A Simple Hedge for Longevity Risk and Reimbursement Risk Using Research-Backed Obligations

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Abstract

Longevity risk is the risk that the promised recipient of lifetime cashflows ends up living much longer than originally anticipated, thus causing a shortfall in funding. A related risk, reimbursement risk is the risk that providers of health insurance face when new and expensive drugs are introduced and the insurer must cover their costs. Longevity and reimbursement risks are particularly acute in domains in which scientific breakthroughs can increase the speed of new drug development. An emerging asset class, research-backed obligations or RBOs (cf., Fernandez et al., 2012), provides a natural mechanism for hedging these risks: RBO equity tranches gain value as new life-extending therapies are developed and do so in proportion to the number of successful therapies introduced. We use the stylized case of annuity underwriting to show how RBO equity could be used to hedge some forms longevity risk on a retirement portfolio. Using the same framework, we then show how RBO securities may be used to hedge a much broader class of reimbursement risks faced by health insurance firms. We demonstrate how to compute hedge ratios to neutralize specific exposures. Although our analytic results are stylized, our simulation results suggest substantial potential for this asset class to reduce financial uncertainty for those institutions exposed to either longevity or reimbursement risks. For example, our simulation results indicate that the correlation between the return on RBO equity and the reimbursement shortfall for a health insurer is about 0.66 under reasonable assumptions. Even under extremely conservative assumptions, this correlation is still 0.34, suggesting that RBO equity offers substantial hedging benefits, producing more favorable outcomes in about 87% of scenarios.

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1 Introduction

Recent advances in science and medicine have rapidly changed the prospects for those afflicted with a range of diseases – many of them life threatening. For example, five years ago, treatments for hepatitis C were able to cure only about 40% of all patients, while today the cure rate exceeds 90% (FDA, 2014). And for patients with certain (but not all) forms of breast cancer, the introduction of the drug Herceptin in a chemotherapy and endocrine therapy regimen appears to significantly increase both the survival rate and the longer-term prognosis, with over 97% of patients surviving five years later and over 80% showing no signs of recurrence eight years after treatment (O’Sullivan et al., 2015).

While society as a whole benefits from, and indeed rejoices in, the development of therapies that extend the lives of those afflicted with cancer and other diseases, in some financial contexts this exuberance is tempered by an analysis of the financial impact that extended life expectancy has on certain classes of financial obligations. One such context is that of a defined benefit pension fund that commits to provide a fixed monthly payment to pensioners from the time they retire until the ends of their lives. To the extent innovations in science and medicine materially extend the lifespans of these pensioners, the funds risk a mismatch between their assets and liabilities since the time period over which they need to provide cashflow increases.

To give a sense of the financial impact of even moderate increases in longevity, consider that in 2014, the New York Employees Retirement System payed pension benefits to 387,389 retired state employees (not including retired police and firefighters), with the average pension payment being $23,268.64 (New York State Office of the State Comptroller, 2015). Extending the time period over which the average retiree collects a pension by even a small number of years could result in material funding consequences.

At the same time health insurance firms are increasingly being called upon to reimburse patients for expensive new specialized treatments which are being developed at an accelerated rate. While again, the societal impact of treating these diseases is overwhelmingly positive, the financial impact of these new and often very expensive drugs can be material for firms that must provide patient reimbursement. This has become a growing concern for such firms: a recent industry report noted that “[T]he major contributors to rising...spend for specialty medications are brand inflation and the accelerating development of expensive, highly targeted therapies.” (Express Scripts Lab, 2015)

Clearly, both for institutions that must reimburse patients for new life-extending therapies as they are developed, and for those that must continue to pay retirement and other lifetime benefits to those individuals whose lifespans are extended though the advent of these new drugs, the uncertainty around the costs of these new scientific advances is of concern.

In this article, we discuss one approach to partially hedging these risks using a newly introduced class of security called a research-backed obligation (RBO), which involves the securitization of early stage biomedical research projects. While previous articles in this lit-
erature have focused on the supply side of the market for RBO securities, i.e., the viability of structuring such securities and their likely payoff-behavior, this is the first article to address the demand side of the market: the specific investor needs that such securities may be used to address and how investments in RBOs may be sized to meet these specific needs.

The structure of RBO securities provides a natural hedge (albeit only a partial one) in the form of a diversifying trade that gains value when new, life-extending drugs are developed. Through our analytic models, we attempt to make more rigorous the intuitive heuristic observation that this new asset class can be used to hedge this type of scientific longevity risk. We examine how RBO equity could be used as a longevity hedge by an underwriter of annuities, which represent a particularly simple class of lifespan-dependent liabilities and by health insurance firms.

However, we acknowledge that many of the drivers of longevity risk are not necessarily directly related to the development of specific drugs for specific diseases, but are rather the results of changes in general health measures (e.g., changes in diet, exercise, better access to health services, etc.). In recognition of this, we next extend our approach to accommodate hedges for reimbursement risk of the sort faced by health insurance firms that must repay patients for the cost of newly developed drugs. In contrast to the longevity case, these risks are quite directly tied to the introduction of new therapies. Our most widely applicable results are thus likely to be those relating to reimbursement risk.

While our analytic results provide intuition for the hedging mechanism, we stress the stylized nature of our current closed-form analytic forms. For this reason, we also conduct more realistic simulation experiments as well.

For example, our simulation results suggest that that the correlation between the return on RBO equity and the reimbursement shortfall for a health insurer is about 0.66 under reasonable assumptions. Even under extremely conservative assumptions, this correlation is still 0.34, implying that RBO equity offers substantial hedging benefit. In about 87% of all simulation paths, the reimbursement shortfall is reduced as a result of the hedge, even after accounting for the cost of the hedge construction.

It is important to note that we make use of a number of stylized assumptions in our modeling. Many of these may be made more realistic through reference to application-specific data sets; nonetheless, to enhance exposition and increase mathematical tractability we have chosen to keep the models simple here. However, because practical application of our results does require simulation (closed form solutions do not appear to exist for the portfolio dynamics), many of these extensions may be incorporated into future versions of the simulation framework as needed.

The organization of this paper is as follows: In Section 2 we discuss the mathematics of annuities and provide a stylized representation of an RBO portfolio. Section 3 uses these constructs to derive hedge ratios based on the characteristics of an annuity underwriter’s portfolio. Section 4 extends this approach to reimbursement risk. Section 5 uses a more
realistic simulation model of an RBO portfolio and cashflows to provide a sense of how a reimbursement hedges might be estimated in practice as well as discussing our results. That section also presents a number of important limitations in our current model and suggests avenues for future work. Section 6 concludes.

2 Annuities, Longevity Risk and Research Backed Obligations

While our main results relate to reimbursement risk, it is instructive to begin with the case of longevity risk since much of the machinery required for analyzing reimbursement risk derives from our results on longevity risk. In addition, in realistic cases in which an annuity underwriter is concerned about hedging out the longevity-related impact of new, potentially wide-reaching drug developments (e.g., the advent of new therapies for certain cancers or for Type 2 diabetes) our longevity analysis provides a practical mechanism for mitigating this risk.

We begin by reviewing the notation and mathematical formulations we will use. In this section we also outline the key results from previous work on RBO structures. We focus on the analysis of annuities, because of their natural relationship to longevity-related obligations.\footnote{Annuities are a popular retirement-planning financial product. In 2013 in the U.S., according to one estimate, just under $230 billion of new annuities were purchased bringing the total outstanding deferred annuity assets to just over $2 trillion (Insurance Information Institute, 2014).} We note however, that defined benefit pension plans effectively underwrite functionally equivalent contracts in the form of promises to pay fixed pension benefits.

2.1 Annuities and the impact of life-extending therapies on annuity cost

It is well known that an annuity that pays a fixed periodic cashflow, $C$, over $T$ periods may be valued as:

$$A(C, r, T) \equiv A = \frac{C}{r} \left(1 - \frac{1}{(1 + r)^T}\right),$$

where

- $C =$ the one period constant cashflow;
- $r =$ the discount rate; and
- $T =$ the number of periods over which the $C$ will be paid.

It will be convenient to distinguish between different values of $T$, the maturity of an annuity of interest. Define the following quantities:
\[ \Delta_j \equiv \text{years lost from a diseased individual’s lifespan due to disease } j; \]
\[ D_j \equiv \text{set of individuals with disease } j; \text{ and} \]
\[ \Pr(i \in D_j) \equiv \text{the probability that individual } i \text{ has disease } j. \]

For convenience we assume that all diseases have the same \( \Delta_j \). Then, depending on the context, we can define the remaining lifespan (r.l.) for an individual in any of the following ways:

\[ T_i \equiv \text{the specific r.l. of individual } i; \]
\[ T_h \equiv \text{the r.l. of a healthy individual}; \]
\[ T_d \equiv \text{the r.l. of a diseased individual} \]
\[ = T_h - \Delta_j; \text{ and} \]
\[ T_u = \Pr(i \in D_j) T_d + (1 - \Pr(i \in D_j)) T_h; \]
\[ \equiv \text{the unconditional r.l. of an individual of unknown disease status}. \]

where \( \Pr(i \in D_j) \) is the probability that individual \( i \) has disease \( j \).\(^2\)

If a therapy for disease \( j \) is discovered at time \( \tau_j < T_d \), and this therapy extends life by \( \Delta_j \) periods for a diseased individual, then, we can derive an exact form of the change in the value of the annuity, which turns out to be particularly compact due to the structure of Eq (1).

Specifically, for an individual with lifespan \( T_i \) and an intervention that extends life by \( \Delta \) years,

\[
\Delta A_i = A(C, r, T_i + \Delta) - A(C, r, T_i)
= \frac{C}{r} \left( 1 - \frac{1}{(1 + r)^{T_i + \Delta}} \right) - \frac{C}{r} \left( 1 - \frac{1}{(1 + r)^{T_i}} \right)
= \frac{C}{r} \left( \frac{(1 + r)^{\Delta} - 1}{(1 + r)^{T_i + \Delta}} \right).
\]

\(^2\)Note that for convenience, and without loss of generality, we assume that this reflects the probability that an individual has the disease and would respond to a new drug in development.
If an annuity is written to individual $i$ who has disease $j$ and who has a lifespan of $T_i = T_d$, but a new therapy is introduced that will extend life for this individual by $\Delta j$ years, the expected change in cost to the underwriter is (2), evaluated at $T_i = T_d$ and $\Delta = \Delta j$:

$$\Delta A_d = \frac{C}{r} \left( \frac{(1 + r)^{\Delta_j} - 1}{(1 + r)^{T_d + \Delta_j}} \right)$$

Note that we have introduced the notation $A_d$ to denote the value of an annuity written to a diseased individual. We will correspondingly denote by $A_h$ and $A_u$ the values of annuities written to healthy individuals and individuals of unknown disease status, respectively.

The more natural case is one in which we do not know $i$’s disease status so that $E[T_i] = T_u$. If a therapy for an arbitrary disease $j^*$ is discovered at a future time, the expected change in $T_i$ as a result of the new drug discovery is given as

$$E[\Delta] = \Pr(\tau_{j^*} < T_d) \Pr(i \in D_{j^*}) \Delta_{j^*}$$

In words, the expected change in $T_i$ is the expected change in lifespan for treating the the disease, multiplied by the probability that individual $i$ has the disease, multiplied in turn by the probability that the new drug is introduced during the lifespan of the diseased individual:\footnote{Note that for simplicity here, we ignore other sources of uncertainty in the fundamental quantities: uncertainty about the realized value of $\Delta_{j^*}$, the change in the specific individual’s lifespan, $T_i$, due to the advent of the therapy; and uncertainty associated with estimates, $T_i$, of the lifespans of diseased and healthy individuals themselves, respectively. We later incorporate the first of these additional sources of uncertainty in our simulations of Section 5.}

$$E[\Delta A_u] = p_{\tau_j} p_{D_j} \Delta A_d + (1 - p_{\tau_j} p_{D_j}) \Delta A_h$$

$$= p_{\tau_j} p_{D_j} \frac{C}{r} \left( \frac{(1 + r)^{\Delta_j} - 1}{(1 + r)^{T_d + \Delta_j}} \right).$$

where $p_{\tau_j} = \Pr(\tau_{j^*} < T_d)$ and $p_{D_j} = \Pr(i \in D_{j^*})$.

Equation 4 gives the expected change in annuity value for an annuity holder $i$ of unknown disease status subject to the introduction of a new therapy for disease $j^*$. For completeness, note that the expected cost of the annuity to the annuity writer is given as:
\[ E[A_u] = p_T p_{D_j} A_d + (1 - p_T p_{D_j}) A_h. \] (5)

While an underwriter can adjust the price of an annuity based on actuarial tables that account for the historically small, but non-zero, probabilities of new therapies that extend the lives of their clients, a larger concern is the possibility that many new therapies become viable at the same time – either by chance, or due to a change in the scientific process or knowledge-base.

For example, if \( T_h \) is the average lifespan of a healthy individual, known to have no diseases, and \( T_j \) is the average lifespan of an individual known to have disease \( j \), then (ignoring individuals with multiple diseases and mangling slightly the notation) a first-order estimate of \( T_i = T_u \) for an individual of unknown disease status (assuming \( T_j < T_u \), i.e., that disease shortens lifespan) is

\[ T_u = T_h - \sum_j (1 - \Pr(\tau_j < T_i)) \Pr(i \in D_j) \Delta_j. \] (6)

The risk to an underwriter, which we call scientific longevity risk or longevity risk for short, is that \( \Pr(\tau_j < T_d) \), the rate of development of new therapies, turns out to be very high, relative to historical levels. Said differently, as the probability of new drugs being developed increases, individuals are more likely to enjoy the lifespan of a healthy individual \( (T_h) \) rather than suffering from the shortened lifespan of a diseased one \( (T_d) \). For large portfolios, even modest shifts in lifespan can have material financial consequences, while more substantial shifts can be catastrophic financially.

To fix ideas, we present a stylized example in the Appendix that use the above representations to calculate the impact of new therapeutic innovations on the value of an annuity and on portfolios of annuities.

For completeness, we now formalize the expected change in the value of the portfolio of annuities, \( E \left[ \frac{\partial P_A}{\partial k} \right] \), for a single new drug approval. If we denote the number of drugs approved for the life of the cohort as \( k \), and, for convenience, assume that for all diseases, \( j \), \( \Pr(i \in D_j) = p_D \) and \( \Delta_j = \Delta_D \), i.e., both quantities are constant across diseases, then for a portfolio of \( N \) annuities:
\[
\frac{\partial A_d}{\partial k} = \frac{C}{r} \left( \frac{(1+r)^{\Delta_D} - 1}{(1+r)^{T_d+\Delta_D}} \right).
\]
\[
\frac{\partial A_h}{\partial k} = 0.
\]
\[
E \left[ \frac{\partial A_p}{\partial k} \right] = \sum_{i=1}^{N} \left[ p_D \frac{\partial A_d}{\partial k} + (1-p_D) \frac{\partial A_h}{\partial k} \right]
= (p_D \times N) \times \frac{C}{r} \left( \frac{(1+r)^{\Delta_D} - 1}{(1+r)^{T_d+\Delta_d}} \right).
\]

Equation (7) provides an intuitive representation of the impact of a new drug on the portfolio of annuities. The expected change in the value of the portfolio of annuities is proportional to the expected number of diseased individuals in the portfolio whose lives are extended as a result of the new therapy.\(^4\)

2.2 Payoffs for portfolios of translational therapies

The motivation for the introduction of research-backed obligations (RBOs) was originally to address funding shortages in the early stages of drug research. However, these securities also offer natural longevity payoffs (as opposed to synthetic payoffs, such as those related to mortality indices) that can offset the increases in liabilities due to life-extending innovations in medicine.\(^5\)

An RBO seeks to pool ownership in many individually risky, but largely uncorrelated, drug development projects and thereby reduce the overall risk of the portfolio (cf., Fernandez et al., 2012). Early papers in this literature showed that portfolios containing early stage cancer therapy candidates could be structured in such a way as to support debt issuance and yield returns consistent with those targeted by large institutional investors. Subsequent extensions of this approach (Fagnan et al., 2014) considered its application to candidate therapies for orphan diseases. Orphan diseases enjoy more favorable regulatory treatment and thus shorter approval times; they are also, in many cases, monogenic diseases making targeting more precise and thus more likely to succeed. The authors showed that such portfolios could be much smaller than those for originally described for cancer therapies (by virtue of the much higher success probabilities of candidate therapies for genetic diseases), and that their profit profiles were correspondingly more favorable.

\(^4\)See footnote 3 for caveats.

\(^5\)Certain classes of life insurance policies may also be structured to provide natural hedges (cf., Milevsky and Promislow, 2001) under specific conditions. In these cases, such firms may seek to hedge the residual longevity risk on their portfolios.
As the RBO market begins to develop for institutional investors, it may present a unique opportunity for firms facing longevity risk. Since the equity tranches of RBO transactions gain value as more therapies are developed, they provide a natural hedge against certain classes of longevity risk, specifically those associated with the introduction of life-extending therapies. RBOs are unique in this regard: their portfolios provide a natural hedge for longevity risk, in contrast to, e.g., longevity swaps which are based on actuarial indices rather than real assets.

In this section we consider a simple analytic model for the returns on a portfolio of translational drug projects. (In a later section of the paper, we detail simulation experiments designed to capture a number of realistic aspects of the drug-development process including path-dependence, heterogeneous valuations of the compounds and the multi-period nature of the drug trial process which requires additional interim payments to fund later stage trials).

To build intuition, the model described in this section reflects a stylized, but informative, view of the portfolio behavior of a basket of drug development projects. We base our model on the motivational model introduced in Fernandez et al. (2012), which similarly used it to develop intuition, before switching to simulation for the main results of that paper.

Assume that a successful therapy has a total NPV of $V$. If there are $k$ successful therapies in the portfolio, then the total value of the portfolio, $V_P$, is given simply as

$$V_P = kV.$$

The change in the portfolio value for an additional successful drug is just

$$\frac{dV_P}{dk} = V. \tag{8}$$

Assume further that any candidate drug in the portfolio has a success probability of $p_S$ and a failure probability of $1 - p_S$, and that the number of successes across the portfolio, $k$, follows a binomial distribution:

$$p(k < k^*) = \sum_{j=0}^{k^*-1} \binom{n}{j} p_S^j (1 - p_S)^{n-j}. \tag{9}$$

Then the mean value of the portfolio is simply

$$E[V_P] = n \times p_S \times V, \tag{10}$$

and an investor wishing to receive $V_I \leq E[V_P]$ in expectation, could simply purchase a $\frac{V_I}{V_P}$ share of the portfolio, assuming that the payoffs on success of the drug trial process were uncorrelated with systematic market factors, and assuming the fund could be made arbitrarily large (to reduce the idiosyncratic risk of the individual projects).
In the absence of correlation and path dependence (we introduce these real-world features in our simulations), the probability of the portfolio generating $F$ or more cashflow ($F \leq nV$) is simply 1 minus the probability in (9) with $k^* = \lceil \frac{F}{V} \rceil$, where $\lceil x \rceil$, indicates the largest integer greater or equal to $x$. The quantity $\lceil \frac{F}{V} \rceil$ is the minimum number of projects that must succeed in order to be confident at a $1 - p (k < \lceil \frac{F}{V} \rceil)$ probability level that there will be at least $F$ of cashflow generated.

This observation forms the basis of debt issuance by the fund: to the extent the fund wishes to use leverage, debt issued with a face value of $F$ will have a probability of default of $PD = p (k < \lceil \frac{F}{V} \rceil)$. Such debt would need to offer at least a market rate of interest but also serves to make riskier, though more profitable the equity investment, which would presumably offer a better expected return than the debt.

Thus, the optimization of the capital structure of the fund becomes a decision problem analogous to that of determining the optimal capital structure of a firm (or any structured financing), which is familiar to students of financial economics. A more detailed discussion of this stylized model, and the impact of leverage on the risk and return of equity can be found in Fernandez et al. (2012). We do not elaborate further on this feature of RBOs as our focus is on use of the equity tranche for hedging, to which we turn in the next section.

3 Hedging some forms of longevity risk

Longevity risk can be seen as a systematic exposure for financial institutions that underwrite lifetime-payment contracts such as pensions or annuities (cf., Aro, 2014). A primary source of longevity risk has been largely statistical: existing models for longevity forecasts (cf., Lee and Carter, 1992) have tended to consistently underestimate future lifespans. (cf., IMF, 2012, Ch. 4). By one estimate, for example, the impact of a one-year shock to longevity would result in a corresponding increase in US pension liabilities of 2-3% or approximately $84 billion (Kisser et al., 2012).

However, another source of longevity risk is due to the increases in health due to a variety of sources such as better diet and nutrition, increased exercise, early detection of some treatable conditions, and so forth. In general, these factors are more difficult to hedge. Indeed, in recognition of the financial impact of longevity risk, and, in order to seek capital relief under some regulatory regimes (e.g., Solvency II), some firms have recently begun structuring insurance contracts to protect against longevity-related increases in liabilities. For example, in a transaction from this emerging sector, BT Group launched its own insurance firm and, in collaboration with Prudential, created longevity insurance for about £16 billion of its approximately £47 billion in pension liabilities (Aglionby and Cumbo, 2014). As another example, Prudential underwrote a $33 billion annuity to GM to effectively buy-out the pension obligations of the firm for 118,000 of GM’s workers (Olsen, 2012).

For a more detailed discussion of the structure of various longevity hedging instruments, see BIS (2013).
Importantly, a subset of health improvement-related increases in lifespan may be tied to new medical advances that extend life through the introduction of new drugs for previously untreated diseases, or of better drugs for disease for which current treatments are less effective.

Although this is a relatively smaller component of longevity risk on average, it is perhaps one of the more substantive sources of extreme changes in longevity. Thus, it represents a form of longevity tail risk, as even modest changes to, for example, cancer mortality rates can have material impacts on the lifespans of the older individuals most likely to be the focus of longevity risk. It has been historically difficult to hedge this form of medical longevity risk of this sort. However, the introduction of RBOs as an asset class, provide new opportunities for hedging longevity risk related to new scientific breakthroughs.

3.1 RBO equity as a natural hedge for scientific longevity risk

Assume an annuity writer maintains a portfolio in which a certain percentage annuity-holders are likely to die of a specific set of diseases and that a therapies for those diseases are being developed within an RBO portfolio.

In principle, an annuity underwriter would desire to purchase an amount of RBO equity, $E_{RBO}$, such that the additional cost of longer lifespans on the part of annuity holders, $E[\Delta A_i]$ is offset by the expected rise in the value of the RBO equity investment. Said differently, when the success rate on the portfolio is higher than the expected (mean) rate, the annuity writer would like the portion of the profit from those successes to offset the costs that the therapies engender in the annuity portfolio (due to lengthened lifespans).

Thus, if $E[V_P] = \sum_{c=1}^{n} p_c V$ is the expected payout for the portfolio, then $\Delta V_P = V_P - E[V_P]$ is the unexpected loss or gain on the RBO portfolio. The underwriter would like to maintain a hedge such that

$$H^* \times \Delta V_P = \Delta A_P,$$

so

$$H^* = \frac{\Delta A_P}{\Delta V_P}.$$ (12)

$H^*$ is simply the hedge ratio for the annuity portfolio against the RBO equity. Of course, ex ante the values of $\Delta A_P$ and $\Delta V_P$ are not known. However, we have already estimated the change in $A_P$ and $V_P$ with respect to successful drug approvals; these are (7) and (8). It is sufficient for these changes to be hedged. We thus have

$$H = \frac{\partial A_P}{\partial k} \frac{dV_P}{dk}.$$ or

12
\[ H = \frac{(p_D \times N) \times \frac{C}{r} \left( \frac{(1+r)^{\Delta D} - 1}{(1+r)^{\Delta D}} \right)}{V}. \]  

(13)

Thus, an underwriter seeking to hedge longevity risk due to the introduction of new therapies would purchase \(SH\) of equity in an RBO tranche for every dollar of the annuity portfolio assuming an annuity portfolio of size \(N\) and annuity value \(A_u\):

\[ E_{RBO} = N \times A_u \times \frac{(p_D \times N) \times \frac{C}{r} \left( \frac{(1+r)^{\Delta D} - 1}{(1+r)^{\Delta D} + \Delta D} \right)}{V}. \]  

(14)

**Example 1. Using RBO equity to hedge longevity risk in a cohort of underwritten annuities**

Consider the highly stylized example of an insurance firm that sells annuities to a cohort of 100,000 40 year old individuals with each annuity paying $10,000 per year for the remainder of the client’s life. We assume that healthy individuals live to age 85 and that a diseased individual’s life-span, \(T_d\), is 60 years, but that the advent of a therapy for the disease would extend life by \(\Delta_d = 25\) years. As before, we assume that the interest rate \(r\) is 5%.

We also assume a total of 100 diseases of interest and that \(\Pr(i \in D_j) = \frac{1}{100}, j = 1 \ldots 100\) so that there are, on average, 1000 individuals with various diseases in the cohort; and that diseases are uniformly distributed across the diseased sub-population, so that on average, 10 individuals will have each disease.

We assume that an RBO is available, supported by a portfolio of 40 candidate drugs each of which has a 5% probability of success. Successful drugs are sold out of the portfolio for a value of \(V = \$250\) million, so the expected value of the portfolio is \$500 million. If the target total return on the fund were 25%, and the fund issued no debt, this would imply (ignoring discounting) \$400 million of equity available on at the launch.\(^7\)

If the underwriter wished to hedge the longevity risk of the annuities, the implied hedge ratio is

\(^7\)For purposes of this simple example, we assume that the fund can acquire a portfolio of compounds and pay for required clinical trials as well as expenses out of this initial investment. In the simulations we present elsewhere, we accommodate much more detailed and realistic assumptions, as well as debt issuance by the RBO.
\[ K = 400,000,000 \equiv \text{Initial drug portfolio capital} \]

\[ H = \frac{(p_D \times N) \times \frac{C}{\gamma} \left( \frac{(1+r)_{T_d} - 1}{(1+r)^{T_d} + \Delta_d} \right)}{V}, \]

\[ = \frac{0.0001 \times 100,000 \times \frac{10,000}{1.05} \left( \frac{(1.05)^{25} - 1}{(1.05)^{20} + 25} \right)}{250,000,000} \]

\[ \approx 0.002124744 \]

\[ E_{RBO} = K \times H \]

\[ \approx 400,000,000 \times 0.002124744 \]

\[ = 849,898. \]

It is useful to observe that the underwriter may not wish to pay for a hedge on the introduction of new drugs that it has already accommodated in its actuarial price assumptions. Said differently, if the underwriter had already priced in the cost of the mathematical expectation of 5 therapies, it would prefer to hedge only the new drug introductions in excess of 5. Using straight equity there is no natural mechanism for doing this. However, the financial engineering techniques that characterize the fuller RBO model (tranching, cashflow triggers, etc.) make such hedges feasible, at least approximately.

There are a number of reasons to believe that a hedge of the sort described in the previous example would be imperfect due to the mathematical properties of the hedge ratio and its components on the one hand, and to the structure of the drug development and discovery market on the other. This latter effect may be exacerbated by realistic limitations on the size of an RBO portfolio.

While a more detailed analysis would account for the mathematical nuances (see Section 5.2 and the Appendix for more details), the structural ones may make perfect hedging practically impossible at this time. This does not mean that practically useful hedges cannot be constructed using RBO equity, but rather that they may remain imperfect for the near term. We discuss these potential limitations, as well as some potential remedies, in Section 5.2.
4 Extending the framework to hedge reimbursement risk for health insurers

In this section, we extend the framework described in Section 3 to consider hedge construction for reimbursement risk. Such hedges would be attractive to those institutions facing uncertain future payouts due to new drug discoveries. Unlike in the case of longevity risk on an annuity portfolio, one of the biggest drivers of reimbursement risk is the introduction of new and expensive therapies for diseased individuals in the insurer’s portfolio. Furthermore, assuming a fixed prevalence rate for a given set of diseases, the financial impact of these new drugs is closely tied to the number of new drugs introduced and their costs, both of which are proxied for by the RBO portfolio.

4.1 Reimbursement risk

Reimbursement risk is a growing problem for providers of health benefits such as health insurance firms and reinsurance companies (cf., Fernandes, 2015). Although insurance providers can accommodate modest shifts in cost structure through annual changes in member premiums, a more pressing concern is the potential for very large changes in expense base associated with, for example, the introduction of many specialty drugs in a short period of time.

Consider the following recent developments:

• 2012 four drugs were approved with annual per-patient costs of over $200,000 (Harper, 2013).

• A study of 47 oral oncologics, found that the patient spend on this subsegment increased by 37% between 2006 and 2011 (Conti et al., 2014).

• Specialty medications represented 32% of all 2014 drug spend while representing just 1% of all U.S. prescriptions (Express Scripts Lab, 2015).

Against this backdrop, the pace of new specialty drug development appears also to be increasing. In a recent survey, PhARMA, an industry association of biotech and biopharmaceutical research firms, reported that over 70% of the drugs in the current development pipeline are so-called “first-in-class” medications – those that use different mechanisms than any currently approved drugs (PhARMA, 2015). This suggests those first-in-class drugs that are ultimately approved drugs will enjoy little or no initial competition should they reach approval and are thus likely to be priced aggressively.\(^8\)

\(^8\)There has also been an increased focus on so-called “orphan diseases” – those that affect fewer than 200,000 Americans. (Similar designations have also been instituted in other jurisdictions in Europe and Asia.) Many of these diseases are genetic in nature and research on their therapies may be expected to benefit from recent advances in genetic sequencing. For example, although it has taken 25 years to sequence about half of all genetic diseases, a recent article (Boycott et al., 2013) estimates that genetic sequencing
As the drug development landscape shifts, such shocks are also becoming increasingly likely. For example, in 2014, the U.S. Food and Drug Administration approved the hepatitis C drug Harvoni® (ledipasvir/sofosbuvir). Despite its affecting about 3,000,000 patients, the high pricing of the drug for patients has been more similar to orphan disease therapies than to drugs targeting broader populations. (Traditionally, orphan status implies conditions affecting fewer than 200,000 patients.) The drug is priced at over $1,000 per tablet implying a monthly cost of over $30,000 (Express Scripts Lab, 2015).

Such sudden increases in costs are not easily transferred to members through increases in premiums; accommodating such drastic reimbursement cost shifts would require unacceptable year-to-year premium inflation. Thus, the goal of many reimbursement paying agents is not to eliminate entirely the costs associated with new drug introduction, but rather to smooth out large spikes in costs, such that the residual of these costs may be incorporated into changes in premium levels in an orderly fashion.

New drugs are often quite expensive due in part to the high cost of development and due to regulatory and legal periods of patent-protection and (sometimes) exclusivity, during which it is difficult or nearly impossible for competing drugs that target the same mechanism to enter the market. This is particularly so in the case of specialty drugs for genetic diseases, which often enjoy extended periods of exclusivity.

4.2 Modeling reimbursement risk

We approach this problem by noting that the risk faced by the reimbursement agent is that they will be required to reimburse patient sub-populations for the treatment costs associated with one or more newly discovered therapies.

Assume that the cost to the health benefit provider of a single therapy is $C_E$ per year while the drug enjoys exclusivity, and $C_O$ once the the drug is “off-exclusivity.” Thus, if the drug enjoys exclusivity for $Y_E$ years, and the patient will be reimbursed for $T$ years, then if new drug is approved today, the total cost is:

$$C = \sum_{t=1}^{Y_E} NPV(C_E, t) + \sum_{t=Y_E+1}^{T} NPV(C_O, t).$$

We may value these cashflows as two annuities. Note first that the present value of an annuity maturing at time $T$, which begins payments at time $\tau > 1$ may be seen as the value of an annuity that begins making payments at time 1 and maturing at time $T$ less

---

for the remaining 50% will be completed by 2020, or in just six years from this writing. These authors assert that the rapid increase in the pace of genetic mapping is the result of dramatic improvements in DNA-sequencing technologies. The impact for patients with these diseases is likely to be faster development of more targeted and effective treatments for the over 7,000 orphan diseases which affect about 1 in 10 individuals (cf., PhARMA, 2013).
the value of a second annuity that begins making payments at time 1, but with maturity \( \tau - 1 \).

It can be shown that the present value of this pair of annuities is:

\[
A(C, r, \tau, T) \equiv A = \frac{C (1 + r)^T - (1 + r)^{\tau-1}}{(1 + r)^{T+\tau-1}}.
\] (15)

Then, assuming the therapy will be required for the duration of the insured term of the patient, the total per-patient reimbursement cost to the agent for a drug approved at time \( t_a \) with \( Y_E \) years of exclusivity is:

\[
A_r = A(C_E, r, t_a, T_E) + A(C_O, r, T_E + 1, T)
\]

\[
= \frac{C_E (1 + r)^{T_E} - (1 + r)^{t_a-1}}{(1 + r)^{T_E+t_a-1}} + \frac{C_O (1 + r)^T - (1 + r)^{T_E}}{(1 + r)^{T+T_E}}
\] (16)

where

\[C_E \equiv \text{the cost of the drug during exclusivity},\]

\[C_O \equiv \text{the cost of the drug after the expiration of exclusivity},\]

\[t_a \equiv \text{the time at which the new drug is approved},\]

\[Y_E \equiv \text{the number of years of exclusivity for the drug},\]

\[T_E \equiv \text{the time of the expiration of exclusivity},\]

\[= t_a + Y_E - 1 \text{ and},\]

\[T \equiv \text{the expiration of the reimbursement obligation}.\]

**Example 2. The expected cost to a health insurer of the discovery of a therapy for a single juvenile disease**

Consider the case of a health insurance firm that insures a family with a newborn infant. Assume that the infant is diagnosed with a rare and terminal condition which, if untreated, would likely be fatal by age 5. However, the year after the baby is born, a new specialty drug for this condition is approved with an exclusivity period of seven years. During this period, the per-patient annual cost of the drug is $150,000. Once the exclusivity ends, the cost of the drug will drop to $20,000 per year. (Consider this pricing to represent a blend of pricing for biologics and small molecules.) Assume also that the child’s insurance will expire on the child’s 18th birthday. For simplicity, we ignore deductibles, copayments, etc. Then we have:

\[C_E = \$150,000,\]

\[C_O = \$20,000,\]

\[t_a = 2,\]

\[Y_E = 7,\]

\[T_O = 8 \text{ and}\]

\[T = 18.\]
If the interest rate $r$ is 5%, then by (17) the cost of this new drug for each child in the insurers portfolio diagnosed with this disease is:

$$A_r = \frac{150,000 (1.05)^8 - (1.05)^1}{0.05} + \frac{20,000 (1.05)^{18} - (1 + 0.05)^8}{0.05} (1.05)^{26}$$

$$= \$931,153.$$

More realistically, if the insurance firm calculated the cost of the reimbursement on the day the drug were approved ($t_a = 1$), then the cost per patient with the disease would be:

$$A_r = \$986,020$$ per patient.

If there were 20 million insured individuals in a firm’s portfolio of which 6% were below the age of 5, there would be 1.2 million children under the age of 5 in the portfolio. If the incidence rate of the disease were $\frac{1}{10,000}$, there would be an expected 120 children diagnosed with the disease and the present value of the total cost to the insurer would be:

$$A_P = 986,020 \times 120$$

$$= \$118,322,434$$ total reimbursement cost.

For comparison, in 2014, according to Aetna’s Inc.’s Annual Report, the firm provided coverage to about 23.5 million medical members and realized a net income of approximately $2.2 billion (Aetna, 2015). For such a firm, the cost of the increased reimbursement expense for the single drug in this stylized example would represent over 5% of the firm’s annual net income.

RBO equity can provide a useful, and more direct, hedge for such drug reimbursement risk than for longevity risk. For practical applications, simulation may be used to estimate hedge ratios for reimbursement risk, and we describe this approach in the next section. To anticipate the results from that discussion, we note that the degree to which an effective hedge can be realized depends to some extent on the prevalence of the disease, the amount of RBO equity available and the amount of leverage on the portfolio.

5 Simulations

While the results of Sections 3 - 4 are illustrative, in practice they cannot be applied directly to determine hedge ratios using real RBO equity. This is because, in practice, neither portfolios of annuities-like instruments nor portfolios of early-stage research compounds behave deterministically. For example, the lifespans of diseased and healthy individuals are stochastic, as are the cost to reimburse patients for new drugs; and the valuations, costs and trial durations of compounds in the RBO portfolio also exhibit stochastic behavior. This latter observation is complicated further by the fact that compounds sold out of the portfolio are typically sold using a structured payment agreement in which portions of the payment to
the seller are withheld pending subsequent success in achieving milestones. Because of this complexity, it is practical to estimate hedge ratios through simulation.

To demonstrate this approach to hedge ratio estimation, we have chosen to focus on hedging strategies for reimbursement risk. We do so because the nature of longevity-exposed annuity portfolios is more complex from an actuarial perspective and would thus require both more numerous and more involved assumptions. Extension of the simulation framework outlined below for use in calculating hedge ratios for longevity-exposed portfolios is straightforward conceptually, if also significantly more involved from an actuarial perspective.

Our simulation considers a portfolio of orphan diseases, as described in Fagnan et al. (2014), although we have updated the simulation parameter assumptions and our performance metrics to reflect both newer research on genetic disease clinical success rates (cf., Hay et al., 2014) and discussions with scientific and industry experts. We have also extended the simulation structure to accommodate a more realistic representation of the drug development process. Genetic diseases are relevant to the reimbursement risk question as they often affect very young children and the drugs that treat them are often very costly.

5.1 Simulation design

We calculate hedge ratios numerically through simulation. To do this, in addition to simulating the evolution of the RBO as in previous work (cf., Fagnan et al., 2014), we must also simulate the co-evolution of a moderately sized portfolio of healthcare benefits recipients. We then use the simulated behavior of both portfolios to calculate the appropriate hedge ratio for each simulation path and use the distribution of these hedge ratios to select an appropriate hedge ratio for the portfolio.

For each path of the simulation we proceed as follows:

1. At the beginning of each path, we simulate the healthcare portfolio using the parameter values described in Table 2.

   (a) We first determine, for each individual in the portfolio, whether the individual is diseased or healthy. This is done probabilistically based on \( p_D \) (the probability of a single disease affecting a single individual). For purposes of this example, we assume that all diseases have the same prevalence rate. Thus, the probability of an individual having any disease for which candidate therapies are included in the portfolio is

   \[
   p_{D^*} = 1 - (1 - p_D)^n,
   \]

   where, \( n \) is the number of therapies in the portfolio.\(^9\)

\(^9\)We assume here that the diseases targeted by the portfolio are monogenic and that each candidate drug targets a different disease.
(b) We then simulate the current age of each insured individual in the portfolio, assuming ages are distributed uniformly in $[0, 5]$. As in our example, we assume that an insured child is insured through the age of 18. (In this example, we focus on an RBO portfolio targeting juvenile diseases, so we assume that the sub-portfolio we are considering represents only the subset of the healthcare portfolio containing members under the age of five.)

2. We next simulate the RBO portfolio to determine the terminal value of the equity. In this simulation we are assuming that drugs are sold out of the portfolio in Phase II. However, unlike in previous work, we also follow all drugs sold out of the RBO portfolio to determine which, if any, are ultimately approved (this may take place a number of years after the RBO winds down). A description of the features of the RBO transaction we simulate for this experiment is given in Table 1.

3. For each approved drug, $j$, we simulate the per-patient cost of the drug:

(a) We assume that the per-patient cost during the exclusivity period, $C_{E}^{j}$, is distributed lognormally,\textsuperscript{10} with the post-exclusivity cost being equal to $C_{O}^{j} \times 0.1$. Values for drug costs are shown in Table 2.

(b) Because it is likely (in the case of genetic diseases) that candidate drugs that sell for high valuations out of the RBO portfolio will also fetch high per-patient costs if approved, we impose correlation between these quantities. In the simulations below, we calibrate such that the correlation between a drug’s portfolio exit price, and its subsequent per-patient reimbursement cost (should it be approved) is 0.6.

4. To determine the impact on the insurance portfolio of the successful drugs in the RBO drug portfolio, we calculate the portfolio unexpected reimbursement-linked funding shortfall, $S_{f}$, for each path:

(a) We first determine which of the diseased individuals in the portfolio will benefit from each new therapy based on the probability of a given therapy for each patient’s disease having been the one developed.

(b) For each diseased individual, $i$, that will receive the therapy, we create a pair of annuities as described in Equation (17) for the cost of the drug during the term of the insurance.

(c) Once all such annuities have been valued, we calculate the cost to the portfolio, as the sum of all such per-patient reimbursement costs.

To calculate the optimal hedge for this path, we first collect $S_{f}$, the reimbursement-linked funding shortfall resulting from the new therapies from Step (4), as well as $R_{c}$, the total cash

\textsuperscript{10}We assume that $C_{E}^{j} \sim \text{LogNormal}(\mu = 3.583, \sigma = 0.8)$. 

20
return for the RBO portfolio due to sales of the compounds from Step (2). The optimal hedge for a given path (with perfect foresight) is then given as:\textsuperscript{11}

\[ H_o = \frac{S_f}{R_c}. \]

\( H_o \) is given in terms of the fraction of the initial RBO equity offering that should be purchased to hedge the reimbursement shortfall along the path. We convert this into a per-member dollar value of equity to be purchased.\textsuperscript{12} By examining the distribution of per-member hedge values, we may determine the trade-offs in selecting more or less conservative hedging strategies.

Our simulations are CPU intensive, even with the use of multi-threaded algorithms. In order to reduce the number of simulations required and the size of our simulated portfolio, we select a somewhat higher than average prevalence rate. While this serves to inflate our results, we also note that the portfolio size we simulate is on the order of less than 1\% of that of a large insurance firm.

5.2 Simulation results and discussion

Table 3 presents summary statistics for the simulation results. We also provide additional details of the simulation graphically in Figure 1.

The table shows the shortfall to the reimbursement agent (\( S_f \)) given various hedging strategies using RBO equity. In the lower portion of the table, we present an analysis of the behavior of hedges calculated by using the median, 75\textsuperscript{th} and 95\textsuperscript{th} percentiles of \( H_o \). For reference, we also present the results on the unhedged portfolio.

We first calculate how much the hedge would cost the provider. We show this on a per-insured cost basis (see the discussion in Section 5.5). We assume that RBO equity is bought “at par,” i.e., that one dollar of equity may be purchased for $1. The remainder of the table shows the performance of the hedges both in absolute terms and, below this, in terms of the percentage of realizations for which the hedger is better off having used the hedge (\textit{after} including the cost of the hedge). Note that the Risk Reduction section shows

\textsuperscript{11}Note that for convenience, we use the total cash return on the portfolio as a proxy for the total value of the cashflows received by equity investors. This does not account for the timing of cashflows either with respect to their discounted value, or with respect to the receipt of the cashflows relative to the incurrance of the increase in the reimbursement costs. In general, investors will recieve RBO cashflows before drugs are approved, so the potential for a mismatch in timing is minimized. Furthermore, because they are received earlier, the NPV of these cashflows should generally be higher than the NPV of the increase in costs, which occurs at the end of the annuity life. However, more sophisticated analyses could incorporate the timing of cashflows on both portfolios to more precisely estimate hedge ratios.

\textsuperscript{12}Alternatively, we could restate \( H_o \) in terms of a percentage of, e.g., the first year’s premium paid by a new member, but this would require more involved assumptions.
### Table 1: Structure of RBO transaction simulated in example

<table>
<thead>
<tr>
<th>Portfolio</th>
<th>25-26 preclinical genetic disease candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target composition</td>
<td>(Mean acquired in baseline simulation 25.97)</td>
</tr>
<tr>
<td>Acquisition schedule</td>
<td>5 projects every 6 months</td>
</tr>
<tr>
<td>Start of portfolio liquidation</td>
<td>Month 90</td>
</tr>
<tr>
<td>Required time to sell compound</td>
<td>12 months</td>
</tr>
<tr>
<td>Target phase for compound exit</td>
<td>Phase II</td>
</tr>
<tr>
<td>Behavior on entering Phase 2</td>
<td>All funding/transitions stop</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Capital Structure</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Capital $(MM)</td>
<td>600</td>
</tr>
<tr>
<td>Debt</td>
<td>180</td>
</tr>
<tr>
<td>Equity</td>
<td>420</td>
</tr>
<tr>
<td>Debt Maturity</td>
<td>4 years</td>
</tr>
<tr>
<td>Debt Coupon</td>
<td>5% p.a.</td>
</tr>
<tr>
<td>Debt Payment Schedule</td>
<td>Semi-annual</td>
</tr>
<tr>
<td>Debt Amortization</td>
<td>Straight line</td>
</tr>
<tr>
<td></td>
<td>Month 36 - 54</td>
</tr>
</tbody>
</table>

This table shows the portfolio composition for the RBO transaction simulated as well as the capital structure and terms & conditions of the debt. All parameters unoptimized for performance.

### Table 2: Structure of health insurance portfolio simulated in example

<table>
<thead>
<tr>
<th>Per patient cost of drugs during exclusivity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost distribution during exclusivity</td>
<td>$C_E^j \sim \text{LogNormal}(3.583, 0.8)$</td>
</tr>
<tr>
<td>Mean</td>
<td>$49,500</td>
</tr>
<tr>
<td>Correlation with RBO exit valuations</td>
<td>0.6</td>
</tr>
<tr>
<td>Cost post-exclusivity</td>
<td>$C_O^j = C_E^j \times 0.1$</td>
</tr>
</tbody>
</table>

| Percentiles (approximate)                  |                                               |
| 0.05                                         | $10,700                                      |
| 0.50                                         | $36,000                                      |
| 0.75                                         | $61,700                                      |
| 0.95                                         | $134,100                                     |
| 0.99                                         | $231,400                                     |

| Reimbursement cost parameters              |                                               |
| Exclusivity period                         | 7 years                                      |
| Term of insurance                          | 18 years                                     |
| Discount rate for payments                 | 5%                                           |

| Disease prevelance                         |                                               |
| Per disease                                | 0.001                                        |

| Age distribution                           | $Age \sim \text{U}(0, 5)$                    |
| Portfolio size (# insured \leq age 5)      | 10,000                                       |
| Simulation paths                           | 25,000                                       |

This table shows composition of the hypothetical healthcare benefits provider portfolio in the simulation. In the upper portion of the table, approximate values are given for the per-patient annual reimbursement cost of new drugs, based on simulation parameters (see Footnote 10).
This figure shows various distributions related to the simulation. The upper left plot shows the distribution of hedge ratios (per-insured individual RBO equity required). The upper right plot shows the distribution of reimbursement-related shortfall ($S_f$). The lower left plot shows the distribution of drugs ultimately approved from the RBO portfolio. The lower left shows the distribution of total return on equity for the RBO.

In general, regardless of the hedging strategy, hedging appears to be prudent. In about 87% of the cases, the hedger is better off for having hedged, primarily because the ROE generally positive for the RBO equity. Unsurprisingly, the more conservative the hedge becomes

the raw shortfall, not including the initial cost of the hedge itself. Here negative numbers indicate positive cashflow (negative costs) beyond the reimbursement shortfall. The section below this reports results after including the initial cost of the hedge.\(^\text{13}\)

In general, regardless of the hedging strategy, hedging appears to be prudent. In about 87% of the cases, the hedger is better off for having hedged, primarily because the ROE generally positive for the RBO equity. Unsurprisingly, the more conservative the hedge becomes

\(^\text{13}\)Note that here we show the results of applying the hedge ratios calculated using the simulation to the simulation paths themselves. In principle, there is a risk of “look-ahead” bias since the sample used to calculate the ratio is also the sample we are using to report the results. However, because the simulation parameters are the same, there is very little difference between doing this and rerunning the simulation using different seeds. To explore this we reran the simulations with new seeds, but using the hedge ratios calculated above. The results were almost identical. A more practical issue in assessing the sensitivity of the results hedge ratio selection, would be to vary simulation parameters. This would best be done in the context of a specific portfolio to be hedged.
Table 3: Economics of the reimbursement hedge

<table>
<thead>
<tr>
<th>RBO</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected IRR</td>
<td>0.227</td>
</tr>
<tr>
<td>RBO bond probability of default</td>
<td>&lt; 1bp</td>
</tr>
<tr>
<td>Mean number of new drugs:</td>
<td>5.1</td>
</tr>
<tr>
<td>Insurance portfolio</td>
<td></td>
</tr>
<tr>
<td>Portfolio size:</td>
<td>10,000</td>
</tr>
<tr>
<td>Mean shortfall ($\bar{S}_f$)</td>
<td>$14,801,156</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No hedge</th>
<th>Median</th>
<th>75th pctle</th>
<th>95th pctle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hedge amt per insured (one-time)</td>
<td>$0</td>
<td>$691</td>
<td>$930</td>
<td>$1,508</td>
</tr>
</tbody>
</table>

Risk reduction:*

Reimbursement shortfall ($S_f$) ($MM$)

\begin{tabular}{lcccr}

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>95th pctle</th>
<th>99th pctle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>14.8</td>
<td>0.3</td>
<td>-4.8</td>
</tr>
<tr>
<td>95th pctile</td>
<td>30.5</td>
<td>11.2</td>
<td>6.8</td>
</tr>
<tr>
<td>99th pctile</td>
<td>40.3</td>
<td>17.8</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Pct time up-front hedge cost < $S_f$ 83.5% 71.5% 42.0%
Pct time better off w/hedge 86.7% 86.7% 86.7%
Pct time hedge eliminates (or better) $S_f$ 11.9% 25.2% 52.3%

*Assuming 0.6 correlation between RBO individual asset sale value and per-patient cost. See Table 4.

This table shows the results of the portfolio simulation. Hedge amounts are calculated per insured individual in the portfolio. $S_f$ is the reimbursement-related shortfall. Risk reduction shows the mean, 95th and 99th percentile shortfalls after adjusting for the RBO hedge. The lower half of the table shows the percentage of times in which the up-front cost of the hedge is lower than the shortfall, the percentage of times the hedge has lower costs as a result of the hedge, and the percentage of times the hedge completely eliminates the shortfall or results in additional positive cashflow to the hedger.

(i.e., the higher quantile of $H_o$ that is chosen), the more it reduces the extreme losses in the tail of the shortfall distribution. However, the cost of the hedge scales in the level of $H_o$. In addition, the percentage of times that cost of the hedge itself is greater than the realized shortfall also increases. (However, note again that that due to the positive ROE, even in these cases, the hedger typically makes a profit.)

Figure 2 shows the relationship between the reimbursement-related shortfall and the return on equity for the RBO portfolio. The left-hand plot shows the unhedged portfolio. The horizontal red line shows the expected (mean) value of the the shortfall, given the number of drugs being developed in the RBO portfolio. As can be seen in the plot, there are a large number of realizations in which the shortfall well exceeds the expected value. On the right, a similar plot shows the same relationship, but this time when the the provider has purchased a hedge (using the 75th percentile hedge ratio). The shortfall is calculated after considering
the cost of the hedge.

In comparing the two figures, it is clear that the hedging provides significant reductions in large shortfalls compared to the unhedged case. Note as well, however, that there is significant density in the region below the expected cost, but above the zero line, suggesting that in these cases, the hedge reduces the shortfall, but does not eliminate it entirely. This is due to a number of issues, some of which we discuss in Section 5.4. In addition, we can also see that in a large number of cases, the hedge actually generates a profit. These cases are shown below the zero line (negative shortfalls are profits).

Indeed, at the more conservative levels, some may consider the portfolio “over-hedged” since, for example, at the 95\textsuperscript{th} percentile of $H_o$, the hedging strategy (after accounting for the cost of the hedge itself) is larger than required more than half the time and thus generates excess cashflow. While these cases result in a profit to the hedge, the cost of the hedge may be high. For example, the cost of the 95\textsuperscript{th} percentile hedge is greater than the unconditional expected shortfall for the portfolio. However, in the most costly cases, it protects the hedger well, all but eliminating largest shortfalls. In the mean case, it also produces a modest return for the hedger.

Thus, hedging a reimbursement risk-exposed portfolio involves trading-off extreme-loss protection against high upfront cost and possibly unutilized hedging capacity. However, as

![Figure 2: RBO return on equity (ROE\textsubscript{RBO}) vs. reimbursement shortfall, hedged and unhedged](image)

This figure shows the relationship between the shortfall due to increased reimbursement costs ($y$-axis) vs. the return on equity for the RBO securities. The left plot shows the unhedged shortfalls and the right plot shows the hedged shortfalls, after accounting for the cost of the hedge. The top (red) line shows the expected shortfall, given the development of the portfolio. 75\textsuperscript{th} percentile hedge used for hedging.
we discussed earlier, hedging with RBO equity may be better thought of as taking a position in a diversifying asset. In this context, underutilization may be acceptable to some hedgers.

The results suggest that there is significant variability in the optimal hedge ratio. It is also clear that even the larger hedges (i.e., those based on large values of $H_o$), are not complete in that for any hedge level there remain cases which would not be fully hedged by the RBO equity. We discuss this in more detail in Section 5.4.

The relationship between the RBO equity performance and the hedge effectiveness is nuanced. Consider that one of the primary sources of variability in the simulation of the reimbursement portfolio is the number of diseased individuals treated, which is, in turn, a function of both the number of diseased individuals and the number of those diseased individuals for whom one of the approved RBO portfolio therapies was appropriate. In general, the RBO equity position will gain value when new therapies are developed, so all else equal, the number of therapies developed should offset, to a significant degree, the increase longevity-linked shortfall. However, when it happens that the number of diseased individuals treated itself is much larger than expected, or the cost of certain drugs is much very much higher than expected (from the initial Phase II valuation of the compound when it was sold out of the RBO portfolio) the hedge may not fully reduce the increased shortfall. Conversely, unless there are an unusually large number of individuals with the disease or unexpectedly high costs, even modest hedges appear to perform well in most cases.

We explore this point in the next subsection in which we discuss the sources of correlation between the return on the RBO equity portfolio and the reimbursement shortfall.

### 5.3 Sensitivity of results to assumptions about correlation between compound valuations at sale and subsequent per patient costs

We make a basic assumption that the price at which the collateral manager sells a compound out of the RBO in Phase II is based on expectations for the future cashflows should the drug be approved (given a specific prevalence rate for the disease). Thus, higher valuations on the compounds at exit should imply higher per-patient pricing of the approved drug (all else equal). In our baseline simulation, we assume that this correlation, $\rho_{VC} = \text{Cor}(V_j, C_{E}^j)$, between the valuation at exit and the per-patient cost, is 0.6.

To give a sense of how the performance of the hedging strategy changes with respect to the level of this correlation, we also simulated the same portfolios using different parameter values for the correlation. These are shown in Table 4. Because one of the values we choose is zero, we may also use the results of these simulations to decompose the drivers of the correlation between the RBO portfolio performance and the effectiveness of the hedge.

We notice first that the hedge performs well regardless of the assumptions about $\rho_{VC}$. 
Table 4: Impact of correlation between compound valuation \( (V_j) \) and per-patient cost \( (C_D^j, C_E^j) \)

<table>
<thead>
<tr>
<th>Economics of hedge evaluated at 75\textsuperscript{th} percentile of hedge ratio simulations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk reduction:</strong></td>
</tr>
<tr>
<td><strong>(negative numbers are profits)</strong></td>
</tr>
<tr>
<td>No hedge</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>95\textsuperscript{th} petile</td>
</tr>
<tr>
<td>99\textsuperscript{th} petile</td>
</tr>
<tr>
<td>Cor((ROE_{RBO}, S_f))</td>
</tr>
</tbody>
</table>

This table shows the performance of the hedging strategy under different assumptions about the correlation between the exit valuation of a candidate drug sold out of the RBO portfolio and the subsequent per-patient cost of that drug in the future. In the table, \(\rho_{VC}\) denotes the assumed value of this correlation in the simulations, \(ROE_{RBO}\) represents the ROE on the RBO portfolio and \(S_f\) represents the shortfall due to increased reimbursement costs. All values are for a hedge using the 75\textsuperscript{th} percentile hedge ratio. (See Table 3.)

The hedged portfolio performs better than the unhedged portfolio in the large majority of cases. In particular, the hedged portfolio always performs better than the unhedged portfolio (even after factoring in the cost of the hedge) in the high quantiles, representing cases of extremely high reimbursement costs.

Furthermore, we can see that even when we assume a correlation of zero between the Phase II sale price and future per-patient costs, the realized value of Cor\((ROE_{RBO}, S_f)\) is 34\%. This represents more than half of the total correlation between \(ROE_{RBO}\) and \(S_f\) that we observe in our base case \(\rho_{VC} = 0.6\). Thus, it seems that substantial correlation is induced simply by virtue of the fact that the total cost of reimbursement for the benefits provider and the value of RBO equity position both depend on the number of approved compounds.

Finally, and not surprisingly, the hedge is more effective as the correlation increases between the RBO exit values and per-patient costs on approved drugs. Although the mean value of the hedge declines as the correlation increases, its effectiveness in lowering the tail risk increases.

5.4 Imprecision of hedge due to incompleteness and non-exclusivity of RBO

Even were the hedge ratio perfectly matched to the number of potential diseased individuals treated, the hedge may still not be a perfect one for a number of reasons. Prominent among...
these are that (a) the drugs in the RBO portfolio are sold in most cases before approval, so the final value of the drug (and thus its likely costs) are only partially known; (b) the portfolio underlying the RBO likely does not contain drugs for all of the possible diseases that may impact the cohort of insured individuals; and (c) even if therapies for the diseases targeted in the portfolio do become available during the lifespan of the diseased individuals in the portfolio, the RBO portfolio (and thus the hedger) only benefit financially from the drug discovery if the therapy that came to market was the one in the portfolio. In this section, we discuss these sources of imprecision in turn.

5.4.1 Therapeutic drugs are sold from portfolio prior to final approval

In general, drugs are sold out of the RBO portfolio after advancing one or more clinical trial phases successfully. However, these drugs have not usually advanced all the way to the end of the trial process. For example, a drug sold out of the portfolio in Phase II still needs to progress through Phase III and NDA before ultimately being approved.

Thus, in some cases, drugs that exit the portfolio never ultimately reach patients. This feature creates the potential for a mismatch between the behavior of the RBO portfolio and the ultimate reimbursement experience of the provider. To some degree, this mismatch is minimized, as for the large majority of the drugs sold out of the portfolio, substantial payments are received only when subsequent trial milestones are met. Nonetheless, this feature introduces imperfections in the degree to which the cashflows of the RBO match those of the reimbursement payments. It also creates uncertainty about the degree to which the cashflows from the sale of the drug out of the portfolio, will match the ultimate costs of the drug. Of course, we assume that generally compounds that are sold at higher than average valuations in, e.g., Phase II will ultimately fetch higher per-dose costs once approved.

5.4.2 Therapeutic drugs for diseases not targeted in the RBO portfolio

It may happen that a new therapy comes to market for a disease not targeted by a compound in the RBO portfolio. This new therapy, against which the reimbursement agent is not hedged though the RBO, may require repayment without providing an offsetting increase in RBO equity value for the underwriter.

A natural mechanism for addressing this is for RBO portfolio managers to explicitly disclose the diseases for which their portfolio is seeking therapies. This may be done confidentially, and with appropriate safeguards, to investors. Investors could then calculate hedge ratios based only on the diseases targeted, thereby hedging out (in expectation) the risk due to potential therapies for those specific conditions, while pursuing alternative risk mitigation for the remainder of the portfolio.

Even if the portfolio were not disclosed, RBO equity investments could still be used to provide an offset against potential risk of breakthrough scientific advancement, such as that currently being experienced in some types of genetic diseases. In this case, the underwriter
might use RBO equity as a means to hedge the general scientific “marketplace” rather than to offset specific positions, albeit with a more obvious mismatch.

This type of mismatch is not uncommon in other asset markets. For example, an investor in a portfolio of small US oil and coal mining exploration firms might seek to hedge this risk using put options on the iShares S&P Global Energy Index Fund (IXC). While it is unlikely that all (or in some cases any) of the firms in the investor’s portfolio would be represented in the index, the investor might reason that the hedge would provide protection against adverse price movements across the sector.

In the same way, RBO equity exposure may provide a hedge for risk that is associated with the more general type of scientific breakthroughs that were discussed at the beginning of this paper. Because changes in scientific regimes will tend to increase the number of successful new drugs overall, underwriters can expect to track these benefits, though perhaps not precisely, regardless of whether the RBO portfolio contains all (and only) those found in the underwritten cohort.

However, such strategies must be constructed carefully. In the case of genetic diseases, for example, the inter-drug scientific correlation is typically considered to be quite low, at least initially. This is due in part to the nature of these therapies which tend to target single genes rather than combinations of genes (as is often the case in some types of cancer) or other broader systemic environments. For such portfolios, only very major breakthroughs (on the order of the Human Genome Project, perhaps) might influence the outcomes of these therapeutic projects.

However, this criticism of RBO-based hedges must also be tempered as this limitation is not unique to RBOs. More generally, there is evidence that the current generation of index-based longevity hedging vehicles may also suffer from basis mismatches. For example, using an augmented Lee and Carter (1992) model, Li and Hardy (2011) estimate that for a model Canadian pension plan, the efficiency of a longevity hedge constructed using $q$-forward contracts (a form of longevity swap based on the LifeMetrics indices) to be 56% of longevity VaR and about 82% of longevity risk.

5.4.3 Therapeutic drugs not in the portfolio but for diseases in the RBO portfolio

Consider the case in which the RBO portfolio manager correctly hedges a disease by investing in a portfolio containing a drug that targets that disease. If a new therapy for the disease makes it to market, but the market therapy was not the one in the portfolio (i.e., another drug development team developed the drug and brought it to market before the RBO’s team), the hedge is worse than ineffective, it is likely costly: the value of the drug in the portfolio will likely go down at the same time that the reimbursement cost goes up.

14It is not uncommon for a genetic breakthrough that initially targets a specific disease to then find applications across a variety of other conditions.
In principle, this can be addressed through a slightly more complicated treatment of $\frac{\partial A}{\partial k}$.

If we define $\Pr(\theta_j \in P | \tau_j \leq T_d) = p_\theta$ as the probability that the therapy brought to market for condition $j$ is the one in the RBO portfolio, given that a therapy is introduced during the lifespan of the affected individuals in the underwritten population, then

$$H_I = \frac{N \times p_D \times \frac{C}{r} \left( \frac{(1+r)^{\Delta - 1}}{(1+r)^{TD + \Delta}} \right)}{p_\theta \times V},$$  

(18) 

where the $I$ subscript indicates an incomplete hedge, i.e., that the RBO cannot provide total coverage of the drug market, even in cases in which the portfolio contains drugs that target all diseases of interest to the underwriter.

Equation (18) provides a fix-up for the uncertain case in which a therapy for disease $j$ becomes available, but the RBO portfolio does not contain it.\footnote{An analogous modification may also be made to the simulation algorithm to reflect the parameter $p_\theta$.} Although, in expectation, the hedge will now provide adequate protection (with missed compounds being made up for by those for which the underwriter receives $1/p_\theta > 1$ instead of $1$), the hedger will still bear more risk in the realization of the portfolio and the variance of the cashflows will increase proportionally. While for large portfolios, this risk may become (relatively) smaller, for more moderate sized portfolios, it may not.

### 5.5 Future research

Although our results suggest substantial benefits to using RBO securities for hedging historically hard-to-hedge risks, our analysis is still stylized in some respects and thus can be fairly criticized along a number of dimensions. While these critiques do not necessarily undermine our fundamental findings, they do suggest a opportunities for future research.

Perhaps most prominent among the limitations of our current work are our assumptions regarding the actuarial properties of various at-risk portfolios and the manner in which these are modeled. For example, the current version of our model does not contemplate stochastic interest rates when valuing annuity-like exposures at the horizon of the RBO securities’ payoffs. As another example, our simulations do not discount annuity cashflows dynamically or attempt to exactly synchronize the valuation times of the annuities with the arrival times of residual “milestone” payments on drugs sold out of the portfolio. We similarly do not consider potential correlation between the cashflows on the RBO equity tranche and the interest rates used to discount the annuity cashflows. We expect future research will explore these dynamics.\footnote{A cursory analysis of the relationship between the yield on five-year treasuries and the value of the iShares Nasdaq Biotechnology Index Fund suggest negative correlation, i.e., discount rates tended to be higher at times when biotech valuations were lower.}

More generally, there is substantial scope for extending the actuarial framework we use in our approach. For example, with respect to longevity risk, recent work on stochastic
longevity models (cf., Cairns et al., 2006) suggest a number of more refined approaches to modeling (and simulating) lifetimes for annuity valuation.

Although our examples are chosen for exposition rather than realism, more realistic examples are no doubt possible, subject to the analysis of historical data on pension and insurance portfolios and based on a more detailed cross-sectional analysis of current ones. For convenience, we assumed homogeneity across prevalence rates and other features of the drugs in the portfolio.

In particular, our assumptions about the impact on a patient’s lifespan of a new drug in our longevity examples are somewhat arbitrary. While drugs that treat certain conditions may indeed extend life well beyond our assumptions, others may offer only a much shorter extension of life. These assumptions, and those used in our reimbursement examples, would need to be tailored to a specific portfolio of diseases, and their financial impact for an underwriter or reimbursement agent would depend also on the makeup of the portfolio of liabilities of that entity. This is also true of our stylized representation of the dynamics of the processes representing both annuity writing and reimbursement, which we have simplified somewhat in our examples and simulations.

We also note that we have left for future work the optimization of hedge strategies. For example, more efficient hedge ratio calculation may be accomplished with more specific information, were it available, about the current health states of the members of the hedger’s portfolio and the specific diseases targeted by the therapies in the RBO portfolio. With more detailed data on the specific diseases in the portfolio, a hedger may determine more precisely the expected cost of a hedge, and factor this into the optimization of the hedge ratio. Similarly, with more detailed information about, for example, the insurance premia paid by individuals in the portfolio, in the case of reimbursement risk, or the contributions of pension fund members, in the case of longevity risk, more exact calculations of net hedging costs are feasible.

This last topic also suggests an interesting opportunity for customizing portfolios to appeal to investors with differential hedging needs. For example, based on portfolio composition, health insurers may be more interested therapies for diseases that affect key demographics in their portfolios; on the other hand, pension funds may prefer portfolios that focus on late-in-life diseases such as certain cancers or neurological disorders.

6 Conclusion

The equity tranche of a research-backed obligation (RBO) is a financial instrument that gains value when individuals live longer. RBO equity thus serves as a potentially attractive natural hedging vehicle for entities exposed to certain types of scientific longevity risk, such as defined benefit pension plans and insurance firms that underwrite annuities to populations of individuals at risk for certain diseases. RBO equity also gains value when new therapies
are developed, making potentially effective for haging for a much broader class of exposures affecting entities that must reimbursement patients for the costs of new and often expensive drugs.

In this paper, we have demonstrated how the equity of a research-backed obligation may be used to hedge longevity risk and reimbursement risk and have shown how an appropriate hedge ratio may be estimated. To do so, we first introduced an analytic model for the case in which all quantities required to calculate hedge ratios were deterministic. Because many of these quantities are, in fact, stochastic (e.g., RBO portfolio exit valuations, numbers of diseased individuals, per-patient costs of approved drugs, etc.) we next proposed a simulation framework for estimating hedge ratios at various levels of confidence. We observed that such hedges may be made arbitrarily effective in expectation, but that care was required in determining the appropriate hedge size because of the dependence of the shortfall on the number of diseased individuals in the portfolio and the less-than-perfect correlation of the exit values of RBO portfolio drugs and the ultimate per-patient costs of approved drugs.

Managing longevity and reimbursement risks continue to be growing challenges for pension funds and insurance firms. The advent of RBO securities provides one possible mechanism for hedging specific dimensions of this risk. As the RBO market continues to develop, we can foresee the potential introduction of bespoke RBO portfolios that are designed to meet the needs of specific institutions. For example, for pension funds in industries that experience higher rates of certain cancers, portfolios targeting those diseases might be constructed to provide hedges. Analogous, “tilts” can be introduced into portfolios to address specific reimbursement concerns.

The ability of an RBO to pool multiple smaller drug development projects to create portfolios large enough to be investable by such financial institution, thereby providing exposure to specific life-extending drug development “factors,” represents a significant step forward in reimbursement and longevity risk mitigation. In addition to being financially attractive, such investments offer the welcome social benefit of providing much-needed funding for drug development, thereby increasing the potential for more and better therapies for millions of patients in need.
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7 Appendix A: The decision to hedge using RBO equity rather than RBO debt

It is useful to reflect on why equity, rather than debt, is the natural hedging vehicle for investors exposed to reimbursement and longevity risk. Notwithstanding the relative ease with which some investors can invest in debt relative equity (e.g., for reasons of regulatory capital requirements), equity is more attractive for hedging purposes for the following reason: With respect to the portfolio value, the upside on any debt is capped, to a first approximation, by the par value of the debt and its credit quality. The case that the hedger is seeking to protect against is the case in which many new therapies are developed in a short time frame. The structure of equity allows the hedger to protect against such outcomes in a manner that scales in the number of new drugs developed.

Consider a simplified example, in which the hedger holds an entire tranche of debt with par value equivalent to the sale value of three successful new therapies out of the portfolio (for the sake of this example, assume that therapies are valued at $200MM each and that the par of the debt is thus $600MM). Given the success of three drugs, the bondholders receive repayment of par at maturity (we ignore interest here). (If they instead sold prior to maturity, but after the three drugs are developed, they might receive slightly more than the original investment, due to improved credit quality.) However, if instead a total of 10 new therapies are developed in the portfolio, the hedger holding the debt tranche will still have a shortfall of the impact of 7 therapies. In contrast, the upside for the hedger holding the equity is unbounded, so they would benefit from all of the therapies developed, rather than just the first three. On the other hand, imagine that NO therapies are developed. The bonds default and the equity is wiped out. The hedger has lost the initial investment, however, the number of therapies is lower than expected so, e.g., the reimbursement costs will be lower than expected. This is similar to the payoff for original position in the bond. (If the hedger could also write a CDS on a high tranche, other strategies would be available.)

8 Appendix B: An extended example of the impact of new drug development on portfolios of annuities

Example 3. An extended example for a portfolio of annuities
Consider the case of an insurance firm that sells a 40 year old individual an annuity that pays $10,000 per year for the remainder of her life. Assume that a healthy individual will live 85 years. If the interest rate $r$ is 5%, then by (1)

$$A_h = \frac{10,000}{0.05} - \frac{10,000}{0.05} \frac{1}{(1.05)^{(85-40)}} = \$177,741.$$
Assume similarly that a forty year old individual with the disease *infirmum corpus* will live only 60 years. Under the same interest rate assumptions as above, by (1)

\[
A_d = \frac{10,000}{0.05} - \frac{10,000}{0.05} \frac{1}{(1.05)^{60-40}}
= \$124,622.
\]

Say a new therapy for *infirmum corpus* becomes available on the day that the diseased individual buys the annuity and that this therapy fully controls *infirmum corpus* and returns diseased a individual’s lifespan to that of an undiseased individual, adding back 25 years of life. Assume further that *infirmum corpus* affects about 1 in 100 individuals. If we did not know an individual’s status the expected change in to that individual’s annuity value, \(A_u\), (which is equivalent to the per-individual increase in cost to the annuity provider) is given by (4):

\[
E[\Delta A_u] = p \tau_j p D_j \frac{C}{r} \left( \frac{(1 + r)^{\Delta} - 1}{(1 + r)^{T_d + \Delta}} \right)
= 1 \times 0.01 \times \frac{10,000}{0.05} \left( \frac{(1 + 0.05)^{25} - 1}{(1 + 0.05)^{20+25}} \right)
= 1 \times 0.01 \times 53,119
\approx \$531.
\]

Of course, for an individual who has *infirmum corpus*, the resulting change in the value of \(A_d\) is \$53,119.

Finally, from (5), the expected cost to the underwriter of writing an annuity to an individual of unknown disease status is:

\[
A_u = p \tau_j p D_j A_d + (1 - p \tau_j p D_j) A_h.
= 0.01 \times \$140,939 + 0.99 \times \$177,741.
= \$177,210
\]

It is interesting to ask what the impact on the cost (value) of \(A\) would be of a therapy that has not yet been developed, but could be in the future. Consider the same insurance company and client population from the previous example. Imagine now, however, that instead of having been approved, the therapy for *infirmum corpus* were currently in Phase 3 trials and that drugs in Phase 3 have about a 1 in 3 chance of becoming approved within five years. Under these assumptions

\[
E[\Delta A_u] = p \tau_j p D_j \frac{C}{r} \left( \frac{(1 + r)^{\Delta} - 1}{(1 + r)^{T_d + \Delta}} \right)
= 0.01 \times 0.33 \times \frac{10,000}{0.05} \left( \frac{(1 + 0.05)^{25} - 1}{(1 + 0.05)^{60+25}} \right)
= 0.01 \times 0.33 \times 53,119
\approx \$177.
\]
Finally, consider the case in which the insurance firm sells annuities to a cohort of 100,000 40 year old individuals. As before, assume that each annuity pays $10,000 per year for the remainder of the client’s life. Then, using the previous results:

\[
A_i = A_u = \$177,210
\]

\[
A_P = \sum_{i=1}^{100,000} A_i
\]

\[
= 100,000 A_i
\]

\[
= \$17,596,330,370.
\]

If, for each disease, there is an historical 5% probability of a new therapy coming to market during the lifespan of the diseased annuity holders, i.e., \( \Pr(\tau_j < T_d) = 0.05 \) and there are a total of 100 diseases of interest \( (j = 1 \ldots 100) \), then the insurance company expects that there will be \( \Pr(\tau_j < \bar{T}_j) \times 100 = 5 \) new therapies available before \( T_d \).

For convenience, assume that \( \Pr(i \in D_j) = \frac{1}{10,000} \), \( j = 1 \ldots 100 \) so that there are, on average, 1000 individuals with various diseases in the cohort. For purposes of this example, we also assume that diseases are uniformly distributed across the diseased sub-population, so that on average, 10 individuals will have each disease. (In this population, it is reasonable to assume that the likelihood of an individual having two of these diseases is negligible).

From our earlier result, we have that the change in cost (value) to the underwriter (holder) of an annuity for a treated diseased individual was $53,119. Thus, for each new therapy introduced, the expected cost to the insurance company is

\[
\Delta A_P = 10 \times \$53,119 = \$531,186.
\]

Since, based on historical data, about five new therapies on average will be introduced before \( T_d \), the total expected cost to the insurance company of new therapeutic agents is

\[
\Delta A_P = 10 \times \$53,119 \times 5 = \$2,655,930.
\]

However, imagine now that new breakthroughs in genetic screening precipitate a rapid increase in effective therapies. Assume further that that now instead of the historical average 5 therapies arriving, 18 arrive. The cost of the introduction of the 18 new therapies is:

\[
\Delta A_P = 10 \times \$53,119 \times 18 = \$9,561,347.
\]

Presumably, the insurance company would have already factored in to its actuarial tables the extension of life due to the expected 5 therapies, so it is natural to think of

\[\text{The practical probability of observing 18 new therapies under the historical assumption of 5% is effectively zero (} p = 0.0000005\). However, if new research on gene therapy moved the probability of success from 5% to 20%, we would expect to see the introduction of 18 or more compounds about 2 out of 3 times. It is notable that the probability of drug approval for pre-clinical therapies targeting orphan diseases is now about 19%, due in part to recent advances in genetic sequencing (cf., Fagnan et al., 2014).\]
losses beyond these as *unexpected*. The total unexpected cost of the extra 18 therapeutic advances would be:

\[\$9,561,347 - \$2,655,930 = \$6,905,417.\]


\[9\] Appendix C: A review of Jensen’s Inequality in the context of annuities

In this paper, we often need to calculate \(A(C, r, T)\) for heterogeneous populations, with heterogeneous lifetimes \((T_i)\). Because of the Jensen effects, we cannot simply take the mean of the \(T_i\) and then calculate a single annuity value. As a simple counter example, assume we had only two individuals 1 and 2 with lifespans \(T_1 = 60\) and \(T_2 = 85\), respectively. Recall that

\[
A(C, r, T) \equiv A = \frac{C}{r} \left(1 - \frac{1}{(1 + r)^T}\right),
\]

where

\[
\begin{align*}
C &= \text{the one period constant cashflow;} \\
r &= \text{the risk-free rate;} \text{ and} \\
T &= \text{the number of periods over which the } C \text{ will be paid.}
\end{align*}
\]

Assume we wish to calculate the mean value of the combined portfolio of two $10,000 annuities, one written to each individual (and using an interest rate of 5%).

The mean of \(T_1\) and \(T_2\) is 72.5. If we were to use this value to calculate \(A\) we get:

\[
A(10,000, 0.05, 72.5) \approx 194,182.
\]

If, on the other hand, we calculated the values of \(A_1\) and \(A_2\) and then take the mean of these, we get:

\[
\begin{align*}
A_1 &= A(10,000, 0.05, 60) \approx 189,292. \\
A_2 &= A(10,000, 0.05, 85) \approx 196,838. \\
\bar{A} &= \frac{(A_1 + A_2)}{2} = 193,066 < 194,182.
\end{align*}
\]