Is 60 the New 50? Examining Changes in Biological Age Over the Past Two Decades

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Abstract

Increasing life expectancy has been interpreted as improving health of a population. However, mortality is not always a reliable proxy for the pace of aging and could instead reflect achievement in keeping ailing people alive. Using data from NHANES III (1988– 1994) and NHANES IV (2007–2010), we examined how biological age, relative to chronological age, changed in the United States between 1988 and 2010, while estimating the contribution of changes in modifiable health behaviors. Results suggest that biological age is lower for more recent periods; however, the degree of improvement varied across age and sex groups. Overall, older adults experienced the greatest improvement or decreases in biological age. Males, especially those in the youngest and oldest groups, experienced greater declines in biological age than females. These differences were partially explained by age- and sex-specific changes in behaviors, such as smoking, obesity, and medication use. Slowing the pace of aging, along with increasing life expectancy, has important social and economic implications; thus, identifying modifiable risk factors that contribute to cohort differences in health and aging is essential.

Introduction

U.S. life expectancy has been rapidly increasing over the past 60 years (Oeppen and Vaupel 2002). Because mortality schedules are often used to estimate the rate of aging, researchers interpreted this change as a slowing of the pace of aging and an improvement in the overall health status of the population (Vaupel 2010). However, life expectancy may not always be a reliable proxy for how fast this population is aging at the biological level (Yashin et al. 2002). For instance, medical interventions aimed at disease treatment rather than prevention will not eliminate disease but may improve survival and physiological functioning of an individual (Rosen and Haglund 2005). In such instances, the extra years of life gained will not be disease-free, but they may be characterized by improved physiology and therefore are probably reflective of improved health status (Crimmins and Beltran-Sanchez 2011).

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By age 65, remaining life expectancy for U.S. males is predicted to be approximately 17.0 years; however, only 8.1 of those years is spent disease-free (Crimmins and Beltran-Sanchez 2011). Similar trends have been shown for U.S. women, who at age 65 have a life expectancy of 19.7 years, 11.3 of which are disease-free (Crimmins and Beltran-Sanchez 2011). As suggested by a phenomenon known as *compression of morbidity*, if humans possess a maximal lifespan, slowing the aging rate would produce a rectangularization of the survival curve (Fries 1983). Additionally, a deceleration of the human aging process, whether accomplished through environment or biomedical intervention, would push the timing of aging-related disease and disability incidence closer to the end of life.

Whether lifespan extension within a population is accompanied by slowing the rate of aging —thus leading to compression of morbidity—could have large economic implications. If coupled with poor health status, increased life expectancy for the U.S. population would likely increase financial strain on national age-based entitlement programs, such as Medicare and Social Security (Daviglus et al. 2004). Conversely, with improved health and slower aging rates, individuals would require fewer health care resources in old age and could continue to contribute to the economy by postponing retirement and collection of Social Security benefits. As a result, rather than looking to mortality trends to assess changes in population health and aging, it may be beneficial to try to estimate biological aging directly in order to determine whether a given population has undergone changes in the pace of aging.

Multisystem composite measures have been developed to quantify an individual's biological aging status (Comfort 1969; Mooradian 1990) and may enable more accurate estimation of changes in the pace of aging for different historical periods. Measures of biological age combine information from multiple physiological systems to estimate an individual's position on the aging trajectory (Klemera and Doubal 2006; Levine 2013). For instance, an individual with a biological age of 50 is estimated to have a physiological status consistent with that observed, on average, for individuals who are 50 years old chronologically. Furthermore, if the given individual is 40 years old chronologically and 50 years old biologically, it may suggest that he/she is aging at an accelerated rate.

Such measures have been found to be reliable predictors of both morbidity and mortality in multiple populations and thus may be suitable for estimating an individual's underlying aging rate (Belsky et al. 2015; Cho et al. 2010; Levine and Crimmins 2014a, b). Other researchers have suggested that for a variable to be considered a reliable and valid measure of biological age, it should meet four criteria: (1) produce realistic measurements, within the limits of recorded life span; (2) be able to identify at-risk individuals prior to entering a disease state; (3) be a better predictor of multiple age-associated biological and functional outcomes than is chronological age; and (4) predict both remaining longevity and disease-specific mortality in a population of which 90 % of the individuals are still alive (Butler et al. 2004; Levine 2013).

The biological age measure used here has been shown to be a better predictor of all-cause and disease-specific mortality when compared with chronological age (Levine 2013) or other composite biomarker measures, such as allostatic load (Levine and Crimmins 2014a).

It has also been found to be associated with outcomes such as cognitive functioning, cognitive change, physical functioning, and facial aging within a birth cohort of young (age 38), disease-free individuals (Belsky et al. 2015; Schaefer et al. 2016). As a result, measures such as the one used in this study present an opportunity for examining age and period differences in biological age above what can be gained by examining changes in disease and functioning outcomes or in individual measures of physiological functioning (e.g., cholesterol, blood pressure, and blood glucose).

Biological aging is believed to be strongly influenced by environmental factors, genetic differences, and some level of stochasticity (Finch and Kirkwood 2000; Kirkwood 2002). For the most part, the genetic makeup of a population does not change much from year to year and therefore would not lead to changes in the pace of aging over a short period, but environments and behaviors do change more rapidly. For instance, a number of recent changes in the prevalence of smoking and obesity could affect the rate of aging over the past few decades. In the United States, smoking prevalence has decreased dramatically since the 1980s, which may be accompanied by health improvements (Wang and Preston 2009). On the other hand, U.S. obesity rates have more than doubled during this time (Finucane et al. 2011), which may counteract the declines in smoking, leading to faster aging rates, increased disease and disability, and overall poorer health status.

Notably, evidence exists that the changes in smoking and obesity prevalence have not been equivalent across U.S. subpopulations: for instance, changes in health behaviors by sex. In U.S. during the mid– to late twentieth century, smoking contributed to significantly more excess deaths for men than for women (Preston and Wang 2006). However, the prevalence of smoking among the sexes has started to equalize, and as a result, the change in physiological aging that can be attributed to smoking cessation should be greater for males. This is one explanation for the decrease in the longevity gender gap since the 1980s, with males gaining more additional years of life than females (National Resarch Council 2011). Additionally, mean body mass index (BMI) has increased faster for females than for males. BMI was higher for males during the latter half of the twentieth century; however, between 1994 and1999, the average BMI of females is estimated to have surpassed that of males (Wang and Beydoun 2007).

Finally, the use of pharmaceuticals to control blood pressure and cholesterol has also increased substantially over the past few decades. For instance, over the decade between 1988 and 2000, both treatment and control of hypertension significantly increased among U.S. adults (Hajjar and Kotchen 2003). Additionally, statin use to control high cholesterol increased by almost tenfold, from approximately 2 % to 25 %, among U.S. adults ages 45 and older. When used as primary or secondary prevention strategies, use of pharmaceuticals has the potential to attenuate some of the age-related decline in physiological functioning related to cardiovascular and metabolic health, and perhaps even postpone death. Nevertheless, the use of such drugs has been more common among men than women (National Center for Health Statistics 2011). The number of Americans on hypertension medication grew between 1988–1991 and 1999–2000, with most of the increase among males (Hajjar and Kotchen 2003). Furthermore, among adults aged 65–74 in 2005–2008,

approximately one-half of all U.S. men (but only one-third of all U.S. women) reported taking a statin drug in the past month.

Using nationally representative data, we aim to examine changes in biological age for the U.S. population between 1988 and 2010, and to estimate the contribution of changes in smoking, obesity, and medication use. Doing so will enable us to estimate whether the aging of the U.S. population is slowing, whether improvements are consistent across age and sex groups, and what proportion of improvements can be attributed to changes in health behaviors or their effects.

Materials and Method

Study Population

Our analytic sample included 21,575 subjects ages 20–79 from the third ($n = 13,426$) and fourth waves ($n = 8,149$) of the National Health and Examination Survey: NHANES III (1988–1994) and NHANES IV (2007–2010), respectively. Our analytic sample was limited to subjects under age 80, given that the functional form of the association between biomarkers and age may be different in the oldest-old, potentially because of mortality selection (Yashin et al. 2013). NHANES III and IV are both cross-sectional waves and thus included different participants. However, both samples are meant to reflect the status of the U.S. adult population at the time of the interview and can therefore be compared to examine how the population changed between the two periods. Unweighted response rates for NHANES III and IV (2009–2010) were 78.0 % and 77.3 %, respectively.

Data for NHANES were collected from at-home interviews as well as examinations that took place at a mobile examination center (MEC). Complete biomarker data (no missing data) were available for approximately 70 % of the age-eligible sample. On average, subjects with missing data were older, were more likely to be black, and had lower levels of education. Apart from missing data, no other exclusion criteria were used.

Biological Age

Parameters for the biological age equation were generated using data pooled across both waves of NHANES (III and IV); sampling weights were used in all calculations. The algorithm incorporates information on chronological age, as well as eight factors that indicate metabolic, cardiovascular, inflammatory, kidney, liver, and lung functioning. These biomarkers are glycosylated hemoglobin, total cholesterol, systolic blood pressure (BP), ratio of forced expiratory volume at 1 second (FEV1) to forced vital capacity, serum creatinine, serum alkaline phosphatase, serum albumin, and C-reactive protein (CRP). These markers have been used in prior work and were found to significantly correlate with chronological age at $r > .10$; when combined using an algorithm developed to estimate biological age, these markers significantly predicted all-cause, cardiovascular, and cancer mortality (Levine 2013; Levine and Crimmins 2014a, b).

Our measure was based on Klemera and Doubal's (2006) proposed algorithm for generating an equation to measure what they called "biological age." This biological age calculation produces estimates that are linearly related to chronological age, with a slope of 1, an

intercept of 0, and residual deviation. As a result, for the population, mean biological age should equal mean chronological age. The equation used to calculate biological age (Eq. (1)) combines information on the participants' measured biomarker values (x_j), as well as the slope (k_j), intercept (q_j), and root mean squared error (s_j) from the equation of each biomarker (j) regressed on chronological age. Additionally, the equation also sets the variance (s_{BA}^2) for the difference between participants' biological and chronological ages.

For more information on the estimation of biological age using this equation as well as the development of the Klemera and Doubal algorithm, on which it is based, see Klemera and Doubal (2006) and Levine (2013).

$$BA = \frac{\sum_{j=1}^{m}(x_j \square q_j)\frac{k_j}{s_j^2} + \frac{CA}{s_{BA}^2}}{\sum_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2 + \frac{1}{s_{BA}^2}}. \quad (1)$$

Smoking and Obesity

Smoking status was self-reported in responses to two questions: (1) "Have you smoked at least 100 cigarettes during your lifetime?," and (2) "Do you currently smoke cigarettes?" Using a commonly employed classification of smoking status, participants were classified as (1) *current smokers* if they answered yes to both questions; (2) *former smokers* if they reported smoking at least 100 cigarettes during their lifetime, but did not currently smoke; and (3) *never smokers* if they answered no to both questions. Body mass index (BMI) was calculated as measured weight (kg) divided by measured height (meters) squared. Participants with a BMI between 25 and 29.9 were classified as overweight, and those with a BMI of 30 or above were classified as obese. Analyses were also conducted using a fourth category: underweight (BMI < 18.5). However, this additional classification did not produce noticeably different results, and thus we chose to collapse the underweight and normal weight categories.

Medications

Medication use was determined using self-reports. NHANES participants were asked whether they were taking prescribed medication for (1) high BP and (2) high cholesterol. Using their answers to these two questions, we recalculated biological age using imputed values for systolic BP and total cholesterol. If participants reported that they were taking prescribed medication for high BP, we recalculated their biological age by substituting 140 for their systolic BP if the level they had when measured was ≥ 140. If participants answered that they were taking prescribed medication for high cholesterol, we recalculated their biological age by substituting 200 for their total cholesterol if the level they had when measured was ≤ 200. For those reporting that they took both types of medication, we recalculated their biological age by using imputed levels for both systolic BP and total cholesterol.

Sociodemographic Characteristics

Race, education, sex, and chronological age were self-reported. Respondents were categorized into four race ethnicity groups: non-Hispanic white, non-Hispanic black, Hispanic, and other. Years of schooling, reflecting the highest grade attended, was used to create four education groups: (1) less than 12 years of schooling, (2) exactly 12 years of schooling, (3) 13–15 years of school, and (4) 16 or more years of schooling. We created a dummy variable for sex, with males coded as 0 and females coded as 1. Finally, subjects were categorized into three 20-year age categories based on whether they were young (20–39), middle-aged (40–59), or old (60–79).

Statistical Analysis

We ran all analyses using sampling weights and controlling for covariates, such as chronological age, race/ethnicity, and education, given that aging outcomes, smoking, and obesity have been shown to vary by such domains. We used ordinary least squares (OLS) regression, with the sample stratified into 20-year age categories, to measure the association between predicted biological age ($\hat{BA}$) and the interaction between period (1988–1994 and 2007–2010) and sex in order to determine (1) the biological age for young, middle-aged, and older males and females during the two periods; (2) whether persons in Period 2 had higher or lower biological ages compared with those in Period 1; and (3) whether period differences in biological age were similar for both sexes (Eq. (2)). Next, we sequentially added interactions with obesity, smoking, and obesity $\times$ smoking into the age-stratified OLS model (Eq. (2)) to examine whether accounting for changes in the levels and effects of these two modifiable health behaviors influenced period-level changes in biological age. Finally, we reran Eq. (2) using a measure of biological age that included imputed levels for participants on hypertension- and cholesterol-lowering medications to determine how much improvement in biological aging could be attributed to increased pharmaceutical therapy.

$$\hat{BA} = \alpha + \beta_1 Female + \beta_2 Period + \beta_3 Female \cdot Period + \beta_4 Age + \beta_5 Black + \beta_6 Hispanic \quad (2)$$
$$+ \beta_7 Other + \beta_8 Edu1 + \beta_9 Edu2 + \beta_{10} Edu3.$$

Results

Sample Description

As shown in Table 1, both chronological and biological age had means of 43.9 years; however, as expected, the standard deviation was slightly larger for biological age (16.2) than for chronological age (15.5). Overall, the sample comprises mostly whites (74.3 %), with only approximately 10 % non-Hispanic black, 11 % Hispanic, and 4.4 % other. Approximately 21 % of the sample never completed high school, 30 % had a high school diploma or GED, 25 % had some college education, and another 25 % completed at least four years of college. Slightly more than one-half of participants are female (50.6 %). Overall, the majority of subjects had a BMI less than 25 (39 %), 33.4 % were overweight (BMI = 25–29.9), and 27.4 % were obese (BMI = 30+). Slightly more than one-half of the sample had some history of smoking, with 25.1 % reporting that they were former smokers,

and 26.4 % reporting that they were current smokers. Approximately 15.8 % of participants reported being on hypertension medications, and 7.5 % reported being on cholesterol-lowering medications. Finally, 59.5 % of participants took part in NHANES between 1988 and 1994, and the other 40.5 % took part in NHNAES between 2007 and 2010.

Period Differences in Biological Age

Participants in all age and sex groups were biologically younger in Period 2, relative to Period 1 (Fig. 1). Biological age for females aged 20–39, 40–59, and 60–79 decreased by 0.63, 2.36, and 3.63 years, respectively, between the two periods; for males, biological age decreased by 1.27, 2.65, and 4.29 years from Period 1 to Period 2, for those aged 20–39, 40–59, and 60–79, respectively. Overall, females in every age group had significantly lower biological ages than males. For instance, for those aged 20–39, 40–59, and 60–79 in Period 1, the average biological age was 3.48, 2.21, and 1.31 years lower for females relative to males, respectively. Similarly, for those aged 20–39, 40–59, and 60–79 in Period 2, biological age was 2.84, 1.91, and 0.65 years lower for females compared with males, respectively.

Although females had consistently lower biological ages than males and all age/sex groups showed improvement between the two periods, results also suggest that sex differences decreased over time. The narrowing of the gender gap was not significant for the middle-aged group ($p = .299$), but it was statistically significant for the youngest age group ($p = .003$) and was marginally significant for the oldest age group ($p = .088$). Moreover, this change suggests that although both males and females had significant improvements in biological age between the two periods, the improvements for males were larger, contributing to a reduction in the gender gap.

Smoking, Obesity, and Biological Age

Before examining whether changes in smoking and obesity accounted for any of the period changes, we examined first how these factors related to biological age as well as how the prevalence of these two factors changed between the two periods. We used OLS regression, with predicted biological age status as the outcome, to estimate the impact of smoking and obesity (using an interaction term). We found that after adjusting for covariates—such as sex, chronological age, race/ethnicity, and education—smoking and obesity were strongly related to biological age (Fig. 2). As expected, both factors were associated with significantly higher biological ages. Furthermore, when we considered them simultaneously, results suggest that they have an additive effect. Compared with never smokers with a normal BMI, never smokers who were overweight had biological ages that were 1.17 years higher, and never smokers who were obese had biological ages that were 2.36 years higher. Similarly, former smokers who were normal weight had biological ages that were about 0.54 years higher than never smokers of normal weight, and current smokers who had normal BMIs had biological ages that were 1.15 years higher. Finally, compared with normal-weight participants who had never smoked, the average biological ages for overweight former smokers were 1.64 years higher; biological ages for overweight current smokers were 2.40 years higher; biological ages for obese former smokers were 2.76 years higher; and scores for obese current smokers were 3.73 years higher. Thus, on average, obese/current smokers

had biological ages that were equivalent to those of normal weight never smokers who were almost 4 years older.

Given the strong association between biological age and smoking and obesity, we estimated how the prevalence of these risk factors changed between the two periods. We used predicted probabilities with controls for age, race/ethnicity, and education to estimate the prevalence of current smoking and obesity for each age by sex category (Fig. 3). Among both males and females, obesity was significantly higher for all age groups in Period 2 compared with Period 1. From 1988–1992 until 2007–2010, obesity prevalence increased for males from 14.8 % to 30.9 % for those aged 20–39; 26.0 % to 35.5 % for those aged 40–59; and 22.8 % to 40.4 % for those aged 60–79. For females, prevalence of obesity increased from 20.1 % to 33.3 % for 20- to 39-year-olds; 29.7 % to 36.8 % for 40- to 59-year-olds; and 26.7 % to 42.6 % for 60- to 79-year-olds.

Among males, the proportion of current smokers significantly decreased for the two older age groups (40–59 and 60–79), with the largest decreases taking place among middle-aged men. During 1988–1992, current smokers made up 32.9 % and 17.2 % of the male population aged 40–59 and 60–79, respectively. However, by 2007–2010, current smokers accounted for 25.8 %, and 14.6 % of males aged 40–59 and 60–79, respectively. Among females, the prevalence of current smoking decreased for those aged 20–39 (from 30.4 % to 25.7 %) and for those aged 60– 79 (from 14.4 % to 11.4 %) between the two periods. However, there was no change in current smoking for females aged 40–59, for whom the prevalence of smoking was 22.5 % for both periods.

Contributions of BMI and Smoking to Decreases in Biological Age Over Time

Next, we examined period changes in biological age after adjusting for the change in the rate and the effect of smoking and obesity individually, as well as jointly, to determine whether changes in these factors could partially explain (1) changes in the aging of the population, and (2) why some age by sex groups experienced greater improvements than others.

When examining the relative role of changes in BMI and smoking prevalence to changes in biological age of the population (Fig. 4), we found that for younger adults, reductions in the prevalence of smoking contribute to decreases in biological age only for females. On the other hand, increases in BMI during this time counteracted the improvements in biological age. Overall, males and females ages 20–39 had biological ages that were 1.27 and 0.63 years lower in Period 2 compared with Period 1, respectively. However, when controlling for differences in the levels and effects of BMI between the two periods, we found that young males and females had biological ages that were 1.75 and 1.08 years lower in Period 2 compared with Period 1, respectively; thus, if the distribution and/or effect of BMI had not changed, males aged 20–39 would have had an additional 38.0 % decrease in biological age, while females aged 20–39 would have had an additional 72.1 % decrease in biological age. Conversely, the decreases in the prevalence (and possibly the effects of smoking) between Periods 1 and 2 contributed to approximately 12.5 % of the decrease in biological age for 20- to 29-year-old females. However, the improvements gained by reduced smoking did not offset the potential loss because of increasing BMI. For instance, if the effects and rates of both smoking and BMI had remained the same between the two periods, males would have

experienced an additional 31.2 % decrease in biological age, whereas females would have experienced an additional 61.3 % decrease in biological age.

Middle-aged females (40–59 years) did not benefit much from reductions in smoking but were somewhat hurt by increases in BMI. Overall, their biological ages were 2.36 years lower in Period 2 than in Period 1. Changes in smoking were found to account for only 5 % of this improvement. However, if BMI had remained constant across the two periods, the group would have had an extra 7.3 % decrease in biological age and if both smoking and BMI remained constant. Females aged 40–59 would have experienced an extra 7.3 % decrease in biological age. Conversely, middle-aged males benefited from reductions in smoking and were only marginally hurt by increases in BMI. Overall, middle-aged males had biological ages that were 2.65 years lower in Period 2 than in Period 1, and approximately 12.5 % of this was due to changes in the rate and/or effect of smoking. On the other hand, controlling for BMI in the model suggests that if BMI levels and effects had not changed between the two periods, males aged 40–59 would have had an additional 3.0 % decrease in biological age; if neither smoking nor BMI had changed, the decrease males aged 40–59 experienced between the two periods would have been reduced by 8.7 %.

Finally, decreases in smoking also appeared to have a large influence on decreases in biological age among older males, whereas changes in BMI had little to no effect. Our results showed that the decreasing prevalence and effects of smoking accounted for 16.0 % of the decrease in biological age among males aged 60–79. On the other hand, changes in BMI had little to no effect on biological age changes for males. Finally, for older females, changes in smoking and BMI appeared to counteract each other. Changes in smoking contributed to an estimated 10.7 % of the decrease in biological age among females aged 60–79, whereas changes in BMI contributed to a 4.3 % loss in potential health improvement. Furthermore, if both BMI and smoking had remained the same over the two periods, females would have experienced a decrease in biological age approximately 4 % less than they actually experienced.

Medication Use and Changes in Biological Age

For participants self-reporting that they took medication for either hypertension or hypercholesterolemia, we reestimated biological ages by setting total cholesterol and systolic blood pressure values just above the cutoffs used for prescribing such treatments. Using OLS regression and controlling for age race/ethnicity and education, we compared the sex-specific differences in biological age between the two periods using our original biological age estimate and the estimate incorporating medication usage (Fig. 5). Overall, it appears that increased medication use accounted for some of the improvements in biological age at every age for both sexes. However, medication use seemed to have the largest influence for older adults. Drug therapy to combat hypertension and hypercholesterolemia was associated with 9.4 % and 20.6 % of the decreases in biological age for males and females aged 20–39, respectively; among those aged 40–59, drug therapy was associated with 21.5 % and 22.0 % of the biological age decreases for males and females, respectively; and among those aged 60–79, medication use was associated with 71.3 % and 74.9 % of the biological age decrease for males and females, respectively.

Discussion

Over the past 20 years, the biological age of the U.S. population seems to have decreased for males and females across the age range. However, the degree of change has not been the same for men and women or by age. Our results showed that young males experienced greater improvements than did young females. This finding may explain why early adult mortality has decreased more for males than females, contributing to a narrowing of the gender mortality gap. Additionally, improvements were also larger for older adults than they were for younger adults.

The finding that some groups did not experience the same degree of declines in biological age as others could have important social and economic implications. For example, if the aging rate of younger adults is not slowing to the same degree as that of their older counterparts, the increases in life expectancy that we have witnessed over the last century could start to taper off. On the other hand, assuming that life expectancy continues to increase at the same rate due to our ability to treat those with illness, the population could experience an expansion rather than a compression of morbidity (Crimmins and Beltran-Sanchez 2011). This shift would translate to individuals spending more of their lives in poor health while contributing to a burden on social systems and increasing medical costs for individuals and programs such as Medicare (Daviglus et al. 2004).

Nevertheless, these issues can potentially be addressed before they arise. Our results suggest that modifiable health behaviors may partially explain why declines in biological age were more dramatic for older adults than younger adults between 1988–1994 and 2007–2010. For instance, our results suggest that decreases in smoking may have disproportionately benefited participants who were older, especially older men. Decreases in smoking prevalence were most pronounced for men aged 60–79, accounting for a significant proportion of their decrease in biological age. Conversely, the changes in biological age of younger adults, especially females, was the most negatively affected by increasing BMI over the past few decades. According to our results, if the proportion of overweight and obese adults (and the effects of being overweight or obese) had not increased over time, younger males would have had an additional 38 % decrease in biological age, and younger females might have had an additional 72 % decrease in biological age, compared with what they actually experienced.

Another explanation for the differences in change over the two periods between younger and older adults is medication use. Similar to previous findings (Cohen et al. 2010; Psaty et al. 2002), we showed that the proportion of persons—especially middle-aged and older adults taking cholesterol- and BP-lowering medications—has increased significantly over recent decades. Given that medications are typically administered at secondary or tertiary prevention stages, younger individuals will not experience benefits (Goetzel 2009) because most of them have yet to cross the clinical thresholds typically used for prescribing these medications, as evidenced when we compared biological ages before and after adjusting for medication usage. Although adjusting for medication use lessened the declines in biological age between the two periods only slightly among the 20- to 39-year-old population, medication use accounted for a large proportion of the declines in biological age for middle-

aged and older adults. Nevertheless, although adjusting for medication use contributed to changes in biological age estimates, it is not possible to differentiate between altering the underlying biological aging process and simply modifying levels of the target biomarkers used in estimating biological age.

Finally, another reason biological age may have improved more for older adults could be that despite variability apparent in young adults (Belsky et al. 2015), the variance in biological age may increase with chronological age. Assuming that negative effects of environment and genes accumulate over the lifetime (Phoenix and de Grey 2007), biological age estimates may not differentiate individuals to the same degree at younger ages. For example, in a heterogeneous population, it may be harder to detect differences in health earlier in life; however, as age and damage increase over the life course, the physiological profile of frail individuals (those with accelerated aging) and robust individuals (those with decelerated aging) may increasingly diverge.

Behavioral factors, such as smoking, obesity, and medication usage, explained some of the period differences in biological age, but a significant proportion of the decreases over time were unaccounted for. Other explanations for the improvements in population health that we were unable to test are better early-life and prenatal conditions and reductions in infectious disease. Studies have consistently supported the links between early-life conditions and later-life health and aging (Crimmins and Finch 2006; Finch and Crimmins 2004; Hayward and Gorman 2004; Heckman 2006). Over the twentieth century, U.S. childhood mortality drastically decreased (Singh and Yu 1996), which suggests an overall improvement in childhood health during this time. Declines in death rates were accompanied by reductions in exposure to infectious diseases (Finch and Crimmins 2004; Smith and Bradshaw 2006), better nutrition, and advances in clinical medicine (Fee 1991). These improvements in early-life health may directly affect the biological aging of these cohorts in later life.

Although we used race/ethnicity and education as covariates in the current analysis, due to their known associations with health behaviors and aging phenotypes, it may be beneficial to examine how biological age has changed by racial/ethnic and social strata over time. For instance, the stagnation for declines in biological age among young females may be driven by a subset of the population (e.g., low-educated whites). In addition to looking at changes by subpopulations, it will also be important to examine changes in the association between racial/ethnic or socioeconomic differences and biological age. For example, having low socioeconomic status may have been more detrimental in recent years than it was in the past, perhaps because social gradients in health behaviors have become stronger.

Limitations in the present study should be acknowledged. First, because of missing biomarker data, our analytic sample included approximately 70 % of NHANES participants aged 20–79, and those excluded from our analysis because of missing data were older, were more likely to be members of racial/ethnic minority groups, and had fewer years of schooling. Although the sample could affect our estimates, the patterns of missing data between the two periods do not appear to differ, and therefore, it should not bias our conclusions regarding changes in biological age over time. Finally, because NHANES collects only cross-sectional data, we were unable to compare changes across individuals or

attenuate for mortality selection. Nevertheless, our study is strengthened by its use of a large nationally representative data that includes multiple biomarker, sociodemographic, and health behavior measures.

In conclusion, we showed that the biological age of the population has improved over the past 20 years in the United States and that the largest improvements have been for males and older adults. We also showed that changes in smoking, obesity, and medication use may partly explain why improvements have not been as dramatic for U.S. females and young adults. In moving forward, it may be useful to examine how cumulative disadvantage linked to socioeconomic factors and psychosocial stressors have influenced changes in biological age over time. Overall, research examining how changing environments affect health and aging is important for our goal of extending healthy lifespan of the population.

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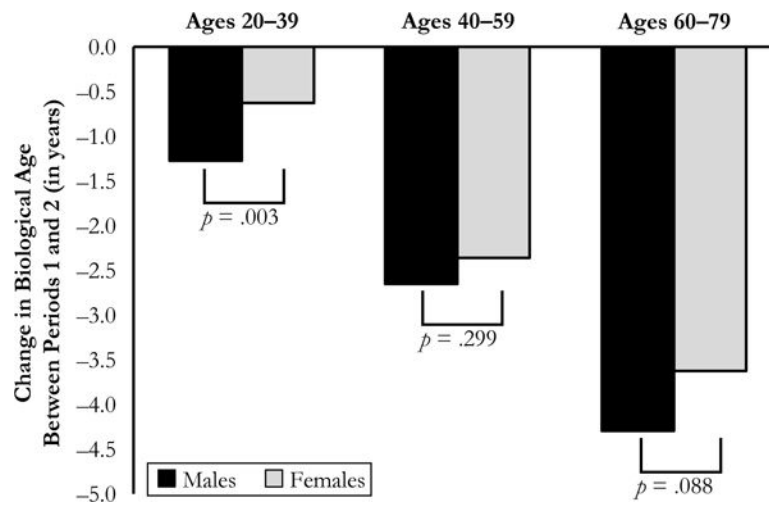
Fig. 1.
Changes in biological age between Period 1 (1988–1994) and Period 2 (2007–2010) by sex and age
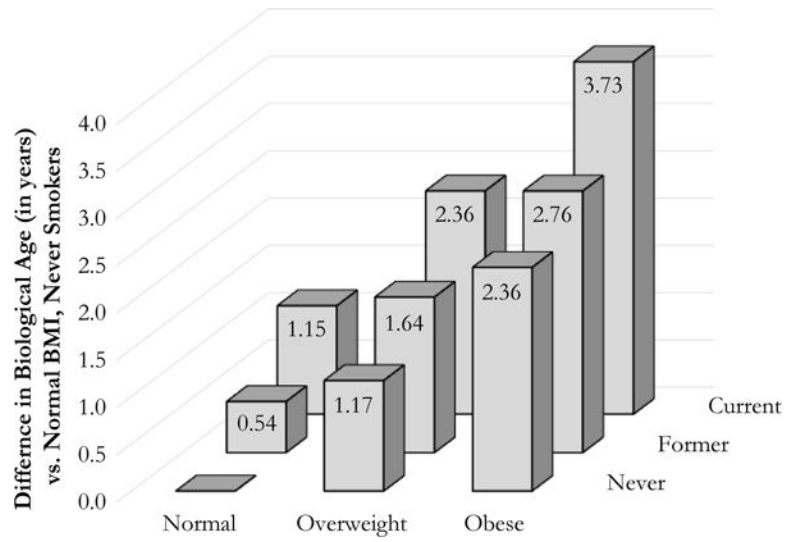
Fig. 2.
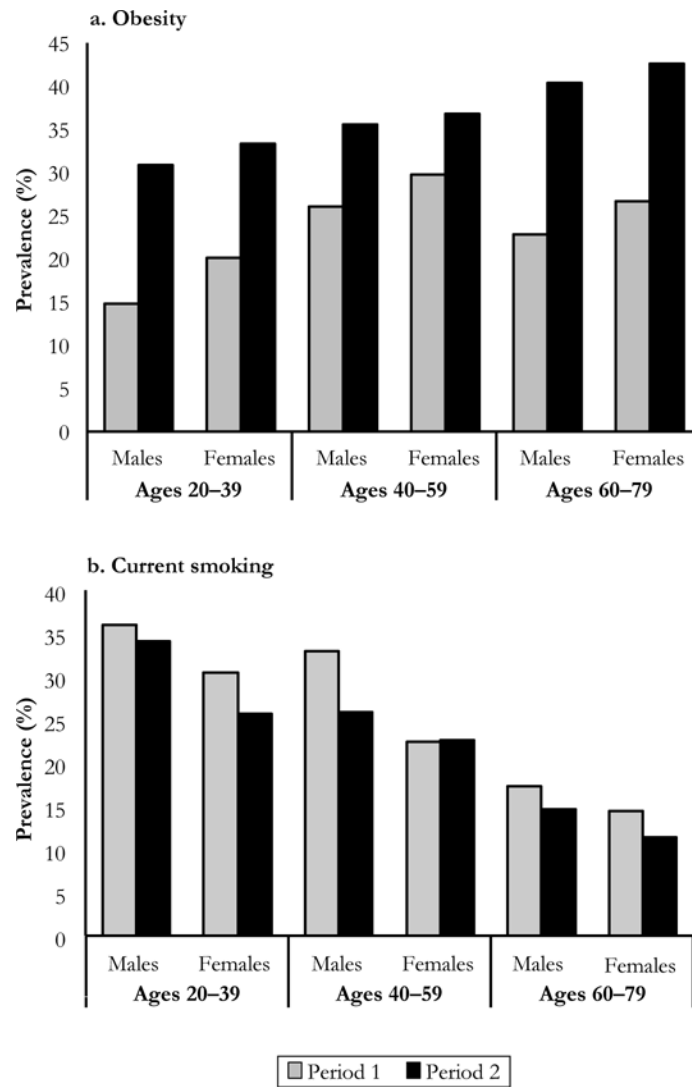Additions to biological age as a function of smoking and obesity

Fig. 3.
Changes in the prevalence of obesity (panel a) and current smoking (panel b) between
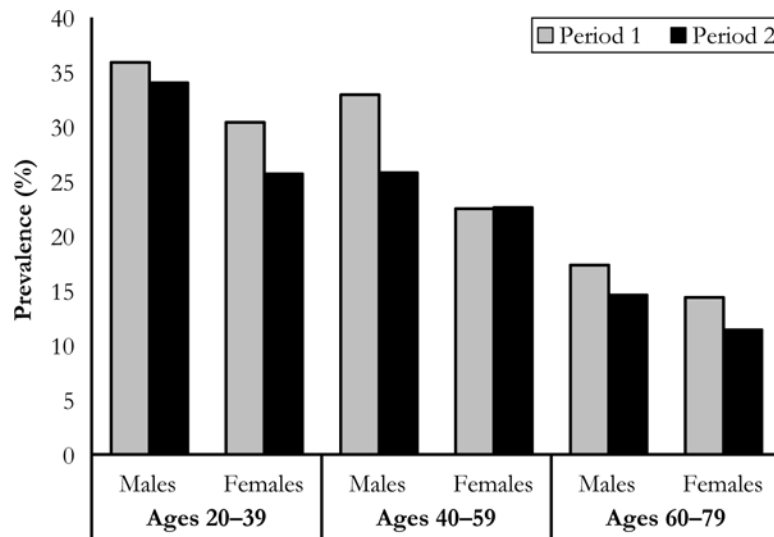Period 1 (1988–1994) and Period 2 (2007–2010)

Fig. 4.

Contributions of BMI and smoking to declines in biological age between **P**eriod 1 (1988–1994) and **P**eriod 2 (2007–2010). **Model 1:** Adjusted for covariates (race/ethnicity, socioeconomic status, and age)

Model 2: Adjusted for covariates plus the interaction with BMI. **Model 3:** Adjusted for covariates plus the interaction with smoking. **Model 4:** Adjusted for covariates plus the interaction with smoking, BMI, and the interaction between smoking and BMI
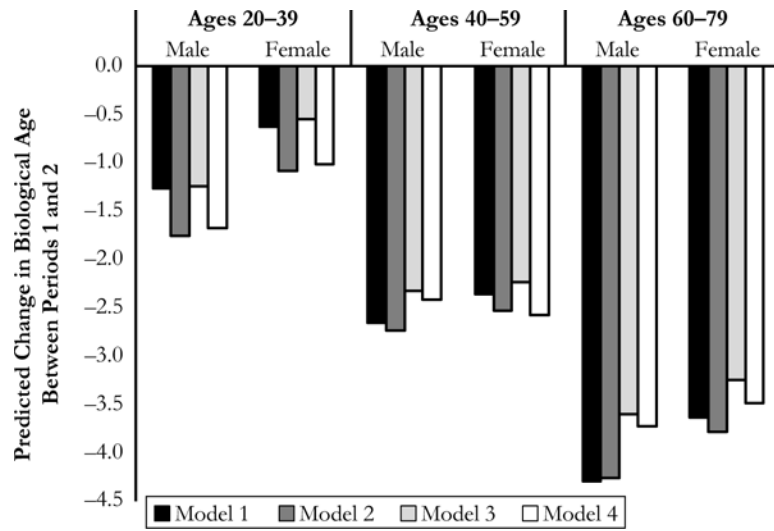
Fig. 5.
Medication use and declines in biological age

Table 1

Sample characteristics ($N = 21,575$)

Characteristic	Statistic (weighted)
Chronological Age (years) (mean)	43.91 (15.5)
Biological Age (years) (mean)	43.91 (17.0)
Female (%)	50.6
Race/Ethnicity (%)	
Non-Hispanic white	74.3
Non-Hispanic black	10.1
Hispanic	11.2
Other	4.4
Education (%)	
< 12 years	21.0
High school diploma/GED	29.9
Some college	24.7
College degree	24.5
BMI (%)	
Overweight	33.4
Obese	27.4
Smoking (%)	
Former	25.1
Current	26.4
Taking Anti-Hypertensive Medication	15.8
Taking Cholesterol-Lowering Medication Period (%)	7.5
1 (1988–1994)	59.5
2 (2007–2010)	40.5

Note: Standard deviations are shown in parentheses.