



HAL
open science

Can Pension Funds Partially Manage Longevity Risk by Investing in a Longevity Megafund?

Edouard Debonneuil, Anne Eyraud-Loisel, Frédéric Planchet

► **To cite this version:**

Edouard Debonneuil, Anne Eyraud-Loisel, Frédéric Planchet. Can Pension Funds Partially Manage Longevity Risk by Investing in a Longevity Megafund?. *Risks*, 2018, 6 (3), pp.67. hal-01571937v3

HAL Id: hal-01571937

<https://hal.science/hal-01571937v3>

Submitted on 10 Dec 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

CONDITIONS OF INTEREST OF A LONGEVITY MEGAFUND FOR PENSION FUNDS

Edouard Debonneuil^α

Anne Eyraud-Loisel*

Frédéric Planchet*

Univ Lyon - Université Claude Bernard Lyon 1,
ISFA, Laboratoire SAF EA2429, F-69366, Lyon, France
Prim'Act, 42 avenue de la Grande Armée, 75017 Paris, France

ActuRx

Version¹ 2.6 du 10/12/2017

ABSTRACT

Pension funds that handle retirement risk need to invest assets in a diversified manner and on long durations while managing interest rate and longevity risks. In the recent years, a new class of investment called a longevity megafund was described, that invests in clinical trials for solutions against age-related diseases. Using simple models, we here study the financial interest for pension funds of investing in a longevity megafund.

Sommaire

1.	Introduction	2
1.1.	Forthcoming anti-aging solutions.....	2
1.2.	Hope for pharmaceutical companies, fear for retirement systems.....	2
1.3.	Longevity megafund: the solution?	3
1.4.	In what conditions is a longevity megafund interesting to hedge longevity risk?	4
2.	Feasibility of hedging longevity risk with a megafund	4
2.1.	What type of retirement systems would benefit from investing in a longevity megafund?	4
2.2.	Needed megafund returns to hedge longevity risks	5
2.2.1.	High returns are crucial to hedge longevity risk.....	5
2.2.2.	High levels of returns can be produced	6
2.3.	Visualization of the financial equilibrium depending on lifespan x.....	7
2.3.1.	Linkage 1: discovery success rate: 10-year megafund returns increase linearly with lifespan.....	9
2.3.2.	Linkage 2: due to breakthroughs, annualized equity returns increase linearly with lifespan	10
2.4.	Comparison between needed and provided returns: a possible hedge.....	11
3.	Impact of investing in a megafund on needed own funds.....	12
3.1.	Refined assumptions.....	12
3.1.1.	Assumptions related to mortality	12
3.1.2.	Assumptions related to population, contributions, investments and benefits	13
3.1.3.	Assumptions related to the megafund	14
3.2.	Simulations, probability of ruin and prudential capital	15
3.3.	Result: needed prudential capital.....	15
4.	Conclusion.....	17
5.	References	17

^α Edouard Debonneuil is founder of ActuRx. Contact: edebonneuil@yahoo.fr

* Anne Eyraud-Loisel and Frédéric Planchet are researcher at SAF laboratory (EA n°2429). Frédéric Planchet is also consulting actuary at Prim'Act. Contact: anne.loisel@univ-lyon1.fr / frederic@planchet.net. Their work benefited partially from the financial support of the ANR project "LoLitA" (ANR-13-BS01-0011).

¹ The authors thank the referees whose comments have significantly improved this work.

1. INTRODUCTION

1.1. FORTHCOMING ANTI-AGING SOLUTIONS

In the 19th and 20th centuries, infant mortality rates and young adult mortality rates have dropped so that the future of life expectancy is now to a large extent a matter of solutions to old age conditions (Vallin 2010).

In this beginning of the 21st century, a series of biomedical discoveries suggest that mortality rates may drop at old age as well. The series started with animal models of human aging and is now turning to humans. The lifespan of laboratory nematodes was extended circa ten times with one single gene change (Ayyadevara, 2008). The lifespan of laboratory mice was extended by 70% through a combination of gene change and diet (Bartke, 2008). There is a vast range of successful methods in animals that are reproduced at the level of cells and tissues in humans and human trials are being discussed (Moskalev 2017). While a different use of existing drugs possibly represents the fastest route to concrete human life extension (Barardo 2017), the graft of bioprinted organs (Ravnic 2017, Mir 2017) and the *in vivo* degradation of old tissues that the body naturally replaces by younger tissue (Fahy 2003, Ocampo 2016, Mosteiro 2016, Mendelsohn 2017) are already being tested in specific clinical settings. Indeed, science is not only on its way to slow down human aging but also to restore youthful characteristics to the body once old.

One may then expect much better health at old ages, which in turn means lower mortality rates and longer lives. By how much? The life expectancy impact of curing diseases can be delicate because beyond the disease there is a largely unknown associated global burden on health (Martin 2003, Arias 2013, Guibert *et al.* 2017). Where models or parameters are to be chosen, psychological ceilings lead to underestimate parameters such as predicting an ultimate average life expectancy limit of 64.75 (Dublin, 1928) or 85 years (Olshansky 1990). Keeping maximum human lifespan around the age of 115 is one of those imaginary ceilings because in the last century it evolved much more slowly than the median age of death. However, the latter evolution is not true when accounting for cause of death; and comparing effects of current interventions in various animal species and humans rather suggests a further increase of 30%, i.e. 150 years of maximal lifespan may be at reasonable reach based on ongoing developments (Ben-Haim 2017).

1.2. HOPE FOR PHARMACEUTICAL COMPANIES, FEAR FOR RETIREMENT SYSTEMS

When will such old-age solutions come? That is a key question for the pharmaceutical industry. The pharmaceutical industry currently suffers from a lack of profitability of investments in research and development due to very low success rates in clinical trials (Scannel 2012), in part due to the attempt to gradually adapt the methods for single, acute diseases to multiple, chronic diseases (Thiem 2011, Roman 2017) instead of targeting the underlying aging and regenerative processes as described above. As many biotech companies now carry that latter approach, various investors reports, books and conferences consider that current retired persons may be the first populations to benefit in large from such advances (Mellon 2017, Pratt 2016, Casquillas 2016). When essentially focusing on hair and skin aging, which were the main anti-aging industry drivers until recently, estimated sizes of the anti-aging market are USD 122 billion in 2013, 140 in 2015,

192 in 2019 and 217 in 2021 (Zion Market Research 2017, Transparency Market Research 2016).

When will such old-age solutions come? That is a key question for retirement systems also: they face the "longevity risk" that retirements must be paid longer than financially planned. Current retirement systems essentially stem from the middle of the 20th century, when most young workers were not expected to reach retirement age, and they depend on various mortality tables that are regularly updated but that empirically underestimate historical life expectancy trends (Antolin 2014, Debonneuil 2017). In the USA only, if deaths caused by cardiovascular diseases and cancer were eliminated, the fiscal imbalance of Social Security and Medicare programs may be as high as USD 87 trillion in present value (Zhavoronkov 2012). May such imbalances be offset by investing retirement contributions in the burgeoning anti-aging market?

1.3. LONGEVITY MEGAFUND: THE SOLUTION?

The concept of "cancer megafund" was developed to face the current pharmaceutical industry crisis that particularly affects cancer research and development: instead of having investors bet high amounts on one risky drug development, the megafund is a financial structure that pools a large number of diversified drug developments and structures investments into debt and equity with low returns but sufficiently low risk (due to the strong diversification) to make investments attractive (Fernandez 2012). The debt part is useful to attract larger investments and to finance long term projects, which is needed for many biomedical developments. The concept has then been and is being studied for various health applications, from rare diseases to biomedical innovation in large, in London, the USA, Australia or Sweden (Swedish Agency for Growth Policy Analysis 2017) and even for non-health-related applications (Hull 2016). In parallel, several remarks have proposed the need for strong contextual attention to properly implement the megafund concept (Boissel 2013, Marko 2013, Tenenbaum 2013, Fagnan 2014, Fagnan 2015, Lo 2014, Lo 2015, Yang 2016).

One of the applications of the megafund concept is the "longevity megafund" (MacMinn 2017, Kahn 2015, Stein 2016). Such a megafund tracks the biomedical innovations that are likely to increase lifespan, as much as possible, and invests in the corresponding developments to become a sort of longevity risk tracker. Such has diverse benefits. By investing in a range of innovations that is wider than cancer therapies, a better diversification of risk is provided which is an essential feature of the megafund concept to make investments attractive. The longevity megafund can notably attract health providers to hedge the risk of reimbursing new, expensive drugs (Stein 2016). By tracking potential solutions to age-related conditions, that correlate with longevity risk, it can attract large investments for the equity part of the megafund: annuity insurance providers and pension funds can invest to cover their longevity risk and this is what we study in this article. The concept of longevity megafund is particularly appealing for the risk management of longevity risk: instead of matching mortality risks of workers who are less than 65 year old with mortality risks of retired persons, it matches mortality risks of retired persons with mortality risks of retired persons. Also, having the income from therapeutic developments come before the treated persons live longer is an interesting feature to possibly pilot retirement benefits in advance.

Some first simulations on life settlements indicate that rightfully investing in a longevity megafund is a better hedge than existing longevity hedges with respect to longevity shocks and basis risk (MacMinn 2017). In this article, is to study the management of longevity risk by investing in a longevity megafund with a more pedestrian approach: the words "covering" or "hedging" (longevity risk) will be used indifferently because the goal is to manage longevity risk without a clear view on the characteristics of the megafund. In particular, due to a lack of historical data on a longevity megafund, the difficulty of knowing what type of health breakthroughs will come first and how well the megafund will capture associated financial returns the article will not claim to find optimal investments to perfectly correlate longevity risk with megafund returns. Instead different scenarios will be proposed to provide examples of longevity risk coverage.

1.4. IN WHAT CONDITIONS IS A LONGEVITY MEGAFUND INTERESTING TO HEDGE LONGEVITY RISK?

We note that, despite so many theoretical advantages, the literature contains little studies about the conditions in which the longevity megafund is interesting to hedge longevity risk. This article aims at investing such conditions at a deeper level.

2. FEASIBILITY OF HEDGING LONGEVITY RISK WITH A MEGAFUND

2.1. WHAT TYPE OF RETIREMENT SYSTEMS WOULD BENEFIT FROM INVESTING IN A LONGEVITY MEGAFUND?

Retirement systems are mainly composed of defined benefits plans, defined contributions plans, pay-as-you-go plans, and insurance retirement contracts. So far, to our knowledge the literature suggests that longevity megafunds may hedge longevity risk, without investigating what type of plans would best benefit from investing in a longevity megafund.

"Defined benefits" means that the pension fund handles investment choices and is entitled to pay benefits until the ends of pensioner lives. The benefits are typically defined as a percentage of the pensionable salary, for example 20% of the average salary over the last three years of work. Investing in a longevity megafund could well be a way for defined benefit pension funds to partially hedge their longevity risk: in case of strong longevity improvements, investment returns are greater so the accumulated capital can pay benefits longer.

In defined contribution plans, employees provide contributions during their working years and make investment choices to build their capital for retirement. Then longevity risk is at the level of the pensioners: if a pensioner uses the whole capital during retirement the pension plan does not need to pay anything more to the pensioner. In recent decades, a shift has occurred from defined benefit plans to defined contribution plans in order to avoid longevity risk. Since they do not directly carry longevity risk, at first sight defined contribution pension funds have no interest in investing in a longevity megafund. At second sight, they may well have an interest as they would then propose a capital that reduces the longevity risk of their pensioners: in case of strong longevity improvements, pensioners would have a greater capital.

Whole life deferred annuities, that are often provided by insurance companies, have an important nuance compared to defined benefit and defined contribution plans: after contributions are collected and invested, benefits are defined as a percentage of

accumulated capital (the percentage is given by a mortality table). This is actually fundamentally different from defining benefits as a percentage of the pensionable salary because here a larger capital will not cover longer durations of benefits. Instead, it provides larger benefits! Longer and larger benefits: the longevity risk is doubled so deferred annuity providers had rather not invest in the equity part of a longevity megafund.

In pay-as-you-go pension plans there is no, or very little, investment: the contributions from workers directly pays the benefits to retired persons. In such a system, that is for example widely spread in France, the lack of investment makes the longevity megafund of no use.

In conclusion, from a first qualitative perspective the equity part of a longevity megafund makes sense for defined benefit and possibly defined contribution pension plans, but a priori not for pay-as-you-go schemes nor for providers of deferred annuities.

Our analysis is somewhat schematic as numerous retirement systems exist and risks can be transferred to stakeholders who have distinct characteristics. For example, insurers providing deferred annuities may transfer their longevity risk to reinsurers who might benefit from investing in a longevity megafund. Also, various practical aspects such as counterparty risk, basis risk and megafund returns – of course – may modulate the conclusions.

2.2. NEEDED MEGAFUND RETURNS TO HEDGE LONGEVITY RISKS

Following that schematic, qualitative analysis we here study the investments returns of a megafund that are needed to hedge the longevity risk of a defined benefit pension plan.

2.2.1. High returns are crucial to hedge longevity risk

Let us start with a very simple model to highlight the orders of magnitude that a longevity megafund should return to offset longevity risk. We consider a pensioner who pays 1 every year from age 25 (included) to age 65 (excluded). Its contributions are invested in funds that are expected to provide the annual return $i=1.5\%$. At age 65, the expected capital is

$$(1+i)^{65-25} + (1+i)^{65-26} + \dots + 1 + i = \frac{(1+i)^{65-25+1} - (1+i)}{i} \approx 55$$

The annual benefits are contractually defined based on that expected capital, to pay the benefits for 20 years for example: up to an expected pensioners lifespan of 85 years. However, let's consider that strong biomedical interventions take place and that pensioners live to 95-100. Benefits must be paid for 30-35 years instead of 20, which is a circa 50% greater duration!

To pay benefits on a 50% greater duration, the capital must be 50% greater. Using the formula with $i = 3.3\%$ instead of 1.5% provides the needed 50% greater capital. It means that the defined benefit pension plan would have offset its longevity risk if all contributions had been invested in a longevity megafund that provides annual returns of 3.3%.

However, pension funds would likely not transfer all their assets into a longevity megafund – a new type of structure – but rather at most for example 20%. The megafund should therefore provide much higher returns so that, when diluted in 80% of returns

at 1.5%, the overall return is 3.3%. Since $3.3\% = (1 - 20\%) \times 1.5\% + 20\% \times 10.5\%$, if pensioners are to live to ages 95-100 on average the megafund should provide 10.5% annual returns. Now, if only 10% of assets were invested in the megafund, it should similarly provide 19.5% annual returns. If 5% of assets were invested in the megafund, it should provide 37.5% annual returns! Offsetting the longevity risk of currently 45-year-old pensioners rather than 25-year-old pensioners is even more demanding: with a 20% or 10% investment in the megafund, required annual returns are 13.8% and 26.1%.

Put differently, *if a longevity megafund cannot generate 10%-20% annual returns in case of material longevity increases, unless pension funds invest surprisingly large percentages of their assets in the megafund it does not seem to be a viable approach to hedge longevity risk.* We then have to check if such a return level is possible?

2.2.2. High levels of returns can be produced

The original cancer megafund paper (Fernandez 2012) provided elements to answer that question: it investigated historical drug development, costs, success rates and sell prices at various stages of development (preclinical, phase I, II, III, approval) in an area that is known to lack financial interest: cancer drugs. It synthesized the observations with two simple models that have the same ten-year annual return of 11.9%: one for blockbusters (drugs with annual revenues more than \$1 billion, after year 10) and one for non-blockbusters. We therefore take this 11.9% revenue as a conservative basis for our models.

The blockbuster model is as follows: N drug development programs each require an initial investment $C_0 = \$200$ million and generate 10 years later a revenue $Y_{10} = \$12.3$ billion (present value of returns starting after 10 years) with a percentage $p = 5\%$ of successful programs (no revenue from unsuccessful programs). The expected 10-year return on investment is then $\rho = \frac{p \times Y_{10} + (1-p) \times 0}{C_0} \approx 3.1$ and the expected annualized return is:

$$r = \left(\frac{p \times Y_{10} + (1-p) \times 0}{C_0} \right)^{\frac{1}{10}} - 1 \approx 11.9\%$$

The non-blockbuster model is the same with $C_0 = \$100$ million, $Y_{10} = \$3.1$ billion, and $p = 10\%$. It also leads to $\rho \approx 3.1$ and $r \approx 11.9\%$.

In what follows, ρ is what matters, or rather the derived equity annualized return i . r is not precisely the return that matters to hedge longevity risk. A megafund must be structured into debt and equity (non-debt). That is because without the debt part it would be difficult to find enough investors to have enough drug development programs financed for the megafund risk to become small compared to returns, hence to be financially attractive. The debt part, composed of "research-backed obligations" (RBOs), provides fixed annual returns: it cannot hedge longevity risk. Therefore i , the annualized return of the equity part of the megafund, that provides gains in excess of RBOs, is the rate that matters to possibly hedge longevity risk:

$$i = \left(\max\left(\frac{\rho - (1 - \alpha) \times 1.05^{10}}{\alpha}, 0 \right), 0 \right)^{\frac{1}{10}} - 1$$

where α is the percentage of investments of the megafund and where we supposed that the interest rate of the RBOs is 5%. Indeed, for αC_0 invested in the equity tranche the

megafund generates 10 years later a revenue of ρC_0 that first pays the RBOs investors who invested $(1 - \alpha)C_0$. If sufficient, the latter receive $(1 - \alpha)C_0 \times 1.05^{10}$ so that equity investors receive the remainder, $\rho C_0 - (1 - \alpha)C_0 \times 1.05^{10}$. This must be compared to the initial αC_0 investment 10 years earlier. When the 10-year return of drug developments is $\rho = 3.1$, having $\alpha = 50\%$ or 25% of investments dedicated to the equity tranche leads to $i = 16.4\%$ or $i = 22.3\%$, respectively: the equity share can be used as a lever to obtain higher returns if there are enough successful drug development programs (at the cost of reducing returns if there are not enough).

Such returns depend of course very much on drug selection and the quality of management of the megafund (Yang 2016), as well as contractual aspects of funds, such as fees and carried interest (Phalippou 2010). Also here we keep the simple assumption that the drug development length is 10 years, in practice numerous details of course need to be taken into account.

But to conclude on the question of interest of investing in a longevity megafund, yes, the equity part can provide sufficient returns to cover the longevity risk of having pensioners live to 100 instead of 85.

2.3. VISUALIZATION OF THE FINANCIAL EQUILIBRIUM DEPENDING ON LIFESPAN X.

To easily visualize and think about the appropriateness of a longevity megafund, we here model mortality as a unique age of death x : we estimate the financial needs of a defined benefit plan as a function of x , we estimate the megafund returns as a function of x and we observe how returns compare to needs as a function of x .

Using Asset Liability Management (ALM) practice standards, we consider employees of different age tranches, each with different salaries and different returns as shown in table 1.

Tab. 1. Age tranches

Age	Number persons	Individual annual contributions	Investment returns
[20-35[4000	3000	$i_1=5\%$
[35-50[4000	4500	$i_2=4\%$
[50-65[4000	6000	$i_3=2\%$

For the sake of simplicity, we consider 4000 employees who all enter the company at age 25 and stay in the company until retirement at 65. From age 20 to 65, the collected and invested annual contributions lead to a total capital of

$$C = 4000 \left[6000 \frac{(1 + i_3)^{16} - 1 - i_3}{i_3} + 4500 \frac{(1 + i_2)^{16} - 1 - i_2}{i_2} (1 + i_3)^{15} + 3000 \frac{(1 + i_1)^{16} - 1 - i_1}{i_1} (1 + i_2)^{15} (1 + i_3)^{15} \right] \approx 1\,587\,000$$

For the sake of simplicity, let us consider that during retirement benefits increase with age at the discount rate such that benefit duration equals retirement length: $x-65$. Considering that benefits are defined so that the capital exactly pays the benefits if pensioners all live to age $x=85$, the first annual benefit is then $(1\,587\,000/4000)/(85-65) = 19\,836$ per pensioner.

Now comes longevity risk and longevity hedge. If pensioners live to age x , the longevity loss for the company is $19\,836 \cdot 4000 \cdot (x-85)$. For example, if pensioners live up to age 100 the loss is 1.2 billion for the pension fund. To offset such losses, the pension fund may have invested a percentage of its assets in the longevity megafund.

Let us consider that the percentage of investment in the megafund depend on the age tranche: for example, $p_1=20\%$, $p_2=15\%$, $p_3=10\%$.

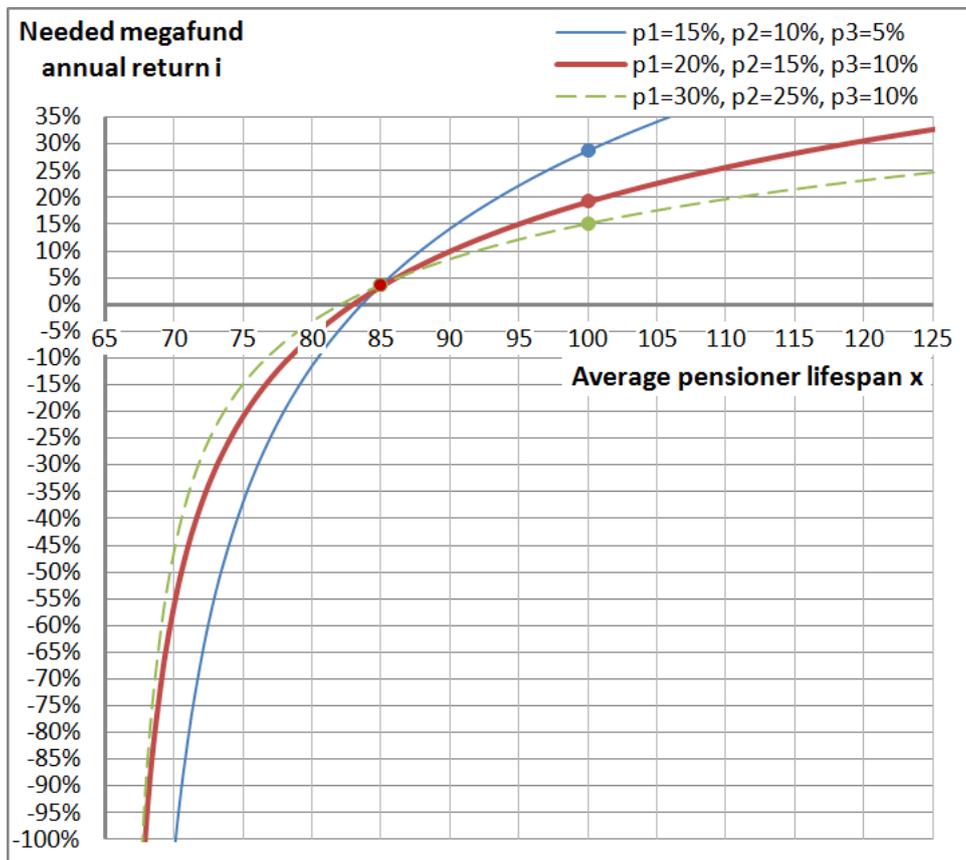
The needed annualized return i of the megafund equity tranche is then such that the greater needed capital (which is proportional to the duration of benefits, see left part of the following formula) is obtained by partially investing contributions in the megafund (right part of the following formula):

$$C \times \frac{x - 65}{85 - 65} = 4000 \left[6000 \frac{(1 + \tilde{i}_3)^{16} - 1 - \tilde{i}_3}{\tilde{i}_3} + 4500 \frac{(1 + \tilde{i}_2)^{16} - 1 - \tilde{i}_2}{\tilde{i}_2} (1 + \tilde{i}_3)^{15} + 3000 \frac{(1 + \tilde{i}_1)^{16} - 1 - \tilde{i}_1}{\tilde{i}_1} (1 + \tilde{i}_2)^{15} (1 + \tilde{i}_3)^{15} \right]$$

where $\tilde{i}_1 = p_1 i + (1 - p_1) i_1$, $\tilde{i}_2 = p_2 i + (1 - p_2) i_2$, $\tilde{i}_3 = p_3 i + (1 - p_3) i_3$.

The formula links pensioner lifespan x and needed megafund annual return i . Accordingly, Figure 1 shows the needed return i that is numerically needed to pay pensioners living to age x given percentages of investment in the megafund.

Fig. 1 - Needed megafund return depending on pensioner lifespan to perfectly hedge longevity risk. Three lines are displayed, they correspond to different percentages of investments in the megafund.



If pensioners on average live to age 70 a full loss of longevity megafund (return of -100%) can be supported by the remaining investments of the pension fund (of course, better

returns are always welcome!). If pensioners live to the expected age of 85, the longevity megafund equity tranche should provide the same average returns as other funds, 3-4% annually. If pensioners live to age 100, 15% or 20% or even 29% annual returns should be provided by the longevity megafund depending on the percentage of investments of the pension fund in the megafund; if pensioners live longer even greater returns are needed. Megafund returns as a function of x .

The link between megafund equity returns and longevity depends on how longevity changes occur and whether the megafund is able to capture them from a financial point of view. A strong longevity increase would typically arise from many health solutions to age-related conditions that affect a large number of persons. We here imagine two types of scenarios.

2.3.1. Linkage 1: discovery success rate: 10-year megafund returns increase linearly with lifespan

A longevity scenario is that a number n of health solution would each provide a given lifespan increase (for example 5 years of added lifespan to 10% of retired persons): the greater the number n the longer the average lifespan, in a proportional manner. The link between the megafund and longevity is that as the number n of meaningful health solutions increases the megafund should be able to capture them in its given resources. The link may be proportional: the proportion p of successful drug development programs should approximately increase in a proportional manner (p is the ratio of successful programs over funded programs, it is closer to 0 than to 1) if the megafund managers are sufficiently able to distinguish important programs from less important ones. In that scenario, the 10-year return on investments, for drug development programs, $\rho = \frac{p \times Y_{10}}{C_0}$, should increase linearly with lifespan:

$$\rho_x = 3.1 + \theta_{(\pm)}(x - 85) + \varepsilon \quad (\text{Linkage 1})$$

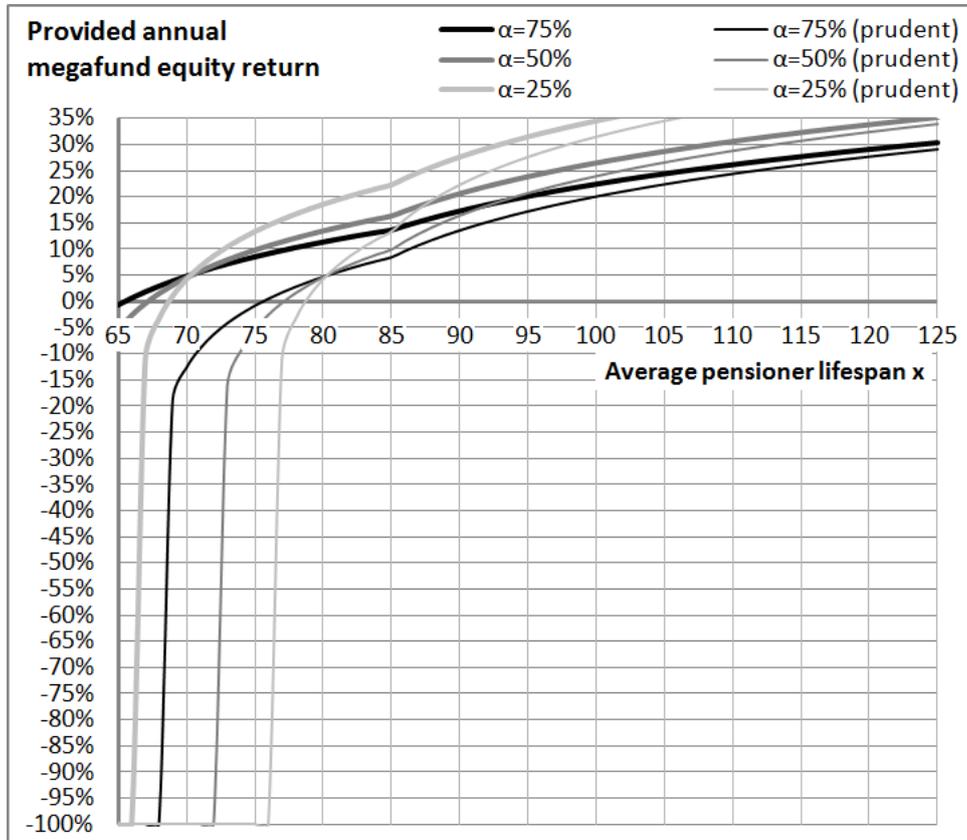
where the coefficient $\theta_{(\pm)}$ and the noise ε remain to be chosen. For increasing lifespan, we take $\theta_+ = 0.2$: if pensioners live to 100 it corresponds to a double of return on investments ($\rho_{100} = 6.1$) and a double of successes in blockbuster and non-blockbuster programs: on the one hand, it is difficult to imagine much higher financial returns so 0.2 may be high, on the other hand it seems that greater successes than 10% of blockbuster programs and 20% non-blockbuster programs may be achieved so 0.2 may be small. For decreasing lifespan, we consider that the biomedical and longevity link is reduced, as a decrease in lifespan would probably largely be driven by pollution, obesity or other aspects that negatively affect health, more than by a lack of biomedical innovation, so we arbitrarily take $\theta_- = 0.1$. We take ε as a uniform random variable between -1 and +1 such that if x is around 85 or lower the link between pharmaceutical results and longevity isn't clear. ε can be seen as the "luck" of the fund; it includes whether the IP of therapeutic developments was sold earlier or later than planned and at a lower or higher price than planned.

Of course, the reader may view those numbers as adequate or not. With the link we established here, equity returns are:

$$i = \left(\max\left(\frac{3.1 + \theta_{(\pm)}(x - 85) + \varepsilon - (1 - \alpha)1.05^{10}}{\alpha}, 0\right) \right)^{\frac{1}{10}} - 1$$

Figure 2 describes the provided returns.

Fig. 2 - Equity returns provided by the longevity megafund, depending on pensioner lifespan, equity share α of megafund investments, and a prudent view on other factors ($\varepsilon = -1$ instead of 0).



2.3.2. Linkage 2: due to breakthroughs, annualized equity returns increase linearly with lifespan

The rate of discoveries is one driver for longevity and it is easy to link it with returns as done just above. However, longevity breakthroughs are to be possibly expected as well, such as tissue regeneration techniques that are currently in labs and that may reach large populations in the forthcoming decades. The link between longevity and returns is less predictable in that scenario because of the novelty of the situation; however, it can be expected to be strong because longevity is then strongly driven by one or a few treatments.

In the previous scenario (linkage 1) the annualized equity return has a concave shape due to the exponent $1/10$. In this scenario (linkage 2), we remove that concave shape by considering that the annualized equity returns increase linearly with lifespan:

$$i = \left(\frac{x - x_0}{85 - x_0} \right) i_{85} + \varepsilon \quad (\text{Linkage 2})$$

where $i_{85} = \left(\max\left(\frac{3.1 + \varepsilon - (1 - \alpha)1.05^{10}}{\alpha}, 0\right) \right)^{\frac{1}{10}} - 1$ is the return in expected conditions with respect to longevity: the return showed at age 85 in Figure 2. x_0 is the age at which i would be expected to be zero and ε is a uniform random number. As Linkage 1 is related to the rate of success of moderate health improvements, we can consider it as a scenario for moderate longevity risk so for Linkage 2 we choose coefficients that align Linkage 1

CONDITIONS OF INTEREST OF A LONGEVITY MEGAFUND FOR PENSION FUNDS

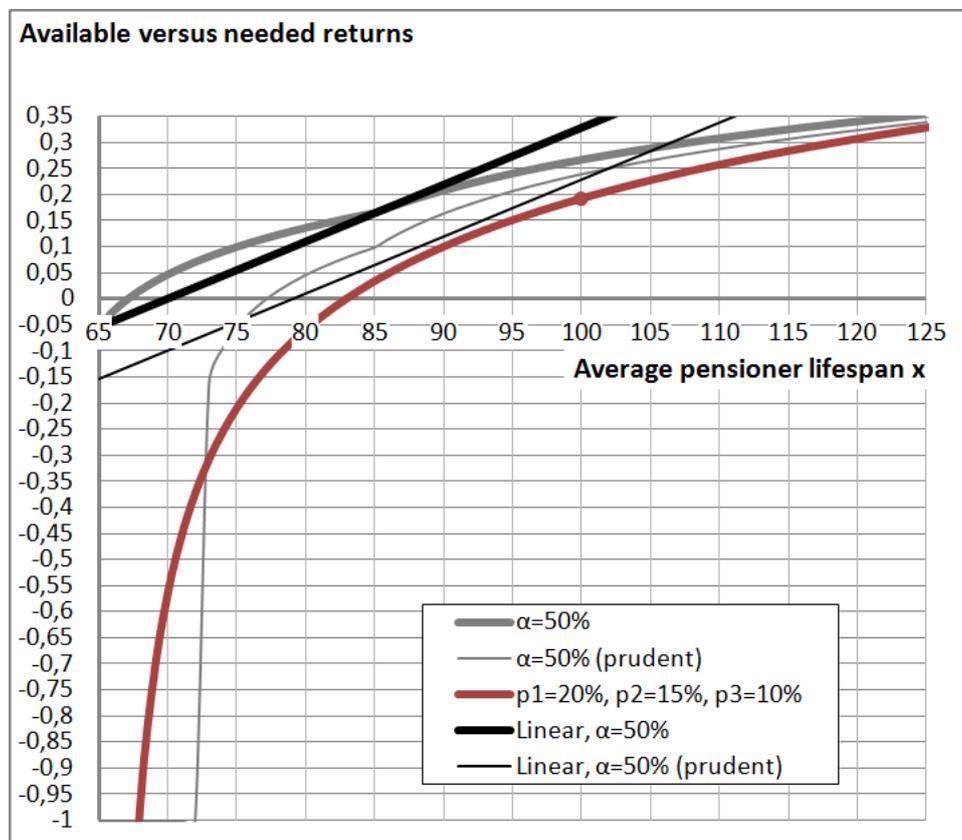
and Linkage 2 around the age of 85: we take $x_0 = 75$ and ε between -20% and +20%. We can see the alignment in Figure 3.

Of note, since longevity may be driven from many discoveries, a small number of key discoveries, and many key discoveries (the combination of both), Linkage 1 is probably prudent.

2.4. COMPARISON BETWEEN NEEDED AND PROVIDED RETURNS: A POSSIBLE HEDGE

Figure 3 superimposes needed returns for the pension fund in the case of approximately 15% investment in the megafund ($p_1=20\%$, $p_2=15\%$, $p_3=10\%$) and provided equity returns by the pension fund, for both Linkage 1 and Linkage 2, in case it has 50% of investments for RBOs.

Fig. 3 - Available megafund equity returns (black and grey lines , prudent or best estimate) versus needed returns for the pension fund. The straight black lines use the second scenario ("Linear"), the curved grey lines use the first scenario.



The megafund seems to provide enough return, except in the prudent Linkage 1 case when longevity decreases. Such is of course the result of models. Other models or other parameters could lead to provide insufficient returns compared to the needed returns for the pension fund. However, we see that the sufficient return stems from the main assumptions that i) the returns are above 5% under current longevity trends, i.e. that the assumptions published for megafunds so far are not absurd, and ii) that the link between longevity and megafund returns are at least like Linkage 1. So, with that simple analysis, there is a sound possibility of hedging longevity risk by investing in a biomedical megafund. Of note, prudence is required. The models and conclusions above assume that the longevity fund is reasonably well handled and that things go reasonably well: if longevity related projects are missed so that longevity increases but the fund doesn't

take a share of the corresponding financial market, a strong mismatch between needed and provided funds may occur. If the megafund bets on an insufficiently diverse set of therapeutic developments, it leads to a poor risk-adjusted profile: the risk is that none of them succeed, or that only a few of them lead to financial gains as other strategies are in competition on the same market. So, the megafund should definitely cover a very diverse range of therapies, and should not position itself on other therapies than competitors: it should in the contrary participate in various external developments to take a share of the overall market. In the worst case that can be imagined, investments would not only be associated with no gain, but with further costs linked to law suits.

On the other hand, various details may in practice improve the hedge compared to the model. Since megafund equity returns are expected to reflect biomedical improvements, it should reflect retirement needs in advance. Hence, if the defined benefit plan leaves some area of adjustment of future benefits, for example regarding the increase of benefits, megafund equity returns may be an input to choose benefit adjustments.

3. IMPACT OF INVESTING IN A MEGAFUND ON NEEDED OWN FUNDS

The above analysis shows that investing in a longevity megafund can in theory provide adequate returns over the years to cover longevity risk, when taking a prudent view compared to a central view. This seems good news for a pension fund because it suggests that large increases of longevity can be managed by having invested in a longevity megafund and holding a minimum amount of prudential capital to face risks, instead of requiring very large amounts of capital to face very large risks.

The above analysis was voluntary schematic for the sake of clarity. Longevity was described by the age x at which everyone dies whereas in practice mortality spreads over ages. Also, the analysis stopped at comparing needed versus provided annualized long-term returns, whereas a sufficient prudential capital is needed at all times to avoid bankruptcy.

Therefore, we adjust the previous analysis of a defined benefit pension plan to incorporate such aspects. After defining refined assumptions to model longevity, pension fund and megafund behaviors, we measure what level of prudential capital is needed today to pay retirement until the last death of current employees.

3.1. REFINED ASSUMPTIONS

3.1.1. Assumptions related to mortality

We consider the following model of annual mortality rates, for someone aged x in t years:

$$q_{x,t} = \frac{0.5}{1 + e^{a-b(x-\varphi t)}}$$

As studied by Debonneuil *et al.* 2017, such a model leads to non-decelerating life expectancy trends and the parameters typically are $a=10.5$, $b=0.1$ and $\varphi=23\%$. With these parameters a and b the model currently has expected behaviors: the current ($t=0$) life expectancy at birth is 84.4 years, it is slightly above the general population life expectancy (the 2015 life expectancy in the UK, France and Japan is respectively 81.2, 82.4 and 83.7) which is desired as it concerns workers and insured persons. With this model also, the current life expectancy at 65 is 22.1 years leading to the average age of 87.1

years, which is expectedly higher than 84.4 years as it doesn't consider people who died before the age of 65.

With $\varphi=23\%$ the model reproduces current major longevity trends. Life expectancy at birth increases by 23% of year annually, which is the "best practice trend" of long lived countries (Vaupel 2010). Current annual mortality improvements are $\frac{q_{70,0}-q_{70,1}}{q_{70,0}} = 2.1\%$ at age 70. For those currently aged 65, it leads to a remaining expected lifespan of 25.6 years, so an expected lifespan of 90.6; such is higher than 87.1 because improvements are expected during these years. For current newborns, it leads to an expected lifespan of 105.8; one shall note that even for newborns of the general population, if current life expectancy trends continue then lifespans of long-lived countries are expected above 100 (Vaupel 2010).

Future longevity trends are however unknown. For the sake of simplicity we suppose that φ is constant over time and lognormally distributed over scenarios of the future, with mean $\log(23\%)$ and standard-deviation of 1: in such conditions, there is as much probability (50%) that probability φ is lower than 23% as greater than 23%. There is also a 7% possibility that $\varphi>1$. Over long periods of time, the latter corresponds to people enjoying better health and reduced mortality risks as time goes, for example because of the emergence and progressive generalization of tissue regeneration techniques. Some may find the latter 7% excessively high and others may find it excessively low (Debonneuil 2016). That is why we will in particular consider four longevity scenarios: $\varphi=0\%$ (no improvement in the future), $\varphi=23\%$ (best practice trend), $\varphi=46\%$ (double trend) and $\varphi=69\%$ (triple trend). Of note, around 1950 Japan had a trend that was clearly above $\varphi=100\%$, suggesting that high trends are possible when hygiene & biomedical knowledge as well as social contexts are adequate. Similarly, over the last decades, life expectancy has increased by more than $\varphi=50\%$ of year annually in countries like Malaysia, Philippines, Vietnam, Laos and Bangladesh (Carbonnier 2013). Of note also, during approximately 70 years after the microbial communications of Louis Pasteur, φ was around 30% in long-lived countries (Vallin 2010); improving hygiene requires complex cultural, technological and urbanization changes, it may be that using anti-aging therapies once they are available is a faster process.

3.1.2. Assumptions related to population, contributions, investments and benefits

Populations. At time $t=0$ we consider 300 persons of age 20, $300(1 - q_{20,0})$ employees of age 21, $300(1 - q_{20,0})(1 - q_{21,0})$ employees of age 22, etc. until age 100. It provides a distribution of the population across ages that is roughly natural. Every year ($t=1, t=2, \dots$) the persons die according to mortality rates and 300 new persons aged 20 arrive. For the sake of simplicity, we do not model arrivals and departures at other ages.

Contributions and investments. As in table 1, persons aged 20-34, 35-49 and 50-54 provide respective annual contributions of 3000, 4500 and 6000. Also, by default investments respectively provide $i_1=5\%$, $i_2=4\%$ and $i_3=2\%$ of expected annual returns, corresponding to three different funds that take different degrees of risk. For each of the three funds the volatility σ is given by a Sharpe ratio of 1.5 (arbitrary number), a risk-free rate of 1% (arbitrary number) and a ρ by ρ correlation of 50% (arbitrary number):

$$\sigma_k = \frac{i_k - 1\%}{1.5} \quad \langle \sigma_k, \sigma_l \rangle_{l>k} = 50\% \quad k, l = 1, 2, 3$$

We consider a 2-by-2 correlation of returns of 50% between the three funds.

Benefits. Regarding contractual benefits, we consider that they have been defined by generation (generations of people contributing since age 20) so that the accumulated capital at age 65 match the remaining lifespan based on the mortality rates with $\varphi=23\%$. Since most actuarial tables have decelerating trends (Debonneuil 2010) actuaries often declare such benefits as prudent when building retirement products. As done in the above stylized models, for the sake of simplicity we suppose that the benefits increase with age like corresponding investment returns so the duration of benefits is equal to the remaining lifespan at age 65: we do not need to model annual benefits, rather the accumulated capital at age 65 and the remaining lifespan. For the computation of contractual benefits, we also take the simplifying approximations that mortality rates before age 65 at those at time $t=0$ and that investments are exactly 5%, 4% and 2% (without considering volatility). We will see in the results that these approximations have a good accuracy.

3.1.3. Assumptions related to the megafund

A percentage of contributions ($p_1=20\%$, $p_2=15\%$, $p_3=10\%$) can be invested in the equity part of the megafund, whose return is correlated with longevity. In line with the previous approach, as a first possible linkage between megafund returns and longevity, the 10-year return of the whole megafund is linked with longevity as follows:

$$\rho_\varphi = 3.1 + \theta_{(\pm)}(\varphi - 23\%) + \varepsilon \quad (\text{Linkage 1})$$

ε is a random uniform number between -1 and 1 drawn once for each scenario of the future in order to represent that the correlation is not deterministic. In the formula, we replaced $(x-85)$ by $(\varphi - 23\%)$, therefore the coefficient $\theta_{(\pm)}$ must be adjusted to the new scale. We do so using age 40 as a sound actuarial age: $\theta_{(\pm)}$ was previously chosen to express the possibility of living to 100 instead of 85, i.e. 15 additional years brought by biomedical discoveries. When $\varphi = 23\%$, people currently aged 40 are expected to live up to the age of 94.5 on average. When $\varphi = 44.5\%$, people currently aged 40 are expected to live up to the age of 109.5: that is also 15 additional years. Consequently, the previous values of $\theta_{(\pm)}$ are multiplied by $\frac{15}{44.5\% - 23\%}$: $\theta_{(\pm)} = 14$ when $\varphi > 23\%$ and $\theta_{(\pm)} = 7$ when $\varphi < 23\%$.

The annualized return of the megafund equity tranche in scenario 1 is then:

$$i = \left(\max\left(\frac{3.1 + \theta_{(\pm)}(\varphi - 23\%) + \varepsilon - (1 - \alpha)1.05^{10}}{\alpha}, 0 \right) \right)^{\frac{1}{10}} - 1$$

By analogy with the previous approach also, a second potential linkage between the megafund and longevity is

$$i = \frac{\varphi}{23\%} \left[\left(\max\left(\frac{3.1 - (1 - \alpha)1.05^{10}}{\alpha}, 0 \right) \right)^{\frac{1}{10}} - 1 \right] + \varepsilon \quad (\text{Linkage 2})$$

where ε is uniform between -10% and 10%.

In the two models of linkage we consider that $\alpha = 50\%$ of the megafund is structured in equity.

3.2. SIMULATIONS, PROBABILITY OF RUIN AND PRUDENTIAL CAPITAL

10,000 scenarios of the future were constructed using the software R. The code is in the supplementary materials. Each scenario draws the longevity trend φ , the "luck" of the megafund ε and, for each future year, the annual returns $i_t^k, k = 1,2,3$ of the three funds (depending on the employee age). Other calculations within a scenario do not require drawing random numbers. A Cholesky decomposition of the covariance matrix $\langle \sigma_k, \sigma_l \rangle$ is used to simulate correlated returns.

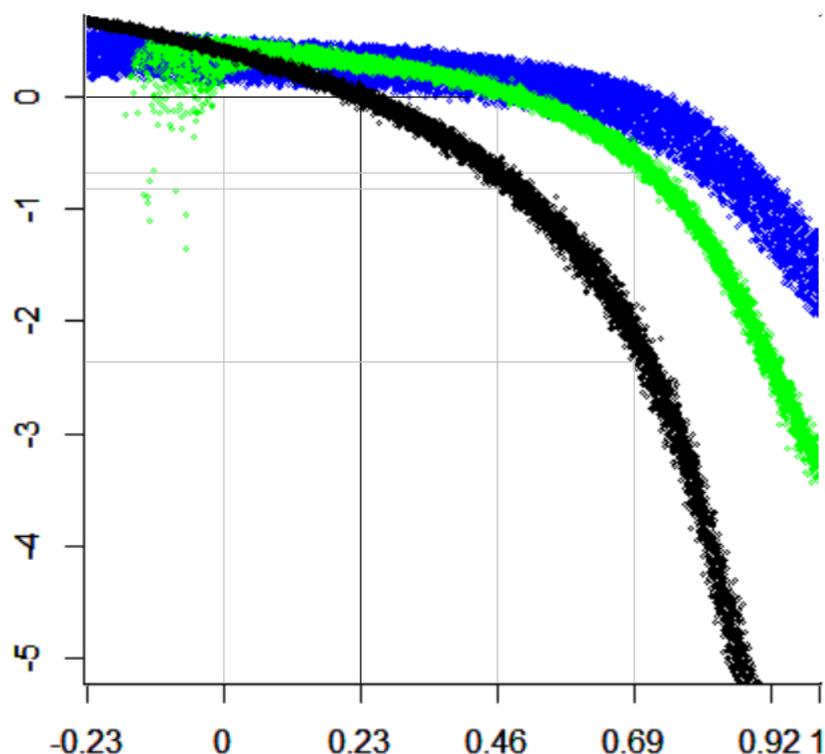
At $t=0$, the defined benefit pension fund starts with its initial population of persons aged 20-65 and an accumulated wealth based on historical mortality rates (modelled with $t=0$ mortality rates) and exactly 5%, 4% and 2% past annual returns on investments. The defined benefit pension fund then either invests p_1, p_2, p_3 in the megafund or does not invest in the megafund. We then simulate scenarios of the future where the longevity trend (φ), the megafund luck (ε) and the returns of funds (i_t^k) intervene. In order to assess the right amount of prudential capital at $t=0$, we instead suppose no initial additional wealth, we allow wealth to become negative (instead of claiming bankruptcy) and for each scenario of the future we measure wealth after all benefits were paid. That measure is discounted using the investment composition of the scenario to represent the initial additional wealth that would have been needed and invested to provide the right amount to pay retirements in the future, without reaching bankruptcy. For the sake of simplicity, the discounting is performed along investments done, i.e. the wealth is divided by the value of an initial investment of 1 when invested in the different funds in the same proportion of contributions. In practice, long term investments choices and associated discounting may be optimized through the use of progressive utility (El Karoui 2014). In fact, considering the returns (i_t^k) of the funds independent from longevity is certainly simplistic.

The needed prudential capital is then arguably defined as the 5% worst initially needed capital across scenarios of the future. This would mean that there is a 5% risk of not paying retirement benefits, however in case of strong risks the wealth provided by new business may be used to pay the older business to some extent, or other adjustments may be provided meanwhile. So, the risk of not paying retirements is arguably lower than 5% (arguably, as events can be worse than modelled and as reactivity can be questioned with respect to retirement systems).

3.3. RESULT: NEEDED PRUDENTIAL CAPITAL

Figure 4 shows the needed amount of additional initial wealth, expressed as a proportion of the initial wealth, depending on the future longevity trend. The first obvious result is that all curves go down on the right side: with these refined assumptions, under extreme longevity scenarios the hedge is partial when investing about $p_2=15\%$ in the longevity megafund. The second obvious result is that the two linkage models lead to approximately the same need of prudential capital (the same bottom of curve) if the future longevity trend isn't three times the current one. The third results is that under such non-too-extreme longevity scenarios, much less prudential capital is needed when investing in the megafund.

Fig. 4 - Needed additional wealth depending on the future longevity trend - Excess initial wealth (or lack of, when <0) as a proportion of the initial wealth²



More precisely, the y-axis shows the actualized remaining wealth after paying retirement benefits for current employees, divided by the current wealth of the pension fund: "-1" means that 100% of additional wealth would be needed today, i.e. that the current wealth should be double. Each dot in the graph is the result of a scenario of the future. In black, no investment is performed in the megafund ($p_1=p_2=p_3=0$). In the light color (light green), the pension fund invests in the megafund which behaves like Linkage 1. In the dark color (blue), the pension fund invests in the megafund which behaves like Linkage 2.

Of note, when not investing in the megafund (nor applying some other major longevity hedge mechanism), if the current longevity trend continues ($\varphi = 23\%$) an additional capital of circa 3.5% of the initial wealth may be considered. Such is due to the risk of the funds -- the thickness of the black curve -- and taking the average (the center of the black curve) instead of a VaR at 5% shows a perfectly neutral initial wealth -- 0 -- indicating that the approximations used to compute benefits are accurate, as expressed above.

If the current longevity trend doubles however ($\varphi = 46\%$) then about 70% of additional initial wealth is needed. Such a strong additional need would be eliminated when investing in a longevity megafund, if the models described here hold well. If instead the trend triples ($\varphi = 69\%$) then about 200% of additional initial wealth is needed, which the megafund reduces to about 50% (60% if the megafund behaves like the linkage1 model, 40% if it behaves like the linkage2 model).

However, if longevity trend is negative, a prudential capital is needed due to the fact to invest in the equity part of a megafund, that would not have been needed otherwise. That is a reality if success rates of drug development programs are lower than historical

² Forthcoming longevity trend φ (was 0.23 in last decades).

pharmaceutical success. The structuring of the megafund may be optimized to reduce that risk, such as having a third tranche of the megafund that absorbs this risk.

These comments are based on specific longevity trends. In practice however, one does not know the future of longevity, so the prudential additional wealth shall cover a wide range of possible longevity trends. Using the lognormal distribution of longevity trends, our simulations suggest that with a 5% probability to have an insufficient initial wealth, the prudential capital would be 8.5 times the initial wealth! Investing in the megafund would reduce it to 4 times under the Linkage 1 behavior, and to 1.7 times under the Linkage 2 behavior. With a 10% VaR, these numbers respectively become 4.1 and 0.5. One might have expected that longevity risk is handled with a prudential capital of 10% or 30% of the initial wealth, such is not the case here because we consider the type of breakthroughs that were described at the beginning of the article and that are burgeoning.

4. CONCLUSION

The current article studied the conditions in which investing in a longevity megafund can hedge longevity risk. With assumptions that such a megafund is reasonably well managed, it appeared that the hedge may work for defined benefit pension plans and with some degree if the change of longevity is too radical.

One might hope that in case of a very radical longevity change, retirement systems are thoroughly adjusted. However, adjusting retirement systems is obviously not easy, and that longevity hedge approach may be considered. The risk analysis performed at the end of this article suggests that the short-term prudential capital risk approach that is currently proposed by diverse regulators, such as the Solvency Capital Requirement in insurance, may not lead to the right order of magnitude of prudence.

The results we obtain depend very largely on models, and not on strong empirical evidence. Indeed, the megafund remains at this stage a theoretical concept. If the biomedical discoveries described at the beginning of the article truly extend human lifespan in a very significant manner, it may be important not to wait too much to develop this longevity megafund solution. It is therefore a good timing to perform more research on the predicted behavior of the megafund depending on its details. For example, aside from mentioned potential refinements of actuarial aspects of the megafund, the pharmaceutical aspects are important. Also, a key dimension in the longevity megafund is intellectual property, and research should be performed on that aspect as well.

5. REFERENCES

Antolin P and Mosher J (2014): [Mortality Assumptions and Longevity Risk](#). Working Party on Private Pensions.

Arias E, Heron M, Tejada-Vera B (2013): [United States life tables eliminating certain causes of death, 1999-2001](#). Natl Vital Stat Rep.;61(9)

Ayyadevara S, Alla R, Thaden JJ, Shmookler Reis RJ (2008): [Remarkable longevity and stress resistance of nematode PI3K-null mutants](#). Aging Cell.;7(1):13-22.

Barardo D, Thornton D, Thoppil H, Walsh M, Sharifi S, Ferreira S, Anžič A, Fernandes M, Monteiro P, Grum T, Cordeiro R, De-Souza EA, Budovsky A, Araujo N, Gruber J, Petrascheck M, Fraifeld VE, Zhavoronkov A, Moskalev A, de Magalhães JP (2017): [The DrugAge database of aging-related drugs](#). Aging Cell.;16(3):594-597.

- Ben-Haim MS, Kanfi Y, Mitchel SJ, Maoz N, Vaughan K, Amariglio N, Lerrer B, de Cabo R, Rechavi G, Cohen HY (2017): [Breaking the Ceiling of Human Maximal Lifespan](#). J Gerontol A Biol Sci Med Sci.
- Boissel FH (2013): [The cancer megafund: mathematical modeling needed to gauge risk](#). Nat Biotechnol.;31(6):494.
- Carbonnier G, Chakraborty P, Dalle Mulle E, Cartografare il presente (2013): [Asian and African Development Trajectories - Revisiting Facts and Figures](#). International Development Policy [Online], Working Papers; DOI : 10.4000/poldev.682
- Casquillas GV (2016): [Human longevity : The giants](#). LongLongLife.org (web page).
- Debonneuil E, Planchet F, Loisel S (2017) [Do actuaries believe in longevity deceleration?](#) Insurance: Mathematics and Economics; *in press*.
- Debonneuil E, He L, Mosher J, Weiss N (2011) [Longevity Risk: Setting the scene](#). Risk books
- Dublin LI (1928): Health and Wealth. A Survey of the Economics of World Health (Harper, New York), page 361
- Fahy GM (2003): [Apparent induction of partial thymic regeneration in a normal human subject: a case report](#). J Anti-Aging Med; 6 (3):219-227
- Fagnan DE, Gromatzky AA, Stein RM, Fernandez JM, Lo AW (2014): [Financing drug discovery for orphan diseases](#). Drug discovery today; 19(5):533–538.
- Fagnan, D.E. et al., (2015): [Financing translation: Analysis of the NCATS rare-diseases portfolio](#). Science translational medicine, 7(276), pp.276ps3–276ps3.
- Fernandez Jose-Maria, Stein Roger M, Lo Andrew W (2012): [Commercializing biomedical research through securitization techniques](#). Nature biotechnology.;30:964–975.
- Guibert Q., Planchet F., Schwarzinger M (2017): Mesure de l'espérance de vie sans dépendance en France. <to be submitted>
- Hull J (2016): [Funding long shots](#). Rotman School of Management Working Paper No. 2773108
- Kahn RN (2015): [A Simple Hedge for Longevity Risk using Research-Backed Obligations](#). JOIM Conference, October 5, 2015 Cambridge
- El Karoui N, Mrad M, Hillairet C (2014): Affine long-term yield curves: An application of the Ramsey rule with progressive utility. Journal of Financial Engineering;1(1)
- MacMinn RD and Zhu N (2017): [Hedging Longevity Risk in Life Settlements Using Biomedical Research-Backed Obligations](#). Journal of Risk and Insurance.;84(1):439-458
- Marko NF (2013): [The cancer megafund: determinants of success](#). Nat Biotechnol.;31(6):492-4.
- Martin GM, LaMarco K, Strauss E, L Kelner K (2003): Research on aging: the end of the beginning. Science.;299(5611)
- Mellon J, Chalabi A (2017): [Juvenescence: Investing in the age of longevity](#). (Book) **In press**

Mendelsohn AR, Larrick JW, Lei JL (2017): [Rejuvenation by Partial Reprogramming of the Epigenome](#). *Rejuvenation Res.*;20(2):146-150.

Mir TA, Nakamura M (2017): [Three-Dimensional Bioprinting: Toward the Era of Manufacturing Human Organs as Spare Parts for Healthcare and Medicine](#). *Tissue Eng Part B Rev.*;23(3):245-256.

Moskalev A, Anisimov V, Aliper A, Artemov A, Asadullah K, Belsky D, Baranova A, de Grey A, Dixit VD, Debonneuil E, Dobrovolskaya E, Fedichev P, Fedintsev A, Fraifeld V, Franceschi C, Freer R, Fülöp T, Feige J, Gems D, Gladyshev V, Gorbunova V, Irincheeva I, Jager S, Jazwinski SM, Kaeberlein M, Kennedy B, Khaltourina D, Kovalchuk I, Kovalchuk O, Kozin S, Kulminski A, Lashmanova E, Lezhnina K, Liu GH, Longo V, Mamoshina P, Maslov A, Pedro de Magalhaes J, Mitchell J, Mitnitski A, Nikolsky Y, Ozerov I, Pasyukova E, Peregudova D, Popov V, Proshkina E, Putin E, Rogaev E, Rogina B, Schastnaya J, Seluanov A, Shaposhnikov M, Simm A, Skulachev V, Skulachev M, Solovev I, Spindler S, Stefanova N, Suh Y, Swick A, Tower J, Gudkov AV, Vijg J, Voronkov A, West M, Wagner W, Yashin A, Zemskaya N, Zhumadilov Z, Zhavoronkov A (2017): [A review of the biomedical innovations for healthy longevity](#). *Aging (Albany NY)*.;9(1):7-25

Mosteiro L, Pantoja C, Alcazar N, Marión RM, Chondronasiou D, Rovira M, Fernandez-Marcos PJ, Muñoz-Martin M, Blanco-Aparicio C, Pastor J, Gómez-López G, De Martino A, Blasco MA, Abad M, Serrano M (2016): [Tissue damage and senescence provide critical signals for cellular reprogramming in vivo](#). *Science*.;354(6315).

Lo AW (2015): [Can Financial Engineering Cure Cancer?](#) [Video] Available on YouTube

Lo AW and Naraharisetti SV (2014): [New Financing Methods in the Biopharma Industry: A Case Study of Royalty Pharma, INC](#). *Journal of Investment Management*.;12:4-19.

Ocampo A, Reddy P, Martinez-Redondo P, Platero-Luengo A, Hatanaka F, Hishida T, Li M, Lam D, Kurita M, Beyret E, Araoka T, Vazquez-Ferrer E, Donoso D, Roman JL, Xu J, Rodriguez Esteban C, Nuñez G, Nuñez Delicado E, Campistol JM, Guillen I, Guillen P, Izpisua Belmonte JC (2016): [In Vivo Amelioration of Age-Associated Hallmarks by Partial Reprogramming](#). *Cell*. 2016 Dec 15;167(7):1719-1733.e12.

Olshansky SJ, Carnes BA, Cassel C (1990): [In Search of Methuselah: Estimating the Upper Limits to Human Longevity](#). *Science*.;250(4981)

Phalippou L (2010): Investing in Private Equity Funds: A Survey. The Research Foundation of CFA Institute

Planchet P and Théron PE (2007): [Allocation d'actifs selon le critère de maximisation des fonds propres économiques en assurance non-vie : présentation et mise en œuvre dans la réglementation française et dans un référentiel de type Solvabilité 2](#). *Bulletin Français d'Actuariat*.;7 (13)

Pratt C (2016): [5 Private Longevity Stocks to Watch: From Calico to Genescent](#). Investing News (web page).

Ravnic DJ, Leberfinger AN, Koduru SV, Hospodiuk M, Moncal KK, Datta P, Dey M, Rizk E, Ozbolat IT (2017): [Transplantation of Bioprinted Tissues and Organs: Technical and Clinical Challenges and Future Perspectives](#). *Ann Surg*.;266(1):48-58.

Román P, Ruiz-Cantero A (2017): [Polypathology, an emerging phenomenon and a challenge for healthcare systems](#). *Rev Clin Esp*.;217(4):229-237

Scannell Jack W, Blanckley Alex, Boldon Helen, Warrington Brian (2012): [Diagnosing the decline in pharmaceutical R&D efficiency](#). Nature reviews Drug discovery.;11:191–200.

Stein RM (2016): [A Simple Hedge for Longevity Risk and Reimbursement Risk Using Research-Backed Obligations](#). MIT Sloan Research Paper No. 5165-16

Swedish Agency for Growth Policy Analysis (2017): [Towards a Swedish megafund for life science innovation](#). Tillväxtanalys;2017/089.

Tenenbaum JM (2013): [The cancer megafund: a catalyst for disruptive innovation](#). Nat Biotechnol.;31(6):491-2.

Thiem U, Hinrichs T, Müller CA, Holt-Noreiks S, Nagl A, Bucchi C, Trampisch U, Moschny A, Platen P, Penner E, Junius-Walker U, Hummers-Pradier E, Theile G, Schmiedl S, Thürmann PA, Scholz S, Greiner W, Klaassen-Mielke R, Pientka L, Trampisch HJ (2011): [Prerequisites for a new health care model for elderly people with multiple morbidities: results and conclusions from 3 years of research in the PRISCUS consortium](#). Z Gerontol Geriatr.;44 Suppl 2:101-12.

Transparency Market Research (2014): [Anti-aging Market \(Anti-wrinkle products, Hair Color, Hair restoration treatment, Breast augmentation and Radio frequency devices\) - Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2013 - 2019](#).

Vallin J et Meslé F (2010): [Espérance de vie: peut-on gagner trois mois par an indéfiniment?](#) Population & Sociétés 473

Vaupel JW (2010): [Biodemography of human ageing](#). Nature;464(7288):536-42

Yang X, Debonneuil E, Zhavoronkov A, Mishra B (2016): [Cancer megafunds with in silico and in vitro validation: Accelerating cancer drug discovery via financial engineering without financial crisis](#). Oncotarget.

Zhavoronkov A, Debonneuil E, Mirza N, Artyuhov I (2012): [Evaluating the impact of recent advances in biomedical sciences and the possible mortality decreases on the future of health care and Social Security in the United States](#). Pensions; 17, 241-251

Zion Market Research (2017): [Anti-Aging Market \(Baby Boomer, Generation X and Generation Y\), by product \(Botox, Anti-Wrinkle Products, Anti-Stretch Mark Products, and Others\), by Services \(Anti-Pigmentation Therapy, Anti-Adult Acne Therapy, Breast Augmentation, Liposuction, Chemical Peel, Hair Restoration Treatment, and Others\), by Device \(Microdermabrasion, Laser Aesthetics, Anti-Cellulite Treatment and Anti-Aging Radio Frequency Devices\) : Global Industry Perspective, Comprehensive Analysis, Size, Share, Growth, Segment, Trends and Forecast, 2015 – 2021](#).