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Towards Longer Lives:

The Ethical Implications of Life Extension by Calorie Restriction and Calorie Restriction Mimetics

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ABBREVIATIONS

CR	Calorie restriction
CRM	Calorie restriction mimetics
2DG	2-deoxy-d-glucose
DHEA	Dehydroepiandrosterone
DHEAS	Dehydroepiandrosterone sulfate
CRS	Caloric Restriction Society
CALERIE	Comprehensive Assessment of Long-term Effects of Reducing Energy Intake
LET	Life Extension Technology
h-LET	Hypothetical Life Extension Technology
USPBC	US Presidential Council on Bioethics
iPSC	Induced Pluripotent Stem Cell
WHO	World Health Organisation
QALY	Quality Adjusted Life Year
NICE	National Institute for Clinical Excellence

FIGURES

ABSTRACT

A significant reduction in calorie intake, known as calorie restriction (CR), has been shown to increase lifespan in a wide variety of animal subjects. If these results translated to humans, CR could substantially increase human lifespans by decelerating ageing. This possibility has led to an effort to develop calorie restriction mimetic drugs (CRMs) that mimic the effects of CR without the need to reduce calorie intake. This project examines the social and ethical implications of extending lifespans using CR and CRMs.

The thesis is in three parts. Part I looks closer at the empirical questions about CR and CRMs, and in particular the issue of whether results from animal studies would translate to humans. I argue that although the evidence is far from conclusive, there are grounds to think that CR could slow ageing and extend lifespan in humans.

Part II examines the implications of prolonging lifespan for individual welfare. I argue that historical and philosophical objections to life extension on the grounds of individual welfare are unsuccessful against CR. CR itself may have some undesirable effects, although these are due to the stringent diet and are unlikely to apply result from CRMs.

Part III discusses the social impact of CRMs, assessing common ethical objections to life extension on the grounds of fairness and social welfare. I claim that it would be fair to distribute CRMs by public health services. Moreover, concerns about the demographic impact of longer lives can be mitigated. Indeed, a wide distribution of life extending technologies could improve social welfare.

Overall, I claim that CR and CRMs are compatible with, and could further, values that are significant for individuals and societies.

INTRODUCTION

Ageing, widely regarded as a progressive decline that makes an organism less capable of survival, is related to a host of maladies including cancers, cardiovascular diseases, diabetes, and Alzheimer's disease. As Harris has suggested, this means that there is a strong chance that treating these and other diseases will have an impact on the rate of ageing and thereby substantially prolong human lives (Harris 2004, 530). This raises the prospect that life extension interventions may arrive largely unheralded.

Thus far, however, only one intervention—caloric restriction (CR)—has been shown to consistently and substantially extend average and maximum lifespan in a wide variety of organisms (Roth et al. 1995).[1] As the name suggests, CR involves a significant reduction in calorie intake. Remarkably this relatively simple intervention has been shown to prolong the lives of rodents by as much as 60% (Speakman and Hambly 2007). If effective in humans it would result in a substantial increase in average and maximum lifespan.[2]

Despite a growing number of CR practitioners, the caloric restriction regime is widely thought to be too demanding for widespread human practice. As a result, biologists and pharmaceutical companies are investigating a number of potential CR mimetics (CRMs)—drugs that might replicate the effects of CR without the need to restrict calories.

Perhaps the most extensively investigated candidate CRMs are rapamycin, resveratrol and metformin.[3] Rapamycin is an immuno-suppressant commonly used in organ transplantation. Metformin is a compound used in the treatment of diabetes. Resveratrol is a polyphenol derived from grapes and found in small quantities in red wine. All of these

[1] For an overview see Masoro 2005.
[2] The extent of this increase is discussed in more detail in Chapter 3.
[3] See Minor et al. 2010 for fuller discussion of recent research on candidate CRMs.

candidate CRMs have been trialled in humans. Indeed resveratrol-based products are widely available without prescription in pharmacies, while metformin is used every day by diabetes sufferers.

Research on CR and CRMs has garnered an increasing amount of attention in well-respected scientific journals, in the media and, significantly, from the pharmaceutical industry. Recently the pharmaceutical giant GlaxoSmithKline bought Sirtris, a biotechnology company aimed at creating effective CRMs, for $720 million—an amount indicative of the financial potential of such drugs.[4] Despite this increased attention, and the fact that life extension has been a human preoccupation for millennia, there is virtually no discussion of the ethical implications of these accessible and potentially lifespan augmenting interventions.

Clearly there is a large body of work, either literary or philosophical, that explores the ethical implications of extending lifespan, and these concerns must be addressed. Yet there is also a growing body of scientific literature yielding clearer ideas about the potential benefits and drawbacks of life extension technologies. Research on CR and CRMs presents the possibility to revisit the more speculative concerns about the impact of substantial life extension on individual welfare with concrete empirical evidence in hand.

This thesis examines these potential ethical implications of prolonging life in light of findings about CR and CRMs. I claim that, although longer lives raise important challenges, research on CR and CRMs provides grounds to think that CRMs in particular could contribute to a better and fairer society with healthier and more long-lived individuals.

[4] http://www.guardian.co.uk/business/2008/apr/23/glaxo.sirtris. Accessed 18 December 2012.

In the remainder of this introduction I discuss the role of empirical studies in this thesis and in applied ethics generally. In doing so, I differentiate this project from other studies of life extension in terms of its scope, and in terms of its focus on factual premises of moral arguments. I also draw attention to a methodological tenet I refer to as 'compatibilism' and discuss its strengths and weaknesses.

i) Applied ethics

Empirical studies play two significant roles in this thesis. First, they function as factual premises in moral arguments; second, they allow a narrower focus that avoids unrealistic and heavily hypothetical life extension scenarios.

The first role of empirical studies is as factual premises in ethical arguments. Below I situate my methodology as a type of applied ethics. I explain the structure of arguments in applied ethics, and the role of factual premises supplied by empirical studies.

The aims of applied ethics

Applied ethics attempts to arrive at justified conclusions about real ethical problems. Its purpose is to inform decisions about what actions or decisions are good or right. The claims that 'abortion is immoral,' or that 'murderers should receive the death penalty' are examples of claims in applied ethics.

This is a thesis in applied ethics. It aims to provide ethical discussion of, and guidance about a potentially problematic technology. More narrowly, it can be regarded as a bioethical study, since it applies ethical principles to an emerging biotechnology.

Argument in applied ethics

An argument in applied ethics must, of course, obey logical rules and has, at minimum, the following components:

1. A moral premise which constitutes a moral conviction, principle or value
2. A factual premise
3. A practical conclusion that is logically entailed by the combination of the moral and factual premises (Tännsjö 2011).

A simplified example is the following:

1. A person should do things that make her healthy
2. Eating vegetables makes a person healthy
3. So a person should eat vegetables

This simple structure means that there are three key ways that an argument in applied ethics can contested. One can challenge the normative premise, the factual premise, or the logical validity of the argument. Below I discuss how a focus on *factual premises* and validity grounds a methodological approach I refer to as 'compatibilism.'

ii) Applied ethics and 'compatibilism'

My approach in this thesis is to accept the normative basis on which objections to life extension are made. That is, I accept a range of normative *moral premises*, which can include values and principles. Instead, I challenge the *factual premises*, and the validity, of arguments about life extension.

I term this approach 'compatibilism,' because my aim is to determine the extent to which life extension by CR and CRMs is compatible with the furtherance of a range of normative

principles. Even if we accept the substantive normative theories that underlie fears about life extension, there may be reason to think that CRMs would be a good thing if these fears are based on misapprehensions about the facts.

This approach is made workable by the narrower focus discussed below. Since I focus on a particular life extending intervention about which much is known, it is possible to examine the factual basis of concerns about life extension. I now discuss some of the strengths of, and motivations for, compatibilism before examining its limitations.

Motivations for compatibilism

One motivation for assessing the compatibility between life extension and value claims is to avoid pervasive disagreement at the level of values. If an intervention can be shown to be compatible with various ethical principles, then it is possible to prevent some of this disagreement. By taking moral premises for granted and instead challenging factual premises, it may be possible to achieve an 'overlapping consensus,' (to use Rawls's (1971) term) on the morality of an intervention.

A further motivation for compatibilism is that if factual premises about an intervention lead to an undesirable conclusion, it is sometimes possible to alter these premises. Facts can sometimes be more malleable than values. Take, for example, the following argument:

1. It is immoral to cause an embryo to die.
2. Stem cell research causes embryos to die.
3. Thus stem cell research is immoral.

Much work in bioethics and applied ethics has focussed on disputing the morality of killing embryos (premise 1). However, more recently, it has become possible to conduct stem cell research that does not make use of embryonic stem cells. Induced pluripotent stem (iPS)

cells can be made from virtually any cell in the body.[5] In effect the factual premise has been altered, rendering false the above argument against the morality of stem cell research.

In a similar way, focusing on factual premises in arguments about life extension might help draw attention to facts that are problematic, and which may similarly be subject to biological manipulation. A relevant example of this, which emerges particularly in Chapters 4 and 9, is the possibility of compressing or shortening morbidity. I highlight this example in more detail the conclusion of this thesis.

These motivations point to ways in which the compatibilist use of empirical studies can shed light on, and potentially resolve, ethical disputes even when moral premises are the subject of deep and pervasive disagreement.

iii) A narrower focus

A second function of empirical studies is that they allows a *narrower* focus on a particular type of life extending intervention. Below I explain what I mean by this by contrasting my focus with broader ethical analyses of substantial life extension.

Broad approaches: life extension and other enhancements

At the broader end of the spectrum, prolonging life might be considered as one of many different types of 'enhancement' technologies: interventions that raise individuals above some level of welfare or health considered 'normal' (Daniels 2000). This type of broad discussion focuses on general features of enhancement technologies and considers their ethical status. Life extension would be judged alongside these.

[5] See for example Cherry and Daley 2012.

This breadth of scope has the advantage of broader applicability, but often ignores more fine-grained details. One example is the likelihood, discussed in Chapters 7 and 8, that although potentially enhancements, CRMs will also be treatments, improving disease conditions.

Narrower focus: substantial life extension itself

More narrowly, ethical theorists focus on a general category of life extending technologies that could hypothetically exist. They attempt to identify ethical problems and sometimes examine whether these problems can be resolved. Such evaluations are useful, since they provide a rich source of potential problems – an ethical gauntlet that a real life extending technology must run. Considering the ethics of longer lives can also, arguably, clarify questions about the meaning of life and why it's good to be alive in the first place.

However, in relation to the implications of life extending technologies themselves, such studies can be hampered by the lack of a factual basis. One can make use of 'thought experiments' about anti-ageing drugs, but it is speculative that these thought experiments will share any features with real technologies. As an example, in Chapter 9, I point out that Singer's argument against life extension fails to apply to CRMs, since it is relies on a hypothetical life extension technology with little basis in fact.

Moreover, the lack of a factual basis often leads writers to focus on unlikely life extension scenarios such as immortality. As Leigh Turner suggests, these discussions can

> skew analysis by moving from legitimate concerns to a far more speculative, less biologically grounded mode of deliberation. (Turner 2004, 220)

Narrower still: particular life extending interventions

At the narrower end of the scale, an ethical analysis of life extension examines the implications of a particular intervention, or category of intervention, given empirical studies. There are very few such analyses because no intervention is known with certainty to substantially extend lifespan in humans.

Nonetheless the focus of this thesis is narrow in this sense. I examine the ethical implications of life extension by CR and CRMs, in the light of empirical studies on CR. This focus enables the making of claims that are more 'biologically grounded,' to use Turner's phrase, than any other claims about life extension that I have encountered.

However, it is important to note that my focus is not as narrow as it gets. If we knew with certainty that an intervention extended lifespan in humans, we could conduct an even narrower ethical inquiry – one without the need for well-grounded, but uncertain, claims. This would obviously be more informative, both scientifically and ethically. However, as I point out in Chapter 3, it is unlikely that we can have certainty that an intervention substantially extends lifespan before it has done so.

iv) Methodological limitations

There are some aspects of the methodology I make use of in this thesis that could be perceived as weaknesses. First, the factual premises I make use of may be shown to be wrong in the long run. They are based on a hypothesis that is not known to be true – that the effects of CR will translate to humans – and a hypothetical intervention – a drug that will mimic these effects. Since the empirical claims are susceptible to falsification, some of the ethical analysis of the effects of CR and CRMs may be rendered incorrect by current and future research. Other accounts that rest less heavily on empirical studies are obviously less susceptible to this outcome.

Second, genuine CRMs may have their own side-effects and ethical complications. It is not possible to take these into account, since, as discussed in Part I, we do not know whether there are any are genuine CRMs.

Despite these potential weaknesses, the claims advanced in this dissertation would have broader applicability, even if some of the empirical claims turn out to be false or incomplete. In the first place, the collection of arguments I discuss provides a *framework* of values and potential problems that is useful for analysing any life extending intervention.

Moreover, a key empirical premise I rely on is that of decelerated or slowed ageing, as outlined in Chapter 2. Even if CR and CRMs do not slow ageing, it is not unlikely that other interventions will. If so, many of the arguments will apply to these interventions.

v) Conclusion

This introduction has attempted to spell out the methodological role of empirical evidence in this thesis. Two advantages are worth re-emphasising. First, the compatibilist focus on acceptance of a variety of moral premises makes it possible to reach agreement about the morality of an intervention despite disagreement about moral values. Second, a narrower focus on a well-known intervention enables more fine-grained and less speculative claims about life extension.

With these methodological points in place, I discuss the empirical evidence that will inform the ethical argument in subsequent parts.

PART I: EMPIRICAL QUESTIONS

INTRODUCTION TO PART I

CR has been shown to increase average and maximum lifespan in multiple organisms including yeast, flies, nematodes, mice, and dogs. This has resulted in a quest to investigate and develop potential CRMs such as resveratrol, rapamycin, and metformin. This part examines the empirical research on CR and CRMs.

Chapter 1 surveys empirical and terminological issues with defining CR and CRMs, and gives examples of candidate CRMs. Chapter 2 discusses research in animals, and the effects of CR on the rate of ageing. Chapter 3 explores the hypothesis, which I refer to as the 'transfer thesis,' that the effects of CR observed in animals will translate to humans.

I claim that while it is difficult to be certain how CR and CRMs will affect humans in the long-term, current findings from animal and human studies suggest that CR, and interventions that mimic it, could slow ageing, leading to a substantially longer life. These claims form the basis for the ethical analysis in subsequent chapters.

1. WHAT ARE CR AND CRMS?

In this chapter I discuss terminological differences in empirical literature that may cause confusion. I also motivate a definition of CRMs, and discuss some interventions that are regarded as potential CRMs.

1.1 What is CR?

Since McCay's seminal studies on restricted food intake (McCay 1935), a number of different experimental protocols have been referred to as calorie restriction. Conversely, many of the very same protocols have been referred to by different names, including food restriction, dietary restriction, energy restriction, and caloric restriction.

Although it is not uncommon to use these terms interchangeably (eg Redman et al 2007), sometimes the use of a particular term has a purpose. For instance, the terms dietary or food restriction are sometimes used operationally when attempting to isolate which aspects of food restriction are responsible for the effects on longevity and ageing. For instance, there have recently been attempts to restrict consumption of various dietary components, such as proteins (Fontana et al 2008), fats (Sanz et al 2006), and molecules such as methionine (Sun et al 2009), in an effort to isolate particular dietary inputs that contribute to the effects of CR on longevity and ageing. The use of the terms food, or dietary restriction in such cases expresses a suspension of judgement about any particular dietary cause.

1.1.1 The term used in this thesis

Dietary restriction and food restriction are broader, encompassing the restriction of calories and other dietary sources that may be responsible for the effects of reduced food intake.

This breadth of meaning means that the terms are somewhat inexact, and have been referred to as 'vague' (Masoro 2006).

Calorie, or caloric, restriction is narrower, referring to the restriction of dietary energy. There is general agreement that the restriction of energy, or calories, plays a large role in the effects of a leaner diet (Masoro 2005). This means that it is somewhat justified to use the term caloric restriction.

Even narrower terms are possible: as mentioned, protein restriction, and the restriction of the amino acid methionine may contribute to the effects of a reduced diet. However, the extent of the roles of protein and methionine are still disputed (*ibid.*). As a result I will use the intermediate terms calorie, or caloric, restriction.

1.1.2 CR protocols

With this terminological query aside, I turn to the issue of what CR entails. Again this is a vexed question. In its broadest formulation, CR involves a restriction of energy intake from *ad libitum* levels, but without a reduction in essential nutrients. There are many difficulties in constructing CR protocols and comparing their results.[6] Here I mention two such problems in order to clarify what CR and *degrees* of CR entail.

The first clarification concerns what is meant by an *ad libitum* or free-feeding diet. Animals that are allowed to eat as much as they wish are often overweight. As a result it has been suggested that some of the gains in longevity achieved by restricting calories may be as a result of counteracting diseases related to overfeeding (Speakman and Mitchell 2011). To eliminate this possibility, it has become common to restrict the calorie intake of

[6] See Speakman and Mitchell 2011 for a more detailed discussion of methodological difficulties in studies of CR.

control mice to 10% of true *ad libitum* levels. This restriction serves as the comparandum for greater reductions in calorie intake. Significantly, this may mean that, for example, a 50% reduction in calories relative to controls is actually a 60% reduction relative to true *ad libitum* levels (Speakman and Hambly 2007). This has consequences for the degree of CR that might be required in humans, and is thus important to mention.

The second clarification concerns interpretations of degrees or percentages of caloric restriction. The extent of CR is expressed in two different ways. Sometimes a diet of 60% that of controls - a reduction of 40% - is referred to as 60% CR, referring to the percentage of an *ad libitum* diet that is consumed. However, the same degree of restriction is sometimes called 40% CR, meaning that the organism's diet is restricted by 40% from normal levels. In this thesis I will use the latter formulation, so that 30% CR is 70% of the diet of controls.

CR thus involves a specified restriction of caloric intake, without malnutrition. In Chapter 3, I will discuss factors that modulate the degree of life extension achieved by CR.

1.2 What are CRMs?

Broadly, CRMs are interventions that mimic the effects of caloric restriction. According to Ingram and colleagues, the function of a CRM is

> to trick the organism into a CR state and thereby activate the protective mechanisms that are induced in CR. Moreover, the parallel objective should be to minimize any reduction in actual caloric consumption. (Ingram et al. 2006, 99)

Ingram et al complain that in much of the literature, CRMs are construed too broadly as including 'any intervention that can evoke similar effects on aging, health, and lifespan to those of CR' (*ibid.*, 98) This suggests there is a need to refine the conceptual scope of

CRMs. At the very least interventions that have radically different modes of action should be excluded.

In order to clarify the aims of research into CRMs, Ingram et al propose that a CRM must fulfil the following conditions:

> (i) it mimics the metabolic, hormonal, and physiological effects of CR; (ii) it does not significantly reduce long-term food intake; (iii) it activates stress response pathways observed in CR and provides protection against a variety of stressors; and (iv) it produces CR-like effects on longevity, reduction of age-related disease and maintenance of function. (*Ibid*.)

However, it is possible that an intervention fulfils all the criteria, but lacks some inessential hormonal, or metabolic effect. Indeed, presumably not all metabolic effects of restricting calories could be replicated without actually restricting food intake. For instance, if food is not restricted, then the metabolic activity of breaking food down to nutrients will not occur to the same extent. This would be a difference in metabolism. So if we're extremely strict about the above definition, it's not clear that anything could be a CRM without being CR itself.

I will not focus extensively on definition of a CRM. Instead I will assert a working definition of a CRM as an intervention that

i) does not involve long-term reduction of food intake and

ii) has identical effects to CR, barring only those effects that are solely consequences of decreasing food intake.

If, for instance, a candidate CRM has exactly the same effects as CR, but doesn't result in weight loss or hunger, and if weight loss and hunger are solely consequences of having less food, the candidate would successfully count as a CRM.

This narrow understanding of a CRM would have the effect of excluding interventions like surgical reduction of the stomach and appetite suppressants, since both involve an actual reduction of calorie intake. It would also inevitably exclude many of the current candidate CRMs discussed below, since none is capable of perfectly mimicking CR. On the other hand this conception of a CRM allows me to examine the ethical implications of CRMs given the store of information that has been accrued across more than 80 years of research on CR.

In the next sub-section I discuss three candidate CRMs, indicating the extent to which they fulfil the criteria for a CRM suggested above.

1.2.1 Candidate CRMs

Numerous candidate CRMs are currently being investigated. These include 2-deoxy-d-glucose (2DG), sirtuins such as resveratrol, rapamycin and rapalogs, and biguanides, such as metformin, phenformin and buformin. Here I will discuss three that are regarded as most promising: resveratrol, rapamycin, and metformin.[7]

Resveratrol is a polyphenol present in diverse dietary sources. It has been widely reported in the media due to the fact that it is found in red wine and purportedly has 'anti-ageing' effects. Interestingly, the consumption of resveratrol-rich red wine has been proposed as an explanation for the French Paradox: the phenomenon that France appears to have low mortality rates, despite a traditionally high-fat diet and the prevalence of cigarette smoking (Vidavalur et al 2006). The attraction of resveratrol is increased due to the fact that it is generally regarded as safe for human consumption (Cottart et al 2010).

[7] See Minor et al 2010 for fuller discussion of recent research on candidate CRMs.

Experiments on resveratrol suggest that, in sufficient quantities, it mimics many of the effects of CR discussed in more detail later. In particular, in mice it has many of the same effects in reducing the incidence of cardio-vascular disease and cancer (Barger et al 2008). However, it has only been shown to be moderately successful in increasing maximum lifespan. Only mice fed a very high fat diet have substantially higher maximum lifespan as a result of resveratrol treatment (Baur et al 2006). Further, resveratrol is not easily absorbed by the human digestive system, and the quantities needed to replicate the effects of resveratrol in humans are thought to be large (Walle 2011).

Nonetheless, findings on resveratrol have been encouraging enough to generate massive investment in developing a marketable version that would be effective in humans. As mentioned in the introduction, Sirtris, a research-based company aimed at making a drug that would have the same effects as resveratrol, was bought by the pharmaceutical company GlaxoSmithKline for a staggering amount of money. Currently Sirtris is conducting clinical trials on a number of resveratrol-derived drugs that may prove to be effective CRMs.

Rapamycin has been shown to increase lifespan in a variety of genetically different rodents (Harrison 2009; Miller 2011). Like CR it has anti-tumor effects, and is believed to slow ageing. These effects have led to the development of rapalogs – drugs derived from rapamycin such as everolimus – that are used in the treatment of cancer (Minor et al 2010).

However, rapamycin is also a potent immune-suppressant used in organ transplantation (*ibid.*). Thus it may have negative effects on the immune system, although it is possible that lower dosage may mimic the life effects of CR without introducing additional deleterious consequences (Kaeberlein 2010). Indeed, some regard rapamycin as a viable

CRM (Blagosklonny 2010) while others suggest that it is the best candidate for the development of CRMs (Sierra et al 2009).

Metformin is the most widely used drug for the treatment of type 2 diabetes. It is regarded as a candidate CRM because it results in similar gene expression patterns (Minor et al. 2010, 2). Like metformin, CR is highly effective in the treatment of diabetes (Jonker et al. 2011). Metformin has also been shown to increase maximum lifespan in mice, though not by as much as CR (Anisimov et al. 2011).

Unlike the above CRM candidates, metformin has been in general use for more than half a century, having been introduced in the United Kingdom in 1958. It is clinically approved and has been used by millions of humans. Significantly, this means it is possible to conduct long-term mortality and morbidity studies in humans. Such studies have indicated that in addition to its on-label effect of treating diabetes, metformin has cardio-protective and anti-atherosclerotic effects (Scarpello 2003). Recent studies also suggest metformin may also have a role in tumour suppression (Scarpello 2008). Again, these effects are similar to those that occur as a result of CR.

It should be borne in mind that metformin may not meet the strict CRM criteria. In particular, I am unaware of any controlled studies comparing the life expectancy of metformin users to that of non-diabetics. Without these studies it is not clear that it increases life expectancy in humans. Even so, metformin is of particular interest as a CRM candidate due to its approved status and the fact that it is already widely used. This makes it perhaps the most realistic target for health policy on CRMs, as discussed in the conclusion of this thesis.

1.3 Conclusion

In this chapter I have discussed some terminological and empirical issues in research on CR and CRMs. I also gave examples of candidate CRMs. Although none of these candidates fully replicate the effects of CR, they are already of ethical interest due to their CR-like effects and their widespread use in humans. Moreover, increased investment in these and other compounds makes it highly plausible that research will lead to the development of CRMs capable of reproducing the effects of CR discussed in Chapters 2 and 3.

2. CR IN ANIMALS: LIFESPAN AND THE RATE OF AGEING

Animal studies suggest that CR extends lifespan by slowing ageing.[8] One influential definition of ageing is the following:

> Aging (senescence) is defined as the deteriorative changes, during the adult period of life, which underlie an increasing vulnerability to challenges, thereby decreasing the ability of the organism to survive (Masoro 2006, 15).

In these terms, ageing is a progressive deterioration that makes an organism less capable of survival. CR is widely regarded as slowing this process, thus allowing organisms to survive for longer.

However, the claim that CR slows ageing is complicated by the fact that several different measures of the rate of ageing are used in empirical studies. In this chapter I outline these measures, and discuss the results that have been achieved in animal models. The discussion below focuses primarily on mammals. Although CR has been shown to have life extending effects in organisms such as yeast, nematodes and fruit flies, studies in mammals are more likely to be of direct relevance to humans ageing.

In discussing different measures of the rate of ageing, I will point out some of their limitations. However, my purpose here is not to privilege any particular measure or to arrive at a clear cut operational account of the rate of ageing. Instead, my aim is to clarify the claim that CR slows ageing. This is important since, as will become clear measures of

[8] Slowed ageing is also referred to as retarded or decelerated senescence. Senescence more commonly refers to cellular, rather than organismic senescence, so I will usually use the term ageing. See Campisi and D'Adda di Fagagna 2007 for a review of the connection between cellular senescence and ageing.

ageing are subject to criticisms both about their usefulness and their relation to ageing itself.

Examining claims of slowed ageing also gives a better understanding of the effects of CR in non-human animals that lead to this attribution. In particular, I will indicate four significant conclusions, each of which corresponds to a particular measure of ageing applied to animal studies. Lifespan measures, rate of mortality measures, disease measures, and biomarker measures of the rate of ageing all point to different respects in which CR slows the rate of ageing in animals.

2.1 Lifespan measures of the rate of ageing

The idea that CR slows the rate of ageing was initially based on the observation that it increases the average and maximum lifespan in populations of animals studied, and reduces the age-relative likelihood of death. In particular, CR mice and rodents have been known to live as much as 60 percent longer than controls.[9]

Studies on rhesus monkeys are in relatively early stage. Although it is too early to know whether CR will increase average and maximum and average lifespan, results so far are promising. As of 2009 only five of thirty-eight CR animals in one study had died of age-related causes, compared to thirteen out of thirty-eight control animals (Colman et al 2009).[10] This is in keeping with studies on rodents that suggest a lower age-relative likelihood of death.

[9] Fontana, Partridge and Longo 2010 provide an overview.

[10] Intriguingly a very recent study has failed to replicate these results (Mattison et al. 2012). Results from this research require further analysis and may provide an opportunity to explore the complex impact of dietary component restriction on the rate of ageing as measured by lifespan.

2.1.1 Limitations of lifespan measures

Determining the rate of ageing on the basis of lifespan has at least one conceptual shortcoming: decreased chance of survival is not all that is important about ageing. Ageing is also associated with increased susceptibility to disease and physical decline. This is a significant reason why we are interested in the rate of ageing in the first place, and lifespan measures alone tell us very little about the prevalence of disease and deterioration.

Lifespan measures of the rate of ageing also present methodological and practical difficulties. In particular, the age at which the oldest organisms die changes with the size of the group studied. Perhaps unsurprisingly the oldest organisms in large samples tend to be older than the oldest organisms in smaller samples (Speakman and Mitchell 2011). As a result, it has become common to record maximum lifespan as the average age of a percentage of the last survivors – often 10%.

A further practical problem is that lifespan measures of the rate of ageing are difficult to apply in studies of longer-lived animals such as humans. For instance, the oldest recorded human is Jeanne Calment, who lived to 122 years and 164 days. If we take Jeanne Calment as our control, according to maximum lifespan measures we would only know if CR slowed ageing in humans if the oldest members of the CR population surpassed this age (or perhaps if the oldest 10% of the CR population lived longer than the oldest 10% of the human population). Clearly it would be useful to find a shorter term method to determine rates of ageing.

2.1.2. Effects of CR on lifespan

Although these limitations are important, lifespan measures of ageing yield a significant finding:

1. CR increases average and maximum lifespan relative to control groups and decreases the age-relative likelihood of death.

The extent to which CR increases lifespan varies in accordance with the degree of CR and the time of life at which the intervention is begun. These factors are discussed in more detail in S3.1.

2.2 Rate of mortality measures

In studies of CR the rate of ageing is often measured on the basis of the rate of mortality. Slowed ageing is said to occur if, after an increase in the number of deaths in a group – which signifies the onset of age-related death – this number takes longer to increase than it does in control groups.

For example, suppose a control group of mice lives to two years before individuals within the group begin to die more frequently. Two months after this acceleration, all are dead. Now suppose another group lives to two years and five months before individuals in the group start dying more frequently. Four months after this acceleration, all are dead.

In this case, *the period in which increased mortality occurs* is extended by an additional two months. Since, after an initial point of increased mortality, deaths occur across a longer span of time than a control group, this is an example of slowed ageing on rate of mortality measures (Merry 2005).

This slowed ageing is in contrast to *delayed ageing*. With delayed ageing only the onset of increased mortality is delayed. After this, animals die at approximately the same rate. In the example above, if the second group of animals lived until two years and five months

before the rate of death increased, and then lived a further two months after increased mortality (the same as the control group), this would be an example of delayed ageing.

A further possibility is *accelerated ageing*. With accelerated ageing the period after the increased onset of age-related mortality is compressed relative to controls. In the example above, accelerated ageing is in evidence if the period between increased mortality and the death of the last animals is less than two months.

Mortality studies on CR rodents point to slowed ageing according to rate of mortality measures. The rate of mortality after the initial age-related increase is slowed down (Weindruch 1996; Weindruch and Sohal 1997; Masoro 2005).

2.2.1 Limitations of rate of mortality measures

Rate of mortality measures of biological ageing are important tools. However, there are obvious shortcomings. Here I will mention four. The first three are held in common with lifespan measures: first, they tell us very little about the health effects of CR; second, they do not tell us about the physiological processes that occur prior to the period of increased mortality; third, they are again very difficult to apply in human experiments or in experiments on other long-lived mammals.

The fourth problem is in direct contrast to lifespan measures. Rate of mortality measures contradict the idea that length of life is an important factor in the rate of ageing. For instance, on these measures it is possible that a group of mice that lived a *shorter* amount of time than a control group would be regarded as having a slower rate of ageing than the control group, or that a group that lived longer than a control group would be regarded as having a faster or equivalent rate of ageing. Indeed the latter finding – increased lifespan, but rapid ageing – was reported by George Sacher upon the administration of procaine

(Sacher 1977). In this case, despite decreased deaths at all ages, rate of mortality measures yielded the conclusion that mice administered procaine aged at the same rate as control mice

This type of finding can occur because the rate of ageing is determined by how quickly animals die after reaching a 'tipping point' of increased group mortality. Nothing that occurs before this tipping point, nor the length of the life as a whole, enters the equation about the rate of ageing. This leads to the above conclusions in Sacher's study, which Masoro describes as 'absurd' (Masoro 2006, 16). Intuitively, there are processes occurring before the tipping point that could be highly relevant to the rate of ageing. This is backed by findings that suggest that age-related decline begins much earlier in life: perhaps earlier than thirty in humans (Sehl and Yates 2001; Nakamura and Miyao 2003.)

2.2.2 Effects of CR on rate of mortality

Despite these limitations, studies that make use of rate of mortality measures lead to a second sense in which CR slows ageing and a second independently significant conclusion:

2. Deaths in CR populations tend to occur across a longer span of time than those in control animals.

2.3 Disease measures

Studies of CR have also concentrated on the occurrence of age-related diseases. Measuring the occurrence of age-related diseases is a promising way to determine the rate at which an organism is ageing. Age-correlated diseases might be regarded as examples of the 'deteriorative changes' that constitute ageing and decrease an organism's chance of survival. Indeed the above approaches have been criticised for their excessive focus on

mortality. Instead critics urge that morbidity, or disease, is 'much more informative about the aging process' than mortality (Sundberg et al 2011).

In the mammals in which it has been applied, CR delays the occurrence of, and slows the development of, age-related diseases (Masoro 2006).[11] In particular, it has been shown to have beneficial effects for the three main causes of death in rodents: it inhibits cancers, and delays or prevents kidney diseases, and heart diseases. It also prevents diabetes, auto-immune disorders, and respiratory diseases (Speakman and Mitchell 2011). Moreover, CR was found to have positive effects in mouse models of debilitating human diseases, including Alzheimer's disease, Huntington's disease, and Parkinson's disease (Omodei and Fontana 2011). Disease measures of the rate of ageing in rodents thus support the idea that CR slows ageing.

Disease measures also have the advantage of taking less time for results than maximum lifespan and rate of mortality measures. As a result studies are beginning to emerge on longer-lived mammals, which are more likely to be of relevance to humans. Perhaps the most striking observations in this respect again come from Colman and colleagues' ongoing study on calorically restricted rhesus monkeys, begun in 1989.

In rhesus monkeys, as in humans, cardiovascular disease, diabetes and cancer are amongst the most prevalent age-related diseases (Colman et al 2009). This is one factor that supports the potential transferability of research on rhesus monkeys to humans.

As of 2009, the monkeys in Colman and colleagues' study were 20 years of age – around half the maximum lifespan of rhesus monkeys. The study found that age-related disease is significantly reduced in the CR population. Remarkably, sixteen of the thirty-eight control

[11] See Pallavi, Giorgio and Pellici 2012 for a discussion of the impact of CR on cancer and healthy ageing.

animals were either diabetic or pre-diabetic, while none of the CR animals showed signs of diabetes.

The incidence of cancer and cardio-vascular disease was reduced by 50% in CR monkeys compared to controls. Eight control monkeys had developed neoplasms, compared to only four CR monkeys. Four control monkeys had developed cardiovascular disease, compared to two in CR monkeys. Overall, age-related disease occurred at about three times the rate in control animals as in CR animals. Although the study is ongoing, disease measures of the rate of ageing indicate that ageing is slowed down in the rhesus monkeys.

2.3.1 Limitations of disease measures

On the basis disease measures, it seems clear that ageing is significantly slowed down in a wide variety of animals. As suggested, these measures have advantages over maximum lifespan and rate of mortality measures. However, their relevance to the ageing process has also been questioned. Some biologists distinguish between primary and secondary ageing. Primary ageing, also referred to as intrinsic ageing, is regarded as

> the inevitable, progressive decline in tissue structure and biological function that occurs with advancing age, independently of disease or harmful lifestyle and environmental factors. (Holloszy and Fontana 2007, 709)

Secondary, or extrinsic ageing is defined as

> the deterioration in tissue structure and biological function that is secondary to disease processes and harmful environmental factors. (*Ibid*.)

If this distinction is accepted, disease does not tell us about the underlying processes of primary ageing, but instead gives a measure of the rate of secondary ageing.

The distinction between primary and secondary ageing has been justified on the grounds that, although all animals age, not all animals experience age-related disease. Some birds, for instance, appear to have in-built 'biological clocks' which result in them dying 'catastrophically' without morbidity (Ricklefs and Scheuerlein 2001). If correct, this distinction implies that disease measures of the effects of CR may only provide evidence of the likelihood of slowed secondary ageing, while telling us nothing about the underlying intrinsic processes of ageing (Masoro 2006; Hayflick 2004).

However, the distinction between basic ageing processes and disease processes is not universally accepted (Sprott 2010). In many animals, it is not always clear how diseases that relate to secondary ageing can be distinguished from 'progressive decline in tissue structure and biological function.'

2.3.2 Effect of CR on diseases

Despite these controversies it is clear that ageing is slowed on disease measures of the rate of ageing. From this I extract a third finding that does not rely on the controversial question of whether disease measures are adequate measures of the rate of ageing per se:

> *3. CR postpones the onset of age-related diseases, and reduces the age-relative likelihood of organisms having age-related diseases.*

If this finding is applicable to humans, it is of obvious ethical importance. In later chapters I will argue that it also has significance for health policy on CRMs.

2.4. Biomarkers of ageing and longevity

Biomarkers of ageing are physiological and behavioural indicators of degrees of ageing. Identifying and testing candidate biomarkers of ageing is a methodologically difficult and

conceptually fraught endeavour (*ibid.*). Miller argues that biomarkers of ageing should be traits that meet the following three conditions:

> 1. The biomarker should predict the outcome of a wide range of age-sensitive tests in multiple physiological and behavioral domains, in an age-coherent way, and do so better than chronological age;
> 2. It should predict remaining longevity at an age at which 90% of the population is still alive, and do so for most of the specific illnesses that afflict the species under study;
> 3. Its measurement should not alter life expectancy or the outcome of subsequent tests of other age-sensitive tests. (in Butler et al 2004, 561)

Ingram and colleagues point out that an ideal of biomarker research is to identify features that are transferable between animal models and humans (Ingram et al. 2001, 1025-6). They suggest that

> [I]f a candidate biomarker is a valid measure of the rate of aging, then the rate of age-related change in the biomarker should be proportional to differences in lifespan among related species. Thus, for example, the rate of change in a candidate biomarker of aging in chimpanzees should be twice that of humans (60 vs 120 years maximum lifespan); in rhesus monkeys three times that of humans (40 vs 120 years maximum lifespan).

Numerous candidate biomarkers have been suggested. Appearance and risk of disease, brain changes, levels of dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), grip strength, and the appearance of grey hair and wrinkles are some examples. Many, if not all of the biomarkers listed above will fail to fully meet the ambitious standards outlined by Miller and Ingram. Nonetheless, I will discuss these purported biomarkers and the results that have been obtained when they are used in studies of caloric restriction.

CR and candidate biomarkers

As discussed, the prevalence and prominence of diseases in animals is sometimes taken as an indicator of the rate of ageing. To the extent that such measures are reliable biomarkers, they point to slowed ageing, as discussed in the previous section.

One characteristic of ageing in humans and primates is brain atrophy. In the above-mentioned study of rhesus monkeys, investigators used brain imaging techniques to examine the effects of CR relative to controls. They found that CR reduced age-associated brain atrophy in several brain regions (Colman et al 2009). Thus if degree of brain atrophy is regarded as a biomarker of ageing, it appears that CR slows ageing according to this measure.

Levels of DHEA and DHEAS have been suggested as candidate biomarkers because levels of these steroids decline with age (Lane et al.1997; Roth et al. 2002). In a study of CR rhesus monkeys levels of DHEA were increased relative to controls, suggesting a slower rate of ageing (Mattison et al 2003).

A relatively successful predictor of age is appearance, or perceived age. Another is physical activity. On the basis of these more mundane biomarkers, humans are able to predict the relative age of organisms – particularly those species whose ageing we are familiar with – with a surprising degree of accuracy (Christensen 2009). Researchers often report that the calorically restricted animals they work with appear much younger than control groups (eg Gems 2011; Colman et al 2009). They are also likely to maintain physical activity for a longer period of time. These easily recognisable biomarkers of ageing suggest that ageing is slowed down in CR populations.

2.4.1 Limitations of biomarker measures

Once again, there are numerous problems with developing effective biomarkers. As is the case with disease measures of ageing, there is no general agreement on which physiological variables track age. Moreover, there are great difficulties associated with the transferability of physiological traits between very different categories of organisms. It is not obvious, for instance, that a successful biomarker of age in a mouse would have an analogue in higher mammals like monkeys or humans.

In addition, it is possible that an intervention that slows ageing in some organ systems may not do so in all systems. This means that even if accepted biomarkers suggest slowed ageing, some organs relevant to mortality and morbidity may age at a different rate. Organismic unity of ageing processes is by no means certain. This means that 'batteries' of biomarkers might be necessary to provide robust predictions about degrees and speeds of ageing (Sprott, 2010).

2.4.2 Effects of CR on biomarkers

Despite these controversies it appears that on the basis of the, albeit imperfect, biomarkers in use, ageing is slowed in a wide variety of organisms. This leads to the fourth conclusion derived from animal studies of ageing rates under CR:

> *4. CR delays the appearance and development of physiological and behavioural traits –biomarkers – associated with ageing.*

2.5 Conclusion

To summarise, measures of the rate of ageing in animals suggest that ageing is slowed in four respects:

1. CR increases average and maximum lifespan relative to control groups and decreases the age-relative risk of death.

2. Deaths in CR populations tend to occur across a longer span of time than those in control animals.
3. CR postpones the onset of age-related diseases, and reduces the age-specific likelihood of organisms having age-related diseases.
4. CR delays the appearance and development of physiological and behavioural traits associated with ageing.

The following chapter examines debates about whether these effects would translate to humans.

3. IMPLICATIONS FOR HUMANS: THE TRANSFER THESIS

A crucial question for ageing research is whether effects observed in calorically restricted animals will be replicated in humans. In what follows I will refer to the claim that these results would translate to humans as the 'transfer thesis'. This chapter examines the predictions and viability of transfer thesis.

The lack of confidence about the effects of CR in humans is due in part to difficulties designing studies in humans. There are obvious practical and methodological problems in conducting sufficiently long-term experiments on free-living humans. This means it is unlikely that fully satisfactory tests of the transfer thesis can be carried out.

Nonetheless, surrogate measures have been developed. Studies of calorically restricted groups such as the participants in the Biosphere Two experiment, members of the caloric restriction society, the CALERIE project, as well as calorically restricted Okinawans provide a basis – albeit a methodologically limited one – for evaluating the transfer thesis.

I begin this chapter outlining the predictions of the transfer thesis with respect to human life expectancy. Thereafter I discuss a number of criticisms that have been made by of the idea that CR will extend lifespan in humans. I argue that these criticisms are themselves subject to doubts, and fail to undermine the viability of the transfer thesis. Finally, I examine the transfer thesis on the basis of human studies. I make the case that the results of such studies suggest that many of the physiological changes that occur in animals are replicated in humans, indicating a likelihood of slowed ageing and increased average and

maximum lifespan. This gives considerable support to the idea that results from animal studies on CRMs would translate to humans.

3.1 Lifespan predictions of the transfer thesis

Before assessing the plausibility of the transfer thesis, it is necessary to clarify its claims with respect to humans. In particular it is necessary to provide estimates of longevity that it predicts in humans, since the effects of CR on human lifespan are the main issue raised by critics of the transfer thesis. Below I outline the factors that influence lifespan increases, and suggest some estimates of longevity that will inform the ethical analysis in chapters to follow.

3.1.1 Modulators of lifespan increase

Speakman and Hambly (2007) point out that two factors heavily influence the degree of life extension achieved by CR animals. The first is the *degree* of caloric restriction; that is, the reduction in food intake relative to controls. The second is the *percentage of life remaining at onset*; that is how early or late in life the intervention is begun. The greatest increases in lifespan occur when CR is initiated very early in life, and when calories are severely restricted. Negligible increases occur when CR is initiated very late in life, or when the degree of CR is very small.

With regard to the effects of different degrees of restriction, the greatest increases in lifespan in rodents have occurred at a restriction of approximately 60% (Speakman and Hambly 2007). That is, animals were restricted to 40% of the diet of control mice. These have been reported to result in an increase in lifespan of 50%. Restrictions of 30% increased average and maximum lifespan by about 20%.

Lifespan gains also differ according to the time of life at which CR is commenced. The above gains were achieved in mice that commenced restriction at a very young age: before they had been weaned. However, studies on rodents suggest that the longevity effect of CR is reduced the later in life that CR is initiated (*ibid*.)

In humans it is unlikely that restriction would begin as early in life as it does in rodents. This is due in part to ethical factors discussed in Chapter 4: such a strict regimen on children appears likely to stunt children's growth. Practising CR much later in life would reduce the extent of life extension achieved. Extrapolations from mouse data suggest that after the age of 50, very little additional life would be gained (see figure 1 below). This means that later restrictors are less likely to achieve the substantial gains in lifespan that might occur if CR was initiated earlier.

3.1.2 Lifespan predictions

If humans experience gains in lifespan proportionate to those in rodents, the lifespan of CR practitioners would increase substantially. The table below details the life extension that could be achieved given different degrees of restriction beginning at different ages, assuming the truth of the transfer thesis.

Percentage life at onset	**Age at onset**	**Years restricting**	**Years added by degree of caloric restriction**				**Average lifespan at 60% restriction**	**Statistical maximum lifespan at 60% restriction**	**Absolute maximum lifespan at 60% restriction**
			60%	*45%*	*30%*	*15%*			
20	*15.6*	62.4	22.4	16.8	11.2	5.6	**100.4**	**131.66**	**157.48**
30	*23.4*	54.6	18.8	14.1	9.4	4.7	**96.8**	**127.72**	**153.26**
40	*31.2*	46.8	13.2	9.9	6.6	3.3	**91.2**	**120.69**	**145.05**
50	*39*	39	9.6	7.2	4.8	2.4	**87.6**	**116.26**	**139.94**
60	*46.8*	31.2	5.6	4.2	2.8	1.4	**83.6**	**110.73**	**133.14**
70	*54.6*	23.4	0.22	0.75	0.5	0.25	**78.22**	**101.44**	**120.61**
80	*62.4*	15.6	0	0	0	0	**78**	**101**	**120**

Figure 1. Lifespan predictions of the transfer thesis. Figure and data adapted from Speakman and Hambly 2007.

The numbers in the above table are adapted from Speakman and Hambly (2007), who extrapolate lifespan data from rodents to humans. They assume that average lifespan is 78 years.

Note that estimates for 60% and 45% are extrapolated from their calculations, but are not included in their text. Similarly, they do not provide estimates for maximum lifespan. Here, maximum lifespan was estimated on the basis of that it is commonly reported that CR increases maximum lifespan by the same proportion of years spent restricting as average lifespan.

The current *statistical* maximum lifespan is taken to be 101. This figure (101 years) is adapted from Willcox and colleagues, who give the maximum lifespan of US and Japanese people as 101.1 and 101.3 respectively (Willcox et al. 2007). Although the *absolute* maximum lifespan achieved is greater than this (just under 123 years), the lower number – statistical maximum lifespan – is in keeping with the lifespan measures discussed earlier (S2.1). That is, it takes the average longevity of a top percentile as the maximum lifespan. The absolute maximum lifespan assumes a current maximum lifespan of 120 years.

On the basis of these figures I suppose that, if the transfer thesis is correct, CR and CRMs would increase the absolute maximum lifespan to at most 160 years and average lifespan to at most 100 years. Of course it is highly unlikely that humans would be able to achieve a 60% reduction in calories, so no-one is likely to reach the upper limit using CR. However, retaining this upper limit for the purposes of ethical analysis is justified, since it may become possible to achieve the effects of 60% CR using a CRM. These figures thus represent good guesses as to the greatest extent of life extension that would be achieved under differing periods and degrees of CR. All this assumes that the transfer thesis can be justified, an issue to which I now turn.

In order to evaluate the transfer thesis I proceed as follows: first, I assess claims that results in animals will not translate to humans; second, I examine the difficulties faced in studying CR in human populations; finally, I discuss studies in humans and indicate the extent to which they provide support for the transfer thesis.

3.2 Doubts about the transfer thesis

Broad questions remain unanswered about the extent to which effects achieved in animal studies can be expected to occur in humans. There are significant genetic differences between different strains of rodents, let alone between rodents and humans. Studies on genetically closer rhesus monkeys mean that this chasm can be narrowed somewhat, but differences remain.

Nonetheless the near ubiquitous inter and intra-species effects of CR on ageing and longevity provide some reason to think that these effects would be retained in humans. Below I discuss the claims of several commentators that dispute this inference and, indeed, the extent to which CR effects are ubiquitous. Many of these arguments are based on evolutionary theories, so it is worth briefly outlining a common evolutionary explanation for the effects of caloric restriction.

The most widely accepted evolutionary account of why there is a CR effect is that it evolved as a response to conditions of famine. In such conditions of reduced availability of energy from food, having more offspring would strain already scarce food resources and reduce survival. In times of famine, then, it may be advantageous to allocate resources from reproduction to maintenance and repair of age-related damage. Doing so may allow organisms to survive to reproduce in times of greater food resources. As such, the CR

effect may be a useful adaptation (Masoro and Austad 1996). In the following sections, I discuss claims that the CR effect would not occur in humans.

3.2.1. Differing energy costs of reproduction

Shanley and Kirkwood, as well as Phelan and Rose claim that CR will not have as great a longevity effect in humans as in rodents, due to the difference in the relative energy costs of reproduction in rodents and humans (Shanley and Kirkwood 2006; Phelan and Rose 2005).

The trade-off hypothesis

These authors suggest that lifespans evolve as a result of strategies involving *trade-offs between increased longevity and increased reproduction*. I refer to this as the trade-off hypothesis. This hypothesis predicts that, other things being equal, organisms with higher reproductive investment and greater fertility will live a shorter time, and organisms with lower reproductive investment will live longer.

The trade-off hypothesis explains, for instance, the fact that the house mouse lives a short time (less than 5 years) in which they reproduce intensively, while the little brown bat can live a very long time (more than 33 years), but reproduces a single offspring per year. The mouse invests heavily in rapid reproduction at a cost to longevity, while the bat invests more in longevity and less in reproduction, and so produces offspring more slowly. Each of these may be a viable evolutionary strategy and results in a different lifespan.

With regard to CR, this reproduction-longevity trade-off suggests that, in conditions of famine, energy resources usually directed to maximising reproduction are instead redirected to maintenance and repair. Again, this is because organisms that defer procreation to more plentiful times have a reproductive and survival advantage. The

increased longevity that results from CR, therefore, is a result of reallocation of the energy resource budget from reproduction to survival.

Lower reproductive investment, less longevity gain

Shanley and Kirkwood and Phelan and Rose note that humans have a much smaller reproductive investment than rodents in relative terms. Rodents have more offspring than humans and at a far greater relative energetic cost. Because humans invest less on reproduction, redirecting resources from reproduction to maintenance would not have as great a longevity effect in humans as it does in rodents. Procreation takes up much less of human beings' energy budget, so saving this fraction and spending it on maintenance wouldn't earn one much more lifespan.

Note that the general evolutionary explanation of the CR effect discussed above need not make this prediction, since it does not postulate a *trade-off* between reproduction and longevity. The general theory suggests that mechanisms that increase maintenance and defer reproduction can be advantageous without predicting that doing so would reduce overall fertility.

Criticisms of the trade-off hypothesis

The idea of evolutionary trade-offs between reproduction and longevity has been criticised on the grounds that some relatively long-lived organisms have a great investment in reproduction. Speakman cites the example of naked mole rats that live up to 28 years, which is exceptional given their size, and which nonetheless produce one of the largest litters of any mammal (Speakman 2011). Cases of this type, involving high levels of both maintenance and reproduction, cast doubt on the broad applicability of the trade-off hypothesis.

Of more direct relevance is the fact that a fundamental prediction of the hypothesis with respect to CR is not borne out in experiments on CR animals. In particular, it predicts animals that have endured CR will have increased lifespan and reduced fertility with respect to controls. However, it has been found that, after emerging from a period of CR, rodents have both increased fertility *and* increased lifespan (Selesniemi 2008). The fact that both reproduction and lifespan are enhanced in animals that have been on CR suggests that a trade-off between them does not explain the CR effect (Speakman and Mitchell 2011).

Conclusions on the trade-off hypothesis

The reproduction-longevity trade-off hypothesis predicts that CR will not extend lifespan as much in humans, since less of our energy budget is directed towards reproduction. However, the hypothesis is faced by problematic counter-examples like the naked mole rat. Moreover, experiments on CR suggest that its effects do not result from a lifetime trade-off between reproduction and longevity. Since this is so there are grounds to doubt the prediction at issue: that CR would not extend lifespan in humans.

3.2.2. Migration as a famine response

Le Bourg claims that species, such as humans, that are capable of migrating and which are relatively fast-moving should not be expected to have increased lifespan. He surmises that rather than reducing reproduction in response to famine, many organisms such as flies, birds capable of flight, and humans would simply migrate. In this way the costs to reproduction could be avoided without the need for a life extension response. I refer to this as the migration thesis.

Le Bourg makes several predictions. In particular he suggests that his hypothesis might be falsified if flighted birds experience life extension in response to CR, and, conversely, if non-flighted birds do not have extended lifespans in response to CR.

Preliminary evidence suggests that hens have increased lifespan (Holmes & Ottinger 2003), in keeping with Le Bourg's hypothesis. Chickens would, as non-flighted birds, potentially be unable to migrate in response to famine. Undergoing the CR effect would thus potentially be useful. However, I am not aware of any studies of life extension under CR in flighted birds.

Problems with the migration thesis

There are, however, other organisms that appear capable of migrating that do show a response to CR. Fish, for example, were amongst the first organisms observed to exhibit the life extending effects of CR (McCay et al 1929; Comfort 1963). However, it could be argued that the fish in the cited experiments – the trout and the guppy – are less adapted to emigration since they are freshwater species. It would be interesting to see if the effects of CR are observed in fish that are more capable of escaping to better conditions.

In addition to this potential empirical problem, there are at least two theoretical problems with Le Bourg's hypothesis. First, it makes assumptions about the degree to which CR is, or is not, an evolutionarily conserved response. If the effects of CR are conserved across multiple lineages, then it is possible that the common ancestor was incapable of escaping famine. If so, then by Le Bourg's hypothesis, humans would have the same CR response as rodents, in keeping with the transfer thesis.

The second problematic assumption is that early humans were capable of escaping a famine. Le Bourg provides no information about the geographic reach of famines, or

humans' ability to travel beyond that reach. It is far from obvious that humans could escape famine at will. These problematic assumptions give Le Bourg's evolutionary hypothesis a rather *ad hoc* feel and diminish its status as a challenge to the transfer thesis.

3.2.3. CR as domestication artefact

It has also been suggested that effects of CR in animals are a result of domestication and breeding adaptations to laboratory conditions, rather than a result of natural evolution (Le Bourg, 2010). It is claimed that applying CR simply undermines these adaptive effects, returning the organism to a wilder state with lower food intake, leaner bodies, more activity and thus greater health. The view, which I refer to as the domestication objection, is that CR works not by slowing ageing, but by undermining faster ageing that has been bred in through years of adaptation to unhealthier conditions.

Again this makes sense within the evolutionary paradigm. It is thought that one common response to surplus food availability is to divert food from maintenance to reproduction. This may have happened in domesticated animals as they adapted to living with humans. For a variety of reasons, laboratory animals may have been selected for increased fecundity and appetite (Speakman and Mitchell 2011).

Limitations of the domestication objection

However, it is not clear that this is relevant to the transfer thesis. Humans in many parts of the world have massively increased in numbers. This is due in part to the ability to avoid food shortages. It has also led to decreases in physical activity in many parts of the world, particularly in recent centuries. Compared to humans like the South African Khoisan and the Australian aborigines, modern civilisations might be said to be more highly adapted to conditions of plenty and less exercise.

Thus, adaptation to living in more plentiful circumstances is not necessarily a disanalogy between rodents and modern humans. Even if CR is a laboratory artefact there's no reason to think we would experience less of a reduction in the rate of ageing than domesticated organisms.

3.2.4. CR in the wild

Laboratory animals are kept in conditions that are different to those experienced by free-living humans. As a result, some physiological features that would be detrimental 'in the wild' might not impact on survival in cages. It is possible that these deleterious effects might cancel out any beneficial effects of CR in terms of longevity, so we should not regard CR effects as transferable.

For example, one effect of CR is that it results in lower bone mass. (Speakman and Hambly 2007). Animals are kept in confined areas with little potential for accidents or damaging activity, so lower bone mass is not detrimental. Humans, on the other hand, are constantly at risk of damage due to injuries and accidents such as falls.

A further difference is that animals are kept in environments that are free from pathogens. As such, if CR had a negative impact on immune systems these would not necessarily be recognised. By contrast, humans are constantly exposed to pathogens that would threaten our survival if immune functions were compromised. The condition of living in the wild might counteract the survival benefits of CR.

Studies on bone quality and immune function

These threats to health may compromise individual welfare, and so are discussed in Chapter 4 on the implications of CR and CRMs for the substantive good of health. There I point to studies on rodents and non-human primates suggest that bone quality and immune

functioning are actually improved under CR. Thus there is no strong reason to think that living in a relatively pathogen-ridden environment would counteract gains in average or maximum lifespan.

3.2.5. Absolute, not proportionate lifespan increase

The previous arguments cast doubt on CR increasing lifespan by pointing to differences between the environments, evolutionary needs and adaptations of model organisms and humans. By contrast, De Grey suggests that a crucial environmental *similarity* undermines the likelihood that CR will substantially extend lifespan in humans (De Grey 2005).

In particular, De Grey claims that the duration of famines is the same for all species. The adaptation of deferred reproduction and slowed ageing would only need to last as long as this duration. Thus we should expect all organisms to gain the same absolute number of years. Any addition to human lifespan should be expected to be *the same as, and not proportionate to*, that experienced in mice and other organisms. This would be enough to secure survival of a famine in order to reproduce.

On the basis of this hypothesis, De Grey holds that the large increases in lifespan reported in some rats will not be replicated in humans. Instead, humans should expect only the same *absolute* number of years as that gained by other organisms. This would only be a moderate maximum lifespan increase of at most two or three years.

De Grey suggests that empirical studies bear out his claims. He cites studies of six organisms that he suggests provide empirical evidence for his hypothesis. Comparison

between nematodes, fruit flies, grasshoppers, mice, dogs and cows all appear to bear out his thesis.[12]

Criticisms of De Grey

Both the evolutionary reasoning in de Grey's argument, and the empirical support cited for his hypothesis has been questioned (Rae 2006). With respect to the evolutionary claims, it is far from clear that famine would not occur more than once in the reproductive life of more long-lived organisms. If it did, slowed ageing might be beneficial more than once and, by de Grey's hypothesis, long-lived organisms might gain a greater reproductive advantage by slowing ageing on more than one occasion. This would increase lifespan more than the duration of a single famine.

Moreover, many evolutionary adaptations can be triggered and maintained in the absence of the environmental factor to which they evolved as a response. For instance, metformin, a potential CRM, works in part by triggering a natural response to excessive glucose. Thus it is possible that a biological mechanism triggered by famine would continue to work in the absence of an actual famine. There's no clear reason that these mechanisms would cease to work after a nominal amount of time.

In addition to these theoretical difficulties, the use of empirical studies cited in De Grey's paper has been heavily criticised on several grounds (Speakman 2011; Rae 2006). There are two central problems. First, the organisms were not restricted to the same degree. As mentioned earlier, the degree of life extension is highly dependent on the extent to which organisms are calorically restricted. If they are not restricted to the same degree then comparisons between extents of life extension are unlikely to be informative. If one

[12] Note that the nematode studies he cites do not achieve close to the same absolute lifespan. He argues that this may be because the maximum lifespan in nematodes has not yet been achieved.

organism is restricted by 30% and another is restricted by 60%, then of course the transfer thesis will not predict the same proportional increase in both. The comparisons in De Grey's study are thus inappropriate tests of whether lifespan increases will be proportionate or absolute.

The second, and related problem is that there is little reason to think that the degree of lifespan extension exhibited in the chosen studies is the *maximum* lifespan the organisms could achieve under CR. Again, this is because the degrees of CR in each study are very different. The mouse study cited is of a 53% calorie reduction, while the study in dogs is only 25%. The response in cows was to a 60% reduction in calories, but interspersed with *ad libitum* feeding. Given that the degree of life extension is sensitive to the consistency and degree of CR, these studies provide little reason to think that the maximum lifespan was achieved in the relevant organisms. The claim that these organisms attain the maximum lifespan increase achievable by *any* organism is thus highly doubtful.

In contrast, comparative studies of species using the same degree of CR appear to directly contradict De Grey's claims. They appear instead to support the idea that

> a given degree of CR imposed on an animal of a given species leads to a similar extension of [lifespan] expressed as a proportion of the species maximum [lifespan] (Rae 2006, 95)

That is, comparative studies appear to support the transferability of CR's effects on longevity between species tested.

3.2.6. Biological limits to lifespan

Carnes, Olshansky, and Grahn claim that there is evidence for 'biological warrantee periods' that are upper limits of maximum and average lifespan (Carnes, Olshansky, and Grahn 2003). Other animals seldom reach these limits because their survival is highly

dependent on extrinsic factors – predation, infectious and parasitic diseases, and the availability of food.

Humans, however, have experienced radical increases in average lifespan across the 20th century due to reductions in these extrinsic causes of mortality. Elimination of many of these causes has revealed an underlying 'intrinsic' life expectancy that is determined by the rate of ageing. Based on patterns of age-related mortality, the authors argue that the biological limit for human lifespan has been reached in many parts of the world. We should not, thus, expect life expectancy to increase much above 85 years of age.

A clarification: lifespan limits and the rate of ageing

It is important to clarify this claim. The authors' contention that there are biological limits to lifespan can be misunderstood as a denial of inability to increase lifespan through medical and biological interventions. However, they explicitly and repeatedly deny this implication (*ibid.;* Carnes & Olshansky 2007). Their claim is instead directed against demographic models that make long-term predictions that simply extrapolate from the life expectancy gains of the 20th century (eg, Vaupel and Gowen 1986). Doing so ignores evidence about an existing intrinsic limit that they argue is likely to prevent, or at least slow down gains in life expectancy.

However, Carnes and colleagues do not deny that the rate of intrinsic ageing can be modulated. On the contrary, they observe that although 'a repetition of the large and rapid gains in life expectancy observed during the 20th century is extremely unlikely', such gains could be achieved if we had the 'ability *to slow the rate of aging'* (Carnes, Olshanky & Grahn 2003, 43. My italics.)

Here they explicitly acknowledge that slowing ageing would increase biological lifespan. As I indicated in Chapter 2, studies indicate that CR slows the rate ageing on a variety of measures. Thus there is no reason to think that Carnes' and colleagues ideas of a biological limit rules out the possibility that CR, or a drug that mimicked it, would result in considerable gains in average and maximum lifespan.

3.2.7 The status of doubts about the transfer thesis

CR is effective in increasing lifespan in a wide variety of organisms. However, the proposals above could cast doubt on the idea that the effects of CR would be transferable to humans. I have argued that these proposals are themselves subject to theoretical and empirical criticisms, or to clarifications that diminish their efficacy as objections to the transfer thesis.

This is not to make a strong claim that CR would have equivalent effects, or that the above proposals are false. Other objections may arise, or the proposals discussed may be vindicated by further studies. However, the difficulties with these challenges mean that the transfer thesis remains plausible.

3.3 Human studies of CR

In the previous chapter I discussed the effects of CR in animal studies, and their implications for slowed ageing and life extension. In this chapter I have examined claims that cast doubt on the likelihood that these effects will be replicated in humans. I argued that they fail to provide convincing evidence that the CR effect will not transfer to humans. In this section I discuss more direct attempts to test the transfer thesis: studies of CR humans.

First I discuss some difficulties with conducting such tests, before providing examples of studies in humans. Though they are by no means conclusive in favour of the transfer thesis, these studies indicate that many of the effects of CR on lifespan and the rate of ageing occur in humans. In combination with the discussion of criticisms of the transfer thesis discussed above, the studies below indicate that CR and interventions that mimic it are worthy of the ethical investigation that follows in later chapters.

3.3.1. Obstacles to empirical studies in humans

As Holloszy and Fontana suggest, 'the only way to be sure that CR 'works' in humans is to conduct studies in people' (Holloszy and Fontana 2007). However, there are obvious practical and methodological difficulties in conducting sufficiently long-term experiments on free-living humans.

The costs of lifelong experiments would be prohibitive. It would also be necessary to control for genetic and environmental factors that affect ageing. All this would have to be done whilst accounting for the range of free human activities that might affect the experiment. Moreover, waiting a significant amount of time for results would significantly delay evaluation of interventions with potentially profound social and ethical importance. They would also be of no help to the thousands of people currently practising CR or making use of candidate CRMs, or to those considering the use of these interventions.

It is thus unlikely that fully satisfactory long-term studies will ever be conducted in humans. Nonetheless there have been attempts to conduct research on humans that that does not require impractical lifelong trials. These make use of the measures of ageing mentioned earlier: lifespan measures, rate of mortality measures, disease measures, and biomarkers of ageing and longevity. Even though these methods are unlikely to lead to

certainty about veracity of the transfer thesis, they mean that we are able to improve our guess about whether CR 'works' in humans.

3.3.2. Examples of studies in humans

Several studies in humans have been undertaken. Below I briefly describe the four most commonly cited studies of calorically restricted humans: Biosphere Two volunteers, members of the Caloric Restriction Society (CRS), participants in the CALERIE study, and the Okinawan cohort.[13] Thereafter, I summarise the results of these studies in terms of the relevant measures of the rate of ageing, and the corresponding claims about CR. Thus far results suggest that the transfer thesis is a viable hypothesis.

Biosphere Two

Biosphere Two was designed to conduct experiments in a closed ecosystem. In 1991 eight volunteers were sealed in the biosphere for two years to study the complex interactions between living processes. One unforeseen consequence of the experiment was that food supplies in the biosphere dropped well below the expected level. As a result, the participants were forced to restrict dietary intake (Walford et al. 2002). Studies of the occupants thus give an indication of the immediate adaptations to a CR diet.

The Caloric Restriction Society

The Caloric Restriction Society (CRS) was founded in 1994 by Roy Walford, one of the participants in the Biosphere Two project. Members of the CRS restrict calories for health and longevity purposes. It has become common for practitioners of a CR diet to volunteer for research, providing data about the short and long-term effects of caloric restriction.

[13] These are discussed by among others, Holloszy and Fontana 2007, Redman and Ravussin 2011, and Roth and Polotsky 2012.

CALERIE

The Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) is the first randomised controlled trial of caloric restriction (http://calerie.pbrc.edu/). The study examines the effects of 25% caloric restriction (75% of weight maintenance requirements) in non-obese women and men between the ages of 25 and 45 years. The trial consists of about 150 calorically restricting participants and is ongoing.

Okinawan studies

The Okinawans – inhabitants of the Japanese Okinawa Prefecture – have one of the highest life expectancies in the world, as well as a disproportionate number of centenarians. The Okinawa Centenarian Study (http://okicent.org) has investigated more than 600 Okinawans in order to discover the reasons for their exceptional longevity. Significantly it was found that a particularly long-lived cohort of Okinawans had a diet that contained substantially fewer calories, leading to the suggestion that their increased longevity may be as a result of CR (Willcox et al. 2007a). This means that Okinawans are perhaps the closest we will get to a lifelong study of CR in humans.

The above studies provide a testing ground for the transfer thesis. Again, the transfer thesis holds that effects observed in animals will be replicated in humans. If the transfer thesis is true:

1. CR humans will have higher average and maximum lifespan relative to non-CR populations, and will have a reduced age-relative risk of mortality.
2. Deaths in populations of CR humans will occur across a longer span of time than those in non-CR humans.

3. In CR humans the onset of age-related diseases will occur later than in non-CR groups, and at any age they will be less likely to have an age-related disease.
4. In CR humans, the appearance and development of other physiological and behavioural traits associated with ageing will be delayed.

Below I discuss the extent to which these claims are justified by human studies.

3.3.3. Lifespan measures of the rate of ageing

As mentioned, it is difficult to conduct scientifically rigorous lifelong studies in humans. However, studies of Okinawans provide the closest available surrogate. These provide some reason to think that the first claim of the transfer thesis will be met.

Willcox and colleagues (2007a) report that the cohort of Okinawans had a high average lifespan of 83.8 years, compared to 82.3 in the rest of Japan and 78.9 in the USA. Similarly, the maximum lifespan of Okinawans was 104.9 years compared to 101.1 in the rest of Japan and 101.3 in the USA. Significantly, Okinawans had higher average and maximum lifespan relative to Japan, the world's longest lived population.

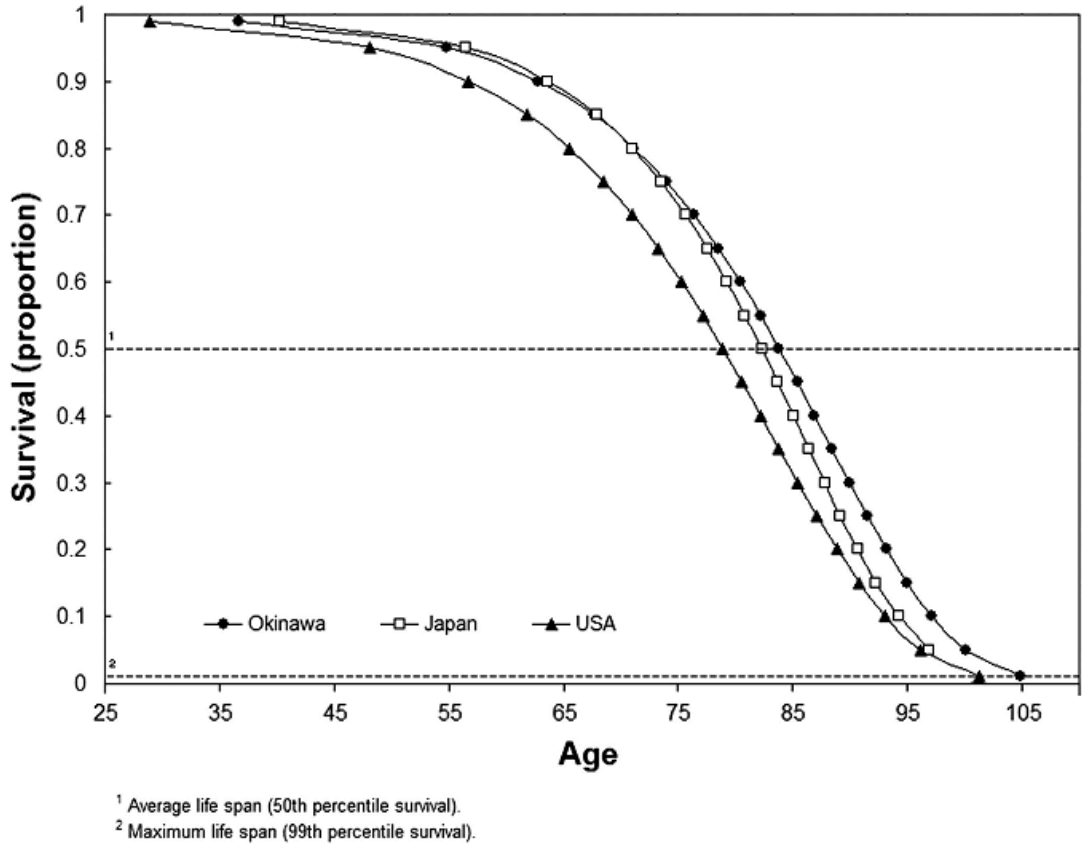

Figure 2 Average and maximum lifespan in Okinawan, Japanese and US groups. (Willcox et al 2007a).

It is important to note that, in keeping with the maximum lifespan measures outlined earlier, Willcox and colleagues did not take the oldest old person in these groups as the maximum lifespan: the oldest old Okinawan person was 114 in 2009,[14] while the oldest American was Sarah Knauss (119 years) and the oldest Japanese person was Tane Ikai (116 years).[15] Instead the average of the top 1% of old people is taken as the maximum lifespan.

Recall, however, that lifespan measures of the rate of ageing a top percentage as identifying the maximum in order to cancel out some of the effects of sample size. As mentioned earlier, there's a higher chance that the oldest member of the larger sample will be older than the oldest member in a smaller sample. Thus it should not be surprising that

[14] http://www.japanupdate.com/?id=9793. Last accessed 19 December 2012. I was unable to provide independent verification for this claim, or discover a recent update. This may be because, as the article claims, the super-centenarian prefers not to be named.
[15] http://en.wikipedia.org/wiki/Supercentenarian. Accessed 19 December 2012.

the oldest member of a relatively small group – the Okinawans – is younger than the oldest member of much larger groups – Japan and America.

Limitations

A further factor to bear in mind is that studies of Okinawans don't account for many of the limitations to human studies mentioned earlier. In particular, it is difficult to exclude the range of genetic and environmental factors other than CR that may have contributed to their impressive longevity. Without this, it is not certain that their diet was the central contributor to increased lifespan. However, Willcox and colleagues note that since the westernisation (increased meat, fat and bread) and Japanisation (more polished white rice) of the Okinawan diet, the 'Okinawan mortality advantage has all but disappeared' (Willcox et al. 2007a, 436). This suggests that calorie intake plays a major role in the increased longevity of older Okinawan groups.

It is also apparent that the increase in lifespan achieved by Okinawans is nowhere near the 60% that has been achieved in animal studies. However, it should be recognised that the degree of CR practiced by Okinawans was estimated to be about 10.9% fewer calories than is recommended to sustain body weight (Willcox et al. 2007a). This is much less than the 60% CR that resulted in drastic life extension in rodents. Moreover the Okinawans studied are only believed to have been under CR for approximately half their adult lives. It may be that reductions greater than this and/or for a greater proportion of life, or CRMs that mimicked such reductions, would result in a higher average and maximum lifespan than that achieved by the Okinawans.

The Okinawans are the closest that we have to a life-long CR study on humans. As a result they are the only humans on which it is possible to conduct studies that make use of lifespan measures of ageing. Use of these measures imply that CR in humans slows ageing

in the first respect above: Okinawans have a higher average and maximum lifespan and reduced age-relative risk of death. Thus available evidence suggests the first aspect of the transfer thesis is borne out.

3.3.4. Rate of mortality measures

Rate of mortality measures equate the rate of ageing with the rate at which organisms die after reaching a tipping point of increased deaths. Again the application of these metrics would require a life-long study in a group such as the Okinawans. Unfortunately, however, I have been unable to find a study that applies rate of mortality measures to the Okinawans.

Nonetheless, the results displayed in figure 2 suggest that Okinawans have a slower rate of ageing relative to mainland Japanese. This is suggested by the widening gap between the two plots that begins between the ages 65 and 75. However, to the naked eye, the gap between the Okinawan and USA plots does not widen, perhaps implying delayed, rather than decelerated ageing. Interpreting the rate of mortality is thus inconclusive. Indeed, attempting to estimate rate of mortality on the basis of the above lifespan plots may be methodologically unsound. Until a rate of mortality analysis is available in humans, it is necessary to make recourse to studies in animals that indicate slowed ageing.

3.3.5. Disease measures

Disease measures of ageing record the incidences of age-related disease. Recall that in rodents and rhesus monkeys it was found that CR reduced the incidence of a wide range of age-related diseases – such as cancer, cardiovascular disease, and diabetes – relative to controls.

Human studies are in keeping with these findings. During the period of CR, calorically restricted occupants of Biosphere Two exhibited improvements in a number of risk factors

for age-related disease. They showed, amongst other beneficial changes, improved levels of cholesterol, blood pressure and low density lipo-proteins, all of which are indicators of the likelihood of cardiovascular disease. They also showed levels of glucose and insulin that indicated a lower risk of diabetes (Walford, 2002).

Similar changes were also evidenced in members of the CRS (Meyer et al 2006), leading Holloszy and Fontana and Omodei and Fontana to contend that they have a decreased risk of atherosclerosis and type 2 diabetes (Holloszy and Fontana 2007; Omodei and Fontana 2011). Similar observations have been made in the CALERIE study. Given acknowledged indicators of age-related diseases, CRS members and subjects in CALERIE appear to have a lower risk of age-related health problems (Stein et al 2012).

Significantly, the CALERIE study also found that CR reduces oxidative damage in humans. Oxidative damage has been implicated as a major cause of ageing and age-related disease. It is, for instance, thought to contribute to cancer, heart failure, atherosclerosis, Parkinson's disease, and Alzheimer's disease (Redman and Ravussin 2011).

Although the findings indicate physiological changes that point strongly to the conclusion that CR would reduce the incidence of disease, none of these studies is life-long. This means that there are no advanced cases of disease in either the control group or the CR group. Despite these positive indications, therefore, it has not been shown conclusively that CR delays the onset of age-related diseases, or reduces the age-relative risk of age-relative diseases in these groups.

The Okinawans again provide the best evidence concerning disease measures of ageing in humans. Willcox and colleagues report that, in keeping with animal studies,

[c]oronary heart disease, and forms of cancer, such as lymphoma, and cancer of the prostate, breast, and colon are remarkably low in age-matched Okinawans versus other Japanese and Americans. (Willcox et al. 2007a, 445)

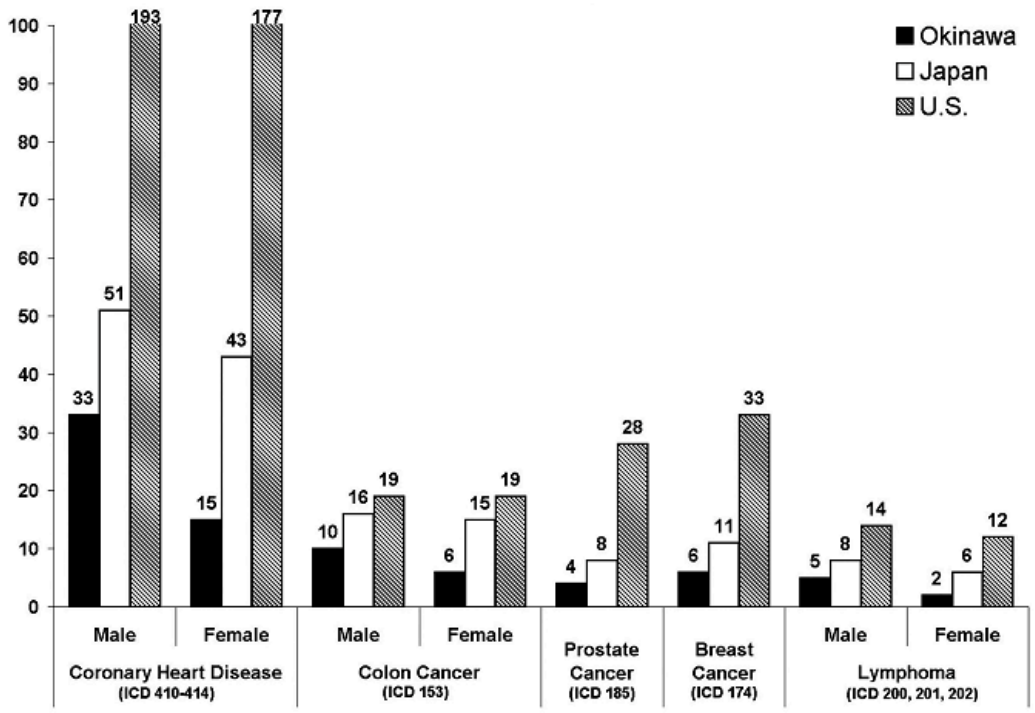

Figure 3 Age-related disease in Okinawans, Japanese and U.S groups. (Willcox et al 2007a).

This means that at any age Okinawans display a lower risk of dying from an age-related disease than Japanese or Americans (see figure 3 above). Moreover, in Okinawans the onset of the period in which age-related disease is more likely is delayed.

Shorter term studies of CR strongly suggest that adaptations occur that will delay the onset of age-related diseases and reduce their likelihood at any age. Studies on Okinawans provide further evidence for this claim. Thus there is a growing body of evidence that the third prediction of the transfer thesis will be fulfilled: in CR humans, as in CR animals, the onset of age-related diseases will occur later than in non-CR groups, and at any age they will be less likely to have an age-related disease.

3.3.6. Biomarkers of ageing and longevity

The fourth way to measure the rate of ageing is to determine physiological traits that deteriorate progressively with age. Again, there are very few, if any, completely reliable inter-species biomarkers. As mentioned earlier, indicators of disease risk are sometimes regarded as biomarkers of ageing. To the extent that they are, the disease measures discussed above indicate that ageing is slowed in humans, replicating findings in animals.

Several other purported biomarkers of ageing have been studied in the human CR groups discussed. These include body temperature, levels of DHEA and DHEAS, physical activity, grip strength and appearance. As discussed below, these tend to indicate slowed ageing on biomarker measures.

Reduced body temperature is a feature that occurs in CR animals and long-lived humans and so may play a significant role in slowed ageing, or provide an indication that similar effects are occurring.[16] In keeping with this indicator, subjects in the CALERIE experiments exhibited the reduced body temperature seen in animals and long-lived humans (Redman and Ravussin 2011).

Levels of DHEA decline progressively with age in rhesus monkeys and also in humans. As a result DHEA is regarded as a candidate biomarker (Lane et al.1997; Roth et al. 2002). In CALERIE participants, no change was observed in levels of DHEA after 6 months under CR, perhaps due to the short duration of the trial. I was unable to find studies about DHEA levels in CRS members, many of whom would have been restricting calories for substantially longer. In the Okinawan cohort, however, DHEA levels were observed to be substantially higher than age-matched controls, suggesting that CR slows the rate of ageing

[16] Given the earlier definition of a biomarker as a physiological trait that deteriorates with age, it is not clear that body temperature should be included in this category. Body temperature does not change predictably with age, so this may disqualify it as a biomarker of ageing on the strict definition discussed in S2.4.

as measured by DHEA. Subsequent publications from the CALERIE study, as well as investigation of DHEA levels in CRS members could provide more information about whether CR slows ageing on the basis of this candidate biomarker.

Other biomarkers provide further support for the idea that CR slows ageing in humans. Okinawans appear physically younger, are more active, and have stronger grip strength than age-matched controls (Willcox et al 2007b). To the extent that available biomarkers can be regarded accurate measures of the rate of ageing, and to the extent that they have been made use of in studies of CR humans, they tend to provide evidence for the fourth aspect of the transfer thesis: in CR humans, the appearance and development of other physiological and behavioural traits associated with ageing are delayed.

3.4 Conclusion

In the above I have attempted to make apparent the limitations of existing research of CR humans. To the extent that studies are available, however, human studies appear to bear out the transfer thesis. Lifespan measures, rate of mortality measures, disease measures, and biomarker measures of the rate of ageing suggest many of the effects observed in animals may be replicated.

CONCLUSION TO PART I

It is impossible, on the basis of the available studies, to be fully confident that CR and CRMs would result in the substantial lifespan gains detailed in S3.1. However, it is worth noting that this lack of certainty in advance is likely with any genuine life extending intervention. Without methodologically rigorous, extremely long-term tests it is impossible to know that an intervention will extend average and maximum lifespan.

In the absence of such long-term evidence we must make decisions on the evidence that is available. The above research on CR provides a strong case for the claim that the effects of CR and drugs that mimicked it would translate to humans, extending lifespan and slowing ageing. This premise, and in particular the four central claims of the transfer thesis, provide the empirical basis for the ethical analysis in chapters to follow.

PART II: CR, CRMS AND INDIVIDUAL WELFARE

INTRODUCTION TO PART II [17]

In the previous chapter, I discussed the transfer thesis – the hypothesis that the effects of CR and CRMs would be replicated in humans. In this chapter I evaluate whether, assuming the truth of the transfer thesis, extending lifespan by using CR or CRMs would, other things equal, be good or bad for a person.

This question can be posed using different terms: would the intervention be in or against a person's interest? Would it harm or benefit her? Would it increase or decrease the value of her life, or make her life go better or worse? Would it be prudent for her to use the intervention, or not? Would it have positive or negative impact on her well-being or welfare? It may be possible to distinguish these questions by appealing to differences in everyday uses between terms such as 'welfare' and 'well-being,' though I have doubts that doing so is useful. Instead, I will treat these questions as equivalent.

i) The significance of individual welfare

Theories of individual welfare provide accounts of what makes a person's life go well and badly for them. If smoking is bad for me, or harms me, theories of welfare should be able to designate the features of smoking that make my life go worse. Similarly, if exercise is good for me, or benefits me, a theory of welfare should be able to account for what it is about exercise that makes my life go better.

[17] The arguments of this Part have benefited from useful discussion at the 2009 Philosophical Society of South Africa (PSSA) Conference, University of Fort Hare, South Africa, the 2012 'Well-being in Contemporary Society (WICS) 2012' conference in, Twente, Netherlands, as well as the '2012 Symposium on Enhancing Human Experience via Emerging Technologies,' in Laval, France. Sections of this Part are forthcoming in *Philosophical Papers* and the *International Journal of Design and Innovation Research*. Thanks to the reviewers for their comments and suggestions.

Individual well-being is significant for prudential and moral individual choices, as well as for policy choices. *Prudential* choices are guided by considerations about whether a particular action will increase or lower one's welfare – whether it would be prudent or wise to make a certain choice. Amongst other things, *moral* choices may require that in pursuing her own welfare a person's choices don't undermine the welfare of others. Some moral systems suggest that we are also obligated to improve the welfare of others.

In biomedical *policy*, beneficence and non-maleficence are regarded as key virtues of political institutions.[18] Other things being equal, institutions should aim to benefit people, increasing the welfare of citizens. Moreover, it is thought that political institutions have an even stronger duty of non-maleficence: to avoid harming, or decreasing the welfare, of individuals. Ethical policy choices may also require that there is a fair distribution of welfare, or opportunities for welfare across society and between individuals.

Well-being may thus play a significant role in ethical individual and policy decisions. As a result, a useful analysis of life extension by CR or CRMs should take into account their effects on well-being.

ii) What makes a life go better or worse?

In this Part, I examine the likely impact of CR and CRMs on the basis of ethical ideas about what values make someone's life go better or worse for her. These accounts of welfare are typically divided into substantive good, desire fulfilment, and mental state accounts.[19]

[18] See, for example, Beauchamps and Childress 2001.

[19] For example, see Parfit 1984, Griffin 1989, Sumner 1996, Scanlon 1998, Crisp 2006, Keller 2004. Substantive good accounts are often referred to as 'objective list' accounts. Here I prefer Scanlon's term, since the term 'list' may invoke an arbitrary string of goods.

Substantive good accounts delineate objectively valuable factors required in order for a person's life to go best. For instance, autonomy, self-development and friendship are often considered to be prerequisites for a high degree of well-being.[20] These goods are seen as intrinsically valuable. They increase welfare whether or not they are wanted by the person and whether or not they have any other good consequences.

Desire satisfactionist accounts hold that a person's welfare depends on whether her desires are fulfilled.[21] If a person desires that her lover is faithful to her, and the lover is not, then she is harmed and her welfare is lowered. On desire satisfactionist accounts, this is so even if she gains in other (un- or less desired) respects, such as having more freedom, or pleasure. The only thing of value for a person is that her desires are satisfied.

Mental state theories hold that a person's life goes well or badly to the extent that she has good or bad mental states. On these theories, only certain experiences have intrinsic value. For instance, hedonist mental state theories hold that a person's life goes better if she has pleasurable experiences and worse if she has painful experiences.[22]

All the above theories have been subjected to criticism. My intention here is not to prefer any particular theory of welfare. Instead I use the theories as a structural device to consider the possible impact of CR-related life extension on individual welfare. That is, the accounts above provide a way to structure arguments and situate objections to life extension in terms of prudential values.

[20] See, for instance, Nussbaum 2000.
[21] For example, Bernard Williams 1973.
[22] Examples of hedonist theories are those of Feldman 1991, and Bradley 2004.

Moreover, considering a variety of claims about welfare is in keeping with the compatibilist methodology outlined in the introduction. Since I address objections on the basis of several accounts of welfare, it is possible that broader agreement may be achieved.

Note that there is obviously some overlap between the prescriptions of these accounts. For instance, no plausible account of value for a person would deny that a degree of happiness is important. They will, however, differ on the justification. Some hedonist accounts, such as those of Mill, Bentham, and Epicurus hold that happiness is the only thing that has intrinsic value. Substantive goods theories may hold that happiness is one good among many, or that it is instrumentally valuable in that it contributes to some other intrinsic good. Desire satisfaction theories will hold that happiness is good because people *want* happiness. Thus, although the accounts of individual benefit can be distinguished, they will often overlap in their recommendations.

iii) Distributions of welfare within a life

The theories of welfare above designate goods and bads that make a person's life go better or worse. However, the value of a life may depend in part on the distribution of these goods within a life (Benatar 2006, 61-64). In particular, individual welfare may involve an interplay between the total, or cumulative goods within a life, as well as the order in which goods occur. I will explain in more detail.

The simplest view of welfare is that a life goes better or worse to the extent that it contains more or less of a particular good. If pleasure is a good, hedonists claim, then a life is better if it contains more pleasure and worse if it contains less. All that matters is the total good accumulated in a life.[23]

[23] For such a view see Bradley 2004.

In addition to cumulative good, David Velleman has argued that the *order* in which these goods are achieved, and the *structure* of a life, also play a role in evaluations of a life (Velleman 1991). For instance, it is usually thought that, other things being equal, a life that goes from worse to better is an improvement over a life that goes from better to worse. Suppose we have to choose between a life of declining happiness and a life of increasing happiness. Velleman holds that if the total good in these lives is the same, most people would choose the second option. This suggests a further contributor to the value of life. In addition to the total good achieved, the structure of the life, and the order in which goods are achieved may be relevant.

iv) Welfare and comparison

In asking whether CRMs make a life go better or worse, it is important to specify *what* the life is better or worse than. That is, it is necessary to indicate the basis or bases of comparison. We think that smoking is bad for a person because it leads to conditions like cancer and cardiovascular disease. If a person smokes she is more likely to have one of these conditions.

Smoking may thus be regarded as bad because it leads from a better to a worse state. From the state of being healthy, one becomes unhealthy. In this case smoking can be said to be bad on the basis of a comparison between a better and a worse state.

Life-death comparisons

This type of comparison is difficult to make in the case of life extending interventions. Assuming that people cease to exist when they die, life extension postpones going from a state of life to a state of non-existence. However, there appears to be a conceptual problem in saying that life is better for a person than non-existence. Silverstein has argued that it is incoherent to assign any value, even zero to times when a person does not exist (Silverstein

1980 & 2000). Since there is no person at such times there can be no value for her.[24] This type of life-death comparison may thus be inappropriate to make. As a result, it is surprisingly difficult to argue that life extension is good for you because it postpones going from a good state (life) to a bad state (death).

Life-life comparisons

In order to avoid this type of life-death comparison, it has become common to invoke a conceptually coherent life-life comparison when considering whether an event is harmful or beneficial.[25] On this view an event is good for you if it makes your life better than it would have been had that event not occurred. Ben Bradley formalises this idea as a general view about harms as follows:

> [t]he overall value for a person x of an actually occurring or obtaining event or state e = the value of x's actual life minus what the value of x's life would have been had e not occurred or obtained. (Bradley 2007, 115)[26]

On this view, then, taking a CRM is good for a person if it makes her life better than it would have been if she had not taken the CRM. Doing so is bad for her if it makes her life worse than it would have been had she not taken the CRM. Suppose, for instance, I take a CRM and, as a result, my life has a value of 10. If I did not take the CRM my life would have had a value of 13. The value of taking a CRM is -3: it is bad for me, since I would have been better off if I had not taken it. On this view something can be bad for me even if it does not result in an absolutely bad state. What matters is that I am comparatively worse off than I would have been.

[24] See my 'Deprivation and the See-saw of Death' 2009 for a detailed discussion of this problem. See also Parfit 1984, 175.
[25] See Nagel 1979, McMahan 2002, Feldman 1991, Bradley 2004.
[26] See McMahan 2002, and Broome 2004, 11 for variants of this claim.

Life-life comparisons and other judgments about welfare

This way of conceiving of harm and benefit avoids the problematic life-death comparison that results from holding that harm involves going from a better to a worse state. However, it also makes sense of some of our other intuitive judgements about benefit and harm, good and bad. For instance, say Maria has a job that she likes, but she applies for another position that would make her better off. Unbeknownst to her, Paolo, a competitor for the position, tells a lie about Maria and, as a result, she does not get the job. Maria continues in her position, at the same level of well-being she was before. Yet it is justified to think she was harmed by Paolo, despite the fact that her level of welfare has not changed. She is harmed because she is worse off than she would have been if Paolo had not lied.

The life-life comparison is effective in a range of cases. It is thus appropriate to use it to determine the prudential value of CR and CRMs. On life-life comparisons, objections to life extension may attempt to show that prolonging one's life would a) add no value to a person's life, so that the intervention would not be worthwhile, or b) would make a person's life worse than it would have been had it not been prolonged.

This latter (b) can occur in two ways: first, a person's life may be made worse because CRMs result in an absolutely bad condition that *subtracts* from the actual value of one's life. This might be the case if, for instance, a CRM resulted in pain so severe that life was not worth living. Alternatively life extension can be bad for me, even if an extended life is good: if taking a CRM *adds less good* to life, and so is *worse*, than not taking the intervention, making use of a CRM is harmful.

v) Structure of arguments

Having delineated relevant axiological conditions for evaluating interventions in terms of their prudential value, I proceed as follows: In each chapter that follows, I outline the

intuitive positive argument for extending lifespan in terms of a relevant value. Thereafter I discuss *general* objections to life extension that have been made on the basis of each value or theory of individual welfare. I determine the extent to which these objections are applicable to CRMs. Where they apply, I assess how damaging they are to the case for life extension by CR and CRMs. Finally, I discuss ethical concerns that have been raised about this *particular* type of intervention, and which are unlikely to have been considered in relation to other life-extending interventions. The overall claim of this part is that, despite some reservations, CRMs are likely to be beneficial.

4. SUBSTANTIVE GOODS

As mentioned above, substantive good accounts designate goods whose presence or absence make a person's life go better or worse. Some examples include 'moral goodness, rational activity, the development of one's abilities, having children and being a good parent, knowledge, and the awareness of true beauty' (Parfit 1984, 499). Martha Nussbaum has a list of central 'capabilities,' which are necessary conditions for a good life. These include, inter alia, life, bodily health, affiliation, and play (Nussbaum 2000).[27]

There is obviously significant dispute about what goods should belong on the list. In this chapter, I restrict the discussion to those substantive goods that have been discussed in relation to life extension: health, procreation, self-development and flourishing, and the value of community.[28] I argue that, contra the objections, CR and CRMs may improve lives on substantive good accounts.

4.1 Health

Health is often regarded as having special value. As early as 380 BC Plato argued that health is desirable in itself and not merely for its consequences (Penner 2003, 312). More recently, Daniels has linked the value of health to its impact on opportunity. He writes:

> [d]isease and disability, by impairing normal functioning, restrict the range of opportunities open to individuals. Health care thus makes a distinct but limited contribution to the protection of equality of opportunity. (Daniels 2001, 2)

However one justifies the value of health, it clearly has key significance to individual welfare. A reasonable standard of physical health is a precondition for having a good life.

[27] See also Nussbaum and Sen 1993.

[28] Note that pleasurable mental states and the satisfaction of desires would form part of most plausible accounts of substantive goods. Thus for substantive good theorists, the sections that follow may be seen as subsets of objective list theory.

Partly for this reason, many concerns about life extension centre on potential negative side-effects that may impact on health related well-being.

Assuming a person had a sufficiently high standard of health, an intervention that postponed death could increase the value of life. By delaying death, a life extending technology (LET) could increase the amount of time spent in a condition that adds to the health-related value of a life. If so, a person's life would have a greater value if she took the intervention than if she did not. On a life-life comparison, the use of the LET would be good for a person.

The objections that follow challenge this idea. The Struldbrug objection makes the point that there are some age-related health conditions that would *detract* from the value of life. Life extension technologies may prolong these conditions, making an extended life worse than a normal one. I argue that, although this may be true, it is not the case with CR and CRMs.

4.1.1 The Struldbrug objection

In a study of community attitudes to life extension, Partridge et al established that one of the major concerns people have about life extension is that gains in length of life come at the expense of losses in quality of life in old age (Partridge *et al.* 2009). Individuals are concerned that new life extending technologies will have what I will call the Struldbrug effect of prolonging and worsening age-related health problems.

The Struldbrugs in Jonathan Swift's *Gulliver's Travels* are an often used example of unhealthy life extension. Swift's Gulliver writes of the Struldbrugs:

> Besides the usual Deformities in extreme old age, they acquired an additional Ghastliness in Proportion to their Number of Years, which is not to be described. (Swift 1826, 89)

These pitiful characters age normally, or at least consistently, but continue to decline physically long after the 'normal' life span. As a result they are tragic and twisted beings with a life of ever-decreasing welfare. This kind of prolonged physical decline is, arguably, increasingly evident in the developed world where lifespan has increased due to medical advances. This has contributed to a rising number of cases of age-associated disorders such as Alzheimer's disease, diabetes, and cancer (Olshansky et al. 2006). In general, getting older is associated with worsening health. Moreover, interventions such as life support machines can lengthen lifespan without increasing health-related quality of life, resulting in lives that many regard as not worth living.

If life extension extends and exacerbates age-related health decline, the contribution it makes to welfare will at some point cease to be positive and the intervention would detract from the health-related value of a person's life. The Struldbrug problem thus captures an important fear that people have about life extension: health decline may make old age so bad that having the additional life is not worthwhile.

A distinction: decreased health minimum and prolonged health decline

To deal with the above fears, it is necessary to distinguish two separate concerns that are present in the case of the Struldbrugs. The first is that an extended lifespan will result in a *decreased minimum* of health. The second concern is *prolonged health decline* – that life extension would stretch out the period of declining health. In the case of the Struldbrugs both concerns are in evidence. The decline in health continues below a minimum, or tolerable level. This decline is also prolonged; in the case of the Struldbrugs it is extended indefinitely without ever 'bottoming out' or being cut short by death.

In response to the Struldbrug objection to life extension, I argue below that CR and CRMs would not result in a decreased health minimum. However, it does appear likely to prolong a period of worse health by decelerating ageing. Although a decreased health minimum would be harmful for individuals, I claim that the prolonged health decline that would result from CRMs may add to the overall health-related value of life. As a result, I argue, the Struldbrug effect is not something that should worry us in the case of CRMs.

Decreased health minimum

As discussed in Chapter 3, several studies of the health effects of CR and CRMs on humans have been and are currently being conducted. The CALERIE project is one of the most recent of these. The study involves the observation of calorically restricting humans, the measurement of health status, and assessment of the biomarkers of ageing.

Thus far the results of the CALERIE study suggest that, far from resulting in a Struldbrug-like scenario, caloric restriction improves the health of subjects, in keeping with rodent and primate studies (Redman and Ravussin 2011). Similar results have been found in a recent clinical trial of a resveratrol-based CRM compound (Kennedy et al. 2010). These shorter term results are in keeping with the transfer thesis outlined in Chapter 3. If the transfer thesis holds true in the longer term, age-related diseases will not be suffered to a worse degree. Instead, since ageing is slowed age-related diseases will be deferred to a later point in life.

Thus, studies on CR and CRMs strongly suggest that life extension by CR derived methods will not to result in the decreased minimum health scenario exemplified by the Struldbrugs. Other healthcare tools such as life support machines may extend life below a minimally tolerable level of health. Existing studies suggest that CRMs will not.

This should go some way to alleviating the fear that about life extension by CRMs would *worsen* health in advanced old age. However, the concern about *prolonged* health decline remains. Although CR and CRMs won't result in a lower minimum of health related welfare, they might result in the decline becoming extended across a longer period. That is, although health will not decrease below normal levels as a result of CR, the period in which health decline occurs might be longer.

Prolonged health decline

Would life extension by CR and CRMs result in prolonged health decline? Some advocates of anti-ageing research claim that anti-ageing technologies may instead result in the *compression* of morbidity (Olshansky et al. 2006, 35). That is, they suggest that rather than extending the existing period of age-related decline, CR shortens it. Lifespan might be extended through a prolongation of what has been termed 'healthspan' – the period of relative health and vitality.

As discussed in the previous chapter, research on animal models points to slowed ageing. As a result, CRMs would most likely delay the onset of diseases related to ageing, *extending* the period of relatively good health before old age. However, slowed ageing also means that the period of decreased health, while postponed, could also be extended. In contrast to the compressed morbidity model, a time of decreased health is not shortened, only put off and perhaps lengthened. If CRMs result in decelerated ageing, as appears likely, there will indeed be a longer period in which age-related diseases will occur.

Compressed morbidity thus does not seem likely to be a consequence of CR. This may strike some as unfortunate, since many people would like to avoid a period of illness at the end of life as much as possible. In a moment I will argue that prolonged morbidity is not,

in fact, a bad thing in terms of individual health. However, for those who regard the compression of morbidity as a goal it may be interesting to point out that there is some evidence that at the level of population, a reduction of late life illness appears to be occurring in the absence of CR (Fries 1983). Compressed morbidity appears unlikely to be achieved by CR itself. However other interventions and lifestyle changes may enable its achievement with or without the intervention at issue in this thesis.

While studies suggest that CRMs won't result in decreased minimum health, it appears they would result in a prolonged period of health decline. This is an aspect that tends to be given little attention in academic literature on CR and CRMs, and it is important for individuals that make use of existing and future CRMs to take this into account.

Benefits of prolonged health decline

Many potential users may be deterred from using a CRM by the thought of a prolonged health decline. However, prolonging health decline isn't necessarily harmful. Indeed, interventions that decelerate ageing and lead to prolonged health decline could contribute beneficially to the overall health-related value of life. This is so for three reasons, discussed below.

First, decelerating ageing means that healthy period before old age would also be extended. One still has more healthy life before health starts to decline. Even if a lengthened period of health decline was regarded as undesirable, some might regard it as a worthy trade-off for an earlier increase in the number of healthy years. The second and third points below go further than this and suggest that this extended period of worse health is actually desirable if it is achieved by CRMs. In this case, the trade-off need not take place.

The second reason why prolonged health decline would be beneficial is that studies on CR suggest that the *number* of diseases suffered will not increase (Gems 2011, 110). Although the length of the 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, the *frequency* of diseases appears to be lower. In this sense prolonged health decline could be regarded as an improvement over normal ageing.

The third reason why prolonging health decline could be a desirable effect of using CRMs is that years spent in imperfect health can benefit one. Even if older people experience a longer period of increased susceptibility to disease this doesn't mean that their lives are *bad for* them or are getting worse on the basis of the value of health. The extra years are simply not as good as they could be. As Christine Overall suggests,

> long-living people who do have an illness or disability are not thereby prevented from leading rich, full lives; to the extent that they are dependent, their dependence should not be interpreted as evidence that increased longevity is bad. (Overall 2003, 188)

Years spent with a disease don't *subtract* from the overall health value of a time, unless they have a *negative* health value.[29] It simply means that less of this good is added to that life.

Another way of putting this third point is that older people generally have good lives, despite declining health and vigour. If a person's life is worth living through most of her old age, an extended old age would still add to the overall or cumulative goodness of her

[29] Note that some measures of health-related quality of life, like the quality adjusted life year (QALY) used by the UK's National Institute for Clinical Excellent (NICE), controversially assign a health value of zero to death. This means that only years spent in a state that is worse than death would detract from the value of life. Years spent in a state better than death would increase the health-related value of life. See Phillips and Thompson 1998.

life, even it would add less good than healthier years would. In comparison to a shorter life without CRMs, then, using the intervention would be beneficial.

These three points provide grounds to think that, far from reducing the quality of a person's life, prolonging the period of health decline might increase it. The possibility that CRMs would result in prolonged health decline is no objection to extending life by these means.

4.1.2 Particular effects of CR on health-related welfare

Above I argued that life extension by CRMs will not result in a Struldbrug situation of indefinitely declining welfare, and that extension of the period of health should not be seen as reducing health related welfare. However, while the slowed ageing that results from CR would not detract from individual health, CRMs may have particular effects with a more problematic impact on well-being. For instance Dirks and Leeuwenburgh caution that CR may result in immune system problems, loss of strength and stamina, decreased blood pressure, bone thinning, osteoporosis, and reduced cognitive performance (Dirks and Leeuwenburgh 2006). Below I discuss the extent to which these problems will apply.

Immune functioning

Results from empirical studies indicate that many of the above concerns are unlikely to affect humans when calorie restriction is practiced without malnutrition.[30] Omodei and Fontana point out that there is insufficient evidence about the long-term effects of calorie restriction on immune function (Omodei and Fontana 2011). However, they cite evidence of improved immune functioning in the short term.

[30] See figure 4 below.

Strength and stamina

With regard to strength and stamina, there appear to be conflicting findings. The CALERIE study found that, although subjects experienced muscle loss, levels of vitality remained the same, while physical functioning increased (Redman et al. 2011). Nonetheless, given reduced calorie intake, it should be expected that severe levels of CR would be incompatible with a high degree of physical activity.

CRMs, as defined in Chapter 1, on the other hand, would have the life extending effects of CR without restrictions in energy intake from food. Although further empirical investigation is required, reduced strength and stamina appear to be the result of reduced food intake, and so are unlikely to be negatively affected. With similar calorie intake there is little reason to think CRMs will contribute to an energy deficit, in the way that CR would.

Bone strength

Bone thickness and strength are significant considerations, since reductions in these contribute to fractures, particularly in the elderly and in malnourished groups. Villareal and colleagues report that, despite a loss in bone density, there is no degradation in bone *quality* (Villareal et al 2010). Since it is lower bone quality that is more strongly associated with fractures in humans, CR practitioners appear to be at no greater risk.

Moreover, even if CR results in decreased bone strength, there is little reason to think that CRMs would do so. The most influential explanation for bone loss is decreased mechanical stress due to decreased weight (*ibid*.). If this explanation is correct, CRMs would not result in decreased bone density, since they do not involve a reduction of food intake and concomitant decreases in weight. Thus there is no reason to think that CRMs would result in decreased bone density.

Hypotension

A further concern expressed by Dirks and Leeuwenburgh is that CR will result in hypotension, or decreased blood pressure. Although blood pressure levels were significantly decreased in human CR subjects, this was not beyond the normal range (Redman 2008). Furthermore, lower blood pressure is associated with reductions in cardiovascular disease, and is only considered problematic in the presence of other symptoms.

Cognitive performance

The CALERIE study also assessed levels of cognitive performance and found that these were not negatively affected (*ibid.*). CR has also been show to improve cognitive function in the elderly (Witte 2009). Further, as discussed in Chapter 2, brain ageing appears to be slowed in CR model organisms. In mice, resveratrol improves later life cognitive performance relative to control mice (Oomen et al 2009). Thus if mouse and primate experiments are transferable to humans, it should be expected that full cognitive function should be retained longer than is normally the case.[31]

Thus the particular concerns mentioned by Dirks and Leeuwenburgh appear unlikely to be problematic in the case of CRMs. Moreover, as part of its investigation of health concerns about calorie restriction and CRMs, the CALERIE study conducted health related quality of life assessment. Such assessments are, for instance, used in health policy to determine whether, and the extent to which an intervention will benefit a person in terms of health. On the basis of this health metric, the researchers concluded that there is little evidence that

[31] This should also offset Glannon's fear that life extension will slow bodily ageing, but not brain ageing, which is a version of the Struldbrug concern discussed above (Glannon 2009).

CR will have unintended consequences, and that there is evidence that the salutary effects observed in animals appear to transfer to humans (Redman et al 2008, 647).

Stunted growth

One health concern derived from animal studies that is not mentioned by Dirks and Leeuwenburgh is that growth may be stunted if the intervention is used when young (Anderson and Weindruch 2012). How should we take this fact? Stunted growth may not be a bad thing in itself. Indeed Liao and colleagues have controversially argued that reducing people's size may be help to reduce carbon emissions (Liao, Sandberg, and Roache 2012).

However, being smaller may have negative effects for individual welfare. In men in particular, shorter size is associated with disadvantages in education, relationships and employment, and many other aspects relevant to welfare (Christensen *et al.* 2007). These possibilities may counsel against making use of the interventions at a young age, even if earlier use would extend lifespan more. At the very least it is important to point out that using the intervention when still growing involves a trade-off between the goods of life extension discussed in this section, and the possibility of size-associated drawbacks.[32]

For the remainder of this thesis I will assume that a person would start the intervention after she is fully grown. It is important to flag that this is a value-laden assumption. That is, I make this assumption because I think it is plausible that, given the *fact* of stunted growth, and the *values* that retarded growth would conflict with, it would be reasonable to postpone taking a CRM.

[32] There is also a further difficult question about who decides whether stunted growth is an acceptable price to pay for a longer life. At the ages at which CR and CRMs could reduce growth, parents are likely to be largely responsible for health decisions regarding the user's welfare. It may thus raise difficult ethical issues about parental responsibility. These are well beyond the scope of this thesis.

Potential health concerns	Recent evidence
Immune problems	Immune decline slowed down, but long-term effects unknown.
Loss of strength and stamina	Muscle loss, but vitality, physical functioning unaffected.
Lower blood pressure	Yes, but not a problem.
Bone thinning, osteoporosis	No decline in bone quality.
Cognitive performance	No reduction. Brain ageing appears to be slowed in rhesus monkeys. Evidence for extended preservation of cognitive function in resveratrol fed mice.
Stunted growth	Likely if used early in life

Figure 4 Recent findings about potential health concerns

4.1.3 Conclusions on health

As it stands, studies of CR in general, and results from the CALERIE project in particular seem positive in terms of the effects of CR on health-related well-being. First, the worry about indefinite decline in health due to extended ageing seems unwarranted, since CR extends the biological ageing process rather than causing it to continue beyond its 'normal' limit. Second, the concern that the period of decline at the end of life will be extended is also mitigated. Although an extended decline may occur, a person is likely to have a satisfactory level of health for longer.

Finally, the available studies indicate, albeit cautiously, that life extension by calorie restriction will not have negative side effects for health. On the contrary, as discussed in Chapters 2 and 3, CRMs may delay or prevent the onset of age-associated health conditions such as cardiovascular diseases, Alzheimer's disease, diabetes and cancers. In terms of the substantive good of health, then, CR and CRMs may have a significant role in enhancing individual welfare.

4.2 Procreation

It is likely that procreation will feature on many lists of substantive goods.[33] Martha Nussbaum, for instance lists reproductive health, and reproductive choice as significant capabilities for a good life (Nussbaum 2000). Similarly, Kass regards procreation as the 'eternal renewal of human possibility' (Kass 2004, 318).

Even if procreation is not given the central significance that Kass and Nussbaum accord it, many people do regard it as an important good. Some regard their own or others' lives as less complete if they don't give rise to other lives. For these, an accompanying decrease in reproductive ability would at least make prolong life less attractive.

In what follows I discuss two ways that a life extension might interfere with procreation. The first potential conflict between life extension and the value of procreation is raised by Kass. He argues that the desire to extend one's lifespan is attitudinally at odds with reproduction. The second problem is that the life extending intervention itself might reduce fertility. I discuss each of these in turn. I claim that desiring to extend lifespan is compatible with procreation. Moreover, fears that CR and CRMs would decrease fertility can be mitigated.

4.2.1 Life extension and attitudes to procreation

Kass has argued that the pursuit of life extension for self-interested reasons displaces procreation as a value in people's lives. Thus, if procreation is a substantive good – one that is good whether or not people want it – and if displacing the value of procreation

[33] Some may associate the good of procreation with the good of health. Here I have kept them separate, since it seems plausible that one can be considered healthy without the ability to procreate. Moreover, as discussed below, there are attitudinal concerns about life extension and procreation that are separable from concerns about health.

prevents or reduces the likelihood of people having children, then desiring life extension might make people's lives worse.[34]

Kass implies that the individual pursuit of increased longevity entails a self-interested attitude which is inimical to reproduction. He claims that

> simply to covet a prolonged life span for ourselves is both a sign and a cause of our failure to open ourselves to procreation … one cannot pursue agelessness for oneself and remain faithful to the spirit and meaning of perpetuation. (Kass 2004, 317)

In other words, wanting to live much longer signals a rejection of the deeper importance of procreation.

There is a weak but important claim here, which is that the immoderate, single-minded focus on selfishly pursuing extended lifespan – 'coveting' a much longer life 'for oneself' – may threaten other values, like procreation, that may be significant for individuals and society. Mythology and popular culture are replete with examples of this. To take an obvious one, the vampire legend promises immortal life at the cost, *inter alia* of losing the ability to reproduce. This warning that a self-interested *obsession* with living longer will detract from other values is surely correct.

However, it might also be possible to extract a stronger claim from the above quote: that wanting to live longer is incompatible with valuing perpetuation, such that if we want longer life, then we are *necessarily* being unfaithful to the value of procreation. This strong claim is implausible. It cannot, for instance, be the case that wanting more happiness – and more happy years – for ourselves entails that a person rejects the value of procreation.

[34] Kass may not view procreation as, in the first instance, an aspect of *individual* welfare. It appears instead to have some metaphysical importance. This is, however one way of interpreting the argument that is relevant in the current context.

Valuing procreation does not require completely forgoing the pursuit of other aspects of one's own welfare.

Kass is right to draw attention to the fact that single-minded desire for longer life can damage and destabilise other values. The value of life is not determined by its length alone. However, it would be misguided to suggest that a wanting a better, longer life for oneself must come at the expense of procreation.

4.2.2 CR, CRMs and reproduction

The second concern about the relation between CRMs and procreation concerns features particular to the intervention itself. A fear that CR and CRMs will impact on reproduction is given credence by evolutionary theories of ageing discussed in Chapter 3, and by studies on a variety of organisms. Nalam and colleagues suggest two central evolutionary reasons that support the idea that CR will reduce reproduction in mammals:

> First, if there is a food shortage, then it would be advantageous for reproduction to be temporarily halted because this would result in conservation of food for existing parents and offspring until the food resources have been replenished. Second, gestation and lactation are energetically costly, so if there is not enough food to support these processes, then mother, child and future offspring would be lost. (Nalam, Pletcher, and Matzuk 2008)

Restricting reproduction in times of decreased food intake is advantageous because it gives adults greater access to food, and reduces energetically costly child-rearing. This evolutionary claim is borne out by a plethora of animal studies demonstrating that reproduction is decreased due to decreased fertility under conditions of calorie restriction.[35]

[35] See Speakman and Mitchell 2011 for a review of the effects of CR on reproduction.

The possibility that CR and CRMs will decrease reproduction in humans may thus seem to argue against their use as life extending techniques. If procreation makes a person's life go better, then one's welfare appears likely to be reduced by CR. Below I discuss five considerations that mitigate this problem. The first is that one can wait until one has reproduced before taking the intervention. The second is that it is possible to interrupt the intervention in order to reproduce. The third is that, empirically, fertility and CR are not as clearly incompatible as the evolutionary argument suggests. The fourth consideration is that CRMs are less likely to result in the fertility-compromising effect of the stringent CR diet. The fifth is that advances in technology mean that levels of fecundity no longer dictate one's ability to procreate.

Mitigating factors

If CR and CRMs prevent reproduction, perhaps one could wait until after having children to commence caloric restriction. If the transfer thesis is correct this means that less lifespan would be gained. If, for instance, one reproduced then, at age 39, commenced the use of an extremely potent CRM, capable of mimicking the life extending effects of a 60% reproduction, one could expect to live to 87 years old.[36] This is less than if the intervention commenced at a younger age. Nonetheless it is still a significant gain in life expectancy, and mitigates concerns about the effects of CRMs on procreation.

A second possibility is that one might interrupt the intervention when one wished to have children. In this way perhaps one could keep lifespan gains earned before reproducing. As mentioned in Chapter 3, in a study on calorically restricted female rats, it was found that fertility increased on return to a normal diet, increasing lifespan and fecundity relative to controls (Selesniemi 2008). If this result is replicated in humans, women could enjoy both fertility and extended life.

[36] See figure 1.

A third consideration that may ameliorate concern about the effects of CR and CRMs is that it has been demonstrated that some genetically modified mice are able to retain the life extending effects of CR whilst retaining normal fertility (Partridge, Gems, and Withers 2005). This raises the possibility that the life extending effects of CR and its effects on fertility are separable. If so, it seems possible that an intervention might be derived that mimics the effects of CR without undermining procreation.

A further factor is that the fertility inhibiting effects of CR are in part due to lower body mass. At a low body mass, females become incapable of menstruation. If low body mass is responsible for declines in fertility, as seems reasonable, then a CRM might not reduce fertility, since a CRM would not require reduced food intake. Some support for this is found in the fact that the most widely used candidate CRM, metformin, can be used before, during, and after pregnancy.[37]

The final mitigating factor is that procreation is less tightly linked to a natural ability to reproduce. People who are less fecund, or infertile can procreate using artificial means. Social factors and technological interventions play an increasingly important role in procreation. Thus, decreasing fecundity does not necessarily defeat the value of procreation.

The above considerations do not entirely remove the concern that CRMs will reduce reproductive ability. More studies in humans are required to determine whether a trade-off between reproductive potential and the likelihood of extended lifespan is avoidable.

[37] It is also thought that metformin *increases* fertility in women with polycystic ovary syndrome. See Morin-Papunen et al. 2012

Nevertheless, given the points above, it is possible to tentatively conclude that the reproduction-life extension trade-off may not be required.

4.3 Self-development and flourishing

The notion of self-development has a strong grounding in the three main families of secular western moral thought. It is apparent in the Aristotle's virtue ethical notion of flourishing, Mill's utilitarian interpretation of the value of liberty, as well as the Kantian idea of autonomy, or self-rule, as deployed in deontology. As such it is unsurprising that self-development is a key value on many substantive good theories. Here I interpret self-development as entailing personal, moral and intellectual growth, since it is on this ground that life extension has been attacked.

On a simple understanding of flourishing as personal growth, it would seem likely that an extended life would provide more opportunities to improve one's personal and moral skills. Given a longer life, it seems plausible that one would gain a greater degree of wisdom, and be able to develop one's skills and interests. However, two objections have been raised against life extension on the grounds that it will fail to contribute to, and perhaps even impede self-development.

The first objection suggests that wanting life extension impedes self-development by causing us to have a damaging focus on hanging onto life. The second concern is based on the idea that personal growth requires progress through certain natural phases. Kass and others have argued that life extension might disrupt these phases, and so impede the natural cycle of development required for a good life.

4.3.1 Life extension as a diversion from living well

Kass argues that the pursuit of 'life-extension will deflect us from realising more fully the aspirations to which our lives naturally point, from living well rather than staying alive' (Kass 2003, 25). This objection is similar to the attitudinal fears about procreation discussed earlier. My response here is the same. Kass is perhaps right to draw attention to the fact that single-minded desire for longer life can come at the expense of living well. However, if, as I argue in this Part, living longer is itself a route to living better in terms of some of the values discussed in this chapter, then there is no conflict been living well and having a longer life. One wants to live longer precisely because it is a way of improving one's life and achieving flourishing.

4.3.2 CRMs, personal growth and the life cycle

In the introduction to this Part, I indicated that some claims about individual welfare hold that the structure of a life and the order in which goods are achieved are significant for welfare. 'Life cycle traditionalism' is one such view.[38] For life cycle traditionalists, personal growth requires that a life progresses naturally through certain phases. Kass puts this idea as follows,

> the 'lived time' of our natural lives has a trajectory and a shape, its meaning derived in part from the fact that we live as links in the chain of generations. For this reason, our flourishing as individuals might depend, in large measure, on the goodness of the natural human life cycle, roughly three multiples of a generation: a time of coming of age; a time of flourishing, ruling and replacing of self; and a time of savoring and understanding. (Kass 2003, 26)

[38] This term is used by Gems 2011.

A life with this structure is paradigmatic of the good life. A life extension technology that disrupted this natural cycle might thus reduce one's chances, or, more strongly, be entirely incompatible with a life of maturity and growth.[39]

Kass's argument is deeply rooted in the Natural Law tradition, or ethical naturalism. This brand of ethical thinking has been heavily criticised in normative ethical theory, not least because it appears to commit the 'naturalistic fallacy.'[40] That is, it has been criticised for jumping from the claim that something is natural to the claim that it is good, without intervening premises that give reasons why we should think that what is natural is good. In the current context, Kass's argument might be criticised for fallaciously moving from the claim that humans *in fact* have a natural life cycle to the claim that the life cycle is a good, and interference with it is bad.

Although the ethical naturalist basis of Kass's argument is controversial, I will not criticise it here. Instead, in keeping with the methodology outlined in the introduction to this thesis, I will pursue a compatibilist approach. That is, I argue below that decelerated senescence is *compatible* with self-development that is bound to life cycles. This is because CRMs would introduce few changes to 'shape' of life, and would not prevent the passage through any of the phases that life cycle traditionalists view as valuable.

CR, CRMs and the life cycle

CR and CRMs slow ageing. This means that the that transition through life's phases would be secured. We would still be children, and then adults, and then elderly. A CRM user would simply spend a longer period of chronological time in each phase. If the passage through the phases is all that matters to self-development, the response to life cycle

[39] Note that procreation is an important aspect of the life cycle as conceived by life cycle traditionalists. Earlier I argued that the use of CRMs is compatible with procreation, so that CRMs shouldn't pose a problem to life cycles in terms of this value.
[40] See for instance Horrobin 2006.

traditionalists is relatively easy. There would be no conflict with self-development because we pass through all the relevant phases of personal growth.

However, life cycle traditionalists may also to be concerned about the *shape* of a life. This might be conceived of as requiring that the phases of life remain in proportion to one another. If we accept this *proportionality requirement* CR and CRMs might be problematic. This is because the intervention would only slow ageing from the point at which the intervention was begun. Phases of growth before this would not be extended. This is a concern given the earlier assumption that the use of CRMs should only commence after a person is fully grown, in order to avoid stunted growth (S4.1.2). If the intervention was begun after a person was full-grown, then later phases would potentially be disproportionately long with respect to the growth phase.

A further way in which the phases of the life cycle could be made disproportionate is if the intervention was stopped earlier. If, for instance, one begun the intervention at adulthood and discontinued the use of a CRM after the middle phase of development – the time of 'ruling and replacing of self' – then the middle phase might be disproportionately long in relation to both the later and the earlier phase.

It is worth pointing out a further concern that does not apply. It might be thought that the last phase - the time of 'savouring and understanding' - could be made disproportionately long relative to the earlier phases. However, as argued in Chapter 1, the degree of lifespan achieved by CRMs is likely to diminish the later the intervention is used. If, for instance, the intervention was begun at 55, there would be almost no increase in lifespan.[41] Increases in lifespan achieved by use of CRMs in the last phase are likely to be negligible. The last phase will not, therefore, be longer relative to both other phases.

[41] See figure 1.

The above considerations mean that there are two ways in which CRMs might make the phases discussed by Kass disproportionate. First, the middle period of 'flourishing, ruling, and replacing of self' and the final period of 'savouring and understanding' might be comparatively longer than the first period of 'coming of age.' Second, the middle period might be made longer than both the initial phase and the final phase.

Would life cycle traditionalists find the relative shortness of earlier and /or later phases problematic in terms of self-development? That is, would they insist on strict proportionality with respect to these phases? The proportionality requirement seems very difficult to argue for. In the first place, it's far from clear that these phases are as distinct as Kass suggests. Moreover, to the extent that it is possible to distinguish between these periods, there's not much reason to think that they are in proportion in the normal case. Intuitively people spend very different amounts of time in each phase. If so, the fact that CRMs alter the proportionality of phases wouldn't represent a substantial departure from what occurs in a normal life.

Life cycle traditionalism at its most plausible should thus be thought of as holding that what is important for a complete life is that one experiences these phases of development and maturation; not that they are proportionate. Since CRMs do not impede this transition to full maturity, a CRM user is at least as likely as anyone else to achieve a life of flourishing and personal growth. Indeed, in a longer life a person might achieve greater development of her personal skills, and moral and intellectual characteristics.

4.4 Creativity and beauty

The value of beauty has historical significance, having been linked with other 'transcendental' values, such as 'goodness' and 'truth' (Blackburn 2010). More recently,

Derek Parfit includes 'awareness of true beauty' as an example of something that might be considered objectively valuable (Parfit 1984, 499). Two separate problems with life extension have been raised in relation to the values of creativity and beauty. The first holds that a sense of mortality underlies the creation and awareness of beauty. The second highlights potential effects of CR on the human body. I claim that the first argument fails because technologies that decelerate ageing do not prevent death. The success of the second argument depends on how highly one values one's own beauty, and may require a trade-off with other values if one is to commence CR. However, CRMs would avoid the second objection altogether.

4.4.1 Mortality as a prerequisite for beauty

Kass has suggested that mortality is a condition for the creation of beauty:

> Perhaps … only a mortal being, aware of his mortality and the transience and vulnerability of all natural things, is moved to make beautiful artifacts, objects that will last, objects whose order will be immune to decay as their maker is not. (Kass 2001, 21)

Kass goes further and implies that, in addition to mortality being a prerequisite for the creation of beautiful objects, it may also be necessary for their appreciation:

> Could the beauty of flowers depend on the fact that they will soon wither? Does the beauty of spring warblers depend upon the fall drabness that precedes and follows? What about the fading, late afternoon winter light or the spreading sunset? Is the beautiful necessarily fleeting, a peak that cannot be sustained? (*Ibid*.)

A number of responses are possible to Kass's considerations. First, it is possible to challenge the idea that impermanence is the source of beauty. It is dubious, for instance that flowers are beautiful just because they will die. Second, even if we accept that impermanence is the sole source of beauty, human death is not the only type of

impermanence. Perhaps we would still be inspired to create beautiful objects by the impermanence of spring warblers and late afternoon winter light.

Though these are possible responses to Kass's claim, I will not argue for them strongly here. It is unnecessary to do so since Kass's argument only targets immortality – interventions that would prevent death altogether. CRMs have no such power and would at most postpone death. As such, they do not remove this potential inspiration for the creation and appreciation of beauty. Thus, if it were raised against the intervention at issue, the argument would fail altogether.

4.4.2 CR and physical beauty

One positive argument in favour of life extension on the basis of the value of beauty is Hackler's suggestion that life extending interventions would have the effect of 'prolonging the period of attractiveness and desire' (Hackler 2004, 192).

However, the effects of CR introduce a problem with the possibility raised by Hackler. In particular, some practitioners of CR complain that the diet worsens their self-perceived aesthetic qualities and makes them less attractive to others.[42] In particular, they are much thinner and less muscular, failing to conform to existing beauty ideals. Thus, rather than prolonging a period of perceived attractiveness, CR may conflict with a person's aesthetic beauty.

Note that this dip in self-perceived attractiveness is not universal. Michael Rae, a biologist who practices CR suggests he prefers being much thinner.[43] Nonetheless, it is a potential side-effect of a severe CR diet that should be taken into account. Practitioners are

[42] http://www.crsociety.org/resources/risks. Last accessed 20 December 2012.
[43] http://www.macleans.ca/science/health/article.jsp?content=20070115_139289_139289. Last accessed 20 December 2012.

confronted with the possibility that efforts to remain biologically younger will reduce their attractiveness. Consequently, in the case of CR itself, this negative effect should be weighed against the positive effects on health and other values outlined in this Part. For some, a reduction of attractiveness may be a sufficient reason not to practice a rigorous diet with perhaps uncertain payoffs.

This difficulty is a further motivation for the development of CRMs. Evidence from studies on mice treated with resveratrol suggests that CRMs could increase healthy lifespan even in overweight mice (Baur *et al* 2006). So a CRM need not result in the emaciated physique that CR practitioners complain of. As a result, there's reason to think that CRMs would not compromise physical beauty in the way that CR would.

Furthermore, in keeping with Hackler's suggestion, CRMs would potentially prolong the time which a person is typically regarded as physically attractive. Since ageing appears to be slowed throughout the organism, phases usually regarded as being times of increased attractiveness will be extended. In this way an effective CRM could contribute to a person's perceived aesthetic value, and also allow more time to experience other things of beauty.

4.5 Community

The importance of community as a *self-interested* value can be derived from the following quote:

> selves tend to be defined or constituted by various communal attachments (e.g., ties to the family or to a religious tradition) so close to us that they can only be set aside at great cost, if at all… [W]e also need to sustain and promote the social attachments crucial to our sense of well-being and respect, many of which have been involuntarily picked up during the course of our upbringing. (Bell 2012)

Understanding community as a prudential value in this way implies that individual welfare is constituted in part by others. Valuing community prudentially means that an insistence on a definite separation between one's own good and the good of (at least some) others becomes untenable. It is at least partly for this reason that communitarians criticise the atomistic pursuit of one's own good that they associate with modern liberalism.[44] If it is true that our own welfare is intertwined with the welfare of others, then the pursuit of our own good necessitates a concern for the well-being of others.

In this section I address the fear that life extension will result in negative changes to the nature and fabric of human relationships. Before I do so, however, I should point to two additional community related issues that are dealt with in subsequent sections. The first is that extending lifespan means that users of CRMs are more likely to be lonely at the end of their lives, and more likely to experience the loss of loved ones. The second concern is that individuals will feel that they are a burden on their community. Although these problems could equally be discussed here, I treat them in the section on mental states welfare in order to retain the unity of the section on the mental state of feeling old (S6.6).

4.5.1 Changing relationships

Temkin suggests that life extension may have further unsettling consequences for our relationships. He mentions the following as potential scenarios that should give us pause about life extension.

> With such changes the lines between generations might well be blurred, and the relations inevitably and profoundly changed… [S]peaking for myself, I think it would be terrible if I came to regard my mother or daughter, not so much as a mother or daughter, but as a peer. Likewise, as lifespans have increased the desirability of lifelong monogamy has been increasingly challenged, and many have started second families in their 50s. If we lived indefinitely, mightn't we

[44] See for example Taylor 1985.

> naturally have *many* spouses over the years? And then, depending on the rules of procreation in play, *many* children or stepchildren? What impact would this have on our notions of familial loyalty and duty? (Temkin 2008, 206)

Here, Temkin highlights that in a longer life the nature of the relationships we have will might change in undesirable ways. If people lived to far greater ages, then the differences between ages would become smaller relative to the length of the life. Substantially extending lifespan would close generational gaps and result in family roles changing across time.

Moreover, in a longer life, it might be expected that people would have larger families since they may have more time to procreate.[45] Temkin implies that with much larger families, the interconnections between community members might become frayed and distant. This might negatively impact on our moral relationships with our families. Perhaps, then extending life would unravel 'social attachments crucial to our sense of well-being and respect.'

It is certainly true that intergenerational relationships change across time. When one is a child the relationship with one's parents may be one of obedience and authority; As the individuals mature the relationship changes – if we're lucky, older generations impart experience, and guide rather than coerce. These adjustments of status can be difficult, but they do not seem, as a rule, to result in relationships that are particularly terrible.

It impossible to know for sure whether, given an *indefinite* life, the great changes in relationships envisioned by Temkin would occur, or would be bad. It seems just as likely that such transitions, although they might undesired from our current perspective, might

[45] This idea is challenged in Chapter 9

contribute positively to our lives. However, I will not press this point here, since my subject is not an indefinite life, but one extended by CRMs.

While the relational changes that would occur in an indefinite life are unforeseeable, it may already be possible to glean information about relationships in a life extended by CRMs. Studies of super-centenarians, people who live to ages of greater than 110, could be useful in this respect since they are relevantly similar in age to those whose lives would be extended by CRMs. As such they are already likely to have experienced relationship transitions described by Temkin. Studies of super-centenarians may thus tell us more about what our relationships would be like if we made use of CRMs.

Unfortunately I have not been able to find studies that assess the quality of relationships between super-centenarians and their families across time. Anecdotally, however, it appears that such relationships are not, or need not be, bad. On the contrary, one family with six living generations (aged 111, 88, 70, 39, 16 and 7 weeks) reported a strong bond, despite relatively small gaps between their ages.[46]

Temkin is right to point out that the character of our relationships with loved ones will change across time. Given a much longer life this change may indeed be substantial. However, it's far from obvious that such changes should be seen as bad for us or our communities. Moreover, even if such changes would be negative in an indefinite, or immortal life, what we know about super-centenarians suggests that there's no reason to think family relationships would change for the worse in a life extended by CRMs.

[46] http://now.msn.com/one-familys-6-generations-of-women-are-still-going-strong. Last accessed 20 December 2012.

4.6 Conclusion

The substantive goods of health, procreation, self-development, beauty, and community provide no strong reasons to think that CR and CRMs would be bad for a person. On the contrary, I argued that, with some reservations discussed in more detail in the conclusion to this Part, CR and CRMs could improve person's life by allowing a longer time to pursue or enjoy these goods. In the next Chapter I discuss arguments to the effect that extending lifespan using CR and CRMs would hinder the fulfilment of desires.

5. DESIRE FULFILMENT

This chapter discusses the impact of life extension by CR and CRMs on the fulfilment of desires. Desire fulfilment accounts of welfare have at their core the idea that what is makes a person's life better is that she gets what she wants. What makes a person's life worse is that her desires are 'set back' or thwarted (Feinberg 1984, 79-95). Desire theories are strongly linked to the values of autonomy and liberty, which emphasise free will in the choice and pursuit of one's ends. Significantly, desire fulfilment theories are formal, rather than substantive. That is, they don't say what a person *should want* in order for her life to go better, but instead claim that what makes her life better is getting what she wants, whatever that may be.

Various versions of desire accounts have been put forward. For instance, it has been argued that the person's desire should be adequately *informed*, so as to rule out the significance of irrational or irrelevant desires on a person's well-being. Fulfilling a desire to know the precise number of blades of grass on a field is, it is suggested on informed desire versions of desire theory, not conducive to an individual's well-being.[47]

Again, I will not provide any critique of the normative ethical theories at issue. To do so would go beyond the methodological scope outlined in the introduction to this thesis. Instead I present a range of arguments that could be brought on the basis of desire theories.

Desire fulfilment in a longer life

It's easy to see how life extension could be good for a person on the grounds of desire satisfaction theories. Most people *want* to live longer. Living longer would allow a person

[47] See Keller 2004 for a short, but informative discussion of the main desire theories and their critics.

more time to fulfil a desire to see their children, grandchildren and perhaps great-grandchildren grow up. In a longer life there is a greater opportunity to engage in projects that one has an interest in, or to see places one wants to see. Indeed, there seem to be very few long term desires that one has that wouldn't stand a greater chance of fulfilment with a greater amount of time.

However, it has been argued that, far from making our lives go better on desire theory, extending lifespan might fail to improve our lives and may even make us worse off. In this chapter, I discuss three objections that purport to show that life extension is either inimical to desire satisfaction, or that desire theory cannot provide prudential grounds for prolonging one's life beyond the current span.

First, David Benatar has argued that if we accept desire satisfaction accounts, we should regard life as bad. If this claim is accepted, perhaps we should regard prolonging life as harmful.

Second, arguing against the desirability of immortality, Bernard Williams claims that two models of an extended life fail to fulfil desire satisfactionist criteria for well-being: if I retain the desires and aims that now make me want more life, then fulfilling them will inevitably become meaningless. If, on the other hand, my future desires are significantly different, then from my perspective now there's no reason to want them, and thus no reason to want that extra life.

The third objection is based on a phenomenon known as Parkinson's law. Parkinson's law holds that the amount of time spent on a project increases to fill the amount of time available for its completion. The effects of this law are well-known. It explains why many tasks are only just completed when the deadline arrives (and sometimes after). If

Parkinson's law holds in the current context, perhaps we would not accomplish more than we actually do in our present lifespan. On desire satisfaction accounts a person would not be better off since the number and quality of desires fulfilled will not be increased.

I examine each of these claims in turn, and argue that they fail to dent the desirability of extending lifespan using CR or CRMs.

5.1 The badness of life

David Benatar argues that if desire fulfilment theories are correct, we should regard life as predominantly bad. If so, this appears to be a reason not to extend life. If life is bad, then it appears that the longer one lives the worse off she becomes: a person has prudential reasons shorten her life, rather than lengthen it. This is a highly counter-intuitive implication, and one that Benatar himself rejects. In this section, I briefly outline his argument that life is bad. Rather than confronting this argument directly, I indicate how it fails to lead to the conclusion that more life is not good for one. Even if life is 'bad' on desire theories, more life can be better. Living longer can provide conditions in which to satisfy our significant desires and so increase the value of life.

5.1.1 Desire theories and the harm of life

Benatar provides four points in support of the claim that life is bad on desire theories. First, and most obviously, many desires will not be fulfilled:

> One yearns to be free, but dies incarcerated or oppressed. One seeks wisdom but never attains it. One hankers after being beautiful but is congenitally and irreversibly ugly. One aspires to great wealth and influence, but remains poor and impotent all one's life. One has a desire not to believe falsehoods, but unknowingly clings to such beliefs all one's life. Very few people ever attain the kind of control over their lives and circumstances that they would like. (Benatar 2006, 75)

Second, much of life is spent in a condition in which even our easily fulfilled desires are unsatisfied. For instance,

> one usually waits at least a couple of hours until hunger is satiated ... One waits still longer to get rest when one is tired. Children wait years to gain independence. Adolescents and adults can wait years to fulfil desires for personal satisfaction or professional success. (*Ibid*.)

Third, even when desires are finally fulfilled the satisfaction of desires quickly gives way to the formation of new, unfulfilled desires. This means that even when our desires have just been fulfilled, we're already taking on new desires. Satisfaction is immediately replaced by dissatisfaction.

The fourth reason that life is bad is that many desires we have that are currently fulfilled will be thwarted in the longer term. For instance,

> [o]ne desires public office and is elected but not re-elected. One's desire to be married is eventually fulfilled, but then one gets divorced. One wants a holiday but it ends (too soon). (*Ibid*.)

As a result of these features, Benatar comes to the sobering conclusion that

> [d]issatisfaction does and must pervade life. There are moments, perhaps even periods, of satisfaction, but they occur against a background of dissatisfied striving. (*Ibid*., 77)

These melancholy considerations seem to have an unfortunate consequence. If one's life is really bad in the sense that harms are always racking up, then it appears that the cumulative value of life must always be decreasing. Life gets worse the longer that it is lived. To extend lifespan *in any way* is to increase the amount of time spent with unfulfilled or thwarted desires. If so, CRMs, and indeed heart transplants, antibiotics and vaccines, are

bad for us. If more life is bad for us, then presumably we have no reason to continue living, and we should not make use of such interventions.

These implications are at the very least counter-intuitive, and perhaps absurd. Indeed, Benatar himself rejects the implication that life is not worth continuing to live, despite his forceful arguments that life is bad. How can this be? To defend the claim that it is better to live longer, it is necessary to a) reject desire theories, or b) undermine Benatar's claim that life is bad on desire theories, or c) show how the claim that life is bad does not lead to the claim that life is not worth continuing.

Since I do not want to reject normative conceptions of welfare, I will not pursue a). Instead, I argue that Bernard Williams' distinction between conditional and unconditional desires makes it possible to accept that life is filled with a large amount of badness while avoiding the conclusion that we should want to shorten our lives. That is, I adopt a version of c). However, I suggest that this route provides grounds for questioning Benatar's claim that life is bad (b).

5.1.2 Conditional and unconditional desires

For Williams, perhaps the most famous proponent of desire theory, *conditional* desires are those that are conditional on our being alive. *If* I continue to exist, I want things to be a certain way. This group of desires contains most of our ordinary desires, like the desire to be able to go to the toilet, to have a holiday, to be in good health, and so on.

Unconditional, or *categorical* desires, on the other hand, contain a more significant class of desires. A categorical desire is one which

> propel[s a person] on into the future, and that desire at least is not one that operates conditionally on [her] being alive, since it itself resolves the question of whether [s]he is going to be alive. (Williams 1973, 86)

Categorical desires are the reasons we have for continuing to live. If, for instance, a person contemplated committing suicide, and decided not to, her reason would take the form of a categorical desire, such as the desire to complete her life's work, to experience more happiness, to have children, or to spend time with her family. Unconditional, categorical desires give a life *purpose*. On Williams' account it is the fulfilment of these desires that is the central source of life's value.

This distinction allows us to make sense of Benatar's claim that life can be worth continuing to live, even if it is characterised by a large degree of desire frustration. It may be that we are often in a state of unfulfilled desire, that many of our desires will be undone, and that many of our desires are ephemeral and quickly replaced. On a desire satisfaction account these conditions are indeed bad. However, if *unconditional*, *categorical* desires are not thwarted, we nonetheless have reasons for continuing to live.

Unconditional desires and the value of living

With Williams' distinction in mind, desire theorists can argue that life only ceases to be worth continuing if all our unconditional, categorical desires will not be satisfied. Arguably this is seldom the case. At the very least it should be acknowledged that the frustration of categorical desires is less pervasive than the omni–present desire frustration described by Benatar. If so, it may be that most lives are worth continuing, even if they are bad in Benatar's sense.

Moreover, the idea of categorical desires casts doubt on Benatar's claim that life is 'bad' on the basis of desire satisfaction accounts. On one ordinary conception of a good life, what makes a life good for one is that one's purposes – one's categorical desires – are fulfilled. Construed in this way, a person can have a 'good' life even if it contains much dissatisfaction. The fulfilment of categorical desires is sufficient for a good life, even against 'a background of dissatisfied striving.'

It is possible that Benatar uses the term 'bad' in an unusual way. Perhaps when he claims that life is bad, he does not mean that it has overall negative value for a person, but instead that it contains many instantiations of badness. Whether or not this is the correct interpretation it remains true that on desire theories, more life can be worth having. Provided a person's categorical desires are furthered, living longer is better. This is so even if important, but less meaningful, conditional desires are often frustrated.

5.1.3 Conclusion

With respect to CRMs, then, Benatar's argument may mean that we have less reason to make use of life extending technologies, or indeed life-saving technologies, than we think. We would experience more frustrated desires and a longer time in a state of dissatisfaction. Despite this, however, if practising CR or using a CRM would allow us to further more of our central reasons for living, then it would increase the value of life on desire satisfaction accounts.

5.2 Persistent desires

The above distinction between conditional and categorical desires undermines a potentially damaging implication of desire theory. However, it has also been employed to argue against the desirability of life extension. Indeed Williams himself claims that two models

of a radically extended life fail to fulfil desire-satisfactionist criteria for well-being due to their effects on categorical desires (Williams 1973).

On the first model, if a person retains the categorical desires and aims that she currently has for a sufficient amount of time, their fulfilment, and thus her continued existence will become meaningless. I call this the *persistent desire* model. Alternatively, on the second model, a person's future categorical desires will be significantly different from those she currently has. If so, then there's no reason to want them and thus no reason to want that extra life. I refer to this as the *changing desires* model. The proponent of radical life extension may find herself on the horns of this dilemma: either the persistent desire model, or the changing desire must be correct. If so, radical extension of lifespan is not good for a person.

In this section, against the problem posed by the persistent desires model, I argue that there's no reason to think that a substantially longer life with unchanging categorical desires would become meaningless. This is because we can have thin and flexible categorical desires like the desire to live a good life, as well as thick, open-ended desires like the desire to perform at the highest level in our particular discipline. The fulfilment of these types of desires could result in a meaningful life. I discuss the changing desires model in S5.3, and claim that an extended life could contribute to a person's well-being even if her desires changed radically. Thus, on both the persistent and changing desires model, extending lifespan using CRMs is desirable, and could contribute to well-being.

5.2.1 The desolation of fulfilled desires

Bernard Williams argued that if individuals retained the same reasons for living in a much longer life, existence would become meaningless since all our categorical desires will be fulfilled. He cites the example of Elina Makropulos, a fictional character granted the

opportunity to live at the physical age of 42 forever. After living for 342 years, she decides to die. Williams diagnoses her as follows:

> Her problem lay in having been at it for too long. Her trouble was it seems, boredom: a boredom connected with the fact that everything that could happen and make sense to one particular human being of 42 had already happened to her. (*Ibid.*, 90)

Although she is physically 42, Makropulos has achieved everything she could want. As a result, her life lacks meaning, resulting in malaise so severe that continued existence has no value for her.

In a similar vein, philosopher and physicist Moritz Schlick writes,

> [o]nce the goal is reached… after the first flush of triumph has passed away, there follows inevitably a mood of desolation. A void remains, which can seemingly find an end only through the emergence of new longings, the setting of new goals. (Schlick 1987, 60)

Satisfaction of desires is followed by an emptiness that only the adoption of new desires can fill. On Williams' persistent desire model, lives may cease to be worth continuing due to the fulfilment of categorical desires and the inability to take on new ones. Eventually we will satisfy all our wants so that only this 'void' remains. This mood of desolation may be part of what drives Elina Makropulos to accept death.

Immortality versus substantial life extension

In considering Williams' claim, it is important to flag the significant difference between the 342 years lived by Makropulos, and the number of years that would be achieved through the use of CR and CRMs. Though the latter would a substantial increase in lifespan, Makropulos has more than 200 years in addition to this before she finally rejects life. Presumably, then, Williams' concerns about the former, much longer, life apply with less force to life extension by CR and CRMs.

Nonetheless, assuming an unchanging personality and a fixed set of achievable categorical desires, it is possible to imagine that one's categorical desires may be exhausted even given an extra twenty or thirty years. Suppose, for instance, my only reason for living was to build myself an enormous mansion. If this desire is achieved, and, by hypothesis, I can take on no more goals, it may be that my life would have no further meaning. Because my reason for living has been realised there is nothing to provide purpose. Thus, even though the objection appears less worrisome in the current context, it retains some force if it is successful. Examining Williams' argument against immortality is thus instructive if substantial life extension is to be regarded as desirable.

5.2.2 Problems with Williams' argument

I claim that a longer life need not lead to a mundane existence even if we retain the same set of desires. This is so for two reasons: first, our categorical desires may be 'thin' enough to give them inexhaustible flexibility; second, we might have 'thick' or substantive desires that are open-ended enough that their fulfilment would not entail their extinction. I will explain these two responses in more detail.

'Thin' desires

The first response is that we can have thin reasons to continue living. Here, a thin desire is one that doesn't contain specific goals or milestones to be achieved. Instead thin desires are more general and inexact. I have in mind things like the desire to have the best life possible, to have purpose, to pursue self-development, and the desire to serve the good. These desires don't appear to have concrete, built-in goals. As a result it is difficult to imagine their becoming exhausted: a person will want things that they think further these thin categorical desires. However, when these subsidiary wants are satisfied, the categorical desires remain and continue to provide impetus for living. So even if people are

stuck with the same set of categorical desires, there's no reason to think that these will be exhausted if they are sufficiently thin.

Open-ended desires

The second response is that a person might have 'thick' desires that are open-ended. By a thick desire I mean one that has substantive content. By open-ended, I mean that the desire has no obvious end point at which it can be said to be exhausted. For example, a person may wish to meet as many of her descendants as she possibly can, or she may want to become the world's greatest musician.[48] These are desires that have clear content, and are potentially achievable, but which are not exhausted by their furtherance.

Consider the desire to meet more of one's descendants. Although this desire is furthered with each new addition to one's lineage, there's no reason to think that this will result in the 'desolation' described by Schlick, or the boredom described by Williams. Instead, since the desire is open-ended, its achievement will be valuable and successive fulfilments of this desire need not become meaningless.

Similarly, if a person's desire is to become the greatest musician, it is unlikely that this desire can be exhausted. Even if she reaches an insurmountable pinnacle in a particular instrument she can always learn and master, and even invent, new instruments. These examples show that there can be substantive open-ended desires that need not be exhausted even in an immortal life. In the context of substantial life extension by CRMs, as opposed to the 342 years lived by Makropulos, it seems even more likely that we can have substantive open-ended categorical desires that will not be exhausted.

[48] Examples discussed by Wisnewski 2005 and Temkin 2008 are of this thick, open-ended type.

Thus there's no reason to think that a substantially longer life with unchanging desires would become meaningless on desire satisfaction accounts. Thin and flexible categorical desires like the desire to serve the good, as well as thick, open-ended desires like the desire to perform at a high level in one's particular discipline can provide purpose.

5.3 Changing desires

It may be true that some people retain categorical desires, such as the desire to see one's family develop, for their entire life. However, it is not obvious that this is always the case. Some individuals may embark on numerous projects which they put to one side upon completion, to be replaced with new reasons for living. For such people a longer existence could mean there is no thread of categorical desire that runs throughout their lives.

This is Williams' second model of an extended life, which I referred to as the changing desire model. Williams holds that at some point in an immortal life all of a person's current categorical desires might be replaced with new reasons to live. If I will have an entirely different set of reasons for living, can I coherently desire that I live that long? Can this additional life benefit me if it will not further categorical desires I currently have? Williams answer is negative: I have no reason to live beyond the achievement of my current desires.

This changing desire model raises an important axiological difficulty concerning the limits of prudential concern. Does a person have any *self-interested* reason for wanting to continue living to a time when she will have reasons for living that are not the same as those she now has? Williams claims that a person has no self-interested reason to extend her life beyond the achievement or extinction of her present categorical desires.

Williams and the 'present desire' account

Williams' argument rests on what might be called the 'present desire' account of the limits of prudential value, which holds that only the fulfilment of a person's current desires can benefit her. On the changing desires model, at some future time none of a person's *current* categorical desires will have survived to be fulfilled. Since her present reasons for living will be extinct, they will not be furthered by the additional life she will have. Because the fulfilment of these current reasons is what matters for well-being, additional life does not further a person's well-being.

The point here can be brought out using an example of a case in which one's desires change so radically that they are in opposition. Say Dumi is currently the leader of a Nazi movement and his *sole* reason for living is to eliminate racial impurity. Suppose that gradually, across time, Dumi's desires change, so that by the age of 110, his categorical desire is to bring an end to any kind of intolerance and disrespect. Williams' claim is that from Dumi's current perspective he has no reason to want that extra life, since it furthers none of his present reasons for living.

The present desire account is a position in normative ethics. Since, as a methodological tenet I wish not to reject any comprehensive normative ethical theory, I will not dispute it here.[49] Instead, I argue that even if the present desire account is correct, a person can coherently want to live beyond a time when her categorical desires have entirely changed.

5.3.1 'Transitive' desires

The most common response to Williams' argument is to claim that self-interested concern is transitive.[50] That is, although a person has no *direct* interest in the welfare of a future

[49] But see Savulescu 1998 for a discussion. He refers to the present desire theory as the 'present aim' theory.
[50] See, for instance, Harris 2004, 83, Temkin 2008, Schloendorn 2006 and McMahan 2002.

self with different categorical desires, she may have an *indirect* interest by virtue of an intermediate whose desires she has an interest in fulfilling.

Jeff McMahan makes this point as follows:

> One need only imagine oneself approaching that later time at which one's *present* interests in continued life would supposedly run out. One would *then* have a strong interest in continuing to live beyond that point. And one has some interest now in assuring the satisfaction of interests one would have then. Perhaps an indefinite iteration of this concern for one's future is sufficient to ensure that almost any future life of one's own would be 'adequately related' to one's present aims to justify some degree of egoistic concern. (McMahan 2002, 102-3)

Transitive desire accounts attempt to show that the fulfilment of desires a person currently has may require the fulfilment of desires that she *doesn't* currently have, but will have later. In essence, they argue that the present desire criterion can commit one to an extended range of desires that you will have at a later time.

For example, suppose at the age of 25, Ben desires that at 75 he will have a higher level of well-being, but doesn't directly care about how his life goes beyond that. At 75, however, Ben desires that he will have a high level of well-being beyond 110. On desire accounts, Ben75's well-being is constituted in part by the fulfilment of his desire to be well at 110. Similarly, since Ben25 wants Ben75 to have a high level of well-being, Ben25 has an indirect interest in fulfilling Ben75's desire for well-being beyond the age of 110.

In this case, It would be good for Ben25 to take steps to improve his well-being at 110 so that he can improve Ben75's well-being. This is despite the fact that, from his current perspective, he doesn't *directly* care about what happens after the age of 75. Whatever interest he has in this time is held via his interest in Ben75's welfare: Ben25 wants Ben75

to be better off. Ben75 is better off if Ben110 is better off, so Ben25 should take steps to make Ben110 better off.

This means that even if Williams' second model of changing categorical desires holds true, a person might have prudential reasons to make use of a CRM. If a person thinks that later in her life she will desire to get to the age of 110 in decent health, and if she currently wants to give herself the opportunity to fulfil desires she will have later in life, then she currently has a reason to make use of a CRM.

5.3.2 Conclusion

In S5.1, I argued that the idea of categorical desires can resolve some difficulties in Benatar's argument for the badness of life. In this section and S5.2, categorical desires were shown to ground a separate concern about life extension: that it would result in a dilemma, both of whose horns entail that life extension is undesirable. In a substantially extended life categorical desires would either persist, in which case life would become mundane, or they would change, in which case I would have no reason to want the additional life.

I argued that neither of these models reduces the desirability of extending lifespan by CRMs. Life need not become mundane if categorical desires remain unchanged: categorical desires can be substantive, and open-ended enough, or thin and flexible enough, that retaining them need not result in life becoming meaningless. Moreover, a person can coherently desire a longer life even if her categorical desires will be different. Even if she has no *direct* desire for the welfare of a distant future self with different categorical desires, she may have an *indirect* desire by virtue of an intermediate whose desires she has an interest in fulfilling. If so, fulfilling this indirect desire would be good for her. It would be better to live longer.

5.4 Desire satisfaction and receding deadlines

The previous sections argue that additional life is worth having if it allows us to fulfil more of our categorical desires. The following objection implicates a curious, but familiar psychological phenomenon known as Parkinson's law and suggests that, in the context of a life, it may entail that we will not achieve more of our categorical desires.

5.4.1 Parkinson's Law

In 1955, C. Northcote Parkinson observed that '[w]ork expands to fulfil the time available for its achievement' (Parkinson 1955, 635).[51] This phenomenon is familiar to anyone who consistently finds themselves working until deadline day, wondering why the task could not have been completed earlier. Since 1955, this 'law' of work expansion has gained an increasing evidential basis and has become an important problem in, for instance, project management (Gutierrez and Kouvelis 1991).

In the context of life extension, Kass raises the following related concern:

> To know and to feel that one goes around only once, and that the deadline is not out of sight, is for many people the necessary spur to the pursuit of something worthwhile. (Kass 2004, 313)

Kass's primary target here is immortality, which would entirely remove the very literal 'deadline' of death. CRMs, on the other hand, would not prevent death, but if the transfer thesis is correct, they would postpone it. This postponement raises the Parkinsonian possibility that, if our deadline is extended, our life's work will simply expand to fill the time available to complete it. As a result, we will fulfil no more of our categorical desires.

[51] Note that this quote, which reflects the common understanding of Parkinson's Law, differs from Parkinson's own explication of his law, which concerns bureaucratic inefficiency.

Thus, if Parkinson's law holds true in the context of a whole life, extending lifespan may not improve our lives.

Kass is not a desire theorist, but his objection seems particularly relevant in the context of categorical desires. Deadlines may sometimes help to further one's categorical desires. Indeed, in some rare cases, categorical desires might only be achieved with the deadline of death. A person estranged from her family might only seek reconciliation when confronting the proximity of death. Or a person who has spent her life working on her magnum opus might finally complete it because of the fear that she will soon die.

However, for the objection to stand, it must be shown that *all* our desires rely on the deadline of death. If the fulfilment of some desires is unaffected by this limit, then it remains the case that a person can further additional desires even though the deadline is postponed. I argue that, in many cases, deadlines are not necessary to further our categorical desires. Moreover, even when deadlines do motivate us to complete projects, the motivation is seldom death. Instead, there are deadlines internal to life that provide the necessary impetus for fulfilling our categorical desires. As such, there's reason to think that the postponement of death would allow us to complete more projects and fulfil more desires.

5.4.2 Desires and the deadline of death

Categorical desires – the reasons for continuing life – are likely to vary from person to person. However, two of the examples I have used in this section include the desire to have more happy experiences, and to spend time with one's family. A person will spend time with her family because she regards doing so as good, and will have happy experiences because she enjoys them. Clearly such projects are pursued even in the complete absence of deadlines. The fact that a person furthers some of one's purposes without deadlines

means that Parkinson's law will not prevent one from achieving these aims to a greater degree given more time.

There are, of course, some desires that *are* furthered by deadlines, in accordance with Parkinson's law. However, the fulfilment of these desires seldom relies on confronting the deadline of *death*. Instead, where deadlines are involved in satisfying categorical desires, they are usually short-term intermediary steps towards larger goals. For instance, achieving a high standard in one's field is likely to require a series of incremental steps, many of which will be marked by deadlines. These shorter term deadlines are dependent on immediate context, and not on when death will occur. A manager does not usually set a project completion date in relation to the time at which her employees are likely to die. This means that the completion of intermediary steps in the fulfilment of categorical desires will often be entirely unresponsive to the time of our death. That is, because independent of death, intermediary deadlines are unlikely to be pushed back if the 'final deadline' is postponed. In this way, the work and time needed to fulfil our desires will not expand to fill the extra time gained by practising CR or using CRMs.

Kass raises one important point that should be acknowledged: it is probably true that when death is imminent one has a greater spur satisfy to one's unfulfilled desires. Considering death can sometimes clarify one's central desires and increase the urgency of their satisfaction. However, I argued that at least some desires are satisfied without any need for deadlines. The time taken to achieve these aims is unlikely to expand to fill additional time. Moreover, in the cases in which deadlines help us to take steps towards the achievement of desires, these time limits are commonly found *within* a life, and are unrelated to ultimate limit of death.

5.5 Conclusion

I argued that, contra Benatar's claims, life is not always bad. I argued against Williams that whether desires change or stay persist in a longer life, we can nonetheless have strong reasons to continue living. Against Kass I claimed that, although the time taken to achieve a desire may sometimes expand to fill additional life gained, many, and perhaps most, of our life's projects are not like this. These considerations mean that additional time can allow a person to fulfil more of her categorical desires, and to satisfy them to a greater extent. As a result, if the transfer thesis is correct, CRMs could make a person's life better by allowing her to further her categorical desires.

6. MENTAL STATES

Thus far I have argued that objective list accounts and desire satisfaction accounts fail to provide convincing reasons to regard CR and CR mimicking interventions as harmful. On the contrary, I claimed that CR-derived life extension may be good for people on the basis of these conceptions of well-being.

I have not yet considered the impact of CR derived life extension on positive mental states such as happiness. This is not because substantive good and desire fulfilment theorists do not regard these states as valuable. They do. However, mental state theories, such as hedonism and forms of utilitarianism, can be regarded as distinct because they regard mental states as the *sole* source of value.

For instance, in his *Letter to Menoeceus,* the Greek hedonist Epicurus, claims that 'all good and evil consist in sensation'(Oates 1940, 30). Similarly, John Stuart Mill claims that

> pleasure, and freedom from pain, are the only things desirable as ends; and that all desirable things (which are as numerous in the utilitarian as in any other scheme) are desirable either for the pleasure inherent in themselves, or as means to the promotion of pleasure and the prevention of pain. (Mill 1998, 55)

Mental states in a longer life

On mental states accounts, the goods described in the previous sections, such as health, and fulfilling categorical desires, are valuable only insofar as they contribute to a pleasurable life.[52] Since I have argued that CRMs would make a person better off on substantive good and desire satisfaction accounts, there is already some reason to think that mental states

[52] Conversely, substantive good theorists might regard positive mental states as a separate objective good, or they might want to categorise some issues concerning mental states, particularly debilitating depressive states, as health issues. Desire theorists are likely to regard happiness a good since most people want to be happy. For structural reasons I treat these here.

theorists would endorse life extension by CRMs. Getting what we want tends to make us happier, as do many substantive goods, such as health and community. Intuitively the presence of these and other sources of positive mental states mean that, in general, it would be better to live longer on mental states accounts. In a longer life one would have more time and thus be able to experience more pleasures.

However, several arguments have been directed against life extension on mental state grounds. The first argument is that there is no reason to live longer, since death is neutral. It has also been claimed that extending lifespan would be bad for a person, since it would result in genuinely bad mental states: suffering, fear, ennui, 'feeling old,' and depression. I claim that there is no compelling reason to think that life extension by CRMs would be neutral or negative in terms of mental states.

6.1 Neutrality

In the introduction to this Part, I pointed out that one way of undermining the potential value of CRMs would be to show that, although not bad, they are also not good for one. One claim to this effect can be derived from Epicurus. Epicurus argued that death doesn't involve any sensations and, since 'all good and evil consist in sensations' death is neither good nor bad. If this is true and death isn't bad, why should one be concerned about living longer? Why should I invest any effort in postponing a condition that doesn't involve bad mental states? There appears to be no reason to prolong one's life, since, were I to die, I would not be harmed by this.

One response is to claim that life is better than death. In comparison to the 'nothing' of death the pleasures of life are a good thing. As I indicated earlier, however, this type of life-death comparison is conceptually difficult. This problem is particularly pronounced on hedonist theories. According to Silverstein, for hedonists even assigning a value of zero to

death would require *some* sensation between the positive of pleasure and the negative of pain (Silverstein 2000). Death, by hypothesis, is nothing and involves no sensations, positive or negative. The idea that living longer is good because death is intrinsically worse is thus deeply problematic on this hedonist account.

6.1.1 The deprivation account of death's badness

Earlier, in response to the problem of determining the harm or benefit of life extending technologies, I argued that the value or disvalue of events or interventions can be determined by the use of a life-life comparison. This type of comparison has been employed to explain the badness of death. It yields what has been called the 'deprivation account' of the harm of death.[53] Death is bad to the extent that it *deprives* one of good experiences. Though it is not intrinsically bad, since it does not have the intrinsically bad property of pain, it is *extrinsically bad.* That is, death is bad if, had a person not died then, her entire life would have had a comparatively higher value.

Thus death can be comparatively bad, even on hedonist accounts that assign value only to pleasurable and painful sensations. Since death can be a harm, then, contra the objection above, there will often be a reason to postpone it. The remainder of this section assesses objections that appear to show that extending life using CRMs would result in mental states that are so bad as to make additional life not worth having.

6.2 Suffering

David Benatar has claimed on hedonist grounds 'even the best lives are not only much worse than people think but also very bad' (Benatar 2006, 14) If so, it may be that life extending technologies make life worse by prolonging a bad thing. In response to this, I

[53] For example Nagel 1979, Feldman 1991, Bradley 2007. See my 'Deprivation and the see-saw of death' for a defence of the deprivation account (Wareham 2009).

concede that that life may often be worse than we think. However, I argue that this does not entail the stronger claim that is required for this to be an objection to life extension. Namely, they do not entail that life is not worth continuing.

Benatar argues that life is much worse in hedonic terms than we commonly think. He catalogues unpleasant mental states that detract from the goodness of life:

> unless one is eating and drinking so regularly as to prevent hunger and thirst or countering them as they arise, one is likely hungry and thirsty for a few hours a day. Unless one is lying about all day, one is probably tired for a substantial portion of one's waking life. How often does one feel neither too hot nor too cold, but exactly right? (*Ibid*., 71)

But the situation is even worse than this:

> The negative mental states mentioned so far, however, are simply the baseline ones characteristic of healthy daily life. Chronic ailments and advancing age make matters worse. Aches, pains, lethargy, and sometimes frustration from disability become an experiential backdrop for everything else.
>
> Now add those discomforts, pains, and sufferings that are experienced either less frequently or only by some (though nonetheless very many) people. These include allergies, headaches, frustration, irritation, colds, menstrual pains, hot flushes, nausea, hypoglycaemia, seizures, guilt, shame, boredom, sadness, depression, loneliness, body-image dissatisfaction, the ravages of AIDS, of cancer, and of other such life-threatening diseases, and grief and bereavement. The reach of negative mental states in ordinary lives is extensive. (*Ibid*., 72)

Benatar claims that we systematically exaggerate the pleasures of life and overlook how much time is spent with these unpleasant mental states. We are able to sustain the illusion of a pleasurable life thanks to Pollyannism – an empirically evidenced tendency to exaggerate positive and de-emphasise negative conditions. For Benatar, a greater awareness of how much time we spend in negative states should cause people to acknowledge that life is bad.

6.2.1 The meaning of 'bad'

If so, why would we wish to extend life? Indeed, Elizabeth Harman claims that if successful, Benatar's claims give strong reason to think we should commit suicide (Harman 2009). As mentioned earlier in relation to desire satisfaction, this conflicts with Benatar's own understanding. Against the claim that his argument entails that suicide is always rational, he holds that

> the existent can have interests in continuing to exist, and thus harms that make life not worth continuing must be sufficiently severe to defeat those interests. (Benatar 2006, 213)

This interest is not *simply* an other-regarding interest in preventing additional grief. That is, it is not an altruistic, as opposed to prudential interest. Benatar is explicit that 'quality of life is not *always* so poor that ceasing to exist is a benefit' (*ibid*.). Thus, it can be good – or in one's interest – to continue living even though life is 'bad' in Benatar's terms.

This appears to conflict with a common sense understanding of the locution 'bad.' Intuitively, life ceases to become worth continuing when it is bad, and will not become good. If one agrees with this alternative use of the term 'bad', then Benatar's suggestion that life is normally bad and yet is worth continuing will strike one as contradictory.

One way of resolving this apparent contradiction is, as I suggested in S2.3.1, to treat Benatar's usage of the term 'bad' as a strange locution, so that even when life is 'bad' in Benatar's terms, it can still contribute positively to the overall value of one's life. Life is 'bad' in the sense that it contains some badness, or is less than perfect. On this understanding, life that is worth continuing adds value to life even though it is 'bad' in the sense of being sub-optimal. The question with regard to life extension then becomes

whether it will result in life that is worth continuing. Living longer can be good for you, in the sense of adding value, even though additional life is 'bad' in Benatar's sense.

Even in this case, Benatar's catalogue of ills raises the possibility that there is often insufficient pleasure to make the myriad pains of life worth suffering. As a result, rational suicide is much more common if his arguments are accepted. Pollyannaism means that we often believe our lives are going better than they are. If so, then perhaps fewer of us have a life worth living. Similarly, extending lifespan would be reasonable in fewer cases. Against this, I claim that hedonist theories provide resources to argue that lives can generally be worth living, even given the terrible conditions Benatar draws our attention to.

6.2.2 Higher pleasures

J.S. Mill famously argued that

> [i]t is better to be a human being dissatisfied than a pig satisfied; it is better to be Socrates dissatisfied than a fool satisfied. (Mill 2009, 19)

This is because certain pleasures are more valuable than others. For Mill, the pleasures gained from intellectual pursuits are, for instance, of a higher value than the pleasure of rolling around in the mud, or eating a delicious cake. Elizabeth Harman gives the following examples of 'higher pleasures:'

> Having loving relationships, doing work that we find rewarding—these experiences can be so valuable that they render the ordinary discomforts Benatar describes comparatively insignificant… some features of a life are very valuable, and can easily outweigh many mundane discomforts. (Harman 2009, 783)

These types of higher pleasures constitute an important response to Benatar's argument. Many of the values discussed in this and previous sections may be sufficiently valuable that they outweigh even the serious pains to which Benatar draws our attention, and give us ample reason to continue living.

6.2.3 Conclusion

Benatar claims that life is bad in hedonic terms since it contains much more pain than we commonly think. I argued that the sense of 'bad' at play is somewhat unclear. However, it avowedly does not mean that life is not worth continuing to live, since Benatar admits that we can still have sufficient reasons to go on living. The prevalence of unpleasant mental states does not entail the prudential rationality of suicide.

Thereafter I introduced the idea that there are higher pleasures capable of outweighing the painful mental states discussed by Benatar. In hedonic terms, then, there may be strong grounds for continuing to live. These grounds strengthen the positive hedonistic argument for the use of life extending technologies like CRMs. Despite the prevalence of pain, a longer life can be better for a person than a shorter life since a person can experience more higher pleasures that add to the value of her life.

6.3 Declining happiness

It is commonly thought that happiness declines with old age. Intuitively, worsening health and being closer to death mean that people will be less happy the older they get. For instance, arguing against life extension, Peter Singer claims that, on average, older people are less healthy and so less happy (Singer 1991).

This is relevant to the current case since, as argued in Chapter 4, CRMs might prolong the period in which one is more likely to experience age-related ill health. It could be argued that if a person is less happy in this period, it would be better for her not to live longer because she would live an extended time in a less happy state.

This objection is the mental states analogue of the Struldbrug case discussed earlier. Again, the lengthening of a miserable, unhealthy old age seems to be one of the most common fears about life extension. Many people seem to abhor the idea of getting old because they imagine it will be an unhappy time of painful hanging on. Why would we extend this period? Two considerations provide reason to do so.

6.3.1 Less happy is not unhappy

The first consideration is similar to that raised in S4.1: even if old age is *less* happy, this time can still be good. As I argued in relation to prolonging a period of worse health, the fact that a person spends time in a less good state doesn't mean that time is bad for her. It just means that less of that good is added to a life. For example: now I'm working. This isn't as fun as being outside in the sunshine. It adds less pleasure, but nonetheless adds some pleasure to my life. For now, the good of happiness is being accumulated at a slower rate.

As Singer acknowledges, a life extending treatment that made a person less happy as time passed could be good for her. Provided a person isn't unhappy, or in serious pain, the additional years, though less happy, can still add to the cumulative hedonic value of the life. Thus, when compared with the life in which she does not take the CRM and dies earlier, a CRM user may have more time to accumulate happy experiences.

6.3.2 Old people are happier

The second, and more significant, consideration is that older people aren't less happy at all. People severely underestimate how happy they will be in later years (Lacey et al 2006).

While it is common to think we'll be unhappy when we're old, a plethora of empirical studies of happiness instead point to *increased* happiness in old age.[54]

This seems to turn the argument on its head. Mark Walker has argued that since old age is strongly correlated with increased happiness, a life extending technology that prolonged the latter part of life would make a person's life even better than prolonging younger years would (Walker 2007). Not only will a person have more happy years, but more of these additional years will be spent in the happier condition of old age. If so, using CRMs would extend the happier times of one's life.

6.3.3 Conclusion

The claim that CRMs would decrease the hedonic value of one's life by extending the later part of one's life thus fails. Periods spent in a less happy state can be good for one. Moreover, studies of age-relative happiness point to increased happiness in old age. Thus extending a period in which one is older appears likely to increase the value of one's life.

6.4 Fear

Kass suggests that life extension will have a negative impact on mental states by increasing the fear of death. Kass writes:

> Who would not want to avoid senility, crippling arthritis, the need for hearing aids and dentures, and the degrading dependencies of old age? But, in the absence of these degenerations, would we remain content to spurn longer life? Would we not become even more disinclined to exit? Would not death become even more of an affront? *Would not the fear and loathing of death increase in the absence of its harbingers?'*(Kass 2004, 310)

Kass is claiming that the health decline at the end of life makes death easier to face, and that life extension technologies will *increase* the health experienced at the end of life. This

[54] See for example studies in Lacey 2006.

deprives us of the cushioning effects of age-related disease. As a result, before the time when our death is likely to occur we will be anxious due to our unwillingness to die and the horror of departing a healthy life.

In support of this idea, Kass approvingly quotes Montaigne:

> when we are led by Nature's hand down a gentle and virtually imperceptible slope, bit by bit, one step at a time, she rolls us into this wretched state and makes us familiar with it. (*Ibid*.)

As a result of depriving us of this 'gentle and imperceptible slope,' life extension results in 'a world increasingly dominated by anxiety over health and the fear of death' (*ibid*.). Mental state welfare is decreased because we experience heightened anxiety in life.

This objection is highly significant given that compressed morbidity – shortening the period of illness before death – is often argued to be a biomedical goal.[55] It is regarded as such due to the economic benefits of healthy old age, but also because it is assumed that a minimising illness and disability in the elderly is good for them. Kass's objection problematises this goal.

At least two responses are possible. The first is that this fear is unlikely to be sufficient to make the additional life not worth living. Although fear is a negative mental state, it's unlikely that it would be so pervasive as to render life *harmful*. Other mental states, such as the higher pleasures mentioned earlier could outweigh the badness of fear, meaning that life is worth continuing. I will not pursue this idea here since the reply below is sufficient.

[55] See for instance Fries 1983.

6.4.1 Fear and compressed morbidity

The second response targets an empirical premise in Kass's argument. From the empirical studies discussed in Part II, it is apparent that the interventions at issue would not result in compressed morbidity. Instead, CR has the effect of decelerating ageing. Ageing is slowed down. As argued in Chapter 4, this may prolong the period in which one is more likely to experience age-related diseases. If so, life would not be so healthy as to make death a subject of increased anxiety. Since we are not deprived of the 'gentle and imperceptible slope' of health decline there is no additional reason to fear death.

Thus, on the basis of empirical studies on CR and CRMs, it is possible to undermine Kass's concern about life extension. Kass's objection is directed at an empirical premise that does not apply in the case of CRMs. That is, he argues against life extending technologies that would result in compressed morbidity. Since studies suggest CRMs would not result in compressed morbidity, the objection does not apply here.

6.5 Boredom

Larry Temkin and Peter Singer have suggested that life extension would involve boredom, or ennui stemming from increased repetition and ever-declining novelty (Temin 2008; Singer 1991).[56] In some cases, this idea has been used as an argument against immortality. In the current context, it could be argued that life extension technologies should be rejected because they will inevitably lead to life-devaluing tedium. Against this, I argue that repetition seldom leads to boredom bad enough to make life not worth continuing. Moreover, even if it could do so in an immortal life, this outcome is unlikely given the comparatively small lifespan gains that would result from CRMs.

[56] This point is sometimes conflated with Bernard Williams' claim that radically extending lifespan would be undesirable because one would fulfil all one's desires. Since that idea is made on the basis of Williams' desire satisfactionist approach, I discussed and rejected it in the previous chapter on desire fulfilment (S5.2).

6.5.1 Repetition and boredom

For Temkin, repetition of activities often leads to boredom. As a result, he questions whether, in a much longer life, activities would become tedious through repetition. He writes,

> [t]he fact is that I've been around the block a few times now, and I'm a lot more jaded than my son, and most of his peers. Yet, crucially, I'm only fifty-three! What if I'd been around the block not just a *few* times, but a *million* times, or more? And even a *billion* times doesn't *begin* to approach the number of blocks I would circle if I were immortal! If I lived forever, would anything still strike me as new, exciting, or bewitching? (Temkin 2008, 202)

Singer similarly argues that the later parts of a person's life will be less good for her, due in part to a decline in novelty. On this issue he quotes Hans Jonas:

> prolonged experience… can never recapture the unique privilege of seeing the world for the first time with new eyes. (Singer 1991, 136)

Both Singer and Temkin question whether a longer life would be as good as we think, given a decline in novelty that results in repetition and boredom.

Boredom is not that bad

However, it is important to point out that neither Singer nor Temkin claims that repetition-induced boredom, or lack of mental freshness is so bad as to *detract* from the total goodness of one's life. Singer acknowledges that years spent experiencing decreased novelty and mental 'freshness' can contribute to the total prudential value of one's life. They can still be good for a person, even though they're not as good as years spent in a mentally fresh state.

Likewise Temkin admits that 'few would find suicide attractive *merely* because their lives were tedious. Even an incredibly boring life may yet be *worth living*, and better than no life at all' (Temkin 2008, 203). Thus, even if we accept that extending lifespan involves repetition and a decline in novelty it is nonetheless beneficial on these accounts. For the

objection to make extending lifespan undesirable, it must be claimed that repetition detracts from the value of a life, or fails to add to it.

That is, for the objection to be forceful against life extending technologies it must be argued that i) repetition devalues experiences and leads to boredom, and that ii) engaging in activities with which one is bored *detracts* from the value of one's life, or contributes no additional value. Moreover, to be effective against CRMs it must hold that iii) life extension will lead to increased repetition of activities in a life with a maximum length of about 140 years.

I argue that none of these claims succeeds. First, I hold that repetition fails to rob many activities of value and can often *add* value. Second, I argue that there's no reason to think that repetition can be as bad as the argument requires: there's no evidence that repetition of activities once deemed pleasurable leads to mental states that could be said to decrease the value of life. Finally, I deny that additional life gained by using CRMs is likely to result in repetition and deprivation of sufficient opportunities for novel experiences.

6.5.2 Repetition and the value of experiences

An initial observation is that the range of activities whose value is decreased by repetition does not appear to be large. Counting stones for eternity would most likely become boring. But this is because the activity was boring in the first place. On the other hand I can't think of many enjoyable activities that become less enjoyable through repetition. Reading, or playing table tennis, or writing a paper can of course become tedious. But when they do, it is usually because the activity has been *sustained* for too long, and not because the activity is repeated. When I become bored of these activities I can stop, and when I return to them they are no longer boring. It's not that playing table tennis loses value and becomes mundane. Instead, I get tired, or want to do something else for some time.

Of course if I watched the same movie over and over again this would result in tedium. But why would I do this? Unless I'm the only person in the world there will always be new instantiations of particular activities. Repeating the exact same activity may result in boredom, but it would be a boredom that could be easily avoided.

Repetition can be good

In addition, there is a range of activities that aren't drained of enjoyment by repetition. Sex is something that is likely to be enjoyable no matter how many times one does it. Conversing with peers, too, is unlikely to become boring (depending on the peers.) If there are always activities available that do not become boring through repetition, it is difficult to see how repetition can lead to a boredom that makes life worse.

In fact, many activities become *more* enjoyable the more they are repeated. Repetition helps one to improve, which in turn increases the enjoyment of the activity. I like table tennis more now that I am better at it. Thus the fact that activities lack novelty is no reason to think they are reduced in value. The claim that repetition inevitably reduces the value of an activity is highly questionable.

6.5.3 Repetition, boredom and the value of life

Even if repeating activities did lead to boredom, it is unlikely that this repetition would make a person's life so intolerable that she no longer wanted it. There is a type of boredom that is closely related to depression, which could plausibly devalue a person's life. In psychological literature this has been referred to as to 'habitual boredom' and involves a pervasive malaise with life in general. This type of tedium has serious consequences for well-being and is associated with destructive behaviour directed at self and society (Bortolotti and Nagasawa 2009).

Habitual boredom is contrasted with 'situational boredom,' in which one is bored with some particular thing. This latter kind of boredom results directly from repetition. Even if we accept that repetition reduces the value of activities within a life and leads to situational boredom, it must be claimed that this reduction is so severe as to make life *bad*. If not, then it would still be good for one to use the life extending technology. It seems necessary, therefore, to argue that situational boredom will result in the more pervasive and life-devaluing habitual boredom.

However, Bortolotti and Nagasawa have claimed that the empirical case that situational boredom is responsible for habitual boredom is weak (*ibid*.). Empirical investigations into the causes of this deeper and more pervasive malaise reveal that, although it can be triggered by situations of low stimulation and reduced novelty, this does not occur in the absence of significant additional factors. In particular,

> [i]t is the failure in developing, pursuing and ultimately achieving life goals that is most likely to determine habitual boredom. (*Ibid*., 273)

Bortolotti and Nagasawa thus conclude that

> [t]he view that some of the alleged features of the immortal life, i.e. the repetition of similar experiences and goal exhaustion, are significant factors in the occurrence of habitual boredom is unsupported and unmotivated. (*Ibid*.)

Although somewhat limited,[57] the empirical evidence the authors offer in support of their claim points to a likelihood that a boredom capable of devaluing a life is not likely to be a result of mere repetition. Instead it must occur against a background of other conditions such a lack of life purpose.

6.5.4 Repetition and boredom in a mortal life

The final point to be made against repetition-induced boredom concerns its status as an

[57] Notably the study on which they base their claim comprised only six subjects.

objection to CRMs as opposed to immortality. While it's conceivable that in an immortal life a person would ultimately repeat every activity available to them, it is unlikely that this would be the case in a life extended to a maximum of, say, 140 years. The range of enjoyable human activities is such that, given an extra twenty or thirty years in reasonably good health, it seems implausible that a person could run out of things to do. Thus, even if repetition did decrease the pleasure of an activity, and even if such devaluation would be severe in an immortal life, the degree of repetition required to devalue life is unlikely to be achieved in a life extended by CRMs.

Thus there is no reason to think repetition would make one's life worse in a life prolonged by CRMs. This is because many pleasures fail to be diminished by repetition, and because evidence suggests that repetition contributes little to a boredom sufficiently bad to devalue a person's life. Moreover, even if repetition could produce a boredom bad enough to make an *immortal* life not worth living, a life extended by CRMs is unlikely to involve sufficient repetition to do so.

6.6 Feeling old

The third argument designates a type of mental state referred to as 'feeling old.' Studies of this condition characterise subjects as 'feeling exhausted in spirit, lacking the energy to find new responses as life changes' (Hauskeller 2011, 395). Hauskeller argues that feeling old is not a function of biological ageing. Instead, the proposal is that *merely existing* for a sufficient amount of time results in a person feeling old. Feeling old designates a type of 'mental ageing' that might occur even if biological ageing is slowed using CRMs. If this occurred, extending lifespan would merely extend and deepen a period of negative mental states.

To determine the soundness of this objection, I question whether feeling old is indeed a

result of existing for a certain amount of time. Drawing on psychological literature, I argue that feeling old is not simply a product of continued existence. Instead, it is the result of contingent contextual and biological factors, including health, the ability to work, and the loss of community members. Although these factors are not decisive against extending lifespan using CRMs, they raise important considerations to be taken into account in decisions about lifespan extension.

6.6.1 Causes of feeling old

It is doubtful that coming to feel old, as characterized above, is really a consequence of merely existing. As mentioned earlier, older people report greater happiness than younger people. Conversely, people who are chronologically younger can experience mental states associated with feeling old. Indeed, as Hauskeller acknowledges, subjective ageing can occur at any point in adulthood (*ibid*., 394).[58] This means that feeling old is not simply due to the passage of time. Instead, factors other than chronological age are likely to be involved.

Nilsson and colleagues suggest several causes of feeling old that, while not exclusive to a longer life, may become more influential. In particular, experiencing ill health, being unable to manage one's own affairs, and losing loved ones and community members are features that appear common to interviewees that self-identified as feeling old (Nilsson et al. 2000). It is not *simply* the passage of time that exacerbates these problems. Nonetheless if these factors would be exacerbated in a life extended by CRMs, they may reduce the appeal of living longer.

Would CRMs entail that above contributors to feeling old play a stronger role? In S4.1, I indicated that health problems would not play a greater role, and may play less of a role in

[58] See also Thompson 1992 on the separability of feeling old and chronological age.

the life of a CRM user than that of a non-user.[59] CR slows biological ageing, reducing the risk of age-associated diseases, cardio-vascular disease, cancer and diabetes. Thus, to the extent that health is a contributor, CRMs may reduce the prevalence of the mental state of feeling old. In the remaining sections I discuss the contributions of personal loss and seeing oneself as a burden to the phenomenon of feeling old. I argue that they will play an increased role in a longer life unless important social changes occur.

6.6.2 Loss and loneliness

As an inevitable function of time's arrow, the more time that goes on, the more losses we experience. These losses add up and contribute to a devaluation of living that, according to Nilsson and colleagues, is strongly related to feeling old. Since the number of losses one experiences increases with the time one lives, living longer could exacerbate this contributor to feeling old.

Hauskeller expresses the idea that loss can contribute to feeling old as follows:

> if our lives lasted forever we might still suffer from, and gradually be wearied down by, the sheer passage of time, which, by its very nature, incurs loss after loss. That may well be part of what makes growing old so hard: not so much the gradual weakening of the body, but the sheer accretion of past in our minds. (Hauskeller 2011, 391)

As a result of mental ageing borne of loss, a person comes to 'feel old.' Empirical studies substantiate the idea that the very old are likely to experience greater loneliness (Ailshire and Crimmins 2011). This points to a type of negative mental state that stems from accumulated losses experienced in life. Because they live longer, those who live to older ages tend to outlive more of their loved ones. The death of a loved one is traumatic in

[59] See also Wareham 2012.

itself, but it may also mean that one is lonelier and less likely to have a community with which they can share and remember experiences.

This is a significant problem that is seldom acknowledged by life extension enthusiasts, such as transhumanists. The possibility of feeling increasingly alone is exacerbated in a longer life, since the longer a person lives, the more likely she is to outlive contemporaries. Faced with the prospect that *only one's own life* would be extended, and the likelihood that one would outlive one's contemporaries, many people, I think, would opt not to take the life extending intervention.

Even so, it could be argued that, since the very old regard their lives as worth living despite loss, substantially extending one's life would be worthwhile. Perhaps one's life would still be good, even though it is worse than if one's loved ones were alive. This may be true, but there can be little doubt that concerns about loss and loneliness are amongst the most significant drawbacks of a life extension technology. Indeed, this prospect was responsible for an unconditional rejection of life extension by some respondents in a recent survey (Partridge et al., 2009, 71).

Loneliness and the distribution of life extension

The possibility of loneliness means that the desirability of the technology depends to an extent on its distribution. With equal distribution, such that everyone in one's community was likely to use the intervention, the chance of outliving one's community of contemporaries may not be increased. This means that this Part's question about the prudential value of longer life overlaps with the question of how life extending technologies should be distributed. This is discussed in the following chapters, in which I argue that wider distribution of CRMs is likely to contribute to significant social goods.

In the present context of prudential, as opposed to social, goods it should be noted that wider distribution would significantly ameliorate problems of loss and loneliness that might result from extending lifespan. The likely distribution of CRMs is thus an important contextual factor in determining the desirability of extending one's life by this means.

6.6.3 Being a burden

The previously cited study by Nilsson and colleagues suggests that being unable to manage one's own affairs is a significant factor in feeling old. In support of this, Partridge and colleagues cite the fear that one would become a burden on one's family or community as one of the common reasons for opposing life extension technologies (*ibid*.). People are concerned that increased frailty in later life will mean that they require more expenditure on care, and are more reliant on others in confronting the challenges of old age.

In a much longer life this sense of reliance could be exacerbated. If one lives longer it may be that one will spend a longer period economically, physically, and emotionally dependent on one's family or nation. If so, since feeling oneself a burden contributes to feeling old, the sensation of feeling old may be worsened by life extending technologies.

Feeling oneself a burden is, again, a serious problem that tends to be overlooked or underplayed by zealous transhumanists. Nonetheless there are some important considerations, about CRMs in particular, that could mitigate one's sense of 'burdensomeness.' In particular, since they slow ageing, CRMs are likely to substantially extend the part of one's life in which individuals tend to be healthier and more productive.[60] This means that one could contribute a greater amount to society, as well as increasing savings for one's (extreme) old age.

[60] I discuss the social significance of this point in more detail in Chapter 9.

Being a burden and contextual factors

Once again, however, the possibility of maintained contribution is dependent on social factors. In particular, in many nations it is compulsory to retire at a certain age, often around 65. This makes it more difficult to contribute economically either to one's society, or to one's future economic needs. As a result of the great increases in lifespan achieved during the 20th century, retirement ages are already being raised in many parts of the world. It should be anticipated that the widespread availability of a life extension technology would make further increases necessary.

Like questions concerning the distribution of CRMs, raising retirement ages faces serious ethical and practical problems. For example, many people don't want to retire later. Moreover, some people who work in labour-intensive jobs should, arguably, not even work as long as they currently do. As a result, a measure aimed at increasing well-being by making one feel less of a burden may have the opposite effect of decreasing welfare by increasing the burden of work.

There may be a happy medium here, such that each individual retires when she is ready. Hervé and colleagues suggest that only the individual is capable of making this judgement, and that a person's perception of her readiness to retire heavily influences life satisfaction in later years (Hervé et al. 2012). Policies that respect this fact may mitigate the feeling of being a burden without the imposition of unwanted labour.

These considerations about feeling old highlight that individual welfare is heavily dependent on social context. In subsequent chapters I argue that CRMs may be widely distributed and have a positive effect on society and individuals' ability to work. If there is wider distribution of CRMs, and if retirement ages keep pace with increased lifespan, then there is no reason to think that extendees should feel lonelier, or more of a burden than

they currently do. Like existing elderly people, CRM users may come to feel old, but policies that allow and encourage contribution as long as one is able would postpone this feeling and thus contribute to an individual's mental state welfare.

6.7 CR, CRMs and Mental States

On the basis of studies on CR, it has been argued that the intervention, and drugs that mimic it, may result in negative mental states. In particular, Dirks and Leeuwenburgh cite evidence that points to the likelihood of

> preoccupation with food, constant hunger, binge eating, emotional deadening and/or depression, mood swings, irritability, anxiety, and social isolation. (Dirks and Leeuwenburgh 2006, 5)

In response to this problem I question whether these consequences are likely to occur. I indicate some studies that suggest that CR may result in improved mental states. Nonetheless, I argue that there may be reasons not to follow a CR diet. This is because the effects on mental states might make life worse if one did so. This risk provides some grounds for rejecting a CR diet, although these are not overwhelming. Finally I claim that this risk does not apply in the case of CRMs. Thus, CRMs might secure the mental state benefits of living longer without the risk of negative mental states that might accompany CR.

A different burden of proof

Before continuing, it is worth pointing out a difference between this objection and those that preceded it. Most of the problems considered above attempted to show that extending lifespan would not be worthwhile, since doing so would result in additional years that detract from the value of life. This required showing that the additional years would not be worth having. The current objection points to a possible decrease in quality not only of the

additional years, but also *in the years a person would normally have*. As a result, the burden of proof here is different. It is not necessary to show that the additional years would be bad, or that years in the life would not be worth living. Instead, for the objection to be successful, it must be shown that the intervention might decrease the hedonic goodness of a life to the extent that additional years are unable to make up for the losses.

Since this objection refers worse mental states within the normal lifespan, it only needs to provide reason to think that using the intervention would result in *less* hedonic good. Moreover, if it can be demonstrated that restricting calories does involve significant hedonic costs, it becomes even more important that the benefits – additional good years – will obtain. There is a greater *risk* involved if restricting calories has some costs, so the benefits should be relatively secure. With these considerations in place, I turn to a discussion of some of the studies about the psychological effects of CR.

6.7.1 Studies on CR and mental states

The Minnesota starvation study was a two year experiment designed to gain information about the results of extreme famine (Kalm and Semba 2005). In it, subjects were fed drastically restricted diets. For 24 weeks participants were restricted to about 50% of the control diet of 3200 calories. The subjects were fed what was regarded as a typical European diet in the latter stages of the second world war: potatoes, turnips, bread, rutabagas, and macaroni.

The results were disastrous in terms of their effects on mental states. Subjects reported many of the conditions cited by Dirks and Leeuwenburgh above, including preoccupation with food, mood swings, and feelings of social isolation. In addition, most participants experienced severe depression that in some cases resulted in self-mutilation. Indeed, one participant chopped off three of his fingers with an axe, and was unable to recall whether it

was accidental or intentional. It is unsurprising, therefore, that the Minnesota study is cited when warning of the potential detrimental effects of CR. If these effects result from a CR diet, there can be no doubt that the intervention is harmful.

CALERIE

However, more recent studies of CR in humans have had different results. Indeed, the CALERIE reported *reduced* depression scores amongst CR practitioners (Heilbron et al. 2006). There are several differences that may contribute to these variations in mental state well-being. Firstly, the degree to which these populations restrict calories is less. The CALERIE study restricted calories to 25% of ad libitum intake. In the Minnesota study, subjects were literally starved. Secondly, the nutritional content in these latter studies is much better than in the Minnesota study, which was designed to test physical and psychological responses to conditions of famine and food shortage. Finally, the CALERIE study is being conducted on overweight humans, while many of the participants in the Minnesota study were considered to be less than the ideal weight at the outset of the experiment.

These differences are significant. The Minnesota study involved severe malnutrition, and so was not 'true' CR as defined by practitioners and biologists. On the other hand, the degree of CR studied by CALERIE may also fall below that required to substantially extend lifespan. Given that a restriction of closer to 30% might be required, CALERIE might not be strongly indicative of what it would be like to restrict calories for the purposes of extending lifespan, as opposed to, say, for the purposes of losing weight.

The Caloric Restriction Society

Better evidence in this regard may come from members of the CRS – a group that restricts calories with optimum nutrition for health and longevity purposes. On the basis of these

studies, it does seem likely that CR will involve some costs. Many, but not all of these subjects, report an increased preoccupation with food, as well as constant hunger.[61] Indeed, even studies of less demanding diets suggest that some of these negative psychological effects would obtain (Warren and Cooper 1988). Despite the fact that CRS members sometimes claim that they simply get used to these mental states, these costs should be taken into account.

Thus Dirks and Leeuwenburgh are right to claim that

> a CR lifestyle should be initiated with extreme caution. The potential for the negative side effects exist and, therefore, those undergoing the classical regimen require medical supervision. (Dirks and Leeuwenburgh 2006, 5)

The effects of CR on mental states are sufficient to cast doubt on the idea that the benefits of additional years gained using a CR diet would outweigh the psychological costs. Thus, on mental state accounts of well-being, there are grounds to doubt that CR would improve the value of one's life.

Note, however, that this is not a conclusive case against the practice of CR. As noted earlier, hedonist theories sometimes claim that there are 'higher pleasures.' Just as these may make it worthwhile to endure much of life's ordinary suffering, perhaps they could outweigh the pains and discomforts that may ensue from CR. This is a very difficult balancing process, and is likely to have different outcomes for different people. It is up to the reader to decide whether the additional pains and deprivation of pleasures involved in restricting calories would be justified.

[61] http://www.psychologytoday.com/articles/200407/the-skinny-calorie-restriction. Last accessed 20 December 2012.

However, this trade-off may not be required. The hunger that results from CR seems likely to be solely a consequence of decreased food intake. If so, an effective CRM, as defined in Chapter 1, would have the same effect on life and healthspan as CR, but without increased hunger.[62] The negative mental states associated with CR diets would not obtain.

6.8 Conclusion

In this chapter I argued against the claim that death is neutral on mental states accounts. Death is bad when it deprives one of pleasurable mental states. Thereafter I examined claims that life extension would result in suffering, fear, boredom, 'feeling old,' and depression – states that could detract from the value of life. In most cases these claims were argued to be false.

However, two reservations about CRMs, and CR in particular are important. First, CR may result in severe hunger. I argued that, if hunger is a solely consequence of reduced diet, CRMs would not result in hunger. Second, an aged extendee may feel *older* due to loneliness or the feeling of being a burden. I claimed that these possibilities depend respectively on the distribution of life extending interventions, and the social context related to work. Given a wider distribution of life extending interventions, and greater opportunity to decide how long one works for, there is little reason to think that life extension by CRMs would be neutral or negative in terms of mental states.

[62] There is an empirical question as to whether effects identical to CR can be achieved without hunger. It may be, for instance, that hunger is an inextricable part of the metabolic response that results in the effects of CR. This question requires further research.

CONCLUSION TO PART II

Focussing narrowly on CR and CRMs has led to conclusions than are more nuanced than is usually the case when the focus is a broader category of life extending enhancements. In this conclusion I draw attention to the key features of, and reservations about, the impact of CR and CRMs on individual welfare.

Although the above considerations are largely in favour of extending lifespan using CR and CRMs, it is important to highlight some reservations. I have raised four concerns about the CR diet. First, the diet would obstruct growth if begun while a person is still developing physically. Second, a CR practitioner would be less capable of procreation unless she suspended the diet. Third, there is a possibility that a practitioner will seem less beautiful, or attractive to herself and others. Fourth, a person on a CR diet is more likely to experience negative mental states related to hunger and restricting food intake.

The above possibilities reduce the appeal of a stringent CR diet, making the development of a CRM a more attractive prospect. By contrast with CR, CRMs would not result in reductions in physical beauty, or unpleasant mental states that occur solely as a result of a stricter diet. It is possible that making use of CRMs too early may stunt growth, and that a person consistently taking CRMs may be less capable of procreation. However, as discussed in S4.1 and S4.2 respectively, these potential drawbacks also seem more likely to be a result of reduced food intake. A CRM, which, as defined in Chapter 1, would not require reduced consumption, may not have even these negative effects.

Additional reservations are heavily influenced by the social context in which a CRM user lives. In deciding whether a CRM would be good for her, a person must consider whether

the distribution of CRMs would be wide enough to prevent increased isolation and loneliness. Moreover, she must consider whether social arrangements will be adapted so that she does not feel herself a burden on others. If these social conditions are not in place, it is possible that additional years of 'feeling old' might detract from the benefit of living longer.

Against these risks, a person considering CR and CRMs must weigh the likely benefits of a longer, healthier life. Such a life would provide an opportunity for more substantive goods, such as self-development. It would also allow us to further our categorical desires, like the desire to spend time with our families. Finally, a longer life would provide the opportunity to have more pleasurable experiences.

One further point leads directly into the next part on social goods. In general, it is good for a person to live in a better society: in a better society a person is more likely to achieve substantively good things, people tend to *want* to live in a good society, and people that live in good societies are likely to be happier. Thus if taking CRMs would be good for society, there appear to be additional prudential grounds for doing so. The next part questions whether this would be the case.

PART III: CRMS AND SOCIAL VALUES

INTRODUCTION TO PART III

Part I examined the hypothesis that results from animal studies of CR will translate to humans, which I referred to as the transfer thesis. In Part II, I argued that the truth of the transfer thesis means that CR and CRMs may be good for individuals given an appropriate social context. However, I suggested that CR has some features that make it less attractive, such as its impact on mental states such as hunger. This makes it unlikely that CR would ever be sufficiently widely practiced to have a large effect on society. By contrast, a life extending CRM would potentially be used by a greater number of people.

As a result, this part examines the potential effects of CRMs, not CR, on society. As in the previous part, the thrust here is to evaluate proposed problems with life extension in the light of findings about CRMs. The overall aim is to assess the extent to which CRMs would further or undermine social values.

i) What makes a society better or worse?

Parfit suggests the following formal features that are likely to be relevant when assessing the social consequences of life extending drugs. He points out that

> when we are choosing between two acts or policies, one relevant fact is how great the resulting benefits would be. For Utilitarians, that is all that matters… But, for egalitarians, it also matters how well off the beneficiaries would be. We should sometimes choose a smaller sum of benefits, for the sake of a better distribution. (Parfit 1997, 202)

This distinction, between the *size* of the benefit, and the *distribution* of the benefit, maps to a distinction between social welfare (or utility) and distributive justice (Hsu, Anen, and Quartz 2008). In assessing whether a given outcome would make a society better off, one can ask whether it will result in a greater total amount of good, and whether that good will be fairly, or justly distributed.

This distinction frames the discussion in this Part. I locate objections to life extension in terms of their impact on *fairness* and *social welfare*, and evaluate these objections in the light of the transfer thesis.

ii) The significance of social values

Social values are significant in terms of individual self-interest, altruistic morality and social policy.

Social values and self-interest

Even if a person cares about solely her own welfare, there are obvious self-interested reasons for caring about the state of her society. If, for instance, a person's society is poverty-stricken and crime-ridden, it is unlikely that her well-being can be entirely insulated from these social circumstances.

On the contrary, even an egoist's well-being is likely to be highly dependent on the state of her society. As discussed in Chapter 4, communitarians suggest that individual welfare is linked to the well-being of those in one's community. In Chapter 6, I also indicated circumstances in which avoiding the feeling of being old might depend on the legal and economic context surrounding retirement ages. The likelihood of loneliness was also seen to depend heavily on how widely life extending drugs are distributed and used.

In addition to this, there is evidence that living in a society one regards as being good and fair has a positive impact on life satisfaction and mental states well-being (Mayhew 2009, 34). Thus the goodness or badness of society is significant as a matter of prudential concern. There are often self-interested reasons for a person to want her society to be better.

Social values and morality

Over and above these prudential interests in social goods, most moral systems accept principles of altruism, whereby it can be morally required to act against one's own interest, particularly if the greater interest of another, or others, is at stake. Ensuring that a society conforms to moral norms of distributive fairness and safeguards broader social welfare is likely to be of central moral significance on most moral theories.

These moral norms are sometimes regarded as *rights* and *duties*. Rights are moral claims, or entitlements that we have against others, while duties are the correlates of such rights. If using a CRM might result in social harm, perhaps individuals have a duty not to make use of them (Overall 2003, ch. 3). On the other hand, if CRMs can be located within the ambit of existing rights, then there are grounds for suggesting a right to CRMs.

Social values and policy

As Hermerén points out, there are important differences between policy-making and philosophical argument. Nonetheless, he affirms that

> [v]alues and ethics are at the heart of public policy, and that public policy recommendations must have an ethical underpinning. (Hermerén 2012, 289)

Social values are significant in the formation of policies. For instance, justice, as well as beneficence and non-maleficence – the duty to promote and avoid reducing welfare

respectively – are regarded as key ethical principles.[63] These social values play an important role in ethical policy on biomedical technologies. It is thus important to examine the impact of CRMs in terms of these.

Moreover, the moral rights and duties discussed above may sometimes be enshrined in legal rights. The rights framework holds sway in policy, since legal rights, though sometimes vague, are a 'reference-point for policy-makers, and a basis for dialogue.' (Hermerén 2012, 289). By locating a moral claim within an existing framework of legal rights, ethical claims can be elevated to the realm of policy. One such right is the right to healthcare, which, I argue in Chapter 8, could justify public provision of CRMs.

These theories and frameworks explain the moral significance of considering the social value of extending lifespan using CRMs.

iii) Outline of arguments

The axiological distinction between fairness and social welfare is the main structuring principle of this part. However, in order to see how these values will be affected, it is important to gain an idea of whether and how CRMs would have a social impact in the first place. Thus I begin this part with a descriptive chapter, suggesting routes whereby research on CRMs may be translated. That is, in Chapter 7, I discuss ways in which CRMs may reach the public. I point out that that several CRM candidates are available over the counter, or are approved by health authorities, and that some are already regarded as cost-effective for the treatment of diseases and provided by health services. This makes it plausible that life prolonging CRMs could be more widely distributed than is usually thought likely.

[63] See for example Beauchamps, and Childress 2001 Chapters 4,5, and 6.

Chapter 8 examines this finding in the light of concerns about distributive fairness. In particular I discuss what I refer to as the Fair Healthspan objection: the idea that life extension technologies will result in disparities in the distribution of healthy lifespan. I point out that this objection rests on a laissez faire distribution of life extending technologies, and that one alternative – banning or preventing the use of life extension – is also likely have unfair consequences. As a result I discuss the possibility of public provision of life extending CRMs. I claim that although not uncomplicated in terms of fairness or other social values, some form of public provision would be preferable to both banning and laissez faire.

Chapter 9 discusses the implications of CRMs for social welfare. I examine concerns related to the social and economic impact of older societies, as well as issues related to population size and the welfare of future generations. I argue that many concerns about life extension are based on empirical claims that are false in the case of CRMs. A society of individuals with lives extended by CRMs would not be more expensive, more dependent, or less innovative than a society that is 'normal', in a sense to be defined. Chapter 9 also makes the case that, although extending lifespan would have an impact on population size and resource usage, it is important to consider this impact alongside other population drivers, such as fertility rates, as well as in comparison to life saving technologies regarded as ethically unobjectionable. Finally, I argue that there is no convincing reason to think the welfare of future generations would be compromised by the widespread use of CRMs.

The conclusion of this part is that a wide, and fair, distribution of CRMs is possible and perhaps likely. Moreover, such a distribution need not impact negatively on social welfare. On the contrary, CRMs might provide a way to mitigate problems, particularly those related to 'greyer' societies. Nonetheless, I reject claims that take an unrealistically positive view of the social value of life extension. The picture is more nuanced than some

have suggested, and requires an interplay between political and psychological factors in order to avoid the worse consequences and extract maximum fair benefit from research on CRMs.

7. TRANSLATION OF CRMS

Both proponents of, and objectors to, life extension tend to take it for granted that an 'anti-ageing pill' would in fact reach consumers. Yet there is potentially a yawning gap between the development of an effective CRM and its translation to, and uptake in, humans. It is important to see how this gap would be filled, in order to know i) how close we how are to having an effective CRM, ii) how widely CRMs would be distributed, and iii) which steps, if any, could be taken to promote, or, if preferred, discourage the use of CRMs. Without this knowledge, it is impossible to prepare for the profound social impact that extended lives may have. The lack of such an account is a significant shortcoming of the literature on life extension generally.

In response to this shortcoming, I describe routes whereby a life extending CRM might be made available to the public, pointing out difficulties in regulating their uptake. I indicate that some candidate CRMs are already available 'over the counter.' Others are in the process of being, or have already been, approved by regulatory bodies. Still others have been accepted or are far along the route to being adopted by health services. As a result, there may be no need to promote the uptake of CRMs, since it will occur, and may already have occurred, through ordinary translational and health policy procedures.

7.1 Over the counter

In recent times there has been an explosion of 'anti-ageing' products with purported health benefits. For the most part, these are marketed as dietary supplements or cosmetic products and are available in shops and pharmacies, or over the internet. Most of these have little or no evidence of efficacy (Butler et al. 2002, B333). Insofar as candidate CRMs are

concerned, at present numerous resveratrol products are available over the counter at pharmacies. However, the efficacy of these is unknown.

Regulating such products is institutionally difficult. Since ageing is not considered a disease, anti-ageing interventions can be marketed as cosmetics or dietary supplements. Juengst and colleagues point out that in the United States there is no burden on manufacturers to demonstrate safety or efficacy for such products.

> Ironically, if anti-aging products were limited to specific pathologies, they would count as drugs or medical devices and proof of safety and efficacy would be required before they could be marketed. But if aging is not considered pathological, then anti-aging products will be assessed like cosmetic medicine.(Juengst et al. 2003, 24)

Such institutional loopholes mean that unregulated and potentially unsafe 'anti-ageing' products abound. If the anti-ageing products work, this has ethical implications for the fair distribution of increased lifespan. On the other hand, if they do not work as intended, this has implications for the exploitation and safety of consumers.

There is, of course, a significant marketing advantage for anti-ageing products that claim efficacy in treating age-related diseases. Once a company makes this claim, however, they fall under the ambit of regulatory authorities, such as the Food and Drugs Administration (FDA) in the USA, or the European Medicines Agency (EMA) in Europe. It appears to be relatively common to claim efficacy in treatment of disease: searching for 'anti-aging' on the FDA's 'warning letters' site results in numerous hits for unapproved drugs, including candidate CRMs such as resveratrol, claiming a beneficial impact on diseases such as cancer. In their letters, the FDA warns that

> The therapeutic claims on your web site establish that the products are drugs because they are intended for use in the cure, mitigation, treatment, or prevention of

> disease. The marketing of these products with these claims violates the [Federal Food, Drug, and Cosmetic] Act.[64]

In order to claim treatment status for an acknowledged disease, an intervention must gain *approval* from an authority such as the FDA or EMA.

7.2 Regulatory approval

To gain approved status as a disease treatment is time-consuming and expensive, comprising numerous phases of clinical trials for safety and efficacy. It takes on average twelve years to get a drug from the laboratory bench to the pharmacy shelf.[65]

Moreover, Sierra and colleagues point out that the testing time for a CRM might be even longer than this

> to test preventive interventions that need to be implemented in middle age or earlier, and possibly maintained for the remaining life span, trials would have to span decades.(Sierra et al. 2009, 465)

This means it is highly unlikely that a CRM would be approved (or rejected) on the basis of its ability to extend lifespan substantially.

Initially, therefore, CRM candidates will attempt to demonstrate shorter term impact on age-related diseases in clinical trials. This is already happening. Thus far, approved CRM candidates include metformin, rapamycin, and rapamycin analogs ('rapalogs'). Searching for 'resveratrol' – a candidate CRM – on the United Sates National Institute of Health Clinical Trials website (ClinicalTrials.gov) yields 58 trials in various phases, for conditions such as diabetes, age-related cognitive impairment, Alzheimer's disease and cancer. Searches for rapamycin and metformin yielded 1398 and 1134 returns respectively.[66] This higher number is perhaps expected, since they are already approved for existing conditions,

[64] See for example http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2010/ucm198452.htm. Accessed 23 November 2012.
[65] http://www.drugs.com/fda-approval-process.html. Accessed 23 November 2012.
[66] Search performed 23 November 2012.

and in many cases are being trialled for other diseases, or for their effect in concert with other drugs.

After initial approval, 'post-market surveillance' – phase IV clinical trials – is required in treated populations. Long-term monitoring would reveal whether an intervention is a CRM in the sense outlined in Part I. Only long-term testing would tell us if an intervention is likely to extend lifespan.

Having completed the approval process, it is not always the case that a CRM would be prescribed by health practitioners. Moreover, drugs approved for treatment of one age-related disease require further approval if they are to be prescribed for additional diseases. Thus metformin, which is approved for diabetes, would require additional, though less time consuming, trials if it is to be approved for cancers, on which it also appears to have positive effects (Decensi et al. 2010).

Despite this, Lucke and colleagues are correct to suggest that

> It is easy … to imagine general practitioners being asked to prescribe 'off-label' drugs that have been approved for other medical purposes in order to increase lifespan. (Lucke et al. 2010, 337)

If a drug is approved for treating a patient's disease and may also have an off-label effect in postponing cancer, or otherwise extending lifespan, there's reason to think that a practitioner would prescribe it, given that it is legal to do so (Dresser and Frader 2009). This is an important path whereby the use of a life extending CRM might become more widespread.

7.3 Provision by health services

There are at least two ways in which CRMs might be taken up and provided by health services. First, they may be adopted as a treatment for an existing age-related disease such as diabetes. Second, they might be promoted or provided as a preventive measure to lower the risk of age-related diseases such as cardio-vascular diseases, cancers and diabetes before any symptoms have occurred.[67] Public health initiatives to promote exercise and a healthy diet are existing examples of this type of preventive measure, as are interventions aimed at encouraging people to quit smoking.

I will briefly outline some general aspects of procedures whereby healthcare providers adopt new interventions before assessing the likelihood that a CRM would be accepted. Of course procedures for the adoption of new drugs will vary between nations and in different institutional contexts. However, 'technology assessment' and cost-effectiveness calculations are likely to occur in any intervention recommendation procedure. I will focus on these two aspects, using the quality adjusted life year (QALY) as an exemplar.[68]

7.3.1 Technology assessment

In seeking to become a 'first line' treatment for a particular disease, a drug manufacturer will make a submission to a public health service or an advisory body, such as the National Institute for Clinical Excellence (NICE) in the UK. The advisory body will in turn evaluate the intervention on the basis of a technology assessment. This assessment is made on the basis of the intervention's contribution to reducing mortality and morbidity. The QALY is

[67] Of course these are not mutually exclusive. For instance, the candidate CRM metformin was introduced as a treatment for diabetes, while a recent systematic review suggests it reduces the incidence of cancer in diabetics by 30% compared to diabetics on other treatments (De Censi et al 2010). In this case the intervention appears to be both risk-reducing and to treat an existing condition.

[68] The QALY is ethically controversial (Harris 1987). Nonetheless, I discuss the QALY because it the most explicit and transparent measure of health benefit I was able to find. Most procedures will take into account mortality, morbidity and cost-effectiveness in assessing an intervention, so my claims here do not hinge particularly on accepting the QALY itself. The discussion of the QALY borrows from Kirkdale and colleagues (Kirkdale et al. 2010).

one method of quantifying this contribution. It is a metric used to evaluate the efficiency of interventions for the purpose of allocating public resources.

Estimating an intervention's QALY contribution involves judging evidence about the *number of years* the intervention will add to a person's life, as well as about the *quality of life* the person is likely to have in her remaining years if she uses the intervention. A year spent in full health is given a value of 1, while anything less than full health has a value of less than 1, tending towards zero as health and disability states worsen.

The intervention will be compared to other interventions targeting the same disease, on the basis of the number of QALYS added, and the cost-effectiveness of adding them. An intervention must be an improvement over the standard treatment in order to be adopted.[69]

7.3.2 Cost-effectiveness

Having estimated the QALYs that would be generated, the intervention is evaluated for cost-effectiveness. A cost per QALY ratio forms the basis for deciding between two interventions. Most nations have a nominal upper bound, or threshold for cost-effectiveness. Currently, in order to be considered cost-effective in the United Kingdom, an intervention must cost less than £30000 pounds per QALY (Kirkdale et al. 2010).

Given these features, under what circumstances would a CRM be adopted by health services? It is commonly assumed that drugs that substantially prolong life would be too costly for healthcare services. Harris, for example suggests that

[69] Note that it is also common to take into account other factors in allocating resources, such as the impact on human dignity, the necessity of the intervention, and the severity of the health condition. See Sabik and Lie (Sabik and Lie 2008) for a discussion of health prioritisation in different nations.

> One thing we do know is that the technology required to produce such results will be expensive. For existing people, with multiple interventions probably required, the costs will be substantial. (Harris 2002, 71)

As a result he claims

> Even in technologically advanced countries therefore … increased life expectancy is likely to be confined to a minority of the population.

Ehni and Marckman are similarly pessimistic about the potential of public health systems to afford anti-ageing technologies:

> It can be doubted whether new interventions decelerating or even halting aging would come at a cheap price. As biological aging is a complex process, many different and most likely expensive interventions… will probably be needed to achieve the desired effect. (Ehni and Marckmann 2009, 289)

I will suggest that, contra these claims, CRMs could cost-effectively add years to lifespan, first as short-term treatments and possibly even when used as very long-term preventive measures.

CRMs as treatments

Rapamycin and 'rapalogs' are already adopted by several health services for the treatment of various cancers. They are also used as immuno-suppressants in organ transplantation (Kaeberlein 2010). Metformin is the first-line treatment for type 2 diabetes.

The initial uptake of CRMs by health services will take place through the cost-effective treatment of age-related diseases. Indeed, the adoption of the CRM candidates above means this may already be happening. However, longer term studies and clinical trials may reveal additional effects on mortality and morbidity. If this occurs, perhaps CRMs might be considered as a risk-reducing preventive measure. In this case, would it be cost-effective to provide long-term, preventive CRMs to healthy subjects?

Cost effectiveness of CRMs as long-term preventive measures

In keeping with the transfer thesis, I am assuming that CRMs, in addition to extending lifespan would postpone age-related diseases. Below I assign some notional figures that are nonetheless consistent with the idea of slowed ageing. I cast doubt on the idea that life extension technologies could not be cost effectively provided.

Instead of health levels being more likely to drop around the age of 65, as is currently the case in the UK,[70] suppose that, if one made use of a CRM, health levels would drop later, at age 80. CRMs would add 20 years life, increasing life expectancy from around 80 years to 100 years. In both cases suppose that the average QALY value in the less healthy years is 0.5.[71]

In the normal case, in which CRMs are not used, this gives us

Normal

65 years of health plus 15 years at an average of 0.5

= 72.5 QALYS

While the healthspan expectancy of a CRM user is

CRM

80 years of full health + 20 years at an average of 0.5

= 90 QALYS

CRM users gain an additional 17.5 QALYS.[72] Could this gain be cost effectively achieved?

[70] Office of National Statistics http://www.ons.gov.uk/ons/rel/disability-and-health-measurement/health-expectancies-at-birth-and-age-65-in-the-united-kingdom/2008-10/index.html. Accessed 19 November 2012.
[71] Later I point out that this assumption of equivalent average health may be somewhat pessimistic. CRMs might make the less healthy later years more healthy than they would be without CRMs.
[72] Note that, if life extension is considered an 'enhancement,' as discussed in the following chapter, additional years above the normal would count less in cost-effectiveness calculations.

Suppose that the intervention would be a preventive daily dose beginning at age 20. This means that if citizens continued to take the intervention for their entire life, they would do so for 80 years. Metformin, a candidate CRM, can currently be bought for less than £1 per tablet.[73] Resveratrol is available for a similar amount.[74] On this basis, I will assume that the drug costs £1 per day.

It may be the case that confirmed CRMs would cost more than this due to the expense of the approval process. However, it is also possible that in the time taken to demonstrate long-term effects, the patent could expire, as has occurred with metformin. Moreover, given the prospect of a larger uptake, the drug price might be lower.

Given this figure, if a person took the drug every day for 80 years it would cost £29200. This would be about £1670 for each of the 17.5 QALYs added. This is well below the QALY cost-effectiveness threshold of £30000. Even if CRMs were substantially more expensive, or extended healthspan less than I assumed above, they could be a cost-effective way to add healthy years to life.

Of course it's impossible to make the stronger case that CRMs would definitely be cost-effective on the basis of this rough and simplified calculation. Such a claim would require a detailed analysis of the long term efficacy of the CRM, in combination with knowledge of its true cost.

Nonetheless, the costs of some candidate CRMs and the healthspan gains that could be achieved by slowed ageing suggest that the provision of CRMs as a long-term preventive

[73] http://www.pharmacy2u.co.uk/Prescriptions/POMSearch.aspx?criteria=metformin . Accessed 19 November 2012.

[74] http://www.amazon.co.uk/gp/product/B001F7B3HQ?ie=UTF8&camp=1634&creative=19450&creativeASIN=B001F7B3HQ&linkCode=as2&redirect=true&tag=www241herbsco-21. Accessed 19 November 2012.

measure could be cost-effective. This should at least dent the common assumption that long term use of life extending drugs would be too expensive for health services to provide. The potential for uptake through health services thus increases the likelihood that CRMs will gain a wide distribution.

7.4 Conclusion

In this chapter, I have outlined routes whereby research on CRMs would be translated into medical practice, made available to markets, and distributed via health services. Below I summarise conclusions about the present and future uptake of CRMs and give an indication of the how these conclusions will impact on the breadth of distribution.

7.4.1 The present

On the basis of the foregoing sections, several conclusions can be drawn about existing CRM candidates:

1. Some CRM candidates are available over the counter at pharmacies, although the effects of these are generally untested.
2. CRM candidates are being trialled for efficacy in the treatment of age-related diseases including type 2 diabetes, cancers, cardiovascular diseases and Alzheimer's disease in humans.
3. Some CRM candidates are in advanced stages of clinical trials for a variety of different diseases.
4. Several CRM candidates are already approved for use in humans for the treatment of particular age-related diseases.
5. At least two CRM candidates – rapamycin and metformin – have been adopted by health services for the treatment of age-related diseases.

7.4.2 The future

On the basis of the above considerations, it is plausible to make the following general claims about the uptake of genuine CRMs:

6. CRMs might be made commercially available without prescription as dietary supplements or cosmetics.
7. Once approved by a regulatory authority, CRMs would initially be made available as treatments for particular diseases.
8. CRMs might legally be prescribed for off-label effects, perhaps including enhanced longevity.
9. CRMs would be adopted by health services as treatments for age-related diseases through normal procedures.
10. It may be cost-effective to provide CRMs as a preventive measure against, rather than a treatment for, age-related diseases.

7.4.3 Breadth of distribution

These conclusions mean that use of CRMs could become prevalent. Purchasing CRMs over the counter, while not necessarily expensive, might not have a great reach. In particular, unproven over the counter life extension drugs are unlikely to be used by groups with less expendable income.

If CRMs gained official approval by regulatory authorities, off-label prescription would be more likely. Doctors may prescribe a drug in the belief that it has substantially life extending side-effects. Public provision by health services for particular diseases would further increase the number of CRM users.

However, the reach of CRMs would be widest if it were part of a preventive campaign against age-related diseases. This step may, however, be a long way off unless well-

researched drugs like metformin can be approved for use in healthy people to reduce the risk of diseases of ageing, a possibility discussed in the conclusion of this dissertation.

It is highly unlikely that CRMs would be approved for the purpose of substantial life extension because doing so would require extremely long test periods, and because procedures focus on efficacy in treating or preventing disease. Nonetheless, the effects of CRMs in combating age-related diseases mean that they would reach the public anyway.

This potentially widespread distribution has significant ethical consequences. The following chapter discusses the possibility that the availability of CRMs will result in increased disparities of healthspan. Thereafter, in Chapter 9, I discuss potential effects on the demographic structure of society.

8. FAIRNESS

Disparities in health have a broader impact on the fair distribution of other goods. Daniels regards the contribution of health to an equal distribution of *opportunities* as the source of its primary social significance (Daniels 2008, ch. 2). Similarly, Sen and Nussbaum (1993) regard health as a core capability enabling people to live *good lives*. These and other grounds are often argued to justify a *right* to health and healthcare (Daniels 2008, ch. 5). Fairness in the distribution of health thus has major implications for significant frameworks implicated in the guidance of a just society.

It is not surprising, then, that concerns about justice in the distribution of healthy lifespan are regarded as 'the major ethical problem with life-extending technologies'(Harris 2002, 71). This chapter examines the Fair Healthspan objection, which claims that life extending technologies would result in increased disparities in healthy lifespan. I argue that some form of public provision by health care services would be fairer than alternatives such as banning and doing nothing.

Outline

In S8.1, I outline two potential policies with respect to life extension and argue that both would result in unfair distributions of health. In S8.2, I discuss a third policy: equal provision. In S8.3, I indicate how equal provision could prevent increased unfairness by benefiting the worse off in both the developed and undeveloped world. However, I discuss the objection that equal provision may result in people being *enhanced*, a prospect that is ethically questionable on what have been called 'fair innings' approaches to the distribution of health interventions. In response to this objection, in S8.4 I examine a fourth

policy of unequal provision. I suggest that such an approach could be made feasible and would be preferable if we apply the fair innings approach strictly. I conclude by discussing the limitations of this claim and its relation to the claims of subsequent chapters.

8.1 The Fair Healthspan objection

The previous chapter pointed out ways in which a CRM might become widely distributed in society. This chapter examines the likelihood that this distribution will be unfair, and steps that could be taken to reduce this unfairness. It has been argued that life extending interventions would exacerbate existing disparities in healthspan, since they would be available only to wealthier groups that are already likely to achieve a greater number of healthy years. Pijnenberg and Leget, for instance, argue that

> inequality, which obtains both between the First World and the Third World and between rich and poor within Western welfare societies, is the main ethical obstacle. How can we justify trying to extend the lives of those who have more already? (Pijnenburg and Leget 585, 2006)

The concern about unfair healthspans also appears to be one of the most common complaints evident in public attitudes to life extension. One respondent in a recent survey suggests that we will

> end up with this society where the poor live their brief little lives and then you know… the rich live forever and have time to accumulate vast resources. (Partridge et al. 2009, 74)

Fears about the unfairness of life extension leading to growing disparities in healthspan can equally be levelled against CRMs. If CRMs will exacerbate disparities in healthy lifespan, they are morally objectionable on the grounds of fairness. I will refer to this problem as the 'Fair Healthspan objection.'

8.2 Flawed responses: Laissez fair and banning

A shortcoming of the Fair Healthspan objection is that its proponents assume that life extension would only be available on a 'laissez faire' or market basis with little or no intervention by relevant authorities. Although this is generally regarded as morally problematic, those that make this objection seldom argue for an alternative to laissez faire distribution.[75]

In this section, I argue that unfairness would indeed stem from laissez faire attitudes to life extension. However, I claim that the presumed alternative – banning – is also deeply flawed both practically and ethically.

8.2.1 Life extension and laissez faire

The real target of the Fair Healthspan objection is a laissez faire policy on life extension. Laissez faire means doing nothing. We simply allow markets to decide who gets life extending treatments. This is likely to be the case if, as outlined in Chapter 7, life extension drugs are available over the counter, or are only available for off-label prescription.

Proponents of the objection are correct that if there is laissez faire distribution, CRMs would increase inequality of healthspan. This type of (non-)policy would entail that those with more resources will be more likely to purchase CRMs for themselves and their in-group. Note that this is not necessarily because CRMs would be expensive. As argued in Chapter 7, they may not be. Poorer people might not use CRMs because they do not have disposable income, or because they are less informed about life extension drugs. As a result, those who already have greater healthy lifespan would live longer, healthier lives than they already do. On the other hand, those that are already on the worse end of this unequal distribution are unlikely to benefit.

[75] See for example Pijnenburg and Leget 2006.

Trickle down of life extension?

One attempt to mitigate this concern is the contention that life extension technologies will 'trickle down' to those that are worse off (Partridge et al. 2009). As drugs improve, prices for old drugs will decrease. Alternatively, drug companies will lower prices and increase awareness in order to conquer larger markets. In this way CRMs will become easily available to poorer or less educated members of society. Just as vaccines and antibiotics have become more easily available to the poor, so might life extension technologies become available to those with lower healthspan expectancy.

However, even if trickling down does occur, this does not undermine the Fair Healthspan objection. Disparities in health are widened, most likely for significant length of time. Bognar stresses that

> [i]t took almost two hundred years, culminating in the public health revolution in the late 19th century, for the benefits of the first health transition to noticeably impact population health. (Bognar 2012, 14)

Inequalities in health that would result from doing nothing are morally objectionable on the basis of fairness. Laissez faire would massively expand the gap between those who already have a healthy lifespan, and those who do not.

For opponents of life extending technologies, the argument sometimes stops there. Inequality of healthspan is the inevitable consequence of life extension. As a result, it may be better to prevent their use, perhaps by banning them. This is the next option I discuss.

8.2.2 Life extension and banning

It is sometimes assumed that preventing or discouraging the use life extension technologies would eliminate the unfairness that would result from laissez-faire distributions of life extension technologies.[76] One way of doing so is to prohibit their sale and use.

However, banning faces obvious practical problems. Firstly, it would be very difficult to police. Purported life extending drugs are already easily available over the internet. It is hard to imagine a successful clampdown on their sale.

Second, prohibition may have negative consequences. As in the case of alcohol and drug prohibition, banning CRMs could lead to dangerous, unregulated products, and also benefit criminal groups willing to engage in illegal trade.

Third, even if national prohibitions could be successfully enforced, a global ban would be required. Without this, the wealthy would be able to engage in 'medical tourism.' That is, they would be able to travel or emigrate to other parts of the world in order to legally receive life extending interventions (Singer 2009). The wealthier portion of society that already has greater prospects, and is able to afford travel, would gain access to the interventions. Inequality would thus be exacerbated.

A fourth problem is ethical in nature. Banning appears to be an instance of ethically questionable levelling down. While other bans, such as the prohibition of narcotics, are generally put in place because the banned substances are thought to reduce welfare, this ban would be explicitly aimed at preventing *increases* in welfare. As Harris points out, such levelling down appears ethically dubious.

[76] See for example respondents in Partridge et al 2009.

> If twins suffer from cancer and one is incurable and the other not, we do not conclude that we should not treat the curable cancer because this would in some sense be unjust to the incurable twin. We don't refuse kidney transplants to some patients unless and until we can provide them for all with renal failure (Harris 2002, 72).

Banning substantial life extension is also complicated by the fact that CRMs are likely to have a range of health effects, such as postponing the incidence of cardiovascular disease, diabetes and cancer. Harris argues that

> it would be impossibly difficult to deny those suffering from treatable disease the chance of a cure on the grounds that the therapy brought the individual too much secondary gain. (*Ibid*. 73)

Denying the opportunity to buy treatments for disease because they might result in life extension is deeply objectionable.

Finally, and importantly, even in the unlikely case that a policy of banning would prevent an *increase* in disparity between haves and have-nots, it would do nothing to *reduce* existing inequalities in healthspan. Bognar points out that

> the gap in average life expectancy in the United States between urban black males and Asian-American females is over 20 years; the life expectancy gap between the best-off and the worst-off social groups is over 15 years for males and almost 13 years for females. In the United Kingdom, the gap in mortality rates between the best-off and the worst-off is greater than at any time during the last 90 years. These inequalities, however, are dwarfed by the 40-year gap in average life expectancy at birth between the least developed countries in Sub-Saharan Africa and the richest countries in the West. (Bognar 2012, 15)

Banning a substantially life extending technology would do nothing to improve the plight of those on the lower end of this healthspan gap. Those worse off would remain worse off.

If other policies are capable of doing better in this respect, then these would be preferable as responses to the Fair Healthspan objection.[77]

These difficulties with banning are often neglected by opponents of extending lifespan. On the other hand, in combination with the trickle-down effect, proponents of lifespan extension sometimes assume that objections to banning constitute a sufficient defence of life extension.[78] Both attitudes are unsatisfactory, since they leave us without a suitable solution to the problem of unfair healthspans. Below I discuss the alternative of public provision and argue that it would be preferable to laissez faire and banning, since it could go some way towards correcting existing inequalities in healthy lifespan.

8.3 Equal access through health services

It has become increasingly common to propose that, rather than doing nothing, or attempting to prevent life extension, it would be fairest to provide life extension technologies through health services. Mackey, for instance proposes that

> [o]ne solution to this problem [of unfair healthspans] is to regulate and fund anti-aging medicine, as well as to require that health insurers cover its expense (or have it available for free via socialized medicine). (Mackey 2003, 194)

In this way

> we could all be universally insured for anti-aging medicine that is proven to work, thereby greatly reducing the concern of a future aging underclass and a relatively ageless upper class. (*Ibid*.)

Thus the goal of fairness might be better served by allocating resources towards public provision of life extending drugs. One way of doing so would be to provide *equal* access through healthcare services. Would equal access avoid the problem of disparate healthspans? Mackey's claim that it would, assumes that making a life extending

[77] This problem also applies to Callahan's idea that we should 'stigmatise' life extension (Stock and Callahan 2005). In addition to being ineffective, stigmatisation would do nothing to benefit those who live for a shorter time.
[78] See, for instance, respondents in Partridge et al 2009.

intervention available to everyone would prevent an increase in the gap between the haves and have-nots. However, there are two fairness-related concerns about this possibility.

The first is that substantial life extension technologies might not benefit those with lower healthspan expectancy. If not, there is no reason to think that equal access is an adequate response to the Fair Healthspan objection. The second problem is that those who already have high healthspan expectancy might benefit *too much*: equal provision might *enhance* some people above a 'fair innings.' I examine these problems in turn.

8.3.1 Benefiting the worse off

Proponents of public provision assume that equal access to anti-ageing drugs would undermine the Fair Healthspan objection by benefiting those who are likely to have shorter and unhealthier lives.

In developed countries this assumption is largely justified. Many with decreased healthspan expectancy would benefit from CRMs. In Europe, for instance, the main causes of death in people under the age of 65 are cardiovascular diseases and cancer, accounting for more than half of deaths (Allender et al. 2008). These are diseases that are heavily related to ageing. As Farrelly points out '[e]veryone – rich, poor, young and old – is susceptible to age-related afflictions' (Farrelly 2010, 10). Because ageing does not only begin when one is old, slowing ageing early could postpone the incidence of age-related diseases in those that are worse off. Providing CRMs to people who would otherwise not live to 65 may thus allow many of these to achieve a longer healthspan.

However, proponents of public provision, such as Mackey and Farrelly, seldom consider whether anti-ageing drugs would benefit the worse off in poorer, developing nations. In low and middle income countries, it might be thought that this assumption is less justified.

This is simply because more people die of causes that would not be remedied by a drug that slows ageing. In low income countries 40% of people do not live beyond the age of fifteen years: people do not grow old enough to have age-related diseases.[79] Providing the population of Swaziland with CRMs would, for instance, have little impact on healthspan expectancy, since many deaths there are caused by HIV/AIDS and other communicable diseases, often in infancy.[80]

Despite this, the impact of age-related diseases, and thus the potential benefits of CRMs, in the developing world should not be underestimated. Abegunde and colleagues report in *Lancet* that:

- In 23 selected countries, which account for around 80% of the total chronic disease mortality burden in developing countries, chronic diseases are responsible for 50% of the total disease burden
- Age-standardised death rates for chronic diseases are more than 50% higher … than in high-income countries…
- As little as a 2% yearly additional reduction in mortality rates from chronic diseases would avert 24 million deaths, with almost 80% of the life-years gained coming from deaths averted in people younger than 70 years…
- Governments have a key role in stimulating the generation of information to reduce the risk of chronic diseases and in ensuring access to preventive and treatment services, *especially for poor people* (Abegunde et al. 2007, 1929. Bullets in original. My italics.)[81]

The burden of chronic, age-related non-communicable diseases is staggeringly heavy in the developing world. Moreover, this burden is set to rise as these populations age.[82] As Daniels points out

[79] World Health Organisation (WHO): http://www.who.int/mediacentre/factsheets/fs310/en/index1.html. Accessed 12 November 2012.
[80] Statistics available from WHO: http://www.who.int/nmh/countries/swz_en.pdf. Accessed 12 November 2012.
[81] Abegunde et al 2007, 1929. Bullets in original.
[82] *Ibid*., 1932. The reduction of non-communicable diseases is also one of the United Nations' high priority Millennium Development goals.

> developing countries are now aging at much faster rates than developed countries did. While the proportion of the elderly in developed countries is due to double over the next fifty years, it is due to triple in East Asia. (Daniels 2008, 164)

Thus, despite the presumption that ageing populations and age-related diseases are a developed world problem, the worse off in the developing world stand to benefit substantially from interventions that impact age-related diseases.

These considerations mean that CRMs could benefit many of those worse off in both the developed and developing world. This is an important point in favour of equal access. In contrast to laissez faire and banning, equal access would work to the benefit of groups with lower healthspan expectancy. In doing so it may at least prevent an increase in unfairness that is likely to result from the other approaches. I now turn to the objection that, in doing so, equal provision may also result in unfair enhancement of the better off.

8.3.2 Equal access and enhancement

In the previous chapter, I argued that equal provision of CRMs might be provided by health services. Above, I suggested that such provision might improve healthspan in those that are worse off. However, two related and controversial approaches to health policy suggest that equal provision might result in unfairness. The 'fair innings' approach, and the idea that life extension is an enhancement require that health services should seek to ensure a 'normal' fair healthspan and no more. I argue that if we accept these ideas, health services should attempt to provide differential, unequal access rather than equal access.

Fair innings and enhancement

The fair innings approach to the distribution of health is an institutional instantiation of the social concern about preventing disparities in life expectancy. It holds that one priority of health services is to ensure that people achieve a 'normal' lifespan.[83]

Influential variations of the fair innings approach suggest that, rather than aiming at a fair *lifespan*, health services should de-prioritise those who will or have achieved a fair number of *healthy years*. Alan Williams, for instance suggests that health services should privilege those who will not achieve a fair span of QALYS (Williams 1997, 117). Williams puts the motivation for this view as follows:

> everyone is entitled to some 'normal' span of health … The implication is that anyone failing to achieve this has in some sense been cheated, whilst anyone getting more than this is 'living on borrowed time.' (*Ibid*., 119)

Put another way, the fair innings approach conforms to the idea that life extension is an 'enhancement,' which there is no obligation for health services to provide (Daniels 2000). Daniels argues that health services are only obligated to restore 'species typical normal functioning' by providing *treatments*. They are not, for instance, required to provide beautifying cosmetic surgery, or other improvements above this 'normal' level.[84] Similarly, the fair innings approach holds that there is a social obligation to *treat* conditions that would cause one to fall below a normal healthspan, but no such obligation to enhance people above this level.[85] Using resources on enhancing people is unfair since it diverts public resources to improving the condition of those who are not badly off.

[83] See for instance Harris 2005 for a criticism of the fair innings approach.
[84] See Callahan 1988 for a similar view; namely that extending the lifespan of the elderly is outside the goals of medicine.
[85] Note that this is a diachronic understanding of 'normal functioning' as living for a 'normal' number of years, rather than a synchronic understanding as functioning normally at a particular time. See for example Ottersen 2012 for a defence of this diachronic understanding of the fair distribution of healthy years.

If the fair innings approach is accepted, then it undermines the desirability of equal provision of CRMs, since, if everyone receives the intervention, some people will be enhanced. This consideration impacts on the QALY calculation of the previous chapter. If health services have obligations to ensure only the normal number of healthy years, then years surplus to this may be de-prioritised. Years above the normal span that would be gained using CRMs may thus carry less weight in QALY calculations. If so, the intervention would be regarded as less cost-effective.

For CRMs to be provided in such a way as to avoid enhancement, they should only be distributed to those that would fall below the normal healthspan threshold. The fair innings approach thus recommends unequal provision.

8.4 Eliminating enhancement by unequal provision

The fair innings approach implies that health services should not enhance those that would achieve a normal lifespan without CRMs. I will first point out potential ethical advantages of unequal access before discussing some ethical and practical worries about this approach. I argue that unequal access is practicable, though imperfect.

8.4.1 Unequal access in practice

In a limited sense, providing CRMs solely as a treatment for acknowledged diseases conditions is already a form of unequal access. Those without a health-threatening disease would not get the drug. However, if health services applied the fair innings approach strictly, they might deny CRMs to those that have already achieved a fair innings, namely the elderly, even if they had a disease.

They might also deny the intervention to those who would eventually exceed a fair innings if their age-related condition is treated with a CRM. If, for instance the patient had

diabetes, and her CRM treatment would result in her living longer than a fair innings, health services might refuse that treatment, or prefer a treatment that would not similarly extend lifespan.

A further way to practice unequal access would be to *promote* the use CRMs amongst those with lower healthspan expectancy, while not doing so for groups with higher healthspan expectancy.

8.4.2 Advantages of unequal access

The first purported advantage of unequal access is that, in keeping with the fair innings approach, unequal access would potentially bring about greater equality of healthspan than laissez-faire, banning, or equal access.

Second, unlike banning, unequal access does not involve levelling down. Excluding the well-off would not *prevent* individuals accessing CRMs using their own funds, or the funds of private health insurance. In this respect, unequal access to CRMs is an improvement over banning.

A third advantage is that unequal access may also be *cheaper* than equal access. Indeed, this is one of the motivations for adopting a fair innings approach more generally. Scarce resources can be allocated to those who have more to gain.

8.4.3 Ethical and practical problems with unequal access

A significant ethical problem is that it is usually thought that public health services are obliged to provide equal access to treatments for diseases like cancer, cardiovascular disease and diabetes, regardless of healthspan expectancy, or age. Persuasive reasons other than the value of fairness, such as solidarity and beneficence, or the moral principle that we

should help those in need might ground such reasoning. Of course, this would be an objection to the fair innings approach itself. In keeping with the compatibilist methodology outlined in the introduction to this dissertation, my purpose is neither to defend or criticise the fair innings approach, but to see if it can accommodate CRMs. However, I return to this point in the conclusion of this chapter.

A further practical problem casts serious doubt on the possibility of distributing CRMs unequally. If health services wished to exclude some people from risk-reducing interventions on the basis of fair innings approaches, they would need to know who will benefit too much, and thereby be enhanced. While it is easy to identify those who have already achieved a fair innings, it is harder to identify in advance who will be worse and better off in terms of healthspan.

Identifying the worse and better off

Identifying those with higher healthspan expectancy is impossible to do with certainty: unexpected misfortunes such as accidents and non-age-related diseases play a role in determining how long people live. However, there are a number of ways a proponent of the differential access solution to providing a fair innings might estimate which individuals are likely to have a shorter healthspan. For instance, they may advocate profiling according to socio-economic indicators such as race or income. As the earlier quote from Bognar makes clear, life expectancy differs substantially along racial and economic lines. The fair innings approach may recommend favouring groups that are statistically worse off in terms of healthspan.

Alternatively, health services might differentiate according to genetic background. If there are robust genetic regularities that correspond to healthspan expectancy, these could be

used to differentiate those that are worse off. Indeed, there is already substantial research into the possibility of 'longevity genes' (eg. Willcox et al. 2006).

These methods are controversial and complex. They would also introduce additional costs to providing differential access. However, if securing a fair innings was regarded as sufficiently important, these options provide a potential, though inevitably imperfect means of identifying worse off and better off groups. Doing so would allow health services to avoid enhancing citizens, whilst still treating those who would otherwise not achieve a normal healthspan.

8.5 Conclusion

I argued that both equal access and unequal access are preferable to banning and laissez faire in terms of fairness. Public provision would prevent increases in healthspan disparity by benefiting many of those that have lower healthspan expectancy, both in the developed and developing world. However, I suggested that equal access could be objected to on the grounds that it would also enhance those that are already better off. Though difficult in practice, unequal access would be preferable if fair innings approaches are accepted.

In this conclusion, I will briefly discuss this finding in the light of values other than fairness. Thereafter, I will indicate how the conclusions of this chapter are limited by those of the next.

8.5.1 The fair innings approach and other values

Although my stated aim in this thesis is not to prefer any particular normative theory, it is important to point out a limitation of the conclusion, based on the fair innings approach, that unequal access would be preferable to equal access. Some values may justify rejection

of fair innings approaches. For instance, Harris argues that a key governing constraint for decisions about resource allocations should be

> the belief that the life and health of each person matters, and matters as much as that of any other and that each person is entitled to be treated with equal concern and respect both in the way health resources are distributed and in the way they are treated generally by health care professionals, however much their personal circumstances may differ from that of others. (Harris 1987, 121)

On this basis he claims that

> To discriminate between people on the grounds of … life-expectancy, is as unwarranted as it would be to discriminate on the grounds of race or gender. (*Ibid.*)

We may think it is morally unjustifiable, *in principle*, to discriminate against individuals or groups in allocations of healthcare resources on the basis of how long they might live. If so, fully equal access to life extending CRMs would be preferable, despite the fact that some people might end up getting more than their fair share of healthy years.

This suggests a conflict between the principles of equal respect, to which Harris refers, and the value that is assigned to an equal distribution of healthy years, and which motivates the fair innings approach. Despite this, it should be clear that both values motivate some form of public provision of CRMs. The issue of whether such provision should be equal, or whether some individuals or groups should be preferred, is a site of significant disagreement. Resolving it is beyond the defined scope of this thesis, since it would require abandoning the compatibilist method outlined in the introduction to this dissertation.

8.5.2 Distribution and social welfare

There remains a further set of problems concerning the effects of extending lifespan on social welfare. Although these are relevant whether we adopt laissez-faire, banning or public provision, it would severely disincentivise the latter if widespread access had negative consequences for social welfare. This possibility is the subject of the next chapter.

9. SOCIAL WELFARE

It might be thought that CRMs would increase the welfare levels of society because, as I argued in Part I, they are likely to make individuals better off. A society with people that have greater well-being is, presumably, better than a society with people that are not as well off. If so, society would be improved with each additional person that took CRMs.

Unfortunately, this is too simplistic. This is because extended lifespans would have a number of demographic effects that could make society as a whole worse off, or which may have undesirable feedback effects on the welfare of individuals. As the arguments of this chapter show, the demographic composition of society can have enormous effects on social goods. In particular, the age composition and the number of people in a society may make a difference to the availability of resources, and the ability to sustain or improve a society's level of welfare.

I introduce the topic by briefly outlining three purported demographic consequences of life extension, and discussing a methodological difficulty with determining the extent to which these would differ in a society in which CRM use was widespread. In subsequent sections I discuss the likelihood of these consequences, the concerns they pose about life extension technologies generally, and the extent to which these problems apply to CRMs. I argue that CRMs can play a role in improving social welfare.

9.1 Social welfare, demography, and slowed ageing

Life extension technologies have been argued to have a three worrying demographic effects.

First, it has been argued that a society in which the use of life extending technologies was widespread would be much *older*. This has led to fears about enhanced economic crises due to an increasingly unhealthy and economically dependent population, as well as a concern that innovation and progress will be negatively impacted. These problems are discussed in S9.2.

Second, it is thought that life extension would result in overpopulation. A decreased number of deaths could result in a larger population. Moreover, if people lived for longer, they may be able to reproduce more, contributing to a population explosion. I discuss these possibilities in S9.3.

Thirdly, It has been argued that life extension would result in a reduction in the number of people that are born, perhaps due to a need to prevent overpopulation. In S9.4, I discuss this implication and its consequences for social welfare.

9.1.1 Social welfare and comparison

Before discussing these demographic effects in more detail, it is important to examine the extent to which the CRM scenario will *differ* from a 'Normal scenario' in which CRMs are not used. It would be incorrect to attribute social harms to CRMs if they would happen anyway. Thus, in order to know whether the CRM scenario would have additional harmful effects for society, it is necessary to compare the CRM scenario to the Normal scenario.

There is, however, an important methodological problem with deciding what the Normal scenario would be like. The difficulty is that many demographic predictions *already assume that substantial life extension will occur*. Oeppen and Vaupel for instance, suggest that

> [b]ecause best-practice life expectancy has increased by 2.5 years per decade for a century and a half, one reasonable scenario would be that this trend will continue in coming decades. If so, record life expectancy will reach 100 in about six decades. (Oeppen and Vaupel 2002, 1029)

This potentially confounds attempts to examine the ethical and demographic impact of particular life extending technologies. CRMs might be one of a broad gamut of life extending technologies that will contribute to the statistical trend towards increased life expectancy. This possibility should blunt the force of criticisms of CRMs in particular, since the demographic changes for which they might be responsible could occur in their absence.

However, in contrast to Oeppen and Vaupel, demographers Carnes, Olshansky, and Grahn are explicit that, in the absence of interventions that *alter the rate of ageing*, life expectancy will not exceed roughly 85 years (Carnes, Olshansky, and Grahn 2003, 45). If they are correct, it is appropriate to compare the CRM scenario in which ageing is slowed, and the Normal scenario, in which it is not, and in which life expectancy does not increase substantially above present levels.

In the following, then, I will assume that there is an upper limit to life expectancy in the absence of interventions that affect the rate of ageing. For ease of calculation in subsequent sections, I will assume this limit is 80 years, while, in keeping with the transfer thesis and the estimations in Chapter 7, I will assume that the CRM scenario will result in slowed ageing and a life expectancy of 100 years. These projections form the initial basis for comparison.

9.1.2 A model of slowed ageing in society

In order to examine the demographic impact of CRMs, I collaborated with a colleague to devise a program that describes the effects of slowed ageing on population size and composition.[86] The program simulates a population of ageing and reproducing organisms. At each time step it updates the age of each organism and generates a 'death' or 'birth' event. For reasons discussed in S9.3.2, the 'birth' probability is calculated so that, on average, every organism gives birth to one child. Thus the population reproduces at replacement rates.

Significantly, the probability of death events is calculated according to the Gompertz law, which describes the increase in the probability of death that occurs with age. It is possible to adjust a parameters of this law in order to reflect slower or faster ageing (Strehler and Mildvan 1960). By doing so, we simulated a CRM population that has a reduced age-relative probability of death. This increases the 'life expectancy' in the population of simulated organisms. Thus, in keeping with lifespan measures discussed in S2.1, the CRM population will have increased average and maximum lifespan relative to control groups and a decreased age-relative likelihood of death. The simulated organisms will age slower.

This model is useful for several reasons. In particular, it removes a reliance on intuitions and allows the testing of hypotheses about the effects of life extension on demography. Importantly, considering population level effects is sometimes conceptually difficult. The use of this model clarified some of the concepts involved. Moreover, the model allowed a more fine-grained analysis: rather than working with a simple average life expectancy, it was possible to give a more detailed account of population effects, based on realistic

[86] I am grateful to Fridolin Groβ for his ingenuity in helping to conceptualise this program, which has clarified some of the issues of this chapter.

probabilities about life lengths in CRM and Normal populations. I will refer the outcomes of this model throughout this chapter.

9.2 Ageing societies

As can be seen in figure 5 below, which was generated using the program discussed above, one consequence of widespread life extension by CRMs is that the average person would, on average, be substantially older. In the Normal scenario the number of people alive at given ages begins to decline after age 50. In CRM, by contrast, this decline occurs later, roughly after age 80. The model thus confirms the idea that society would have far higher proportion of chronologically older people.

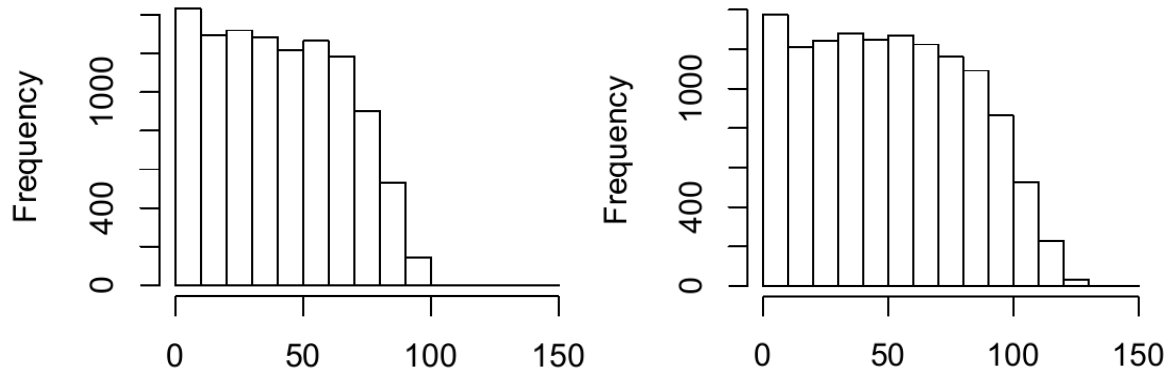

Figure 5 Number of people at any age after 200 years of No life extension (left) and after 200 years of slowed ageing (right).

Extrapolating from existing developed world trends towards older populations raises important problems for social welfare and the utility of life extension. In particular, it has been argued that longer lives would entail i) greater expenditure on health care for the elderly, ii) an 'enslaved' population of workers supporting a burgeoning population of pensioners, and iii) a decline in innovation and progress. I examine these in turn.

9.2.1 Health care expenditure

The greatest expenditures on health increase dramatically after the age of 50 (Alemayehu and Warner 2004). Since societies are 'greying' – the average age and the proportion of elderly people is growing – health expenditure is already increasing. Recent research

suggests that per capita health expenditures will rise by one fifth by the year 2030 if changes are not made to healthcare systems (*ibid*., 640).

If life extension technologies became widespread, the average age of society, and the proportion of people above the age of 50 would increase still further. Fukuyama thus warns of a

> national nursing home scenario, in which people routinely live to be 150 but spend the last fifty years in a state of childlike dependence on caretakers. (Fukuyama 2002, 69)

Fukuyama envisions a situation in which disease and disability states are significantly prolonged. Such a scenario would exacerbate a difficult situation and imply greater, and perhaps unsustainable health costs. Would widespread life extension by CRMs have similar effects? I will suggest that even if CRMs lengthened the period in which a person has an increased likelihood of age-related diseases, the costs of healthcare could nonetheless be reduced.

Prolonged health decline and health expenditure

CRMs would postpone the period of increased disability and disease that occurs in the elderly. However, although disease occurs later, it may still be the case that the time span in which a person is more likely to experience age-related diseases will be expanded. This is the 'prolonged health decline' discussed in Chapter 4.

In keeping with the figures in Chapter 7, suppose again that normal healthspan expectancy is 65 and life expectancy is 80. Suppose further that CRMs increased healthspan expectancy to 80 and life expectancy to 100. In this case the CRM adds 15 years of healthy lifespan, but also results in an additional 5 years spent with an increased likelihood of

disease. In Chapter 4, I argued that this would be good for individuals; the question here is whether it would result in additional health costs.

There are several reasons to think it would not. First, healthcare costs are strongly related to proximity to death, rather than to age itself (McCrail et al 2000; Felder, Meier, and Schmitt 2000; Yang, Norton, and Stearns 2003). Pan and colleagues point out that 'it is not aging as such that creates healthcare expenditure but services needed when death is imminent' (Pan, Chai, and Farber 2008). As a result, if death is postponed, the costs of treating the elderly should not substantially increase, since the majority of the expense would be postponed. This has led Lubitz and colleagues to claim that

> [h]ealth promotion efforts in the non-elderly population that have payoffs in better health and longer life for the elderly will not increase health care spending among the elderly. (Lubitz et al. 2003, 1048)

This provides an initial reason to think that a CRM that prolonged health decline would not substantially increase health expenditure. Since a CRM would postpone death, it should be expected that the greatest proportion of expenditure would be deferred and not increased. The costs that may increase would be those incurred as a result of additional *healthier* years, which are proportionately low.

Reduced health expenditure

In addition, there is some reason to think that CRMs may even *decrease* health expenditure by comparison with a Normal greying society. As argued in Chapter 4, the *frequency* of age-related diseases would be lower. Thus it is likely that, at any time, less people would be making use of health services to treat age-related diseases. The pressure on health services may be eased to some extent by comparison with Normal aged populations.

Moreover, CRMs appear likely to *treat* expensive age-related diseases like Alzheimer's. As discussed earlier, CR improves conditions like diabetes, Alzheimer's disease and cancer in animals. Treating and caring for sufferers of these maladies is predicted to be one of the greatest expenditures in ageing populations (Olshansky et al. 2006, 31). CRMs could reduce this burden.

A further argument that extending lifespan could reduce health expenditure is provided by Harris. He argues that interventions that delay the incidence of age-related diseases, as CRMs would, allow health services to defer costs. Given economic growth, then, the relative costs of treating diseases at the end of life will be lowered.

> immortality so far from increasing health costs per individual might actually dramatically reduce them, there might in short be an economic discounting argument for the public funding of 'immortality' interventions. (Harris 2010, 70)

The economic gain of increasing lifespan would be greater in the indefinite lifespan Harris envisages. However, the point also applies in the context of a smaller lifespan increase.

Against these claims, it could be objected that although CRMs might reduce health expenditure on individual elderly people, expenses would nonetheless increase because there would be *a greater proportion of elderly people.* This is certainly true in the sense that there would ultimately be a larger proportion above a given age, say 65. This is evident in the comparison in figure 5 above.

However, people over the age of 65 in the CRM scenario will be biologically younger and will incur lower health expenses than their age-matched cohorts in the Normal scenario. If other things, such as fertility rates, are held equal, the proportion of citizens who are less healthy is unlikely to be affected.

Conclusion on health expenditure

Far from increasing health expenditures and resulting in a 'national nursing home' scenario, CRMs could alleviate some of the existing expenses that occur as a result of ageing societies, even if it prolonged the period of health decline. This is not to suggest the overly rosy picture that CRMs would solve the pressing difficulties related to providing healthcare in 'greyer' societies, but instead to point out that CRMs, in increasing healthy lifespan, could mitigate them to some extent.

However, the fact that CRMs would result in less use of health resources would be undermined if they also resulted in an economic situation in which less funds were generated due to a smaller workforce. I now discuss this possibility.

9.2.2. Unfavourable support ratios

The past century and a half has seen great increases in life expectancy, with few increases in the average age of retirement (Mayhew 2009). In addition, people are having fewer children. This means that the ratio of working people to retired people is decreasing. Fukuyama gives the following example:

> Japan… will go from a situation in which there were four active workers for every retired person at the end of the twentieth century, to one in which there are only two workers per retired person a generation or so down the road. (Fukuyama 2002, 62)

The ratio of workers to non-workers is known as the 'support ratio,' or 'dependency ratio.' The unfavourable support ratio that currently exists in ageing societies is a major contributor to the 'pensions crisis,' which is essentially a decline in the resources available to pay the pensions of retirees.

McConnell and Turner argue that problems related to the support ratio would be exacerbated if people lived even longer than they currently do, since they would then be

above pensioning age for an even greater proportion of their lives (McConnel and Turner 2005). If people on CRMs continued to draw a pension from age 65, and could be expected to live until 100, how could the deficit be made up? Fukuyama, similarly, gestures at the dystopian possibility that workers may eventually 'feel enslaved to the two, three, or more generations of ancestors dependent on them'(Fukuyama 2002, 97).

In this section I outline the claim, made by Olshansky and colleagues, that anti-ageing technologies would improve the current situation, since they would compress morbidity and allow people to work for longer. I argue that, although the authors may overstate impact of anti-ageing technologies, CRMs could once again mitigate some of difficulties related to support ratios.

Anti-ageing as an economic boon

Olshansky and colleagues argue that anti-ageing interventions would result in a

> compression of mortality and morbidity [that] would create financial gains not only because aging populations will have more years to contribute, but also because there will be more years during which age-entitlement and healthcare programs are not used. (Olshansky et al. 2006, 35)

The claim here is that people who used anti-ageing interventions would have more years of healthy, active life that could be spent contributing. As such, the proportion of working to non-working years could be increased. Public coffers will be boosted by relative decreases in the use of pension and healthcare schemes, and increased income from taxation on earnings later in life. If so, then far from exacerbating the problems resulting from greying societies, anti-ageing interventions may provide an effective way to ameliorate them.

There are, however, two major problems with this possibility. The first is that CRMs may not compress the period of morbidity at the end of life. Secondly, it is not clear that citizens' *ability* to make an increased contribution means that they would *in fact* make an

increased contribution. There are numerous legal, social, and psychological obstacles to citizens working longer. Below I discuss these two problems and the potential impact of CRMs on support ratios.

CRMs and ability to work

Olshansky and colleagues' optimistic assessment is that anti-ageing technologies, by compressing morbidity, would increase the proportion of years in which citizens are able to work relative to the Normal scenario. Could this outcome also be a consequence of the use of CRMs that do not compress morbidity? I argue that it could.

The ability to work is strongly influenced by one's healthy life expectancy, in the sense that healthspan

> creates the necessary conditions for any economic activity to be undertaken and influences the decision to remain economically active for longer. (Mayhew 2009, 10)

Given this, I will suppose, as I did above, that healthy life expectancy in the Normal scenario is 65 and that life expectancy is 80. As a result, one is able to work until 65, which is roughly the current pensioning age. Healthy life expectancy in the CRM scenario is 80 and life expectancy is 100. Thus in the CRM scenario one is able to work until 80. Suppose further, that in both scenarios one finishes education at the age of 20. Thus, in the Normal scenario one is unable to work for 35 years of one's total lifespan, due to education (20 years) and declining health (15 years). In the CRM scenario, the number of years in which one is unable to work is greater, 40 years, due to a longer period of health decline (20 years).

However, despite a greater absolute number of years spent in retirement, the proportion of working to non-working years is more favourable in the CRM scenario. In the Normal scenario the average person will spend 45 years working and 35 years not working. About 55% of a person's life will be spent working. In the CRM scenario the average person will spend 60 years working and 40 years not working: 60% of a life will be spent working.

As a result, slowing ageing may increase the percentage of society able to contribute, relative to the Normal scenario. Though doing so would not increase productive potential as much as compressing morbidity entirely, perhaps Olshansky and colleagues' prediction of financial gains might be nonetheless be realised.

Non-health-related limitations on working life expectancy

However, although health is regarded as a 'necessary condition' for longer working life expectancy, it is not sufficient. As mentioned, the fact that people are *able* to work more does not mean they will *in fact* work more.

Improving citizens' ability to contribute creates the potential to work longer, but there are numerous obstacles to realising this potential. These include psychological factors such as individual preferences and ingrained expectations about work, as well as social factors such as attitudes to older people in the workplace, existing company and government policies, and laws with respect to retirement and pensions. If citizens are required to be economically productive for longer, extending healthy life expectancy is not enough: policies must identify and exploit the psychological, social and legal influences on retirement ages.

Conclusion

These challenges already exist in greying societies. They entail that that neither CRMs nor any other anti-aging intervention should be regarded as a panacea to the possibility of economically dependent elderly populations. It is unrealistic to think these challenges could be resolved by drugs alone. Political, economic and social factors play a far greater role.

Even so, the above points suggest that, with respect to the potential to improve support ratios, the CRM scenario has an advantage over the Normal scenario. However, this advantage would be undermined if a society with older workers is likely to undermine scientific, moral and political progress, as some have claimed. This is the topic of the next section.

9.2.3 Progress

Contra the concerns of the previous section, which stemmed from people working for too short a fraction of life, it has been claimed that people might work *too long*, leading to declines in innovation and progress.

Having older people contributing for longer might be thought likely to contribute to social, economic and scientific progress. Older people are stores of knowledge and experience. They are also more highly skilled than novices. Moreover, it is often thought that increased life expectancy epitomises progress. Vaupel and Kistowski rank the rise in life expectancy in the last century as 'a crowning achievement of modern civilisation' (Vaupel and Kistowski 2008, 256).

It is perhaps ironic, then, that critics of life extension have argued that extending lifespan would result in a decline in innovation. Scientific and technological progress, as well as moral and political progress might be retarded in a much older society. This is argued to be

likely on the basis of three claims about older people: first, old people are inflexible and less able to adapt to changing contexts; second, old people are less innovative, so an older society would innovate less; third, old people are conservative, so that progressive younger generations would be ignored or suppressed by conservative age-based hierarchies.

I outline these claims and argue that they are empirically disputed. To the extent that they can be verified, there are psychological and social factors that account for differences between the productivity and innovation of older generations. Awareness of these points the way to furthering progress both in existing ageing societies and in the CRM society.

Are the elderly less able to adapt?

The first difficulty highlighted by Fukuyama is that progress might be slowed as individuals become less capable of adapting to new work environments and technologies as they age, since 'past a certain age, the correlation between age and ability begins to go in the opposite direction' (Fukuyama 2002, 64). If it is true that older workers adapt worse, it may be that an older work force would be less able to maintain the rate of progress and growth.

If older people do adapt less easily, we should expect that they will be less productive in the workplace. The claim that there is such a decline in productivity is the subject of empirical dispute (McEvoy and Cascio 1989; Waldman and Avolio 1986). However, there is evidence that older people tend to retire earlier in industries in which the pace of progress is rapid (Bartel and Sicherman 1993). This lends some support to the idea that the elderly are less able to adapt to new demands. Several reasons are given for this. The most commonly cited are biological factors:

> a worker's health tends to deteriorate over the life cycle … In addition, it is argued that cognitive abilities generally decrease with age. (Lallemand and Rycx 2009, 274)

As suggested in the previous section, to the extent that productivity and the ability to adapt are based on biological age and health, CRMs would enable workers to continue to adapt for much longer.

However, there may be additional factors, to some extent independent of biology, that make it more difficult for older people to adapt. Other factors thought to decrease older workers productivity include the possibility that

> older people might be less willing to invest in training programmes since they are closer to retirement … Moreover, employers might be more reluctant to invest in training for older workers because they have a shorter period of time to benefit from on-the-job training. (*Ibid*.)

In other words, the proximity of retirement may play a large role in employees' willingness to learn new skills, as well as employers' willingness to invest in training. In turn, levels of training influence employees ability to meet technological challenges and to be productive in changing work environments. In support of this, it has been found that older workers who continue to receive training are substantially less likely to retire early (Fouarge and Schils 2009).

This suggests, perhaps unsurprisingly, that older people have no inherent inability to adapt that is not related to health problems that naturally accompany old age. The productivity of older workers would be improved if compulsory retirement ages were raised, and if they continued to attend training. Steps towards these ends are already being taken in contemporary ageing societies. With similar initiatives, there is little reason to think the CRM scenario, in which people worked for longer, would be less progressive than the

Normal scenario. Indeed, CRMs would postpone age-related sources of decreased productivity, allowing the most skilled and experienced workers to remain productive for longer.

Are older people less innovative?

A further problem, suggested by former US President George W. Bush's Council on Bioethics (USPCB) is that, since younger people are more risk-taking and innovative, older societies are less likely to supply the innovative force required to maintain the rate of progress. The Council argues that

> [s]erious innovation… is therefore often the function of a new generation of leaders, with new ideas to try and a different sense of the institution's mission and environment. (Kass and the USPCB 2003, 195)

There is some evidence for this claim. In particular, peak scientific productivity, measured primarily by patent applications and Nobel Prize winners appears to occur between the ages of 30 and 40 (National Research Council 2012, Ch 6). However, evidence from the business sphere suggests the opposite may be true. Recent studies suggest that older age groups have a significantly higher rate of entrepreneurial activity (Stangler 2009; Wadhwa, Freeman, and Rissing 2008). The empirical evidence is thus mixed and it is difficult to draw a conclusion abut levels of innovation in different age groups.

Nonetheless, even if it were proven that younger people are more innovative, a further claim would be required in order to provide grounds to think that 'greyer societies' would innovate less: either there would need to be fewer young people, or the opinions of young people must be less likely to come to light.

Thus far, I have not discussed whether fewer people would be born in the CRM scenario. In S9.3 I argue that increases in longevity need not result in decreases in fertility. If not, then CRMs would not result in there being fewer young innovators than the Normal ageing societies scenario. Indeed, the model of slowed ageing discussed earlier suggests that would be *more* young people (figure 5).[87] Thus, to the extent that innovation depends on the *number* of innovators, life extension by CRMs would not compromise innovation.

In sum, then, the evidence that older people innovate less is limited. Moreover, CRMs would not result in there being fewer young innovators. As a result, it is unjustified to claim that older societies would innovate less.

Would the conservative elderly stifle innovation?

However, the USPCB has suggested there may be other ways in which an elderly population could slow progress and dampen innovation.

> If individuals did not age…it might just be that societies …would experience their own sort of senescence—a hardening of the vital social pathways, a stiffening and loss of flexibility, a setting of the ways and views. (Kass and the PBC 2003, 197)

It is argued that it may become more difficult for younger, more innovative citizens to oust outmoded or immoral paradigms, entrenched and 'inflexible', held by increasingly older and ideologically conservative generations. Epistemic and moral progress might be compromised because outdated doctrines survive for longer, while the development of new ideas is hampered.

This claim rests on the idea that older people are more conservative and less likely to accept innovation. Again this is an empirical claim, and the evidence appears to be

[87] This is in part due to an increased population. If it became necessary to reduce reproduction to avoid overpopulation some of the innovation-related benefits of having more young people might be lost.

weighted against it. Numerous studies suggest that older people are no more ideologically conservative, and are at least as likely to adapt their moral and political viewpoints as younger people.[88] If older people's attitudes to progressive innovations in morality, politics and the sciences are no more rigid than those of younger people, then the fact that they live longer makes them no more likely to impose attitudinal obstacles to progress.

One final way of buttressing the idea that innovation would be suppressed in a CRM society is to claim that, even though many older people will embrace innovation, even a few 'reactionaries' might be sufficient to undermine the social benefits of longer lives. This possibility is most evident in the political sphere, where, David Gems writes,

> [h]istorically, a great benefit of aging has been deliverance from tyranny. It is biology's analog of the most successful feature of parliamentary democracy: an effective means to dispose of bad leadership. Even under tyranny one can at least wait, and hope to outlive one's oppressor. (Gems 2003, 34)

It is possible that using CRMs might allow powerful dictators to live longer and suppress social progress in some contexts.

However, it is no less likely that this stultifying effect of injustice would be heavily outweighed by the benefits externalised by aged figures like Nelson Mandela, as well as those of potentially billions of other good people. In this respect, viewing a life extension technology as a social ill because it might prolong dictatorships seems analogous to regarding life-saving vaccines as problematic because the patient might turn out to be a criminal. The claim that life extension is an ill because it might allow progress to be curtailed by a handful of dictators is thus irredeemably unjustified.

[88] See for instance Campbell and Strate 1981, Danigelis and Cutler1991, Hummert et al. 1995, Fullerton and Dixon 2010, Danigelis, Hardy, and Cutler 2007.

Conclusion on CRMs and progress

This section has examined the idea that the older society that would result from CRMs would be less innovative and progressive. This claim was found to rely on unqualified or unjustified stereotypes about older people, namely that old people are less able to adapt to changing work environments, that they are less innovative, and that they are conservative and more likely to suppress novel ideas.

While keeping older workers in the workplace for longer presents challenges for both contemporary greyer societies and the CRM scenario, there's no reason to think that such challenges will be insurmountable, or that older workers will inhibit the rate of progress through an inability to adapt.

Older generations can provide experience and criticism that guide and spur progress and help direct innovation. If people lived longer, the valuable commodities of accumulated skill, wisdom, and experience could increase the rate of progress by enabling the avoidance of repeated error and unproductive paths. Moreover, as mentioned, extending lifespan and healthspan is often regarded as a hallmark of social progress. These benefits are likely to outweigh purported declines in innovation, which, in any event, appear to have scant evidential basis.

9.3 Overpopulation (at a time)

There is a growing concern that even the current population of the planet may be too large to support. One of the commonly expressed fears about life extension is that it would increase populations, taxing already strained planetary resources. Barazzetti and Reichlin, for instance argue that,

> one of the consequences of an increase in the lifespan would be the increase in the population; if this is so, it seems likely that the scientific success of life-extending

> technologies would impose an unbearable burden on the environment and its resources. (Barazzetti and Reichlin 2011, w13181)

Population size is determined by the starting population, the number of births, the number of deaths, as well as immigration and emigration. Since the concern is expressed in terms of global resources, I will leave aside immigration and emigration. Below I discuss the likely influence of CRMs on births and deaths. I argue that the numerous influences on fertility mean that it is plausible to hold fertility rates equal in the comparison between CRM and Normal societies. However, I argue that doing so would, as Barazzetti and Reichlin fear, increase a population's size. I examine the ethical implications of this possibility.

9.3.1 CRMs and fertility

The impact of CRMs on population size will depend to a large extent on their effect, if any, on fertility and birth rates. In Chapter 4, I argued that CRMs would not reduce the ability to procreate. Nonetheless it might be thought that longer life, in itself, might have an impact on fertility. For instance, if citizens live longer, and are able to reproduce for longer, perhaps they will want more children. On the other hand, past increases in longevity have coincided with *decreases* in fertility, resulting in a 'fertility crisis' in much of the developed world (Caldwell and Schindlmayr 2003). Far from increasing fertility, longer lives have corresponded with a *decrease* in reproduction. Which, if either, of these consequences is more likely, and would CRMs have any impact on them?

Longevity may play some role in fertility rates. In general, where such a role is postulated, longer life is thought to likely to reduce fertility. This is what has occurred in most of the developed world (Westendorp and Kirkwood 1998). If this is the likely outcome, it is

tempting to conclude that overpopulation would be an unlikely consequence of extending lifespan by CRMs.

However, this would be too simplistic, in part because the role of longevity in reducing fertility is disputed (Gavrilova et al. 2004), but more importantly because fertility rates have an array of social determinants. Explanations for variations in fertility include government policies, numbers of women in the workplace, the availability of contraception, levels of education, the stability of parental relationships, religion, the expense of raising children, and the expense of living generally (Hirschman 1994). In light of these, it is an immense over-simplification to suggest that longevity alone would result in a decline in fertility and thereby exert a strong effect on population size.

Since this is the case, the rate of fertility in a society in which CRMs became widespread is something of an imponderable. Other determinants of fertility might mean that people with increased reproductive lifespan might have more children. Alternatively, they may reproduce less. Since this is the case it is reasonable to assume the same fertility rate will obtain in both scenarios. I now discuss the effects on population size that would result from slowed ageing, given equivalent fertility rates.

9.3.2 Slowed ageing and population size

I hypothesised that the rate of population growth would initially increase, due to decreased frequency of deaths in the CRM scenario. After this, growth would stabilise as extendees began to die at a regular rate. Population size would increase, but only for a time. The model discussed earlier bore out this prediction. As can be seen in figure 6, population size increased from an initial population of 10000 to roughly 12500 with slowed ageing.

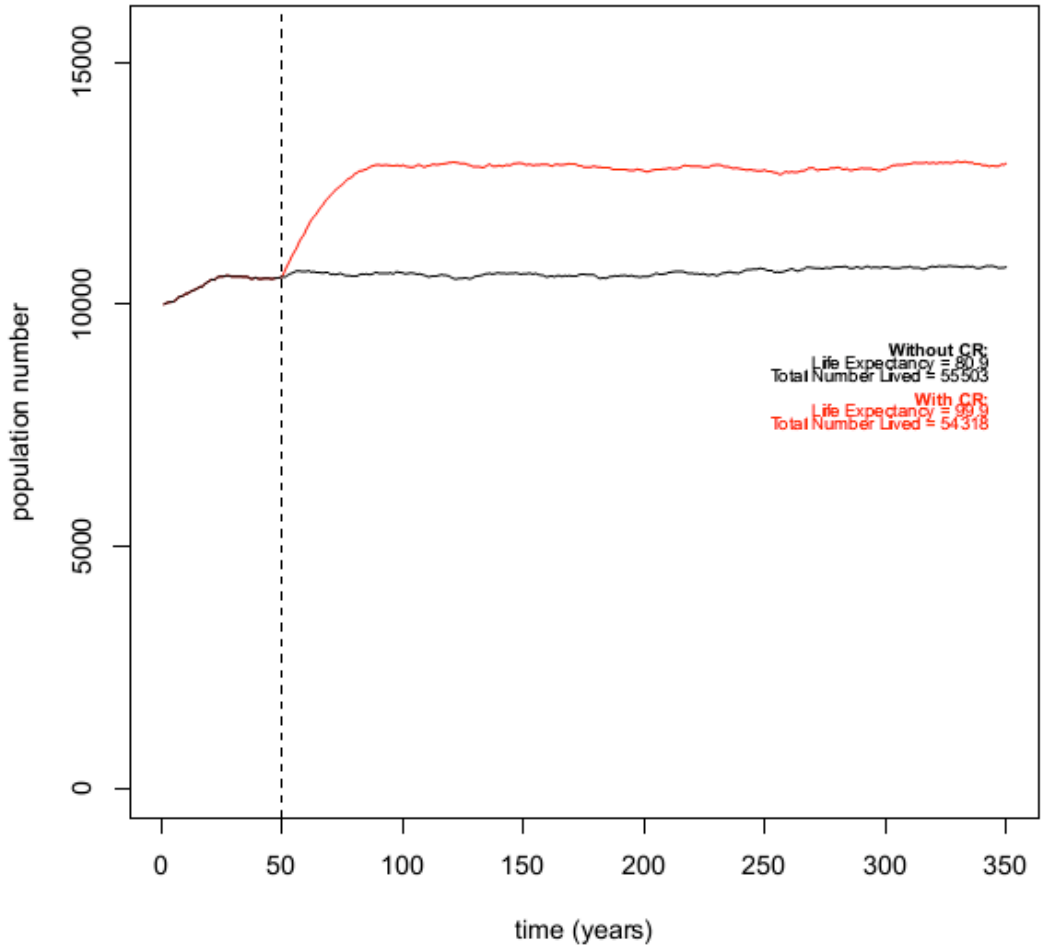

Figure 6 Change in population size in CRM compared to Normal, given replacement rates

The model assumes reproduction at replacement rates.[89] If individuals had more than one child per person, the increase in population would be greater, since more people would be born in the period in which the frequency of death decreased. Once again, however, the rate of growth would eventually return to that experienced in the normal scenario. This means that if a population reproduced above replacement rates, and there was an environmental tipping point, life extension would get us there sooner, but not much sooner, since the rate of population growth would revert.

In reality, of course, the uptake of CRMs would be much more gradual, meaning that the population would grow more slowly. Moreover, even with widespread public health

[89] Note that the model uses actual replacement, and not the commonly agreed figure of 2.1 children per female.

campaigns promoting CRM use, not everyone would make use of the intervention. The impact of CRMs on population size would be smaller, though nonetheless significant.

9.3.3. The ethical status of CRMs given overpopulation

The possibility of hastened overpopulation is an ethical problem, since it might contribute to a decline in the welfare of individuals in society. Planetary resources might not be sufficient for everyone. The question is how this should influence decisions about substantial life extension by CRMs.

In this respect, it is important to recognise that it is not just a substantial increase in life expectancy that would contribute to this problem. The creation of lives through reproduction makes a greater contribution to population growth, as does saving lives with other medical advances. As David Gems notes,

> advances in medicine along with improved nutrition and hygiene have greatly reduced infant mortality during the last century. This has led to dramatic increases in population, but no one has called reducing infant mortality undesirable. (Gems 2003, 34)

This means that the possibility of overpopulation, in itself, should not cause us to believe that life extending technologies are harmful. Instead, if steps are required to avert overpopulation, it is necessary to compare alternative courses.

One such course is to prevent the use of technologies that substantially prolong lifespan. However, given the smaller impact of such a step on population size, it may be more effective to reduce the number of people that are born. In the following section, I examine an argument that suggests that a reduction in births that might accompany the use of life extending technologies would be undesirable, thus providing a reason for preventing the widespread use of CRMs. I argue that the case that CRMs would reduce total welfare is

weak. If so, then reducing fertility may be a more effective and no less morally justifiable alternative to reducing population size than preventing life extension.

9.4 Under-population (across time)

The previous objection was that welfare might be reduced because too many people are alive *at a particular time*. The objection of this section is that social welfare might be decreased because there will be fewer people *across time*. Peter Singer has argued that life extension might result in a reduction of total welfare if fewer people come into existence. I will refer to this as 'the under-population argument.'

9.4.1 The under-population argument

The under-population argument, proposed by Peter Singer, runs as follows:

1. If life expectancy is substantially raised, a smaller number of people will be born across time.
2. A smaller number of people across time will have comparatively lower total welfare.
3. We should maximise present and future welfare.
4. So we should prevent substantial rises in life expectancy. (Singer 1991)

I will outline premises 1 and 3, before examining premise 2. I claim that premise 2 may be correct in the case of CRMs, but by such a narrow margin that it is unconvincing as an argument against the widespread use of CRMs.

Fewer people in total

One reason for thinking that there will be fewer people in the life extension CRM scenario is the possibility of overpopulation discussed in the previous section. If life prolonging

interventions are more widely used, they could contribute to a tipping point at which resources are so scarce that the number of children born would need to be reduced.

Such checks were notoriously instituted in China where high reproduction rates meant that population growth was regarded as unsustainable. As a result, in 1978, laws were introduced to discourage people from having more than one child. The laws themselves, and the means used to implement them are widely regarded as unethical.[90]

Of course, checks on population size would not necessarily be coercive. Instead, efforts are currently undertaken to impact on the drivers of fertility discussed earlier. By educating and empowering women, in particular, it is thought that fertility rates will be lowered, as has occurred in the developed world (Presser 1997). Reducing fertility in these ways is seldom regarded as ethically objectionable.

However, CRMs would result in a smaller number of people across time even if fertility rates were the same in both scenarios. Because CRM people live for longer, but have the same number of children, a smaller number of children will be born in a given period of time. This hypothesis is again borne out by the model discussed in S9.1.2.[91] Thus, it seems plausible that fewer people will be born in the CRM scenario, even without reductions in fertility.

Total utilitarianism

The third premise, that we should maximise present and future welfare, rests on a view sometimes referred to as *total utilitarianism.* According to total utilitarianism we should aim to maximise total welfare without regard to the number of individuals to whom the

[90] See Hvistendahl 2010 for an account of the methods used by the Chinese authorities and their effects.
[91] See 'Total number lived' in fig.6. Note that, despite fewer births at a time, population rose due to fewer deaths. Greater fertility reduction would be required to lower population size in CRM.

benefit accrues, or the degree of benefit experienced by each. All that matters is the overall 'pool' of welfare. It is best contrasted with average utilitarianism, which holds that we should raise the average welfare of each individual in society and focus on making individuals better off.

Total utilitarianism commonly integrates what Singer refers to as 'the principle of impartiality over time': the idea that we should be impartial between the welfare of existing and future people (Singer 1991, 143). In combination with temporal impartiality, total utilitarianism entails that, if we had a choice between a) raising the welfare of existing and future people and b) conceiving a greater number of people who would be individually less happy, but would have a greater total welfare, we should choose b). We should *conceive a greater number of happy people*, rather than making existing and future people happier.

Some regard total utilitarianism, and the idea of temporal impartiality, as counter-intuitive.[92] But, in keeping with my compatibilist methodology, I will not dispute these here. It is thus necessary to challenge premise 2: the claim that a society with fewer people in total would result in lower total welfare.

9.4.2 Singer's thought experiment: under-population and the h-LET

Singer argues that a society that produced a smaller number of people with longer lives may be worse than a society that produces a greater number of people with shorter lives. In support of this premise, Singer proposes the following thought experiment: A scientist develops a drug that increases life expectancy to about 150 years. However, the drug has no effect until middle age. After this, later life is prolonged. The hypothetical life extension

[92] See for example Narveson 1967, 67 for a critique of this type of impersonal harm.

technology (h-LET) only extends the latter part of a person's life: a 'Fountain of Prolonged Middle Age.'

In Singer's thought experiment the period in which health decline occurs – during and after middle age – is drastically extended. As a result, a much larger proportion of a person's life is spent in decline and so the average health across the life is decreased relative to a normal life, although the total health in each life is nonetheless greater.

Singer accepts that each individual h-LET user will be better off; health decline isn't bad, just worse than full health. Living longer in lower health still adds to welfare. Nonetheless he argues that using the drug would, paradoxically, make the society worse in terms of total health utility. This is so for two reasons: firstly, because, compared to the Normal scenario, the ratio of healthy to unhealthy years would be less favourable. Secondly, although individual lives will have greater total health utility, across time there will be *fewer of these lives*. For reasons outlined above, less people will come into existence. As a result, the total health utility would be lower than it would be if people had shorter lives with a higher proportion of healthy years.

If the premises above are accepted, then, in terms of social good, it would be better if the society chooses the reproduction strategy rather than developing Singer's h-LET. Preventing the use of the h-LET would increase total health and therefore total welfare.

However, since Singer's h-LET is imaginary, the argument is by no means conclusive against life extension in general. Nor is it intended to be. Instead, the thought experiment should be seen as raising considerations about the conditions in which a life extending intervention would be a good thing in terms of the total welfare of present and future generations.

In what follows I examine the implications of Singer's thought experiment for CRMs. I argue that if we substitute the assumptions of the thought experiment with the assumptions of the transfer thesis, the margins become too close to call and the objection is less effective.

9.4.3 Under-population and CRMs

There are three differences between the h-LET and CRMs. The first is that the extent of life extension is likely to be less than 150 years. I have suggested an expectancy of about 100 years.

The second difference is that, as argued in Chapter 4, a CRM would decelerate ageing earlier in life. Unlike the h-LET, then, *a CRM would extend the earlier, healthier, part of life* in which a person has less chance of experiencing age-associated health problems. The healthspan of subjects is increased. This difference is highly significant, since it means that the number of years spent in good health will be greater than in Singer's scenario.

The third difference between the h-LET and CRMs is that *the prolongation of the period of health decline is likely to be far less*, regardless of when the intervention starts. If one begins using a CRM late in life, there will most likely be little or no extension of life.[93] If, on the other hand, the intervention is started earlier and decelerates ageing there may be a slight prolongation of age-related health decline, but much less than in Singer's scenario.

Combining this third difference with the second point above, it becomes evident that the *proportion* of healthy years to unhealthy years will be more favourable than in Singer's thought experiment. Healthspan is substantially extended, while unhealthier period would

[93] See Chapter 3.

be extended to a lesser degree. What does this mean in terms of the total health utility of CRMs relative to Normal?

The healthy utility of Normal versus CRM

To know whether Normal is preferable to CRM on the basis of healthy years, it is necessary to estimate the total number of healthy years that would obtain in each. That is, we must estimate how many people would exist in each scenario, and how much health each would have.

In order to calculate this, I will assign some plausible numbers that are fairly easy to work with. To compare the health utility of the Normal and CRM scenarios, I will assume that each healthy year as counts as 1, while years spent in a less healthy state count as less than 1, depending on the severity of the illness or disability. A very severe illness, or death, might reduce one's health level to zero. This is similar to the QALY discussed earlier.

I will again assume that until 65 a person will be in full health. After this, a person's health declines for 15 years until she dies. In keeping with the QALY calculation of Chapter 7, I will assume that for these 15 years her average health is 0.5. Again, this means that an average normal life will have a health value of 72.5 healthy years (65 + (15 x 0.5)).

Now suppose the maximum population is 1 million. Everyone begins at age zero. Birth and death rates are well-matched so that, across time, on average, there is no deviation from the total population. We are interested in a period of 400 years. This gives us:

Normal

65 years of health plus 15 years at an average of 0.5

= 72.5 healthy years x 1million (constant population) x 5 (number of generations of 80 year olds in 400 years) = *362.5 million healthy years*

Now consider slowed ageing. CRMs increase healthspan expectancy to 80 and life expectancy to 100. This results in 20 years with an increased likelihood of disease. Let us again assume that the 20 years of declining health have an average value of 0.5. This time there will be four generations of 100 year olds in the 400 years we're interested in. These considerations give us:

CRM

80 years of full health + 20 years at an average of 0.5

= 90 healthy years x 1 million x 4 = *360 million healthy years*

Like the h-LET, a CRM would result in lower total health utility than Normal. Compared to the Normal scenario, two and a half million healthy years might be lost across four hundred years. Assuming a capped population, if we were making a decision entirely on the basis of total health utility, and that these figures are the basis of our decision, we should prevent the use of the CRM. Rather than that slowing ageing we should choose to add a larger number of new people with normal lives.

9.4.4 Mitigating factors and imponderables

Several points serve to render this conclusion unconvincing. The first is that the assumption that the average in the last 20 years will be 0.5 is quite pessimistic. It stands to reason that, in general, a person's worst health will occur in the year or so before death. This is a larger fraction of 15 years than it is of 20 years. If so, the comparatively longer time spent in better, though imperfect health would raise average health in later years in the CRM scenario.

Moreover, it is likely that CRMs would decrease the amount of time with chronic diseases in the period of health decline, since, as I have stressed, CRMs are also likely to be used as treatments for age-related diseases. Interestingly, if the estimate of 0.5 is pushed up to a less pessimistic 0.6, CRM results in an advantage of 5.5 million healthy years over Normal. Such fine margins mean that neither CRM nor Normal is a convincing winner in terms of total utility.

9.4.5 Conclusion on under-population across time

Singer's thought experiment highlights a curious problem that total utilitarianism poses for population ethics. It entails that, given certain assumptions, life extension can be good for everyone, yet reduce welfare. If we accept total utilitarianism, extending lifespan can be worse for society, even if people that exist have better lives.

However, the fact that CRMs would greatly increase healthy lifespan means that the total utility of a CRM society is roughly commensurate with that of a Normal society with many more people. CRMs could contribute to social welfare, even if it was necessary to restrict population size. Since the alternative of shorter lives with less well-being is not convincingly better in terms of total welfare, even total utilitarians can have no strong objection against the widespread use of CRMs.

Moreover, the abstract nature of Singer's argument hides the fact that if any policy really prevented the use of CRMs, this would harm real people by causing them to die earlier. Such a harm to individuals becomes less easy to justify if one considers that preventing the existence of additional people would harm no-one, since the would-be beneficiaries need not exist.

9.5 Conclusion

In this chapter I have argued that life extension is likely to result in three demographic scenarios: an older society, an increase in population size and a decrease in the number of people that exist across time. However, I argued that the prospect of an greyer society is less troublesome because, although older in years, citizens would be younger biologically.

I made the case that the increase in population size would be smaller than is sometimes thought likely. As a result, the influence of life extension on population size should be compared to that of other, stronger, determinants of population size, such as fertility.

Finally, I claimed that if extending lifespans required a smaller number of people across time, the substantial gains in health achieved using CRMs mean that a CRM society might have greater welfare than a Normal society.

CONCLUSION TO PART III

This part has examined questions about the distribution of life prolonging CRMs, and their impact on justice and social welfare. I have argued that CRMs may become widespread even in the absence of conclusive evidence of their life extending effects. I claimed that in order to reduce the likelihood of unfair healthspans it would be better if citizens had access to CRMs through health services. Finally I argued that the impact of CRMs on social welfare is uncertain, but that, in combination with forward thinking social policies, many of which are already in place, the social dangers of life extension can be avoided, and the social benefits of increased healthy lifespan can be realised. The conclusion that follows discusses the import of these claims.

CONCLUSIONS

Below I discuss the central ethical conclusions of this dissertation, and its implications for health and social policy. Finally I suggest directions for future research.

i) Ethical conclusions

Biogerontologist David Gems suggests that life extension may be a matter of 'tragic inevitability' and that '[t]he only serious option is to adapt as best we can to a future involving even greater extension of lifespan' (Gems 2011, 111).

The arguments of this thesis suggest that there may indeed be a degree of inevitability about life extension. The arguments of Chapter 7, in particular, point to a strong likelihood that the uptake of life extending interventions will occur, and may already be occurring, without any concerted efforts to promote or discourage it.

However, it is wrong to claim that this is a 'tragic' consequence. My aim in this dissertation has been to assess CR and CRMs on the basis of values that have been argued to be inimical to prolonging lifespan. In all cases I have claimed that research on CR leads us to hold that interventions that mimic it without reducing food intake would be compatible with these values.

The arguments of Part II show that, given the right social context, life extension by CRMs would be good for individuals. Moreover, there is little reason to think that life extending CRMs would have a negative impact on this context. CRMs can further the social value of fairness, and have the potential to improve social welfare. In most cases, facts about this

promising candidate for a life extending drug dissolve speculative fears about prolonging lifespan.

This will, I hope, allow broader agreement about the acceptability of CRMs. While not everyone will agree that life extension more generally is ethical, there is no reason to think that this particular category of intervention is ethically problematic. On the contrary, individual lives and society at large may be improved due to longer, healthier, more productive lives.

ii) Conclusion on health policy

A significant finding is that, as argued in Chapter 7, substantial life extension is likely to come about through existing health policy procedures that promote health and treat disease.

Moreover, with longer term analysis, it may be desirable to consider the adoption of CRMs as long-term preventive or risk-reducing measures, rather than just as treatments for diseases. As argued in Chapter 8, a widespread provision of CRMs as preventives would be fairer than alternatives such as doing nothing or banning because CRMs would benefit the worse off.

However, CRMs, like other interventions that raise lifespan above a normal level, raise a question about who should benefit. Should only those worse off in terms of healthspan expectancy receive the intervention, so as to reduce the gap between wealthier and poorer groups? Or should everyone have equal access, perhaps reflecting the value of equal respect? These questions are, as discussed in Chapter 8, outside my current scope. Their answer requires a difficult weighting of moral claims that puts them beyond the compatibilist method outlined in the introduction.

Nonetheless, some form of public provision of risk-reducing CRMs, be it equal or unequal, will be preferable. A preventive campaign of either type will require more research and long-term clinical trials. As discussed below, investigating a broader use of metformin would be a step in this direction. Only if such studies are conducted will we know whether CRMs are an efficacious and cost-effective means for reducing the incidence of age-related diseases in the developed and developing world.

Trials on candidate CRMs may reveal long-term efficacy in reducing the risk of age-related diseases. If so, there is no reason why encouraging the use of CRMs should not be considered alongside other interesting preventive or risk-reducing measures, such as proposed initiatives to give statins to healthy people (McCartney 2012), to encourage a small daily amount of aspirin for the prevention of cancer (Chan and Cook 2012), and perhaps even efforts to improve health through smoking reduction and a healthy diet. It is an empirical question whether provision of CRMs would be more effective than these public health initiatives in increasing healthy lifespan in the developing and developed world. Studies on metformin and other CRM candidates would enable greater clarity about the answer to this question.

The continued drive towards healthy ageing promises benefits for individuals and society. It is in the context of this health policy goal, and not in the context of futuristic immortality interventions, that CRMs, and indeed any socially feasible life extending interventions, should be seen.

iii) Directions for empirical research

In addition to justifying continued research on CR and CRMs, the arguments of this thesis suggest two further promising directions for empirical research. The first is to investigate

possibilities for compressing morbidity. The second is to investigate candidate CRMs, and particularly metformin, as preventive measures against disease.

Towards a compression of morbidity

In the introduction to this thesis, I argued that, in addition to wider agreement, an advantage of the compatibilist approach I have adopted is that it could help identify ethical goals for scientific research. I pointed to research on iPS cells as an example of a case in which an ethical problem was mitigated by scientific and not ethical research.

In this vein, it is significant that many of the objections to prolonging lifespan focussed on the idea that doing so would also prolong morbidity – the period in which age-related diseases are suffered. I argued that although CRMs might lengthen this period, this prolongation is insufficient to dent their acceptability.

Nonetheless, it is worth pointing out that an intervention that compressed morbidity to some extent would fare even better against these criticisms. Doing so would increase the proportion of life spent in good health, with all the individual, economic and social benefits that this entails. This is a worthy goal, of which biologists of ageing are well aware (Sinclair 2008).

Investigation of metformin

A further suggestion for empirical research is to investigate metformin as a preventive measure in healthy people. As mentioned above, this type of initiative has recently been undertaken with statins, which are used in the treatment of cardiovascular diseases. Metformin could be investigated towards a similar end.

Metformin may not be a genuine CRM in the sense described in Chapter 1, since its effect on lifespan does not appear to be as dramatic. Nonetheless features held in common with CR – such as its similar preventive impact on cancers, cardiovascular diseases, and diabetes – make it an intriguing test case for some of the arguments of this dissertation. Moreover, the fact that it has been used in human populations for more than 60 years means that long-term data in a large population of users may be available.

iv) Conclusion on social policy

I argued in Chapter 7 that CRMs would be taken up by health services in the course of treating age-related diseases. As a result, the main social policy conclusions do not concern what to do about CRMs, since there is no reason to treat them differently to other interventions. Instead they concern the social conditions in older societies generally.

Vaupel and Kitowski point out a widely accepted conclusion about 'greying' societies:

> As people benefit from longer, healthier lives, they will have to work longer. European economies cannot afford to see active, healthy people step out of the workforce long before official retirement age, especially if these people can be expected to live three or four more decades in good health. (Vaupel and Kistowski 2008, 260)

Measures to encourage training for older workers, and to defer or remove compulsory retirement ages are amongst the important and controversial challenges for policy makers. These challenges are already pressing in existing ageing societies. With longer lives, whether due to CRMs or other interventions, similar measures will continue to be relevant.

v) Concluding remark

Research on CR and CRMs promises to contribute to biological potential for longer, healthier and more productive lives. Moreover, this promise is compatible with, and could

further, values that are important for individuals and societies. Empirically informed individual choices and policies will enable the realisation of these benefits.

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