A Vaccine for the Pandemic of Aging? Conceptual and Ethical Issues

15

Christopher Simon Wareham and Pablo Garcia-Barranquero

Abstract

In this chapter, we develop and extend the above analogy by means of a thought experiment in which a vaccine for the pandemic of aging is developed. We ask first, whether the concept of a vaccine for the pandemic of aging is *conceptually* coherent, and second whether such a vaccine (or similar aging preventive) is ethically desirable. This chapter makes the case that, while there are some clear disanalogies between aging and typical pandemics like the COVID-19 pandemic, there are some striking similarities that advocate for similar degrees of urgency. Moreover, the comparison throws important light on some of the flawed objections to healthy life-extending technologies.

Keywords

Ageing · Anti-ageing · Vaccine · Covid · Life extension · Ethics

C. S. Wareham (✉)
The Ethics Institute, Utrecht University, Utrecht, Netherlands

Steve Biko Centre for Bioethics, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
e-mail: c.s.wareham@uu.nl

P. Garcia-Barranquero
Department of Philosophy, University of Malaga, Málaga, Spain
e-mail: pablogarcia@uma.es

S. I. Rizvi (ed.), *Emerging Anti-Aging Strategies*,
https://doi.org/10.1007/978-981-19-7443-4_15

15.1 Introduction

Writing against the backdrop of the COVID-19 pandemic, Aubrey De Grey provocatively claimed that we are living in a "pandemic of aging" drawing an analogy between interventions against aging and treatments for other medical conditions (De Grey 2020, p. 92). The implication is that aging ought to be treated like so many diseases, and if it were, it would become an absolute research priority, leapfrogging even the COVID-19 pandemic in terms of urgency. However, De Grey stops short of proposing what might be referred to as a "vaccine for aging," and considering its value relative to a COVID-19 vaccine.

In this chapter, we develop and extend the above analogy by means of a thought experiment in which a vaccine for the pandemic of aging is developed. [1] We ask first, whether the concept of a vaccine for the pandemic of aging is *conceptually* coherent, and, second, whether such a vaccine (or similar aging preventive) is ethically desirable.

We begin in Sect. 15.2 by outlining a thought experiment in which a "vaccine for the pandemic of aging" is proposed. In Sects 15.3 and 15.4, we consider whether the concept of a vaccine for the aging pandemic is a coherent one. In particular, in Sect. 15.3, we question whether aging is indeed a "pandemic" and, in Sect. 15.4, whether "vaccine" is a concept that could be appropriately applied to a treatment that prevents aging. In Sect. 15.5, we raise three bioethical questions about the "vaccine" for aging. First, is it an intervention that would be good for people? Second, would its development as high a priority as de Grey suggests it ought to be? Third, how should such a preventive be distributed?

The thought experiment we propose is not the first thought experiment regarding an anti-aging treatment. [2] However, part of the contribution of this article is to explicitly compare a vaccine for the pandemic of aging, to a modern-day emergency—the COVID-19 pandemic. This provides an opportunity to revisit problems and objections, and to explore analogies and disanalogies with the aging vaccine. This chapter makes the case that, while there are some clear disanalogies, there are some striking similarities that advocate for similar degrees of urgency. Moreover, the comparison throws important light on some of the flawed objections to healthy life-extending technologies.

15.2 A Revolutionary Proposal

This section proposes a thought experiment. The function of thought experiments is to draw out relevant considerations in evaluating outcomes, to determine whether the outcomes are desirable, and to clarify concepts. at all. A significant purpose is to

[1] Parts of this chapter are reworked from an article which appears in Spanish in the journal *Pasajes.*

[2] See, e.g., Bostrom (2005); De Grey (2007); Gems (2011); Williams (2009). All these thought experiments are different, as are their the philosophical and ethical implications.

cause us to reflect on the *ends* of an activity, in this case, scientific research into aging. In order to do this, thought experiments are typically permitted to depart from what is strictly considered realistic. With this clarification in place, consider the proposal below.

15.2.1 A "Vaccine for the Pandemic of Aging"

Suppose that, in the near future, a renowned scientist, Professor Makropulos, claims that with 18 billion dollars, [3] her team will be able to fast-track a technique allowing the development of "vaccine for the pandemic of aging" within a year. The vaccine, though expensive to develop, is unlikely to be particularly expensive to develop or produce, and probably no more expensive than the COVID-19 vaccine. From this point, she claims anyone who takes the vaccine will be drastically protected from biological aging. She anticipates that most of the people given the vaccine will no longer age at all, and those who do age will age slower, and will experience the symptoms of aging with far less severity. People with complete protection from aging will no longer experience, or die of age-related causes, and their susceptibility to these diseases will not increase with chronological age. Those nonetheless age, will experience significant, though incomplete protection from age-related causes of death. They may age, though it will be far slower, and their (chronological) age-relative risk of dying from age-related causes will be far lower.

Professor Makropulos is careful to point out that her vaccine is *not* an immortality drug (her surname also belonging to the infamous immortal Elina Makropulos is just a curious coincidence (Williams 2009)). It will be necessary to take a "booster" vaccine every year, and if one wishes to age, one can choose not to take the vaccine. People who take the drug will still die of various conditions. Non-age-related cancers and heart disease are still possible, so the vaccine-protected person would still need to be watchful of her health. Moreover, like everyone else, they will need to be careful crossing the street, driving a car, or going to countries with a high crime rate or prevalence of infectious diseases. [4]

On the other hand, as time progresses, they will not have cause to be quite as fearful as a biologically older person would be of, for instance, pandemics like the COVID-19 pandemic. While a person who takes the vaccine can still die of innumerable causes, they are far less likely to die from aging, or diseases that mainly afflict those with advanced age. Their chances of dying of these causes will increase more slowly with chronological age, and in some cases, will not increase at all.

[3] This is the amount invested in Operation Warpspeed, the US government's project to develop a COVID-19 vaccine (Kim et al. 2021). However, other projections place the figure much higher https://www.devex.com/news/interactive-who-s-funding-the-covid-19-response-and-what-are-the-priorities-96833

[4] There is also the possibility of non-aging-related biological causes of death that correlate with chronological age, as in the case of birds that die "catastrophically" (Ricklefs and Scheuerlein 2001). In this case, we would die without aging.

Professor Makropulos is a highly well-respected gerontologist, and her consistently groundbreaking work has for a long time hinted at this possibility. So there are good reasons to think that she is onto something that really could achieve this result. However, she is making some very strong, and, some suggest, outlandish or simply erroneous claims about what we will refer to as the "Makropulosjab." Does her claim about a "vaccine" for "pandemic" of aging make scientific and conceptual sense. Furthermore, do we have strong moral reasons to give her the 18 million dollars required?

15.3 Is Aging a Pandemic?

The scientific and conceptual questions of whether the Makropulosjab could justifiably be called a vaccine for an aging pandemic should be treated in two parts. In this section, drawing on the example of the COVID-19 pandemic, we discuss various criteria for a pandemic and question the extent to which aging can justifiably be seen as a *pandemic*. In Sect. 15.4, we turn to the question of whether the concept of an aging *vaccine* makes conceptual sense.

15.3.1 What Is a Pandemic?

In scientific terms, COVID-19 is an exemplary pandemic. Morens et al. (2009) suggest key characteristics that are definitive of a pandemic (Morens et al. 2009). [5] These characteristics provide additional detail to the three previously mentioned conditions. After briefly discussing these, we will assess whether aging fits the same framework for COVID-19.

1. *The wide geographical extension* of the disease over large geographical areas (interregional, transregional, or global).
2. The *spread and movement of the disease* through transmission that can be traced from one location to another.
3. High disease attack rates and *strong detrimental effects* on people's health, including the possibility of death. The most notorious health crises have tended to exhibit a more explosive character, i.e., multiple cases appearing in a short time).
4. Minimal population immunity is a form of natural resistance against the most severe effects of the disease.
5. The disease must be *novel* or at least be associated with different variants of existing microorganisms.
6. The disease has a robust *infectious character*.

[5] See also, Sampath et al., (2021).

Table 15.1 Comparison between COVID and aging in light of the essential characteristics of a pandemic

	COVID-19	Aging
Wide geographical extension	Yes	Yes
Disease movement	Yes	No
High attack rates and explosiveness	Yes	No
Minimal population immunity	Yes	Yes
Novelty	Yes	No
Infectiousness	Yes	No
Contagiousness	Yes	No

7. The disease *is highly contagious* by one or more means of transmission (either between members of different species or between members of the same species).

Not all of these characteristics are equally important when defining what a pandemic is. For instance, while most pandemics, including the COVID-19 pandemic, do have the characteristic of novelty, we would be justified in attributing the term to less novel diseases if the other conditions were met.

15.3.2 Is Aging a Pandemic?

These clarifications notwithstanding, the criteria discussed present good reasons why aging would not match the ordinary scientific understandings of a pandemic. As shown in Table 15.1, the conceptualization of aging as a pandemic is problematic from this scientific point of view. Of course, it might be suggested that, even more than COVID-19, aging has a "wide geographical extension." Indeed, other things being equal, it is a universally experienced condition. It could also be suggested that there is minimal population immunity to aging—there is no immunity at all, an issue we return to in the next section when we consider whether the Makropulos drug is a vaccine. However, acceptance of Professor Makropulos's idea of an "aging pandemic" on these or other grounds seems to stretch ordinary scientific understandings of the term pandemic.

15.3.3 Is Aging a Disease?

In addition to the above, there is perhaps a deeper reason why many would be disinclined to refer to aging as a pandemic: typically a pandemic is a term referring to *diseases*. The idea that aging is a disease is extremely controversial. Considering whether this classification is possible is one of the most important philosophical questions relevant to geroscience (Lemoine 2020, pp. 2–3). On the face of it, if any other condition caused organisms to suffer progressively greater cognitive and physical deterioration, ultimately resulting in death, we would be strongly inclined to treat them as a disease. Then why not aging? Some approaches argue that it is not a disease (Hayflick 2000; Schramme 2013); others that it is (Caplan 2005; De Winter

2015); still others argue that it is helpful to view it as a disease, and not merely dismissed as a "natural" process (Murphy 1986; Callahan and Topinkova 1998). We cannot do justice to this significant conceptual debate here, but will instead adopt a "pragmatist" approach to the possibility that aging is a disease. Philosophical pragmatism is, roughly, the idea that the words and concepts ought to serve a practical function, and, further, that the meaning of concepts should be guided by, and perhaps exhausted by their practical usefulness. Saborido and García-Barranquero note that

> The history of medicine shows many conceptual changes of this type—conditions that cease to be diseases or begin to be interpreted as such—and presumably more conceptual changes will happen in the future because medicine is in constant evolution. New diseases will arise and old diseases will change their meanings in the cases in which such changes prove useful to achieve the goals of medicine (Saborido and García-Barranquero 2022).

In this kind of view, the definition of the concept of disease is not determined by who has the best scientific or philosophical arguments. Instead, whether aging is a disease will depend upon whether viewing aging as a disease has useful results, for example, in terms of medical practice. One such useful result of employing the "aging as disease" concept might be highlighting the possibility of a treatment for aging.

> Whether adopting the conception of "aging as a disease" is beneficial or not is something that gerontology will decide depending on whether it helps to achieve its epistemic goals. Treating aging as a disease would make it such (Saborido and García-Barranquero 2022).

In this case, we might say that the question of whether aging is a disease is an open question, one which will have a clearer answer when it is obvious whether or not treating aging as a disease has a pragmatic purpose.

15.3.4 A Broader Understanding of "Pandemic"

So far in this section, we have discussed narrower, technical conceptions of a pandemic, some of which incorporate the idea that pandemics must involve disease. Methodologically, these more technical conceptions draw on the history of disease pandemics in defining what a pandemic is in the epidemiological context (Morens et al. 2009). However, this is neither the only context in which the term pandemic is used, nor is this the only methodology that we could use in determining the correct usage of the term pandemic. Below, we suggest that it would be possible to interpret Professor Makrupulos's claim in a broader etymological way, which nonetheless coincides with other common uses of the term.

First, we consider it relevant to approach the word's etymology. The origin of the word pandemic is found in the Greek word *pandēmos*. This is made of two words

pan (all) and *dēmos* (all the people), i.e., "that which affects the whole people." [6] This definition underlies the one that states that a pandemic implies a contagious epidemic disease that spreads to several countries and attacks many individuals simultaneously. We could say that the meanings discussed earlier are narrower and more technical and require more specific conditions than the one that refers only to its broader etymological meaning. From this latter reading, it is logical to point out that aging is a biological process that *all* humans undergo, arguably throughout our lives (Gems 2014; Lemoine 2020). This inherent condition of aging will (in the absence of an anti-aging intervention) accompany us throughout our existence without exception. In this sense, aging seems to fit squarely with the original meaning of the term pandemic, indeed perhaps better than disease pandemics themselves, since the latter spare at least *some* people.

In addition to this etymological approach, there are some "common usage" reasons to regard Makropulos's broader usage of the term as appropriate. Certainly, a less restrictive approach is employed in speaking of the "pandemic of obesity" or the "smoking pandemic"(Moodie et al. 2013; Meldrum et al. 2017). Both problems can lead to other conditions that drastically reduce our quality of life (whether due to disorders, illnesses, or stigma). Thus, even if we do not accept that aging can be classified as a (new) disease, it is unclear that all pandemics should be governed by this criterion. A less rigid disease-based concept allows us to reflect on what is important about pandemics. In all these cases, there are concomitant health problems that cause a decrease in the well-being of many people. Seen in this way, we are motivated to reverse pandemics with medical, public health, and social measures. This theoretical framework shows a practical aim of the term pandemic that is arguably understated by purely epidemiological definitions: to urge the development of measures that can improve human health and generate greater widespread awareness of the problem to be remedied.

From the above considerations it is clear that, when the term pandemic is understood in a narrow, technical, epidemiological sense, *aging* cannot be seen as a pandemic. This is partly because there is doubt over whether it can be classified as a disease, although, as we suggest there may be pragmatic reasons to do so. However, this narrower conception is not the only conception. "Pandemic" can be understood *etymologically* as a condition that affects *everyone*, or in *common usage* as a ubiquitous cause of health problems. In these latter senses, aging ought arguably to be seen as the greatest pandemic of all since absent other causes of death, it affects everyone, without exception.

[6] https://bcmj.org/blog/origin-pandemic-related-words

15.4 A Vaccine for Aging?

The above is not to suggest that the broader conception of the pandemic should have priority. However, it does present a clear sense in which Makropulos is justified in claiming that there is a "pandemic of aging." The next question is whether her use of the term "vaccine" could be justified. In the same way that we have written about the term "pandemic," we will start by considering the typical scientific definition.

15.4.1 What Is a Vaccine?

Vaccination is a preventive approach that consists of administering a substance to a healthy subject to generate its own immunity against a disease. Such diseases are generally mediated by a virus, bacterium, and, exceptionally, parasites, as in the case of malaria. Vaccines are substances that prepare the immune system to fight a disease-causing germ or other pathogens by imitating an infection. They train the immune system into making a "memory"' of that germ, so that when the immune system encounters the real pathogen—whether a virus, bacterium, or other microbes—the immune system is better prepared to fight infection. [7] As a result, the vaccinated person gains a degree of protection from the effects of the infectant. It should be noted that RNA vaccines generated a change in the understanding of a vaccine. Before the RNA vaccines developed for COVID-19, acquired immunity was generated by the use of an antigen—a substance, usually a protein that generates an immune response. By contrast, RNA vaccines do not involve the physical introduction of an antigen. Instead, these novel vaccines use the machinery of our cells to generate the antigen (Kwok et al. 2021). According to some, this modifies the vaccine concept. Although the global definition does not appear to be affected, vaccine denialists have nonetheless used this to cast doubt aspersions on COVID-19 vaccines.

15.4.2 A Vaccine for Aging?

Aging is clearly not transmitted by viruses or other foreign infectious elements. Indeed a major point of disanalogy between the function of vaccines and the function of an anti-aging intervention is that vaccines typically function by discriminating between "self" and "non-self," and eliminating "non-self," while leaving "self" intact (Kwok et al. 2021). This is different in the case of aging, since aging cells are *our own* cells. So it appears conceptually problematic to suggest that our own aging cells are something that can be vaccinated against. Nonetheless, being

[7] WHO "Vaccines and Immunization: What is vaccination" https://www.who.int/news-room/questions-and-answers/item/vaccines-and-immunization-what-is-vaccination

Table 15.2 Comparison between COVID and aging in light of the essential characteristics of a vaccine

	COVID-19 vaccine	Aging vaccine
Uses acquired immune response	Yes	Yes, but partially
Distinguishes between self and a foreign biological agent	Yes	No
Removes a proliferative agent that is harmful to the organism	Yes	No

open-minded, we might consider what approaches to an anti-aging preventive might share similarities with the vaccine paradigm.

Loosely, a vaccine trains the immune system what to detect as foreign, and, therefore, what to attack. This enables the creation of cells prepared to identify a specific enemy (the specific antigen) and eliminate it from the system. If there were a vaccine against aging, a specific marker of aging would have to be identified that would distinguish the aged cell as foreign. The immune system would have to be trained or otherwise altered to recognize and eliminate cells carrying the marker. In this way, when a cell ages, the marker would become identifiable by the immune system and the aged cell would be eliminated by the body, removing it from circulation and preventing it from making other aged cells.

Arguably, a similar approach is employed in immunotherapy, whereby, roughly, T cells are genetically modified to eliminate cancer cells expressing relevant makers, before being reintroduced to the patient to eliminate cancers (Provinciali and Smorlesi 2005). Perhaps even more relevantly, there is an ongoing effort to develop cancer vaccines (Kwok et al. 2021). Such efforts derive their plausibility in part from the idea that cancers routinely form, but are often eliminated by the immune system (Shankaran et al. 2001). However, applying this idea to *aging* is merely notional and faces serious difficulties. For instance, cancer cells are harmful due to their tendency to proliferate, so that eliminating them is beneficial. Normal aging cells are however beneficial generally and contribute to the homeostasis of the organism. Eliminating aging cells from the body appears likely to damage the functioning of the organism (Table 15.2).

Thus, if Makropulos's "vaccine" used these or similar methods that employ the immune system machinery, she would be involved in a hitherto rather unexplored field. The incredulity of gerontologists, vaccinologists, and the scientific community might well be justified. Without further reasons to the contrary (which we are unable to provide) it might be most charitable to treat Makropulos's claim that the intervention is a vaccine as at best metaphorical. [8] She is proposing that her intervention

[8] Perhaps, for instance, Makropulos believes that a hormesis paradigm, which is sometimes implicated in the effects of caloric restriction, underlies both her intervention and the success of some vaccines (Masoro 2005; Calabrese et al. 2013). Hormesis is, roughly, the idea that small doses of something often induces a response that is favorable to health (Calabrese et al. 2013). Again, though pointing to a similar mode of action would not make her intervention a vaccine.

could somehow prevent or slow the progression of, or reduce the effects of aging *preemptively*, just as vaccines prevent or slow the progression, or reduce the effects of some diseases *preemptively*. Without further evidence, the idea that such an intervention might employ the immune system in a way that would justify the use of the term "vaccine" seems, at best, far-fetched.

15.5 Ethical Implications

Returning to the thought experiment, what should we conclude about Dr. Makropulos's claim to be able to develop a vaccine for a pandemic for aging? Though imprecise, metaphorical, and somewhat rhetorical, it is not entirely outlandish or necessarily disingenuous (at least not unusually so for a funding proposal). Considered alone, the conceptual stretches in Makropulos's public claim provide no strong reason to turn the request down. Moreover, per the thought experiment, we should assume the scientific aspects of her proposal are credible and there is a real prospect that her research could slow or halt aging. [9]

The question then moves to the *rationale* for funding the research. If we assume that Makropulos's work could successfully slow or prevent aging, are there reasons (not) to give her the 18 million dollars? From a public health perspective, biogerontologists and biodemographers have argued that there are enormous financial gains to be achieved from anti-aging interventions (Olshansky et al. 2006, 2007; Huber and Sierra 2009; Miller 2009). Assuming this to be the case, what ethical considerations ought to be considered? While the ethical need for a functional covid vaccine is clear, the desirability of intervening in aging has been debated for millennia. Would it ethically desirable to "immunize" (again, metaphorically) against aging?

In what follows, we consider and rely on three objections to this developing and using the Makropulos "vaccine": First, that slowing aging would be harmful to the individual; second that it would be harmful to society, and third that it would compromise the social values of equality and fairness.

15.5.1 Would Extending Lifespan Using Makropulos Vaccines Be Harmful to the Individual?

As we age we tend to become less healthy. Older people are more likely to have diseases like cancer, cardiovascular disease, diabetes, and Alzheimer's disease. As a

[9] We might think of this as science fictional, but one function of ethics thought experiments is to draw out relevant considerations in evaluating outcomes, to see whether the outcomes are desirable at all. In other words, they cause us to reflect on the ends of an activity, in this case, scientific research.

result, some fear that if we take a life-extending intervention like the Makropulos vaccine, we will simply live longer in a very unhealthy state(Partridge et al. 2009).

For example, suppose that, on average, people are fully healthy until 65, after which they tend to become progressively less healthy until they die at 80. A concern is that if people lived longer than 80 they would age normally until that point, with the increased frequency of disease that typically characterizes old age. Thereafter, they would get even less and less healthy until life became unbearable(De Grey 2008). If this possibility holds true, if we take the life-extending Makropulos vaccine we will eventually have more age-related diseases like cancers, and more disabling mental diseases like Alzheimer's disease. Even though we live longer, we might wish we had not taken the life-prolonging vaccine. Reaching 120 years old, for example, will not be a blessing, but a curse. There is no reason to extend lifespan since doing so would be bad for us. [10]

To some extent, the realization of this unpleasant scenario, along with other negative side effects of this vaccine is an empirical question, the answer to which will depend on the nature of the vaccine developed by Makropulos and may only be discovered in the very long term. In advance of this information, though, it would be reasonable to consider evidence from studies of slowed aging in calorically restricted (CR) organisms. Biologists investigating calorie restriction have observed that CR extends lifespan by slowing down the processes of aging (Giacomello and Toniolo 2021). Because aging is decelerated throughout life, healthy lifespan is extended, postponing the onset of age-related diseases until later in life. This means that, depending on when one initiated the vaccine, rather than health beginning to decline at 65, one might live in good health until 80, and live much longer after that.

Nonetheless, if the healthier part of the aging process is slowed down and extended, perhaps it is possible that the unhealthy part would be slowed down and extended. Just as pulling on the ends of a rubber band elongates all the rubber segments, slowing aging will extend both the healthy and unhealthy segments of our lives (Gems 2011). If we take Makropulos vaccines, it could be that the unhealthy part of life at the end of life will also be extended. And if we take it when we are older, we will be unhealthy for a greater proportion of our lives.

Again, it makes sense to consider evidence from studies of slowed aging in calorically restricted organisms. Some biologists suggest that slowing aging will shorten, rather than lengthen, the period of reduced health at the end of life. Health in late life may actually be improved. While it remains possible that the time in which one experiences worse health will be prolonged, studies on CR suggest that the number of diseases suffered will not increase (Gems 2011, p. 110). That is, although the length of time in which a person is more likely to get sick is longer, at any point during extended old age she is less likely to have a particular age-related disease. So despite the fact that one would be more susceptible to age-related diseases for longer,

[10] An immediate thought is that if life reached the state in which it is not worth living, we might simply end it (Harris 2002). However, this option might not be available or simple to some, for example, for religious reasons.

the frequency of diseases appears to be lower. In this sense, prolonged health decline should be seen as an improvement over normal aging.

Importantly, although health is not as good as when they were younger, older people live good lives. Indeed, studies suggest that older people tend to be far happier than middle-aged people (Blanchflower and Oswald 2008). Thus, although later years are not as healthy, one can still benefit from them, even if one benefits less than one would if one was in full health (Wareham 2012). Provided a life-extending intervention would not reduce well-being below a desirable threshold—and there is no reason to think Makropulos's "vaccine" would do this—later years in an extended life can be as good as the last years of a normal elderly person's life. Since these years are worth having, there is reason to think that even extending this period of worse health would be beneficial. Certainly, there is no strong reason to think the Makropulos vaccine would be harmful to the person who uses it.

15.5.2 Would the Makropulos Vaccine Be Harmful to Society?

It might be thought that the Makropulos vaccine would increase the welfare levels of society if it made individuals better off. A society with citizens that have greater well-being is, generally better than a society with citizens that are not as well off. If so, there is an argument that society would be improved with each additional person that took the anti-aging vaccine.

However, this simple argument ignores population-level effects that are extremely important for public health ethics. In the last century, life expectancy has already risen substantially. One extremely important demographic consequence of people living longer is that the proportion of elderly people in most parts of the world has increased substantially (Fukuyama 2002). If the maximum lifespan was further increased as a result of the Makropulos vaccine, it should be expected that this proportion would be even greater. Many think that the effects of an older society will eventually reduce welfare (Fukuyama 2002). Would population aging that would occur due to the use of the Makropulos vaccine be bad for society?

One reason to think so is the possibility of unsustainable dependency. The past century has already seen great increases in life expectancy, with few increases in the average age of retirement. This means that the ratio of working people to retired people is decreasing. If people using the Makropulos vaccine continued to draw a pension from age 65, and could be expected to live until 100, an even greater proportion of people would then be above pensioning age. In this circumstance, perhaps a diminishing proportion of workers would need to support an expanding population of retirees. If so, this could place an unsustainable burden on society, since less money would be available for social programs such as public healthcare (Fukuyama 2002).

It is true that if citizens continued to retire at age 65 and lived longer afterward, this could pose serious difficulties. Is this an argument against the use of the Makropulos vaccine? As an initial consideration, it might be illuminating to consider this objection in light of our attitudes to the COVID-19 vaccines. These were treated

as life-saving and valuable interventions, in major part because of their implications for preventing death in the very elderly. The idea that we should not use these vaccines because the elderly place a burden on health and social systems would rightly be considered monstrous. Why should this argument be acceptable in the context of the Makropulos vaccine? At minimum, we would have to see the likely social cost as extremely high and very likely if we are to reject the Makropulos drug on these social grounds.

With that said, are there reasons to think the Makropulos vaccine would be harmful to society more broadly? If citizens made use of the Makropulos vaccine, they would—as discussed in the previous section on individual welfare—age more slowly and be healthy for longer. Ill health in later life is arguably one of the main reasons for having a retirement age in the first place. Older people who remain healthy tend to work for longer (Clark et al. 2008). Thus, if people remained healthy for longer, citizens could contribute productively for longer. Indeed many nations have policies to gradually increase retirement ages. The successful development of a Makropulos vaccine would require careful thought about how to arrange the distribution of work and social benefits in society. In a super-aged nation, the longer lived population that made use of the intervention would have to be *healthy* to avoid depletion of the proportion of workers. Though not guaranteed, given available knowledge of slowed aging, this condition appears likely to be fulfilled.

15.5.3 Should Life-Extending Vaccines Be Fairly Distributed?

People who are poorer tend, on average, to die younger. This is already a serious ethical problem. A significant concern is that lifespan gaps might widen even further if life-prolonging interventions became available. The wealthy would make greater use of life-extending vaccines because they tend to be better educated and have more disposable income (Pijnenburg and Leget 2007).

One way to respond to this problem is to suggest that Makropulos vaccines should be provided to everyone by the state, much as COVID-19 vaccines have been (Wareham 2016). Given their health effects, in countries with universal public health cover, perhaps public health services should supply Makropulos vaccines in the same way that other health interventions are. Doing so might go some way towards preventing the lifespan gap from expanding.

However, there are important ethical arguments for and against this type of universal provision of healthy life-extending vaccines. One objection to the wider provision of the Makropulos vaccine is that, typically, health services are obligated only to provide treatments for diseases or disabilities(Mackey 2003). They should restore a person to health. Health services do not typically provide enhancements—such as beautifying cosmetic surgery—that improve a person's condition above a normal level. The Makropulos vaccine would raise people above a normal level by allowing them to live much longer than a normal person. They would therefore constitute an enhancement, which health services do not—and perhaps should not—provide(Barazzetti and Reichlin 2011).

Against this, proponents of the public provision of Makropulos vaccines could argue that the interventions do not *aim* to enhance above normal health. Instead, they should be considered as treatments, since they would cure, prevent or postpone acknowledged diseases like cardiovascular disease, diabetes, and cancer. As such, Makropulos vaccines should fall into the category of preventive interventions. Their provision should be regarded as similar to public health interventions to reduce smoking and obesity (Wareham 2016), and indeed COVID. These are regarded as pivotal and valuable aims of public health services. Thus, if Makropulos vaccines are similarly effective, there are reasons to think that their provision should be prioritized alongside these. At least in the developing world, provision of Makropulos vaccines would be fairer, since it would benefit the worse off.

On the other hand, lower income nations often have different health priorities and emphases. In some contexts, the use of public resources to undermine the causes of infant mortality and curing and preventing HIV/AIDS would prevent more premature deaths than slowing aging. In such contexts, anti-aging interventions would not be fair or effective, since people mainly die of non-age-related causes. Nonetheless, even in lower income nations, the burden of age-related disease is extremely high (Christensen et al. 2009). Noncommunicable diseases, which are often related to aging, represent a large fraction of premature deaths in the developing world. Moreover, these populations are aging at a much faster rate than those of the developed world (Abegunde et al. 2007). Thanks to better healthcare, more people are reaching adulthood. This means that more people will die of age-related diseases, rather than communicable diseases. As a result, even in worse-off nations, forward-thinking policy-makers would have an interest in provision of Makropulos vaccines to slow the large, and growing, burden of age-related disease. Doing so will benefit many people who would otherwise die prematurely. Thus, respecting fairness is not an argument against developing the Makropulos vaccine. Instead, it provides strong reasons to develop and distribute it fairly.

15.6 Conclusion

Anti-aging interventions prevent a wide array of conceptual and ethical challenges. To investigate some of these challenges, this article proposed a thought experiment in which a researcher proposes a "vaccine for the pandemic of aging." The above sections made the case that Makropulos's use of the term pandemic of aging is a departure from the ordinary scientific use, but accords with a broader etymological understanding, as well as common usage. The use of the term "vaccine" was even more problematic, since it is difficult to see how an anti-aging intervention would employ the immune system in the required sense.

Nonetheless, allowing for some colorful and metaphorical language, it could be permitted that Makropulos could have developed a preventive anti-aging intervention. This raises ethical questions: should such an intervention be permitted, or, as with COVID-19 vaccines, should states *provide* it? The relative priorities and values of individual states play a role in this. However, for states that value fairness, there

appear to be strong reasons to disseminate the drug, so as to increase the lifespans of those who die of age-related causes.

In conclusion, it is important to note two disturbing disanalogies between our response to the "pandemic of aging" and the COVID-19 pandemic. Firstly, it would be considered monstrous to suggest that one should not develop a COVID-19 vaccine because death by COVID-19 prevents people from experiencing the harms of aging. Yet, as discussed above, this is the objection that is often made against life extension. That is, a common objection to life extension is the fear of ill health in old age. But very few would have thought it acceptable to fail to develop COVID-19 vaccines so that old people die earlier and thereby be spared age-related health decline by death.

Secondly, suggesting that it was not worth developing the COVID-19 vaccine because longer lived old people increase dependency and place a drain on the economy would have been considered immoral in extreme. Again, this is precisely the sort of consideration presented against the Makropulos "vaccine" above. These apparent inconsistencies in our attitudes demand ethical attention. If we think 18 million USD is too high a price to pay for Makropulos's drug, it is important to consider and justify why aging is treated with nothing approaching the urgency of the COVID-19 pandemic.

Acknowledgments Christopher Wareham's contribution is part of the research program Ethics of Socially Disruptive Technologies, which is funded through the Gravitation programme of the Dutch Ministry of Education, Culture, and Science and the Netherlands Organization for Scientific Research (NWO grant number 024.004.031).

References

Abegunde DO et al (2007) The burden and costs of chronic diseases in low-income and middle-income countries. Lancet 370(9603):1929–1938. https://doi.org/10.1016/S0140-6736(07)61696-1

Barazzetti G, Reichlin M (2011) Life extension: a biomedical goal? Scientific prospects, ethical concerns. Swiss Med Wkly 141:1–7. https://doi.org/10.4414/smw.2011.13181

Blanchflower DG, Oswald AJ (2008) Is well-being U-shaped over the life cycle ? Soc Sci Med 66:1733–1749

Bostrom N (2005) The fable of the dragon tyrant. J Med Ethics 31(5):273–277

Calabrese EJ, Iavicoli I, Calabrese V (2013) Hormesis: its impact on medicine and health. Hum Exp Toxicol 32(2):120–152

Callahan D, Topinkova E (1998) Is aging a preventable or curable disease? Drugs Aging 13(2):93–97. https://doi.org/10.2165/00002512-199813020-00001

Caplan AL (2005) Death as an unnatural process. EMBO Rep 6:S72–S75

Christensen K et al (2009) Ageing populations: the challenges ahead. Lancet 374(9696):1196–1208. https://doi.org/10.1016/S0140-6736(09)61460-4

Clark RL et al (2008) Older workers and national productivity in Japan. Popul Dev Rev 34:257–274

De Grey ADNJ (2007) Aging and airborne HIV: a reassuring analogy. Rejuvenation Res 10(1):1–3. https://doi.org/10.1089/rej.2006.9099

De Grey ADNJ (2008) Combating the Tithonus error: what works? Rejuvenation Res. https://doi.org/10.1089/rej.2008.0775

De Grey ADNJ (2020) Being rational about health: the Pandemic's long-term silver lining? Rejuvenation Res 23(2):91–92. https://doi.org/10.1089/rej.2020.2336
De Winter G (2015) Aging as disease. Med Health Care Philos 18(2). https://doi.org/10.1007/s11019-014-9600-y
Fukuyama F (2002) Our Posthuman Future. Farrar, Straus, and Giroux, New York
Gems D (2011) Tragedy and delight: the ethics of decelerated ageing. Philos Trans R Soc Lond Ser B Biol Sci 366(1561):108–112. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3001315&tool=pmcentrez&rendertype=abstract
Gems D (2014) What is an anti-aging treatment? Exp Gerontol 58:14–18
Giacomello E, Toniolo L (2021) The potential of calorie restriction and calorie restriction mimetics in delaying aging: focus on experimental models. Nutrients 13(7):2346
Harris J (2002) Intimations of Immortality: the ethics and justice of life extending therapies. Curr Legal Probl 55(1):65–95. https://doi.org/10.1093/clp/55.1.65
Hayflick L (2000) The future of ageing. Nature 408(6809):267–269. https://doi.org/10.1017/S1062798702000261
Huber WR, Sierra F (2009) The longevity dividend: why invest in basic aging research? Can J Aging 28(4):391–394; French 395-398
Kim JH et al (2021) Operation warp speed: implications for global vaccine security. Lancet Glob Health 9(7):e1017–e1021
Kwok M, Fritsch EF, Wu CJ (2021) Cancer and COVID-19: on the quest for effective vaccines. Blood Cancer Discov 2(1):13–18
Lemoine M (2020) Defining aging. Biol Philos 35(5). https://doi.org/10.1007/s10539-020-09765-z
Mackey T (2003) An ethical assessment of anti-aging medicine. J Anti Aging Med 6(3):187–204. https://doi.org/10.1089/109454503322733045
Masoro EJ (2005) Overview of caloric restriction and ageing. Mech Ageing Dev 126(9):913–922. http://www.ncbi.nlm.nih.gov/pubmed/15885745
Meldrum DR, Morris MA, Gambone JC (2017) Obesity pandemic: causes, consequences, and solutions—but do we have the will? Fertil Steril 107(4):833–839. https://doi.org/10.1016/j.fertnstert.2017.02.104
Miller RA (2009) "Dividends" from research on aging - can biogerontologists, at long last, find something useful to do? J Gerontol Ser A Biol Sci Med Sci 64(2):157–160. https://doi.org/10.1093/gerona/gln062
Moodie R et al (2013) Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultra-processed food and drink industries. Lancet 381(9867):670–679. https://doi.org/10.1016/S0140-6736(12)62089-3
Morens DM, Folkers GK, Fauci AS (2009) What is a pandemic? J Infect Dis. https://doi.org/10.1086/644537
Murphy TF (1986) A cure for aging? J Med Philos 11(3):237–255
Olshansky SJ et al (2006) In pursuit of the longevity dividend. Scientist 20(3):28–36
Olshansky SJ et al (2007) Pursuing the longevity dividend: scientific goals for an aging world. Ann N Y Acad Sci 1114:11–13. http://www.ncbi.nlm.nih.gov/pubmed/17986572
Partridge B et al (2009) Ethical concerns in the community about technologies to extend human life span. Am J Bioethics Ajob 9(12):68–76. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20013509
Pijnenburg M, Leget C (2007) Who wants to live forever? Three arguments against extending the human lifespan. J Med Ethics 33(10):585–587. https://doi.org/10.1136/jme.2006.017822
Provinciali M, Smorlesi A (2005) Immunoprevention and immunotherapy of cancer in ageing. Cancer Immunol Immunother 54(2):93–106
Ricklefs RE, Scheuerlein A (2001) Comparison of aging-related mortality among birds and mammals. Exp Gerontol 36(4–6):845–857. http://www.ncbi.nlm.nih.gov/pubmed/11295518
Saborido C, García-Barranquero P (2022) Is aging a disease? The theoretical definition of aging in the light of the philosophy of medicine. J Med Philosop [Preprint]

Sampath S et al (2021) Pandemics throughout the history. Cureus 13(9):e18136. https://doi.org/10.7759/cureus.18136

Schramme T (2013) "I hope that I get old before I die": ageing and the concept of disease. Theor Med Bioeth 34(3). https://doi.org/10.1007/s11017-013-9256-2

Shankaran V et al (2001) IFNγ and lymphocytes prevent primary tumour development and shape tumour immunogenicity. Nature 410(6832):1107–1111

Wareham CS (2012) Substantial life extension and quality of life. In: ACM International Conference Proceeding Series. https://doi.org/10.1145/2331714.2331728

Wareham CS (2016) Substantial life extension and the fair distribution of healthspans. J Med Philos 41(5):521–539. https://doi.org/10.1093/jmp/jhw021

Williams B (2009) The Makropulos case: reflections on the tedium of immortality. In: Problems of the self. Cambridge University Press, Cambridge. https://doi.org/10.1017/cbo9780511621253.008