Determining Transition Probabilities:

Confusion and Suggestions

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Confusion regarding proper use of the terms rate and risk persists in the literature. This has implications for the proper modeling of prognosis and transition between health states in decision analysis and related techniques. The issue is complicated by the plethora of terms related to rate and risk. Although the suggestion to use the terms force and probability as substitutes for rate and risk has some appeal, the change in terminology by itself is unlikely to solve all the confusion or misuse of terms. This paper clarifies the proper definitions and estimations of rates and risks and suggests critical factors for the decision analyst to remember when using, modeling, or interpreting transition rates and risks. *Key words*: decision models; rate; risk; force; probability; transitions. **(Med Decis Making 1994;14:52–58)**

Concern has been raised in the medical decision making literature regarding confusion about the terms rate, force, and probability, and the effect of this confusion on accurate modeling of transitions from one health state to another.[1,2] Depending on the model, this confusion may have little practical importance or may introduce significant errors into the decision making model. As an example of the latter, in the work by Silverstein et al.[3] on prognosis in systemic lupus erythematosus, had the analysts made the single mistake of treating the 50% probability of transitting between flare and death as a rate (transforming it to a 39.3% probability), the life expectancy of their cohort would have been estimated at 33.7 years rather than the correct 29.6 years, a 14% error. Other incorrect applications of rates and risk would have further distorted their model.

Confusion about rate, risk, and related terms is certainly not new.[4,5] While attempts have been made to clarify the terminology in the decision making literature,[1,2] we believe that considerable opportunity for misunderstanding and misapplication continues.[6] The purposes of this paper are fourfold: to clarify definitions related to transition rate (or force)[2] and risk (or probability)[2]; to review sources of confusion; to demonstrate proper estimation of rate- and risk-related measures; and to offer suggestions for correct application of these measures in decision modeling despite problems of variably correct use of terms.

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Proper Terminology: Concepts and Practical Aspects

Measurement of transition from one health state to another involves estimation of the pressure to transit and the probability of transitting over a period of time. The transition may relate to movement from alive to dead ("mortality"), from a disease- or event-free state to an occurrence of the disease or event ("incidence"), or from one disease state to another. The propensity to transit can be represented either as the potential for transitting at any point in time or as the likelihood of transitting over a period of time. These two concepts are represented by the terms "rate" and "risk," respectively, in proper epidemiologic usage.[4] Thus rate represents the same concept as does "force" used by Beck[2] and Stalpers et al.,[1] and risk refers to the same concept as "probability" in Beck's proposed usage.[2] (Both force and probability, of course, can be applied to any transition, not just the mortality transition discussed by those authors.)

RATE

In conceptual terms, rate (table 1) represents the *instantaneous potential* for change in one variable per unit change in another variable. In mathematical terms, rate represents the first derivative of the first variable relative to the second.[4,7,8] In medical research, the second variable is usually time and the change is described relative to the size of the candidate population ("relative rate").[4,7,9] Representing an instantaneous potential, a rate theoretically has no upper bound. For example, the *annual* mortality rate on a small island the instant it is swamped by a massive tidal wave approaches infinity.[9]

Because rate is an event pressure over an infinitely small period of time, it cannot be measured directly but must be inferred from measurement on a population taken over time (denoted an "average rate") and

Table 1 • Essential Aspects of Rate (Force) and Risk (Probability)*

	Rate (Force)	Risk (Probability)
Concept	Instantaneous potential for change in one variable per unit change in another variable; usually expressed as a relative rate in medical usage. Representing an instantaneous potential, rate theoretically has no upper bound.	Probability that a person will experience a change in health state *within* a specified time period. As a conditional probability a risk measure can vary between zero and one and is dimensionless.
Mathematical definition	*General form*[4,7]: $-dY/dX$ at time t. *Specific form (relative rate)*[8]: $\frac{-d(N_t')/dt}{N_t'}$, at time t, where N_t' denotes the size of the candidate population at time t.	$(N_0' - N_t')/N_0'$, where N_0' represents the size of the population eligible to transit at beginning of the interval, and N_t' represents the number remaining eligible to transit at time t.
Relationship to time	The measure refers to an infinitely small period of time but in practical terms must be inferred from measurement on a population taken over time (i.e., an "average rate").	Risks require period referents that describe the time or age span over which transitions occur. The period referent varies by disease process under consideration.
Practical aspects	Usually measured as events/population–time. In a fixed cohort an individual's time occurring after a transition but still in the measurement interval is removed from the population–time denominator. Estimation must be based on group data, not individual outcomes.	Usually measured as persons experiencing a transition per total population at risk over the relevant time period. In a fixed cohort a person experiencing a transition during the interval is considered part of the denominator for the duration of the measurement interval. In a dynamic cohort risk is usually estimated from rate using the density method.[7] Estimates may be based on individual outcomes (e.g., Kaplan-Meier).[10]
Typically encountered in	Epidemiologic studies of chronic diseases with extended risk periods using dynamic cohorts.	Studies of diseases with restricted risk periods (usually acute conditions). Most clinical studies.
Use in medical decision making	To provide flexible derivation of probabilities over varying time periods.[11] To estimate life expectancy using the DEALE[12] and related techniques.[13]	In decision trees, Markov processes, and other methods to estimate number of persons affected (or probability for a single person) over a given time period.

*For reference citations, see the reference list.

is usually measured as events per population–time. Rates can be estimated directly from observations of a *fixed cohort* observed over a defined period of time. In a *dynamic cohort* (i.e., participants enter and leave at different times) with known individual follow-up periods, the design can be artificially converted to a fixed cohort by considering each subject's time of entry into the study as the common starting time (usually using the actuarial method).[7] In either case person–time occurring after a transition but still in the measurement interval is not included in the population–time denominator, a difference from that which occurs when estimating probabilities (risks). When individual follow-up periods in a dynamic cohort are not known, rates can be estimated from serial cross-sectional observations over time if the major variables within the population do not change (indicating that persons transitting out of the susceptible population are equally balanced by new entrants, in terms of both numbers and levels of risk factors). This is the approach usually taken in community studies.[7] In this case person–time occurring after a transition is not formally removed from the population–time denominator but is considered to have been balanced by time contributed by new entrants. The studies in which rates (correctly measured) are typically encountered are delineated in table 1, as are the typical uses of rates in medical decision making.

RISK

As opposed to rate, risk (table 1) conceptually represents the *probability* that an individual will transit from one state to another *within* a specified time period.[4,9] Although risk requires a period referent, as a probability it is dimensionless and varies between zero and one.

When measured directly, risks are usually estimated from observations of a fixed cohort or a dynamic cohort that can be artificially converted to a fixed cohort. When risks are being estimated, a person experiencing a transition is considered part of the cohort for the duration of the measurement interval during which the transition occurred but not for subsequent measurement intervals. Risks are difficult to measure di-

Table 2 • Intended Relationships of Terms Found in the Medical Literature to the Concepts of Rate and Risk*

Rate	Risk
Force	Probability
Hazard	Likelihood
Potential	Cumulative incidence
Person–time incidence rate	Product–limit (Kaplan-Meier)
Force of morbidity	
Incidence density	
Instantaneous risk	

*The reader is cautioned that these terms are frequently misapplied in the medical literature. Their appearance in a research report in no way assures that the measures were appropriately estimated and thus represent the originally intended meaning.

rectly from dynamic cohorts in the community but can be estimated from rates using the density method (described below).[7] The studies in which risks (probabilities) are commonly encountered and typical uses in medical decision making are described in table 1.

RELATIONSHIP BETWEEN RISK AND RATE

Risk represents the accumulated effect of the transition rate throughout the chosen time period. More often than not, rates vary over time. Therefore, an important judgmental task is the choice of time interval over which to represent risks. For example, the most important time interval after surgery to evaluate transitions may be two hours, two days, one month, six months, or some other interval, depending on the clinical question. Once the risk interval is chosen, the accumulated effect of (a varying) transition rate over that time interval can be determined.

CURRENT LEVEL OF MISUSE

As a rough evaluation of the level of terminology misuse in the current medical literature, we selected a random sample of 20 original articles from *Abridged Index Medicus* journals published in 1989 with the term "mortality rate" in either title or abstract. Review articles were excluded. One of us (DKM) evaluated each article to determine whether the indicated mortality rate represented a true rate (force) or a risk (probability). In one article, not enough information was provided to make the determination. In the other 19, including reports in both the medical and surgical literature, "mortality rate" incorrectly referred to a risk (probability); that is, to the number of events over a finite period of time without removal of person–time after transition.

Twenty-seven "mortality rates" (mean "rate" 19%, range 1.9% to 70%) were reported in the 19 studies. If the reported results had been treated as true rates and transformed to probabilities, the now-incorrect probability estimates would have averaged 16% (range 1.9% to 50%). Thus the incorrect estimates would have introduced absolute errors averaging 3% and as high as 20%. Sixteen of the 27 mortality probabilities were greater than 10%; mistakes this large can cause serious problems with the validity of decision models.[2,7]

Sources of Confusion

Several factors contribute to confusion in the use of terms such as rate and risk. First, time is handled differently in the proper estimation of rates and risks, but the relationship to time is often transposed between the two terms or otherwise misinterpreted.[4] Second, a number of non-epidemiologic terms in common use employ "rate" in a manner other than that sanctioned here; examples are employment rate and tax rate.[8]

Third, even though a term's accepted meaning is well understood, it still may be used incorrectly. For instance, even while supporting proper use of terms in general, the editor of the *American Journal of Epidemiology* condoned misapplication of the word rate in occasional instances of traditional use. The example he cited was "prevalence rate,"[5,14] which constitutes an impossible concept from the view of proper terminology.[4] Other epidemiologists also support this use of the term prevalence rate.[8]

A fourth potential for problems stems from the multiple methods for determining transition rate and risk, each of which frequently has its own terminology. Several of these expressions are represented in table 2. The term instantaneous risk, intended to represent the concept of rate, is particularly worth noting. Obviously use of the word risk in this manner can be confusing. When any of these terms appears in the medical literature, the reader must be concerned not only about the intended meaning of the term but also that the data were properly managed so that the term truly represents the intended meaning.

Other potential sources of confusion relate to the attempted clarification of these issues in recent *Medical Decision Making* articles.[1,2] In a brief editor's note,[2] Beck described the correct transformation of a *n*-year survival probability to an annual probability but did not proceed to general formulations for other time periods or transition probabilities other than survival. It is also of some concern that Beck's important clarification may be missed in a small editor's note. A succeeding paper by Stalpers et al.[1] clarified some points but added to the confusion in others. Of particular concern was the term "instantaneous mortality rate," which is actually a one-year mortality risk (probability). The term could cause misunderstanding in part because it used the word "rate" differently (as a probability) from correct epidemiologic usage and the convention suggested by Beck.[2] In addition, linkage of the word "instantaneous" to a probability was confusing

because "probability" always implies activity over a finite period of time. It makes more sense to us to reserve the word "instantaneous" for reference to rates or forces.

Another source of confusion in understanding and correctly computing transition probabilities (risks) relates to models of multiple transitions from a single state (e.g., from well to small stroke, to large stroke with residual, or to death). Correct determination of annual probabilities for multiple transitions from a single state using n-year data usually involves a difficult choice among several possible n^{th} root solutions of the transition matrix.[15; D. G. Fryback, personal communication, 12/17/90] However, full explanation of this issue is beyond the scope of the present paper.

Proper Estimation of Rate and Risk

Using the notation of Kleinbaum and colleagues,[7] we review acceptable methods for estimating rates and risks.

RATE

Let N_0' represent the initial size of the population eligible to transit (e.g., disease-free subjects to be followed for Δt years for first incidence of disease) and N_t' be the number remaining eligible to transit at time t. The *instantaneous incidence rate* (also known as the "hazard function"[10]) is given by $[-d(N_t')/dt]/N_t'$, where the numerator is simply the slope of the line tangent to N_t' at time t. In practice the instantaneous rate is often approximated by estimating the *average incidence rate*, also known as the *incidence density*, ID (t_0, t). Mathematically $ID(t_0, t)$ represents the number of new cases divided by the integral of $N_t'(dt)$ from t_0 to t. If the incidence rate is constant, then the number of eligible subjects (N_t') at time t is an exponential function such that $N_t' = N_0' \exp[-ID(\Delta)]$, where $\Delta = (t - t_0) \leq \Delta t$.

As usually measured, the true ID of an entire cohort is estimated by the number of new cases, I, divided by the accrued population-time, PT:

$$\hat{ID}\ (t_0, t) = I/PT \qquad (1)$$

Estimating average incidence rate in this manner is similar to using distance traveled over a period of time as an estimate of average velocity.[7] When individual follow-up periods are known, PT may be calculated by summing each subject's time exposed to the possibility of transitting. PT should not include time occurring after a transition or withdrawal. Withdrawal refers to all reasons for removal from the candidate population *other than* the transitions of interest (e.g., follow-up loss, death from another cause, or use of non-study procedures that remove the person from the candidate population). When individual follow-up periods are not known and the population is stable over time, PT may be estimated by multiplying the size of the candidate population by the actual duration of the study follow-up; that is, $PT = N'(\Delta t)$, where N' represents the size of the stable candidate population and Δt denotes the duration of follow-up.[7]

Estimation of the average rate by I/PT may obscure variations in the instantaneous rate. For example, consider the situation where the instantaneous rate declines over time. In this situation the $\hat{ID}$ based on a large cohort followed for a short time (e.g., 1,000 persons followed one year) would be larger than the $\hat{ID}$ based on a smaller cohort followed for a longer period (e.g., 100 persons followed ten years). Notice also that rate estimation needs to be based on group data; otherwise $\hat{ID}$'s vary too widely.

RISK

Risks may be estimated by any of three methods: the simple cumulative method, the actuarial method, and the density method based on estimation of average rates.[7] In the attempt to prevent additional confusion introduced by notation, we use the symbol $\hat{P}$ to represent risks (probabilities) in place of the traditional epidemiologic $\hat{R}$.[7]

1. For a fixed cohort of individuals, all of whom are followed for Δt years, *the simple cumulative method* estimates the t-year risk, $\hat{P}(t_0, t)$, as the number of new cases (I) diagnosed during the period (t_0, t) divided by the number of disease-free individuals (N_0') at time t_0[7]:

$$\hat{P}(t_0, t) = (N_0' - N_t')/N_0' = I/N_0' \qquad (2)$$

2. When members of the cohort are not all followed for Δt duration, the *actuarial* (or life-table) *method* permits calculation of risks from grouped data for a cohort in which withdrawals may be present. The denominator, N_0', is adjusted by subtracting half of the number of study withdrawals (W) under the assumption that the mean withdrawal time occurs halfway through the period (t_0, t). The resulting estimate of risk is[7]:

$$\hat{P}(t_0, t) = I/[N_0' - (W/2)] \qquad (3a)$$

To estimate the Δ-year risk, $P(t_0, t_j)$, over an accumulated period (t_0, t_j) of Δ years (1 year $\leq \Delta \leq \Delta t$), the one-year estimates of risk, $\hat{P}_j$, can be combined by using the formula[7]:

$$\hat{P}(t_0, t_j) = 1 - \prod_{j'=1}^{j} (1 - \hat{P}_{j'}) \qquad (3b)$$

where $\hat{P}_{j'}$ is the one-year transition risk for the j^{th} time

interval, (t_{j-1}, t_j), and Π represents the product of the $(1 - \hat{P}_{j'}$'s. Other time periods can be treated in a similar fashion. If the true transition rate can be assumed to remain constant over the time period, the common $\hat{P}_j$ can be estimated from $\hat{P}(t_0, t_j)$ using the equation:

$$\hat{P}_j = 1 - [1 - \hat{P}(t_0, t_j)]^{1/j} \quad (3c)$$

where j represents the number of equal time intervals.

The actuarial life-table method requires a moderately large number of observations, at least 30, so that transition times [or, alternatively, retention ("survival") times] can be grouped into intervals. When data cannot be easily grouped (usually because of small numbers), the Kaplan–Meier product-limit estimator can be used to estimate transition (or retention) probabilities. Thus the product-limit method represents a special case of the life-table method where each measurement interval contains only one observation.[10]

3. The third method of risk estimation, the *density method*, uses estimated group-specific incidence densities (i.e., rates) to estimate risk for a specified group or time interval. Assuming that the instantaneous transition rate remains constant during the entire period (i.e., exponential reduction in eligible population), the Δ-year risk, $P(t_0, t)$, is estimated by:

$$\hat{P}(t_0, t) = 1 - (N_t'/N_0') = 1 - \exp[-\hat{ID}(\Delta)] \quad (4a)$$

where $\hat{ID}$ is the estimated average rate (previously defined) and Δ is the elapsed time, $(t - t_0)$. The assumption that the rate is constant is essential for a correct estimation. If the rate varies over the entire period, total Δ may be divided into small enough intervals that the assumption of constant rate is reasonably met for each interval. Estimated risk for the total period can then be calculated by determining $\hat{P}_j$ for each interval using equation 4a and combining interval risks using equation 3b.

The Δ-year risk can also be estimated by combining the interval $\hat{ID}$s directly as follows[7]:

$$\hat{P}(t_0, t_j) = 1 - \exp\left[-\sum_{j'=1}^{j} \hat{ID}_{j'}(\Delta_{j'})\right] \quad (4b)$$

where $\Delta_{j'}$ represents the j^{th} risk interval, $\hat{ID}_{j'}$ represents the $\hat{ID}$ for the j^{th} interval, and Σ represents the arithmetic sum of $\hat{ID}_j$s over the entire period t_0 to t_j. This approach can be particularly helpful when the $\hat{ID}$s are already known. If the true transition rate can be assumed to be constant over the relevant time period, equation 4b can be rewritten:

$$\hat{P}(t_0, t_j) = 1 - \exp(-\hat{ID}_j j) = 1 - e^{-\hat{ID}_j j} \quad (4c)$$

where $\hat{ID}_j$ represents the common transition rate over each $\Delta_{j'}$ time interval and j represents the number of equal $\Delta_{j'}$ intervals.[11] Reversing the process and again assuming constant transition rate, $\hat{ID}$ can be determined from a multi-time period probability by solving for it in equation 4c as follows:

$$\hat{ID}_j = \frac{-\ln[1 - \hat{P}(t_0, t_j)]}{j} \quad (4d)$$

Example

To illustrate the three methods for estimating risk, consider an example provided by Beck and Pauker.[16:423–4] They modeled a clinical problem in which 100 well patients were followed for three years (i.e., a fixed cohort). There were apparently no withdrawals, and 70 became ill over the three-year period. Beck and Pauker calculated the average annual transition rate as 70 transitions / (100 patients × 3 years), or 0.233 transitions per patient–year. They neglected, however, to remove the time occurring after transitions from the population–time denominator. They went on to determine the one-year annual transition probability (assuming constant transition rate throughout the year) as $1 - e^{-\text{annual rate}} = 1 - e^{-0.233} = 0.208$.

Using these results and the actuarial method, the one-year estimated risks and corresponding numbers of annual incident cases are computed and reported in table 3. Notice that using 0.208 as the annual morbidity risk results in a total of only 50 incident cases over three years, as opposed to the 70 reported. In the following we model correct ways to determine the transition probability (risk) using the methods described above.

The *simple three-year cumulative incidence*, $\hat{P}_{(0,3)}$, is 70/100, or 70%. Because there are no withdrawals, the *actuarial three-year cumulative incidence* is also 70%. If the cycle length for the Markov model is one year and we assume the incidence rate remains constant within the three-year interval, the *one-year probability* can be determined directly from the 70% probability using the actuarial method or via rates using the density method. Using equation 3c for the actuarial method and assuming constant rate, the one-year incidence can be estimated directly from the three-year rate:

$$\hat{P}_1 = 1 - [1 - \hat{P}_{(0,3)}]^{1/3} = 1 - [1 - 0.7]^{1/3} = 0.3306$$

Alternatively, $\hat{P}_j$ can be estimated via rates in the following manner. First $\hat{ID}$ is estimated using equation 4d:

$$\hat{ID}_j = \frac{-\ln[1 - \hat{P}(0, 3)]}{3} = \frac{-\ln[1 - 0.7]}{3} = 0.4013$$

$\hat{P}_1$ can then be determined from $\hat{ID}_j$ using equation 4a:

$$\hat{P}_j = 1 - \exp[-\hat{ID}_j(\Delta)]$$

$$= 1 - \exp[-0.4013\ (1)] = 0.3306$$

This approach, while appearing more cumbersome, can provide greater flexibility in estimating probabilities over varying time periods.[11]

Using constant $\hat{P}_j$s of 0.3306, the results are recalculated in table 4. We see that the total number of incident cases during the three-year period now totals 70.

Table 3 • Estimation of the Risk of Becoming Ill for the Hypothetical Cohort of 100 Individuals, by One-year Intervals, using the Beck and Pauker[16] Approach

Year j	Interval (t_{j-1}, t_j)	Number Entering Interval N_{0j}	Number of Incident Cases I	1-Year Estimated Risk $\hat{P}_j$
1	(0, 1)	100	21	0.208
2	(0, 1)	79	16	0.208
3	(2, 3)	63	13	0.208
TOTAL			50	

Table 4 • Estimation of the Risk of Becoming Ill for the Hypothetical Cohort of 100 Individuals, by One-year Intervals, Using the Actuarial Method*

Year j	Interval (t_{j-1}, t_j)	Number Entering Interval N_{0j}	Number of Incident Cases I	1-Year Estimated Risk $\hat{P}_j$	Δ-Year Estimated Risk for Accumulated Period $\hat{P}(t_0, t_j)$†
1	(0, 1)	100	33	0.3306	0.3306
2	(1, 2)	67	22	0.3306	0.5519
2	(2, 3)	45	15	0.3306	0.7000
TOTAL			70		

*See Kleinbaum et al.,[7] pp. 104–6.
†Formula (3b) in text.

Discussion

The medical literature supplies the parameter estimates for most models in the decision-making literature, and the words rate and risk are frequently used in terms to describe these parameter estimates. However, given the problems enumerated above, it is not surprising that the terms rate and risk are often misused. Thus the decision analyst can rarely assume that they represent what they are supposed to represent. Although the suggestion of Beck to use the terms force and probability instead of rate and risk[2] has some merit, there is no guarantee, considering the complexity of these issues, that these terms will be properly applied by other authors either; consider the problem that Beck himself had in his earlier paper with Pauker,[16] as detailed above. Even during the writing of this paper, there were several times that the two authors had to remind each other of the proper use of the terms. The subject matter is inherently tricky. Further, even if the analyst knows how the terms force and probability ought to be applied, he or she will still have to deal with the plethora of terms in the literature and the variable correctness in their use.

For communication within the medical decision community, one of us (DKM) favors Beck's suggestion[2] to use force for the concept of rate and probability for the concept of risk. The other (SMH) believes that the terms rate and risk are so ingrained in the medical and related literature that avoidance is impossible and the decision-making community may as well learn how to use them properly. In any event, extra care in application of the proper concepts (rate vs risk or force vs probability) and use of correct terminology so that audiences are not confused is warranted.

In short, there is no substitute for the decision analyst's understanding the basic characteristics of a measure to decide whether that measure represents a rate/force or a risk/probability. The analyst needs to keep the following in mind:

1. The two concepts (rate/force vs risk/probability) have different relationships to time. Rate represents a pressure to transit at one point in time, while risk represents actual transitions over a period of time. As a consequence, rate and risk treat person–time occurring after a transition but during the measurement interval differently.

2. How subjects enter the susceptible population affects how risks (probabilities) are measured. In a fixed cohort risks can be measured directly, but in dynamic cohorts in the community they must be derived from initial estimates of rate (force).

3. When measuring transitions, the duration of the measurement interval relative to the time it takes for transitions to occur is important. If the measurement interval is long compared with the speed of transition, it is generally better to estimate a risk (probability) directly. However, if the measurement interval is short compared with the speed of transition or measurements are taken from a community-based dynamic cohort, then estimation of rate first and transforming

the rate to a risk secondarily is usually more appropriate than direct estimation of risk.[7]

When a decision analyst is using parameter estimates from the literature for his or her model, we suggest the following:

1. Determine whether a mis-substitution of risk for rate (or vice versa) would make a difference to the outcome of the analysis. Generally, if the proportion transitting over the *total duration of the analysis* is less than 0.10, then the difference will be small and unlikely to make a major change in the outcome.[2,7] This rule of thumb, however, may vary by the specific application.

2. If an incorrectly estimated transition parameter would have a sizeable impact on the analytic outcome, attempt to determine from the primary studies whether the parameter was estimated using methods appropriate for measuring rate (force) or risk (probability) and modify the analytic model appropriately.

3. If review of the relevant papers fails to settle the issue, consider contacting the authors of the major studies for clarification. Alternatively, include an estimate assuming rate and one assuming risk in the sensitivity analysis.

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