Fighting Aging as an Effective Altruism Cause:

A Model of the Impact of the Clinical Trials

of Simple Interventions

*Alexey Turchin\*, Michael Batin, Anastatia Egorova*

Science for Life Extension Foundation, Moscow

\*alexeiturchin@gmail.com, corresponding author

*Elena Milova*

Life Extension Advocacy Foundation

*David Denkenberger*

Global Catastrophic Risk Institute (GCRI);

Tennessee State University;

Alliance to Feed the Earth in Disasters (ALLFED).

**Abstract**: The effective altruism movement aims to save lives in the most cost-effective ways. In the future, technology will allow radical life extension, and anyone who survives until that time will gain potentially indefinite life extension. Fighting aging now increases the number of people who will survive until radical life extension becomes possible. We suggest a simple model, where radical life extension is achieved in 2100, the human population is 10 billion, and life expectancy is increased by simple geroprotectors like metformin or nicotinamide mononucleotide by three more years on average, so an additional 750 million people survive until “immortality”. The cost of clinical trials to prove that metformin is a real geroprotector is $65 million. In this simplified case, the price of a life saved is around eight cents, 10 000 times cheaper than saving a life from malaria by providing bed nets. However, fighting aging should not be done in place of fighting existential risks, as they are complementary causes.

**Keywords**: aging, life extension, immortality, metformin, effective altruism, clinical trials.

**Highlights:**

* Aging and death are the main causes of human suffering now.
* Simple interventions could extend human lives until aging is defeated.
* These interventions need to be clinically tested before FDA approval.
* A trial of the life extension drug metformin is delayed by lack of funds.
* Starting trials now will save 750 million people from death, at a cost of $0.08 for each life saved.

[1. Introduction 3](#_Toc509152654)

[1. Aging is currently the leading cause of human suffering on Earth 5](#_Toc509152655)

[2.1. Nature of aging 5](#_Toc509152656)

[2.2. Reasons biological aging is the greatest challenge of the 21st century 6](#_Toc509152657)

[2.3. Aging as a major cause of human suffering in the world 7](#_Toc509152658)

[2.4. Aging is the main cause of death in the US and in the world 8](#_Toc509152659)

[3. “Badness” of death 9](#_Toc509152660)

[3.1. Negative utility of death in preference utilitarianism 9](#_Toc509152661)

[3.2. Death of investor paradox 10](#_Toc509152662)

[3.3. Willingness to pay as a measure of the preference not to die 11](#_Toc509152663)

[3.4. Reasons why death is bad 11](#_Toc509152664)

[3.5. False arguments against badness of death 12](#_Toc509152665)

[3.6. Number of saved lives and years of increased life expectancy is the best measure of cost-effectiveness, not QALY 13](#_Toc509152666)

[4. Fighting aging is possible via cost-effective interventions, for which research is underfunded 14](#_Toc509152667)

[4.1. Human aging can probably be delayed by rather simple interventions 14](#_Toc509152668)

[4.2. Problems with clinical trials of antiaging therapies in humans 14](#_Toc509152669)

[4.3 Total research budgets on the fundamental problem of aging 16](#_Toc509152670)

[4.4. Life extension as a market failure: clinical trials could be funded only by governments, donations, or patients’ organizations 16](#_Toc509152671)

[4.5 Multiple approaches to fight aging 17](#_Toc509152672)

[5. The need for extensive clinical trials of simple interventions 18](#_Toc509152673)

[5.1 Long duration of proper clinical trials of the geroprotectors 18](#_Toc509152674)

[5.2 The need of fundamental research in fighting aging 19](#_Toc509152675)

[5.3 The biggest cost in clinical trials is paperwork 19](#_Toc509152676)

[5.4. The need for geroprotectors to be extremely safe drugs 19](#_Toc509152677)

[5.5 Several cost-effective interventions, which are able to extend human life 20](#_Toc509152678)

[6. Three cost-effective clinical trials 21](#_Toc509152679)

[6.1. Metformin as the potentially effective geroprotector, for which clinical trials are underfunded 21](#_Toc509152680)

[6.1.1 Effects of metformin on life expectancy 21](#_Toc509152681)

[6.1.2 TAME study as an icebreaker for future research 22](#_Toc509152682)

[6.1.3 Model of the impact of metformin trials on life expectancy and survival until radical life extension is developed 22](#_Toc509152683)

[6.1.4. Metformin safety 25](#_Toc509152684)

[6.2. Crowdfunding of simple important experiments on mice 25](#_Toc509152685)

[6.3. Clinical trials of diets in patient organizations 26](#_Toc509152686)

[7. Additional reductions in the price of life-extension solutions 27](#_Toc509152687)

[7.1. The price of anti-aging intervention could be negative, as it will lower insurance premiums 27](#_Toc509152688)

[7.2. Social changes could be the most cost-effective actions to increase global life expectancy 27](#_Toc509152689)

[7.3 Delivery problem could be solved by obligatory food fortification 28](#_Toc509152690)

[8. Fighting aging and research of existential risks 28](#_Toc509152691)

[8.1. How fighting aging could help in the research of existential risks 28](#_Toc509152692)

[8.2. How fighting aging and x-risks may contradict each other 28](#_Toc509152693)

[8.3. Preventing aging of x-risks researchers 29](#_Toc509152694)

[Conclusion 29](#_Toc509152695)

[Disclaimer 30](#_Toc509152696)

[Acknowledgments 30](#_Toc509152697)

[References: 30](#_Toc509152698)

# 1. Introduction

In this article, we will demonstrate that bringing aging under medical control is vital for reducing global suffering, and that there are untapped cost-effective interventions, which could save one human life, under certain assumptions, for $0.08. Such an approach is much more effective than one of the most effective current charities, which saves lives via malaria bed nets for around $1 500 per life saved (Pulkki-Brännström, Wolff, Brännström, & Skordis-Worrall, 2012).

A growing movement of “effective altruism” (EA) has appeared in recent years (MacAskill, 2015; P. Singer, 2015). It aims to do good globally in the most cost-effective ways, in a cause-neutral approach. The movement is represented by organizations such as “Give Well”, “Open Philanthropy”, and “80,000 Hours”. They aim to evaluate of the cost-effectiveness of philanthropy and to find efficient ways to create the biggest impact on the most important global problems. The EA movement attracts a lot of media attention and is securing increasing amounts of funding.

Currently, there are three main fields which EA has established as providing the biggest impact, based on dollars spent: global poverty prevention, including curing diseases common in the developing world, like malaria; reducing animal suffering; and global risk prevention, especially in the area of AI safety (Global Prioritisation Project, 2015). Some possible areas are surprisingly neglected, like political change [(Kissel, 2017)](file:///C%3A%5CUsers%5CAdministrator%5CAppData%5CLocal%5CTemp%5C%28Kissel%2C%202017%29) and curing depression (Plant, 2015).

More funding is now allocated according to EA recommendations, and donors, consciously or subconsciously, are orienting on EA narrative. As a result, other fields of philanthropy must now invest in proving their cause is important from the point of view of a large reduction in global suffering, and that the way they address their case is cost-effective. For example, Denkenberger (Denkenberger, 2017) recently wrote an article demonstrating that spending as little as $0.20 could be enough to save a human life by improving preparedness for food global crises.

Other fields could have a larger impact in suffering reduction but are currently neglected or minimally discussed. One such field is investment in fighting aging and life extension research. There are several organizations that accept donations and have performed high quality fundamental research on the nature of aging, including the TAME experiment, Buck Institute, and SENS Foundation.

Fluttershy did a comparison of healthy life years gained by anticancer research and by funding the SENS Foundation, which works on strategies for engineered negligible senescence (Fluttershy, 2015). He concluded that one health life year bought by cancer research costs around $3 000, and if this money were to be used on strategies for engineered negligible senescence, the price would be $0.059 for one year of life lived—not per life saved. The beneficial economical effects of the wide adoption of geroprotectors have been analyzed, as well (S. Bulterijs, 2016).

Gwern analyzed economical impacts of metformin and vitamin D as possible life extension interventions (Gwern, 2015). He concluded that “The expected life expectancy gain is 0.33 years or $16,800, while total cost of vitamin D supplementation is estimated at $761, for a profit of $15,300” based on his estimation of QALY price as 50 000 USD. For metformin, he gets 1 year of the life expectancy increase.

We will examine approaches other than SENS; these approaches may be even more cost-effective and closer to implementation. The first will be use of geroprotectors, especially metformin. Several other geroprotectors may have comparable or higher effects, including vitamin D (Mark et al., 2016), but none of these are as close to FDA approval as an anti-aging drug as metformin, which could be its main advantage.

We identify delays in clinical trials, and the first TAME trial of metformin to prevent aging (N. R. Barzilai, 2017) as a critical point, where intervention could help global life extension. The TAME study is expected to be supported by crowdfunding and thus doesn’t depend on either “big pharma” or government funding. The total cost of the study is estimated at $65 million. If it succeeds, and the FDA approves its use, it may pave the way to the global use of metformin as an aging prophylaxis drug. We expect it would increase median life expectancy by about three years, starting approximately 20 years after the start of the trial. Given that, in the future, other life-extension interventions will be available, hundreds of millions more people will survive until *longevity escape velocity,* and thus will be saved from death for an indefinitely long time. Thus, investing $65 million could save several hundreds of millions of lives, not least by accelerating the acceptance of geroprotectors.

Metformin, and several other simple interventions, could be tested via experiments with predictable price, time and design, as well as a high expected probability of success based on previous animal trials. People could implement these interventions on their own, as they are based on generally safe and cheap drugs, which are already approved by regulators for other conditions. Such drugs will have a negative cost for consumers, as they will delay age-related illnesses, and reduce expenditure on more expensive drugs; insurance companies may even lower premiums for those who take them.

Fighting global catastrophic risks (X-risks) may have an even bigger impact and cost-effectiveness under certain assumptions. We will compare fighting aging with preventing X-risks and demonstrate that the effectiveness of interventions against each is in fact similar, and such interventions are synergistic.

In Section 2 we explore the importance of the problem of aging, and demonstrate that aging and death are the main causes of suffering in the contemporary world. In Section 3 we review the problem of badness of death and the ways to quantify it. In Section 4 we demonstrate that untapped cost-effective mechanisms to fight aging exist, and in Section 5 we suggest a simple model to estimate such cost-effectiveness, using an example of funding experiments that prove the geroprotective properties of metformin. In Section 6 we explore other ways to cost-effectively fight aging, including social changes. In Section 7 we compare fighting aging with existential risk prevention, and demonstrate that they are, in fact, similar tasks.

# Aging is currently the leading cause of human suffering on Earth

## 2.1. Nature of aging

According to the WHO, “At the biological level, ageing results from the impact of the accumulation of a wide variety of molecular and cellular damage over time. This leads to a gradual decrease in physical and mental capacity, a growing risk of disease, and ultimately, death” (WHO, 2015).

Since aging represents a gradual accumulation of damage, age-related health deterioration manifests in later life. The first signs of health damage as a result of the aging processes can be observed in the 40s (e.g. wrinkles, onset of osteoporosis, decrease in muscle mass). Although these changes are neither linear nor consistent, most people will experience manifestation of some age-related diseases by their 60s.

## 2.2. Reasons biological aging is the greatest challenge of the 21st century

Life expectancy at birth is projected to rise globally from 70 years in 2015 to 77 years in 2050 and 83 years in 2100. At the same time, estimates of global fertility project a reduction from 2.5 children per woman in 2010–2015 to 2.4 in 2025–2030 and 2.0 in 2095–2100 (United Nations, 2015a). Taken together, these two trends will lead to rapid global *population aging.*

In 2015, there were 901 million people aged 60 or over, comprising 12 percent of the global population. This cohort is currently growing at a rate of approximately three percent per year. Some regions experience higher rates of population aging, like Germany (21.2% of people aged 65+) or Japan (26.3% of people aged 65+) (United Nations, 2015b). It is estimated that by 2050 all continents except Africa will have a quarter or more of their populations aged 60 or over.

In absolute numbers, the older population is estimated to be 1.4 billion by 2030 and 2.1 billion by 2050; it could rise to 3.2 billion in 2100. Experts believe this increase is inevitable in the short-to-medium term.

One of the consequences of population aging is changes in morbidity structure, or so-called epidemiological transition. Morbidity from infectious diseases is decreasing due to the spread of universal healthcare, but infectious diseases are replaced by non-communicable diseases (NCDs). The list of leading causes of disease and death in developed countries now mainly consists of age-related pathologies (Rao, Lopez, & Hemed, 2006). We can expect that by 2050, due to economic development and universal healthcare coverage, epidemiological transition will affect most countries. In that case, the list of leading causes of disability and death world-wide will correspond to today’s list in developed countries.

There are many age-related diseases that do not themselves cause death, but cause disability, rendering people unable to work and care for themselves. Such diseases include osteoarthritis, hearing loss, cataracts, and glaucoma, among others. Even older people who are willing to work and wish to remain relatively independent are often not able to do so because of deteriorating health. Loss of income because of disability leads to poverty, social isolation and other secondary negative social consequences (Cuaresma, Loichinger, & Vincelette, 2016).

The growing share of older people can also have another negative impact: an increase in the old-age dependency ratio—the number of dependent persons aged 65+ per 100 people of working age, 20–64. Recent study in the EU (a region experiencing very fast population aging) have shown that a higher old-age dependency ratio is related to lower per capita income growth for European countries over the last two decades. The research groups suggest that there are potential negative effects of population aging on the future economic growth of Europe (Cuaresma et al., 2016).

## 2.3. Aging as a major cause of human suffering in the world

Although this topic is rarely publicly discussed, aging represents the leading cause of human suffering globally. Other than the harm of death, aging also causes suffering, both directly for an individual, and through impacts on friends and family.

This relationship is not obvious, as we are culturally adapted to see age-related changes as normal, and economically based surveys show a u-shaped relation between satisfaction and age (Cheng, Powdthavee, & Oswald, 2017). However, if all objective and subjective data are taken into account, a plot of this relationship produces a convex form with peak of quality of life at 18, followed by decline (Easterlin, 2006).

Direct impacts of aging include increased suffering due to disease, inability to derive pleasure from things which were pleasant at younger ages (Bennett, Clarke, Kowalski, & Crocker, 2017), loss of memory (Leibing & Cohen, 2018), and other end-of-life experiences, as well as depression. Impacts of aging on families include mortality and morbidity of relatives.

Poverty is regarded as one of the current main sources of suffering on Earth, and it is important to compare it to the suffering of aging. The main difference is that there are two types of poverty: the poverty of the young and of the old. The poverty of young people is potentially temporary because of the potential for migration and economic growth, and it could also be compensated for by many cheap pleasures of youth, like sex, playing football, spending time with friends, etc. The poverty of the old, though, has no end except death.

Poverty is especially difficult for older people (Stolz, Mayerl, Waxenegger, & Freidl, 2017), who have no chance of escaping it. To be poor and old is completely different from being poor and young. The elderly need more expensive healthcare and can’t compensate for poverty with cheap pleasures like younger people. Hunger could end, but aging ends only with death. Global extreme poverty declined from 40 percent in 1980 to 10 percent in 2017, and if this trend continues, it will disappear in 10 years (Roser & Ortiz-Ospina, 2017). While extreme poverty is declining, the aging population is growing, and thus aging-related suffering is becoming a bigger problem.

People suffer from aging in many different ways: they can’t find work, they can’t have (healthy) children, they often suffer from chronic pain, sleep problems, and depression (Braun, Kopecky, & Koreshkova, 2017). They are less active, rarely play sports, and meet friends less frequently (Hawkley & Cacioppo, 2007). Their mental performance declines, and dementia is more probable (Gado, Hughes, Danziger, & Chi, 1983). Their beauty, sex life and libido decline (Mulligan, Retchin, Chinchilli, & Bettinger, 1988), their emotions are blunted and become more stereotypical, they lose their memories and can’t learn. They become lonelier, and they know that their condition will only deteriorate.

Humans also suffer from aging indirectly when their loved ones age and die—parents, siblings, friends, and even pets. Several times in life, a person experiences the age-related death of a close relative, typically parents and grandparents, but also sometimes spouses.

As most cases of cancer are associated with aging (Yancik, 2005), and for many cancer patients, effective pain therapy is not available, aging is the main cause of cancer suffering. Cancer pain is one of the most intensive and long-lasting pain.

More people are suffering from the effects of aging than are suffering from hunger in the world now (901 million vs. 795 million) (WorldHunger, 2016). Surprisingly, there are some data that hunger could help those suffering from it live longer because of the effects of calorie restriction (Everitt, Couteur, & David, 2007); however, children who suffer from hunger age faster (Abeliansky & Strulik, 2017).

Aging affects everyone. We can cure people of infections and alleviate poverty, but we can’t stop aging. The median age of the world population is now 30 (Statista, 2018); and soon after this age the first signs of aging typically become visible and may be felt. Women start to feel discomfiting effects of aging at about 25–30 years of age, and men soon after. Aging lowers mating and job prospects and increases healthcare expenditures. In our quickly changing world, older people have significantly fewer economic opportunities. Learning capacities decline with age, and it becomes increasingly difficult for them to prevent knowledge and professional skills from becoming obsolete. In addition, a larger older population means smaller average pension benefits.

Aging has not been the main source of suffering and death throughout human history: Poverty, wars and infectious diseases have prevailed in previous centuries, but now all of them are in decline, and only cultural inertia makes us pay more attention to these older causes of suffering.

The primary reason for aging being the main source of suffering is that it is currently the main cause of death in the world.

## 2.4. Aging is the main cause of death in the US and in the world

Cardiovascular diseases account for most NCD deaths, or 17.5 million people annually in world, followed by cancers (8.2 million), respiratory diseases (4 million), and diabetes (1.5 million). These four groups of diseases account for 82% of all NCD deaths (WHO, 2017).

It is important to consider that although most people die because of these diseases, overall health becomes more fragile as we age, and thus deaths from influenza (Sprenger, Mulder, Beyer, Van Strik, & Masurel, 1993), falls (Agnew & Suruda, 1993), and even car accidents (Katayama et al., 2018), positively correlate with aging.

The probability of death in actuarial science is presented by *Gompertz-Makeham’s law of mortality*, which consists of time-independent probability of death and a time-dependent exponential element (Gompertz law) (Gavrilov & Gavrilova, 1991). Technically, if there was no aging, only time-independent components would define human mortality. Now we will calculate maximum human life expectancy if there is no aging:

If we exclude the age-dependent component of mortality by extrapolating the minimal probability of death for 10-year-old white American girls, which is 0.000084 for a year (Actuarial Life Table, 2017), calculated life expectancy is 5925 years. Increasing the probability of death by including the factor of age, though, lowers it to 81. Hence, aging lowers the maximum human life expectancy by 73 times, or in other words, 98.3 per cent of white women in the US die because of aging.

To properly estimate negative value of aging, we need a way to calculate “badness” of death, which we will do in the next section.

Discussion of the question—is aging a disease?—is still active. Many scientists have demonstrated that it has many properties characteristic of disease, including changes in DNA expression and effects on mortality (Gavrilov & Gavrilova, 2017; Moscalev, 2017). In some sense, aging could be regarded as a meta-disease, similar to AIDS, as it is able to produce many other diseases.

# 3. “Badness” of death

## 3.1. Negative utility of death in preference utilitarianism

It is surprising that we must prove that death is bad. However, a special field of philosophy exists which studies the problem of badness of death (Bavelaar, 2016; Bercic, 2004; Blatti, 2012), plus some transhumanist authors are very vocal about death wrongness (Minerva & Sandberg, 2017), (Stolyarov, 2013), (Istvan, 2013).

Some may think that death is not bad, as it is the end of suffering; however, there are two ways to define suffering:

1) *Suffering is the experience of the qualia of pain.*

2) *Suffering is an event which has extreme negative utility, according to one’s value system*, as defined by "preference utilitarianism" (Peter Singer, 2011).

Based on the second definition, death is infinitely bad, as it means infinitely long non-existence. Humans value existence, plus the death is bad itself according to the values of most people.

Death is invariantly bad for most time-continuous utility functions. Regardless of what you want—fame, money, pleasure—the end of your existence means that you stop getting it; thus, death is equal to the loss of infinite utility. This makes death universally bad—that is, bad to almost any utility function—but our society has adapted to death in a way that ignores its extreme negative value, using constructions like religion, myths about overpopulation, steep discount rates, far mode thinking, etc.

It is certainly possible to imagine a human utility function in which death is not bad, for example, the sadomasochistic pleasure of self-killing, but this is rare, and bad from the point of view of others. Most people feel that death is very bad, but only when they discuss it in a near mode of thinking; thus, they fear death only if it is near. There are likely reasons based in evolutionary psychology that cause humans to ignore long-term threats of death.

Despite the claim that one can’t “feel” death, anticipation of the future death could be felt in the form of the fear of death, which is constantly present in adult life and may spoil quality of life (Cicirelli, 2006; Green, 1982).

## 3.2. Death of investor paradox

To address death from a utilitarian point of view, it is better to view it, not from the point of pain-suffering, but from the perspective of economics. It may be called the “death of investor” paradox. Imagine that an investor measures utility by the amount of money he has, multiplied by time he has owned it: dollar-years. If we calculate this utility, death becomes an infinitely large loss for the investor. Exponential types of discounting could cap the loss, but it would still be very large.

Humans, typically, have a rather large discount rate of 17 percent in financial decisions (Warner & Pleeter, 2001), but our discount rate takes into account our own mortality. We want to spend money before we die, and thus it can’t be extrapolated to an “immortal investor”. However, immortality implies infinite possible future utility, and thus can’t be discounted (at least in some models).

An interesting model of the effects of longevity on economics and demographics was presented by (Bogojevic, Balaz, & Karapandza, 2008), in which life extension is a commodity.

## 3.3. Willingness to pay as a measure of the preference not to die

 The willingness of people not to die could be indirectly estimated by their willingness to pay for expensive cures or risk reduction. It was estimated based on meta-analysis of 42 studies, that humans are ready to pay between $100K-400K for QALY, that is only for one year (Hirth, Chernew, Miller, Fendrick, & Weissert, 2000), while the median *household* income at the time of the study was only $37,000 in inflation non-adjusted dollars (US Census Bureau, 1997). Thus, US citizens in 1997 valued one year of their life 3–10 times more than the wellbeing of the whole family for the same period. The median size of the US family was around three people, so if this estimation is adjusted to one person, it equates to 9–30 years of economic wellbeing being equal to one additional year of life.

 With only a slight stretch, we can say that the typical American fears death 10 times more than poverty.

## 3.4. Reasons why death is bad

Now we list some other considerations of why death is bad:

1. *Death is the end of everything,* so any positive thing which is associated with life also ends with death (Bradley, 2013), e.g., if you like flowers, there are no flowers.
2. *Non-existence itself is known to create existential fear* (Baillie, 2013). Thus, the inevitability of death creates pain before death.
3. *The moments before death* *are often the most emotionally and physically painful*. The time before death often includes prolonged periods of unbearable pain of unthinkably strong intensity. Cancer, death by fire and asphyxiation are all known to cause unbearable suffering. By definition, the moments just before death are never reported.
4. *Death means that a person can't finish projects*, and in particular, will stop being useful as an effective altruist.
5. *Death is the loss of the information*, the human memory, the majority of which is unique.
6. *Death is unpredictable in both time and form*, and thus poses an extreme burden on any planning. The standard deviation of the moment of death by aging is around 15 years, and this uncertainty creates a large economic burden (Edwards, 2013).
7. *Deaths of relatives create intense, long-term emotional suffering* in those left behind (Marks, Jun, & Song, 2007). Even the most successful people have to deal with the deaths of parents and grandparents.
8. *Death in the 21st century is an enormous cost opportunity,* as survival up to a currently unknown threshold of new technologies could provide an almost unlimited lifespan in a completely new world full of new opportunities (De Grey & Rae, 2007).
9. *There is only a small probability that death is not the end,* because of the possibility of a simulation (Bostrom, 2003a), an afterlife, or because of “quantum immortality” (Almond, 2008). Any hypothetical existence after death is at best unpredictable, and at worst, equivalent to eternal torture (Aranyosi, 2012). Even the most religious people can’t be sure that they will end up in a paradise.

## 3.5. False arguments against badness of death

 There are several misconceptions that lead to the belief that ending death due to aging is bad:

1. *Stopping death will create “bad immortality”,* an infinite linear existence in time equal to infinite suffering because of boredom. But no-death means only “potentially indefinite life extension”, which could still be ended voluntarily, or could have some other endpoints. We cannot now understand such endpoints, but they may involve circular timelines or integration with superintelligent AI. Boredom was disproved by Bortolotti & Nagasawa (2009), and by Yudkowsky, who suggested the “general theory of fun” (Yudkowsky, 2009).
2. *Stopping death will result in overpopulation*. Only the number of births counts for overpopulation (Gavrilov & Gavrilova, 2010), and short-lived organisms like lemmings are the type of species that suffers from overpopulation.
3. *Stopping death could result in stagnation, infinite totalitarianism, or other bad social outcomes*. Our world changes so quickly that there is no time for such “stability” to take root.
4. *Stopping death takes opportunity from non-born people, who would be born if resources were freed up by death of aging humans*. The idea of an infinite universe where everything is possible kills the objection.
5. *Death can’t be experienced, so it can’t be bad.* This is so-called Epicurean conjecture (Blom, 1992). However, the badness of death is explicitly presented inside a human value system, for obvious reasons rooted in evolutionary psychology: most humans who haven’t feared death, have died.
6. *Death is needed to bring “meaning” to human lives*. To have meaning, someone must be alive, so this is a self-contradictory requirement. Moreover, the feeling of meaningless of life is a sign of depression or age-related brain changes, and it can be cured by methods short of death. In addition, knowing that everything you value will be destroyed is the perfect recipe to destroy a person’s feeling of meaning in life.
7. *Torture is worse than death*. Marcus Aurelius said: “When pain is unbearable, it destroys us; when it does not, it is bearable” (Aurelius, 170AD). There is no natural level of “unbearable” pain, only a decision level of unbearableness, where someone tries to stop pain by killing himself. However, if he survives the attempt, he will probably decide that it was the right decision to not kill himself because of pain. Research shows that sufferings become “unbearable” only if include psychological component of hopelessness (Dees, Vernooij-Dassen, Dekkers, Vissers, & Weel, 2011).
8. *Most people believe, or at least hope, that there is some form of afterlife*. The willingness to pay for not dying discussed above demonstrates that such a belief is not strong and is further diminishing in the current secularized society. Only Islamic State terrorists and some other radical groups seem to actually believe in a positive heaven in the contemporary world, but even they still need to be constantly brainwashed to act on this belief.

 In another article, Turchin showed (Turchin, 2018) that, because of the small probability of eternal suffering after death, connected with possibility of so-called “quantum immortality”, euthanasia is bad, but it could be replaced with cryotanasia (Minerva & Sandberg, 2017), that is a combination of euthanasia and cryonics, which mitigates this risk.

## 3.6. Number of saved lives and years of increased life expectancy is the best measure of cost-effectiveness, not QALY

There is a viewpoint that we should strive for “healthy aging”, which could be measured via quality-adjusted life years (QALY) (Hansen & Kennedy, 2016). However, this view is applicable only to a stable world, in which there is no technological progress.

If we take into account exponential technological progress, then the biggest impact on the utility of one’s life will be one’s ability to survive until some really good things arrive, the first of which will be new medical technologies.

Hence, surviving even 10 years in a poor physical state is better than three years in a perfect state, as it increases the possibility of surviving until some moment in the future, which will probably be the creation of beneficial superintelligent AI, which will help to dramatically increase life expectancy, as well as quality of life.

We will take a rather late date of 2100 for the arrival of AI, when it will happen with a probability of around 70 percent, according to aggregated expert opinion (Grace, 2017). We have shown that, for the purposes of AI risks we should take an earlier date of AI arrival, and for medical AI, we need a later date (Batin, Turchin, Markov, Zhila, & Denkenberger, 2018).

For example, if anyone who survives to 2100 gets an additional 1 000 years of life expectancy, and every year is 10 times better than his life before AI, then the total utility of his life “after AI” will be 100 times greater than the utility of life in the 21st century.

# 4. Fighting aging is possible via cost-effective interventions, for which research is underfunded

## 4.1. Human aging can probably be delayed by rather simple interventions

Aging has been slowed in many animal models using cheap, safe, long-term tested drugs, like metformin, enalapril, and aspirin (Alexey Moskalev, Chernyagina, Kudryavtseva, & Shaposhnikov, 2017). Aging has been slowed in mice by more than 30 percent through administration of rather simple drugs (see data at <http://geroprotectors.org/>).

But we can’t know how the geroprotector experimental data would transfer to humans, without experiments with human participants (Alexey Moskalev et al., 2016). We have some cohort studies which showed, for example, that diabetics who took metformin lived longer than a control group of healthy people (Bannister et al., 2014). People who had hot chili pepper in their diet had a six percent increase in lifespan, according to a recent cohort study (Chopan & Littenberg, 2017). But cohort studies provide weaker evidence than controlled, double-blind placebo-controlled clinical studies.

Negligibly senescent animals exist, like the naked mole rat (Ruby, Smith, & Buffenstein, 2018). The probability of death for these species doesn’t depend on time, and they live much longer than similar organisms. Therefore, aging is not universal. There are mammals that live longer than humans, like whales, which can live at least 200 years (Dovey, 2015).

All these factors combine to suggest that human aging may be slowed down by rather simple interventions.

## 4.2. Problems with clinical trials of antiaging therapies in humans

Most potential to fight aging is untapped, because until recently, little scientific research on slowing aging in humans has been done. It is quite likely that some simple interventions would work on slowing aging, but we have not tried them. Here are some reasons why aging research is rare compared to, say, cancer research:

1. *Such tests will take a very long time, because humans have long life spans*. There are ways to make such studies shorter, such as using biomarkers of aging (AA Moskalev & Batin, 2011) as substitute end points for mortality. Many simple experiments, which could have been done in the middle of the 20th century or earlier, have not been carried out until recently. Such experiments may have a rather simple design, like vitamin supplementation during life, but they should be longitudinal by nature, that is, they should be as long as human life in order to supply meaningful data. Thus, if such experiments started in the middle of the 20th century, we would be able to use their results now; however, if we start the same experiments now, it will take decades before they produce meaningful results, and during this time other technologies for life extension will mature.
2. *Research on the aging of humans is difficult because aging is not considered a disease under WHO classification* *(ICD)*. (Sven Bulterijs, Hull, Björk, & Roy, 2015; Zhavoronkov & Bhullar, 2015). Thus, the pharmaceutical industry is not interested in new anti-aging drugs, as it can’t sell them without FDA approval, and the FDA can’t approve a drug that lacks nosology and isn’t included in the ICD of the WHO.
3. *Many promising geroprotector candidates (drugs slowing aging) can’t be patented* as they have existed for decades. Thus, pharma and startups are not interested in investing in clinical trials.
4. *There was an idea that extending human life is immoral* even among gerontologists, as it was thought it would result in overpopulation (it will not), or create a larger burden on retirement plans (it will not) (De Grey & Rae, 2007).
5. *The field is a case of market failure: despite large demand, only a small percentage of money is going into actual research.* A large amount of money is spent on snake oil solutions, while really interesting experiments are underfunded. The total market of anti-aging supplements and other untested solutions is around 200 billion USD (Ghumare, 2015). The total research budget on the fundamental mechanism of aging, though, is only a small part of this figure and is not funded through these sales. This is also a problem with critical thinking and lack of communication between scientists and the public, that is, of human rationality.

*Many interventions, which are known to slow down aging, and generally improve health, are not implemented by the majority of the population*. This includes a healthy diet, physical activity, and reductions in smoking and alcohol consumption. These lifestyle interventions require will, and a fight with addictions, neither of which is easy to implement. The sugar and tobacco industries have also contributed to the promotion of their unhealthy products. Easily implementable anti-aging solutions should not be burden for the human will; ideally it would be as easy a pill, taken once a day (or less). However, even taking one pill a day is a large burden for many people; for example, many hypertension patients stop taking their medicine after several months. This basis of this problem is the same as that has led governments to add supplemental iodine to salt. A combination of drugs clinically proven to slow down cardiovascular risks, *Polypill*, is commercially available; it may offer geroprotective effects (Polypill.com, 2018). This is the type of solution that will be necessary.

1. As antiaging treatment will be applied to healthy middle-aged people before the onset of age-related diseases, *in the same way as vaccination, it must be extremely safe.* Safety must be ensured by extensive trials, and by personalized protection against rare adversarial cases.

In 2015, the US Food and Drug Administration (FDA) approved the first-ever test of metformin for slowing aging, called MILES (“Metformin in Longevity Study”). The study, which will be a rather short several-week experiment, is taking place at the Albert Einstein College of Medicine in New York (ClinicalTrials.gov, 2015). It seems that the experiment is still not complete as of February 2018.

One small trial is not enough to prove anything, but it is an important step for future trials, as it creates a precedent of FDA approval. The law system of the US is based on precedents, so it is especially important to create such a positive precedent as early as possible.

In parallel, another trial was announced by Nick Barzilai (N. R. Barzilai, 2017), TAME, Targeting Aging with Metformin. The expected cost of the experiment is 65 million USD, but only half of that amount was available in 2017, so the experiment has not yet started. The trial is expected to run for six years with 3 000 participants and will check for the frequency of various comorbidities.

## 4.3 Total research budgets on the fundamental problem of aging

The biggest player here is the *National Institute of Aging* in the US, with a budget of 1.2 billion USD annually. Not all of its spending is devoted to the research of the fundamental mechanisms of aging; instead, some is spent on age-related diseases, like Alzheimer’s (Nelson, 2015). The next-largest player is Google’s Calico, with total (not annual) funding of 500 million USD. All other players combined have smaller budgets, including the famous SENS by Grey, which in 2015, had a budget of around 4 million USD per year (Nelson, 2015). If we exclude age-related diseases, the total budget on fundamental research on aging could be estimated at an order of magnitude of 100 million USD in 2015. In the subsequent two years a growth of interest in human longevity research was observed, but mostly in the form of startups, which are not interested in long-term non-patentable research.

## 4.4. Life extension as a market failure: clinical trials could be funded only by governments, donations, or patients’ organizations

We could use the following metaphor. There are two islands, and there is no bridge between them:

**Demand island:** On this island of demand for antiaging are older people, women who want to be younger, children who want to prevent their parents from aging, etc. These people, who are old or ill now, may regret that they did not pay for the creation of general prevention drugs. They want to spend a lot to prevent aging. The visible part of this demand is a 200 billion USD annual spend on unproven anti-aging therapies (Ghumare, 2015). But the real part of this demand is larger, as most rational customers understand that there are no current working solutions.

**Supply island:** On this island are scientists, who have ideas how to fight aging, but don’t have money for experiments.

But there is no bridge between these two islands, because there are three types of sharks in the murky waters: scammers, religion, and the FDA.

1. Scammers sell untested solutions and use the revenue for personal advertising. The nature of any anti-aging drug is that real effects can’t be immediately observed, and this results in market failure. That problem was solved in the case of vaccination and can be solved for this case as well.
2. Religion, and in general, traditions, are psychological defenses against fear of death. They promise that immortality already exists in heaven, and that life extension is unnatural. Thus, religion is the biggest scammer, and the biggest seller on the market for immortality. But it is also an example of “Stockholm syndrome”: people take the side of death to escape fear of it, and thus are driven to say that death is natural.
3. The FDA doesn’t recognize aging as a disease, and so pharma can’t register clinical trials of anti-aging drugs, and government can’t spend money on the allegedly non-existent disease.

In recent years, interest in the idea of fighting aging has grown, manifested in the creation of companies such as Calico and many startups. Governments have started to recognize that life expectancy is a great proxy to measure overall good in their country, among them Russian prime minister Medvedev (Markelov, 2017). But this growth alone is not adequate to address the problem.

## 4.5 Multiple approaches to fight aging

The fight against aging is gaining traction, and multiple startups are exploring various approaches, however most of these approaches require extensive animal, safety and human efficacy tests, so their global implementation could be decades from now. Many people will not survive to this time, but if they do, they will have a chance to access several powerful therapies, which will ensure reaching longevity escape velocity. These therapies include:

* Stem cell-based therapies (Neves, Sousa-Victor, & Jasper, 2017)
* Anti-inflammatory drugs (Pedersen, 2009)
* Elimination of damaged and senescent cells (Naylor, Baker, & Deursen, 2013)
* Telomerase reactivation (Jaskelioff et al., 2011)
* Epigenetic drugs (Vaiserman & Pasyukova, 2012)
* Activation of chaperones and proteolytic systems (Calderwood, Murshid, & Prince, 2009)
* IIS and mTOR inhibition (Johnson, Rabinovitch, & Kaeberlein, 2013), AMPK (Burkewitz, Zhang, & Mair, 2014) and sirtuin activation (Houtkooper, Pirinen, & Auwerx, 2012)
* Mitohormetics (Ristow & Schmeisser, 2014), mitophagy (Lemasters, 2005)
* Blood borne rejuvenation factors (Castellano, Kirby, & Wyss-Coray, 2015)
* Genetic therapy (de Jesus et al., 2012)
* Microbiome regulation (Heintz & Mair, 2014)

When these interventions are combined, they could provide decades of additional life expectancy, and if we account for expected success in medical AI, we could achieve even larger gains (Batin et al., 2018), but we need to survive until that time, and that is why we need fast track trials that are simple, safe and easily implementable on a global scale.

# 5. The need for extensive clinical trials of simple interventions

## 5.1 Long duration of proper clinical trials of the geroprotectors

As human aging takes decades, the duration of the experiments which actually measure the effects of any simple intervention are also very long. Decades of possible research have been lost because proper simple experiments were not done. If such experiments had been started in the middle of the 20th century, we might already know which simple vitamins or drugs like aspirin actually extend human life.

There are several ways to accelerate such experiments, by using biomarkers of aging, animal models and AI (Batin et al., 2018; Moskalev & Batin, 2011), but even calibrating biomarkers requires time.

Long experiments are also more expensive if they are done according to the protocols with a lot of paperwork. However, the design of such experiments may be extremely simple: a large group of people should take a supplement every day and then its mortality will be compared with a control group.

## 5.2 The need of fundamental research in fighting aging

This highlights the more general need of fundamental research in the nature of aging, that is research which is not aimed at immediate commercialization, but on understanding the nature of aging, which is also longitudinal by nature.

## 5.3 The biggest cost in clinical trials is paperwork

It is important to note that most of the cost of the trial is organizational, as the price of the drug used (based on two cents for pill) is 15 000 USD, and the participants are volunteers.

Lowering the price for clinical trials using AI, using distributed data collected via wearable gadgets and volunteers, is another cost-effective intervention, as well as more test-friendly regulations, with lower legal costs (Batin et al., 2018). Organizations such as the Open Longevity project may also be able to help; it is currently working on organizing distributed clinical trials via volunteers (“Open Longevity,” 2017).

Scott Alexander recently described a small study which may have great benefit for bipolar disorder, which had had died because of Kafkian requirements in the paperwork. The study was just a poll, but thousands of hours were spent on absurd requirements that, in addition to increased cost, also undermined the blind structure of the study (Scott, 2017).

Other jurisdictions like China may have simpler laws but suffer from other scientific problems like fraud. Moving studies to jurisdictions with more permissive regulations is an established strategy; for example, a study funded by Peter Thiel recently moved to St. Kitts study of a herpes vaccine to St. Kitts to escape regulatory difficulties (Brown, 2017).

## 5.4. The need for geroprotectors to be extremely safe drugs

One suggested approach for the safe use of geroprotectors is to use them in smaller doses than during medical therapy.

Prophylaxis of aging could be compared with vaccination, as a cheap, early intervention, which can increase life expectancy. In general, like vaccines, the safety of geroprotectors must be higher than safety of other drugs, as they will be given to a larger, healthier, and relatively younger population. Even an extremely rare complication will create a negative PR effect, and slow down early adoption, as well as the development of new anti-aging drugs.

There are many examples of bad PR from early experiments delaying research for decades. For example, the first (and last) xenotransplantation of a baboon heart was in the 1970s; its failure resulted in harsh criticism and cessation of research (Bailey, Nehlsen-Cannarella, Concepcion, & Jolley, 1985). Early failures in gene therapies have led to barriers in this field. Extreme events in the early years of the preventive intervention would mean a large loss of healthy life years. For perspective, remember that even walking and running can be dangerous, if we include risks of falls, accidents, and crimes. Such risks depend on age, terrain, and the social risks of the neighborhood.

There are several substances which have consumed by humans for millennia, and thus are known to be extremely safe, and are also culturally accepted. Green tea, curcuma, olive oil, grapes and peppers have all been shown to have life-extending benefits. We could even say that these plants co-evolved with humans for mutual longevity. However, no clinical trials have been conducted to their life extension properties on humans.

If we have a bunch of extremely safe interventions, it seems that combining them could have a net positive effect on life expectancy, *even if some of them do not work*. If we can prove this, theoretically, small dietary changes could increase human life expectancy.

## 5.5 Several cost-effective interventions, which are able to extend human life

We could identify criteria of simple cost-effective interventions for life extension:

1. They are already implemented by large group of healthy adults on anon-prescription basis, and cohort studies support their effects on life extension.
2. They are cheap enough to be bought by almost everyone.
3. They are easy to implement, without requirement of enormous will.
4. They could be quickly implemented globally without overstretching limited supplies of some types of resources, so billions of people could have access to it.

Now we will look at several already suggested interventions with this point of view in mind:

* + - 1. *Mediterranean diet with large amount of fish and olive oil*. However, it can’t be currently provided to all, as olive oil is limited resource, as well as wild fish. However, maybe balanced nature of the *Mediterranean* diet is the key (Martinez-Gonzalez & Martin-Calvo, 2016)
			2. *Limiting smoking*. Quitting smoking is personally difficult, but replacing it with vaping may be simpler. However, the relative safety of vaping should be proved (Levy et al., 2018).
			3. *Physical activity.* It is well known that more activity is beneficial to health but it is not known how to help people move more. Runners live 3 years longer (Lee et al., 2017).
			4. *Limiting sugar consumption*. Again, sugar is addictive and supported by large companies, but its consumption could be limited by tax increase on sweet beverages (Long et al., 2015).
			5. *Vitamin D*. It seems current RDAs for vitamin D are non-adequate, and there is a lot of research about its benefits. (Bjelakovic et al., 2014).
			6. *Ten cups a day of green tea*. It is not clear whether it is possible to provide enough green tea for billions of people without overstretching agriculture. But some active compounds could be identified and synthesized (Nakachi, Eguchi, & Imai, 2003).

# 6. Three cost-effective clinical trials

## 6.1. Metformin as the potentially effective geroprotector, for which clinical trials are underfunded

### 6.1.1 Effects of metformin on life expectancy

Human clinical trials of metformin may demonstrate it as an effective geroprotector, a drug that slows all signs of aging in humans and increases health span and total life span.

Metformin has been extensively studied for life extension in animals and has demonstrated relatively minor but consistently positive results. Metformin administration leads to life extension in humans according to a cohort study (S. Bulterijs, 2017). The drug has minor side effects compared with other candidate geroprotectors.

One of the most recent reviews at time of publication is “Metformin reduces all-cause mortality and diseases of ageing, independent of its effect on diabetes control: A systematic review and meta-analysis” (Campbell, Bellman, Stephenson, & Lisy, 2017). The meta-analysis of 200 previous publications concluded that “Diabetics taking metformin had significantly lower all-cause mortality than non-diabetics (hazard ratio (HR) = 0.93”. This means that ill people had a 7 percent *lower* mortality rate than healthy people if they were on this drug. The hazard ratio was 28 percent lower in metformin cases than for diabetics on other therapies, like insulin.

Lower mortality is achieved due to a reduction in the risk of age-related diseases, so it is possible to conclude that metformin slows down the main pathways associated with aging. Unfortunately, a 7 percent lower hazard ratio cannot be translated to a 7 percent increase in life extension because of the exponential nature of the Gompertz curve (Dehbi, Royston, & Hackshaw, 2017). For example, a 1.13 hazard ratio (associated with meat consumption) is a loss of only one year of life expectancy, according to an online calculator (David, 2012). The TAME study expected that the size of an effect on mortality of 30 percent translates into an increase of approximately three years of life expectancy.

The main mechanism of action of metformin is as an insulin sensitizer, but in fact it also targets many mechanisms of aging, including mTOR, DNA damage, and inflammation (N. Barzilai, Crandall, Kritchevsky, & Espeland, 2016). Thus, its effect on life expectancy effect occurs, not by curing one disease, but by *slowing aging in general*, represented by slowing all age-related diseases.

The effects of metformin on life extension decline with age: one must start taking it as early as possible: “When started early in life, the mean lifespan was increased by 14%, but with initiation at older ages, this effect declined” (N. Barzilai et al., 2016). Tests in mice gave different results: the maximum life extension was reported as 40 percent in outbred female mice (Anisimov et al., 2011), and the median in all mouse types was reported as 4–6 percent (Martin-Montalvo et al., 2013).

### 6.1.2 TAME study as an icebreaker for future research

The expected benefits of the TAME study include not only examination of the life-extension properties of metformin, but also the opening of a pipeline for tests of other drug candidates and combinations. It will also pioneer refinements in the methodology of human tests for life extension, including pharma-independent crowdfunding. Thus, even if TAME fails to demonstrate that metformin possesses life-extending properties, it will still accelerate development of life extension therapies.

Dr. Barzilai, head of the TAME study, has said: “Our goal is to establish the principle of using a drug, or two in combination, to extend health span. The best we can expect from metformin is two or three additional years of healthy aging. But the next generation of drugs will be much more potent” (Brody, 2016). It seems that many scientists are afraid to say that by delaying aging they will also extend the human life span. “In 1980, Dr. James F. Fries, a Stanford University physician who studied chronic disease and aging, proposed that a ‘compression of morbidity’ would enable most people to remain healthy until a certain age, perhaps 85, then die naturally, or after only a brief illness” (Brody, 2016). But in most animal trials, metformin not only delayed the onset of aging diseases, but also extended life.

### 6.1.3 Model of the impact of metformin trials on life expectancy and survival until radical life extension is developed

Technologies are developing that provide the possibility of radical life extension by means of cyborgisation, brain uploading, and nanotech. The rise of these technologies as viable strategies will happen gradually, but many people alive now will not survive that long.

For simplicity’s sake, we will use a one-step model, where everybody who survives until 2100 gets “potentially indefinite life extension” of thousands and maybe even millions or billions of years. They will live as long as they want to, not limited by involuntary death or any type of suffering. In other words, they will completely escape the risks of involuntary death.

By many projections, the human population will be ~10 billion people around 2100 (United Nations, 2017b). Their life expectancy, if we account for other improvements to quality of life and medicine, but not for specialized anti-aging therapy, will be similar to the life expectancy in the most advanced countries in the world now, around 80 years. There is uncertainty of about ± 2 billion people in this estimate of total population, connected with potential variance of fertility and mortality rates (United Nations, 2017a); however, variance in mortality has only a minimal impact.

Here, we assume that the problems of sustainable development will be solved by future technological advances, which will occur in parallel to the technologies which will provide life extension, like genetic engineering.

Calculation of the exact effects on population of an increase in average life expectancy is difficult, because of the complex age structure. For simplification, assume:

1. Five billion people will be born in 2020 and will have a life expectancy, without geroprotectors, of 80 years. Assume another 7.5 billion were born at a different time or haven’t taken metformin; in that case, only 2.5 billion of them survive until 2100, because life expectancy is 80. This is the main simplification of our model, as in reality, most of these five billion will be born during the first half of the 21st century.
2. Total population (without metformin) in 2100 is 10 billion.
3. This year (2100) sees the sudden appearance of a powerful new life-extension technology, which will mostly solve the problem of death due to aging.
4. Human life expectancy could be extended by three years, i.e., 3.75 percent, a number that seems to be achievable by wide and early adoption of metformin as a geroprotector, if clinical trials confirm its efficacy. From which 1 years of life expectancy increase comes from metformin (gwern, 2015), and 2 more from combination of all other simple interventions which could be tested and implemented during with 80 years period and which tests become possible after trail-blazing metformin test. Combination of geroprotectors is the most promising instrument for low-tech life extension (Batin et al., 2018).
5. Every year of delay in the start of the first clinical trial, results in one year of delay in the start of global adoption *of all possible* geroprotectors, which translates to a 1/80 decrease of the population effect in 2100.

Because of the steep curve of the Gompertz law, a three-year increase in life expectancy is equivalent to lowering mortality by 30 percent, the expected size of the effect in the TAME study. This means that 30 percent more people (of the old cohort) will survive until 2100, in our model 0.3 х 2.5 х 109 = **750 million people**. This is a surprisingly large result, made possible by the steep nature of the age-mortality curve.

Each year of delay in the global implementation of antiaging therapy is equal to a loss of life of approximately 1/80 = 1.25 percent of those who could benefit from it by surviving until strong AI, in our case, **9.375 million people**. Bostrom’s “Astronomical Waste” offers similar logic, where a small delay in the implementation of beneficial AI results in enormous future loss (Bostrom, 2003b). Note that in this model we assume that the delay in the metformin trial will not produce a delay in final medical AI implementation. Given this, along with the many other potential sources of uncertainty, we can only indicate the order of magnitude for most effects.

Proving the geroprotection properties of any drug, including metformin, will require quite a long study, which will include several experiments. However, none of these experiments can start if the first proof of concept experiment is not performed. In our case, every year of delay in starting the TAME study is equal to the loss of almost 10 million human lives.

Given that the full price of the TAME study is 60 million USD, saving 750 million lives translates into approximately 0.08 USD for each saved life. The economic effects of such a study will also include cheaper health care. In his interview “[Barzilai estimated that]…even a 20 percent cut in how fast people age could save more than $7 trillion over the next half-century in the United States alone” (Brody, 2016).

Metformin costs $0.02 per pill, and for the purpose of life extension a smaller dose than used in diabetes therapy may be appropriate. For life extension, it may even be taken in courses, which would reduce costs even more. Bulk prices of the metformin may be even cheaper, but in western pharmacies it is much more expensive. As we show in the next section, it will have a net negative price for a customer, because of consumer savings on cheaper medical insurance.

Even if slowing down aging is more expensive than 8 cents per life saved, it is still cost-effective, at 10 000 times the margin of the next competitor—fighting malaria via bed nets. Only prevention of x-risks and food crises may be as effective in saving lives.

 In developed countries, saving one life, for example, by improving road safety, typically costs 1–10 million USD (Robinson, 2008). This cost is 10–100 million more time more expensive than saving lives via funding clinical trials for geroprotectors.

### 6.1.4. Metformin safety

This article should not be interpreted as medical advice to start taking metformin for personal life extension, as the results of clinical trials are not yet in, and confirming safety is one of the primary objectives of clinical trials for all new therapies. Barzilai suggested a deeper analysis of metformin’s safety profile (N. Barzilai et al., 2016).

There are two main concerns about metformin safety. One is the risk of lactoacidosis. This is a very rare condition, but it could affect people rather randomly, and could even result in death. Some researchers claim that it never occurs in healthy people on metformin (Lalau et al., 2017). Another potential risk is metformin-accelerated accumulation of beta-amyloid, which may increase the risk of dementia. This effect has appeared only in some studies, while others demonstrate improved cognitive outcomes (Wang, Lorenzo, Habib, Jo, & Espinoza, 2017).

Publication and other biases could demonstrate risks of many types, including those related to the placebo effect; some statistical abnormalities will always appear in any study. But the potential risks of metformin still need to be addressed by clinical trials, as well as personalization of the therapy. Tests of renal function as well as genetic tests should find those people who may suffer from these negative outcomes. Easily-available test strips for lactoacidosis, or other noninvasive measures, like smartphone apps, may also reduce rates of negative outcomes, and help reduce fear of the new drug.

## 6.2. Crowdfunding of simple important experiments on mice

As many human clinical trials are expensive because of their length and safety conditions, much cheaper tests may be done on mice. The same experiment on mice is approximately 1000 times cheaper than on humans, but not all mice results are directly translatable to humans.

However, mice experiments are the first step required for many useful human experiments, and it may be surprising that even some simple mice experiments are underfunded or postponed by ethical concerns (like head transplantation and organ transplantation between clones).

There are many ideas for interesting experiments on mice, but even they require funding in the order of 1 USD for 1 day for 1 mouse. As life extension experiments are long by definition, and their effects are small, a large population of mice is needed in order to observe differences in mortality.

For example, testing all already existing drugs on mice for life extension effects could be a great experiment for identifying potential geroprotectors. Gudkov and Chikunov did such experiments on 1000 mice groups, but the small size of the groups and large number of them increased the probability of noise. They decided not to publish the results and tried for a commercialization pass.

Commercialization and its detrimental effects on research quality could be escaped if the experiments were crowdfunded, and thus their results are publicly owned.

That is why Lifespan.io ran small crowdfunding campaigns, all six of which were overfunded. the small number of curated projects guaranteed that the projects would be attractive enough money to start the experiments. The size of the projects is between 20,000 and 50,000 USD.

Many mice experiments are needed to identify new potential geroprotectors or useful combinations of them. Many experiments need to be repeated in multiple conditions and labs in order to exclude errors, and many experiments will produce negative results. We estimate that between 100 and 1000 mice experiments are needed to get information which is useful for human life extension (and getting this information also requires tests on larger and longer living animals, which will be more expensive.)

Lifespan.io is working on identifying which underfunded experiments could have the biggest impact via their novelty on the future of life extension research, and which scientists are able to perform these experiments. People can support Lifespan.io via their recurrent Life Span Hero fundraising which pays for the management of the projects.

## 6.3. Clinical trials of diets in patient organizations

Calorie restriction has been shown to extend the life of mice, for several reasons, but it is not known if it works for primates. Intermittent fasting is also works great on mice, but humans will have obvious difficulties to fast 5 days every month it will spoil their productivity. That is why V.Longo suggested *fast mimicking diet* (FMD) in which only protein content and calories are limited but the food is still very delicious and diverse. Tests of this diet on mice showed lowering of IGF-1, which is associated with longer lifespan (Brandhorst et al., 2015). However, the “FMD” brand is patent protected and can’t be tested independently.

Many people are experimenting themselves with various forms of dietary interventions, and also implementing medical tests on themselves, but most of these data are lost for science, as people do not share it and they don’t become big data, which could be analyzed by contemporary machine learning systems. If a lot of people were to upload the data in some form of social network in an anti-aging patient organization, it would be equal to clinical trials of dietary interventions without the typical costs of such trials.

It is important to organize people in such a way that all of them make the same array of tests before and after dietary intervention, and this array of tests should be maximally close to the biomarkers of aging. As patients will pay for their own tests and for the dietary intervention, and since they would have these costs regardless, the only cost is creating a computer interface which could collect the data from them.

*Horizontal patient organizations* will make clinical trials cheaper, and will reduce fraud, as they will bypass the biggest part of bureaucracy, and the participants will volunteer for free.

One such organization which accepts donations and is preparing clinical trials of diets is *Open Longevity,* which was able to attract thousands of volunteers with an estimated budget of around 70,000 USD collected via ICO.

# 7. Additional reductions in the price of life-extension solutions

## 7.1. The price of anti-aging intervention could be negative, as it will lower insurance premiums

The price of a lifetime supply of metformin, 500 USD, will pay for an additional three years of life expectancy and a proportional delay of age-related diseases.

However, the actual price of the therapy for a person could be negative, because medical insurance companies will be interested once people start taking age-slowing drugs, as it will delay payments on medical bills. Insurance companies could gain interest on this money. For example, if 100K of medical bills is delayed by three years, and the interest rate is two percent, the insurance company will earn 6 000 USD on later billing. Thus, insurance companies could provide incentives such as discounts or free aging treatments to those who use antiaging therapies.

## 7.2. Social changes could be the most cost-effective actions to increase global life expectancy

Attracting 60 million USD via crowdfunding for the TAME trial is still very difficult. The biggest donations to the SENS foundation, the most famous anti-aging organization, were on the order of $1–3 million (Barrett, 2018). Thus, even more cost-effective solutions are needed, and we identify some cheaper solutions where some work has already been done:

1. *Lobbying WHO to recognize aging as a disease*, this will give big pharma a legal right to run research on life extension drugs. (Jin, Simpkins, Ji, Leis, & Stambler, 2015; Stambler, 2017; Zhavoronkov & Bhullar, 2015).
2. *Creation of political parties, like the German party for medical research (Partei für Gesundheitsforschung)* that recently won around one percent of the vote in a local election in Berlin, could help to funnel government money into scientific research (Partei für Gesundheitsforschung, 2018).
3. *Horizontal patient organizations*.

## 7.3 Delivery problem could be solved by obligatory food fortification

One of the main problems is not only identifying cheap life extending intervention, but cost-effectively delivering it to billions of people. Selling it as a supplement will not work much, as most people will not take it, for either economical or cognitive overload reasons.

However, the problem has been solved for some other essential and extremely safe nutrients, like iodine, which is added to salt in low levels.

Because of the need to check for side effects, metformin food fortification is not possible. However, some AI empowered system where people take an obligatory (if they signed for the program) daily pill, and also have a test every day (may be of a person’s pee in a smart house restroom) could solve the global delivery problem, as discussed in (Batin et al., 2018).

# 8. Fighting aging and research of existential risks

## 8.1. How fighting aging could help in the research of existential risks

Fighting x-risks is reasonable only if one thinks that human life has value. The same is true for life extension and fighting aging. Basically, it is the same task—preventing death—on two different levels, personal and civilizational.

People who live longer have a greater chance of dying from x-risks, so they may be more interested in their prevention. Risk aversion is a personal trait, and many people are interested in both topics. By promoting life extension, we simultaneously promote the idea of x-risks prevention, as these two interests correlate.

## 8.2. How fighting aging and x-risks may contradict each other

A popular objection is that more research into the biology of aging will increase the chances of global catastrophe connected with synthetic biology.

While the risks of biocatastrophe are very serious (Millett & Snyder-Beattie, 2017), they are dominated by the risks of multipandemic created by biohackers or rogue states (Turchin, Green, & Dekenbergern, 2017). Multipandemic could result from the exponential progress of biotechnologies, and there is little that can be done about this risk.

In anti-aging research, hypothetical global risks are associated with artificial viruses which will deliver genetic therapy; hypothetically, such viruses could run out of control, but this is not a danger associated with simple chemical geroprotectors.

Dangerous experiments with viruses for self-modification may contribute to the creation of a multipandemic. But such a contribution could be rendered negligibly small if it is done in a controlled environment, in professional labs. Lis Parish created viral vectors and injected herself with them; this was genetic therapy outside of a controlled environment, which could be alarming (Parrish, 2015).

## 8.3. Preventing aging of x-risks researchers

Many AGI safety researchers and EA activists are currently in their 20s, and it is natural to them to ignore the risks of aging at this age. They may rationally expect that they will survive until the creation of strong AI anyway, so the only difference for them will be whether this AGI is safe or not.

But creation of AI alignment theory may take decades, and AGI safety researchers will age in that time. Eliezer Yudkowsky will be 38 in 2018, and Nick Bostrom will be 45. The peak of productivity for physicists is estimated to be age 48 (Choi, 2011); after age 50, productivity declines, as can be seen in the performance of chess masters. Many of the best brains in the field of AI safety could start to age before they have a chance to create safe AGI theory, or their performance will be suboptimal because of brain aging. Brain aging happens at different rates in different people, so some start to decline much earlier; these individuals will benefit the most from solutions that slow brain-aging.

# Conclusion

Geroprotectors are probably the cheapest way to fight aging, as most research on their safety, chemistry and side effects has been already done. There are other approaches, like genetic therapy for aging, but these require much *de novo* research. High tech approaches could also increase the risks of dual-use technology: as medical and as military, which can’t happen with classical geroprotectors. As a result, their testing for safety and mass adoption will take much longer, and they will not have a global effect for decades.

Many promising geroprotectors are over-the-counter drugs or are almost freely available. Pharmaceutical companies can’t make money from such treatments, and the general population are unaware of their potential for slowing aging. Funding geroprotector tests is a promising area, in which inexpensive altruistic action could have a large effect on the public good.

# Disclaimer

Alexey Turchin and Michael Batin works on non-repayable terms for the Science for Life Extension Foundation in Moscow. Elena Milova works for Lifespan.io. No commercial interest is connected with the TAME metformin trial. This article represents the views of the authors and does not necessarily represent the views of the Global Catastrophic Risk Institute.

# Acknowledgments

We would like to thank Elvira Kinzina and members of the *effective-altruism collective editing* group for help in improving this article. All possible errors are ours.

# References:

1. Abeliansky, A., & Strulik, H. (2017). Hungry children age faster. *Discussion Papers*, *322*. Retrieved from https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3040909
2. Actuarial Life Table. (2017). Actuarial Life Table. Social security. Retrieved from https://www.ssa.gov/oact/STATS/table4c6.html
3. Agnew, J., & Suruda, A. J. (1993). Age and Fatal Work-Related Falls: SHORT NOTE. *Human Factors*, *35*(4), 731–736. https://doi.org/10.1177/001872089303500411
4. Almond, P. (2008). Quantum Suicide and Inconsistency: Assuming you will survive quantum suicide may be simplistic. Retrieved from https://web.archive.org/web/20120309233248/http://www.paul-almond.com/QuantumSuicideInconsistency.pdf
5. Anisimov, V. N., Berstein, L. M., Popovich, I. G., Zabezhinski, M. A., Egormin, P. A., Piskunova, T. S., … Kovalenko, I. G. (2011). If started early in life, metformin treatment increases life span and postpones tumors in female SHR mice. *Aging (Albany NY)*, *3*(2), 148.
6. Aranyosi, I. (2012). Should we fear quantum torment? *Ratio*, *25*(3), 249–259.
7. Aurelius, M. (170AD). *Meditations*. Everyman’s Library.
8. Bailey, L. L., Nehlsen-Cannarella, S. L., Concepcion, W., & Jolley, W. B. (1985). Baboon-to-Human Cardiac Xenotransplantation in a Neonate. *JAMA*, *254*(23), 3321–3329. https://doi.org/10.1001/jama.1985.03360230053022
9. Baillie, J. (2013). The expectation of nothingness. *Philosophical Studies*, *166*(1), 185–203.
10. Bannister, C. 1, Holden, S. E., Jenkins-Jones, S., Morgan, C. L., Halcox, J. P., Schernthaner, G., … Currie, C. J. (2014). Can people with type 2 diabetes live longer than those without? A comparison of mortality in people initiated with metformin or sulphonylurea monotherapy and matched, non-diabetic controls. *Diabetes, Obesity and Metabolism*, *16*(11), 1165–1173.
11. Barrett, J. (2018, February 2). SRF Receives $2.4M Ethereum Donation from Vitalik Buterin. Retrieved February 8, 2018, from http://www.sens.org/outreach/press-releases/srf-receives-24m-ethereum-donation-from-vitalik-buterin
12. Barzilai, N., Crandall, J. P., Kritchevsky, S. B., & Espeland, M. A. (2016). Metformin as a tool to target aging. *Cell Metabolism*, *23*(6), 1060–1065.
13. Barzilai, N. R. (2017). Targeting aging with metformin (TAME). *Innovation in Aging*, 743–743.
14. Batin, M., Turchin, A., Markov, S., Zhila, A., & Denkenberger, D. (2018). Artificial Intelligence in Life Extension: from Deep Learning to Superintelligence. *Informatica (Slovenia)*, *41*, 401.
15. Bavelaar, K. T. (2016). *Puzzling with nonexistence: can death be bad for the one who dies?* (Master’s Thesis).
16. Bennett, E. V., Clarke, L. H., Kowalski, K. C., & Crocker, P. R. (2017). From pleasure and pride to the fear of decline: Exploring the emotions in older women’s physical activity narratives. *Psychology of Sport and Exercise*, *33*, 113–122.
17. Bercic, B. (2004). Death.
18. Bjelakovic, G., Gluud, L. L., Nikolova, D., Whitfield, K., Wetterslev, J., Simonetti, R. G., … Gluud, C. (2014). Vitamin D supplementation for prevention of mortality in adults. *The Cochrane Database of Systematic Reviews*, (1), CD007470. https://doi.org/10.1002/14651858.CD007470.pub3
19. Blatti, S. (2012). Death’s distinctive harm. *American Philosophical Quarterly*, *49*(4), 317–330.
20. Blom, A. J. M. (1992). *In Defence of Euthanasia: The Epicurean View of Death* (PhD Thesis). University of Waterloo (Canada).
21. Bogojevic, A., Balaz, A., & Karapandza, R. (2008). Consequences of increased longevity for wealth, fertility, and population growth. *Physica A: Statistical Mechanics and Its Applications*, *387*(2–3), 543–550. https://doi.org/10.1016/j.physa.2007.09.004
22. Bortolotti, L., & Nagasawa, Y. (2009). Immortality Without Boredom. *Ratio*, *22*(3), 261–277.
23. Bostrom, N. (2003a). Are You Living In a Computer Simulation? *Published in Philosophical Quarterly (2003) Vol. 53, No. 211, Pp. 243-255.*
24. Bostrom, N. (2003b). Astronomical waste: The opportunity cost of delayed technological development. *Utilitas*, *15*(3), 308–314.
25. Bradley, B. (2013). How Bad Is Death? *Canadian Journal of Philosophy*, *37*, 111–127. https://doi.org/10.1353/cjp.2007.0007
26. Brandhorst, S., Choi, I. Y., Wei, M., Cheng, C. W., Sedrakyan, S., Navarrete, G., … Longo, V. D. (2015). A periodic diet that mimics fasting promotes multi-system regeneration, enhanced cognitive performance and healthspan. *Cell Metabolism*, *22*(1), 86–99. https://doi.org/10.1016/j.cmet.2015.05.012
27. Braun, R. A., Kopecky, K. A., & Koreshkova, T. (2017). Old, sick, alone, and poor: A welfare analysis of old-age social insurance programmes. *The Review of Economic Studies*, *84*(2), 580–612.
28. Brody, J. E. (2016). Finding a Drug for Healthy Aging. *Well.Blogs.NYtimes.* Retrieved from https://well.blogs.nytimes.com/2016/02/01/pursuing-the-dream-of-healthy-aging/
29. Brown, K. (2017). Report: Peter Thiel Is Funding a Totally Shady Offshore Herpes Vaccine Trial. *Gizmondo*. Retrieved from https://gizmodo.com/report-peter-thiel-is-funding-a-totally-shady-offshore-1798496015
30. Bulterijs, S. (2016). The Longevity Dividend: The Economic Advantages Of Geroprotective Treatments. Retrieved February 6, 2018, from http://longevityreporter.org/blog/2016/6/6/the-longevity-dividend-the-economic-advantages-of-geroprotective-treatments
31. Bulterijs, S. (2017). Geroprotector review: metformin. Sven’s Science Column (LongeCity). Retrieved from http://www.longecity.org/forum/blog/201/entry-3593-geroprotector-review-metformin/
32. Bulterijs, S., Hull, R. S., Björk, V. C. E., & Roy, A. G. (2015). It is time to classify biological aging as a disease. *Frontiers in Genetics*, *6*. https://doi.org/10.3389/fgene.2015.00205
33. Burkewitz, K., Zhang, Y., & Mair, W. B. (2014). AMPK at the nexus of energetics and aging. *Cell Metabolism*, *20*(1), 10–25.
34. Calderwood, S. K., Murshid, A., & Prince, T. (2009). The Shock of Aging: Molecular Chaperones and the Heat Shock Response in Longevity and Aging – A Mini-Review. *Gerontology*, *55*(5), 550–558. https://doi.org/10.1159/000225957
35. Campbell, J. M., Bellman, S. M., Stephenson, M. D., & Lisy, K. (2017). Metformin reduces all-cause mortality and diseases of ageing independent of its effect on diabetes control: A systematic review and meta-analysis. *Ageing Research Reviews*, *40*, 31–44. https://doi.org/10.1016/j.arr.2017.08.003
36. Castellano, J. M., Kirby, E. D., & Wyss-Coray, T. (2015). Blood-borne revitalization of the aged brain. *JAMA Neurology*, *72*(10), 1191–1194.
37. Cheng, T. C., Powdthavee, N., & Oswald, A. J. (2017). Longitudinal Evidence for a Midlife Nadir in Human Well-being: Results from Four Data Sets. *The Economic Journal*, *127*(599), 126–142. https://doi.org/10.1111/ecoj.12256
38. Choi, C. Q. (2011). The Stroke of Genius Strikes Later in Modern Life. *Live Science*. Retrieved from https://www.livescience.com/16911-scientific-breakthroughs-genius-aging.html
39. Chopan, M., & Littenberg, B. (2017). The Association of Hot Red Chili Pepper Consumption and Mortality: A Large Population-Based Cohort Study. *PLOS ONE*, *12*(1), e0169876. https://doi.org/10.1371/journal.pone.0169876
40. Cicirelli, V. G. (2006). Fear of Death in Mid-Old Age. *The Journals of Gerontology: Series B*, *61*(2), P75–P81. https://doi.org/10.1093/geronb/61.2.P75
41. ClinicalTrials.gov. (2015). Metformin in Longevity Study. Retrieved February 6, 2018, from https://clinicaltrials.gov/ct2/show/NCT02432287
42. Cuaresma, J. C., Loichinger, E., & Vincelette, G. A. (2016). Aging and income convergence in Europe: A survey of the literature and insights from a demographic projection exercise. *Economic Systems*, *40*(1), 4–17.
43. David. (2012). What does a 13% increased risk of death mean? | Understanding Uncertainty. Retrieved February 6, 2018, from https://understandinguncertainty.org/what-does-13-increased-risk-death-mean
44. De Grey, A., & Rae, M. (2007). *Ending aging: The rejuvenation breakthroughs that could reverse human aging in our lifetime*. St. Martin’s Press.
45. de Jesus, B. B., Vera, E., Schneeberger, K., Tejera, A. M., Ayuso, E., Bosch, F., & Blasco, M. A. (2012). Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer. *EMBO Molecular Medicine*, *4*(8), 691–704.
46. Dees, M. K., Vernooij-Dassen, M. J., Dekkers, W. J., Vissers, K. C., & Weel, C. van. (2011). “Unbearable Suffering”: A Qualitative Study on the Perspectives of Patients Who Request Assistance in Dying. *Journal of Medical Ethics*, *37*(12), 727–734.
47. Dehbi, H.-M., Royston, P., & Hackshaw, A. (2017). Life expectancy difference and life expectancy ratio: two measures of treatment effects in randomised trials with non-proportional hazards. *BMJ*, *357*, j2250. https://doi.org/10.1136/bmj.j2250
48. Denkenberger, D. (2017). How you can save expected lives for $0.20-$400 each and reduce X risk - Effective Altruism Forum. Retrieved February 7, 2018, from http://effective-altruism.com/ea/1hq/how\_you\_can\_save\_expected\_lives\_for\_020400\_each/
49. Dovey, D. (2015, January 6). Can Marine Biology Help Us Live Forever? Bowhead Whale Can Live 200 Years, Is Cancer Resistant. *Medical Daily*. Retrieved from http://www.medicaldaily.com/can-marine-biology-help-us-live-forever-bowhead-whale-can-live-200-years-cancer-316424
50. Easterlin, R. A. (2006). Life cycle happiness and its sources: Intersections of psychology, economics, and demography. *Journal of Economic Psychology*, *27*(4), 463–482. https://doi.org/10.1016/j.joep.2006.05.002
51. Edwards, R. D. (2013). The cost of uncertain life span. *Journal of Population Economics*, *26*(4), 1485–1522.
52. Everitt, A. V., Couteur, L., & David, G. (2007). Life extension by calorie restriction in humans. *Annals of the New York Academy of Sciences*, *1114*(1), 428–433.
53. Fluttershy. (2015). Tentative Thoughts on the SENS Foundation - Effective Altruism Forum. Retrieved February 7, 2018, from http://effective-altruism.com/ea/dh/tentative\_thoughts\_on\_the\_sens\_foundation/
54. Gado, M., Hughes, C. P., Danziger, W., & Chi, D. (1983). Aging, dementia, and brain atrophy: a longitudinal computed tomographic study. *American Journal of Neuroradiology*, *4*(3), 699–702.
55. Gavrilov, L., & Gavrilova, N. (2017). Is aging a disease? The point of view of biodemographs. *Adv. Gerond. Vol. 30, No 6, P. 843-844*.
56. Gavrilov, L., & Gavrilova, N. S. (1991). The biology of life span: a quantitative approach.
57. Gavrilov, L., & Gavrilova, N. S. (2010). Demographic Consequences of Defeating Aging. *Rejuvenation Research*, *13*(2–3), 329–334. https://doi.org/10.1089/rej.2009.0977
58. Ghumare, N. (2015). Anti-aging Market is estimated to be worth USD 191.7 Billion Globally by 2019: Transparency Market Research. *Globe Newswire*. Retrieved from http://globenewswire.com/news-release/2015/05/21/737992/10135534/en/Anti-aging-Market-is-estimated-to-be-worth-USD-191-7-Billion-Globally-by-2019-Transparency-Market-Research.html
59. Global Prioritisation Project. (2015). How can we help the world? A flowchart. Retrieved February 7, 2018, from http://globalprioritiesproject.org/2015/09/flowhart/
60. Grace, K. (2017). When Will AI Exceed Human Performance? Evidence from AI Experts. Retrieved from https://arxiv.org/pdf/1705.08807.pdf
61. Green, O. H. (1982). Fear of death. *Philosophy and Phenomenological Research*, *43*(1), 99–105.
62. gwern. (2015, June 1). Life Extension Cost-Benefits - Gwern.net. Retrieved March 17, 2018, from https://www.gwern.net/Longevity
63. Hansen, M., & Kennedy, B. K. (2016). Does longer lifespan mean longer healthspan? *Trends in Cell Biology*, *26*(8), 565–568.
64. Hawkley, L. C., & Cacioppo, J. T. (2007). Aging and loneliness: Downhill quickly? *Current Directions in Psychological Science*, *16*(4), 187–191.
65. Heintz, C., & Mair, W. (2014). You are what you host: microbiome modulation of the aging process. *Cell*, *156*(3), 408–411.
66. Hirth, R. A., Chernew, M. E., Miller, E., Fendrick, A. M., & Weissert, W. G. (2000). Willingness to Pay for a Quality-adjusted Life Year: In Search of a Standard. *Medical Decision Making*, *20*(3), 332–342. https://doi.org/10.1177/0272989X0002000310
67. Houtkooper, R. H., Pirinen, E., & Auwerx, J. (2012). Sirtuins as regulators of metabolism and healthspan. *Nature Reviews Molecular Cell Biology*, *13*(4), 225.
68. Istvan, Z. (2013). *The transhumanist wager*. Futurity Imagine Media LLC.
69. Jaskelioff, M., Muller, F. L., Paik, J.-H., Thomas, E., Jiang, S., Adams, A., … DePinho, R. A. (2011). Telomerase reactivation reverses tissue degeneration in aged telomerase deficient mice. *Nature*, *469*(7328), 102–106. https://doi.org/10.1038/nature09603
70. Jin, K., Simpkins, J. W., Ji, X., Leis, M., & Stambler, I. (2015). The critical need to promote research of aging and aging-related diseases to improve health and longevity of the elderly population. *Aging and Disease*, *6*(1), 1.
71. Johnson, S. C., Rabinovitch, P. S., & Kaeberlein, M. (2013). mTOR is a key modulator of ageing and age-related disease. *Nature*, *493*(7432), 338.
72. Katayama, Y., Kitamura, T., Kiyohara, K., Iwami, T., Kawamura, T., Hayashida, S., … Shimazu, T. (2018). Factors associated with prehospital death among traffic accident patients in Osaka City, Japan: a population-based study. *Traffic Injury Prevention*, *19*(1), 49–53.
73. Lalau, J.-D., Kajbaf, F., Protti, A., Christensen, M. M., De Broe, M. E., & Wiernsperger, N. (2017). Metformin-associated lactic acidosis (MALA): Moving towards a new paradigm. *Diabetes, Obesity & Metabolism*, *19*(11), 1502–1512. https://doi.org/10.1111/dom.12974
74. Lee, D.-C., Brellenthin, A. G., Thompson, P. D., Sui, X., Lee, I.-M., & Lavie, C. J. (2017). Running as a Key Lifestyle Medicine for Longevity. *Progress in Cardiovascular Diseases*, *60*(1), 45–55. https://doi.org/10.1016/j.pcad.2017.03.005
75. Leibing, A., & Cohen, L. (2018). *Thinking about dementia: Culture, loss, and the anthropology of senility*. Rutgers University Press.
76. Lemasters, J. J. (2005). Selective mitochondrial autophagy, or mitophagy, as a targeted defense against oxidative stress, mitochondrial dysfunction, and aging. *Rejuvenation Research*, *8*(1), 3–5.
77. Levy, D. T., Borland, R., Lindblom, E. N., Goniewicz, M. L., Meza, R., Holford, T. R., … Abrams, D. B. (2018). Potential deaths averted in USA by replacing cigarettes with e-cigarettes. *Tobacco Control*, *27*(1), 18–25. https://doi.org/10.1136/tobaccocontrol-2017-053759
78. Long, M. W., Gortmaker, S. L., Ward, Z. J., Resch, S. C., Moodie, M. L., Sacks, G., … Claire Wang, Y. (2015). Cost Effectiveness of a Sugar-Sweetened Beverage Excise Tax in the U.S. *American Journal of Preventive Medicine*, *49*(1), 112–123. https://doi.org/10.1016/j.amepre.2015.03.004
79. MacAskill, W. (2015). *Doing good better: Effective altruism and a radical new way to make a difference*. Guardian Faber Publishing.
80. Mark, K. A., Dumas, K. J., Bhaumik, D., Schilling, B., Davis, S., Oron, T. R., … Melov, S. (2016). Vitamin D promotes protein homeostasis and longevity via the stress response pathway genes skn-1, ire-1, and xbp-1. *Cell Reports*, *17*(5), 1227–1237.
81. Markelov, R. (2017). Медведев поручил Минздраву повысить продолжительность жизни до 76 лет. *Российская газета*. Retrieved from https://rg.ru/2017/04/11/medvedev-poruchil-minzdravu-povysit-prodolzhitelnost-zhizni-do-76-let.html
82. Marks, N. F., Jun, H., & Song, J. (2007). Death of Parents and Adult Psychological and Physical Well-Being: A Prospective U.S. National Study. *Journal of Family Issues*, *28*(12), 1611–1638. https://doi.org/10.1177/0192513X07302728
83. Martinez-Gonzalez, M. A., & Martin-Calvo, N. (2016). Mediterranean diet and life expectancy; beyond olive oil, fruits, and vegetables. *Current Opinion in Clinical Nutrition and Metabolic Care*, *19*(6), 401–407. https://doi.org/10.1097/MCO.0000000000000316
84. Martin-Montalvo, A., Mercken, E. M., Mitchell, S. J., Palacios, H. H., Mote, P. L., Scheibye-Knudsen, M., … Blouin, M.-J. (2013). Metformin improves healthspan and lifespan in mice. *Nature Communications*, *4*, 2192.
85. Millett, P., & Snyder-Beattie, A. (2017). Existential Risk and Cost-Effective Biosecurity. *Health Security*, *15*(4), 373–383. https://doi.org/10.1089/hs.2017.0028
86. Minerva, F., & Sandberg, A. (2017). Euthanasia and cryothanasia. *Bioethics*, *31*(7), 526–533.
87. Moscalev, A. (2017). Is aging a disease? Genetist’ point of view. *Adv. Geront Vol. 30 N6*. Retrieved from https://www.facebook.com/alexey.moskalev/posts/1804202862943427
88. Moskalev, A., & Batin, M. (2011). Biomarkers of aging and aging-related pathologies. *Department of Bioengineering and Bioinformatics of MV Lomonosov Moscow State University*, 63.
89. Moskalev, A., Chernyagina, E., Kudryavtseva, A., & Shaposhnikov, M. (2017). Geroprotectors: A Unified Concept and Screening Approaches. *Aging and Disease*, *8*(3), 354–363. https://doi.org/10.14336/AD.2016.1022
90. Moskalev, A., Chernyagina, E., Tsvetkov, V., Fedintsev, A., Shaposhnikov, M., Krut’ko, V., … Kennedy, B. K. (2016). Developing criteria for evaluation of geroprotectors as a key stage toward translation to the clinic. *Aging Cell*, *15*(3), 407–415. https://doi.org/10.1111/acel.12463
91. Mulligan, T., Retchin, S. M., Chinchilli, V. M., & Bettinger, C. B. (1988). The role of aging and chronic disease in sexual dysfunction. *Journal of the American Geriatrics Society*, *36*(6), 520–524.
92. Nakachi, K., Eguchi, H., & Imai, K. (2003). Can teatime increase one’s lifetime? *Ageing Research Reviews*, *2*(1), 1–10.
93. Naylor, R. M., Baker, D. J., & Deursen, J. van. (2013). Senescent cells: a novel therapeutic target for aging and age-related diseases. *Clinical Pharmacology & Therapeutics*, *93*(1), 105–116.
94. Nelson, C. (2015). Who Funds Basic Research in Aging in the US? | SAGE. Retrieved February 6, 2018, from http://sage.buckinstitute.org/who-funds-basic-research-in-aging-in-the-us/
95. Neves, J., Sousa-Victor, P., & Jasper, H. (2017). Rejuvenating Strategies for Stem Cell-Based Therapies in Aging. *Cell Stem Cell*, *20*(2), 161–175. https://doi.org/10.1016/j.stem.2017.01.008
96. Open Longevity. (2017). Open Longevity. Retrieved from http://openlongevity.org/
97. Parrish, E. (2015). Liz Parrish speaks at People Unlimited on transcending the aging paradigm with gene therapy. Retrieved from https://bioviva-science.com/video/2017/4/2/liz-parrish-speaks-at-people-unlimited-on-transcending-the-aging-paradigm-with-gene-therapy
98. Partei für Gesundheitsforschung. (2018). Partei für Gesundheitsforschung. Retrieved February 7, 2018, from https://parteifuergesundheitsforschung.de/
99. Pedersen, B. K. (2009). Anti-inflammation – just another word for anti-ageing? *The Journal of Physiology*, *587*(Pt 23), 5515. https://doi.org/10.1113/jphysiol.2009.183152
100. Plant, M. (2015). Is effective altruism overlooking human happiness and mental health? I argue it is. - Effective Altruism Forum. Retrieved February 7, 2018, from http://effective-altruism.com/ea/yv/is\_effective\_altruism\_overlooking\_human\_happiness/
101. Polypill.com. (2018). What is the Polypill Prevention Programme? -. Retrieved February 8, 2018, from https://www.polypill.com/Home/WhatIsIt
102. Pulkki-Brännström, A.-M., Wolff, C., Brännström, N., & Skordis-Worrall, J. (2012). Cost and cost effectiveness of long-lasting insecticide-treated bed nets - a model-based analysis. *Cost Effectiveness and Resource Allocation : C/E*, *10*, 5. https://doi.org/10.1186/1478-7547-10-5
103. Rao, C., Lopez, A. D., & Hemed, Y. (2006). Causes of Death. In D. T. Jamison, R. G. Feachem, M. W. Makgoba, E. R. Bos, F. K. Baingana, K. J. Hofman, & K. O. Rogo (Eds.), *Disease and Mortality in Sub-Saharan Africa* (2nd ed.). Washington (DC): World Bank. Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK2298/
104. Ristow, M., & Schmeisser, K. (2014). Mitohormesis: promoting health and lifespan by increased levels of reactive oxygen species (ROS). *Dose-Response*, *12*(2), dose–response.
105. Robinson, L. (2008). How US Government Agencies Value Mortality Risk Reductions. *Review of Environmental Economics and Policy*, (1(2): 283–299). Retrieved from http://opim.wharton.upenn.edu/risk/downloads/RiskSeminar\_2008-09-23\_Robinson.pdf
106. Roser, M., & Ortiz-Ospina, E. (2017). Global extreme poverty. *Our World in Data*.
107. Ruby, J. G., Smith, M., & Buffenstein, R. (2018). Naked mole-rat mortality rates defy Gompertzian laws by not increasing with age. *ELife*, *7*. https://doi.org/10.7554/eLife.31157
108. Scott, A. (2017). My IRB Nightmare | Slate Star Codex. Retrieved February 6, 2018, from http://slatestarcodex.com/2017/08/29/my-irb-nightmare/#comments
109. Singer, P. (2011). *Practical ethics*. Cambridge university press.
110. Singer, P. (2015). The Most Good You Can Do: How Effective Altruism Is Changing Ideas About Living Ethically. *The Most Good You Can Do: How Effective Altruism Is Changing Ideas About Living Ethically*, 1–211.
111. Sprenger, M. J. W., Mulder, P. G. H., Beyer, W. E. P., Van Strik, R., & Masurel, N. (1993). Impact of Influenza on Mortality in Relation to Age and Underlying Disease, 1967–1989. *International Journal of Epidemiology*, *22*(2), 334–340. https://doi.org/10.1093/ije/22.2.334
112. Stambler, I. (2017). Recognizing Degenerative Aging as a Treatable Medical Condition: Methodology and Policy. *Aging and Disease*, *8*(5), 583.
113. Statista. (2018). Median age of the world population from 1990 to 2100 | Statistic. Retrieved February 7, 2018, from https://www.statista.com/statistics/268766/median-age-of-the-world-population/
114. Stolyarov, G. (2013). *Death is Wrong*. Rational Argumentator Press. Retrieved from https://www.amazon.com/Death-Wrong-Gennady-Stolyarov-II/dp/0615932045
115. Stolz, E., Mayerl, H., Waxenegger, A., & Freidl, W. (2017). Explaining the Impact of Poverty Risk on Frailty Trajectories in Old Age Using Growth Curve Models. *World Academy of Science, Engineering and Technology, International Journal of Humanities and Social Sciences*, *4*(6).
116. Turchin, A. (2018). *Forever and Again: Necessary Conditions for the “Quantum Immortality” and its Practical Implications*.
117. Turchin, A., Green, B., & Dekenbergern, D. (2017). Multiple Simultaneous Pandemics as Most Dangerous Global Catastrophic Risk Connected with Bioweapons and Synthetic Biology. *Forthcoming*.
118. United Nations. (2015a). World Population Prospects: The 2015 Revision, Key Findings and Advance Tables. In *Working Paper No. ESA/P/WP. 241* (pp. 1–59). Retrieved from https://esa.un.org/unpd/wpp/Publications/Files/Key\_Findings\_WPP\_2015.pdf
119. United Nations. (2015b). World Population Prospects: The 2015 Revision, Volume II: Demographic Profiles. Retrieved from https://esa.un.org/unpd/wpp/publications/Files/WPP2015\_Volume-II-Demographic-Profiles.pdf
120. United Nations. (2017a). The impact of population momentum on future population growth. Retrieved from https://esa.un.org/unpd/wpp/Publications/Files/PopFacts\_2017-4\_Population-Momentum.pdf
121. United Nations. (2017b). World Population Prospects. The 2017 Revision. Retrieved from https://esa.un.org/unpd/wpp/Publications/Files/WPP2017\_KeyFindings.pdf
122. US Census Bureau. (1997). Household income. Retrieved from https://www.census.gov/prod/3/98pubs/p60-200.pdf
123. Vaiserman, A. M., & Pasyukova, E. G. (2012). Epigenetic drugs: a novel anti-aging strategy? *Frontiers in Genetics*, *3*. https://doi.org/10.3389/fgene.2012.00224
124. Wang, C.-P., Lorenzo, C., Habib, S. L., Jo, B., & Espinoza, S. E. (2017). Differential effects of metformin on age related comorbidities in older men with type 2 diabetes. *Journal of Diabetes and Its Complications*, *31*(4), 679–686.
125. Warner, J. T., & Pleeter, S. (2001). The personal discount rate: Evidence from military downsizing programs. *American Economic Review*, *91*(1), 33–53.
126. WHO. (2015). Ageing and health fact sheet number 404. *WHO, Geneva*. Retrieved from http://who.int/mediacentre/factsheets/fs404/en/
127. WHO. (2017). WHO | Noncommunicable diseases. Retrieved from http://www.who.int/mediacentre/factsheets/fs355/en/
128. WorldHunger. (2016). How many people are hungry in the world? Retrieved February 7, 2018, from https://www.worldhunger.org/2015-world-hunger-and-poverty-facts-and-statistics/
129. Yancik, R. (2005). Population Aging and Cancer: A Cross-National Concern. *The Cancer Journal*, *11*(6), 437–441.
130. Yudkowsky, E. (2009). The Fun Theory Sequence - Less Wrong. Retrieved February 21, 2018, from http://lesswrong.com/lw/xy/the\_fun\_theory\_sequence/
131. Zhavoronkov, A., & Bhullar, B. (2015). Classifying aging as a disease in the context of ICD-11. *Frontiers in Genetics*, *6*.