







# Impact of within-visit systolic blood pressure change patterns on blood pressure classification: the Cardiovascular Risk in Young Finns Study

Yaxing Meng <sup>1</sup>, Costan G. Magnussen<sup>1,2,3,4</sup>, Feitong Wu <sup>1</sup>, Markus Juonala <sup>5,6</sup>, Marie-Jeanne Buscot <sup>1</sup>, Katja Pahkala<sup>2,3,7</sup>, Nina Hutri-Kähönen<sup>8</sup>, Mika Kähönen <sup>9</sup>, Tomi Laitinen<sup>10</sup>, Jorma S.A. Viikari<sup>5,6</sup>, Olli T. Raitakari<sup>2,3,11†</sup>, and James E. Sharman <sup>1†\*</sup>

<sup>1</sup>Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia; <sup>2</sup>Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland; <sup>3</sup>Centre for Population Health Research, Turku University Hospital, University of Turku, Turku, Finland; <sup>4</sup>Baker Heart and Diabetes Institute, Melbourne, Victoria, Australia; <sup>5</sup>Department of Medicine, University of Turku, Turku, Finland; <sup>6</sup>Division of Medicine, Turku University Hospital, Turku, Finland; <sup>7</sup>Paavo Nurmi Centre, Sports & Exercise Medicine Unit, Department of Physical Activity and Health, University of Turku, Turku, Finland; <sup>8</sup>Department of Pediatrics, Tampere University and Tampere University Hospital, Tampere, Finland; <sup>9</sup>Department of Clinical Physiology, Tampere University Hospital and Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; <sup>10</sup>Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital and University of Eastern Finland, Kuopio, Finland; and <sup>11</sup>Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku, Finland

Received 21 December 2021; revised 19 May 2022; editorial decision 20 May 2022; accepted 21 May 2022; online publish-ahead-of-print 2 June 2022

See the editorial comment for this article 'New answers to an old question: how many office blood pressure measurements are needed?', by G. Bilo *et al.*, <https://doi.org/10.1093/eurjpc/zwac158>.

## Aims

Most international guidelines recommend that repeat blood pressure (BP) readings are required for BP classification. Two international guidelines diverge from this by recommending that no further BP measurements are required if the first clinic BP is below a hypertension threshold. The extent to which within-visit BP variability patterns change over time, and whether this could impact BP classification is unknown. We sought to examine this.

## Methods and results

Data were from the Cardiovascular Risk in Young Finns Study, a prospective cohort study. Up to 2799 participants were followed from childhood (9–15 years) to adulthood (18–49 years) over up to six visits. Patterns of within-visit systolic BP (SBP) variability were defined as no-change, decrease, increase between consecutive readings (with 5 mmHg change thresholds). Classification of SBP (normal, high-normal, hypertension) using the first reading was compared with repeat readings. On average, SBP decreased with subsequent measures, but with major individual variability (no-change: 56.9–62.7%; decrease: 24.1–31.6%; increase: 11.5–16.8%). Patterns of SBP variability were broadly similar from childhood to adulthood, with the highest prevalence of an increase among participants categorized with normal SBP (12.6–20.3%). The highest prevalence of SBP reclassification occurred among participants with hypertension (28.9–45.3% reclassified as normal or high-normal). The prevalence of reclassification increased with the magnitude of change between readings.

## Conclusion

There is a major individual variation of within-visit SBP change in childhood and adulthood and can influence BP classification. This highlights the importance of consistency among guidelines recommending that repeat BP measurements are needed for BP classification.

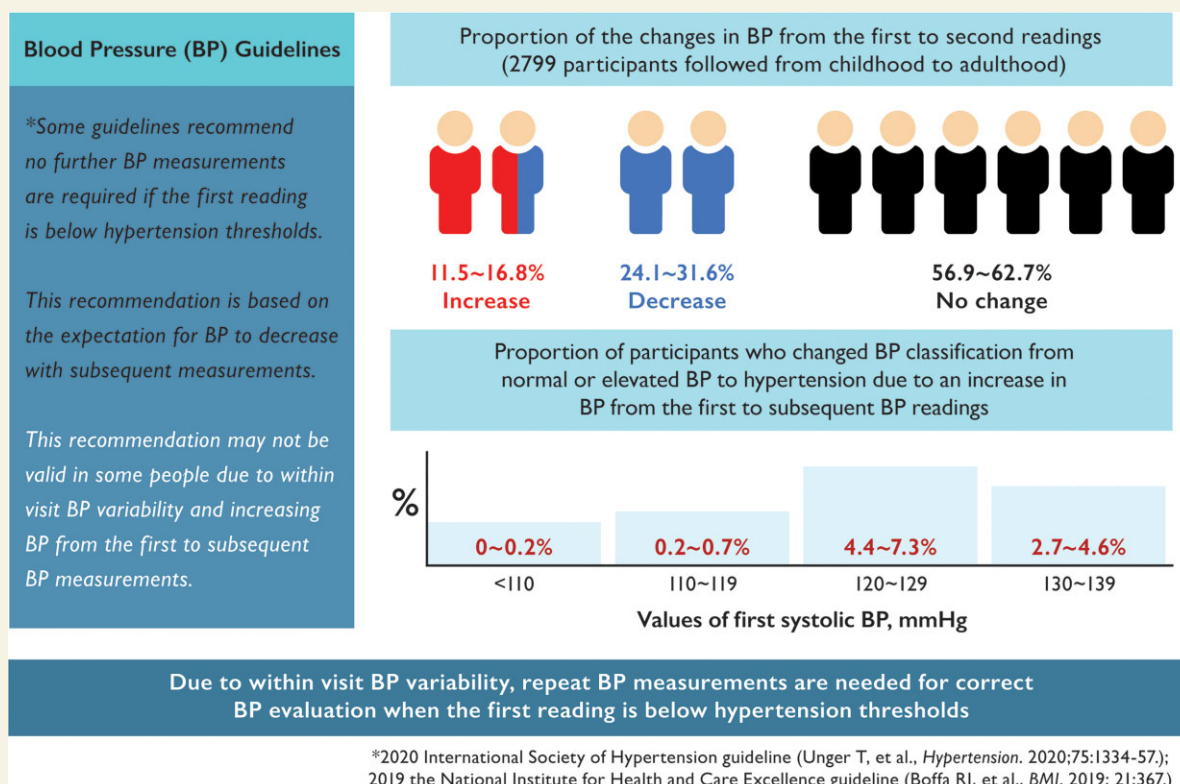
\* Corresponding author. Tel.: +61 3 6226 4709, Fax: +61 3 6226 7704, Email: [james.sharman@utas.edu.au](mailto:james.sharman@utas.edu.au)

† These authors contributed equally.

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

## Graphical Abstract



## Keywords

Blood pressure classification • Clinic blood pressure • Hypertension guidelines • Longitudinal study

## Introduction

In-office measured blood pressure (BP) is the basis for diagnosis and management of hypertension.<sup>1</sup> However, BP changes dynamically among consecutive readings in a single clinic visit, known as within-visit BP variability (WVV), and this might affect the accuracy of in-office BP evaluation.<sup>2</sup> Population-level data show that the mean of the first BP reading within a clinic visit is typically highest and that on average BP decreases upon successive readings.<sup>3</sup> This appears to underlie the rationale for the National Institute for Health and Care Excellence in the United Kingdom to recommend that no further BP measurements are required if the first clinic BP is <140/90 mmHg (Supplementary material online, Table S1).<sup>4</sup> Only one other international society recommends such an approach, but is based on the lower hypertension threshold of <130/85 mmHg (Supplementary material online, Table S1).<sup>5</sup>

The above rationale of only taking one BP reading could be flawed on the basis of individual-level analysis of cross-sectional data in adults<sup>6</sup> and young people<sup>7</sup> in which highly variable WVV change patterns were observed between consecutive BP readings (i.e. no change, decrease, increase). These changes could be of such a magnitude to potentially influence BP classification, especially if only one BP reading is relied upon for diagnostic workup. To our knowledge, there has never been a longitudinal analysis on the individual variation in the patterns of

WVV over time, nor the extent to which WVV could impact BP classification. In this study, we sought to examine this in the population-based Cardiovascular Risk in Young Finns Study in which repeat measures of WVV were recorded from childhood to adulthood.

## Methods

### Study design and setting

Data were available from the Cardiovascular Risk in Young Finns Study, a population-based ongoing prospective cohort study. Full details of the methodology and study design of the Cardiovascular Risk in Young Finns Study have been presented elsewhere.<sup>8</sup> In brief, participants from five Finnish cities and their rural surroundings who were representative of the underlying population were recruited to a population-based prospective cohort study to examine risk factors and precursors of cardiovascular disease from childhood to adulthood. In 1980, the first cross-sectional study was carried out among 3596 participants aged 3, 6, 9, 12, 15, and 18 years. Thereafter, follow-up surveys were conducted in 1983, 1986, 1989, 1992, 2001, 2007, and 2011 (Supplementary material online, Table S2).

### Participants

BP was recorded at each survey visit using the same protocol.<sup>8</sup> However, there was a change in BP devices in 1986, thus for this analysis, data were only included for those participants who had completed three BP

readings at each visit using the same device from 1986 (when participants were aged 9–24 years) to 2011 (when participants were aged 34–49 years) (Supplementary material online, Table S2). Written informed consent was provided by all participants or their guardians. The study followed the guiding principles of the Helsinki Declaration and had local ethics committee approval.

## BP measurement and classification

BP was measured with a random zero sphygmomanometer (Hawksley & Sons, Lancin, UK) using an appropriate cuff size by trained nurses using a standardized protocol.<sup>8</sup> All BP measures were performed between 8 am and 10 am from the right arm after participants had been seated and rested for 5 min. The proper cuff size was selected at each survey according to the circumference and length of the upper arm at the time of BP measurement. There were two choices of cuff size (9.5 cm × 28 cm and 13 cm × 40 cm) for children, with the most appropriate cuff covering at least two-thirds of the upper arm surface. In adults, there were three choices of cuff size: 12 cm wide (for arm circumference 26–32 cm), 14 or 15 cm wide (for arm circumference 33–41 cm), and 18 cm wide (for arm circumference >41 cm). BP measurements were undertaken in outpatient clinics of the Departments of Paediatrics for participants in the cities, and at public health centres for participants in the rural communes. Three measurements were performed with a 2- to 3-min interval between successive readings. This study focused on WVV of systolic BP (SBP) because SBP is the most important single component of BP and the main determinant of cardiovascular events irrespective of age.<sup>9</sup> The SBP values analysed at each visit included one of the three single readings (SBP1, SBP2, SBP3), the mean of the first two or last two successive readings (SBP1 and SBP2 or SBP2 and SBP3), and mean of all three readings. For completeness, some analyses were also conducted for the WVV in diastolic BP (DBP), following the same convention as described for SBP above.

For participants aged <18 years, BP classification was determined by the 2016 European Society of Hypertension (ESH) guidelines in children and adolescents.<sup>10</sup> For participants aged ≥18 years, BP classification was determined by the 2018 European Society of Cardiology (ESC)/ESH guidelines in adults.<sup>11</sup> At the ages of 9, 12, and 15 years, BP classification was defined as normal (<90th percentile for age, sex, and height), high-normal (≥90th to <95th percentile), or hypertension (≥95th percentile).<sup>10</sup> At the age of ≥18 years, BP classification was defined as optimal (<120/80 mmHg), normal (<130/85 mmHg), high-normal (130–139/85–90 mmHg), or hypertension (≥140/90 mmHg).<sup>11</sup> For the purpose of consistent BP classification from childhood (aged 9, 12, and 15 years) to adulthood (aged 18–49 years), the categories of 'optimal' and 'normal' were combined and referred to as 'normal' for participants aged ≥18 years. In this study, BP was first classified based on the first BP measure, then the change of BP classification compared with using the mean of two or three readings was referred to 'reclassification'. Reclassification included 'down-reclassification' (either from high-normal to normal BP, or from hypertension to high-normal or normal BP) and 'up-reclassification' (either from high-normal to hypertension BP, or from normal to high-normal or hypertension BP).

## Patterns of change in WVV

The patterns of no-change, decrease, or increase in WVV were analysed separately at each study time point and defined according to 5 mmHg change thresholds as follows: no change (SBP2 minus SBP1 from –4 to 4 mmHg); decrease (SBP2 minus SBP1 ≥–5 mmHg); and increase (SBP2 minus SBP1 ≥5 mmHg). The threshold change of 5 mmHg was determined on the basis that it was reasonable to expect a small amount of random error in SBP measurement, and a magnitude of >5 mmHg

change in SBP has clinical significance.<sup>12</sup> A threshold change of 10 mmHg was also analysed. Additionally, analysis was undertaken using the change patterns between SBP2 and the third SBP reading (SBP3), between SBP1 and SBP3, as well as between SBP1 and the mean values of SBP2 and SBP3 (meanSBP23).

## Weight status

At all surveys, height and weight were measured and the body mass index (BMI) was calculated as weight in kilograms divided by height in m<sup>2</sup>. Weight status was determined by the BMI. Participants aged ≤18 years were classified as underweight if the BMI was <5th age- and sex-specific percentile, normal if the BMI was ≥5th and <85th percentile, overweight if the BMI was ≥85th and <95th percentile, obesity if the BMI was ≥95th percentile.<sup>13</sup> Weight status in participants aged >18 years were classified as underweight if the BMI was <18.5 kg/m<sup>2</sup>, normal if the BMI was ≥18.5 and <25 kg/m<sup>2</sup>, overweight if the BMI was ≥25 and <30 kg/m<sup>2</sup>, obesity if the BMI was ≥30 kg/m<sup>2</sup>.<sup>14</sup> Owing to the small proportion of the sample that met the criteria for underweight at each time-point, the categories of 'underweight' and 'normal weight' were combined and referred to as 'normal'.

## Statistical methods

Data were presented as mean (standard deviation, SD) or as percentages (%). Analyses were performed using Stata 16.0 (StataCorp, College Station, USA) with a two-tailed *P*-value <0.05 regarded as statistically significant. Cross-tabulation was applied to assess the reclassification of the SBP category (normal, high-normal, hypertension) based on SBP1 compared with the mean of SBP1 and SBP2 (meanSBP12), the mean of SBP2 and SBP3 and the mean of all three readings (meanSBP123). Seven age groups were generated to calculate age-specific BP reclassification. The ages of 9, 12, and 15 years were combined (childhood) as the first age group, and the remaining discrete time points in adulthood aged 18–49 years were divided into six subgroups according to 3- to 4-year intervals between successive subgroups. Given regression to the mean may influence change patterns,<sup>15</sup> we assessed the regression to the mean and regression dilution ratios among repeated SBP readings at each study time point using the following two methods: the MacMahon method,<sup>16</sup> where participants were divided into five groups according to 10 mmHg strata of SBP1 (<110, 110–119, 120–129, 130–139, ≥140 mmHg), then regression dilution ratios were calculated as the range between the mean values of highest (≥140 mmHg) and lowest (<110 mmHg) SBP groups of SBP3 divided by the range between the mean values of the highest and lowest SBP groups of SBP1; the Rosner method,<sup>17</sup> where the slope of the regression line was calculated after regression of SBP3 on SBP1, which represented the regression dilution ratio. Given that SBP1 level, age,<sup>6</sup> sex, and weight status may affect WVV patterns, we examined the distribution of the patterns across SBP status classified from SBP1 and stratified by baseline age, sex, and weight status. Given SBP1 levels may affect the reclassification of the SBP category, we examined reclassification of the SBP category stratified by different SBP groups according to percentiles (childhood) or 5 mmHg (adulthood) strata of SBP1 (childhood: <80th, 80–84th, 85–89th, 90–94th, 95–98th, ≥99th percentile for age, sex, and height; adulthood: <110, 110–119, 120–129, 130–139, 140–149, ≥150 mmHg). Given weight status may affect the reclassifications of the SBP category and SBP1 levels, we further assessed the reclassification of BP categories stratified by weight status and SBP1 levels. Given DBP increased earlier than SBP and predicts the risk of cardiovascular mortality, we assessed patterns of within-visit DBP variability and examined reclassifications of DBP categories. Given that DBP also determines BP classification, this study additionally assessed the reclassification of BP status using a different number and combination of BP measurements, considering SBP and DBP together. Because anti-

**Table 1** Participant demographics and systolic blood pressure indices at six surveys of the Cardiovascular Risk in Young Finns Study

	Study year											
	1986		1989		1992		2001		2007		2011	
	n	Values	n	Values	n	Values	n	Values	n	Values	n	Values
<i>Demographic characteristics</i>												
Female, n (%)	2493	1312 (53.0)	376	194 (51.6)	446	234 (52.5)	2254	1239 (55.0)	2182	1198 (55.0)	2032	1108 (55.0)
Age (years)	2493	16.0 (5.0)	376	19.0 (5.0)	446	22.0 (5.1)	2254	31.5 (5.0)	2182	37.7 (5.0)	2032	41.8 (5.0)
Body mass index (kg/m <sup>2</sup> )	2492	20.0 (3.4)	375	21.9 (3.7)	443	22.7 (3.9)	2247	25.1 (4.4)	2152	26.0 (4.8)	2026	26.5 (5.1)
Overweight or obesity <sup>a</sup> , n (%)	2492	303 (12.2)	375	64 (17.1)	443	104 (23.5)	2247	978 (43.5)	2152	1147 (53.3)	2026	1155 (57.0)
<i>SBP indices</i>												
SBP1	2493	116 (14)	376	116 (12)	446	117 (12)	2254	118 (14)	2182	122 (15)	2032	120 (15)
SBP2	2493	113 (13)	376	114 (11)	446	115 (12)	2254	116 (14)	2182	121 (15)	2032	119 (14)
SBP3	2493	112 (13)	376	113 (10)	446	114 (12)	2254	115 (13)	2182	120 (14)	2032	118 (14)
Mean of SBP1 and SBP2	2493	114 (13)	376	115 (11)	446	116 (11)	2254	117 (13)	2182	121 (15)	2032	119 (14)
Mean of SBP2 and SBP3	2493	113 (13)	376	114 (10)	446	114 (11)	2254	116 (13)	2182	120 (14)	2032	118 (14)
Mean of SBP1, SBP2 and SBP3	2493	114 (13)	376	115 (11)	446	115 (11)	2254	117 (131)	2182	121 (14)	2032	119 (14)

Values are continuous data with normal distribution expressed as mean (standard deviation); categorical data expressed as proportions.

SBP1, the first SBP reading at each visit; SBP2, the second SBP reading at each visit; SBP3, the third SBP reading at each visit.

<sup>a</sup>Participants aged >18 years were classified as overweight or obesity if body mass index  $\geq 25$  kg/m<sup>2</sup>. Participants aged  $\leq 18$  years were classified as overweight or obesity if body mass index was at least 85th age- and sex-specific percentile.

**Table 2** Distribution of patterns of within-visit systolic blood pressure variability from first to second reading at each survey time-point

	1986 n (%)	2001 n (%)	2007 n (%)	2011 n (%)
<i>5 mmHg threshold</i>				
No change	1419 (56.9)	1321 (58.6)	1278 (58.6)	1273 (62.7)
Decrease	787 (31.6)	642 (28.5)	538 (24.7)	489 (24.1)
Increase	287 (11.5)	291 (12.9)	366 (16.8)	270 (13.3)
<i>10 mmHg threshold</i>				
No change	2053 (82.4)	1887 (83.7)	1791 (82.1)	1774 (87.3)
Decrease	344 (13.8)	271 (12.0)	216 (9.9)	175 (8.6)
Increase	96 (3.9)	96 (4.3)	175 (8.0)	83 (4.1)

All participants with complete three systolic blood pressure readings at each visit. Because the limitation in the sampling size in 1989 and 1992, this table did not show the measures in these 2 years.

hypertensive medication usage might affect BP categories, we also examined the reclassification of SBP categories after excluding participants who had ever used anti-hypertensive medication. Given the heterogeneities among the participants regarding the different number of visits and the length of follow-up, we repeated the above analyses among the participants who attended all surveys from 1986 to 2011.

## Results

### Distribution of patterns of WVV from childhood to adulthood

The mean (SD) length of follow-up was 16.8 (9.8) years and the mean (SD) number of separate visits at which WVV was measured

was 3.1 (1.4). [Table 1](#) shows participant demographics and the mean values from the first to third SBP reading at each visit. On average, SBP decreased with subsequent measures. However, there was major individual variability in the direction of change from SBP1 to SBP2, as shown in [Table 2](#) (56.9–62.7% no change; 24.1–31.6% decrease; 11.5–16.8% increase). The distribution patterns of WVV from SBP1 to SBP2 were broadly similar across each visit from childhood to adulthood. The distribution of WVV patterns from SBP1 to SBP2 was consistent irrespective of different age groups at baseline or sex (data are not shown). The distribution of WVV patterns from SBP1 to SBP2 was consistent by weight status (Normal weight: 56.9–63.6% no-change; 22.3–31.2% decrease; 11.9–16.5% increase; overweight or obesity: 56.4–61.8% no-change; 25.2–34.7% decrease; 8.6–16.7% increase). The distribution patterns of WVV from SBP1 to SBP2 among 1191 participants who attended all surveys from 1986 to 2011 were essentially unchanged (57.0–63.1% no change; 24.3–31.3% decrease; 11.7–17.8% increase). With a change threshold of 10 mmHg about 80% of participants had no change from SBP1 to SBP2 whereas between 9 and 14% of participants had a decrease and 4–8% had an increase from SBP1 to SBP2. The results were largely consistent for change patterns between SBP2 and SBP3, as well as between SBP1 and SBP3 (data are not shown). [Table 3](#) shows that there was a considerable proportion of participants with an increase in SBP with consecutive readings among all BP categories determined by SBP1. The highest prevalence of an increase in SBP (either from SBP1 to SBP2 or SBP1 to meanSBP23) was among those participants categorized with normal SBP1. For these participants, the prevalence of an increase in SBP ranged from 12.6 to 20.3% between SBP1 and SBP2, and 11.4 to 17.1% between SBP1 and meanSBP23. These results were similar when BP categories were determined by first SBP and first diastolic BP readings together (data are not shown). The



**Table 3** Distribution of patterns of within-visit systolic blood pressure variability at each visit across systolic blood pressure categories classified from the first measured systolic blood pressure

BP category	1986 n (%)	2001 n (%)	2007 n (%)	2011 n (%)
<i>From first to second SBP reading</i>				
<i>Normal<sup>a</sup></i>				
No change <sup>b</sup>	1182 (60.4)	1086 (61.1)	891 (58.2)	1032 (66.9)
Decrease <sup>b</sup>	529 (27.0)	438 (24.6)	329 (21.5)	288 (18.7)
Increase <sup>b</sup>	247 (12.6)	254 (14.3)	310 (20.3)	223 (14.5)
<i>High normal<sup>a</sup></i>				
No change <sup>b</sup>	144 (48.7)	172 (54.4)	225 (61.3)	145 (55.3)
Decrease <sup>b</sup>	124 (41.9)	122 (38.6)	102 (27.8)	96 (36.6)
Increase <sup>b</sup>	28 (9.5)	22 (7.0)	40 (10.9)	21 (8.0)
<i>Hypertension<sup>a</sup></i>				
No change <sup>b</sup>	93 (38.9)	63 (39.4)	162 (56.8)	96 (42.3)
Decrease <sup>b</sup>	134 (56.1)	82 (51.3)	107 (37.5)	105 (46.3)
Increase <sup>b</sup>	12 (5.0)	15 (9.4)	16 (5.6)	26 (11.5)
<i>From first SBP reading to the mean of second and third readings</i>				
<i>Normal<sup>a</sup></i>				
No change <sup>b</sup>	1126 (57.5)	1027 (57.8)	932 (60.9)	1036 (67.1)
Decrease <sup>b</sup>	608 (31.1)	520 (29.3)	336 (22.0)	307 (19.9)
Increase <sup>b</sup>	224 (11.4)	231 (13.0)	262 (17.1)	200 (13.0)
<i>High normal<sup>a</sup></i>				
No change <sup>b</sup>	130 (43.9)	161 (51.0)	221 (60.2)	147 (56.1)
Decrease <sup>b</sup>	146 (49.3)	136 (43.0)	119 (32.4)	100 (38.2)
Increase <sup>b</sup>	20 (6.8)	19 (6.0)	27 (7.4)	15 (5.7)
<i>Hypertension<sup>a</sup></i>				
No change <sup>b</sup>	75 (31.4)	63 (39.4)	140 (49.1)	95 (41.9)
Decrease <sup>b</sup>	153 (64.0)	92 (57.5)	134 (47.0)	112 (49.3)
Increase <sup>b</sup>	11 (4.6)	5 (3.1)	11 (3.9)	20 (8.8)

Data are from participants with three complete SBP readings at each visit. Because the limitation in the sampling size in 1989 and 1992, this table did not show the measures in these 2 years.

<sup>a</sup>At ages of 9, 12, 15 years, SBP was classified as: normal (<90th percentile), high-normal (≥90th to <95th percentile), hypertension (≥95th percentile). At the age of ≥18 years, SBP was classified as: normal (SBP <130 mmHg), high-normal (SBP ≥130–139 mmHg), hypertension (SBP ≥140 mmHg).

<sup>b</sup>No change means that the difference between the first and second SBP reading or the mean of second and third readings is from −4 to 4 mmHg. Decrease means that the difference between first and second SBP reading or the mean of second and third readings is ≤−5 mmHg. Increase means that the difference between first and second SBP reading or the mean of second and third readings is ≥5 mmHg.

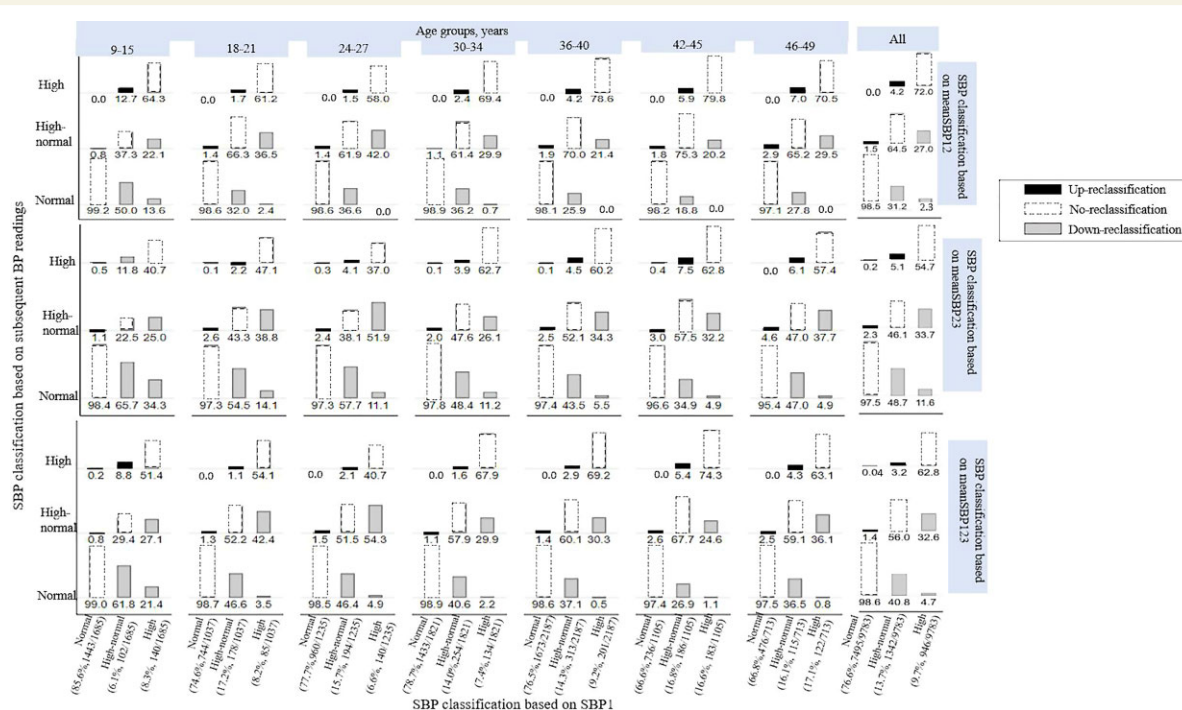
consistency of the individual variations of WVV patterns using a 5 mmHg threshold was evaluated among participants who attended baseline (1986) and all follow-up surveys in 2001, 2007, and 2011. Of the 139 participants who had an increase from SBP1 to SBP2 at baseline, 10.8–15.8% continued to have an increase in SBP at each subsequent follow-up survey. Of the 373 participants who had a decrease from SBP1 to SBP2 at baseline, 21.5–29.2% maintained this pattern at each subsequent follow-up survey (Supplementary material online, Table S3). Similar results were observed when we considered only those with two consecutive surveys (i.e. between 1986 and 2001, between 2001 and 2007, between 2007 and 2011) (Supplementary material online,

Figure S1). For example, among 212 participants who had an increase from SBP1 to SBP2 in 2007, 14.6% maintained this WVV pattern in 2011. The distribution of WVV patterns were similar for DBP (with a change threshold of 5 mmHg: no-change: 58–70%; decrease:16–23%; increase:14–19%).

**Reclassification of BP based on SBP1 compared with subsequent readings**

Across all participants, 76.6% were categorized as normal using SBP1, whereas 13.7 and 9.7% were categorized as high-normal and hypertension, respectively (Figure 1). Irrespective of age, there was a low prevalence of BP reclassification among people with normal SBP1, whereas there was a larger prevalence of BP reclassification among people with higher SBP1 (Figure 1). Specifically, of those categorized with normal SBP using SBP1, only 1.5% (110/7495) were reclassified as high-normal or hypertension using meanSBP12. Furthermore, only 2.5% (191/7495) were reclassified using meanSBP23, and only 1.5% (109/7495) were reclassified using meanSBP123 (Figure 1). Conversely, of those categorized with hypertension using SBP1, 29.0% (274/946) were reclassified as normal or high-normal using meanSBP12. Furthermore, 45.3% (429/946) were reclassified using meanSBP23, and 37.2% (352/946) were reclassified using meanSBP123 (Figure 1). Reclassification increased the closer SBP1 was to the BP classification threshold (i.e. childhood: age-, sex-, and height-specific percentile: 90<sup>th</sup> for normal SBP, 95<sup>th</sup> for high SBP; adulthood: 130 mmHg for normal SBP, 140 mmHg for high SBP) (Supplementary material online, Figure S2). The reclassifications of SBP categories were consistent by weight categories (Supplementary material online, Figure S3). After excluding participants who had ever used antihypertensive medication, the results were essentially unchanged. For example, of those categorized with normal SBP using SBP1, 1.2% (86/7046) were reclassified as high-normal or hypertension using meanSBP12, 2.0% (144/7046) were reclassified using meanSBP23, and 1.0% (85/7046) were reclassified using meanSBP123. Of those categorized with hypertension using SBP1, 31.1% (224/721) were reclassified as normal or high-normal using meanSBP12, 48.0% (346/721) were reclassified using meanSBP23, and 40.0% (289/721) were reclassified using meanSBP123. Furthermore, the reclassifications of SBP categories were similar among 1191 participants with complete SBP data across 1986, 2001, 2007, and 2011 (data are not shown). The reclassifications were similar for DBP. For example, of those categorized with normal DBP using the first DBP reading, 1.8% (146/8329) were reclassified as high-normal or hypertension using the mean of the first and second reading, 3.6% (283/8329) were reclassified using the mean of the second and third readings, and 1.6% (109/8329) were reclassified using the mean of all three readings. The results were also similar when BP categories were determined by both SBP and DBP together (Supplementary material online, Table S4).

Supplementary material online, Figure S4 shows the percentage of reclassification in BP category according to the patterns of WVV (i.e. no-change, decrease, increase) from SBP1 to SBP2 using a threshold change of 5 mmHg. In general, the prevalence of reclassification increased with the magnitude of the change between readings. For example, those with an increase from SBP1 to SBP2 ranging from 5 to



**Figure 1** Age-specific systolic blood pressure classification based on the first systolic blood pressure reading compared with the mean of two or three systolic blood pressure readings among individuals with three complete systolic blood pressure readings at a single visit aged 9–49 years. Values (%) indicate the percentage of the reclassification of systolic blood pressure categories based on the first reading compared with using the mean of two or three readings. Down-reclassification was either from high-normal to normal systolic blood pressure, or from hypertension to high-normal or normal. No-reclassification indicates the blood pressure classification did not change. Up-reclassification was either from high-normal to hypertension, or from normal to high-normal or hypertension. meanSBP12, mean of the first and second systolic blood pressure readings at each visit; meanSBP23, mean of the second and third systolic blood pressure readings at each visit; meanSBP123, mean of the first, second and third systolic blood pressure readings at each visit. For measures collected at ages 9, 12, 15 years, systolic blood pressure was classified as: normal (<90th percentile), high-normal (≥90th to <95th percentile), hypertension (≥95th percentile). For measures collected at ≥18 years, systolic blood pressure was classified as: normal (<130 mmHg), high-normal (≥130–139 mmHg), hypertension (≥140 mmHg).

10 mmHg, 7.8% were reclassified to a higher BP category (up-reclassification) using meanSBP12, 9.6% had up-reclassification using meanSBP23, and 5.6% had up-reclassification using meanSBP123. Whereas there was about a two-fold increase in this pattern of reclassification when the magnitude of the increase from SBP1 to SBP2 was more than 10 mmHg.

Regression to the mean analyses among within-visit consecutive SBP readings is shown in [Supplementary material online, Figure S5](#) (MacMahon method) and [Supplementary material online, Figure S6](#) (Rosner method). [Supplementary material online, Figure S5](#) shows general trends towards regression to the mean from SBP1 to SBP3 among those with higher SBP upon first measurement, but with high regression dilution ratios (ranging from 0.836 to 0.867 for the MacMahon method and from 0.832 to 0.866 for the Rosner method) altogether indicating a minimal influence of regression to the mean. The results were essentially unchanged when the regression to the mean analyses were constructed using SBP1 and SBP2 (regression dilution ratios: the MacMahon method, 0.866–0.892; the Rosner method, 0.858–0.890) and using SBP2 and SBP3 (regression dilution ratios: the MacMahon method, 0.963–0.971; the Rosner method, 0.910–0.939).

## Discussion

In this population-based longitudinal study, we found large individual variability in the change in BP with repeat measures at a single clinic visit. Consistent with other studies,<sup>3,18</sup> we showed that BP declines on average with repeated measurement, but a novel observation was that a sizeable percentage of participants had an increase among their consecutive within-visit SBP readings, and this is similar at each observed time-point from childhood to adulthood. The most important consequence of individual variations of patterns of WVV was a change in BP classification when using a single SBP reading versus subsequent readings. This was most pronounced among people who were hypertensive according to their first SBP reading and were reclassified as normal or high-normal by the average of repeat measures. Critically, reclassification also occurred in the opposite direction among people who had increases in SBP with consecutive readings (albeit with lower prevalence). The results were consistent when BP categories were determined by either SBP or diastolic BP. Overall, these findings have implications regarding the recommended protocols for accurate BP measurement and hypertension diagnosis in childhood and adulthood.

## Comparison with other studies

To our knowledge, this is the first study to examine individual variation in patterns of WVV from childhood to adulthood, encompassing an extensive follow-up time (31 years). The variability in the direction of BP changes from one reading to the next are broadly similar to other research that has examined this using a cross-sectional design. In 20716 adults from a general population with a mean age of 45 years, 18% of subjects had an increase, 33% had a decrease and 49% had no change in SBP from the first to the second BP readings according to 5 mmHg as the threshold of a change.<sup>6</sup> Another analysis using data from 3047 children and adolescents, aged 5–17 years, showed that from the first to second BP measurements, SBP decreased in 58% (95%CI 56–60) of subjects, did not change in 10% (95%CI 9–12), and increased in the remaining 32% (95%CI 29–34) of the population.<sup>7</sup> Our study extends on these observations showing that there is a similar distribution of variability of within clinic BP (no-change, decrease, increase) over many years of measurement, with nearly 10–15% of people maintaining the subsequently increase across the observed lifespan. This study also provides the first evidence that these individual variations in patterns of WVV result in reclassification of BP categories when using a single reading compared with repeated readings in childhood and adulthood. These data are relevant to international guideline recommendations on BP measurement and underscore the need to use repeated measurements for BP classification across all guidelines.

## Interpretation of results and implications

Currently there are subtle variations between international hypertension practice guidelines on the recommended protocols to measure BP. Most guidelines recommend taking at least two BP readings, or more if there are major differences between BP readings.<sup>1,11,19–21</sup> However, the 2019 National Institute for Health and Care Excellence guideline for the United Kingdom only recommends taking additional BP measures if the first reading is  $\geq 140/90$  mmHg.<sup>4</sup> Similarly, the 2020 worldwide practice guidelines developed by the International Society of Hypertension advise that no further BP measurement is required if the first reading is  $<130/85$  mmHg.<sup>5</sup> These protocols would be optimal for accurate diagnosis if the first BP reading was always higher than subsequent readings. Certainly, this is true for the average of consecutive BP readings at the population level, but is not the case at the individual level according to our findings, nor those of other recent analyses showing that BP increases upon repeat measures in about 11–18% of the population.<sup>6,7</sup> Our findings argue that a second BP measurement is needed in those with normal BP on the first measurement, based on the relatively consistent individual variation of WVV across multiple time-points (Supplementary material online, Table S3 and Supplementary material online, Figure S1) and the sizeable proportion that subsequently increase (Table 3), rather than the relatively small impact this has on reclassification of those who are 'normal' from the first measurement (Figure 1). Nevertheless, the proportion reclassified is more pronounced the closer SBP1 values are to the BP classification threshold (Supplementary material online, Figure S2). The other important finding of this current study was that it was not uncommon for large differences between consecutive BP readings to occur ( $>10$  mmHg), and this was related to a higher prevalence of BP

recategorization. Altogether our study emphasizes that accurate BP measurement should be based on the average of repeated readings, regardless of whether the first value is normal or high especially when SBP1 levels are closer to the classification threshold.

According to the threshold changed of 5 mmHg, about 40% of the study sample experienced an increase or decrease from the first SBP reading to consecutive readings, and this was consistent in both childhood and adulthood. These data relating to decreases in SBP may be partly explained by regression to the mean, whereby those participants with higher SBP at first measurement had a trend towards lower SBP reading at the final measurement. However, there was less evidence of regression to the mean among participants with low SBP at first measurement, and statistical tests overall indicated minimal influence of regression to the mean (Supplementary material online, Figure S5 and S6). It is less likely that the measurement method itself has contributed to the SBP variability between readings because a standardized auscultatory method by trained operators using the same device was undertaken. On the other hand, if automated BP devices were used instead, this could have been a source of random error in BP measurement.<sup>22</sup> Spontaneous variability of BP occurring over minutes or between beats (due to many factors, such as emotional stimuli, respiratory variation or local vasomotor phenomena<sup>23</sup>) could have contributed to the study findings. We cannot rule out that the BP changes observed between readings in this study represent real physiological variability that must be considered in BP measurement protocols, and again supports the importance of using repeated BP readings during diagnostic workup regardless of the first BP value.

## Strengths and limitations

The main strengths of this study are using a large, established, and well-characterized, longitudinal study derived from the general population. Furthermore, each BP measurement was undertaken with manual auscultation using a standardized, international protocol. This will reduce the potential influence from measurement error. A possible study limitation is bias due to differential loss to follow-up. However, compared with other similar studies, participant retention in the Young Finns Study was high, with non-participants at earlier surveys re-entering at later time-points. Furthermore, baseline risk factor levels between participants and non-participants in adult surveys have largely been comparable.<sup>24</sup> Another study limitation was that all BP measures at each survey in the Young Finns Study were performed on the right arm and did not consider between-arm difference as suggested by the BP guidelines (Supplementary material online, Table S1). Thus, our protocol was not the same as that recommended in either the NICE or ISH guidelines, and this could influence the interpretation of our results as they relate to these guidelines. Our study population was young at baseline and the oldest age at follow up was 49 years. Thus, our findings may not be generalizable to older age strata, which is a population most likely to be affected by hypertension. Finally, as surveys in the Young Finns Study were conducted a minimum of 3-years apart [median (interquartile range), 6 (4–15) years], BP status was classified according to BP readings collected at a single visit, rather than at repeat clinic visits or using out-of-clinic measures to confirm clinical diagnosis as recommended by the guidelines (Supplementary material online, Table S1).

## Conclusion

WVV change patterns are highly variable at the individual-level whereby BP does not drop with repeated measurements for a sizeable proportion of the population. These individual variations in patterns of WVV result in reclassification of BP category when using a single reading versus the mean of repeated readings, and this is evident across childhood to adulthood. Irrespective of age, reclassification was most pronounced in those who were hypertensive based on the first SBP reading and were below the hypertension threshold on repeat measurements. Importantly, reclassification also occurred in the opposite direction, albeit with lower prevalence. These findings have implications for BP guidelines on how to measure BP for both children and adults. Accurate BP evaluation should be based on the average of repeated readings, regardless of whether the first value is normal or high.

## Financial support

None.

## Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

## Authors' Contribution

Y.M. processed and analysed the data and wrote and finalized the manuscript. C.G.M. and J.E.S. provided advice on the analysis, helped with the development of the manuscript, and modified the manuscript. F.W. and M.-J.B. provided advice on the analysis. All of other authors contributed to the design of the study and participated in data collection. All authors contributed to critical review of the manuscript, read, and approved the final draft.

## Acknowledgment

We thank all staff and participants in the Young Finns Study.

**Conflict of interest:** No support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

## References

- Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbigele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension* 2018;**71**:e140–e144.
- Parati G, Stergiou GS, Dolan E, Bilo G. Blood pressure variability: clinical relevance and application. *J Clin Hypertens (Greenwich)* 2018;**20**:1133–1137.
- Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in humans and experimental animals. *Circulation* 2005;**111**:697–716.
- National Guideline C. *National institute for health and care excellence: clinical guidelines. Hypertension in adults: diagnosis and management*. London: National Institute for Health and Care Excellence (UK); 2019.
- Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, Wainford RD, Williams B, Schutte AE. 2020 international society of hypertension global hypertension practice guidelines. *Hypertension* 2020;**75**:1334–1357.
- Veloudi P, Blizzard CL, Srikanth VK, Breslin M, Schultz MG, Sharman JE. Age-dependent changes in blood pressure over consecutive office measurements: impact on hypertension diagnosis and implications for international guidelines. *J Hypertens* 2017;**35**:753–760.
- Veloudi P, Blizzard CL, Srikanth VK, Schultz MG, Sharman JE. Influence of blood pressure level and age on within-visit blood pressure variability in children and adolescents. *Eur J Pediatr* 2018;**177**:205–210.
- Raitakari OT, Juonala M, Rönnemaa T, Keltikangas-Järvinen L, Rasanen L, Pietikainen M, Hutri-Kahonen N, Taittonen L, Jokinen E, Marniemi J, Jula A, Telama R, Kahonen M, Lehtimäki T, Akerblom HK, Viikari JS. Cohort profile: the cardiovascular risk in young finns study. *Int J Epidemiol* 2008;**37**:1220–1226.
- Williams B, Lindholm LH, Sever P. Systolic pressure is all that matters. *The Lancet* 2008;**371**:2219–2221.
- Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, Invitti C, Litwin M, Mancia G, Pall D, Rascher W, Redon J, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wühl E, Zanchetti A. European society of hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens* 2016;**34**:1887–1920.
- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I, De Backer G, Heagerty AM, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;**39**:3021–3104.
- Campbell NRC, Schutte AE, Varghese CV, Ordunez P, Zhang X-H, Khan T, Sharman JE, Whelton PK, Parati G, Weber MA, O'riás M, Jaffe MG, Moran AE, Liane Plavnik F, Ram VS, Brainin M, Owolabi MO, Ramirez AJ, Barbosa E, Bortolotto LA, Lackland DT. São Paulo call to action for the prevention and control of high blood pressure: 2020. *J Clin Hypertens (Greenwich)* 2019;**21**:1744–1752.
- Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Mei Z, Wei R, Curtin LR, Roche AF, Johnson CL. 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat* 2000;**246**:1–190.
- Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1995. vol. 854, p. 1–452.
- Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol* 2004;**34**:215–220.
- MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, Abbott R, Godwin J, Dyer A, Stamler J. Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet* 1990;**335**:765–774.
- Rosner B, Willett WC, Spiegelman D. Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. *Stat Med* 1989;**8**:1051–1069.
- Schulze MB, Kroke A, Bergmann MM, Boeing H. Differences of blood pressure estimates between consecutive measurements on one occasion: implications for inter-study comparability of epidemiologic studies. *Eur J Epidemiol* 2000;**16**:891–898.
- Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E, Persu A, Mancia G, Kreutz R. 2021 European society of hypertension practice guidelines for office and out-of-office blood pressure measurement. *J Hypertens* 2021;**39**:1293–1302.
- Leung AA, Nerenberg K, Daskalopoulou SS, McBrien K, Zarnke KB, Dasgupta K, Cloutier L, Gelfer M, Lamarre-Cliche M, Milot A, Bolli P, Tremblay G, McLean D, Tobe SW, Ruzicka M, Burns KD, Vallée M, Prasad GVR, Lebel M, Feldman RD, Selby P, Pipe A, Schiffrin EL, McFarlane PA, Oh P, Hegele RA, Khara M, Wilson TW, Penner SB, Burgess E, et al. Hypertension Canada's 2016 Canadian hypertension education program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol* 2016;**32**:569–588.
- Gabb GM, Mangoni AA, Anderson CS, Cowley D, Dowden JS, Gollidge J, Hankey GJ, Howes FS, Leckie L, Perkovic V, Schlaich M, Zwar NA, Medley TL, Arnold A. Guideline for the diagnosis and management of hypertension in adults — 2016. *Med J Aust* 2016;**205**:85–89.



22. Sharman JE, Padwal R, Campbell NRC. Global marketing and sale of accurate cuff blood pressure measurement devices. *Circulation* 2020;**142**:321–323.
23. Mancia G. Short- and long-term blood pressure variability: present and future. *Hypertension* 2012;**60**:512–517.
24. Dwyer T, Sun C, Magnussen CG, Raitakari OT, Schork NJ, Venn A, Burns TL, Juonala M, Steinberger J, Sinaiko AR, Prineas RJ, Davis PH, Woo JG, Morrison JA, Daniels SR, Chen W, Srinivasan SR, Viikari JS, Berenson GS. Cohort profile: the international childhood cardiovascular cohort (i3c) consortium. *Int J Epidemiol* 2013;**42**:86–96.