Modeling Disability-Adjusted Life Years for Policy and Decision Analysis

Abstract

This study outlines a methodological framework for joint modeling of Disability- and Quality-Adjusted Life Year outcomes.

Plain Language Summary

Modeling Disability-Adjusted Life Years for Policy and Decision Analysis

0.1 Introduction

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Disability-adjusted life years (DALYs) measure disease burden in a population. Conceptualized in the Global Burden of Disease (GBD) study (C. J. Murray & Lopez, 1997), DALYs quantify the total sum of years of life lost due to disability attributable to a disease (YLD), plus years of life lost to premature mortality from the disease (YLL; i.e., DALY = YLD + YLL).

In addition to their role in describing levels and trends in disease burdens worldwide, DALYs are a primary health outcome in evaluations of health interventions in low- and middle-income countries (LMICs). In these settings, resource allocation decisions are guided by modeled assessments of the incremental costs per DALY averted under alternative (often competing) strategies to improve population health.[1]

Despite the prominent role of DALYs in global health policy, scant methodological guidance is available for adapting and/or structuring decision analytic models for DALY outcomes. This methodological gap has its roots in health economics education, where textbooks and training exercises focus almost exclusively on Quality-Adjusted Life Year (QALY) outcomes—the primary health outcome used for health technology assessments (HTAs) and policy decisionmaking in high-income countries (HICs). DALYs differ from QALYs in important and model-relevant respects, including the use of reference life tables to calculate YLLs and standardized disability weights to calculate YLDs.[2] To the extent DALY-specific modeling considerations are taught, they are often considered in isolation and without a firm methodological grounding in *how* one might structure a model to measure DALY outcomes.

As a consequence, and in practice, health economic applications often resort to shortcuts and other "hacks" for calculating DALYs. For example, practitioners may simply estimate a "QALY-like" DALY that is based on a diseased state occupancy payoff of one minus the disability weight. Other approaches define a diseased-state payoff using the disability weight as an estimate of YLDs, and accumulate person-years in an absorbing death state (due to disease) as an estimate of YLLs. As this study will show, these shortcuts do not provide an accurate representation of DALY levels in a population.

This tutorial outlines a framework for direct incorporation of DALY outcomes in common decision modeling environments. Our primary focus is on discrete-time Markov cohort models—however, our framework extends directly to microsimulation and is also easily adapted for continuous time discrete event simulation (DES) models. As such, our study provides a comprehensive roadmap for incorporating DALY outcomes into common decision modeling frameworks.

[1] The adoption of DALYs over other common health outcomes in health economics (e.g., quality-adjusted life years, or QALYs) stems from several practical and theoretical considerations. See Feng et al. (2020) and Wilkinson et al. (2016) for futher discussion.

[2] In contrast, QALYs are calculated based on utility weights derived from general and patient surveys. See Feng et al. (2020) and Wilkinson et al. (2016) for futher discussion.

To maintain consistency within the literature, we build on an existing didactic disease progression model (Alarid-Escudero et al., 2023). The underlying discrete time Markov cohort model is time homogeneous—that is, transition probabilities do not vary as a function of age/time in model. However, our methods and code are developed to accomodate time-inhomogenous models. Finally, recognizing the wide spectrum of experience and programming comfort level among practitioners, we offer three approaches for modeling DALYs (beginner, intermediate and advanced) and provide replication materials for implementing our approaches in R and Microsoft Excel.

0.2 Background

This section provides background information sufficient for conceptual understaning of DALYs and how to estimate them in a decision-analytic model; it is not intended as a comprehensive treatment of the subject. For extensive discussion of the history, assumptions and controversies around DALYs, see TK.

DALYs are the sum of two components: a morbidity component called years lost to disability (YLD), and a premature mortality component called years of life lost to disease (YLL) (WHO, 2013). To quantify YLDs, conditions are assigned disability weights (D) ranging from zero to one, with zero representing the absence of the condition and one representing the highest burden a condition can inflict. Disability weights are elicited from expert panels, are standardized across geographies, and are routinely updated and published as part of the GBD (WHO, 2013).

For a given condition c, YLDs are defined as the condition's disability weight multiplied by the average number of years a person lives with the disease (L_c):

$$YLD(c) = D_c \cdot L_c \tag{1}$$

YLLs are determined by a loss function, which is typically defined as the number of years lost to premature mortality at age a. This value is often taken directly from a life table that provides information on remaining life expectancy ($Ex(a)$) at a given age.

$$YLL(a) = Ex(a) \tag{2}$$

.

Choices over the specific value of remaining life expectancy will depend on the context and research question at hand (Anand & Reddy, 2019). Historically, the GBD has utilized an *exogenous*, external reference life table based on the maximum potential life span among humans (Global Burden of Disease Collaborative Network, 2021; WHO, 2013). More recent GBD estimates draw on reference life tables based on the lowest observed age-specific mortality rates among geographies with populations over 5 million in 2016 (Global Burden of Disease Collaborative Network, 2021).

Finally, DALYS are simply the sum of these two components:

$$DALY(c, a) = YLD(c) + YLL(a) \tag{3}$$

0.2.1 Discounting

In the original GBD study, additional age-weighting and time discounting practices were applied to DALY calculations (C. J. Murray & Lopez, 1997). These methods respectively weighted the burden of illness more during adulthood than early childhood and old age, and valued present health over future years of illness by discounting YLD and YLL measures by 3% per year. From 2010 onwards, both practices were discontinued to make the DALY a more descriptive measure (WHO, 2013).

While the GBD no longer uses age and time discounting, the World Health Organization's Choosing Interventions that are Cost-Effective (WHO-CHOICE) program recommends consideration of time discounting of health outcomes (Bertram et al., 2021; C. J. L. Murray et al., 2020). We therefore adopt the WHO-CHOICE recommendation and include discounting in our DALY modeling approach.[3] We do, however, maintain the continuous-time discounting used in the original GBD DALY equations—which differs slightly from the more common use of discrete time discounting in Markov cohort models.

For an annual discount rate r, for condition c, and at age a, the equation for YLDs is,

$$YLD(c) = D_c \left(\frac{1}{r} \left(1 - e^{-r(L_c)} \right) \right). \tag{4}$$

Similarly, YLLs are calculated as,

$$YLL(a) = \frac{1}{r} \left(1 - e^{-rEx(a)} \right). \tag{5}$$

It is important to note that the discounting shown in Equation 4 and Equation 5 yield the present value of YLD and YLL outcomes at a single point in time, when the duration of disease (L_c) and time of death from disease (a) are known. For a decision model where not all cohort members start off ill, that point in time very likely occurs at some point after the baseline period—and different illness durations and death times will, of course, occur across individuals in a modeled cohort. As such, to be consistent with standard practice with WHO-CHOICE, we must discount YLL and YLD outcomes further—all the way back to the baseline (time $t = 0$) period. This additional discounting step will become apparent in Section 0.5 below.

0.3 Model Overview

We build on an existing progressive disease model in which healthy individuals develop a disease with two health states ("Sick" and "Sicker"; Alarid-Escudero et al. (2023)). Individuals can also transition to an absorbing death state due to causes unrelated to the disease (i.e., "background" mortality), or due to disease-specific causes.

We consider outcomes under four strategies:

- A **Standard of Care** strategy based on the baseline model parameters.
- **Strategy A**, which improves the quality of life among individuals with the disease, but does not affect disease progression.
- **Strategy B**, which reduces the rate of progression from Sick to Sicker by 40%.
- **Composite Strategy AB**, which jointly implements strategies A and B.

A state transition diagram is shown in Figure 1. In the figure, nodes are health states and edges depict possible transitions among them. Edge labels are defined in terms of transition intensities (rates). Other key model parameters are summarized in Table 1.

As depicted in Figure 1, and as parameterized in our replication code, the underlying Markov model is time homogeneous—that is, transition rates do not vary as a function of time (e.g., the background mortality rate is fixed and does not

[3] Practitioners who do not wish to discount DALY outcomes can simply set the annual discount rate r to zero.

increase with age). This is merely a simplification that builds on an existing time-homogeneous model constructed for didactic purposes (Alarid-Escudero et al., 2023). We do, however, index all formulas and other model-relevant objects with the subscript t to allow for time-inhomogenous models. Our replication code is also written to easily accomodate time-inhomogeneous models.

An additional observation is worth highlighting. In our implementation of the Sick-Sicker model, disability weights are defined as one minus the utility weight. This is not generally the case, as DALY disability weights are derived from expert valuations and are standardized across countries and regions (Sassi, 2006; WHO, 2013). Utility weights, by contrast, are often derived from general population and/or patient samples and therefore differ across geographies (Sassi, 2006). We have elected to parameterize our model in this way to hold this methodological difference fixed—that is, we aim to show how differences in methodological choices shape estimates of DALYs while holding fixed *additional* differences that might occur due to differences in the derivation of disability and utility weights.

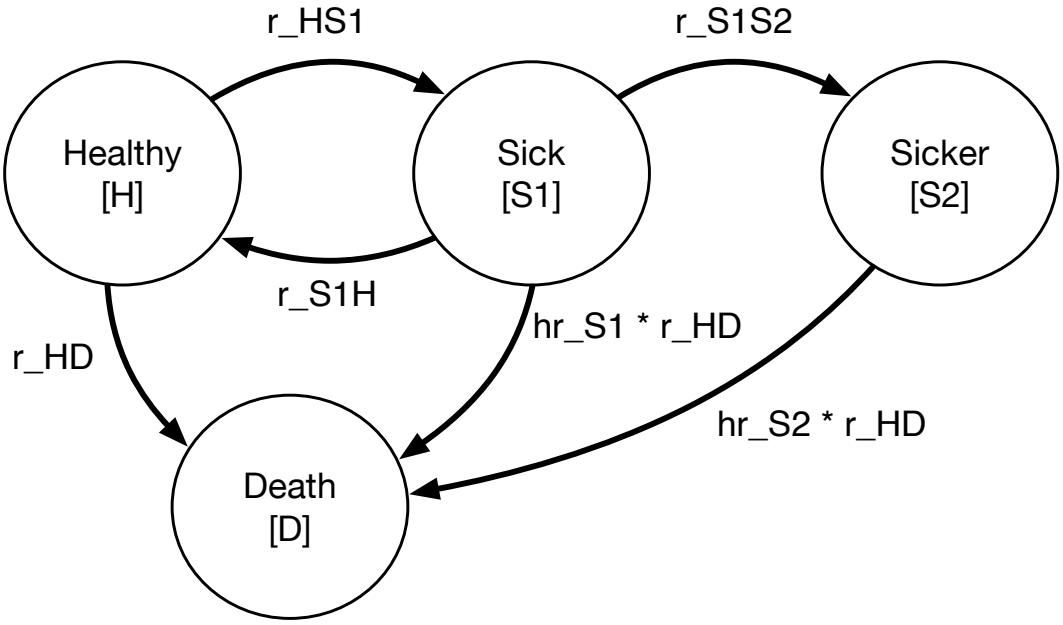

Figure 1: State transition diagram for progressive disease model

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0.4 Transition Matrices

With the model parameterized, our next step is to define the matrices that govern transitions in the model. The state transition diagram represented in Figure 1 is not well-suited to calculate DALY outcomes, however. A primary reason is that transitions to the absorbing death state capture transitions due to all causes of death. To calculate YLLs, we need to separately track the timing and number of deaths *due to disease*.

Table 1: Model Parameters

Parameter	Value	Description
v_tx_names	(SoC,A,B,AB)'	Treatment strategies (vector)
n_tx	4	Number of treatment strategies
cycle_correction	half-cycle	Cycle correction method
v_tr_names	(H,S1,S2)'	Transient health state names (vector)
v_ab_names	(DOC,DS)'	Absorbing health state names (vector)
n_states	5	Total number of health states
horizon	400	Model time horizon (years)
r_v_disc_h	0.03	Annual discount rate for health outcomes
r_v_disc_c	0.03	Annual discount rate for cost outcomes
Delta_t	1	Time step (cycle length; 1=annual, 1/12=monthly, etc.)
age0	25	Age at baseline
r_HS1	0.15	Transition rate: healthy to sick
r_S1H	0.5	Transition rate: sick to healthy
r_S1S2	0.105	Transition rate: sick to sicker
r_HD	0.002	Transition rate: Disease-free background mortality
hr_S1	3	Hazard ratio: mortality from sick state
hr_S2	10	Hazard ratio: mortality from sicker state
u_H	1	Utility weight: healthy [H]
u_S1	0.75	Utility weight: sick [S1]
u_S2	0.5	Utility weight: sick [S2]
u_D	0	Utility weight: death [D]
dw_S1	0.25	Disability weight: sick [S1]
dw_S2	0.5	Disability weight: sicker [S2]
c_H	2000	Cycle occupancy cost: healthy [H]
c_S1	4000	Cycle occupancy cost: sick [S1]
c_S2	15000	Cycle occupancy cost: sicker [S2]
c_D	0	Cycle occupancy cost: death [D]
c_trtA	12000	Cycle occupancy cost: treatment A [S1,S2]
u_trtA	0.95	Utility weight: treatment A [S1]
dw_trtA	0.05	Disbility weight: treatment A [S1]
c_trtB	12000	Cycle occupancy cost: treatment B [S1,S2]
hr_S1S2_trtB	0.6	Hazard Ratio: S1 to S2 disease progression under treatment B

To accommodate this need, several approaches are available. We categorize each based on the level of experience and skill required (beginner, intermediate, advanced):

1. **Approach 1 (Beginner): Separate Death State**: Re-define the health states to include a separate cause-specific death state as depicted in Figure 2.[4] We then draw on the resulting Markov trace and use changes in the number of cause-specific deaths in each cycle to calculate YLLs.

2. **Approach 2 (Intermediate): Non-Markovian Trackers**: Include a non-Markovian transition state for cause-specific deaths in the transition probability matrix. This approach allows for direct calculation of YLD, YLL and DALY outcomes because it sidesteps the need to derive a separate cause-related death transition vector from the Markov trace (as in Approach 1).

3. **Approach 3 (Advanced): Markov Chain with Rewards** Define a block matrix Markov chain with rewards for occupancy (YLDs) and disease-related death transitions (YLLs) by adapting the methods in Caswell & van Daalen (2021). This approach draws on matrix calculus and solves for expected outcomes as well as higher order moments such as variance and skewness.

Each approach facilitates the design and execution of a decision-analytic model that correctly calculates YLD, YLL, and DALY outcomes—as well as other common outcomes such as life-years (LYs), QALYs and costs. In practice, Approaches (1) and (2) will produce identical results. Approach (3) draws on slightly different assumptions on partial payoffs for partial occupancy in a cycle, but will yield results very similar to (1) and (2). We show in Section 0.7 that other shortcut-based approaches previously used in the literature—such as modeling a QALY-like DALY and/or accumulating time in the absorbing death state—will not in general yield similar results.

0.4.1 Approach 1 (Beginner): Cause-Specific Death State

Under this approach, we separate out deaths from disease vs. other causes by defining a separate health state for cause-specific mortality; an updated state transition diagram is shown in Figure 2.

Transitions among health states are defined in terms of continuous rates ("intensities") and are captured within an intensity matrix $\mathbf{Q}_t$,

$$\mathbf{Q_t} = \begin{array}{c} \\ \text{H} \\ \text{S1} \\ \text{S2} \\ \text{DOC} \\ \text{DS} \end{array} \begin{array}{c} \begin{array}{ccccc} \text{H} & \text{S1} & \text{S2} & \text{DOC} & \text{DS} \end{array} \\ \begin{pmatrix} -(\texttt{r\_HS1}_t+\texttt{r\_HD}_t) & \texttt{r\_HS1}_t & 0 & \texttt{r\_HD}_t & 0 \\ \texttt{r\_S1H}_t & -(\texttt{r\_S1H}_t+\texttt{r\_S1S2}_t+\texttt{hr\_S1}_t\cdot\texttt{r\_HD}_t) & \texttt{r\_S1S2}_t & \texttt{r\_HD}_t & \texttt{hr\_S1}_t\cdot\texttt{r\_HD}_t-\texttt{r\_HD}_t \\ 0 & 0 & -(\texttt{hr\_S2}\cdot\texttt{r\_HD}_t) & \texttt{r\_HD}_t & \texttt{hr\_S2}_t\cdot\texttt{r\_HD}_t-\texttt{r\_HD}_t \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \end{array}$$

Figure 3: Transition Intensity Matrix for Approach 1

[4] In this example, disease-specific death rates are goverened by a hazard ratio applied to the background mortality rate. Because we are operating on the rate scale, we can separate out disease-related deaths from other-cause mortality by simply taking a difference in the rates. Other applications for prevalent conditions with high death rates, however, may require us to construct a cause-deleted life table to obtain background mortality rates that net out deaths from the modeled disease.

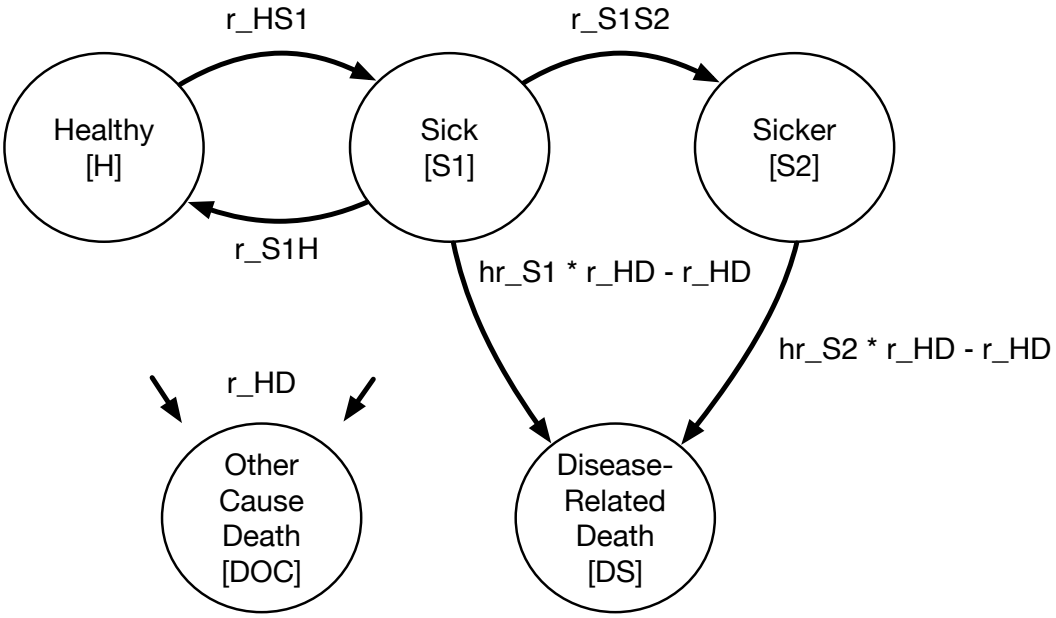

Figure 2: State transition diagram for progressive disease model with separate cause-specific death state

Cell values in row i, column j of $\mathbf{Q}_t$ capture the (continuous time) transition rate from health state i to health state j. $\mathbf{Q}_t$ has diagonal elements defined as the negative sum of the off-diagonal row values (i.e., the row sums of $\mathbf{Q}_t$ are zero). This ensures that the Markov model is "closed"—that is, the total cohort size neither grows nor shrinks over time.

We next embed the transition intensity matrix into a discrete time transition probability matrix by taking the matrix exponential of $\mathbf{Q}_t$ for a defined time step (i.e., "cycle length") Δt:[5]

$$\mathbf{P}_t = e^{\mathbf{Q}_t \Delta t} \tag{6}$$

Embedding the Sick-Sicker model results in a transition probability matrix $\mathbf{P}_t$ with the following probabilities defined:

[5] In Markov theory, $\mathbf{P}$ is called the "discrete skeleton" of the continuous model (Iosifescu, 1980). The conversion formula used to calculate $mathbfP$ is the matrix analogue to the standard rate-to-probability formula commonly taught in health economics textbooks, i.e., $p = 1 - e^{r\Delta t}$, where r is the rate and Δt is the time step (i.e., "cycle length").

$$\mathbf{P}_t = \begin{array}{c} \\ \text{H} \\ \text{S1} \\ \text{S2} \\ \text{DOC} \\ \text{DS} \end{array} \begin{array}{c} \begin{array}{ccccc} \text{H} & \text{S1} & \text{S2} & \text{DOC} & \text{DS} \end{array} \\ \begin{pmatrix} \texttt{p\_HH}_t & \texttt{p\_HS1}_t & \texttt{p\_HS2}_t & \texttt{p\_HDOC}_t & \texttt{p\_HDS}_t \\ \texttt{p\_S1H}_t & \texttt{p\_S1S1}_t & \texttt{p\_S1S2}_t & \texttt{p\_S1DOC}_t & \texttt{p\_S1DS}_t \\ 0 & 0 & \texttt{p\_S2S2}_t & \texttt{p\_S2DOC}_t & \texttt{p\_S2DS}_t \\ 0 & 0 & 0 & 1.0 & 0 \\ 0 & 0 & 0 & 0 & 1.0 \end{pmatrix} \end{array}$$

Figure 4: Transition Probability Matrix for Approach 1

Embedding the transition probability matrix using the matrix exponential ensures that the resulting transition probabilities capture the underlying continuous time disease process. In particular, $\mathbf{P}$ will capture the probability of compound ("jumpover") transitions within a single cycle.[6]

0.4.2 Approach 2 (Intermediate): Non-Markovian Tracking States

Under this approach, we maintain the overall structure as depicted in the original Figure 1, but augment the transition probability matrix with non-Markovian components to facilitate accounting of disease-related deaths.[7] Approach 2 offers a more generalized method that allows practitioners to accurately account for costs and/or health payoffs (such as YLLs) that are defined by *transitions* among health states, rather than occupancy in a health state. DALY outcomes can also be calculated directly, without the need to derive a vector of disease-related death transitions from the Markov trace (as required for Approach 1).

Figure 5 shows a state transition diagram with the tracking state added. The tracking state (shown as red nodes) simply records transitions as cohort members move from either diseased state to the absorbing death state due to causes related to the disease.

In general, tracking states can either count the total number of transitions that have occurred up to a given cycle (i.e., an "accumulator" state), or can track the total number of new transitions that occur within a single cycle (i.e., a "transition"

[6] For example, in the continuous time rate matrix $\mathbf{Q}_t$ above, there is a zero-valued rate defined for progressions from Healthy (H) to Disease-related death (DS), since individuals must first become ill before they can die from disease-related causes. However, after embedding, the matrix $\mathbf{P}$ has a non-zero cycle transition probability from Healthy (H) to Disease-related death (DS) (i.e., `p_HDS`). This value captures the probability of a compound or "jumpover" transition from Healthy and through the Sick and/or Sicker state to death from disease-related causes within the same discrete time cycle; see Graves et al. (2021) for further discussion, and Iosifescu (1980) for additional theory.[^comparison]

[7] Tracking states also allow for accurate bookeeping for other outcomes such as costs. For example, if developing the disease incurs a one-time diagnosis or treatment cost, the compound transitions implied by the embedded transition probability matrix indicate that some individuals will transiently enter (and then exit) the Sick state in a single cycle. When calculating costs, practitioners may want to include a tracking state for the Sick state to be sure to capture these one-time costs, which would be masked if cost payoffs are simply multiplied by state occupancy at the end of each cycle (e.g., costs for individuals with a sojourn through the Sick state in a single cycle would not be accounted for).

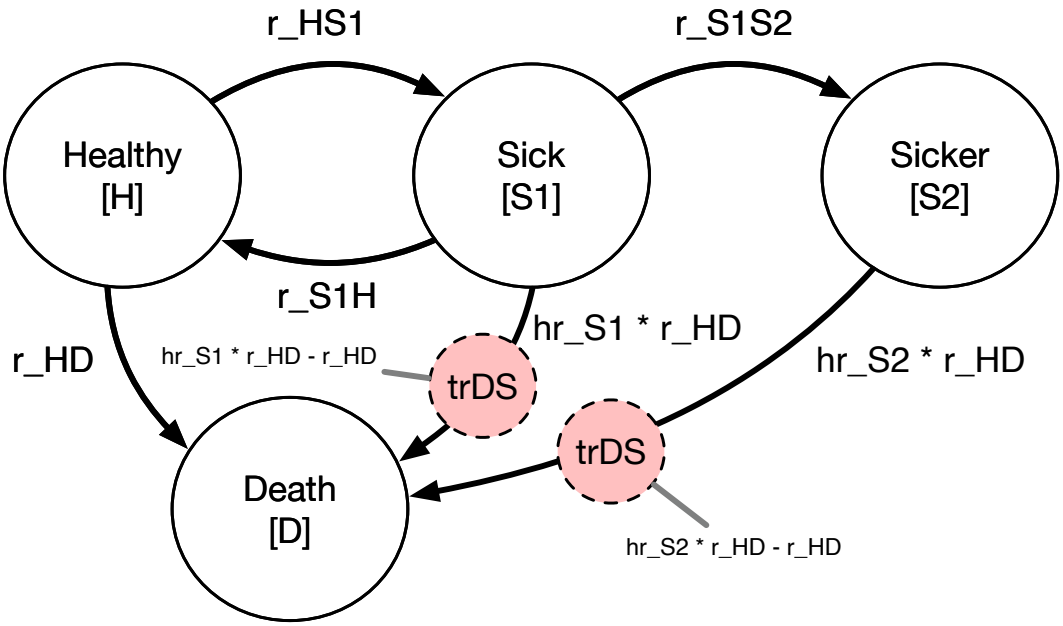

Figure 5: State Transition Diagram with Transition State (Red)

state).[8] To calculate YLL outcomes we will add a transition state that records the total number of new disease-related deaths in each cycle.

To implement Approach 2, we add a transition state row and column to the transition intensity matrix. This transition state, called `trDS`, is included in the augmented intensity matrix $\mathbf{Q}_t$ below:

$$\mathbf{Q}_t = \begin{array}{c} \\ \text{H} \\ \text{S1} \\ \text{S2} \\ \text{D} \\ \text{trDS} \end{array} \begin{array}{c} \begin{array}{ccccc} \text{H} & \text{S1} & \text{S2} & \text{D} & \text{trDS} \end{array} \\ \left(\begin{array}{ccccc:c} -(\texttt{r\_HS1}_t+\texttt{r\_HD}_t) & \texttt{r\_HS1}_t & 0 & \texttt{r\_HD}_t & 0 \\ \texttt{r\_S1H}_t & -(\texttt{r\_S1H}_t+\texttt{r\_S1S2}_t+\texttt{hr\_S1}_t\cdot\texttt{r\_HD}_t) & \texttt{r\_S1S2}_t & \texttt{hr\_S1}_t\cdot\texttt{r\_HD}_t & \texttt{hr\_S1}_t\cdot\texttt{r\_HD}_t-\texttt{r\_HD}_t \\ 0 & 0 & -(\texttt{hr\_S2}_t\cdot\texttt{r\_HD}_t) & \texttt{hr\_S2}_t\cdot\texttt{r\_HD}_t & \texttt{hr\_S2}_t\cdot\texttt{r\_HD}_t-\texttt{r\_HD}_t \\ 0 & 0 & 0 & 0 & 0 \\ \hdashline 0 & 0 & 0 & 0 & 0 \end{array}\right) \end{array}$$

Figure 6: Transition intensity matrix with transition state added

Two aspects of $\mathbf{Q}_t$ are worth highlighting. First, $\mathbf{Q}_t$ is divided into a Markovian submatrix and the non-Markovian tracking row and column. This division is made apparent using dotted vertical and horizontal lines. Critically, the Markovian submatrix remains closed—that is, the diagonal elements remain unchanged so that the row sums of the submatrix remain zero, even after the addition of the tracking

[8] More generally, accumulator and transition states can be defined for any number of transition types, as they are useful for capturing one-time costs in the model, or for for calculating other decision-relevant outcomes such as the total number of people who developed the disease or died from the disease as secondary outcomes.

column along the "edges" of $\mathbf{Q}_t$. This ensures that the Markovian submatrix can be used to calculate state occupancy for a closed cohort that neither gains nor loses cohort members over time.

Second, two transition intensities—from the S1 (Sick) and S2 (Sicker) states to Death—appear in the tracking column. This ensures that `trDeadDisease` will track all relevant transitions to death due to the disease. Because we are operating on the rate scale, we can net out non-disease related deaths as captured by the background mortality rate among healthy individuals (i.e., `r_HD`). Other approaches might draw on cause-deleted life tables to incorporate death transition rates that net out deaths from the disease itself.[9]

As above, we obtain the transition probability matrix by embedding $\mathbf{Q}_t$ into the discrete time step (Equation 6). However, the resulting transition probability matrix treats `trDS` as an absorbing state (i.e., individuals are retained in the `trDS` with probability one). Using the terminology introduced above, this absorbing state could serve as an **accumulator** state that (in the constructed Markov trace) records the total number of people who have died from the disease up to any given cycle. This may be a decision-relevant health outcome to consider on its own; indeed, so long as the Markovian submatrix remains closed, there is no limit to the number of accumulator and/or transition states one might add along the "edges" of a model.[10]

To change `trDS` to a **transition** state, we simply replace the absorbing probability of one in the cell [`trDS`, `trDS`] with a zero. This cell-level change is highlighted in grey in the bottom right cell of $\mathbf{P}$ below:

$$\mathbf{P}_t = \begin{array}{c} \\ \text{H} \\ \text{S1} \\ \text{S2} \\ \text{D} \\ \text{trDS} \end{array} \begin{array}{c} \begin{array}{ccccc} \text{H} & \text{S1} & \text{S2} & \text{D} & \text{trDS} \end{array} \\ \begin{pmatrix} \texttt{p\_HH}_t & \texttt{p\_HS1}_t & \texttt{p\_HS2}_t & \texttt{p\_HD}_t & \texttt{p\_HDS}_t \\ \texttt{p\_S1H}_t & \texttt{p\_S1S1}_t & \texttt{p\_S1S2}_t & \texttt{p\_S1D}_t & \texttt{p\_S1DS}_t \\ 0 & 0 & \texttt{p\_S2S2}_t & \texttt{p\_S2D}_t & \texttt{p\_S2DS}_t \\ 0 & 0 & 0 & 1.0 & 0 \\ 0 & 0 & 0 & 0 & 0.0 \end{pmatrix} \end{array}$$

Figure 7: Transition Probability Matrix for Approach 2

Source: Article Notebook

0.4.3 Approach 3 (Advanced): Markov Chain With Rewards

Our final approach adapts methods from mathematical demography to estimate YLD, YLL and DALY outcomes (Caswell & van Daalen, 2021).[11] This approach

[9] For an example of how to do this using Global Burden of Disease cause of death and life table data, see the example here

[10] To build on the example of compound "jumpover" transitions above, suppose an individual starts off healthy in a cycle, then rapidly transitions through the Sick and Sicker state and dies due to disease-related causes within the same cycle. If there is some treatment cost associated with being in the Sicker state, a traditional approach that applies cost payoffs to state occupancy at the (beginning) end of the cycle would miss treatment costs for this individual because they *transition* through the Sicker state, but never occupy it at the beginning or end of a cycle. Adding a non-Markovian transition state to the model facilitates more accurate bookkeeping because the transition state would pick up on this transition through the Sicker state.

[11] The method also easily accomodates other common outcomes such as QALYs and costs.

requires a separate disease-related absorbing state as shown in Figure 2. While our focus here is on expected outcomes, this method can also be used to estimate higher order moments (e.g., variance, skewness). It is also quite flexible and can estimate separate outcomes for any combination of health states and age classes (e.g., disease-free survival among those aged 40-45, etc.); see Caswell & Zarulli (2018) and Caswell & van Daalen (2021) for details.

To implement Approach 3 we define some additional parameters:

$$
\begin{aligned}
\tau &= \text{Number of transient (non-absorbing) states} \\
\alpha &= \text{Number of absorbing states} \\
\omega &= \text{Number of cycles (age classes)} \\
s &= \text{Total number of states; } s = \tau\omega + \alpha \\
\mathbf{K} &= \text{vec-permutation matrix; parameters } \tau, \omega \\
\mathbf{U}_t &= \text{Transition matrix at time } t, \text{for } t = 1, \dots, \omega \\
\mathbf{M}_t &= \text{Mortality matrix at time } t, \text{for } t = 1, \dots \omega \\
\mathbf{D}_j &= \text{Age advancement matrix for stage } j, \text{for } j = 1, \dots, \tau
\end{aligned}
$$

In the above notation, $\mathbf{K}$ is a permutation matrix known as the vec-permutation matrix.[12] The matrix $\mathbf{U}_t$ captures transition probabilities among transient (i.e., non-absorbing) health states, while $\mathbf{M}_t$ contains transition probabilities from transient health states to the absorbing (death) states.

To construct $\mathbf{U}_t$ and $\mathbf{M}_t$ we define transition rate ("intensity") matrices as in Approaches 1 and 2 above. One important (minor) difference is that the rows in $\mathbf{Q}_t$, $\mathbf{V}_t$, and $\mathbf{S}_t$ now correspond to the final state, while the columns correspond to the starting state; this is essentially the transpose of the rate matrices defined for Approaches 1 and 2, where rows corresponded to the initial health state and columns to the final health state.

The overall intensity matrix $\mathbf{Q}_t$ is given by

$$
\mathbf{Q}_t = \left(\begin{array}{c|c} \mathbf{V}_t & \mathbf{0} \\ \hline \mathbf{S}_t & \mathbf{0} \end{array} \right) \tag{7}
$$

where $\mathbf{V}_t$ is the rate matrix for the transitory (i.e., non-absorbing) states and $\mathbf{S}_t$ is the rate matrix for the absorbing states. The diagonal elements of $\mathbf{Q}_t$ are the negative sum of the non-diagonal column elements, thus making the column sums of $\mathbf{Q}_t$ zero (i.e., the model is "closed" and does not gain or lose cohort members over time).

For the defined time step Δ_t, the discrete time transition probability matrix $\mathbf{P}_t$ is again obtained by taking the matrix exponential of the intensity matrix ($\mathbf{Q}_t$) multiplied by the time step (Δ_t), i.e., Equation 6:

$$
\mathbf{P}_t = e^{\mathbf{Q}_t \Delta t}
$$

We obtain $\mathbf{U}_t$ and $\mathbf{M}_t$ from the block matrix structure of $\mathbf{P}_t$:

$$
\mathbf{P}_t = \left(\begin{array}{c|c} \mathbf{U}_t & \mathbf{0} \\ \hline \mathbf{M}_t & \mathbf{0} \end{array} \right) \tag{8}
$$

[12] See Henderson & Searle (1981) and Appendix B in Caswell & van Daalen (2021) for further information. A function to construct a vec-permultation matrix is provided within our replication code.

In addition, the matrix $\mathbf{D}_j$ defines age advancement in the Markov chain. Borrowing from an example in Caswell & van Daalen (2021), if $\omega = 3$ then

$$\mathbf{D}_j = \begin{pmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & [1] \end{pmatrix} \quad j = 1, \ldots, \tau \tag{9}$$

In our implementation, we include the (optional) value of one in the lower right corner; this assumes that after the last specified age, the cohort continues to experience transitions among health states according to the transition probabilities defined for the last age class. If this value is zero, the model will assume that everyone dies after the last cycle.

We next combine the transition matrices (for all age classes as defined by discrete time cycles) together into a series of block-structured matrices as follows:

$$\mathbb{U} = \left(\begin{array}{c|c|c} \mathbf{U}_1 & \cdots & \mathbf{0} \\ \hline & \ddots & \\ \hline \mathbf{0} & \cdots & \mathbf{U}_\omega \end{array}\right) \tag{10}$$

$$\mathbb{D} = \left(\begin{array}{c|c|c} \mathbf{D}_1 & \cdots & \mathbf{0} \\ \hline & \ddots & \\ \hline \mathbf{0} & \cdots & \mathbf{D}_\tau \end{array}\right) \tag{11}$$

$$\widetilde{\mathbf{U}} = \mathbf{K}^\top \mathbb{D} \mathbf{K} \mathbb{U} \quad \tau\omega \times \tau\omega \tag{12}$$

where $^\top$ is the transpose operator.

We also define

$$\widetilde{\mathbf{M}} = \begin{pmatrix} \mathbf{M}_1 & \cdots & \mathbf{M}_\omega \end{pmatrix} \quad \alpha \times \tau\omega \tag{13}$$

Finally, we capture the entire Markov chain in a block transition matrix,

$$\widetilde{\mathbf{P}} = \left(\begin{array}{c|c} \widetilde{\mathbf{U}} & \mathbf{0}_{\tau\omega \times \alpha} \\ \hline \widetilde{\mathbf{M}} & \mathbf{I}_{\alpha \times \alpha} \end{array}\right) \quad (\tau\omega + \alpha) \times (\tau\omega + \alpha) \tag{14}$$

where $\mathbf{I}$ is the identity matrix and $\mathbf{0}$ is a matrix of zeros.

$\widetilde{\mathbf{P}}$ is the analogue to the transition matrix $\mathbf{P}$ (Equation 6) under Approaches 1 and 2 above.

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0.5 DALY Outcomes Under Approaches 1 and 2

With transition matrices and other relevant model objects defined, we next define formulas for estimating outcomes. Our three approaches differ in how total (or expected) outcomes are calculated. Approach 1 requires a Markov trace that tracks occupancy in each cycle; for YLL outcomes, we use this information to calculate the number of new disease-related deaths in each cycle. Approach 2 does not require this extra step, as both cycle-specific and total outcomes are calculated directly. Finally, Approach 3 differs insofar as it directly solves for expected outcomes (i.e., the approach does not require calculation of cycle-specific values).

0.5.1 Markov Trace

YLL outcomes calculated under Approach 1 requires a Markov trace, or a matrix summarizing occupancy in each health state in each cycle. Define $\mathbf{s}_0$ as the initial state occupancy (column) vector at time $t = 0$. The vector $\mathbf{s}_0$ has size k, where k is the total number of states (including transition tracking states, if applicable). This vector summarizes the number or fraction of the cohort in each health state at baseline. Health state occupancy at time t is is calculated as:

$$\mathbf{s}_t^\top = \mathbf{s}_0^\top \mathbf{P}_1 \mathbf{P}_2 \dots \mathbf{P}_t \tag{15}$$

where $\mathbf{P}_t$ is the $k \times k$ transition probability matrix at time t.[13]

We apply Equation 15 at each cycle to construct a Markov trace $\mathbf{S}$, which has dimensions $\omega \times k$,

$$\mathbf{S} = \begin{bmatrix} s_{01} & s_{02} & \cdots & s_{0k} \\ s_{11} & s_{12} & \cdots & s_{1k} \\ \vdots & \vdots & \ddots & \vdots \\ s_{\omega-1,1} & s_{\omega-1,2} & \cdots & s_{\omega-1,k} \end{bmatrix} \tag{16}$$

where each row represents state occupancy at time $t = 0, 1, \dots, \omega - 1$.

Note that the rows in $\mathbf{S}$ run from $t = 0$ to $\omega - 1$; this assumes that all health state transitions occur at the end of each cycle. If we were to instead assume transitions occur at the beginning of the cycle, we would set the matrix to run from $t = 1$ to ω.

0.5.2 Years of Life Lived with Disability (YLD)

To calculate YLDs, we define a $k \times 1$ disability weight payoff vector $\mathbf{d}_{YLD}$. For the model as represented in Figure 2, define,

$$\mathbf{d}_{YLD} = \begin{matrix} \text{H} \\ \text{S1} \\ \text{S2} \\ \text{DOC} \\ \text{DS} \end{matrix} \begin{pmatrix} 0 \\ \texttt{dwS1} \frac{1}{r_{\Delta_t}}(1 - e^{-r_{\Delta_t}})\Delta_t \\ \texttt{dwS2} \frac{1}{r_{\Delta_t}}(1 - e^{-r_{\Delta_t}})\Delta_t \\ 0 \\ 0 \end{pmatrix}$$

where `dwS1` and `dwS2` are the disability weights for the Sick and Sicker states, respectively. In addition, r_{Δ_t} is the cycle discount rate, which is calculated as,

$$r_{\Delta_t} = r\Delta_t \tag{17}$$

where r is the annual discount rate and Δ_t is the cycle length.

In the YLD payoff vector, the term $\frac{1}{r_{\Delta_t}}(1 - e^{-r_{\Delta_t}})$ is included as a continuous-time discounting factor for the defined time step Δ_t. This term is included to discount time *within* each cycle in order to maintain the continuous-time discounting approach used in the original GBD equations (Larson, 2013).[14]

[13] For a time-homogeneous model, Equation 15 simplifies to $\mathbf{s}_t' = \mathbf{s}_0' \mathbf{P}^t$.

[14] Common discounting formulas, such as the discrete time discount factor $\frac{1}{(1+r)^t}$, as well as the continuous time discount factor e^{-rt}, are designed for a series of discrete "payoffs" at specific time points. By comparison, the continuous time discounting used in the GBD DALY equations (Equation 4 and Equation 5) is based on an assumption that payffs accrue in a continuous stream. The discount adjustment factor shown here ($\frac{1}{r}(1 - e^{-rt})$)—and introduced in Larson (2013))—essentially "smooths out" the discrete YLD weight applied in each cycle to reflect this continuous flow. We have verified that application of this factor in our approach exactly replicate the example results using the GBD equations in Fox-Rushby & Hanson (2001); see the Supplementary Appendix for these examples and code.

To fully discount outcomes, we still must discount all future outcome values back to baseline ($t = 0$). Discounted years of life lost to disability (YLD) at cycle t is given by

$$YLD_t = \mathbf{s}_0' \mathbf{P}_1 \mathbf{P}_2 ... \mathbf{P}_t \mathbf{d}_{YLD} \times e^{-r_{\Delta_t} t} \tag{18}$$

Total discounted YLDs are obtained by summing cycle-specific discounted YLD outcomes,

$$YLD = \sum_{t=0}^{\omega-1} YLD_t \tag{19}$$

We can incorporate additional cycle adjustments (e.g., half-cycle adjustment or an adjustment based on Simpson's rule) by defining a adjustment factor c_t that multiplies the cycle-specific discounting factor (i.e., $e^{-r_{\Delta_t} t}$) with other cycle-specific adjustment values,

$$YLD = \sum_{t=0}^{\omega-1} YLD(t) = \sum_{t=0}^{\omega-1} (\mathbf{s}_0' \mathbf{P}_1 \mathbf{P}_2 ... \mathbf{P}_t \mathbf{d}_{YLD} \times c_t) \tag{20}$$

where, at a minimum, $c_t = e^{-r\Delta_t t}$ and can also include any other cycle-correction value (e.g., 0.5 for half-cycle correction or a Simpson's rule coefficient, etc.).

Finally, an equivalent way to calculate YLD outcomes is through matrix multiplication of the Markov trace matrix and the YLD payoff vector,

$$YLD = \sum_{t=0}^{\omega-1} \mathbf{S} \mathbf{d}_{YLD} \odot \mathbf{c} \tag{21}$$

where $\mathbf{c}$ is an $\omega \times 1$ vector of cycle discoutning/correction factors c_t and $\odot$ is the element-wise multiplication (Hadamard product) operator.

0.5.3 Years of Life Lost to Disease (YLLs): Approach 1

As noted in Section 0.2 and in Equation 5, YLLs are based on the present value of remaining life expectancy among disease-related deaths. In a discrete time Markov model, these deaths may occur in any cycle—though, like YLDs, the fully-discounted value is calculated relative to baseline ($t = 0$).

Define a_t as the age of the cohort at cycle t, i.e.,

$$a_t = a_0 + t \cdot \Delta_t \tag{22}$$

where a_0 is the age of the cohort at $t = 0$.

We next define Ex_t as the present value of remaining life expectancy of the cohort in cycle t.

Following the GBD discounting approach, Ex_t is given by

$$Ex_t = \frac{1}{r}(1 - e^{-rEx(a_t)}) \tag{23}$$

where $Ex(a_t)$ is the remaining life expectancy at age a. $Ex(a_t)$ is drawn from either an exogenous (reference) life table, or an endogenous life table, depending on the objectives of the modeling exercise (Anand & Reddy, 2019).

To calculate YLLs, we use the Markov trace to calculate m_t, the total number of new deaths from disease-related causes in each cycle. We calculate m_t by taking the

difference in state occupancy in the disease-related death column (`DS`) in adjacent cycles. As above, we can incorporate additional discounting and cycle adjustments into a cycle correction term c_t and calculate total discounted (and cycle-corrected) YLLs as

$$YLL_t = m_t Ex_t \times c_t \tag{24}$$

Total discounted YLLs are given by,

$$YLL = \sum_{t=1}^{\omega-1} YLL_t = \sum_{t=1}^{\omega-1} m_t Ex_t \times c_t \tag{25}$$

0.5.4 Years of Life Lost to Disease (YLLs): Approach 2

YLLs under Approach 2 can be calculated in a similar way as YLDs, since we have augmented the model with a transition tracking state that directly etimates new deaths in each cycle. Define the YLL payoff vector $\mathbf{d}_{YLL,t}$, which has value Ex_t for the transition tracker health state (`trDS`) and zeros elsewhere,

$$\mathbf{d}_{YLL,t} = \begin{matrix} \text{H} \\ \text{S1} \\ \text{S2} \\ \text{D} \\ \text{trDS} \end{matrix} \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \frac{1}{r}\left(1-e^{-rEx(a_t)}\right) \end{pmatrix}$$

We can now apply similar equations as used for YLD outcomes to calculate fully discounted YLLs,

$$YLL = \sum_{t=0}^{\omega-1} YLD(t) = \sum_{t=0}^{\omega-1} \left(\mathbf{s}_0' \mathbf{P}_1 \mathbf{P}_2 \dots \mathbf{P}_t \mathbf{d}_{YLL,t} \times c_t\right) \tag{26}$$

Alternatively, using the Markov trace, we stack each $k \times 1$ payoff vector (using $\mathbf{d}_{YLL,t}^\top$ as rows) into an $\omega \times k$ payoff matrix $\mathbf{D}$, and obtain total adjusted YLLs as

$$YLL = \sum_{t=0}^{\omega-1} \text{sum}(\mathbf{S} \odot \mathbf{D}) \odot \mathbf{c} \tag{27}$$

where the sum() operator sums each row across the k columns that result from $\mathbf{S} \odot \mathbf{D}$.

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0.6 DALY Outcomes Under Approach 3

Our advanced approach draws on Markov chain with rewards methods that define reward matrices for occupancy-based (YLD) and transition-based (YLL) outcomes. These reward matrices allow us to estimate outcomes for any combination of health states and/or ages. Reward matrices have notation $\mathbf{R}_m$, where m indexes the moment of interest (e.g., expected value, variance, etc.). We focus here on expected outcomes (i.e., outcomes based on $\mathbf{R}_1$)—though equations are available to estimate higher-order moments and objects such as variance, skewness, the coefficient of variation, etc.

0.6.1 Years of Life Lived With Disease (YLD)

To calculate occupancy-based outcomes such as YLDs, we first define a $\tau \times \omega$ reward matrix $\mathbf{H}$, which has dimensions $\tau \times \omega$ and is structured as shown in Figure 8:

	Cycle					
	1	**2**	**3**	**4**	**...**	ω
Healthy	0	0	0	0	0	0
S1	1	1	1	1	1	1
S2	1	1	1	1	1	1

Figure 8: YLD reward matrix $\mathbf{H}$

Cell values within this matrix can be set to one if we want to potentially "reward" that health state-age combination in our outcome measure, and zero otherwise.

We use this matrix to define the reward vector $\mathbf{h}$:[15]

$$\mathbf{h} = \text{vec } \mathbf{H}$$

We also define $\neg\mathbf{h}$ as the complement of $\mathbf{h}$, (i.e., values of 1.0 become 0, and vice versa).

We next define additional matrix $\mathbf{V}$, which has the same structure as $\mathbf{H}$ but includes the (fully discounted) disability weight:

	Cycle					
	1	**2**	**3**	**4**	**...**	ω
Healthy	0	0	0	0	0	0
S1	`dwS1*`	`dwS1*`	`dwS1*`	`dwS1*`	`dwS1*`	`dwS1*`
S2	`dwS2*`	`dwS2*`	`dwS2*`	`dwS2*`	`dwS2*`	`dwS2*`

Figure 9: YLD reward matrix $\mathbf{V}$

where $\texttt{dwS1*} = \texttt{dwS1} \times \Delta_t \times \frac{1}{r_{\Delta_t}}(1 - e^{-r_{\Delta_t}}) \times e^{-r_{\Delta_t} t}$, etc.

We similarly define an occupancy indicator vector $\mathbf{v}$ just as we did for $\mathbf{h}$:

$$\mathbf{v}_m = \text{vec } \mathbf{V}_m$$

0.6.1.1 Partial Occupancy

Because we are modeling a continuous-time disease progression progress in discrete time, it is useful to make corrections for partial occupancy in a cycle. Similar to a half-cycle correction often used in health economic applications, the Markov chain with rewards approach does so by assuming transitions occur half-way through a cycle. We operationalize this assumption by defining,

[15] The vec operator stacks the columns of an $m \times n$ matrix into a $mn \times 1$ vector.

$$\widetilde{\mathbf{B}}_1 = \mathbf{h}\mathbf{v}_1^\top + \frac{1}{2}(\neg\mathbf{h})\,(\mathbf{v}_1^\top) + \frac{1}{2}\,(\mathbf{v}_1)\,(\neg\mathbf{h}^\top)$$

and

$$\widetilde{\mathbf{C}}_1 = \frac{1}{2}\mathbf{1}_\alpha \mathbf{v_1}^\top$$

where $\mathbf{1}_\alpha$ is a vector of ones with length α.

We combine $\widetilde{\mathbf{B}}_1$ and $\widetilde{\mathbf{C}}_1$ to obtain:

$$\widetilde{\mathbf{R}}_1^{YLD} = \left(\begin{array}{c|c} \widetilde{\mathbf{B}}_1 & \mathbf{0} \\ \hline \widetilde{\mathbf{C}}_1 & \mathbf{0} \end{array}\right)$$

which has same block structure and dimensions as the transition probability matrix $\widetilde{\mathbf{P}}$ (Equation 14).

0.6.2 Years of Life Lost to Disease (YLL)

For transition-based outcomes such as YLLs, we define the first moment of remaining life expectancy as the vector $\tilde{\eta}^\top$. This vector has dimensions $\tau\omega \times 1$ and has the following basic structure:

$$\tilde{} = \left(\begin{array}{c} \eta_{11} \\ \vdots \\ \hline \eta_{\tau 1} \\ \hline \vdots \\ \hline \eta_{1\omega} \\ \vdots \\ \eta_{\tau\omega} \end{array}\right)$$

where η_{ix} is remaining life expectancy for an individual in health state i at a given age x. In this structure, remaining life expectancy for each health state is grouped within age classes. Remaining life expectancy should also enter η_{ix} as fully discounted back to $t = 0$.

We next construct the reward matrices:

$$\widetilde{\mathbf{B}}_1 = (\mathbf{0}_{\tau\omega\times\tau\omega})$$
$$\widetilde{\mathbf{C}}_1 = \left(\begin{array}{c} \tilde{\eta}_1^\top \\ \mathbf{0}_{1\times\tau\omega} \end{array}\right).$$

and

$$\widetilde{\mathbf{R}}_1^{YLL} = \left(\begin{array}{c|c} \mathbf{0}_{\tau\omega\times\tau\omega} & \mathbf{0}_{\tau\omega\times 2} \\ \hline \tilde{\eta}_1^\top & \mathbf{0}_{1\times 2} \\ \mathbf{0}_{1\times\tau\omega} & \mathbf{0}_{1\times 2} \end{array}\right)$$

0.6.3 Expected YLD and YLL Outcomes

The expected value of outcome Y (where $Y \in \{YLD, YLL\}$) is estimated by,

$$\tilde{\rho}_1^Y = \widetilde{\mathbf{N}}^\top \mathbf{Z}\left(\widetilde{\mathbf{P}} \odot \widetilde{\mathbf{R}}_1^Y\right)^\top \mathbf{1}_s \tag{28}$$

where $\widetilde{\mathbf{N}}$ is the fundamental matrix,

$$\widetilde{\mathbf{N}} = (\mathbf{I} - \widetilde{\mathbf{U}})^{-1}$$

Table 2: Markov Trace Under Approach 1

cycle	H	S1	S2	DOC	DS	deaths_disease
0	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000
1	0.8870	0.1046	0.0062	0.0020	0.0003	0.0003
2	0.8232	0.1521	0.0197	0.0040	0.0010	0.0008
3	0.7832	0.1723	0.0363	0.0060	0.0022	0.0012
4	0.7547	0.1796	0.0540	0.0080	0.0037	0.0015
5	0.7321	0.1808	0.0717	0.0099	0.0056	0.0019

and $\mathbf{Z}$ is

$$\mathbf{Z} = (\mathbf{I}_{\tau\omega} \mid \mathbf{0}_{\tau\omega\times\alpha})$$

Total (across all ages) outcomes for each starting health state are calculated as

$$\rho_1^{Y,\text{stage}}\left(\text{cycle}\, t\right) = \left(\mathbf{e}_t^\top \otimes \mathbf{I}_\tau\right) \tilde{\rho}_1^Y \quad \tau \times 1 \tag{29}$$

where $\otimes$ is the Kronecker operator and $\mathbf{e}_t$ is a vector of length ω with a value of one in the first position and zero elsewhere; this facilitates calculating expected outcomes from the baseline period (i.e., $t = 0$).

Alternatively, we may wish to calculate outcomes separately under different starting ages, and for a specified starting health state (e.g., healthy). This is given by

$$\rho_1^{Y,\text{age}}\left(\text{ stage } i\right) = \left(\mathbf{I}_\omega \otimes \mathbf{e}_i^\top\right) \tilde{\rho}_1^Y \quad \omega \times 1, \tag{30}$$

where $\mathbf{e}_i$ is a vector of length τ with a value of one in the initial health state position of interest (e.g., `Healthy`) and zero elsewhere.

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0.7 Results

Table 2 shows the Markov trace for the first five cycles under Approach 1, while Table 3 shows the trace under Approach 2. Table 2 also includes a new column (`deaths_disease`) that is calculated as the difference in state occupancy in the `DS` column between cycles. This extra step will be necessary later for calculating YLL outcomes. The trace shown under Approach 2 (Table 3), by comparison, automatically calculates new deaths through the inclusion of the transition state `trDS`; the values under `deaths_disease` and `trDS` are identical, again highlighting that either approach can be used to calculate the number of disease-related deaths in each cycle.

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Table 3: Markov Trace Under Approach 2

cycle	H	S1	S2	D	trDS
0	1.0000	0.0000	0.0000	0.0000	0.0000
1	1.0000	0.0000	0.0000	0.0000	0.0000
2	0.8870	0.1046	0.0062	0.0023	0.0003
3	0.8232	0.1521	0.0197	0.0050	0.0008
4	0.7832	0.1723	0.0363	0.0082	0.0012
5	0.7547	0.1796	0.0540	0.0117	0.0015

Scenario	Life-Years	YLDs	YLLs	DALYs	DALY-Hack	QALY-like DALY	QALY	Costs
Approaches 1 and 2 (Markov Trace)								
SoC	86.567	4.608	2.683	7.291	9.624	21.872	21.872	158566.1
A	86.567	3.901	2.683	6.584	8.917	22.590	22.590	292352.4
B	103.352	3.820	2.028	5.847	7.741	23.699	23.699	255608.1
AB	103.352	2.953	2.028	4.981	6.875	24.579	24.579	375043.1
Approach 3 (Markov Chain With Rewards)								
SoC	86.644	4.637	2.810	7.447			22.309	158365.5
A	86.644	3.896	2.810	6.706			23.024	291128.7
B	103.717	3.844	2.124	5.969			24.142	254886.6
AB	103.717	2.949	2.124	5.074			25.019	373515.0

Strategy	Cost	Effect	Inc_Cost	Inc_Effect	ICER	Status
QALY - Approaches 1 & 2						
SoC	158566	21.872				ND
B	255608	23.699	97042	1.827	53119	ND
AB	375043	24.579	119435	0.879	135813	ND
A	292352	22.590				D
QALY - Approach 3						
SoC	158365	22.309				ND
B	254887	24.142	96521	1.833	52656	ND
AB	373515	25.019	118628	0.877	135271	ND
A	291129	23.024				D
DALY - Approaches 1 & 2						
SoC	158566	7.291				ND
B	255608	5.847	97042	1.444	67203	ND
AB	375043	4.981	119435	0.866	137860	ND
A	292352	6.584				D
DALY - Approach 3						
SoC	158365	7.447				ND
B	254887	5.969	96521	1.478	65287	ND
AB	373515	5.074	118628	0.895	132583	ND
A	291129	6.706				D
DALY-Hack						
SoC	158566	9.624				ND
B	255608	7.741	97042	1.883	51524	ND
AB	375043	6.875	119435	0.866	137860	ND
A	292352	8.917				D
QALY-like DALY						
SoC	158566	21.872				ND
B	255608	23.699	97042	1.827	53119	ND
AB	375043	24.579	119435	0.879	135813	ND
A	292352	22.590				D

0.8 Conclusion

0.9 To Incorporate

- Link
- Link ## References {.unnumbered}

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