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Systolic blood pressure decline in very old individuals is explained by deteriorating health

Longitudinal changes from Umeå85+/GERDA

Bodil Weidung, MD, PhD[a,b,*], Annika Toots, PT, PhD[a,c], Peter Nordström, MD, PhD[a], Bo Carlberg, MD, PhD[d], Yngve Gustafson, MD, PhD[a]

Abstract

Declining systolic blood pressure (SBP) is common in very old age and is associated with adverse events, such as dementia. Knowledge of factors associated with SBP changes could explain the etiology of this decline in SBP. This study investigated longitudinal changes in socioeconomic factors, medical conditions, drug prescriptions, and assessments and their associations with SBP changes among very old followed individuals.

The study was based on data from the Umeå85+/Gerontological Regional Database (GERDA) cohort study, which provided cross-sectional and longitudinal data on participants aged 85, 90, and ≥95 years from 2000 to 2015. Follow-up assessments were conducted after 5 years. The main outcome was a change in SBP. Factors associated with SBP changes were assessed using multivariate linear regression models.

In the Umeå85+/GERDA study, 454 surviving individuals underwent follow-up assessment after 5 years. Of these, 297 had SBP measured at baseline and follow-up. The mean change ± standard deviation in SBP was −12 ± 25 mm Hg. SBP decline was associated independently with later investigation year ($P = .009$), higher baseline SBP ($P < .001$), baseline antidepressant prescription ($P = .011$), incident acute myocardial infarction during follow-up ($P = .003$), new diuretic prescription during follow-up ($P = .044$), and a decline in the Barthel Activities of Daily Living index at follow-up ($P < .001$).

In conclusion, SBP declines among very old individuals. This decline seems to be associated with initial SBP level, investigation year, and health-related factors.

Abbreviations: ACE = angiotensin-converting enzyme, ADL = activities of daily living, AMI = acute myocardial infarction, BMI = body mass index, BP = blood pressure, GDS = Geriatric Depression Scale, GERDA = Gerontological Regional Database, MMSE = Mini-Mental State Examination, SBP = systolic blood pressure, SSRI = selective serotonin reuptake inhibitor.

Keywords: aged 80 and over, cohort effect, cohort studies, hypertension, hypotension, longitudinal studies

1. Introduction

Declining systolic blood pressure (SBP) is common in old age[1–12] and has been shown to precede dementia,[11,12] cardiovascular events,[1] and mortality[1–3,5,13] by 1 to 10 years. In very old age (≥80 years), about two-thirds of individuals seem to experience SBP declines of at least 5 mm Hg over 5 years,[11] and the average SBP decline may be 1.5 to 2.9 mm Hg/year.[3,4,11] SBP decline has been associated with greater age,[1,4,7] male sex,[7] higher initial SBP,[1,4,7] medication use,[14] antihypertensive treatment,[4] poor health,[1,4,14] depression,[15,16] anxiety,[17] ventricular hypertrophy,[4] socioeconomic status,[14] serum lipid concentrations,[4] and transfer to care facility residence.[4] SBP may also decline with the Mini-Mental State Examination (MMSE) score.[8,11,18,19] Although previous results indicate that health-related factors are important, the ability of individual diseases, drug prescriptions, and assessments to predict SBP changes has not to our knowledge been tested in multivariate models.

Adequate mapping of normal SBP changes in very old age could provide a reference for the detection of pathological changes. Knowledge of factors associated independently with SBP decline might help to explain the etiology of SBP decline. In addition, this knowledge might aid the identification of individuals at risk of such decline and could be used in future prevention studies. Previous knowledge from studies of younger

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[a] Department of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, Umeå, [b] Department of Public Health and Caring Sciences, Geriatric Medicine, Uppsala University, Uppsala, [c] Department of Community Medicine and Rehabilitation, Physiotherapy, [d] Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden.

[*] Correspondence: Bodil Weidung, Department of Public Health and Caring Sciences, Geriatric Medicine, Uppsala University, 751 85 Uppsala, Sweden (e-mail: bodil.weidung@pubcare.uu.se).

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old individuals may not apply to the very old population, in which blood pressure trajectories differ and the risk of adverse drug reactions is greater.[20] The aim of this study was to investigate 5-year changes in SBP and associated factors in a representative sample of very old individuals followed for 5 years.

2. Methods

2.1. Setting

This study was based on data from the Umeå 85+/Gerontological Regional Database (GERDA) study, conducted by Umeå University, Sweden, in collaboration with Åbo Akademi University and the University of Vaasa, Finland. The objectives of the Umeå85+/GERDA study are to increase knowledge about the living conditions of very old people, increase quality of life in this population, and provide data to support planning of future elder care. Cross-sectional and longitudinal data were collected from 3 population-based age cohorts (85, 90, and ≥95 years) in 2000 to 2002, 2005 to 2007, 2010 to 2012, and 2015.

2.2. Design

Every other individual aged 85 years and all individuals aged 90 and ≥95 years living in 8 municipalities in northern Sweden and western Finland, as listed in population registers, were eligible to participate in the Umeå85+/GERDA study. Eligible participants were sent written information about the study by mail and were contacted by phone thereafter. Trained assessors collected information at participants' homes using tests, assessment scales, measurements, and a standardized questionnaire. Information was also collected from relatives and health care professionals as proxy respondents, and from medical records of general practitioners, hospitals, and care institutions. Informed consent was obtained from all included participants. A close relative also gave consent in each case of diagnosed or suspected cognitive impairment. Data collection is repeated every 5 years, with the addition of a new cohort and longitudinal follow-up data to the database. The Umeå 85+/GERDA study has been approved by the Regional Ethical Review Board in Umeå (§99–326, §05–063M, §09–178M, §2015–296–31) and the Ethics Committee of Vaasa Central Hospital (§05–87, §10–54).

2.3. Participants

All participants in the Umeå 85+/GERDA study were included in the present study. Data from the first participation were used as the baseline assessment. In cases of multiple follow-up measurements, only data from the first follow-up were used, except for 3 participants with missing baseline SBP values. Data from these participants' second and third follow-up measurements were used as their baseline and follow-up assessments, respectively. A subsample was formed including all participants with baseline and follow-up SBP values to investigate longitudinal SBP changes.

2.4. Measures

The outcome of the present study was the difference in SBP between the baseline and follow-up measurements (ΔSBP). SBP was measured according to a standardized procedure with the participant in the supine position using a calibrated, manual sphygmomanometer and stethoscope after 5 minutes rest.

Information on cohabitation, education, smoking status, diagnoses, medical conditions, and drug prescriptions was collected from the respondents and from medical records. The total number of drugs included all prescribed drugs according to medical records and other drugs taken regularly, as reported by respondents. An experienced specialist in geriatric medicine verified all medical diagnoses using all available data, including assessments and medical records. Dementia and depression were diagnosed according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision.[21] Body mass index (BMI; kg/m^2) was calculated from height and weight, measured using a measuring stick and a calibrated portable scale, respectively. The MMSE was used to assess cognition on a scale of 0 to 30, with higher scores indicating better cognitive function.[22] The Geriatric Depression Scale (GDS) was used to assess depressive symptoms on a scale of 0 to 15, with higher scores indicating more depressive symptoms.[23] Incomplete GDS scores with ≥10 items answered were imputed using individual mean scores. Dependency in personal activities of daily living (ADL) was assessed on a scale of 0 to 20 using the Barthel ADL index, with higher scores indicating lesser degrees of dependence in personal ADLs.[24] Gait speed from a standstill was measured over 2.4 m at usual pace, with the use of a walking aid, but no personal assistance or support from nearby structures, permitted. The mean of 2 measurements was used.

2.5. Statistical analysis

Different statistical tests were used to analyze cross-sectional and longitudinal differences between samples. Differences at baseline between participants with and without baseline SBP values were compared using Student *t* test for numerical variables and Pearson Chi-squared test for nominal variables. Differences at baseline between followed participants with and without SBP measurement were compared using Student *t* test for numerical, parametric variables; the Mann–Whitney *U* test for numerical, nonparametric variables; and Pearson Chi-squared test for categorical variables. Among followed participants, differences between baseline and follow-up measurements were analyzed using the paired-samples *t* test for numerical, parametric variables; Wilcoxon signed-rank test for numerical, nonparametric variables; and McNemar test for nominal variables.

Changes in all variables (Δvariables) were calculated by subtracting baseline from follow-up values. For binary variables, the derived Δvariables took 3 possible values, treated as ordinal: –1 (removed diagnosis or discontinued drug prescription during follow-up), 0 (no change), and 1 (new diagnosis or drug prescription during follow-up). ΔCerebrovascular disease (CVD), Δacute myocardial infarction (AMI), and Δhip fracture, characterized by events occurring during follow-up rather than prevalence were binary.

Multiple linear regression was used to predict ΔSBP in the subsample. The associations of variables with ΔSBP were tested using linear regression in 2 models; model 1 included baseline variables and model 2 included Δvariables. The models were constructed with baseline age, sex, investigation year, baseline SBP, and variables associated with ΔSBP at $P \leq .15$ according to Student *t* test and bivariate correlations [model 1: care facility residency, CVD, rheumatic disorder, and antidepressant prescription; model 2: Δdiabetes, Δcongestive heart failure (CHF), Δatrial fibrillation, ΔAMI, Δdementia, Δangiotensin-converting enzyme (ACE) inhibitor prescription, Δbeta blocker prescription, Δdiuretic prescription, Δbenzodiazepine prescription, Δneuroleptic prescription, Δtotal number of drugs, ΔMMSE score, ΔGDS score, and ΔBarthel ADL index]. Multicollinearity between variables was tested using

bivariate correlations. The variables of baseline depression and warfarin prescription were removed from model 1 due to high degrees of correlation with antidepressant prescription and atrial fibrillation ($r = 0.569$ and $r = 0.568$, respectively); the variable with the strongest association with ΔSBP was kept. No other correlation exceeded $r = 0.5$. Model 3 was constructed with baseline age, sex, investigation year, baseline SBP, and predictors associated with ΔSBP at $P \leq .15$ from models 1 and 2 (rheumatic disorder, antidepressant prescription, ΔAMI, ΔBarthel ADL index, Δdiuretic prescription, and Δneuroleptic prescription). Residuals were distributed normally in all models. Some covariates had missing data and analyses were restricted to individuals with complete data.

All analyses were performed using SPSS software (version 23.0; IBM Corporation, Armonk, NY). All analyses were 2-tailed and $P < .05$ was considered to be significant.

3. Results

Figure 1 shows the flow of participants in the Umeå85+/GERDA study and the present substudy. The participation rate in the Umeå85+/GERDA study was 84.3% of invited individuals, with 1425 first-time participants. Of these, 454 individuals participated in the 5-year follow-up and 916 were deceased. Baseline and follow-up SBP measurements were performed in 297 participants, who were included in the subsample.

Table 1 summarizes cross-sectional data for all first-time Umeå85+/GERDA participants and longitudinal data for all followed participants. Many baseline diseases and drug prescriptions, including CHF, atrial fibrillation, dementia, hip fracture, depression, angina pectoris, and prescriptions for ACE inhibitors, diuretics, benzodiazepines, antidepressants, opioids, neuroleptics, paracetamol, and statins, differed significantly between followed and not followed participants; all except statin prescription were less prevalent among followed participants. All baseline assessment scores differed significantly between followed and not followed participants [SBP, mean ± standard deviation (SD): 152 ± 22 vs 144 ± 23 mm Hg; $P < .001$].

During follow-up, almost one-third (31%) of community-living participants became care facility residents. Most drug prescriptions and diseases, such as dementia (+27%), CHF (+18%), angina pectoris (+16%), depression (+13%), atrial fibrillation (+10%), hip fracture (+10%), CVD (+7%), and diabetes (+5%), became more prevalent. Of the drug prescriptions, only statin prescription became less prevalent. BMI, MMSE score, Barthel ADL index, and gait speed decreased, while GDS score increased.

Table 2 summarizes longitudinal data for participants in the subsample of followed participants with SBP measured at baseline and follow-up. Table 3 and Fig. 2 show ΔSBPs according to 10 mm Hg categories of baseline SBP. Mean ± SD follow-up time was 4.7 ± .33 years. The mean ± SD baseline and follow-up

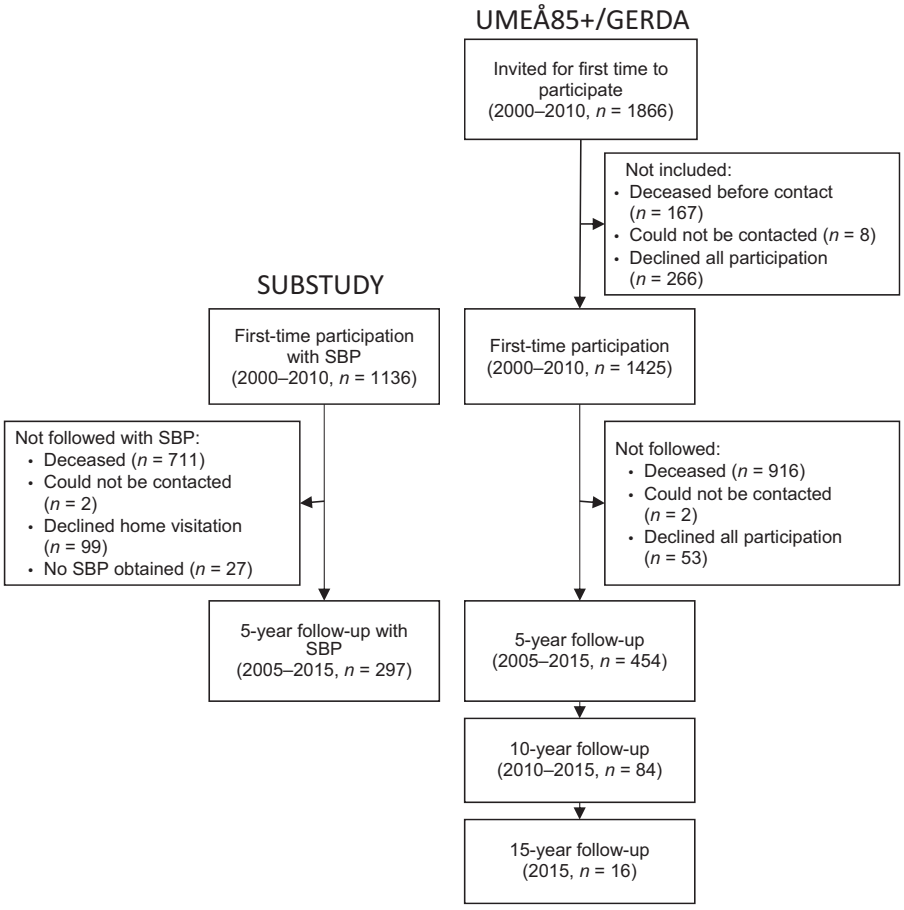

Figure 1. Flow chart of participation in the Umeå85+/GERDA study and in the present substudy. GERDA = Gerontological Regional Database; SBP = systolic blood pressure.

Table 1

Characteristics of Umeå85+/GERDA study participants.

Characteristic	First-time participants		Followed participants			P†
	N	Baseline*	n	Baseline*	5-year follow-up*	
Investigation year	1425	2006.1 ± 4.0	454	2005.8 ± 3.8	2010.3 ± 3.8	
Age, y	1425	89.4 ± 4.7	454	87.3 ± 3.4	91.9 ± 3.4	
Sex (female)	1425	979 (69)	454	322 (71)	322 (71)	
Care facility residency	1353	530 (39)	411	59 (14)	182 (44)	<.001
Living alone	1314	1044 (80)	387	284 (73)	316 (82)	<.001
Education <8 y	1143	841 (74)	377	257 (68)	257 (68)	1
Current smoker	1227	39 (3)	369	13 (4)	9 (2)	.34
Former smoker	1225	344 (28)	367	117 (32)	102 (28)	.03
Diagnoses and medical conditions						
Diabetes, ever	1425	206 (15)	454	55 (12)	76 (17)	<.001
Congestive heart failure	1425	446 (31)	454	80 (18)	162 (36)	<.001
Atrial fibrillation	1425	329 (23)	454	69 (15)	113 (25)	<.001
AMI, previous year	1425	40 (3)	450	8 (2)	7 (2)	1
Cerebrovascular disease	1425	305 (21)	454	89 (20)	121 (27)	<.001
Cancer, previous 5 y	1424	178 (13)	451	53 (12)	63 (14)	.28
Dementia	1422	277 (20)	453	29 (6)	151 (33)	<.001
Hip fracture, ever	1425	270 (19)	454	50 (11)	94 (21)	<.001
COPD	1425	244 (17)	454	71 (16)	91 (20)	<.001
Depression	1424	478 (34)	452	110 (24)	169 (37)	<.001
Rheumatic disorder, ever	1425	190 (13)	454	64 (14)	78 (17)	<.001
Angina pectoris	1425	396 (28)	454	107 (24)	180 (40)	<.001
Drug prescription						
ACE inhibitors	1424	271 (19)	452	62 (14)	90 (20)	<.001
Beta blockers	1424	461 (32)	452	157 (36)	180 (40)	.02
Calcium channel blockers	1424	217 (15)	452	78 (17)	85 (19)	.48
Diuretics	1424	704 (49)	452	194 (43)	217 (48)	.03
Benzodiazepines	1424	361 (25)	452	93 (21)	116 (26)	.02
Antidepressants	1424	275 (19)	452	58 (13)	100 (22)	<.001
ASA	1424	558 (39)	452	172 (38)	170 (38)	.93
Opioids	1424	210 (15)	452	49 (11)	49 (11)	1
Neuroleptics	1424	177 (12)	452	26 (6)	32 (7)	.42
Warfarin	1424	114 (8)	452	35 (8)	41 (9)	.31
Paracetamol	1424	496 (35)	452	99 (22)	174 (38)	<.001
NSAIDs	1424	88 (6)	449	31 (7)	24 (5)	.37
Statins	1421	136 (10)	449	59 (13)	36 (8)	<.001
Total no. of drugs	1388	7.7 ± 4.6	436	6.4 ± 4.3	8.7 ± 4.6	<.001
Assessments						
Body mass index	1114	25.4 ± 4.4	316	25.7 ± 3.9	25.0 ± 3.9	<.001
MMSE score	1133	23 (17–27)	308	26 (23–28)	22 (16–26)	<.001
GDS score	949	3 (2–5)	283	2 (1–4)	3 (2–5)	.001
Barthel ADL index	1208	19 (13–20)	345	20 (19–20)	18 (12–20)	<.001
Gait speed, m/s	876	0.53 ± 0.23	240	0.65 ± 0.23	0.50 ± 0.18	<.001
Systolic blood pressure, mm Hg	1136	145.9 ± 23.3	297	151.6 ± 22.3	139.6 ± 20.0	<.001
Diastolic blood pressure, mm Hg	1132	74.1 ± 11.3	293	75.5 ± 10.6	71.1 ± 12.3	.001

ACE = angiotensin-converting enzyme, ADL = activities of daily living, AMI = acute myocardial infarction, ASA = acetylsalicylic acid, COPD = chronic obstructive pulmonary disease, GDS = Geriatric Depression Scale, MMSE = Mini-Mental State Examination, NSAID = nonsteroidal anti-inflammatory drug.

* Data are presented as n (%), mean ± standard deviation, or median (interquartile range).

† *P* values for differences between baseline and follow-up calculated using the paired-samples *t* test, Wilcoxon signed-rank test, and McNemar test.

SBP was 152 ± 22 and 140 ± 20 mm Hg. The mean ± SD ΔSBP during follow-up was –12 ± 25 mm Hg (2.6 ± 5.4 mm Hg/year). Most variables changed significantly during follow-up.

The prevalence of several baseline characteristics and longitudinal changes was significantly lower in the subsample than in other followed participants (numbers shown for variables in model 3): investigation year (mean ± SD: 2005.4 ± 3.5 vs 2006.5 ± 4.1, $P = .005$), proportion of women (65.7% vs 80.9%, $P = .001$), care facility residency, hip fracture, depression, antidepressant prescription (8.8% vs 21%, $P < .001$), neuroleptic prescription (3.4% vs 10.2%, $P = .006$), warfarin prescription, number of drugs, Δdementia, Δhip fracture, Δparacetamol, ΔMMSE score, and ΔBarthel ADL index [median (interquartile range): –1 (–3 to 0) vs –3 (–10 to –1), $P < .001$]. Baseline antidepressant prescriptions in the subsample were selective serotonin reuptake inhibitors (SSRIs; n = 20, 77%), tricyclic antidepressants (n = 2, 8%), and "other" (n = 5, 20%, including mianserin and mirtazapine). One participant had both SSRI and "other" prescriptions at baseline. The main reason for the failure to obtain baseline or follow-up SBP measurement was decline of home visitation (n = 137, 87%). Three (2%) participants terminated their participation before SBP measurement, and SBP was not measured in 17 (11%) participants for unknown reasons.

Table 2

Characteristics of followed participants with baseline and follow-up systolic blood pressure measurements.

Characteristic	n	Baseline*	5-y follow-up*	P†
Investigation year	297	2005.4 ± 3.5	2010.0 ± 3.5	
Age, y	297	87.4 ± 3.3	92.0 ± 3.4	
Sex (female)	297	195 (66)	195 (66)	
Care facility residency	291	33 (13)	113 (39)	<.001
Living alone	292	211 (72)	237 (81)	<.001
Education <8 y	293	193 (66)	193 (66)	1
Current smoker	297	10 (3)	8 (3)	.72
Former smoker	295	96 (33)	82 (28)	.04
Diagnoses and medical conditions				
Diabetes, ever	296	36 (12)	50 (17)	<.001
Congestive heart failure	296	56 (19)	117 (40)	<.001
Atrial fibrillation	295	48 (16)	79 (27)	<.001
AMI, previous year‡	295	4 (1)	5 (2)	1
Cerebrovascular disease	295	54 (18)	73 (25)	<.001
Cancer, previous 5 y	296	39 (13)	44 (15)	.55
Dementia	296	18 (6)	82 (28)	<.001
Hip fracture, ever	296	26 (9)	42 (14)	<.001
COPD	296	51 (17)	64 (22)	<.001
Depression	296	58 (20)	102 (35)	<.001
Rheumatic disorder, ever	295	36 (12)	48 (16)	<.001
Angina pectoris	296	73 (25)	127 (43)	<.001
Drug prescription				
ACE inhibitors	296	42 (14)	63 (21)	.001
Beta blockers	296	112 (38)	130 (44)	.03
Calcium channel blockers	296	53 (18)	57 (19)	.67
Diuretics	296	126 (43)	147 (50)	.02
Benzodiazepines	296	61 (21)	77 (26)	.04
Antidepressants	296	26 (9)	53 (18)	<.001
ASA	296	118 (40)	118 (40)	1
Opioids	296	27 (9)	32 (11)	.49
Neuroleptics	296	10 (3)	18 (6)	.10
Warfarin	296	31 (10)	37 (13)	.26
Paracetamol	296	61 (21)	99 (33)	<.001
NSAIDs	293	18 (6)	16 (6)	.85
Statins	293	39 (13)	29 (10)	.08
Total no. of drugs	296	6.1 ± 4.2	8.8 ± 4.5	<.001
Assessments				
Body mass index	290	26 ± 3.9	25 ± 3.8	<.001
MMSE score	291	26 (24–28)	23 (17–26)	<.001
GDS score	267	3 (1–4)	3 (2–5)	.001
Barthel ADL index	294	20 (19–20)	19 (15–20)	<.001
Gait speed, m/s	234	0.63 ± 0.24	0.50 ± 0.18	<.001
Systolic blood pressure, mm Hg	297	152 ± 22	140 ± 20	<.001
Diastolic blood pressure, mm Hg	293	76 ± 11	71 ± 12	<.001

ACE = angiotensin-converting enzyme, ADL = activities of daily living, AMI = acute myocardial infarction, ASA = acetylsalicylic acid, COPD = chronic obstructive pulmonary disease, GDS = Geriatric Depression Scale, MMSE = Mini-Mental State Examination, NSAID = nonsteroidal anti-inflammatory drug.

* Data are presented as n (%), mean ± standard deviation, or median (interquartile range).

† *P* values for differences between baseline and follow-up calculated using the paired-samples *t* test, Wilcoxon signed-rank test, and McNemar test.

‡ During the entire follow-up period, 31 (10.5%) participants had AMIs.

Table 3

Average systolic blood pressure of followed participants at baseline and follow-up, according to 10 mm Hg categories of baseline systolic blood pressure*.

SBP category	N	Baseline	5-y follow-up
<120	11	109 ± 6	129 ± 14
120–129	25	122 ± 3	131 ± 20
130–139	45	132 ± 3	135 ± 19
140–149	53	142 ± 3	137 ± 16
150–159	47	152 ± 3	142 ± 18
160–169	48	162 ± 3	141 ± 19
170–179	29	171 ± 2	146 ± 22
180–189	26	181 ± 2	145 ± 22
≥190	13	207 ± 17	156 ± 25

SBP = systolic blood pressure.

* SBP is presented as mean ± standard deviation, in mm Hg.

Table 4 summarizes the results of the linear regression models. In model 1, only investigation year, baseline SBP, and antidepressant prescription were associated independently with ΔSBP. In model 2, investigation year, age, baseline SBP, ΔAMI, and ΔBarthel ADL index were associated independently with ΔSBP. In model 3, ΔSBP was associated independently with investigation year, baseline SBP, baseline antidepressant prescription, ΔAMI, ΔBarthel ADL index, and Δdiuretic prescription during follow-up. Baseline SBP had the largest standardized beta coefficient (model 3: −0.66). Significant regression equations were found [model 1: $F[8, 288] = 30.815$, $P < .001$, $r^2 = 0.461$; model 2: $F[18, 247] = 15.483$, $P < .001$, $r^2 = 0.530$; model 3: $F[10, 282] = 29.878$, $P < .001$, $r^2 = 0.497$].

4. Discussion

In this longitudinal study of very old individuals, mean SBP declined during the 5-year follow-up. In a multivariate model,

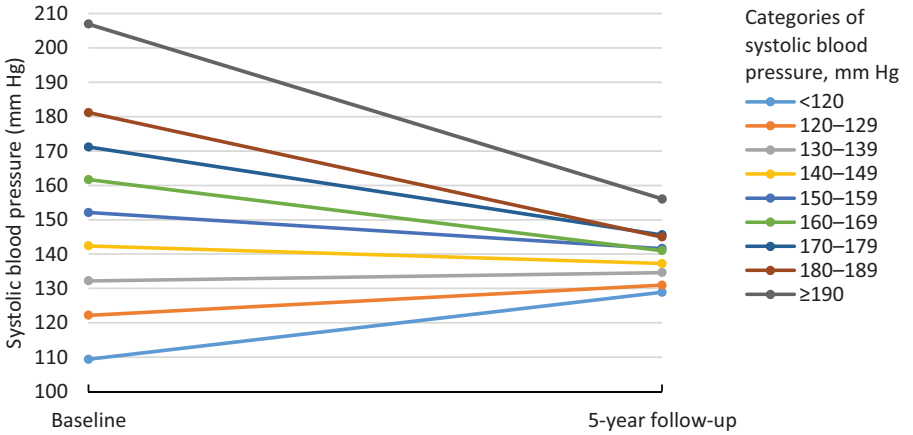

Figure 2. Average systolic blood pressure of followed participants at baseline and the 5-year follow-up, according to 10 mm Hg categories of baseline systolic blood pressure.

Table 4

Multivariate associations with systolic blood pressure change*.

	Unstandardized B	SE	Standardized beta	*P*
Model 1 (n = 297)				
(Constant)	1329.94	641.09		.04
Investigation year	−0.63	0.32	−0.09	.05
Age	0.35	0.34	0.05	.30
Sex (female vs male)	3.60	2.36	0.07	.13
SBP, mm Hg	−0.75	0.05	−0.67	<.001
Care facility residency	1.95	3.69	0.03	.60
Cerebrovascular disease	−0.14	2.89	−0.002	.96
Rheumatic disorder	5.85	3.37	0.08	.08
Antidepressants	−11.96	3.91	−3.06	.002
Model 2 (n = 266)				
(Constant)	2162.07	685.17		.002
Investigation year	−1.07	0.34	−0.15	.002
Age	0.84	0.37	0.11	.024
Sex (female vs male)	3.36	2.42	0.06	.17
SBP, mm Hg	−0.71	0.05	−0.64	<.001
ΔDiabetes	5.05	4.71	0.05	.29
ΔHeart failure	−0.92	2.69	−0.02	.73
ΔAtrial fibrillation	−2.12	3.32	−0.03	.53
ΔAMI	−8.79	3.66	−0.11	.02
ΔDementia	−0.56	3.36	−0.01	.87
ΔACE inhibitors	−4.39	3.19	−0.06	.17
ΔBeta blockers	−3.44	2.59	−0.06	.19
ΔDiuretics	−3.80	2.50	−0.07	.13
ΔBenzodiazepines	1.94	2.89	0.03	.50
ΔNeuroleptics	−9.10	4.70	−0.09	.05
ΔTotal number of drugs	−0.27	0.33	−0.04	.42
ΔMMSE score	0.41	0.31	0.08	.19
ΔGDS score	−0.19	0.45	−0.02	.68
ΔBarthel ADL index	0.73	0.32	0.12	.03
Model 3 (n = 293)				
(Constant)	1667.84	624.37		.008
Investigation year	−0.81	0.31	−0.11	.009
Age	0.61	0.33	0.08	.063
Sex (female vs male)	3.09	2.27	0.06	.18
SBP, mm Hg	−0.75	0.05	−0.66	<.001
Rheumatic disorder	5.50	3.22	0.07	.09
Antidepressants	−9.85	3.83	−0.11	.01
ΔAMI	−10.12	3.44	−0.12	.003
ΔBarthel ADL index	0.86	0.24	0.16	<.001
ΔDiuretics	−4.44	2.19	−0.09	.04
ΔNeuroleptics	−5.75	4.40	−0.06	.19

ACE = angiotensin-converting enzyme, ADL = activities of daily living, AMI = acute myocardial infarction, GDS = geriatric depression scale, MMSE = mini-mental state examination, SBP = systolic blood pressure, SE = standard error.

* Coefficients and *P* values were calculated using multiple linear regression.

longitudinal decline in SBP was associated independently with later investigation year, higher baseline SBP level, baseline antidepressant prescription, incident AMI during follow-up, new diuretic prescription during follow-up, and declining Barthel ADL index during follow-up.

4.1. Longitudinal trends

The average SBP decline of 2.6 mm Hg/year during the follow-up period in this study is in accordance with findings of previous longitudinal studies, where average SBP decline has been reported to be 1.5 to 2.9 mm Hg.[3,4,11] Most medical conditions and drug prescriptions increased, whereas BMI, MMSE score, Barthel ADL index, and gait speed decreased. However, followed participants were healthier than average at baseline, according to a comparison with all first-time Umeå85+/GERDA participants, likely due to survival bias. For instance, very small proportions of followed participants had dementia, depression, or neuroleptic prescriptions, or were care facility residents at baseline, compared with all first-time Umeå85+/GERDA participants, probably due to the high mortality risks associated with these factors.[25–27] Similarly, baseline SBP, which is an indicator of increased survival among very old individuals,[28–30] was higher among followed participants than among all first-time Umeå85+/GERDA participants. Longitudinal trends in some variables (diabetes, CVD, chronic obstructive pulmonary disease, rheumatic disease, and beta blocker prescription) may have been less affected by survival bias, as baseline prevalences were similar to those among all first-time Umeå85+/GERDA participants. Some drug prescriptions that did not increase (e.g., those for neuroleptics, calcium channel blockers, opioids, warfarin, and nonsteroidal anti-inflammatory drugs) are associated with adverse drug reactions in old age,[31,32] and the stable trends may indicate awareness of this risk among prescribing doctors.[33]

4.2. Factors associated with SBP change

In line with previous studies,[1,4,7] the present study demonstrated a strong influence of baseline SBP on SBP change, which may be attributed in part to regression toward the mean. SBP declined with later investigation year, indicating a cohort effect, which is in accord with previous findings from cross-sectional stud-

ies.[7,10,34,35] Several health-related factors associated independently with SBP change in the present study. The final multivariate model explained about half of the variation in SBP change, and uninvestigated factors may also be important.

Some previous findings were not repeated in the present study. Age was not associated independently with SBP change in the final model in the present study, in contrast to results from previous studies, including Umeå85+/GERDA.[1,4,7] However, those studies did not involve adjustment for health-related variables or the cohort effect, which seem to confound the association between age and SBP change in old individuals.[10,14] Similarly, SBP change was not associated independently with sex, care facility residence, or changing MMSE score or depressive symptoms, in contrast to findings from previous studies,[4,8,11,16,18,19] also possibly due to confounding of health-related variables, such as dependence in ADL, which is related closely to these factors.[36,37] Socioeconomic indicators were associated significantly with SBP change in a previous study,[14] but not in the present study, probably due to the use of different indicators (previous occupation and deprivation index of residential area vs education in the present study).

Different classes of antidepressant have been found to shift autonomic regulatory control over the heart in different directions, independently of underlying depressive disorder. SSRIs, which formed the most commonly prescribed antidepressant drug class in the present study, may decrease cardiac sympathetic control and reduce SBP.[38,39] Alternatively, the association may be explained by underlying conditions for which antidepressants are prescribed, such as depression, which was correlated strongly with antidepressant prescription in the present study, or anxiety.[15,17]

The blood pressure lowering effect of incident AMI during follow-up may be mediated by impaired cardiac function with secondary heart failure, treatment, or secondary prevention. AMI may also contribute to the previous observation of an increased mortality risk after SBP decline.[1–3,5,13,40]

The blood pressure lowering effect of new diuretic prescription is most likely therapeutic. However, discontinued or new prescriptions for ACE inhibitors, beta blockers, and calcium channel blockers were not associated significantly with SBP change in this study. These drugs may be prescribed predominantly for different indications, such as hypertension, atrial fibrillation, and CHF, and their effects on SBP may differ according to indication.

The association between changing Barthel ADL index and SBP change may be due to a common factor, such as the development of dementia or another cerebrovascular pathology.[10,11,41] Decreasing SBP and the ability to perform personal ADLs may also be consequences of debilitating end-stage cardiac disease, although CHF was not associated significantly with SBP change in the present study.

4.3. Prevention

Several health-related variables could be targeted for prevention of SBP decline, which would have obvious direct benefits other than the maintenance of stable SBP. However, prevention of associated variables may not influence SBP decline or related adverse outcomes, as these relationships may not be causal.[1,3] Furthermore, high SBP may also be associated with increased risks of adverse outcomes.[20,28,42–44]

Prevention of AMI is already implemented in clinical practice and involves control of cardiovascular risk factors, such as hypertension and hypercholesterolemia, although incidence rate reductions are not as large in very old age as in middle age.[45,46] Depression may be treated with nonpharmacological interventions, such as high-intensity functional exercise and social activities.[47–49] Physical activity may also improve dependency in personal ADL.[50]

4.4. Limitations

As SBP was measured with participants in the supine position in this study, values may be higher than if measurements were conducted in the standard seated position. Additional measurements between the baseline and follow-up assessment were not performed but could have contributed with valuable information on trends. Some factors that may be associated with changes in SBP, such as anxiety,[17] serum cholesterol and triglyceride levels, plasma dehydroepiandrosterone sulfate, and ventricular hypertrophy,[4] were not investigated in the present study. Some conditions may have been underrepresented in the present study, as very old individuals and care facility residents may not visit the hospital for investigation. To minimize data loss, information was collected directly from participants or proxy respondents in addition to collection from medical records. However, follow-up information was not collected from participants who were deceased before the 5-year follow-up timepoint, causing survival bias. Consequently, the subsample of followed participants is not representative of the general very old population, but rather of a selected portion of survivors. Indeed, only 36% of first-time participants survived. Furthermore, the subsample was healthier at baseline than were followed participants without SBP measurement. The main reason for the failure of SBP measurement at baseline or follow-up in followed participants was decline of home visitation, which may have been due to health reasons and thus may have caused healthy user bias. In addition, the final subsample of 297 individuals may have been too small for the sufficient assessment of some variables.

5. Conclusion

To our knowledge, this study is the first to investigate factors associated with longitudinal SBP change in comprehensively adjusted models, including individual diseases, drug prescriptions, and assessments. In a sample of very old followed individuals, mean SBP declined by 12 mm Hg during the 5-year follow-up period. The decline in SBP in very old age seems to be explained by higher baseline SBP, later investigation year, and health-related factors (incident AMI, baseline antidepressant prescription, new diuretic prescription, and increased dependency in personal ADLs). The clinical importance and causality of these associations remain to be determined. However, knowledge about the magnitude and etiology of SBP decline could help clinicians detect, understand, manage, and possibly prevent SBP decline in very old individuals, in whom this decline may precede adverse events.

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References

[1] Satish S, Zhang DD, Goodwin JS. Clinical significance of falling blood pressure among older adults. J Clin Epidemiol 2001;54:961–7.
[2] Lernfelt B, Svanborg A. Change in blood pressure in the age interval 70–90. Late blood pressure peak related to longer survival. Blood Press 2002;11:206–12.

[3] Poortvliet RK, de Ruijter W, de Craen AJ, et al. Blood pressure trends and mortality: the Leiden 85-plus Study. J Hypertens 2013;31:63–70.
[4] Hakala SM, Tilvis RS. Determinants and significance of declining blood pressure in old age: a prospective birth cohort study. Eur Heart J 1998;19:1872–8.
[5] Heikinheimo RJ, Haavisto MV, Kaarela RH, et al. Blood pressure in the very old. J Hypertens 1990;8:361–7.
[6] Landahl S, Bengtsson C, Sigurdsson JA, et al. Age-related changes in blood pressure. Hypertension 1986;8:1044–9.
[7] 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;27:197–203.
[8] Nilsson SE, Read S, Berg S, et al. Low systolic blood pressure is associated with impaired cognitive function in the oldest old: longitudinal observations in a population-based sample 80 years and older. Aging Clin Exp Res 2007;19:41–7.
[9] 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:e1000440.
[10] Bush TL, Linkens R, Maggi S, et al. Blood pressure changes with aging: evidence for a cohort effect. Aging (Milan, Italy) 1989;1:39–45.
[11] Molander L, Gustafson Y, Lövheim H. Longitudinal associations between blood pressure and dementia in the very old. Dement Geriatr Cogn Disord 2010;30:269–76.
[12] Skoog I, Lernfelt B, Landahl S, et al. 15-year longitudinal study of blood pressure and dementia. Lancet 1996;347:1141–5.
[13] Reinikainen J, Laatikainen T, Karvanen J, et al. Lifetime cumulative risk factors predict cardiovascular disease mortality in a 50-year follow-up study in Finland. Int J Epidemiol 2015;44:108–16.
[14] Starr JM, Inch S, Cross S, et al. Seven-year follow-up of blood pressure in the Healthy Old People in Edinburgh (HOPE) cohort. J Hum Hypertens 2000;14:773–8.
[15] Siennicki-Lantz A, André-Petersson L, Elmståhl S. Decreasing blood pressure over time is the strongest predictor of depressive symptoms in octogenarian men. Am J Geriatr Psychiatry 2013;21: 863–71.
[16] Paterniti S, Verdier-Taillefer M-H, Geneste C, et al. Low blood pressure and risk of depression in the elderly. A prospective community-based study. Br J Psychiatry 2000;176:464–7.
[17] Hildrum B, Romild U, Holmen J. Anxiety and depression lowers blood pressure: 22-year follow-up of the population based HUNT study, Norway. BMC Pub Health 2011;11:601.
[18] Zhu L, Viitanen M, Guo Z, et al. Blood pressure reduction, cardiovascular diseases, and cognitive decline in the Mini-Mental State Examination in a community population of normal very old people: a three-year follow-up. J Clin Epidemiol 1998;51:385–91.
[19] Kähönen-Väre M, Brunni-Hakala S, Lindroos M, et al. Left ventricular hypertrophy and blood pressure as predictors of cognitive decline in old age. Aging Clin Exp Res 2004;16:147–52.
[20] Butt DA, Harvey PJ. Benefits and risks of antihypertensive medications in the elderly. J Intern Med 2015;278:599–626.
[21] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th edition, Text Revision. Washington, DC: American Psychiatric Publishing, Inc.; 2000.
[22] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
[23] Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clin Gerontol 1986; 5:165–73.
[24] Collin C, Wade DT, Davies S, et al. The Barthel ADL Index: a reliability study. Int Disabil Stud 1988;10:61–3.
[25] Scafato E, Galluzzo L, Ghirini S, et al. Changes in severity of depressive symptoms and mortality: the Italian Longitudinal Study on Aging. Psychol Med 2012;42:2619–29.
[26] Börjesson-Hanson A, Gustafson D, Skoog I. Five-year mortality in relation to dementia and cognitive function in 95-year-olds. Neurology 2007;69:2069–75.
[27] Ray WA, Chung CP, Murray KT, et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Eng J Med 2009;360:225–35.
[28] Weidung B, Boström G, Toots A, et al. Blood pressure, gait speed, and mortality in very old individuals: a population-based cohort study. J Am Med Dir Assoc 2015;16:208–14.
[29] Boshuizen HC, Izaks GJ, van Buuren S, et al. Blood pressure and mortality in elderly people aged 85 and older: community based study. BMJ 1998;316:1780–4.
[30] Jacobs JM, Stessman J, Ein-Mor E, et al. Hypertension and 5-year mortality among 85-year-olds: the Jerusalem Longitudinal Study. J Am Med Dir Assoc 2012;13:759.e1–6.
[31] Davies EA, O'Mahony MS. Adverse drug reactions in special populations: the elderly. Br J Clin Pharmacol 2015;80:796–807.
[32] Rochon PA, Normand S, Gomes T, et al. Antipsychotic therapy and short-term serious events in older adults with dementia. Arch Intern Med 2008;168:1090–6.
[33] Hovstadius B, Petersson G, Hellström L, et al. Trends in inappropriate drug therapy prescription in the elderly in Sweden from 2006 to 2013: assessment using national indicators. Drugs Aging 2014;31:379–86.
[34] Hopstock LA, Bønaa KH, Eggen AE, et al. Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: the Tromsø Study 1979 to 2008. Hypertension 2015;66:496–501.
[35] Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. Lancet 2011;377:568–77.
[36] den Ouden MEM, Schuurmans MJ, Mueller-Schotte S, et al. Domains contributing to disability in activities of daily living. J Am Med Dir Assoc 2013;14:18–24.
[37] Gaugler JE, Duval S, Anderson KA, et al. Predicting nursing home admission in the U.S: a meta-analysis. BMC Geriatr 2007;7:13.
[38] Licht CMM, de Geus EJC, van Dyck R, et al. Longitudinal evidence for unfavorable effects of antidepressants on heart rate variability. Biol Psychiatry 2010;68:861–8.
[39] Licht CMM, Penninx BWJH, de Geus EJC. Effects of antidepressants, but not psychopathology, on cardiac sympathetic control: a longitudinal study. Neuropsychopharmacology 2012;37:2487–95.
[40] Desta L, Jernberg T, Lofman I, et al. Incidence, temporal trends, and prognostic impact of heart failure complicating acute myocardial infarction. The SWEDEHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): a study of 199,851 patients admitted with index acute myocardial infarctions, 1996 to 2008. JACC Heart Fail 2015;3:234–42.
[41] Baune BT, Schmidt WP, Roesler A, et al. Functional consequences of subcortical white matter lesions and MRI-defined brain infarct in an elderly general population. J Geriatr Psychiatry Neurol 2009;22:266–73.
[42] Aronow WS, Fleg JL, Pepine CJ, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. Circulation 2011;123:2434–506.
[43] Weidung B, Littbrand H, Nordström P, et al. The association between SBP and mortality risk differs with level of cognitive function in very old individuals. J Hypertens 2016;34:745–52.
[44] Hörnsten C, Weidung B, Littbrand H, et al. High blood pressure as a risk factor for incident stroke among very old people: a population-based cohort study. J Hypertens 2016;34:2059–65.
[45] Wilhelmsen L, Welin L, Svärdsudd K, et al. Secular changes in cardiovascular risk factors and attack rate of myocardial infarction among men aged 50 in Gothenburg, Sweden. Accurate prediction using risk models. J Intern Med 2008;263:636–43.
[46] Koopman C, Bots ML, van Oeffelen AA, et al. Population trends and inequalities in incidence and short-term outcome of acute myocardial infarction between 1998 and 2007. Int J Cardiol 2013;168:993–8.
[47] Boström G, Conradsson M, Hörnsten C, et al. Effects of a high-intensity functional exercise program on depressive symptoms among people with dementia in residential care: a randomized controlled trial. Int J Geriatr Psychiatry 2016;31:868–78.
[48] Cooney GM, Dwan K, Greig CA, et al. Exercise for depression. Cochrane Database Syst Rev 2013;9:CD004366.
[49] Bridle C, Spanjers K, Patel S, et al. Effect of exercise on depression severity in older people: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry 2012;201:180–5.
[50] Giné-Garriga M, Roqué-Fíguls M, Coll-Planas L, et al. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: a systematic review and meta-analysis. Arch Phys Med Rehabil 2014;95:753–69. e3.