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Translating Evidence from Continuous Outcomes into Transition Probabilities in Markov Models: A Systematic Review of Current Practice and Methodological Gaps in Health Technology Assessment

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BACKGROUND

Markov models require transition probabilities (TPs) to represent disease progression and treatment effects, whereas evidence syntheses frequently report treatment effects for continuous outcomes as mean differences (MDs) or standardized mean differences (SMDs). How evidence derived from continuous outcomes is translated into TPs remains poorly described.

OBJECTIVE

This study aimed to identify and classify approaches used to incorporate continuous outcome evidence into Markov-based economic evaluations.

METHOD

A systematic review was conducted using the INAHTA database. Health technology assessment (HTA) reports published between 1st January 2018 and 4th September 2025 were searched. Eligible studies included both a systematic review and an original economic evaluation, with detailed inclusion and exclusion criteria was in table 1. Included studies were reviewed to identify methods for translating continuous outcome evidence into TPs.

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• A systematic review and original model-based economic evaluations using continuous outcomes from clinical trials, either as individual patient data, aggregate results, or trial-based evidence synthesis. • Continuous outcomes used to define model health states or generate or adjust transition probabilities, event risks, state-allocation probabilities, or transition matrices. • Trial-stage conversion of continuous outcomes into categorical or time-to-event data was eligible when these data, directly or after evidence synthesis, informed model probabilities.	• Studies without accessible full texts • Reviews or secondary descriptions without an original economic model. • No eligible trial-derived continuous outcome, or continuous outcomes used solely for utility mapping or resource use, without informing model probabilities. • Cost-consequence or cost-minimization analyses. • Partitioned survival models • Area-under-the-curve models without relevant state-transition probabilities; HTA reports with unreported or confidential model structures. • Reports published in languages other than English or Chinese.

RESULTS

Database searches identified 3,323 records, with one additional report identified manually. Following screening, 195 studies were included: 48 used patient-level models and 147 used cohort-level models. Among cohort-level studies, 55 used categorical or survival outcomes derived from continuous measures during clinical trials, 57 estimated model probabilities from clinical-trial individual patient data or external-cohort data, and 35 translated continuous-outcome summary statistics into model probabilities—the focus of this review.

Six transformation categories were identified: **risk-equation methods (n=15), distribution- and threshold-based transformation (n=8), clinical mapping functions (n=5), relative-effect transformation (n=4), statistical formula transformation (n=3), and scale range and algorithm-based transformation (n=1)**. One study contributed to two categories. Applicability depended on available outcome statistics, external evidence and model state definitions. Depending on the method, additional inputs included variability estimates, thresholds and baseline probabilities. Outputs informed decision-tree branches, initial state allocation and subsequent state transitions.

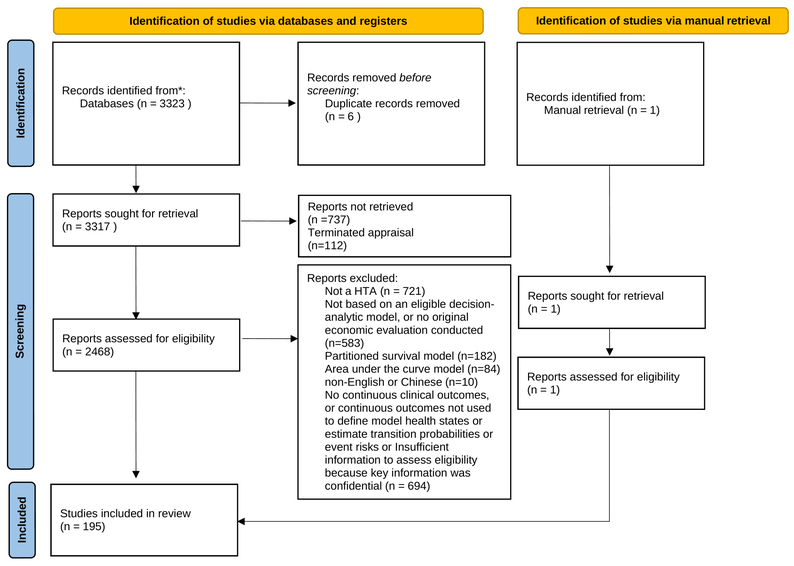


Figure 1. PRISMA flow diagram of study identification, screening, and inclusion

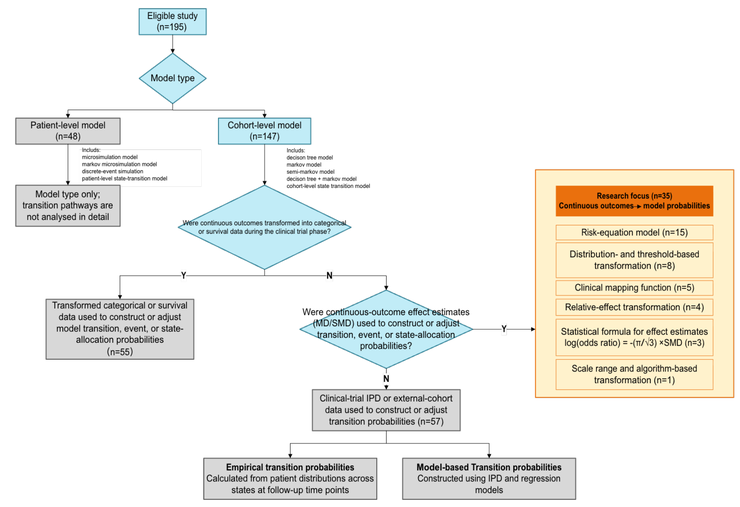


Figure 2. Classification of methods for translating continuous outcomes into model probabilities

Table 2. Methods for transforming continuous outcomes into model probabilities

Subtype / method (study count)	Definition	Outcome / state types	Data required	General pathway and example
I Risk-equation method: estimate event risk from absolute levels or changes in continuous measures using risk functions or associations (n=15)				
I-1 Risk-factor updating (n=4)	Update continuous risk factors and re-estimate risk using a risk function.	① / d	Mean change / MD / post-treatment mean; baseline levels; risk function.	General: Mean change / MD / post-treatment mean → update risk-function inputs → event probability. Example: SBP MD → updated SBP → QRISK3 cardiovascular risk.*
I-2 External per-unit risk association (n=11)	Adjust baseline risk using the association between a unit change in the measure and risk.	①/ a, b, c, d	Mean change / MD; per-unit risk association; baseline risk or event rate.	General: Mean change / MD → external risk association from meta-analysis or observational studies → adjusted event / transition probability. Example: LDL-C reduction → per-unit event ratio → adjusted annual event probability.
II Distribution- and threshold-based transformation: derive category probabilities from outcome distributions and thresholds or state boundaries (n=8)				
II-1 Treatment-threshold probabilities (n=5)	Simulate post-treatment levels or changes from their distributions; estimate probabilities within thresholds or intervals.	① ② ③ / a, b, d	Mean change / MD / post-treatment mean; SD and distribution; threshold.	General: Outcome-level / change distribution → threshold classification → response, state-allocation or conditional transition probability. Example: QMG change distribution → reduction ≥3 points → response probability.
II-2 Baseline-distribution and threshold probabilities (n=3)	Simulate baseline values and changes from their distributions, construct trajectories and count the resulting states.	① ② ③ / a, b, d	Baseline mean and SD; mean change / change distribution; state boundaries.	General: Baseline mean / SD + mean change → simulated trajectories → state-allocation / conditional transition probabilities. Example: Simulated CD4 trajectories → interval classification → state-transition probabilities between adjacent time points.
III Clinical mapping function: map continuous outcomes to intermediate clinical measures (n=5)				
Clinical mapping function (n=5)	Map continuous outcomes to disease progression or intermediate clinical outcomes.	①, ③ / a, d	Change / MD / absolute level / median; mapping function; progression rules.	General: Change / level / median → clinical mapping → progression probability or deterministic state update. Example: IOP reduction → VF decline rate → time to the next state → reciprocal as monthly progression probability.
IV Relative-effect transformation: use continuous-effect ratios to adjust relative effects or probabilities (n=4)				
IV-1 Proxy relative effect (n=2)	Use a ratio of changes as a proxy HR or RR.	② / a, c	Arm-specific mean changes / slopes; baseline progression parameters.	General: Arm-specific mean changes / slopes → proxy HR / RR → adjusted progression probability. Example: CDR-SB change ratio → proxy HR → adjusted MCI-to-mild-AD progression.*
IV-2 Existing relative-effect adjustment (n=1)	Adjust a reference HR / RR / OR using a ratio of changes.	② / d	Comparable mean changes / MDs; reference HR / RR / OR; baseline probability.	General: Mean change / MD → adjusted HR / RR / OR → event probability. Example: ESS-effect ratio r → $\ln(OR_{new}) = r \ln(OR_{ref})$ → adjusted event probability.*
IV-3 Direct probability adjustment (n=1)	Multiply or divide transition-matrix probabilities by a ratio of changes.	③ / a	Arm-specific changes, or reference-arm change and MD; baseline transition matrix.	General: Arm-specific mean changes → change ratio → adjusted transition matrix. Example: OFF-time ratio r → worsening probability × r; improvement probability ÷ r → recalculate diagonal probabilities.
V Statistical formula transformation: convert SMDs to ORs using a statistical formula (n=3)				
Statistical formula transformation (n=3)	Convert an SMD to an OR and then to an event probability.	② / b	SMD; SMD-to-log-OR relationship; baseline response / remission probability.	General: SMD → log OR → response / remission probability calculated with the baseline probability. Example: PTSD SMD → log OR = $-\frac{\pi}{\sqrt{3}} \times$ SMD → remission probability.
VI Scale range and algorithm-based transformation: assign probabilities using scale boundaries and transformation rules (n=1)				
Scale range and algorithm-based transformation (n=1)	Assign probabilities using scale boundaries and transformation rules.	② / a	MD; scale range; state boundaries; lookup rules; baseline probabilities.	General: MD → assumed probabilities inferred by counting feasible change combinations → direct use or RR-based adjustment of transition probabilities. Example: Pain MD → lookup of assumed NRS probabilities → approximate RR → Markov transition probabilities.*

Outcome types

① Physiological, biochemical, and objective functional measures: objective physiological, laboratory or functional measurements, such as blood pressure, cholesterol, cell counts and walking speed.

② Symptom, functional, and disease severity scores: patient-reported or clinician-rated scales of symptoms, functioning or disease severity.

③ Measures of disease burden: frequency, duration, and extent: numerical measures such as headache days, symptom duration or affected body area.

Model state types

a Continuous-outcome intervals: numerical ranges defining severity or health states.

b Treatment response or remission: states defined by an explicit improvement threshold or remission criterion.

c Clinical stage or functioning: states defined by disease stage, functional ability or dependence.

d Disease, complications or event history: disease or event states, decision-tree branches, standalone model events, post-event states and death.

Abbreviations

MD, mean difference; SMD, standardised mean difference; SD, standard deviation; SE, standard error; HR, hazard ratio; RR, relative risk (risk ratio); OR, odds ratio; log OR, natural logarithm of the odds ratio; n, number of studies. SBP, systolic blood pressure; LDL-C, low-density lipoprotein cholesterol; QMG, Quantitative Myasthenia Gravis; CD4, cluster of differentiation 4; IOP, intraocular pressure; VF, visual field; CDR-SB, Clinical Dementia Rating–Sum of Boxes; MCI, mild cognitive impairment; AD, Alzheimer's disease; ESS, Epworth Sleepiness Scale; PTSD, post-traumatic stress disorder; NRS, numerical rating scale. OFF time denotes periods of inadequate Parkinson's disease symptom control. QRISK3 is a cardiovascular risk prediction algorithm; ln denotes the natural logarithm; r denotes a continuous-effect ratio.

DISCUSSION AND CONCLUSION

- Continuous outcomes can inform economic models through several distinct transformation methods; no single approach is suitable for all settings. Method selection should reflect the available summary statistics, external evidence, and model health-state definitions.
- This classification provides a practical framework for selecting and reporting transformation methods.

REFERENCES

1. Health Technology Wales. Renal denervation to treat people with resistant hypertension. Evidence Appraisal Report EAR042. 2023.
2. National Institute for Health and Care Excellence. Bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia: committee papers. NICE; 2020.
3. Tice JA, Touchette DR, Nikitin D, et al. Eculizumab and efgartigimod for the treatment of myasthenia gravis: effectiveness and value. Institute for Clinical and Economic Review; 2021.
4. National Institute for Health and Care Excellence. Cabotegravir and rilpivirine for treating HIV-1: committee papers. NICE; 2021.
5. Canadian Agency for Drugs and Technologies in Health. Optimal use of minimally invasive glaucoma surgery: a health technology assessment. Ottawa: CADTH; 2019.
6. Lin GA, Whittington MD, Synnott PG, et al. Aducanumab for Alzheimer's disease: effectiveness and value. Institute for Clinical and Economic Review; 2021.
7. National Institute for Health and Care Excellence. Pitolisant hydrochloride for treating excessive daytime sleepiness caused by obstructive sleep apnoea: committee papers. NICE; 2021.
8. National Institute for Health and Care Excellence. Foslevodopa-foscarbidopa for treating Parkinson's disease with motor symptoms: committee papers. NICE; 2023.
9. National Guideline Alliance. Post-traumatic stress disorder: evidence review D. Psychological, psychosocial and other non-pharmacological interventions for the treatment of PTSD in adults. NICE guideline NG116. 2018
10. Riley P, Glenny AM, Worthington HV, et al. Oral splints for patients with temporomandibular disorders or bruxism: a systematic review and economic evaluation. Health Technol Assess. 2020;24(7):1-224.