The Half-Cycle Correction Revisited: Redemption of a Kludge

Article *in* Medical Decision Making · October 2013

DOI: 10.1177/0272989X13501558 · Source: PubMed

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The Half-Cycle Correction Revisited: Redemption of a Kludge

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Decision-analytic software commonly used to implement discrete Markov models requires transitions to occur between simulated health states either at the beginning or at the end of each cycle. The result is an over- or underestimation, respectively, of quality-adjusted life expectancy and cost, compared with the results that would be obtained if transitions were modeled to occur randomly throughout each cycle. The standard half-cycle correction (HCC) is used to remedy the bias. However, the standard approach to the HCC is problematic: It does not account for discounting or for the shape of intermediate state membership functions. Application of the standard approach to the HCC also has no numerical effect on the resulting incremental cost-effectiveness ratio or change in net health benefit under certain circumstances. Alternatives to the standard HCC, in order of ease of use, include no correction, the life-table approach, the cycle-tree method, and a correction based on Simpson's rule. For less complex decision models in which the computational burden is not large, reducing the cycle length to a month or less and using no correction should result in small estimation biases. With more complex models, where cycle lengths larger than 1 month may be necessary to make computation feasible, we recommend the cycle tree approach. The latter is relatively easy to apply and has an intuitive appeal: Hypothetical subjects who transition from one state to another, on average halfway through a cycle, should receive half of the value associated with the state from which they come and half the value of the state to which they are going. ***Key words:*** *discrete state transition models; Markov models; half-cycle correction.* ***(Med Decis Making 2013;33:961–970)***

Hollenberg[1] devised the Markov cycle tree in 1984 as a practical way to implement discrete-time, state transition models. He recognized that discrete models have an inherent bias compared with those in which time is modeled continuously, and he implemented a half-cycle correction (HCC) method in his SMLTREE program to reduce the bias. In that program, parameters were created for each health state that specified the amount of utility or cost to assign at the beginning of the transition process. Hollenberg[1] as well as Sonnenberg and Beck[2] found that setting the value of the initial parameter to a half-cycle's worth of utility or cost remedied the bias induced by discrete processes. The latter approach has been adopted by other widely used software applications, such as Decision Maker[3] and TreeAge, and use of the HCC was recommended in a recent best-practice guideline.[4]

We have found that students in the introductory course on decision analysis at the University of Toronto often have trouble understanding the standard application of the HCC. Thus, in a previous article in this journal,[5] our group sought to provide 2 alternative approaches to explaining the HCC. Our focus was narrow and pedagogic: We did not consider the value of applying the HCC per se, merely how to teach the concept.

In response, Barendregt[6] pointed out that not only was the HCC difficult to teach, but its application may actually lead to erroneous results. He described a life-table-based method as a better way to solve the fundamental problem of discrete Markov state transition models: the over- or underestimation of life expectancy (or any value term) when state membership is

Received 20 September 2012 from the Department of Medicine, University of Toronto, Toronto, ON, Canada (DMJN, MDK); Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada (DMJN, NNK); and Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada (MDK). Revision accepted for publication 24 July 2013.

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DOI: 10.1177/0272989X13501558

counted at the beginning or end of a cycle, respectively. In the present paper, we corroborate and extend the concerns about the standard application of the HCC raised by Barendregt. We then explore alternatives to the standard method and compare their relative performance using an example of a discrete health state transition model. Our aim was to find an alternative to the standard HCC that is less ''kludge''-like than Barendregt suggests.

THE STANDARD HCC APPLICATION

In discrete-time, state transition (Markov) models, hypothetical subjects exist in one of several mutually exclusive health states. Time from the initiation of the Markov process is broken up into discrete segments or cycles. As the cycle number increases, a discrete Markov simulation traces the movement of a hypothetical cohort of subjects as they make transitions among the health states. Eventually, they enter an absorbing state, such as ''Dead,'' from which they cannot exit. With each cycle, subjects typically contribute quality-adjusted life-months (incremental utility) or incremental costs to a cumulative total for the cohort. As the proportion of the cohort in the absorbing states nears 1.0, the cumulative total quality-adjusted life-months or costs for the cohort approach asymptotes. Those values, when divided by the initial size of the cohort, provide estimates of its quality-adjusted life expectancy and expected cost per subject, respectively.

During the course of a cycle, a subject may remain in the current state or else experience chance events that result in a transition to another. Actual subjects followed over time would likely experience transitions between health states throughout a given cycle. However, commonly used software, which implements Markov models, accounts for state membership either at the beginning or at the end of each cycle. For example, TreeAge counts state membership at the beginning of each cycle. This results in an overestimation of the cumulative quality-adjusted life-months and costs experienced by the cohort compared with the value that would be obtained if transitions had occurred at random times during the cycle (Figure 1). The overestimation is approximately equal to half of a cycle's worth of incremental utility or cost.[5] By subtracting these quantities from the cumulative total for the state, the overestimation is corrected. Other software applications for discrete state transition models, such as SMLTREE and Decision Maker, account for state membership at the end of each cycle and therefore underestimate the cumulative quality-adjusted life expectancy and costs compared with a model that allows transitions throughout the cycle. For these applications, it is necessary to add a half-cycle's worth of incremental utility and cost to the cumulative totals for each state.

SMLTREE, Decision Maker, and TreeAge provide a convenient method for implementing the HCC. Three utility or cost parameters can be specified for each state. *Initial values* correspond to the number of quality-adjusted life-months or costs to be assigned to the members of a health state at the beginning of the Markov process (at cycle 0). *Incremental values* correspond to the quality-adjusted life-months or costs to be assigned to members of the state while in the midst of the process. *Final values* correspond to the number of quality-adjusted life-months or costs to be assigned to any members of the cohort who remain in the state when the Markov process ends.

In the standard implementation of the HCC, decision analysts use the initial utility and cost parameters. For example, imagine that a particular state, labeled ''Well,'' has an incremental utility, uWell, and an incremental cost, cWell. In the TreeAge context, if the analyst decides not to use the HCC, the initial utility and cost values during cycle 0 would be set equal to their incremental values, that is, 1.0*uWell and 1.0*cWell. In contrast, to implement the HCC, the analyst sets the initial values to half of their incremental values: 0.5*uWell and 0.5*cWell. The net effect is that the cumulative total utility and cost for the state are each a half-cycle *less* than the totals would be if no HCC had been applied, and the discrete overestimation is therefore remedied.

The initial utility and cost expressions look the same for Decision Maker but they have a different meaning. In this context, if the analyst decides not to use the HCC, the initial utility and cost values during cycle 0 would be set to zero. However, if the HCC were to be used, and because Decision Maker counts state membership at the end of each cycle, the initial cost and utility values would be set to half of their incremental values. In this case, the net effect is that the cumulative total utility and cost for the state are each a half-cycle *more* than the totals would be if no HCC had been applied, and the discrete underestimation is resolved.

As we showed in our previous paper,[5] the latter correction is too large if the Markov process ends early while subjects still inhabit nonabsorbing states. In that case, a half-cycle's worth of incremental utility or cost should be added back for each subject (or for the proportion of subjects) left in a state in the

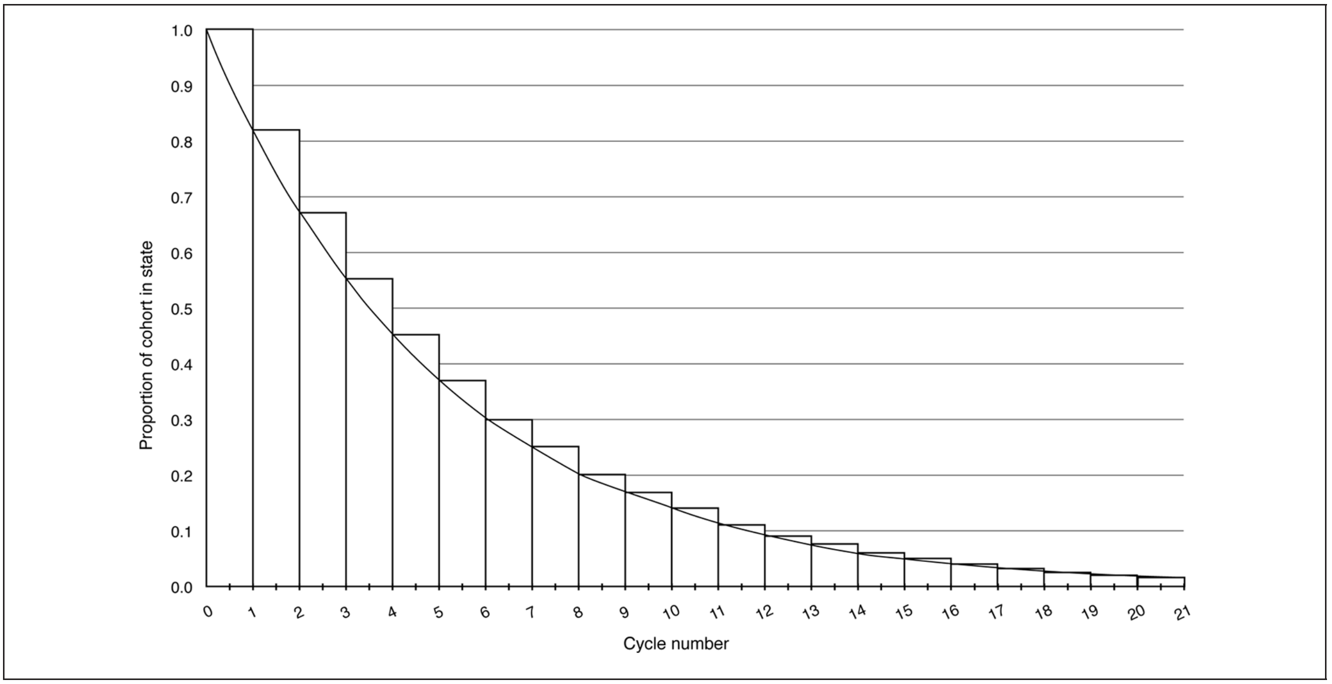

Figure 1 *A state membership curve, representing the proportion of a hypothetical cohort existing in a state as a function of cycle number, with a declining monotonic shape. The number of life-months (whether quality adjusted or not) is overestimated by discrete Markov models (area of the rectangles) when membership in the state is counted at the beginning of a cycle compared with the value that would be obtained if transition out of the state were to occur randomly during a cycle (area under the smooth curve).*

TreeAge context and should be subtracted from the total for the state in Decision Maker. Thus, the full HCC specification for the utility terms for the Well state would be as shown in Table 1.

PROBLEMS WITH THE STANDARD HCC APPROACH

One issue with the standard approach to the HCC has to do with discounting. Common practice in Markov state transition models is to discount the incremental utility and costs associated with membership in particular state by a fixed proportion (usually 3%–5%) per annum. The standard HCC method does not allow for discounting. By subtracting a half-cycle's worth of utility or cost from the total for a state, the implicit assumption is that the overestimated quantities due to the discrete process for later cycles in the Markov process have their full undiscounted value. Writing a properly discounted expression for the HCC as the initial utility or cost parameter for a state would be extremely cumbersome.

The second concern with the standard HCC implementation has to do with the shape of state membership curves. The latter are defined as graphs of the proportion of the cohort in a given state as a function of cycle number. Nonabsorbing Markov states can have 2 types of shapes: declining monotonic and nonmonotonic. Declining monotonic states are those in which no subjects who were not in that state at the beginning of the process may enter during the course of the process. In essence, declining monotonic states are the opposite of absorbing states. The state membership curve for a declining monotonic state, as its name suggests, declines monotonically from the proportion in the state at cycle 0. In contrast, intermediate, nonmonotonic states accept subjects from other states during the course of the Markov process and may have a larger proportion of them during a particular cycle than they did at cycle 0. The state membership curve for a nonmonotonic state rises when the number of subjects entering the state exceeds the number leaving and then falls when the opposite is true.

The standard approach to the HCC assumes that the state membership curve is declining and monotonic. However, the standard HCC is not appropriate for nonmonotonic states. As shown in Figure 2, when state membership is counted at the beginning of

Table 1 Example of the Standard Approach to the Half-Cycle Correction (HCC) for a State Labeled ''Well,'' Which Has an Incremental Utility of ''uWell''

Application	Parameter Type	No HCC	HCC
TreeAge	Initial	uWell	0.5*uWell
	Incremental	uWell	uWell
	Final	0	0.5*uWell
Decision Maker	Initial	0	0.5*uWell
	Incremental	uWell	uWell
	Final	0	−0.5*uWell

Note: Initial utilities refer to quantities evaluated at cycle 0, whereas final utilities refer to quantities to be calculated when the discrete-time, state transition process ends. Note that for exposition, discounting expressions have been omitted. In the TreeAge environment, initial utility and cost values are set to half of the amount they would have without the HCC. As a result, the cumulative total for the state is less than would be the case without the HCC, and the overestimation due to counting state membership at the beginning of each cycle is remedied. If subjects remain in the state after termination of the Markov process, the HCC reduction would be too large and a final amount of utility and cost equal to half of a cycle for the proportion of the cohort still residing in the state must be added back. In the Decision Maker environment, initial utility and cost values are set to half of their incremental values. As a result, the cumulative total for the state is more than would be the case without the HCC, and the underestimation due to counting state membership at the end of each cycle is remedied. If subjects remain in the state after termination of the Markov process, the HCC increase would be too large and a final amount of utility and cost equal to half of a cycle for the proportion of the cohort still residing in the state must be subtracted.

a cycle, the discrete approach underestimates the true number of life-months or costs accrued by the cohort when the state membership curve is rising and overestimates the true quantity when the curve is falling. If, the state membership curve is symmetric, one might assume that the under- and overestimations would cancel out and no HCC would be required. However, with discounting, the relative values of the under- and overestimations are different. The more likely scenario is that the state membership curve is not symmetric (Figure 3). In that case, even if discounting is ignored, it is unclear what HCC expression the analyst should place in the initial utility or cost boxes.

The last concern with the standard HCC has to do with the effect that the HCC has on the incremental cost-effectiveness ratio (ICER) or change in net health benefit (ΔNHB) when 2 strategies are compared using a discrete Markov-based approach. Not uncommonly, Markov processes are allowed to run until nearly the entire hypothetical cohort has been absorbed and until the contribution to the cumulative utility and costs from subjects remaining in the non-absorbing states are negligible. In this situation, the value for the final utility and costs for each state in the processes are set to 0. Assuming that the states are the same for 2 strategies to be compared (i.e., that the branches of the Markov nodes are identical), then the HCC quantities can be written as $U_{hcc,1}$ and $C_{hcc,1}$, which refer to half of the weighted sum of the initial utilities and costs, respectively, across the health states for the first strategy; similarly, $U_{hcc,2}$ and $C_{hcc,2}$ can be written for the second strategy. The weights correspond to the proportions of the cohort that occupy each of the states at the beginning of the Markov process. Since the HCC quantities refer to values on the first cycle, they do not have to be discounted. Also, as is commonly the case, if the initial utility and costs are the same for each of the states and the proportion of the cohort who start in each state is the same under both strategies, then $U_{hcc,1} = U_{hcc,2} = U_{hcc}$ and $C_{hcc,1} = C_{hcc,2} = C_{hcc}$.

Now consider the effect of applying these HCC quantities to the ICER and ΔNHB. In the case of the ICER, the value obtained without applying the HCC would be

$$ICER_{(no\ HCC)} = (QALE_1 - QALE_2)/(C_1 - C_2).$$

Here, QALE refers to the quality-adjusted life expectancy and C to the expected cost that are obtained from the Markov process associated with the strategy denoted by the subscripts. Given that the structure of the Markov process is the same for the 2 strategies, that the incremental utilities and costs for the states are the same, and that the distribution among the states at cycle 0 is identical, then

$$\begin{aligned} ICER_{(HCC)} &= [(QALE_1 - U_{hc}) - (QALE_2 - U_{hc})]/ \\ &\quad [(C_1 - C_{hc}) - (C_2 - C_{hc})]. \\ &= (QALE_1 - QALE_2)/(C_1 - C_2) = ICER_{(no\ HCC)}. \end{aligned}$$

Thus, under the conditions described above, application of the HCC in the standard fashion makes no difference to the ICER when membership in non-absorbing states is negligible at the termination of the Markov process.

The same is true for the difference in net health benefits.

$$NHB_1 = QALE_1 - C_1/W$$
$$NHB_2 = QALE_2 - C_2/W.$$

Here, W refers to the willingness-to-pay ratio (dollars per quality-adjusted life-month).

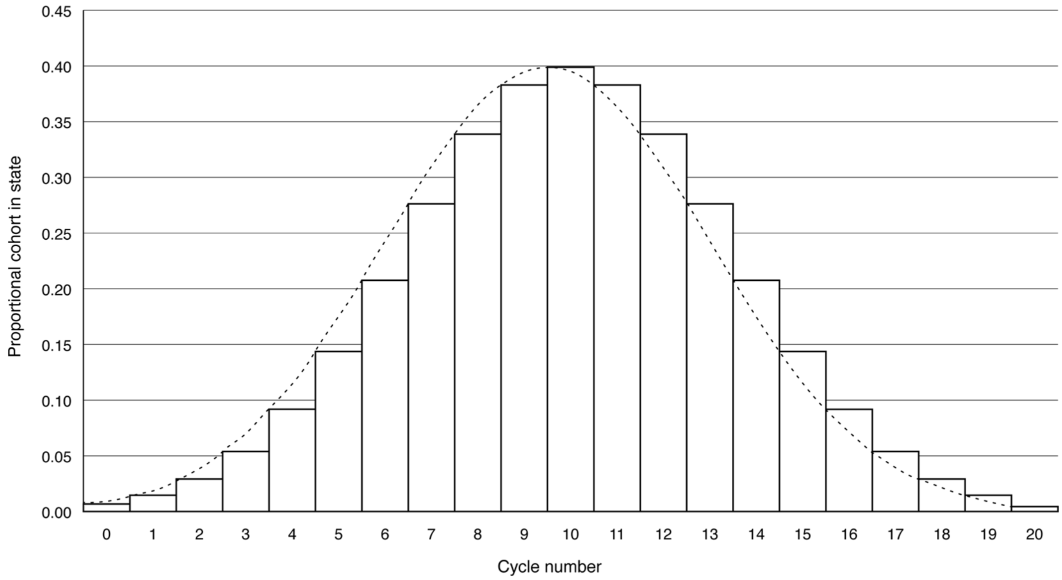

Figure 2 A state membership curve representing the proportion of a hypothetical cohort existing in a state as a function of cycle number, with a nonmonotonic, symmetric shape. The number of life-months (whether quality adjusted or not) is underestimated by discrete Markov models (area of the rectangles) when membership in the state is counted at the beginning of a cycle and the membership curve is rising compared with the value that would be obtained if transition out of the state were to occur randomly during a cycle (area under the smooth curve). When the state membership curve declines, the number of life-months is overestimated by the discrete process. If the state membership curve is symmetric and the value of later cycles is not discounted, then the under- and overestimated quantities would approximately cancel out. With discounting, the relative value of the under- and overestimated quantities would be different.

$$\Delta NHB_{(\text{no HCC})} = (QALE_1 - QALE_2) + (C_2 - C_1)/W$$

$$\Delta NHB_{(\text{HCC})} = [(QALE_1 - U_{hc}) - (QALE_2 - U_{hc})] + [(C_2 - C_{hc}) - (C_1 - C_{hc})]/W$$

$$= (QALE_1 - QALE_2) + (C_2 - C_1)/W = \Delta NHB_{(\text{No HCC})}.$$

When one is using the Decision Maker application, since state membership is counted at the end of each cycle, the HCC quantities would be added to rather than subtracted from the cumulative totals for quality-adjusted life expectancies and costs but the effect would be the same: The ICER and ΔNHB with and without the application of the HCC would be identical.

In summary, the standard application of the HCC does not account for discounting of future incremental utility and costs, does not accurately reflect the degree of estimation error for nonmonotonic states, and, for analyses in which 2 strategies use the same Markov structure and which run to completion, makes no difference to the ICER or ΔNHB.

ALTERNATIVES TO THE STANDARD HCC METHOD

For the remainder of this paper, we will assume that the software application used to implement Markov processes counts state membership at the beginning of each cycle as TreeAge does.

The Cycle Tree Method

As an alternative to the standard HCC application, the analyst accounts for transitions when they actually happen, that is, within the cycle trees for a given state, rather than at the beginning of the process. The cycle tree method relies on a principle that should be intuitive for students of Markov decision models to understand: If subjects make transitions between states, on average, halfway through a cycle, they should be given half of a credit for the state from which they are making the transition and half a credit for the state to which they are going. The principle holds true whether the ‘‘receiving’’ state is the same as the ‘‘transmitting’’ state or whether the receiving

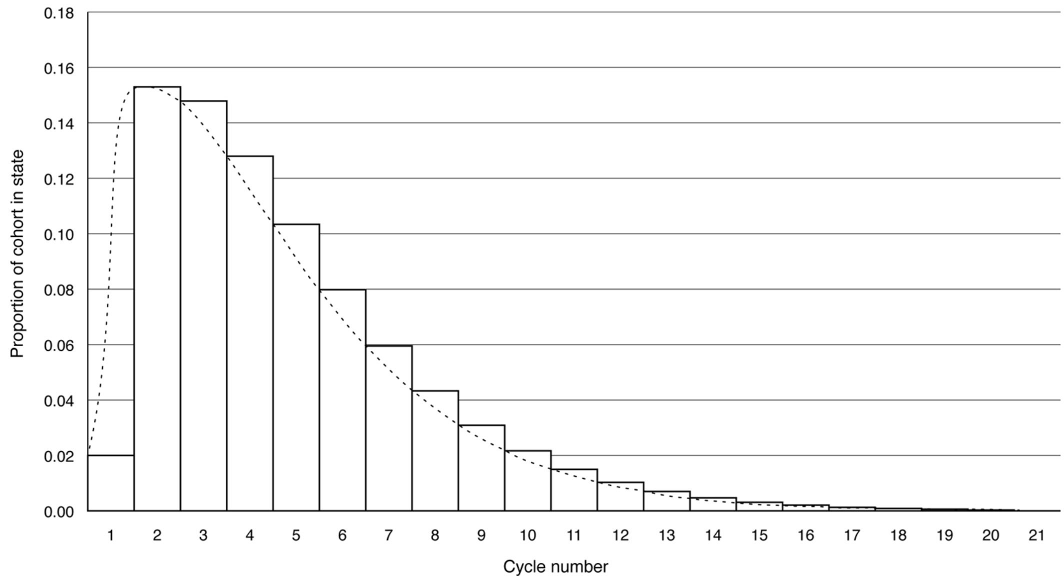

Figure 3 A state membership curve representing the proportion of a hypothetical cohort existing in a state as a function of cycle number, with a nonmonotonic and asymmetric shape. The number of life-months (whether quality adjusted or not) is underestimated by discrete Markov models (area of the rectangles) when membership in the state is counted at the beginning of a cycle and the membership curve is rising compared with the value that would be obtained if transition out of the state were to occur randomly during a cycle (area under the smooth curve). When the state membership curve declines, the number of life-months is overestimated by the discrete process. Because of the asymmetry of the curve, the under- and overestimated quantities would be different.

state is an absorbing one with zero value or cost per cycle.

In practice, both the initial and incremental utilities and costs are set to half of the values they would have in an uncorrected Markov process while the final utility parameters are set to 0. For example, for the Well state, the initial and incremental utilities would be set to 0.5*uWell*DR and the initial and incremental cost would be set to 0.5*cWell*DR. DR represents a discounting function that has the value of 1.0 on the first cycle and then, subsequently, reduces the utility and cost associated with the Well state by some proportion per annum. Note that if the DR function is set as a function of the cycle counter, it is important that the behavior of the counter in various software applications be considered (i.e., whether the cycle counter starts at 0 or 1.0).

The cycle-tree HCC is then implemented as a set of tolls (''transition rewards'' in the TreeAge nomenclature) within the branches of the cycle tree for a state. For example, on terminal branches for the Well cycle tree that lead to the ''Sick'' state, the tolls would be 0.5*uSick*DR and 0.5*cSick*DR. On terminal branches that lead back to the Well state, the tolls would be 0.5*uWell*DR and 0.5*cWell*DR.

If we use incremental utility as an example, the total for a subject who transitions from the Well to the Sick state would be equal to the sum of the amount assigned at the beginning of the cycle and the tolls encountered on the pathway within the cycle tree:

$$0.5^{*}\mathrm{uWell}^{*}\mathrm{DR} + 0.5^{*}\mathrm{uSick}^{*}\mathrm{DR} = 0.5^{*}(\mathrm{uWell} + \mathrm{uSick})^{*}\mathrm{DR},$$

which is the average of the discounted incremental utility of the Well and the Sick states. The incremental utility for a subject who remains in the Well state would be

$$0.5^{*}\mathrm{uWell}^{*}\mathrm{DR} + 0.5^{*}\mathrm{uWell}^{*}\mathrm{DR} = \mathrm{uWell}^{*}\mathrm{DR}.$$

The toll expressions are not necessary on terminal branches that lead to absorbing states that have zero incremental utility or costs associated with them because

$$0.5^{*}\mathrm{uWell}^{*}\mathrm{DR} + 0.5^{*}0^{*}\mathrm{DR} = 0.5^{*}\mathrm{uWell}^{*}\mathrm{DR}.$$

That is, subjects who are absorbed from the Well state will do so, on average, halfway through the cycle and therefore generate only a half-cycle's worth of incremental utility. The same reasoning holds for the incremental cost tolls. Similarly, tolls can be set for the other states of the Markov process.

The Barendregt Life-Table Method

The Barendregt life-table method for the HCC is similar to the cycle-tree approach except that HCCs are made only between nonabsorbing and absorbing states. Both the initial and incremental utilities and costs are set to the values they would have in an uncorrected Markov process, while the final utility parameters are set to 0. For example, for the Well state, the initial and incremental utilities would be set to uWell*DR and the initial and incremental cost would be set to cWell*DR. Tolls are set on branches of cycle trees that lead to an absorbing state. For example, on a terminal branch leading from the Well state to an absorbing state, the tolls would be −0.5*uWell*DR and −0.5*cWell*DR.

For transitions between nonabsorbing and absorbing states, and in the case where quality adjustment of the value of state membership is not considered, the cycle-tree HCC method is numerically identical to the life-table approach. The difference between the latter approach and former is that the cycle tree method accounts for transitions between nonabsorbing states that have different quality assignments, whereas the life-table approach does not.

A Correction Method Based on Simpson's Rule

Simpson's rule is a method of numerical integration of functions.[7] The calculation of cumulative quality-adjusted life expectancy and cost in a health state transition model is a type of discrete integration, and this fact forms the rationale for the application of Simpson's rule to remedy the HCC problem. If *f(x)* is a function of a continuous variable, x, and if a and b are values of x such that $b > a$, then

$$\int_a^b f(x)dx \approx \frac{b-a}{6}\left(f(a) + 4\cdot f\left(\frac{a+b}{2}\right) + f(b)\right).$$

In a decision modeling context, the definite integral represents the area under the state membership curve during the course of one cycle (i.e., $b - a = 1$). The quantity *f(a)* represents the proportion of the cohort that exists in the state at the beginning of the cycle, whereas *f(b)* represents the proportion at the end of the cycle. In the TreeAge environment, *f(a)* and *f(b)* can be obtained by using the StateProb() and Global() functions, which provide, respectively, the proportion of the cohort existing in the state where the function is evaluated and a matrix that can store and retrieve values during a Markov process.

Tolls are placed on each terminal branch of each cycle tree, which stores the current value of StateProb() in a cell of the matrix. These stored values can then be used as the *f(a)* value in the subsequent cycle. For example, on the terminal branches of the Well state, the tolls would be 0*Global(1;1;StateProb()) and for the Sick state, 0*Global(1;2;StateProb()), where Global(i;j;value) results in the placement of the quantity ''value'' in the *i*th row and *j*th column of the matrix and Global(i;j) retrieves it. Note that the Global() function may return a nonzero value when called. Multiplying the function by zero eliminates that value should it be returned. A call to the StateProb() function in the incremental utility box of a state provides the *f(b)* value. TreeAge cannot report the $f[(a + b)/2]$ quantity, but it can be estimated by $[f(a) + f(b)]/2$. The magnitude of the bias produced by this approximation will depend on the cycle length.

Thus the area under the state membership curve for the Well state is estimated by

$$\begin{aligned}&(\text{Global}(1;1) + (2^*(\text{Global}(1;1)\\ &+ \text{StateProb}()))) + \text{StateProb}())/6.\end{aligned}$$

The latter expression can be placed in the incremental utility box of the Well state. However, since TreeAge automatically multiplies the value in the incremental utility box by the proportion of the cohort in the cycle the area under the state membership curve for the Well state, aWell should be written as

$$\begin{aligned}&(\text{Global}(1;1) + (2^*(\text{Global}(1;1) + \text{StateProb}())))\\ &+ \text{StateProb}())/(6^*\text{StateProb}()).\end{aligned}$$

Then the incremental utility for the Well state would be

$$\text{uWell}^*\text{aWell}^*\text{DR}.$$

Similar expressions can be written for the cost of being in the Well state and for the parameters of the Sick state. Care should be taken to properly initialize the matrix at the start of Markov process; otherwise, an error may occur. Also, since the Simpson's rule approach requires information from previous cycles, and none exist for cycle 0, initial

Table 2 Parameters for the Example Model (Figure 4) to Show the Effect of Either Not Using a Half-Cycle Correction v. Applying the Standard and Alternative Methods for the Half-Cycle Correction

Variable	Value
Cycle length	1–12 months
Discount rate (per annum)	5%
Probability of becoming sick (per annum)	0.1
Probability of death (per annum)	0.05
Relative risk of death (sick v. well)	5
Proportion of cohort starting in the well state	0.5
Incremental utility of being well	1.0
Incremental utility of being sick	0.6

utility expressions for the Well and Sick states could be written, respectively, as

$$\text{uWell} + (0^*(\text{Global}(1;1;1) + \text{Global}(1;2;1)))$$

and

$$\text{uSick} + (0^*(\text{Global}(1;1;1) + \text{Global}(1;2;1)))$$

Similar initial cost expressions could also be written.

RELATIVE PERFORMANCE OF THE CORRECTION METHODS

To assess the relative performance of the alternatives to the standard HCC method, we constructed a simple Markov process as shown in Figure 4. We chose this particular model structure because it is the simplest one in which there are at least 2 nonabsorbing states with different incremental quality adjustments and where there is at least 1 intermediate, nonmonotonic, state. We used values shown in Table 2 as fixed parameters for the process except for the cycle length, which was allowed to vary from 1 to 12 months. For illustration, we ran the process for incremental utilities and not costs. To generate the ''true'' QALE estimate, we ran the Markov process for 120 years using hour-long cycles, which yielded 47.05 quality-adjusted life-months. Figure 5 shows the magnitude of the difference between the ''true'' QALE and estimates obtained after using either no HCC or those mentioned above. As cycle length increased, a positive bias was introduced to the QALE estimates when no HCC was used. The bias was reduced but not eliminated by the Simpson's rule approach. The other methods resulted in an overcorrection of the positive bias. In this example model, the cycle-tree method introduced the least amount of overcorrection. Figure 5 illustrates that no HCC method solves the overcorrection problem perfectly and that for cycle-lengths of 1 month or less, the difference between methods, including no correction, becomes quite small.

DISCUSSION

As we have demonstrated in this paper, discrete state transition models will tend to produce biased estimates of quality-adjusted life expectancy and average cost when compared with models where transitions can occur at random times throughout a cycle. The standard HCC approach is to either add or subtract—depending on the particular software application used—a half-cycle's worth of quality-adjusted utility or cost to the cumulative total for a state. We show that this approach does not appropriately discount the quantities to be added or subtracted and it does not appropriately correct for the bias in intermediate, nonmonotonic states. Furthermore, in the common situation in which 2 strategies use the same Markov structure and run to completion, the standard HCC approach makes no difference to the resulting ICER or ΔNHB.

We provide an estimate of the size of the bias and the effect of applying no correction, the standard HCC, and several alternatives to the standard for a particular 3-state model with a variety of cycle lengths. The magnitude of the bias would be difficult to forecast a priori for more complex models, in particular, those with more than 1 intermediate state. In general, for a given Markov structure, the fewer the average number of effective cycles in the process—either because of long cycle lengths, a high discount rate, or rapid absorption—the greater the expected bias would be and therefore the greater the effect of a given HCC method.

For relatively simple models with a low computational burden, the simplest approach would be to omit an HCC and to use a cycle length of a month or less. In the situation where a model is complex and longer cycle lengths are required to make computation feasible, we would recommend that one of the HCC methods be used. We have shown that the standard HCC is inappropriate, and therefore, currently, the analyst must choose between the cycle tree, life-table, or Simpson's rule approaches. In terms of the number and complexity of the additional expressions

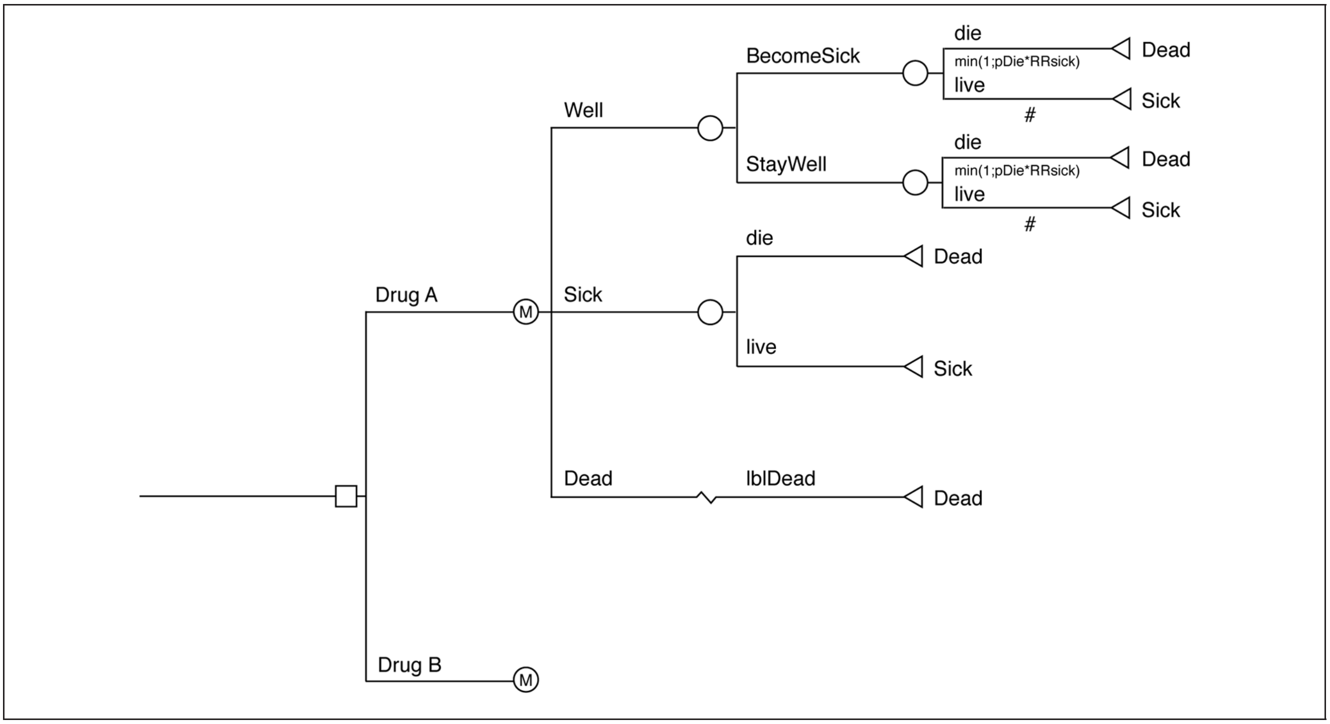

Figure 4 A simple 3-state Markov process used to demonstrate the magnitude of the effect of applying the half-cycle correction. The same Markov structure, but with different transition probabilities, would be attached to the Drug B Markov node (not shown).

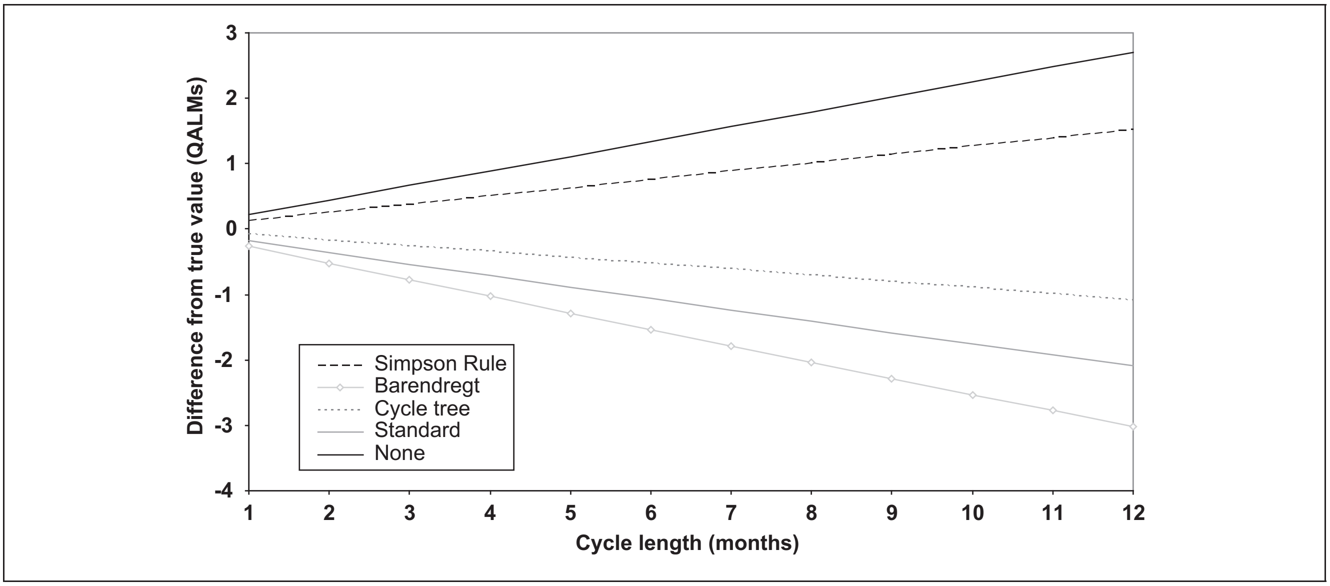

Figure 5 The magnitude of the bias in the estimated number of quality-adjusted life-months (QALMs) obtained for the Drug A strategy of an example Markov process (Figure 4) as a function of cycle length. The mean values of the parameters shown in Table 2 were used to generate the estimate. Separate lines are shown for each correction method: none, the standard half-cycle correction (HCC) method, the cycle tree HCC method, the Barendregt life-table HCC method, and a method based on Simpson's rule.

that must be added to a model, with the inherent risk of coding errors, the life-table approach is the most simple and the Simpson's rule–based method is the most complex. Our preference is to use the cycle-tree method because it is only marginally more difficult to implement than the life-table approach and because it has intuitive appeal: Hypothetical subjects who transition between states should be given half the value or cost for the state they are leaving and half of the credit for the state to which they are going.

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