Blood pressure as a predictor of mortality in old age

Jeanet W. Blom¹, Wouter de Ruijter¹, Jacqueline C.M. Witteman², Willem J.J. Assendelft¹, Rudi G.J. Westendorp³, Albert Hofman², Jacobijn Gussekloo¹

1. Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, the Netherlands.
2. Department of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlands.
3. Department of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, the Netherlands.

Submitted
Abstract

Background: Following observational findings that high systolic blood pressure (SBP) is related to decreased cardiovascular mortality in the oldest old, clinicians in daily practice do not know until what age measurement of blood pressure is useful, in particular regarding risk prediction in primary preventive settings.

Objective: To investigate age-specific all cause and cause-specific mortality risks related to SBP and diastolic blood pressure (DBP), in people from age 55 years onwards with no history of cardiovascular disease (CVD).

Methods: From the Rotterdam Study, a population-based prospective cohort study among participants aged 55 years and over, 4612 participants (2858 women, 1754 men) with no history of CVD were included. The mean follow-up duration was 11.2 years (range 0-15.6 years). Within four age strata (55-64, 65-74, 75-84 and ≥85 years) relationships between baseline SBP (and DBP), and all cause and (non) cardiovascular mortality were estimated (reference groups SBP <140 mmHg and DBP <90 mmHg).

Results: At baseline, 42.9% of participants had SBP ≥140 mmHg and 15.0% had SBP ≥160 mmHg. In participants aged 55-64 years, high SBP was related to increased all cause mortality (HR140-159 1.3, 95% CI 1.9-1.7; HR160 1.7, 95% CI 1.2-2.4, p for trend <0.001), adjusted for sex. In participants aged 75-84 years, this relationship disappeared (HR140-159 1.0, 95% CI 0.8-1.2; HR160 1.2, 95% CI 0.9-1.5, p for trend = 0.271). From age 85 years onwards, SBP ≥140 mmHg was related to decreased all cause mortality (HR140-159 0.7, 95% CI 0.4-1.0; HR160 0.6, 95% CI 0.4-0.8, p for trend = 0.007). Comparable results were observed for cardiovascular and non-cardiovascular mortality. For DBP ≥90 mmHg, present in 401/4612 (8.7%), no clear trends with age as seen in SBP were observed.

Conclusion: From age 75 years onwards, SBP levels ≥140 mmHg are no longer related to an increased mortality risk in people with no history of CVD, and from age 85 years onwards this risk even reverses. Since SBP does not predict all cause mortality or cardiovascular mortality from age 75 years onwards, it should no longer be used to this end in such older populations.
**Introduction**

At present it is generally known that systolic blood pressure (SBP) is an important risk factor for cardiovascular disease. Therefore, SBP control is one of the cornerstones of secondary prevention after previous cardiovascular events and has proven to be effective up to high ages.\(^1\)\(^-\)\(^5\) As yet, there aren’t any studies that have demonstrated that lowering, withdrawal or not initiating antihypertensive treatment in (very) old patients after previous cardiovascular events is beneficial. Therefore, regular SBP measurement in such patients in order to monitor antihypertensive treatment is to be continued up to very high ages.

Regarding primary prevention, however, the aim of SBP measurement is different: SBP is one of the key risk factors used to predict cardiovascular risk in people with no history of cardiovascular disease so far. In daily practice, SBP is universally used in that way in people of all ages. However, this method of risk prediction may not be adequate in older persons from age 75 years onwards, since several studies have confirmed that the relationship of SBP with cardiovascular mortality and morbidity in very old age reverses.\(^6\)\(^-\)\(^13\) However, thus far it is still unknown at what age this risk actually reverses.

Given the high prevalence of hypertension in the older age groups this question has high relevance for daily practice.

Therefore, we sought to elucidate the value of SBP (as well as DBP) as a predictor of all-cause and cardiovascular mortality in patients with no history of cardiovascular disease, in older persons from 55 years onwards.

**Methods**

**Study population**

The Rotterdam Study is a population-based prospective cohort study, including 7983 participants (4878 women and 3105 men) of 55 years and over, living in an urban district of Rotterdam, the Netherlands. The study has been described in detail previously.\(^14\) The Medical Ethics Committee of the Erasmus University of Rotterdam approved the study. Written informed consent was obtained from all participants.

For the current study, all participants with a history of cardiovascular disease, defined as myocardial infarction, coronary interventions (percutaneous coronary interventions or coronary artery bypass grafts), ischemic and hemorrhagic stroke, atrial fibrillation and peripheral arterial disease, were excluded (n=2294); 308 participants were excluded because data on cardiovascular history were missing. From the thus included participants (n=5381), blood pressure data were available for n=4612 (85.7 %), which was the final sample size in the present study.
Measurements
Between 1989 and 1993 participants visited the research center for the baseline examination, where blood pressure measurements were obtained. Blood samples were taken for measurement of total cholesterol and high-density cholesterol measurements, and body mass index was assessed, as well as participants’ history of smoking and diabetes mellitus. Blood pressure measurements were carried out by research assistants using a standardized protocol. Systolic (Korotkoff phase I) and diastolic (Korotkoff phase V) blood pressure were measured in duplicate on the right arm using a random-zero sphygmomanometer with a 14 cm x 38 cm cuff, after the participant had been seated for at least 5 minutes. The mean of the two blood pressures values was used in the analyses. For SBP, three fixed categories for blood pressure were used, according to categories in the European guidelines on cardiovascular disease prevention in clinical practice, namely ‘normal’ (SBP <140 mmHg), ‘grade 1 hypertension’ (SBP 140-159 mmHg) or ‘grade 2 hypertension or higher’ (SBP ≥160 mmHg). For DBP, three categories were used corresponding with DBP values of <90 mmHg, 90-99 mmHg and ≥100 mm Hg, respectively. Data on the use of antihypertensive medication (ATC-codes: C02, C03, C07) were collected through interviews. Medication containers were checked during the interview. A SBP ≥160 mmHg and/or DBP ≥100 mmHg was reported to participant’s general practitioner, unless the general practitioner was already informed about participant’s hypertension.

Follow-up
Follow-up was completed until 1 January 2005. The mean follow-up duration was 11.2 years (range 0-15.6 years). Information on vital status of the participants was obtained at regular intervals from the municipal register in Rotterdam. Information on fatal and non-fatal endpoints was obtained on a weekly basis from the general practitioners working within the study district, and yearly from general practitioners working outside. Complete follow-up information was available for 4273 (92.6%) participants. Participants with incomplete follow-up were on average 2.4 years younger and generally had a 0.5 mmHg lower SBP and a 1.2 mmHg higher DBP.

Endpoints
All information on possible events was obtained from the general practitioners of the participants and subsequently classified independently by two research physicians. Cardiovascular mortality was defined as mortality from coronary heart disease or stroke. Coronary heart disease morbidity was defined as myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft operation. Stroke morbidity was defined as non-fatal stroke. In case of disagreement consensus was reached in a plenary session. A medical expert in the field of cardiovascular disease verified all these events. This verification was considered definite. Classification of events was based on the International Classification of Diseases, 10th revision.
Data analysis
Within strata by age group (at baseline 55-64 years, 65-74, 75-84 and >85 years), we calculated risk estimates for the association between blood pressure at baseline, and all cause and cause-specific (cardiovascular and non-cardiovascular) mortality, using a Cox proportional hazards model. Since our objective was to determine the predictive value of SBP and DBP, as opposed to exploring etiological pathways, results were adjusted for sex only. Analyses were repeated in strata according to baseline use of antihypertensive medication. To evaluate the influence of the arbitrarily chosen age groups, all analyses were repeated in 5-year interval age groups (at baseline 55-59 years, 60-64, 65-69, 70-74, 75-79, 80-84 and >85 years), as well as different 10-year interval age groups (at baseline 55-59 years, 60-69, 70-79 and >80 years). Finally, within two age groups (at baseline 55-79 years and >80 years) and for SBP only, analyses were repeated for 'coronary heart disease' and 'stroke' separately, with fatal events (mortality), non-fatal events (morbidity) and a combined endpoint (mortality plus morbidity) as outcomes.

Analyses were performed using SPSS 16.0 for Windows (SPSS, Chicago, IL, USA).

Results
Table 1 shows baseline characteristics of the participants, including their other cardiovascular risk factors. The mean age of the participants at baseline was 67.4 years (range 55.0-106.2). The proportion of participants with SBP ≥160 mmHg was 15.0%, and 57.1% had SBP <140 mmHg. For DBP, 1.4% had DBP ≥100 mmHg and 91.3% had DBP <90 mmHg.

During follow-up, overall mortality increased from 10.7/1000 person years (0.2% in the first year of follow-up) in those 55-64 years old to 171.9/1000 person years (12.3% in the first year of follow-up) in participants aged 85 years and over.

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of participants (n=4612).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
</tr>
<tr>
<td>Median duration of follow-up in years (IQR)</td>
</tr>
<tr>
<td>Age groups (%)</td>
</tr>
<tr>
<td>55-64 years</td>
</tr>
<tr>
<td>65-74 years</td>
</tr>
<tr>
<td>75-84 years</td>
</tr>
<tr>
<td>≥ 85 years</td>
</tr>
<tr>
<td>Median systolic blood pressure in mmHg (IQR)</td>
</tr>
<tr>
<td>Median diastolic blood pressure in mmHg (IQR)</td>
</tr>
<tr>
<td>Participants with antihypertensive medication (%)</td>
</tr>
<tr>
<td>Other cardiovascular risk factors</td>
</tr>
<tr>
<td>Median total cholesterol in mmol/L (IQR)</td>
</tr>
<tr>
<td>Median HDL cholesterol in mmol/L (IQR)</td>
</tr>
<tr>
<td>Median BMI (IQR)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
</tr>
<tr>
<td>Smoking (%)</td>
</tr>
</tbody>
</table>

* Antihypertensive medication defined as ATC-codes C02, C03 and C07
Systolic blood pressure
For both categories of SBP (140-159 mmHg and ≥160 mmHg), with increasing age group, all cause mortality and cause-specific mortality (cardiovascular and non-cardiovascular) decreased (p for trend <0.001). In age group 55-64 years old, a robust correlation was observed between increasing SBP and all cause and cardiovascular mortality (p for trend <0.001), as well as non-cardiovascular mortality (p for trend 0.025) (Table 2).

Risk of all cause mortality
In participants aged 55-64 year, SBP ≥140 mmHg was related to an increased all cause mortality (HR_{140-159} 1.3, 95% CI: 1.0-1.7 and HR_{≥160} 1.7, 95% CI: 1.2-2.4, p for trend <0.001) compared to those with SBP <140 mmHg, adjusted for sex. Relative mortality risks decreased to unity in those aged 75-84 year (HR_{140-159} 1.0, 95% CI: 0.8-1.2 and HR_{≥160} 1.2, 95% CI: 0.9-1.5, p for trend = 0.271).

From age 85 years onwards, SBP ≥140 mmHg was related to decreased all cause mortality (HR_{140-159} 0.7, 95% CI: 0.4-1.0 and HR_{≥160} 0.6, 95% CI: 0.4-0.8, p for trend = 0.007) (Table 2, Figure 2).

Figure 1 shows the all cause mortality rate (n/1000 person years) depending on two levels of SBP: <140 mmHg and ≥160 mmHg. At some age between 75 and 85 years, the mortality risk reverses, with SBP <140mmHg being related to higher mortality than SBP ≥160 mmHg.

![Figure 1. Incidence of death by age group, depending on different levels of systolic blood pressure.](image-url)
Table 2. All cause and cause-specific mortality risks for participants with no history of cardiovascular disease (n=4612) by baseline systolic and diastolic blood pressure categories, adjusted for sex.

<table>
<thead>
<tr>
<th>Events</th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All*</td>
<td>&lt; 140</td>
<td>140-159</td>
<td>160+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 140</td>
<td>n=164</td>
<td>n=1288</td>
<td>n=465</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64 yrs</td>
<td>261</td>
<td>9.4</td>
<td>1</td>
<td>1.3 (1.1-1.7)</td>
<td>1.7 (1.2-2.3)</td>
<td>&lt;0.001*</td>
<td>10.1</td>
<td>1</td>
<td>1.4 (0.9-2.1)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>249</td>
<td>24.9</td>
<td>1</td>
<td>1.3 (1.1-1.5)</td>
<td>1.3 (1.1-1.7)</td>
<td>0.004*</td>
<td>28.6</td>
<td>1</td>
<td>1.1 (0.8-1.5)</td>
</tr>
<tr>
<td>≥ 85 yrs</td>
<td>49</td>
<td>225.9</td>
<td>1</td>
<td>0.7 (0.4-1.4)</td>
<td>0.6 (0.4-1.2)</td>
<td>0.007*</td>
<td>171.3</td>
<td>1</td>
<td>1.0 (0.5-1.9)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64 yrs</td>
<td>23</td>
<td>1.3</td>
<td>1</td>
<td>2.0 (1.8-3.8)</td>
<td>2.6 (1.9-4.7)</td>
<td>&lt;0.001*</td>
<td>1.6</td>
<td>1</td>
<td>3.0 (1.5-6.0)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>49</td>
<td>4.9</td>
<td>1</td>
<td>1.2 (0.6-1.9)</td>
<td>1.5 (0.8-2.3)</td>
<td>0.013*</td>
<td>5.3</td>
<td>1</td>
<td>1.0 (0.5-2.1)</td>
</tr>
<tr>
<td>≥ 85 yrs</td>
<td>79</td>
<td>13.6</td>
<td>1</td>
<td>1.1 (0.7-1.7)</td>
<td>1.4 (0.8-2.3)</td>
<td>0.160</td>
<td>13.8</td>
<td>1</td>
<td>1.9 (1.1-3.7)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64 yrs</td>
<td>23</td>
<td>1.3</td>
<td>1</td>
<td>2.0 (1.8-3.8)</td>
<td>2.6 (1.9-4.7)</td>
<td>&lt;0.001*</td>
<td>1.6</td>
<td>1</td>
<td>3.0 (1.5-6.0)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>49</td>
<td>4.9</td>
<td>1</td>
<td>1.2 (0.6-1.9)</td>
<td>1.5 (0.8-2.3)</td>
<td>0.013*</td>
<td>5.3</td>
<td>1</td>
<td>1.0 (0.5-2.1)</td>
</tr>
<tr>
<td>≥ 85 yrs</td>
<td>79</td>
<td>13.6</td>
<td>1</td>
<td>1.1 (0.7-1.7)</td>
<td>1.4 (0.8-2.3)</td>
<td>0.160</td>
<td>13.8</td>
<td>1</td>
<td>1.9 (1.1-3.7)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cardiovascular mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64 yrs</td>
<td>138</td>
<td>8.0</td>
<td>1</td>
<td>1.2 (0.8-1.6)</td>
<td>1.6 (1.0-2.3)</td>
<td>0.029*</td>
<td>8.4</td>
<td>1</td>
<td>1.1 (0.7-1.8)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>200</td>
<td>20.0</td>
<td>1</td>
<td>1.2 (1.1-1.5)</td>
<td>1.3 (0.9-1.7)</td>
<td>0.003*</td>
<td>21.3</td>
<td>1</td>
<td>1.1 (0.8-1.6)</td>
</tr>
<tr>
<td>≥ 85 yrs</td>
<td>154</td>
<td>53.4</td>
<td>1</td>
<td>1.0 (0.8-1.2)</td>
<td>1.1 (0.9-1.3)</td>
<td>0.504</td>
<td>58.1</td>
<td>1</td>
<td>1.2 (0.8-1.8)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*AR=absolute risk per 1000 person years; *statistically significant.
Figure 2. Relationship of different levels of systolic blood pressure with all cause and cause-specific mortality by age group.
Risk of cause-specific mortality
1. Cardiovascular mortality
In the age group 55-64 years old, the risk of cardiovascular mortality was increased for participants with SBP ≥140 mmHg (HR_{140-159} 2.0, 95% CI: 1.0-3.8 and HR_{160} 2.6, 95% CI: 1.2-5.7, p for trend <0.001) compared to those with SBP <140 mmHg. In the higher age groups this risk decreases. At the age of 85 years and over, the relative risk related to SBP ≥160 mmHg is similar to the risk related to SBP <140 mmHg: HR_{160} 0.8, 95% CI: 0.3-2.1 (Table 2, Figure 2). When participants were categorized into different age groups, the increased risk with higher SBPs is present up to age 80 years: in age group 70-79 years old the HR_{140-159} is 1.5 (95% CI: 1.0-2.4) and the HR_{160} is 1.6 (95% CI: 1.0-2.7), whereas in age group 80 years and over the HRs reach unity (HR_{140-159} 1.0, 95% CI: 0.6-1.7 and HR_{160} 1.0, 95% CI: 0.6-1.8). This was also observed when participants were categorized into 5-year age groups (data not shown).

2. Non-cardiovascular mortality
Non-cardiovascular mortality is increased with higher SBPs in the younger age groups, but in the age group 75-84 years old the relative risk reaches unity. For participants aged 85 years and over, the risk for non-cardiovascular mortality was decreased for participants with SBP ≥140 mmHg compared to those with SBP <140 mmHg (HR_{140-159} 0.5, 95% CI: 0.3-0.8, and HR_{160} 0.5, 95% CI: 0.3-0.8, p for trend = 0.005) (Table 2, Figure 2).

Risk of (fatal and non-fatal) coronary heart disease and stroke separately
Table 3 shows mortality risks for coronary heart disease and stroke separately, as well as morbidity risks (non-fatal events), again depending on different baseline SBP categories. Since from our preliminary analyses age 80 years appeared to be pivotal, and in order to preserve power, we dichotomized our group of participants into a group of 55-79 year olds versus those 80 years and over. For coronary heart disease and stroke alike, the relationship of increased SBP with the combined endpoint ‘mortality plus morbidity’ reaches unity in age group 80 years and over, whereas robust increases of hazard ratios are observed in age group 55-79 years (Table 3).
Diastolic blood pressure
In this population, the prevalence of DBP ≥90 mmHg is low (8.7%), therefore point estimates of hazard ratios have wide confidence intervals.

Risk of all cause mortality
DBP ≥90 mmHg was related to an increased mortality in age group 55-64 years (HR90-99 1.4, 95% CI 0.9-2.1 and HR≥100 2.5, 95% CI 1.3-5.0, p for trend = 0.016). A trend with increasing age as seen in SBP could also be observed (p for trend <0.001), although less clear (Table 2).

Risk of cause-specific mortality
For cardiovascular and non-cardiovascular mortality there is no clear change with age in risk related to DBP ≥90 mmHg compared to DBP <90 mmHg, although p’s for trend are all <0.01 (Table 2).

Additional analyses (data not shown)
When participants were stratified according to the use of antihypertensive medication at baseline, results in both strata were essentially the same as the overall results. Excluding participants who died in the first year of follow-up showed similar results. No difference in pattern of relative risks was observed between men and women, although in women the effect of the inversing relationship for cardiovascular mortality was less clear.
Discussion

This analysis in the Rotterdam study shows that, for individuals with no history of cardiovascular disease, starting at the age of 75 years, systolic blood pressure $\geq 140$ mmHg is no longer related to an increased risk of mortality. In contrast, above the age of 85 years high SBP was related to decreased mortality. With regard to primary prevention of cardiovascular disease, SBP therefore is probably no longer a predictor of cardiovascular (and all cause) mortality from age 75 years onwards, and definitely not after the age of 80 years.

Already in 1992 a review of observational population studies, relating blood pressure to mortality in older persons, reported a weaker relationship between blood pressure and mortality, SBP as well as DBP, from age 75 onwards.\textsuperscript{17} Since then, several studies have reported on the fading relationship between blood pressure and mortality and cardiovascular morbidity in older persons.\textsuperscript{6,18-24} In contrast with our study, which included a true 'primary prevention' population as would be detected by screening for risk factors in people with no history of CVD, these studies usually included older persons without considering their history of CVD, or they included patients from a population with a known high prevalence of cardiovascular disease. Also, few of these studies were stratified by age, or they evaluated relationships in the oldest old only.

The interpretation of the reversed relationship between blood pressure and mortality in old age is complex. It has been suggested that the population of oldest old includes relatively many 'false normals', since SBP is known to decrease in the last years before dying. In fact, in the oldest old about a quarter of the population has had SBP falls of $\geq 20$ mmHg over the preceding 3 years.\textsuperscript{25} SBP falls have been interpreted as signs of imminent heart failure, and this could underlie the observed worse prognosis in these individuals.\textsuperscript{26,27} Conversely, very old people with higher SBPs have been shown to have larger stroke volumes, larger ejection fractions and lower heart rates, as well as a better renal function.\textsuperscript{21,27} Apparently, with rising age, people with higher SBPs ('afterloads') and resulting better perfusion pressures are better off.

Our population-based study has several strengths. The population that was studied is highly representative for people with no history of CVD in the general population, and therefore reflects the population that would be addressed with systematic screening as a means of primary prevention of CVD. A high response rate and almost complete follow-up reinforce internal validity and generalizability. Our study further distinguishes itself by stratifying into age groups, in various ways, allowing for determination of the specific age where the relationship between SBP and mortality disappears and subsequently reverses. We also showed that the age-dependent effects on cardiovascular outcomes of various levels of SBP are not only carried by coronary heart disease, but also by stroke: the risk of non-fatal strokes with rising SBP levels also reaches unity in age 80 years and over, as does the combined risk of fatal and non-fatal stroke. From an etiological perspective,
which was not the objective of our study, it could be seen as a limitation of the study that we did not measure individual changes in blood pressure over time. However, from a prognostic perspective, all currently applied risk scores also use cross-sectional blood pressure measurements.\textsuperscript{28-32} It could also be seen as a weakness that general practitioners were informed about previously unrecognized hypertension, potentially causing information bias and type-II error. Since in the younger age groups (up to age 75 years) robust correlations of high SBP and increased mortality risk were observed, and it is unlikely that participants in these age groups are treated less strict than those in older age groups,\textsuperscript{33} this almost certainly did not influence our results.

The most important clinical implication of our findings is that, contrary to current practice, SBP probably cannot be used as a predictor for cardiovascular mortality or morbidity in day-to-day care for community-dwelling people over 75 years of age with no history of CVD, certainly not in those over 80 years of age. As it is likely that in old age similar inversions of risk exist for other risk factors, it is recommended that age specific risk scores for older people be developed. Finally, the effects of lowering or discontinuation of antihypertensive medication in very old people, in particular those with no history of CVD, needs to be investigated, as the target SBP level for this group may well be higher than assumed thus far.

It is appropriate to indicate that studies that describe an inversion of the relationship between SBP and mortality in (very) old age, as the present study does, do not per se provide evidence that lowering high SBP in old age is counter-effective. In fact, clinical trials and a Cochrane review from 2006 suggest that antihypertensive treatment in the elderly improves the prognosis of patients with high SBP.\textsuperscript{34} Also, in 2008 the results of the Hypertension in the Very Elderly Trial (HYVET) were published, yielding an important reduction of cardiovascular mortality, and a 21% reduction in all cause mortality.\textsuperscript{2;35} Although concerns exist about the generalizability of the HYVET results to primary preventive populations,\textsuperscript{36} treating hypertension in the very old for primary preventive reasons may, to some extent, be beneficial. However, here we showed that very old people with ‘hypertension’ are not the ones with the highest mortality and cardiovascular morbidity risks. So, from the perspective of risk selection in primary preventive strategies, screening for high SBP in people over 75 years of age cannot be recommended.

In conclusion, after the age of 75 years SBP levels $\geq$140 mmHg are no longer related to an increased risk of mortality in people with no history of cardiovascular disease, and above the age of 85 years the mortality risk even reverses. SBP therefore is no longer a reliable predictor of cardiovascular (and all cause) mortality from age 75 years onwards, and should no longer be used to this end, not as individual risk factor, and probably also not as a component of a risk score.
References


