Sex differences in time trends of blood pressure among Swedish septuagenarians examined three decades apart: a longitudinal population study

Erik Joas, Xinxin Guo, Silke Kern, Svante Östling, and Ingmar Skoog

Objective: The aim of this study was to analyze the influence of birth cohort, sex and age on the trajectories of SBP and DBP in two birth cohorts of 70-year-olds, examined 3 decades apart and followed up at ages 75 and 79–80 years.

Methods: Two population samples of 70-year-olds from Gothenburg, Sweden, were examined. The first, born in 1901–1902, was examined in 1971–1972 (n = 973). The second, born in 1930, was examined in 2000 (n = 509). Both samples were re-examined at ages 75 and 79–80 years.

Results: We found that SBP and DBP were considerably lower in septuagenarian men and women born 1930 compared with those born 1901–1902, also when adjusting for antihypertensive treatment in different ways. The decline was especially pronounced in women. Blood pressure was higher in women than in men in the 1970s, whereas there were no sex differences in the 2000s. The age-related decline in SBP started earlier and was more accentuated in those born in 1930 than in those born in 1901–1902.

Conclusion: Blood pressure decreased, and the age-related decline in SBP started earlier in septuagenarians examined in the 2000s compared with those examined in the 1970s. The decrease was especially pronounced in women and diminished the sex differences. Antihypertensive treatment only partly explained our findings, suggesting that other mostly unknown factors played an important role.

Keywords: cohort difference, hypertension, sex differences, time trends

INTRODUCTION

High blood pressure (BP) is a risk factor for cardiovascular disease and other disorders, such as dementia [1,2]. High BP is a key risk factor contributing to disease burden and mortality globally, and is estimated to account for 7% of disability adjusted life-years (20% among those older than 70 years) and 9.4 million deaths in 2010 [3]. Mean BP has decreased in high-income countries during the past decades, both in the general population and among the elderly [4–8], whereas BP has increased in low-income and middle-income countries [4]. A variety of explanations have been suggested for the decrease in BP in high-income countries, such as changes in early life factors, diet, smoking habits, changes in guidelines, and a rising prevalence of antihypertensive treatment [5,9–11]. On the other hand, an observed rise in the frequency of obesity [12] and diabetes mellitus [13] would be expected to increase BP [1], thus a large part of the decrease in BP is still unexplained [5,9,10].

Most studies report that midlife BP is higher in men than in women, with a reverse in old age leading to higher BP in women among the elderly [1,14]. A number of different biological and social explanations for this sex difference have been suggested [15]. During the last decades, large changes in sex roles occurred in Sweden and in the Western world, for example female participation in the labor force increased dramatically [16] and inequality between sexes in higher education diminished [17]. This convergence of sex roles could also impact biological measurements through risk factors such as stress and diet. However, trends in other risk factors for hypertension such as cholesterol and BMI seem not to have differed between men and women across recent decades [12,18,19].

The pattern of BP trajectories through life is complex. SBP is suggested to increase from adolescence to late life followed by a decline around the age of 80 years [1,20]. The decline in DBP starts earlier, at around 50–60 years of age. Age is thus one of strongest predictors of BP [1]. It is not clear whether BP trajectories in old age have changed during the past decades. However, age-related trajectories of BP in old age may be important in relation to different outcomes. For example, although high BP in midlife is linked to late-life dementia [21], several studies also report that BP decreases the years before dementia onset [2,22], maybe due to incipient brain changes. To our knowledge,
few longitudinal studies have specifically examined time trends in trajectories of BP among the elderly [8,23]. High BP is an important risk factor for disorders such as stroke, cardiovascular disease and dementia. Changes in BP might therefore be important for projections of future disease burden and may also indirectly indicate to what extent primary and secondary prevention interventions have lowered BP in the general population.

The aim of this study was to analyze sex and birth cohort differences in the trajectories of SBP and DBP in two birth cohorts of 70-year-olds, examined in 1971–1972 and 2000–2001, and followed up at ages 75 and 79 years.

**METHODS**

The multidisciplinary H70-study was initiated in 1971. The first study comprised a representative sample of 70-year-olds born in 1901–1902 and living in Gothenburg, Sweden. The sample was systematically drawn from the Swedish Population Register by inviting individuals born on dates ending with 2, 5 or 8 between 1 July 1901 and 30 June 1902. In 1971–1972, 973 individuals took part in a medical examination [response rate (RR) 84.8%] [24], out of these 140 individuals died before the follow-up examination in 1976–1977. Follow-up examinations were conducted at age 75 years in 1976–1977 (n = 744, RR 89.1% from the survivors of the participants in 1971–1972, out of these 125 individuals died before the next follow-up) and at age 79 years in 1980–1981 (n = 537, RR 86.5% from the survivors of the participants in 1971–1972).

In 2000–2001, a new H70 study was conducted on a representative sample born in 1930 on dates 3, 6, 12, 18, 21, 24 or 30 [25]. Of those invited, 509 participated in a medical examination (RR 65.3%), out of these 18 individuals died before the follow-up in 2005–2006. Some of the women (n = 165) who participated in this new study had previously taken part in the Prospective Population study of Women. Follow-ups were conducted at age 75 years in 2005–2006 with an enlarged sample [19], in which 768 individuals participated in the somatic examination (RR = 61.2%, out of these 73 individuals died before the follow-up in 2009–2010), and at age 79–80 years in 2009–2010, in which 555 (RR 70.3%) individuals took part in the examination (which only included individuals who had taken part in previous examinations).

Informed consent was obtained from all participants. The study was approved by the Ethics Committee for Medical Research at the University of Gothenburg.

**Examinations**

The general examinations included physical examinations, psychiatric examinations, neuropsychological examinations and laboratory tests including ECG and extensive biochemical evaluations.

BP was recorded in the sitting position after 5-min rest using a standard cuff and mercury sphygmomanometer. SBP and DBP were registered to the nearest 2 mmHg. DBP was defined as Korotkoff phase 5. Independent investigators between studies measured BP. The investigators were blinded in relation to previous BP measurements. Antihypertensive treatment was documented from self-report and medication lists. Information on diabetes was given by self-report. Cholesterol was measured using standard measurements at the Sahlgrenska University Hospital.

**Statistics**

SBP and DBP were analyzed separately. Linear mixed effects models with a random intercepts were used to analyze differences in mean BP and trajectories of BP from age 70 to 79 years. These models are suitable for analyzing data with repeated measurements, as they account for intraclass correlations [26]. In these analyses, SBP and DBP were dependent variables in separate analyses with birth cohort, age and sex as independent variables. Age was centered at 70 years in all analyses. To allow for nonlinear trajectories over time, a breakpoint in slope was used at age 75 years.

Our initial model included time, time after 75, cohort, sex and their two-way and three-way interactions. Higher order interaction terms were removed on the basis of likelihood ratio tests. Linear combinations of some parameter combinations from the model are given in the text.

We also conducted some analyses to study the effect of antihypertensive treatment on cohort differences. First, we used antihypertensive treatment as a confounder. This approach is, however, problematic as individuals on antihypertensive medication generally have a higher BP (the indication for treatment) compared with the rest of the population. At the same time, treatment lowers BP. Thus, the variable ‘treatment’ contains both the indication (i.e. high BP) and the effect of treatment (lowering of BP). Using antihypertensive treatment as a confounder in a regression model cannot separate between these effects [27]. Previous studies [27] have addressed this problem by imputing a fixed constant of 10 mmHg for SBP to obtain an estimate of pretreatment BP in individuals on antihypertensive treatment. This value is based on an estimated general effect of antihypertensive treatment [20,27–29]. In a second analysis, we therefore analyzed data after adding 10 mmHg for SBP and 5 mmHg for DBP in those who were on antihypertensive treatment. As the number of different types of antihypertensive medications increased during the study period, the number of different antihypertensive medications per individual also increased. In a third analysis, we therefore used a model that was sensitive to the number of antihypertensive medications per individual. In these analyses, we added 10 mmHg in SBP and 5 mmHg in DBP for every type of antihypertensive drug. In these analyses, we also added a term to account for the fact that a majority of the women in the second cohort had previously taken part in an epidemiological study, and thus probably had a more careful health monitoring than other participants. Fourth, we also included the confounders BMI, cholesterol, education, smoking and diabetes to study their impact on birth cohort differences in BP. Fifth, to analyze the sensitivity of the findings due to increased survival in the 1930 cohort, we analyzed a subset comprising only those who participated in all three examinations. Sixth, we also stratified the analysis based on BP treatment. However, as the recommended level of BP for initiation of antihypertensive treatment has changed during the study period [30,31], the
level of BP would have fallen both in the untreated and in the treated groups even without a cohort effect. However, this would be an artifact of diagnostic norms, as those with the ‘highest’ BP in the previously untreated group have entered into the treated group, thus declining the BP in the treated group.

SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA) and R 3.2.2 [32] were used for all calculations. The R function line in the nlme-package was used to estimate the linear mixed effects models [33].

**RESULTS**

Sample characteristics are presented in Table 1. The prevalence of antihypertensive treatment was higher in those born in 1901–1902 than in those born in 1930 for men at all ages 70 and 75 years (0.42 mmHg, SE = 0.23, P = 0.02) and decreased between ages 75 and 79 years (−1.36, SE = 0.26, P = 0.01). BP increased with age between ages 70 and 75 years (0.42 mmHg, SE = 0.18, P = 0.02) and decreased between ages 75 and 79 years (−1.03 mmHg, SE = 0.24, P < 0.01) in cohort 1901–1902. In cohort 1930, SBP decreased in both men and women between ages 70 and 79 years, with an accelerated decrease after age 75 years (age 70–75 years: −0.56 mmHg/year, SE = 0.26, P = 0.03, and age 75–79 years: −2.9 mmHg/year, SE = 0.23, P < 0.01).

The findings were similar when adjusting for antihypertensive treatment, additional confounders and in the sensitivity analyses. In the analyses adjusted for antihypertensive treatment as a covariate, the cohort differences increased slightly. In the analyses imputing estimated pretreatment levels of SBP, the differences were attenuated (Table S4, http://links.lww.com/HJH/A760 in the online data supplement), with some exceptions. When adjusting for antihypertensive treatment by imputing 10 mmHg in those treated, and when imputing 10 mmHg per number of antihypertensive drugs, the small cohort difference in men at age 70 years was no longer significant. Results were similar when only individuals who participated at all examinations (n = 788) were analyzed, except that the cohort difference between men at the baseline age of 70 years was no longer significant. In analyses stratified by antihypertensive treatment, the cohort differences were even larger. The cohort difference in SBP at

**TABLE 1. Characteristics of the sample**

| Examination | Participants with information on SBP and antihypertensive treatment | | | | | |
|-------------|--------------------------------------------------------------------|---|---|---|---|
|             | Cohort born in 1901–1902                                           | 70 | 75 | 79 | 70 | 75 | 79 |
|             | n (%)                                                               | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
|             |                                                                     | 973 | 738 | 536 | 505 | 704 | 534 |
| Antihypertensive treatment | 291 (29.9) | 292 (39.6) | 240 (44.8) | 186 (36.8) | 355 (50.4) | 358 (67) |
| Females     | 524 (53.9) | 409 (55.4) | 328 (61.2) | 264 (52.3) | 398 (56.5) | 299 (56) |
| Smoking     |                                                                     |       |       |       |       |       |       |
| Never       | 504 (51.8) | 410 (56.2) | 310 (58.9) | 223 (44.7) | 336 (47.9) | 250 (47.3) |
| Former      | 181 (18.6) | 151 (20.7) | 130 (24.7) | 201 (40.3) | 280 (39.9) | 230 (43.6) |
| Current     | 288 (29.6) | 169 (23.2) | 86 (16.3) | 75 (15) | 86 (12.3) | 48 (9.1) |
| Education (> mandatory) | 152 (15.9) | 119 (16.3) | 86 (16.2) | 196 (39.4) | 317 (45.6) | 257 (48.5) |
| Age 70      | 70.13 (0.12) | 75.12 (0.24) | 79.23 (0.18) | 70.52 (0.22) | 75.66 (0.38) | 80.07 (0.16) |
| SBP         | 165.63 (24.72) | 167.17 (25.32) | 163.26 (24.55) | 154.71 (21.89) | 150.87 (21.28) | 138.05 (18.98) |
| Cholesterol | 5.9 (1.43) | 5.89 (1.22) | 5.89 (1.2) | 5.31 (1.04) | 5.29 (1.09) | 5.29 (1.09) |
| BMI         | 25.8 (3.91) | 25.4 (3.85) | 25.22 (3.89) | 26.04 (4.1) | 26.04 (4.1) | 26.04 (4.1) |

**TABLE 2. Mixed effects models of the development of SBP (mmHg) from 70 to 79–80 years of age**

<table>
<thead>
<tr>
<th>Estimate (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>160.05 (158.08; 162.01)</td>
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<tr>
<td>Cohort (reference born in 1901–1902)</td>
<td>−4.28 (−7.46; −1.10)</td>
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<td></td>
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<tr>
<td>Sex (reference male)</td>
<td>10.26 (7.82; 12.70)</td>
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<tr>
<td>Age</td>
<td>0.43 (0.07; 0.78)</td>
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<tr>
<td>Age 75+</td>
<td>−1.46 (−2.18; −0.74)</td>
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<tr>
<td>Cohort × sex</td>
<td>−10.78 (−14.38; −7.18)</td>
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<tr>
<td>Cohort × age</td>
<td>−0.98 (−1.60; −0.37)</td>
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<tr>
<td>Cohort × age 75+</td>
<td>−0.87 (−1.96; 0.23)</td>
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<tr>
<td>Num. obs.</td>
<td>3990</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Num. individuals</td>
<td>1842</td>
<td></td>
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<tr>
<td>Residual SD</td>
<td>17.12</td>
<td></td>
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<tr>
<td>Random intercept SD</td>
<td>15.20</td>
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</tr>
</tbody>
</table>

*0 outside the confidence interval (CI).*
ages 70, 75 and 79 years for men and women, when using different methods for examining the effect of antihypertensive treatment on birth cohort differences, can be seen in Table S5, http://links.lww.com/HJH/A760.

The relation between DBP and birth cohort, age and sex is given in the Table 3 and in Fig. 2. The results for DBP in relation to age, cohort, sex and between-individual variations were similar as for SBP. Both women and men had lower DBP in the second cohort. Women had higher DBP than men in the first cohort at age 70 years (2.17 mmHg, SE = 0.72, P < 0.01), whereas there was no difference in DBP in the second cohort (1.43 mmHg, SE = 0.84, P = 0.09) at age 70 years. There were no differences in slope between cohorts, but there were differences in slope between sexes, with women having a shallower decrease in DBP after age 75 years. The findings when adjusting for antihypertensive treatment, additional confounders and in the sensitivity analyses were quite similar as for SBP (Table S6, http://links.lww.com/HJH/A760 in the online data supplement). The results were also similar when only analyzing those who participated in all three examinations. In analyses stratified by antihypertensive treatment, the cohort differences were even larger. The cohort difference in DBP for men and women when using different methods for examining the effect of antihypertensive treatment on birth cohort differences can be seen in Table S7, http://links.lww.com/HJH/A760.

DISCUSSION

We found that SBP and DBP were lower among septuagenarians born in 1930 and examined in the 2000s compared with those born 1901–1902 examined in the 1970s, even after adjusting for antihypertensive treatment. The decrease was especially pronounced in women and diminished the sex difference observed in the 1970s. In the 1970s, women had higher SBP and DBP than men, whereas in the second cohort there were no sex differences. The age-related

<table>
<thead>
<tr>
<th>TABLE 3. Mixed effects models of the development of DBP (mmHg) from 70 to 79–80 years of age</th>
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<tbody>
<tr>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td>Intercept</td>
</tr>
<tr>
<td>Cohort (reference born in 1901–1902)</td>
</tr>
<tr>
<td>Sex (reference male)</td>
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<tr>
<td>Age</td>
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<tr>
<td>Age 75+</td>
</tr>
<tr>
<td>Cohort × sex</td>
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<tr>
<td>Sex × age</td>
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<tr>
<td>Sex × age 75+</td>
</tr>
<tr>
<td>Num. obs.</td>
</tr>
<tr>
<td>Num. individuals</td>
</tr>
<tr>
<td>Residual SD</td>
</tr>
<tr>
<td>Random intercept SD</td>
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</tbody>
</table>

*0 outside the confidence interval (CI).
decline in SBP started earlier and was more pronounced in the cohort born in 1930 than in those born in 1901–1902. Thus, the cohort differences in BP widened with age. A previous report on the cohort born in 1901–1902 with a follow-up to age 92 years noted that SBP started to decline after age 75 years in that cohort [34].

The strengths of this study include the representative samples and the longitudinal and similar design of both cohort studies. In addition, the statistical methods give a comprehensive overview of the cohort differences both regarding intraindividual change and cross-sectional cohort differences. There are also several limitations. First, our study is not nearly as large as recent large-scale collaborations [35]. Second, an observational study as this cannot prove causal effects from treatment or risk factors. However, the use of longitudinal data measured similarly three decades apart in cohorts from the same area is rare and puts new insights into the modifiability of BP trajectories in late life in a real-life context. Third, only single measures of BP at each examination were taken, which might overestimate BP levels. Fourth, the RR was lower in the second cohort. This could potentially lead to an overestimation of the differences, as participation bias often means that unhealthy individuals are less likely to take part in the study. This is only partly supported by our finding that dropouts during follow-up in the first cohort had slightly higher BP at age 70 years than participants, whereas there was no difference in BP between participants and dropouts in the cohort born in 1930. Fifth, medication lists were used to assess antihypertensive medication, which probably overestimates the use of antihypertensive medications as several of the medications, may be prescribed for other reasons. However, they probably still influence BP levels irrespective of indication for treatment. In addition, both birth cohorts probably had a higher prescription of antihypertensive medications during follow-up than in the general population, as individuals with hypertension were referred to their general practitioner. Sixth, we used a single imputed constant to account for the impact of all antihypertensive medications. As newer medications were available for the second cohort born in 1930, this might influence our results. In addition, antihypertensive treatment before age 70 years was not recorded, which could influence our results as BP control might be easier to achieve if treatment is initiated early. Seventh, there are some results showing that physicians obtain higher BP readings than nurses [36]. White-coat hypertension could have been increased in the cohort examined in the 1970s, when physicians performed the examinations, compared with the 2000s, when nurses measured BP.

The cohort differences were larger among women than among men, in agreement with other studies from mainly younger samples from the developed world [4,9]. It might be that birth cohort or period changes have had more dramatic effects on BP in women, maybe due to changing sex roles,
such as for example increased labor force participation [16] and higher educational achievement [17] in women. BP was higher in women than in men in those examined in the 1970s, in agreement with previous studies [14]. In the 2000s, this sex difference had almost reversed. Different biological hypotheses regarding the higher BP of women in old age have been suggested, for example sex differences in aortic stiffening with age [15]. Our finding that the sex differences disappeared in the 2000s suggests that lifestyle factors have been underestimated as explanations. We have previously reported in 75-year-olds that both sexes had a decline in the prevalence of cardiovascular disorders between 1975–1976 and 2005–2006, a decline that was more pronounced in women [19]. Cardiovascular disorders were thus more common in women in the 1970s and more common in men in the 2000s [19]. These findings mirror the current results on BP. It seems that factors that influence BP in the elderly have changed more dramatically in women than in men. Although we tested several factors, we could not test the influence of many potentially important lifestyle factors, such as physical activity, diet or stress, as we did not have comparable measures on all occasions. A previous publication from our group showed that physical inactivity at age 75 years decreased in both men and women between the cohort born in 1930 with a cohort born in 1911–1912 [37]. In addition, sexual activity was higher in 70-year-olds born 1930 and those born in 1901–1902 [25]. However, it is not likely that a single factor can explain these birth cohort differences [38].

Our finding that BP was lower in the later born birth cohort is in line with previous studies across all ages in the developed world [4, 9]. This suggests that changes in BP may be a period rather than a birth cohort effect. It is not likely that genetic factors played a role in these birth cohort or period changes, although prenatal and perinatal epigenetic influences might have modified gene expression [39]. Instead, it highlights the importance of environmental factors, such as changes in salt consumption [40], more exercise [37] and better hygiene, and societal changes in relation to maternal and perinatal care [41, 42], urbanization, education [17], working conditions, housing and general health services, might all have contributed to these changes. Previous researches have shown the importance of early-life factors in BP development [43]. More people are also treated for vascular diseases, for example the proportion on antihypertensive treatment increased dramatically in the Western world during the last decades [1]. Broad prevention with antihypertensive treatment at the population level started in the late 1960s, when the first cohort was above age 65 years. As late as in the early 1990s, it was suggested that DBP above 94 mmHg was an indication for treatment and that isolated systolic hypertension was not a treatment target until the Systolic Hypertension in the Elderly Program [44]. Thus, SBP was not a treatment target in the first cohort, and it was not a target until the second cohort was above age 60 years.

The birth cohorts also differed regarding the proportion of survivors at 70 years of age. In the 1901–1902 cohort, only 60% women and 51% of men survived until age 70 years, compared with 78% of women and 66% men in the cohort born in 1930 (Source: Statistics Sweden). Thus composition of survivors at age 70 years may also have changed in a way that influences BP, due to, for example, changes in early and mid-life factors, such as decrease in childhood mortality [45].

SBP is suggested to increase rapidly in adolescence, followed by a slower increase in early adulthood, a rapid increase in mid-life, a slow increase in late life followed by a decline around age 80 years [1, 20]. The decline in DBP starts earlier. Based on cross-sectional data, it has been suggested that BP has a slower rise in mid-life in more recently born cohorts [9], whereas another longitudinal study found no time trends in SBP rise [46]. In our study, the age-related decline in BP started earlier in the cohort born in 1930 compared with the cohort born in 1901–1902. One reason may be changes in guidelines, as discussed above [11]. However, the importance of environmental factors for BP trajectories may be illustrated by findings from several select populations. In nonmodernized societies [47] and in nuns in a secluded order [48], age-related BP rise was much less pronounced than in population-based studies in modern societies. Furthermore, white-collar workers in the United Kingdom had a shallower increase in BP than a general population-based sample [20].

In conclusion, BP decreased, and the age-related decline in SBP started earlier in septuagenarians examined in the 2000s compared with those examined in the 1970s. The decrease was especially pronounced in women. Our findings further illustrate the importance of taking historical context into consideration when analyzing trajectories of BP across the life course.

ACKNOWLEDGEMENTS


Previous presentations: The work was presented partly as a poster at the 22nd Nordic Congress of Gerontology.

Conflicts of interest

I.S. has received consultancy fees from Takeda.

REFERENCES

Reviewers’ Summary Evaluation

Reviewer 2
The study strengths include the longitudinal design adopted and assessment of multiple birth cohorts. The study limitations include that the evaluation of blood pressure was based on a single measurement. In addition, use of antihypertensive treatments was documented according to patient recall and/or medication lists. As a result, the present study findings should be interpreted in light of the potential occurrence of systematic measurement and/or recall biases.