Since population is a dynamic continuum of generations, there are issues in every age group to deal with to secure healthy longevity as a whole.

We declare that we have no conflicts of interest.

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In their Review on ageing populations,[1] Kaare Christensen and colleagues take a critical view of Fries' "rectangularised survival curve". Such a view is not new, however. Back in the 1980s it was clear that the idea of a fixed maximum lifespan was erroneous, and that the numbers of the very old, including centenarians, was increasing rapidly.[2] Indeed, Roger Thatcher[3] showed in the late 1990s that mortality at age 80 years had been declining steadily during the second half of the 20th century, especially from the 1970s onwards. This, Thatcher explained, was the reason for the rising number of centenarians in high-income countries such as the UK.

In approaching the health profile of older populations, it is important, as Christensen and colleagues note, to distinguish between mild, moderate, and severe forms of morbidity and disability. To do otherwise is to run the risk of characterising old age tout court as dependent or incapacitated. Research has shown over many years that even after the ages of 85 or 90 years, life is characterised by diversity.[4] This suggests that the distinction between the "third age" and the "fourth age" (first developed by the historical sociologist, Peter Laslett[5]) is highly problematic, with the fourth age (of "decline and decrepitude", to quote Laslett) becoming the repository for our fears and negative sentiments on ageing.

Given the increasing population of older people, and especially the very old, morbidity compression could be accompanied by a rise in the number of individuals with moderate or severe disabling conditions, and longer dying trajectories. Research and practice needs to develop a coherent view of ageing that combines realistic appraisal of rising health needs with age and a recognition that varied experience is characteristic of all stages of the life course.

I declare that I have no conflicts of interest.

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Authors' reply

Jay Olshansky and Bruce Carnes raise incorrect or misleading objections. Our first paragraph describes our forecasting method. A 12-fold or 25-fold increase in the number of centenarians over the next century is exceeded by the increase of about 100-fold on average seen between 1900–07 and 2000–07. If death rates are declining at older ages, cohort life expectancy can be considerably greater than period life expectancy.

The legend to table 1 and the pertinent text indicate that the information is based on forecasts. Comparison of increases in life expectancy with new records for sprints is misleading: we do not suggest that all of us will live as long as the world record (currently 122 years). Our figure 1 shows that life expectancy is increasing at roughly the same rate in many developed countries. We discuss the poor performance of the USA.

We do not attribute "recent increases in life expectancy... to decelerated biological ageing" but to reductions in death rates at older ages. First published in 1994,[1] the discovery that deaths at older ages are being postponed is a key finding about the biology of ageing.

We agree with Ulf Jakobsson that psychosocial factors in ageing populations must be considered together with physical health problems. Although the incidence of clinically diagnosed depression declines after age 60 years, the frequency of self-reported symptoms of depression increases.[2,3] A longitudinal study of the entire Danish 1905 cohort from age 92 to 100 years with multiple assessments showed that, although on an individual level depression symptomatology and cognitive disabilities increased with age, the overall depression level and cognitive functioning changed very little within this age range, because those surviving tended to be those with the best health, mood, and cognitive function.[4] This suggests that most individuals can expect to experience cognitive decline and increase in depression symptomatology close to their death, but also that postponement of this individual decline makes it possible for us to live in reasonable good physical and psychological health to the highest ages.

Takeharu Koga and Yuichi Oshita point out that increasing childhood obesity and declining physical abilities of younger generations may counteract progress in health and lifespan. The remarkable increase in life expectancy since World War II was

achieved despite widespread tobacco use. Hence, progress can be made even given negative developments.

We concur with Michael Bury that there is no indication of a well defined fourth age and that a critical view of Fries' "rectangularised survival curve" is not new.[1] The absolute number of people with disabilities is likely to increase due to the large baby boomer cohorts approaching high ages. Available data suggest that the period of ill health that often precedes death is being delayed, not protracted: people are generally reaching older ages in better health.

We declare that we have no conflicts of interest.

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Allow me to respond to the article by Kaare Christensen and colleagues.[1] Ageing well is perhaps more easily grasped by writers, poets, philosophers, or anthropologists than by demographers. Christensen and colleagues refer consistently to the ability to do activities of daily living, but hardly mention joy, passion, creativity, purpose, or non-conformity.

A study of American centenarians able to live independently in the community[2] showed that they shared a common trait: those who scored highest on "life satisfaction" displayed a measure of non-conformity that had characterised them throughout their life. The nuns' study[3] found that future novices who showed more imagination in essays written in their last year of secondary school fared better intellectually and emotionally when assessed 60 or 70 years later.

Simone de Beauvoir addressed the issue of passion invigorating life in her book *La force de l'âge*, and the great American psychiatrist George E Vaillant warns on the cover of his masterpiece, *Aging Well*: "Think diet and exercise are keys to a long, healthy life? Think again!"

Quite so. I consult in a small nursing home that boasts two centenarians. One, a tall man, plays the harmonica readily whenever requested to do so. The other, a tiny woman in a wheelchair, joyfully knits coverlets for adults and for babies; she gives them to staff, family, and friends. Neither one of these centenarians will ever need my services because of depression.

I declare that I have no conflicts of interest.

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Combination therapy with clopidogrel and proton-pump inhibitors

Michelle O'Donoghue and colleagues' post-hoc analysis of TRITON-TIMI 38 and PRINCIPLE-TIMI 44 (Sept 19, p 989)[1] suggests that use of a proton-pump inhibitor (PPI) does not increase cardiovascular events in patients taking clopidogrel, despite pharmacokinetic resistance. However, methodological limitations, unanswered questions, and the findings' contrast with those of large observational analyses[2-4] suggest that confirmation of the safety of co-administration is warranted before clinical practice changes.

The liver enzyme CYP2C19 converts clopidogrel's prodrug to an active metabolite, and reduced CYP2C19 activity has been correlated with inhibition of platelet aggregation and increased cardiovascular events.[5] Omeprazole is a moderately strong CYP2C19 inhibitor. In O'Donoghue and colleagues' analysis, PPI users were heterogeneous because 60% received moderately strong CYP2C19 inhibitors, whereas 40% received pantoprazole. Subsequently, there are questions that must be answered. Can a moderately strong CYP2C19 inhibitor induce a state similar to a CYP2C19 polymorphism? In other words, can omeprazole block inhibition of platelet aggregation and does this portend adverse events? Furthermore, is there a potentially hazardous interaction between clopidogrel and use of a strong CYP2C19 inhibitor in patients with polymorphisms other than *1?

Discrepancies in the study's data analysis exist. Compared with O'Donoghue and colleagues' earlier work, the current study showed numerical differences in CYP2C19 polymorphism DNA samples, with the current study identifying 38 (11%) fewer.

The unpublished COGENT trial offers little because of a low event rate, lower risk cohort, and use of a non-standard omeprazole formulation. It also leaves our questions unresolved. Therefore, we will continue to use H2 antagonists in patients on clopidogrel unless there is a clear indication for PPIs.

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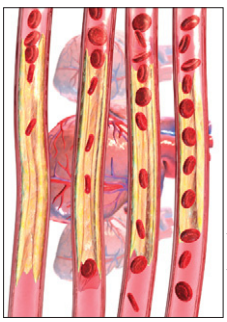
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