

Blood Pressure Trajectories in the 20 Years Before Death

João Delgado, PhD; Kirsty Bowman, MPH; Alessandro Ble, MD; Jane Masoli, MBChB; Yang Han, PhD; William Henley, PhD; Scott Welsh, MD; George A. Kuchel, MD; Luigi Ferrucci, MD, PhD; David Melzer, MBBCh, PhD

IMPORTANCE There is mixed evidence that blood pressure (BP) stabilizes or decreases in later life. It is also unclear whether BP trajectories reflect advancing age, proximity to end of life, or selective survival of persons free from hypertension.

OBJECTIVE To estimate individual patient BP for each of the 20 years before death and identify potential mechanisms that may explain trajectories.

DESIGN, STUDY, AND PARTICIPANTS We analyzed population-based Clinical Practice Research Datalink primary care and linked hospitalization electronic medical records from the United Kingdom, using retrospective cohort approaches with generalized linear mixed-effects modeling. Participants were all available individuals with BP measures over 20 years, yielding 46 634 participants dying aged at least 60 years, from 2010 to 2014. We also compared BP slopes from 10 to 3 years before death for 20 207 participants who died, plus 20 207 birth-year and sex-matched participants surviving longer than 9 years.

MAIN OUTCOMES AND MEASURES Clinically recorded individual patient repeated systolic BP (SBP) and diastolic BP (DBP).

RESULTS In 46 634 participants (51.7% female; mean [SD] age at death, 82.4 [9.0] years), SBPs and DBPs peaked 18 to 14 years before death and then decreased progressively. Mean changes in SBP from peak values ranged from -8.5 mm Hg (95% CI, -9.4 to -7.7) for those dying aged 60 to 69 years to -22.0 mm Hg (95% CI, -22.6 to -21.4) for those dying at 90 years or older; overall, 64.0% of individuals had SBP changes of greater than -10 mm Hg. Decreases in BP appeared linear from 10 to 3 years before death, with steeper decreases in the last 2 years of life. Decreases in SBP from 10 to 3 years before death were present in individuals not treated with antihypertensive medications, but mean yearly changes were steepest in patients with hypertension (-1.58 ; 95% CI, -1.56 to -1.60 mm Hg vs -0.70 ; 95% CI, -0.65 to -0.76 mm Hg), dementia (-1.81 ; 95% CI, -1.77 to -1.87 mm Hg vs -1.41 ; 95% CI, -1.38 to -1.43 mm Hg), heart failure (-1.66 ; 95% CI, -1.62 to -1.69 mm Hg vs -1.37 ; 95% CI, -1.34 to -1.39 mm Hg), and late-life weight loss.

CONCLUSIONS AND RELEVANCE Mean SBP and DBP decreased for more than a decade before death in patients dying at 60 years and older. These BP decreases are not simply attributable to age, treatment of hypertension, or better survival without hypertension. Late-life BP decreases may have implications for risk estimation, treatment monitoring, and trial design.

JAMA Intern Med. 2018;178(1):93-99. doi:10.1001/jamainternmed.2017.7023
Published online December 4, 2017.

← Invited Commentary page 100

+ Supplemental content

Author Affiliations: Epidemiology and Public Health, Institute of Biomedical and Clinical Science, University of Exeter Medical School, Exeter, United Kingdom (Delgado, Bowman, Ble, Masoli, Melzer); Health Statistics Research Group, Institute of Health Research, University of Exeter Medical School, St Luke's Campus, Exeter, United Kingdom (Han, Henley); University of Connecticut Center on Aging, University of Connecticut Health, Farmington (Welsh, Kuchel); Longitudinal Studies Section, National Institutes of Health, Harbor Hospital, Baltimore, Maryland (Ferrucci).

Corresponding Author: David Melzer, MBBCh, PhD, Epidemiology and Public Health, University of Exeter Medical School, Medical Research, RILD Level 3 South, Barrack Rd, Exeter EX2 5DW, UK (d.melzer@exeter.ac.uk).

Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) follow progressive upward trajectories from childhood to middle age, but blood pressure (BP) trends at older ages are unclear.¹ Several studies reported flattening of the upward trend or a decrease in BP at advanced ages,¹⁻⁴ although a few have reported continued BP increases.^{5,6} Blood pressure decreases in older age have been associated with poorer health, onset of dementia, and excess mortality.⁷⁻¹⁰ Hypothesized explanations for BP decreases in later life include (1) advancing age; (2) increasing end-of-life disease, especially heart failure, suggesting a link to the years before death rather than to age; (3) more intensive use of antihypertensive medications; or (4) that excess mortality of hypertensive individuals leaves healthy survivors with lower BP.^{1,10} Data to test these hypotheses are currently limited. Two analyses combined several longitudinal studies to estimate BP trajectories but did not observe the same individuals and did not follow up to death.^{1,11}

Observing individuals with multiple repeated BP measures over time could help clarify the causes underlying trends. If increasing end-of-life disease explains BP changes, then similar downward BP trajectories should not be observed in age- and sex-matched controls who die much later. For example, Rogers et al¹² compared 4-year BP changes in 404 patients with diabetes who died during follow-up against 3362 who survived and found greater BP decreases in those who died. Similar data on the general older population or longer-term BP trajectories in individual older patients are not available.

In this study, we used the population-based Clinical Practice Research Datalink (CPRD)¹³ to estimate clinically measured SBP and DBP trajectories for 20 years prior to death, for individuals dying at 60 years and older. Second, we compared the linear SBP trends for years 10 to 3 years before death in patients who died and age- and sex-matched controls who survived at least 9 years. These approaches aimed to separate age from end-of-life associations, and avoid healthy survivor biases.

Methods

Data Source

This study was approved by the Independent Scientific Advisory Committee for UK Medicines and Healthcare Products Regulatory Agency database research. Individual patient consent for this analysis was waived, as only deidentified routinely collected data were used, following CPRD approval for our research protocol. The CPRD is the UK National Health Service observational data service for research, covering 674 UK primary care practices.¹³ We used CPRD primary care electronic medical records linked to Hospital Episode Statistics data for hospitalizations, and UK Government Office for National Statistics death certificate data.¹⁴ Registration with primary care is nearly complete for older people in the UK: age and sex distribution data are similar to the UK population, and comparable for ethnicity and body mass index.^{13,15} The CPRD has good ascertainment of major diagnoses.^{13,15}

Key Points

Question Do blood pressures (BPs) decrease in older patients, and if so are decreases related to age, proximity to death, or better survival without hypertension?

Findings In a 20-year cohort analysis of medical records, systolic and diastolic BPs decreased for 14 to 18 years before death. Decreases were present in patients not treated for hypertension but were steepest in patients with hypertension, dementia, heart failure, and late-life weight loss.

Meaning Substantial BP decreases toward the end of life may have implications for treatment monitoring, and decreases in BP may also bias risk estimation and complicate trial design.

The 20-Year BP Trend Sample

For 20-year BP trends, we selected 54 856 individuals with death certificates or registered as deceased in their general practitioner practice, from January 1, 2010, to November 14, 2014. Patients were included if registered and remaining with a practice for 20 years prior to death. We excluded 773 patients younger than 60 years old at death and 7449 with BP recorded less than 6 times; 46 634 individuals met inclusion criteria. Age at death (range, 60-111 years) was classified into 60 to 69, 70 to 79, 80 to 89, and at least 90 years.

Matched Cohort of Dying vs Survivors (Last 10 to 3 Years of Life)

Separate groups were selected for comparing linear SBP trajectories from 10 to 3 years before death. The case group (n = 20 207) were at least 60 years old and died January 1, 2000, to November 14, 2005. Survivors were matched by year of birth, sex, and SBP at start of follow-up, but survived at least 9 years longer than paired cases (n = 20 207). Index date was date of death of cases. We aimed for a 1:1 case-survivor matching. Individuals were included if registered for 10 years prior to index date, with BP recorded in at least 3 studied years.

Blood Pressure Measurements

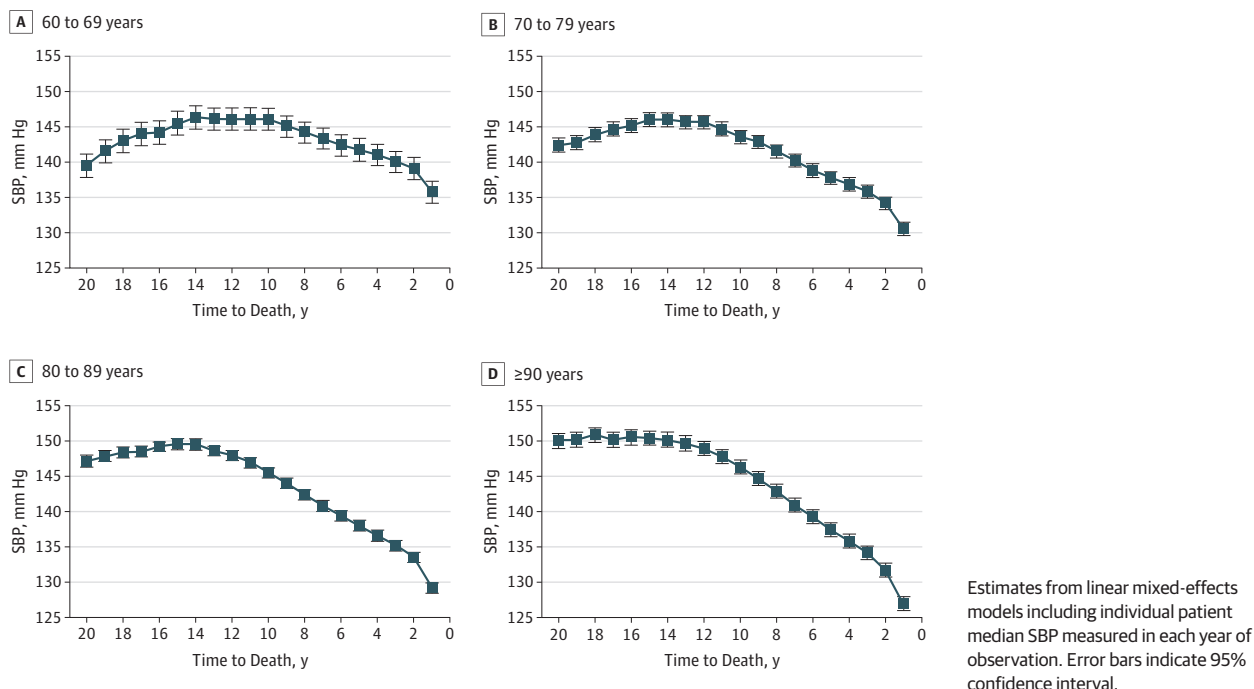
Blood pressures were measured during routine consultations and recorded by general practitioners, nurses, or other practice staff.¹³ National guidelines recommend a minimum of 2 consecutive measurements to ascertain elevated BP,^{16,17} but in CPRD a single BP measurement is recorded from each consultation, likely the measure considered of greatest clinical relevance.^{13,18}

Annual median SBPs and DBPs were calculated for each calendar year; these were based on a mean of 2.98 (range, 1-165) separate recorded BPs and were available for a mean (SD) of 12.5 (3.86) of 20 years observed. Based on clinical and statistical advice, we used median recorded BPs in each year to avoid biases that could arise from analyzing possibly skewed distributions from atypical measures, for example, recorded during acute clinical events.¹⁹

Diagnoses at the Time of Death

We investigated BP trend associations with hypertension and cardiovascular conditions (heart failure, atrial fibrillation, and

Figure 1. Estimated Mean Systolic Blood Pressure (SBP) in the 20 Years Prior to Death, by Age at Death (60-69, 70-79, 80-89, ≥90 Years)



stroke or transient ischemic attack) at any time before death, plus cumulative burden of disease, measured by the Charlson comorbidity index (CCI), and the Rockwood frailty index (RFI)^{20,21} adapted for electronic medical records. Hypertension diagnoses were removed from indexes to avoid circularity. The CCI was based on 16 diagnoses any time before death, and the RFI, on 36 diagnoses 15 years or less before death. Analysis compared first quintile (least comorbidity: CCI ≤2; RFI ≤0.09) with fifth quintile (most comorbidity: CCI ≥9; RFI ≥0.26) during 20-year follow-up.

Statistical Analyses of Trajectories

We used linear mixed-effects models to estimate trajectories of SBP and DBP. Trajectories were modeled as a function of years until death, after adjustment for calendar year of death and sex, the age at death (as years from individual's death age to mean death age of age group), study entry year, and individual-level Index of Multiple Deprivation (a postal code-based socioeconomic marker). Separate models were run for the 4 age-at-death groups. The linear mixed-effects model allowed for correlations between repeated measurements on the same individuals.²² The selected model for SBP used indicator variables for each year before death to account for the nonlinear form of trajectories (hereafter referred to as the *step function* model).

The step function model was compared with 5 more parsimonious mixed models with time to death represented by linear, quadratic, cubic, and piecewise linear functions (1 knot and 2 knots) (eFigure 1 in the Supplement). The Akaike information criterion was used to select the best-fitting model (details in eTable 1 in the Supplement). Figure 1 displays esti-

mated trajectories of SBP, constructed by plotting coefficients from the step function model for each time point t .

Analysis of Matched Cohort of Dying vs Survivors

Matched cohort analyses were performed by fitting linear mixed-effect models with BP as dependent variable and time as a linear function, adjusting for sex, age at index date, calendar year of index date, and Index of Multiple Deprivation. Interactions were tested using likelihood ratio tests and retained in the model if likelihood ratio $\chi^2 P < .05$.

Analyses of Diagnoses and Related Measures

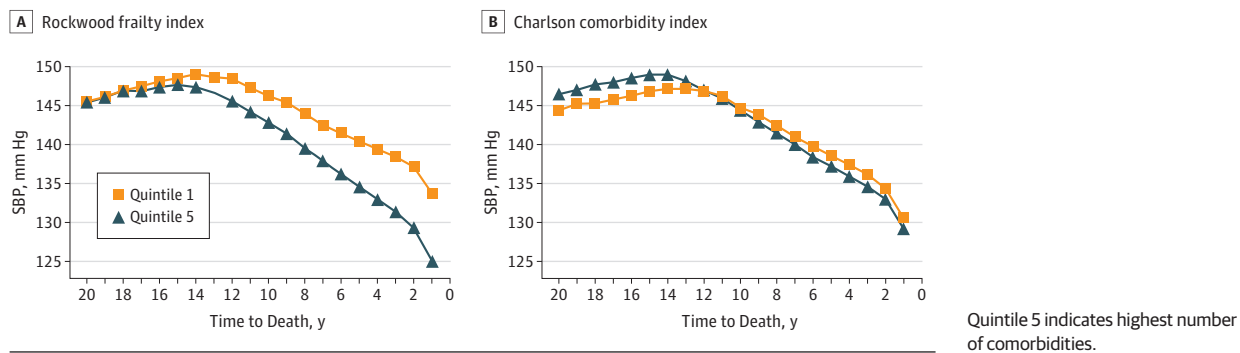
We analyzed independent associations between 15 common primary care diagnoses and change to SBP from 10 years to 3 years before death. This analysis included 39 370 individuals from our main cohort with information available to calculate changes in SBP. Medical conditions included asthma, atrial fibrillation, coronary heart disease, cancer, chronic kidney disease (stage 3-5), chronic obstructive pulmonary disease, dementia, depression, diabetes mellitus, epilepsy, heart failure, hypertension, severe mental conditions (psychoses),²³ stroke or transient ischemic attack, and hypothyroidism. We used multivariate regression analysis, adjusted for the same covariates as the main step function model. Sensitivity analyses assessed effects of antihypertensive treatment, weight loss, smoking status, and physical activity. Weight loss was defined as maximum recorded weight in the first 10 years of follow-up minus last weight in the last 3 years of life. Physical activity and smoking status were from records in the last 10 years (closest to death).

Table 1. Measured Change in Systolic Blood Pressure (SBP) From Peak to Year of Death, by Age Group^a

Age at Death, y	Overall SBP Change, mm Hg, Mean (95% CI)	Proportion of Sample With Decrease in SBP, mm Hg, %		
		≥10	≥20	≥30
60-69	-8.5 (-9.4 to -7.7)	48.4	31.8	17.1
70-79	-13.8 (-14.3 to -13.2)	58.2	39.7	24.1
80-89	-19.1 (-19.5 to -18.7)	67.1	49.9	32.7
≥90	-22.0 (-22.6 to -21.4)	71.2	55.0	39.1
Total	-17.4 (-17.7 to -17.2)	64.0	46.8	30.5

^a Decrease estimated as the difference between SBP values recorded at the age groups' peak (year 14 before death for age 60-69 and 70-79 years, year 15 for 80-89 years, and 18 for ≥90 years) and values recorded in the year prior to death; this was estimated based on the records of 27 918 individuals with data available in both years.

Figure 2. Mean Systolic Blood Pressure (SBP) in the 20 Years Before Death by Charlson Comorbidity Index and Adapted Rockwood Frailty Index Quintiles, Both Excluding Hypertension Diagnoses



All analyses were conducted using Stata 14. Two-sided *P* values were estimated using the mixed-effect models. The level of statistical significance used was $\alpha = .05$.

Results

A total of 46 634 individuals met the inclusion criteria for 20-year BP trajectory estimation. Women were 45.5% of those dying aged 60 to 69 years vs 64.6% of those dying aged at least 90 years (eTable 2 in the Supplement). Hypertension was diagnosed at any time before death in 55.2% of the youngest and 67.2% of the oldest, and heart failure, in 7.7% of the youngest vs 18.6% of the oldest.

Twenty years before death, estimated mean SBPs increased with increasing age at death (60-69 years, 139.5; 95% CI, 137.9-141.2 mm Hg; ≥90 years, 150.0; 95% CI, 149.0-151.1 mm Hg). All age-at-death groups initially experienced increasing SBP, reaching peak values and then declining with proximity to death (Figure 1). Peak SBPs occurred 14 years before death in those dying aged 60 to 69 years (mean peak SBP, 146.3; 95% CI, 144.7-148.0 mm Hg) to 18 years before death for those dying aged at least 90 years (mean peak SBP, 150.8; 95% CI, 149.8-151.9 mm Hg). In individuals with data on peak-year SBP and last year of life SBP (*n* = 27 918) (Table 1), mean SBP change ranged from -8.5 mm Hg (95% CI, -9.4 to -7.7) for dying at 60 to 69 years to -22.0 mm Hg (95% CI, -22.6 to -21.4) for those dying aged at least 90 years. Overall, 64.0% of individuals experienced SBP decrease of more than 10 mm Hg. Decreases in DBP (eFigure 2 in the Supplement) were proportionately similar to SBP decreases, although smaller in absolute numbers: for example, at 70 to 79 years, DBP decreased by a mean of 11.3 mm Hg, or 13.2%, from

peak values, compared with mean SBP decreases of 15.4 mm Hg, or 10.6% (eTable 3 in the Supplement).

We examined 20-year SBP trajectories by multimorbidity (Figure 2), using the CCI and adapted RFI (counting 36 common comorbidities), both excluding hypertension (see Methods). Overall trajectories appeared similar, with approximately 14-year linear decreases in SBP, but were a little steeper with more comorbidity on the RFI. Accounting for time-dependent effects of hypertension, atrial fibrillation, heart failure, and cancer diagnosis date, plus accumulating morbidities (CCI) in the last 20 years of life, changed SBP trends little (eFigure 3 in the Supplement).

Antihypertensive medication was prescribed to 85.1% of patients for at least 1 year during the analysis period: mean SBP changed by -20.8 mm Hg from peak to year of death in those treated vs -11.2 mm Hg in those not treated. Peak SBP occurred at a mean of 15 years before death in the treated vs 14 years in those not treated. Adjustment for antihypertensive treatment made little difference to the main model results (eFigure 4 in the Supplement).

Smoking status, alcohol consumption, and levels of physical activity measured in the 20 years prior to death had little association with SBP decreases (eFigure 5 in the Supplement). Weight loss (the difference between the maximum weight during the first 10 years of follow-up and weight in the final year) findings showed that patients losing at least 20 kg experienced a bigger absolute SBP decrease (mean, -24.87; 95% CI, -24.90 to -24.83 mm Hg) compared with those who did not lose weight (mean, -15.91; 95% CI, -15.94 to -15.87 mm Hg).

The trajectories of SBP from 10 to 3 years before death appeared linear, so our analyses focused on this period, excluding accelerated SBP decreases in the last 2 years before death.²⁴

Table 2. Annual Changes in Systolic Blood Pressure (SBP) by Diagnosis, From 10 to 3 Years Prior to Death

Diagnosis	Change in SBP per Year, mm Hg (95% CI)		Interaction Term Effect Size ^a
	Diagnosis Present	Diagnosis Absent	
Cardiovascular disease	-1.57 (-1.53 to -1.62)	-1.44 (-1.42 to -1.47)	0.12
Hypertension	-1.58 (-1.56 to -1.60)	-0.70 (-0.65 to -0.76)	0.87
Heart failure	-1.66 (-1.62 to -1.69)	-1.37 (-1.34 to -1.39)	0.29
Atrial fibrillation	-1.66 (-1.63 to -1.69)	-1.36 (-1.33 to -1.39)	0.30
Stroke or transient ischemic attack	-1.58 (-1.54 to -1.62)	-1.44 (-1.41 to -1.46)	0.14
Dementia	-1.81 (-1.77 to -1.87)	-1.41 (-1.38 to -1.43)	0.41

^a Interaction term for the effect of each diagnosis on yearly change in SBP: a separate analysis provided *P* values, using a mixed-effects model with additional adjustment for the respective diagnosed conditions and (diagnosis of condition multiplied by year to death). *P* < .001 for all.

Table 3. Dying vs Survivor^a Estimated Slopes of Change in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in Years 10 to 3 Before Death

Age at Death, y	Change in SBP per Year (95% CI), mm Hg		Interaction Term ^b	
	Case	Survivor	Effect Size	<i>P</i> Value
SBP				
60-69	-0.18 (-0.26 to -0.09)	-0.05 (-0.13 to 0.03)	0.14	.02
70-79	-0.48 (-0.54 to -0.44)	-0.16 (-0.21 to -0.11)	0.33	<.001
80-89	-0.69 (-0.75 to -0.63)	-0.17 (-0.23 to -0.11)	0.52	<.001
≥90	-0.94 (-1.25 to -0.63)	0.04 (-0.30 to 0.38)	0.96	<.001
DBP				
60-69	-0.50 (-0.55 to -0.46)	-0.36 (-0.41 to -0.32)	0.13	<.001
70-79	-0.64 (-0.66 to -0.61)	-0.50 (-0.53 to -0.48)	0.13	<.001
80-89	-0.63 (-0.66 to -0.60)	-0.47 (-0.50 to -0.44)	0.16	<.001
≥90	-0.49 (-0.65 to -0.34)	-0.38 (-0.56 to -0.22)	0.10	.37

^a Survived at least 9 more years, with matching for initial (10 y) SBP.

^b Interaction term testing for dying vs survivors control status in the slope of blood pressure decrease in the 10 years prior to index date: a separate analysis provided *P* values, using a mixed-effects model with additional adjustment including for case/control and (case/control multiplied by year to death).

Systolic BP decreased in individuals who did not have hypertension, heart failure, atrial fibrillation, or stroke or transient ischemic attack (all diagnosed at any time before death) (Table 2), but decreases were greater with each condition, especially hypertension: mean annual SBP decrease of -1.6 vs -0.7 mm Hg without hypertension (interaction term, *P* < .001).

Independent associations of 15 chronic conditions against change in SBP from 10 to 3 years before death were tested by means of multiple regression. The mean overall adjusted change (regression constant) in SBP was -0.55 (95% CI, -0.71 to -0.39) mm Hg per annum, with larger decreases with hypertension, dementia, and heart failure (eTable 4 in the Supplement), followed by atrial fibrillation, chronic kidney disease, and chronic obstructive pulmonary disease. The estimated independent SBP decrease with coronary artery disease alone (ie, adjusted for hypertension and all other conditions) and cancer was a little smaller than the overall trend.

Last, a matched cohort analysis of cases who died vs survivors who lived at least another 9 years focused on linear BP trends from 10 to 3 years to death. Decreases in SBP were more marked in cases (Table 3).

Discussion

Previous studies have suggested that mean SBPs plateau or decrease in older populations, but the mechanisms involved were unclear.^{1,11} In this analysis, we estimated individual patient BP trajectories for 20 years to death, in a large representative older population. For all age-at-death groups studied, mean SBP in-

creased to a peak 18 to 14 years before death. Peak values were followed by substantial BP decreases. Overall, 64.0% of patients experienced SBP decreases of greater than 10 mm Hg. Decreases in SBP were present without antihypertensive treatment but were steepest in patients with treated hypertension, dementia, heart failure, and late-life weight loss. To our knowledge, this analysis provides the first evidence that SBP and DBP decrease for 14 or more years before death.

Worldwide, BPs have decreased over recent decades, but from 2005 to 2015, SBP in high-income countries reportedly decreased by 4 mm Hg or less in older groups (eTable 4 in Zhou et al²⁵). This is a small difference compared with trajectories that we found observing individual patients in the years before death, and background trend effects would have been present in both our cases and survivors in the matched cohort analysis.

Limitations

We have used recorded BP measures from routine clinical practice rather than standardized research approaches,²⁶ but obtaining research BPs in representative older populations for 20 years to death would be challenging. We have necessarily limited the analysis to patients with sufficient numbers of recorded pressures. It may be that this selected patients targeted by primary care for more frequent BP measures, but our sensitivity analysis including patients with at least 1 year of recorded BPs (rather than ≥5 separate years) made little difference to results (eFigure 6 in the Supplement), suggesting that measurement frequency is not a major influence on the trajectories observed.

Treatment for hypertension has been hypothesized as explaining late-life decreased BPs, but decreasing BP slopes were also present in those without hypertension diagnoses or antihypertensive medication prescriptions. Changes in antihypertensive prescriptions over time are often complex. Unfortunately, CPRD records often contain limited detail and accounting for dose equivalence of different preparation combinations is complex. Changes in medication are recorded without explanation, including whether they are related to decreasing BP near death, raising the possibility of confusing cause and effect. We have therefore not accounted for specific treatment changes when modeling changing treatment status over time. As noted herein, however, decreases in BP were present in those not receiving antihypertensive treatment, indicating that treatment and treatment changes cannot provide a complete explanation for the trajectories observed. Toward the end of life it is common for antihypertensive medication use to be lessened or withdrawn, but this should have increased BPs rather than causing decreases.

In most models, we tested associations between diagnoses at any time during study periods rather than accounting for date of diagnosis. This was because many disease conditions in older people develop over protracted periods long before diagnosis, and because BP measurements may have been more likely when clinical events including diagnoses occurred. Also, correlations over time before death may be difficult to validly disentangle. More extensive testing of potential correlates of the BP decreases may be justified in cases in which systematic data on baseline and changing exposure status over time are available, although distinguishing between cause and effect can be challenging: for example, decreasing weight may merely reflect the effects of the disease processes leading to death.

Major strengths of our analysis include using large-scale data on essentially complete older populations because virtually all older people in the UK are registered with primary care. This population representativeness removes potentially serious healthier and cognitively intact response and retention biases frequently seen in volunteer studies of older groups.⁹⁻¹¹ The inclusion of data over a 20-year period before death is also exceptional.

As noted in the Introduction, several previous studies (but not all) reported a plateau or decrease in BP late in life, although there have been few published data on individual trajectories before death. Molander et al²⁷ and Londos et al²⁸ described steeper decreases in BP with incident dementia and lower Mini-Mental State Examination scores.²⁸ Londos et al²⁸ described an association between lower SBP and diagnoses of depression, polypharmacy, and increased comorbidities. Rogers et al¹² found a steeper decrease in both SBP and DBP in patients with a diagnosis of diabetes. Decreasing SBP has also been associated with an increase in all-cause mortality and cardiovascular mortality.²⁹ In our analysis, we found that longer-term decreases in BP occurred with or without the presence of hypertension, heart failure, atrial fibrillation, or stroke. Additionally, these decreases occurred at all studied levels of comorbidity. These results are in line with studies that found decreases in indicators of cognitive (although not SBP), sensory, and physical health to be associated with time to death.³⁰⁻³²

More work is needed to elucidate the specific mechanisms involved in late-life BP dynamics. Such studies may also be useful in addressing ways of optimizing the clinical care of older patients who experience decreasing BP. Also, downward BP trajectories before death have the potential to introduce reverse causation or “reverse epidemiology” effects in risk analyses, yielding misleading associations between BP and outcomes in older patients. Predeath trajectories of BP might also introduce heterogeneity into trials of interventions.

Conclusions

In this large-scale analysis of individual patient trajectories, mean SBP and DBP decreased for 14 or more years before death. Decreases in SBP were present in individuals not treated with antihypertensive medications but were steepest in patients with treated hypertension, dementia, heart failure, and late-life weight loss. The trajectories may bias risk estimation in later life, and introduce heterogeneity into clinical trials of interventions. These findings may also have implications for treatment monitoring in later life. More work is needed to better elucidate the mechanisms explaining these long-term BP decreases toward the end of life.

ARTICLE INFORMATION

Accepted for Publication: September 10, 2017.

Published Online: December 4, 2017.

doi:10.1001/jamainternmed.2017.7023

Author Contributions: Drs Delgado and Melzer had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Delgado, Bowman, Ble, Masoli, Henley, Kuchel, Ferrucci, Melzer.

Acquisition, analysis, or interpretation of data:

Delgado, Bowman, Ble, Masoli, Han, Henley, Welsh, Kuchel, Melzer.

Drafting of the manuscript: Delgado, Masoli, Han, Henley, Melzer.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Delgado, Masoli, Han, Henley.

Obtained funding: Kuchel, Melzer.

Administrative, technical, or material support:

Bowman, Masoli, Kuchel.

Study supervision: Henley, Kuchel, Melzer.

Conflict of Interest Disclosures: No disclosures are reported.

Funding/Support: This work was supported by the National Institute for Health Research (NIHR) School for Public Health Research (SPHR) Ageing Well programme. The SPHR is funded by the NIHR. Dr Masoli is supported by NIHR Doctoral Research Fellowship DRF-2014-07-177. Dr Henley received support from the NIHR Collaboration for Leadership in Applied Health Research and Care for the South West Peninsula. This analysis was also supported in part by the Intramural Research Program of the

National Institute of Aging, National Institutes of Health, Baltimore, Maryland.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The views expressed in this publication are those of the authors and not necessarily those of the UK National Health Service, the NIHR, or the Department of Health.

REFERENCES

1. Wills AK, Lawlor DA, Matthews FE, et al. Life course trajectories of systolic blood pressure using

- longitudinal data from eight UK cohorts. *PLoS Med*. 2011;8(6):e1000440.
2. Molander L, Lövheim H. Blood pressure change and antihypertensive treatment in old and very old people: evidence of age, sex and cohort effects. *J Hum Hypertens*. 2013;27(3):197-203.
 3. Kristjansson K, Sigurdsson JA, Lissner L, Sundh V, Bengtsson C. Blood pressure and pulse pressure development in a population sample of women with special reference to basal body mass and distribution of body fat and their changes during 24 years. *Int J Obes Relat Metab Disord*. 2003;27(1):128-133.
 4. Landahl S, Bengtsson C, Sigurdsson JA, Svanborg A, Svärdsudd K. Age-related changes in blood pressure. *Hypertension*. 1986;8(11):1044-1049.
 5. Pearson JD, Morrell CH, Brant LJ, Landis PK, Fleg JL. Age-associated changes in blood pressure in a longitudinal study of healthy men and women. *J Gerontol A Biol Sci Med Sci*. 1997;52(3):M177-M183.
 6. Franklin SS, Gustin W IV, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure: the Framingham Heart Study. *Circulation*. 1997;96(1):308-315.
 7. Skoog I, Lernfelt B, Landahl S, et al. 15-year longitudinal study of blood pressure and dementia. *Lancet*. 1996;347(9009):1141-1145.
 8. Stewart R, Xue Q-L, Masaki K, et al. Change in blood pressure and incident dementia: a 32-year prospective study. *Hypertension*. 2009;54(2):233-240.
 9. Starr JM, Inch S, Cross S, MacLennan WJ, Deary IJ. Blood pressure and ageing: longitudinal cohort study. *BMJ*. 1998;317(7157):513-514.
 10. Hakala SM, Tilvis RS. Determinants and significance of declining blood pressure in old age: a prospective birth cohort study. *Eur Heart J*. 1998;19(12):1872-1878.
 11. Muniz-Terrera G, Bakra E, Hardy R, Matthews FE, Lunn D; FALCon Collaboration Group. Modelling life course blood pressure trajectories using Bayesian adaptive splines. *Stat Methods Med Res*. 2016;25(6):2767-2780.
 12. Rogers MAM, Ward K, Gure TR, et al. Blood pressure trajectories prior to death in patients with diabetes. *Diabetes Care*. 2011;34(7):1534-1539.
 13. Herrett E, Gallagher AM, Bhaskaran K, et al. Data resource profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol*. 2015;44(3):827-836.
 14. Williams T, van Staa T, Puri S, Eaton S. Recent advances in the utility and use of the General Practice Research Database as an example of a UK primary care data resource. *Ther Adv Drug Saf*. 2012;3(2):89-99.
 15. Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol*. 2010;69(1):4-14.
 16. O'Brien E, Asmar R, Beilin L, et al; European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*. 2003;21(5):821-848.
 17. National Institute for Health and Care Excellence (NICE). Hypertension in adults: diagnosis and management. NICE; 2011. Updated November 2016. <https://www.nice.org.uk/guidance/cg127/chapter/1-Guidance#measuring-blood-pressure>. Accessed August 20, 2017.
 18. Walley T, Mantgani A. The UK General Practice Research Database. *Lancet*. 1997;350(9084):1097-1099.
 19. Choi PT. Statistics for the reader: what to ask before believing the results. *Can J Anaesth*. 2005;52(suppl 1):R46.
 20. Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing*. 2016;45(3):353-360.
 21. Khan NF, Perera R, Harper S, Rose PW. Adaptation and validation of the Charlson Index for Read/OXMIS coded databases. *BMC Fam Pract*. 2010;11(1):1-7.
 22. Alley DE, Metter EJ, Griswold ME, et al. Changes in weight at the end of life: characterizing weight loss by time to death in a cohort study of older men. *Am J Epidemiol*. 2010;172(5):558-565.
 23. Melzer D, Delgado J, Winder R, Masoli J, Richards S, Ble A. The Age UK almanac of disease profiles in later life (August 2015). London, England: Age UK; 2015. https://www.ageuk.org.uk/Documents/EN-GB/For-professionals/Research/Age_UK_almanac_FINAL_9Oct15.pdf?dtrk=true. Accessed October 18, 2017.
 24. Ravindrarajah R, Hazra NC, Hamada S, et al. Systolic blood pressure trajectory, frailty and all-cause mortality over 80 years of age: cohort study using electronic health records. *Circulation*. 2017;135(24):2357-2368.
 25. Zhou B, Bentham J, Di Cesare M, et al; NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet*. 2017;389(10064):37-55.
 26. Kornegay C, Segal J. Selection of data sources. In: Velentgas P, Dreyer NA, Nourjah P, et al, eds. *Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide*. Rockville, MD: Agency for Healthcare Research and Quality; 2013:1-208. <https://www.ncbi.nlm.nih.gov/books/NBK126195/>. Accessed October 18, 2017.
 27. Molander L, Gustafson Y, Lövheim H. Longitudinal associations between blood pressure and dementia in the very old. *Dement Geriatr Cogn Disord*. 2010;30(3):269-276.
 28. Londos E, Passant U, Gustafson L. Blood pressure and drug treatment in clinically diagnosed Lewy body dementia and Alzheimer's disease. *Arch Gerontol Geriatr*. 2000;30(1):35-46.
 29. Satish S, Zhang DD, Goodwin JS. Clinical significance of falling blood pressure among older adults. *J Clin Epidemiol*. 2001;54(9):961-967.
 30. Diehr P, Williamson J, Burke GL, Psaty BM. The aging and dying processes and the health of older adults. *J Clin Epidemiol*. 2002;55(3):269-278.
 31. Gerstorff D, Ram N, Lindenberger U, Smith J. Age and time-to-death trajectories of change in indicators of cognitive, sensory, physical, health, social, and self-related functions. *Dev Psychol*. 2013;49(10):1805-1821.
 32. Diehr PH, Thielke SM, Newman AB, Hirsch C, Tracy R. Decline in health for older adults: five-year change in 13 key measures of standardized health. *J Gerontol A Biol Sci Med Sci*. 2013;68(9):1059-1067.