eAPPENDIX: supplemental digital content

1 Growth mixture modelling

eTable 1. Model fit indices and class information from the growth mixture models with increasing numbers of classes.

Classes:		Men				Women			
		BIC	**LRT (p)**	**Entropy**	**Class sizes**	**BIC**	**LRT (p)**	**Entropy**	**Class sizes**
SBP	**1**	39220	-	-	1840	39517	-	-	1819
	2	39111	0.001	0.82	1736, 104	39363	<0.001	0.98	1794, 25
	3	39103	0.78	0.84	1709, 100, 31	39316	0.008	0.84	1687, 108, 24
	4	39094		0.82	1671, 68, 33, 68	39316	0.20	0.78	1519, 117, 86, 17
	5	39104		0.81	1629, 98, 35, 16, 72	39307		0.78	2, 1563, 110, 20, 124
DBP	**1**	36401	-	-	1840	36412	-		1819
	2	36359	0.005	0.84	1795, 45	36344	<0.001	0.97	1802, 17
	3	36366	0.013	0.87	1777, 4, 59	36292	<0.001	0.92	21, 48, 1750
	4	36367	0.165	0.72	1599, 9, 62, 170	36306	0.334	0.89	17, 30, 32, 1740
	5	36370		0.74	1567, 11, 188, 4, 70	36317		0.90	1737, 7, 7, 37, 31
PP	**1**	36820	-	-	1840	36762	-	-	1819
	2	36688	0.107	0.87	1769, 71	36594	0.003	0.77	1694, 125
	3	36631	0.003	0.89	1744, 71, 25	36515	0.002	0.83	1677, 12, 130
	4	36627	0.117	0.86	4, 1700, 27, 109	36524	0.8	0.84	1652, 6, 11, 147
	5	36623		0.84	19, 71, 67, 5, 1678	36522		0.67	58, 10, 375, 56, 1320

SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; BIC: Bayesian information criterion; LRT: Lo-Mendell-Rubin Likelihood ratio test.

2 Sensitivity analyses

2.1 Choice of constant for treatment effect

The models reported in the paper corrected values that were observed while on antihypertensive medication by adding constants of 10mmHg for systolic blood pressure (SBP) and 5mmHg for diastolic blood pressure (DBP). We examined the sensitivity of the extracted latent classes and class membership to this choice of constant by refitting the models assuming a higher treatment effect of 15mmHg for SBP and 10mmHg for DBP.

Compared to the main models in the paper, the number of extracted classes remained the same for SBP and DBP (pulse pressure is unchanged in this scenario since it is calculated as SBP minus DBP). The concordance between the classes was also very good (eTable 2). In men, none of the original 'Increaser' class were discordant, and the latent trajectories were very similar (not shown). There was a slight increase in the number of people in the 'Increaser' class. Similar results were found in women with the exception of 5 individuals (0.3%) who were in the non 'Normative' classes using the main models being classified into the 'Normative' class in models that used a higher treatment effect.

eTable 2: Class concordance in men when assuming different blood pressure treatment effects

	Sensitivity models (assuming a bigger treatment effect)†			
	SBP		DBP	
	Norm.	Inc.	Norm.	Inc.
Main Models‡				
SBP n (%)				
Norm.	1719 (99.0)	17 (1.0)		
Inc.	0 (0)	104 (100)		
DBP n (%)				
Norm.			1777 (99.0	18 (1.0)
Inc.			0 (0)	45 (100)

† A constant of +15 for SBP and +10mmHg for DBP was added to values observed on antihypertensive medication
‡ A constant of 10mmHg for SBP and 5mmHg for DBP was added to values observed on antihypertensive medication. These are the main models presented in the paper.
SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure;
Norm.: Normative class; Inc.: Increaser class; Dec.: Decreaser class

eTable 3: Class concordance in women when assuming different blood pressure treatment effects

	Sensitivity models (assuming a bigger treatment effect)†					
	SBP			DBP		
	Norm.	Inc.	High	Norm.	Inc.	High
Main Models‡						
SBP n (%)						
Norm.	1641 (97.3)	46 (2.7)	0 (0)			
Inc.	0 (0)	108 (100)	0 (0)			
High.	0 (0)	0 (0)	24 (100)			
DBP n (%)						
Norm.				1742 (99.5)	5 (0.3)	3 (0.2)
Inc.				1 (4.8)	20 (95.2)	0 (0)
High				4 (8.3)	0 (0)	44 (91.7)

† A constant of +15 for SBP and +10mmHg for DBP was added to values observed on antihypertensive medication
‡ A constant of 10mmHg for SBP and 5mmHg for DBP was added to values observed on antihypertensive medication. These are the main models presented in the paper.
SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure;
Norm.: Normative class; Inc.: Increaser class;

2.2 Treatment censored blood pressure

To further examine the influence of including treated blood pressure on the extracted latent classes, we refitted models after censoring an individual's BP trajectory from the time of first treatment for high BP.

Compared to the main models in the paper, the number of extracted classes was the same and the mean trajectories for each class were broadly similar (eFigure 1). The one exception was the DBP 'Increaser' class in women, which contained fewer individuals and had a steeper slope in the censored models. There was some disagreement in the classification of individuals between the models generated using the censored BP data and the main models using uncensored BP (eTable 4 and 5). Generally this disagreement was approximately 30%, and mainly in the direction of individuals who were classified in a non 'Normative' trajectory class in the main analysis being classified as a 'Normative' in the censored analysis.

That the mean trajectories of the extracted classes were generally similar in the two sets of analyses (eFigure 1), suggests there were other reasons for the classification discordance other than the latent trajectories being fundamentally different. We investigated whether a lack of data points could be a reason for this differential classification since censoring may cause a loss of information on key parts of an individual's trajectory that are used to classify individuals. Following up the finding that the majority of discordance occurred because the censored models classified more individuals into a 'Normative' class, we compared the medication prevalence and number of BP observations between individuals who were discordant 'Normatives' using the censored models with individuals who were concordant non 'Normatives'. eTable 6 shows that with the exception of female DBP, the discordant individuals generally had fewer BP observation points and were more likely to have a treatment censored trajectory. This highlights the need for multiple data points to ensure robust class classification.

eTable 4: Class concordance in men between models generated from data where an individuals BP trajectory was censored at the point of first treatment for high BP and models that don't censor treated individuals.

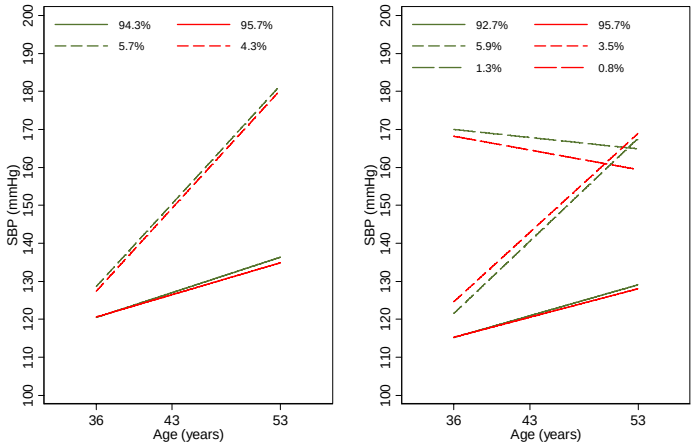
	Sensitivity models (treated BP censored)†						
	SBP		DBP		PP		
	Norm.	Inc.	Norm.	Inc.	Norm.	Inc.	Dec.
Uncensored BP‡							
SBP n (%)							
Norm.	1702 (0.5)	8 (0.5)					
Inc.	30 (30.0)	70 (70.0)					
DBP n (%)							
Norm.			1766 (99.9)	2 (0.1)			
Inc.			15 (35.7)	27 (64.3)			
PP n (%)							
Norm.					1699 (98.8)	16 (0.93)	4 (0.2)
Inc.					21 (31.3)	46 (68.7)	0 (0)
Dec.					1 (4.2)	0 (0)	23 (95.8)

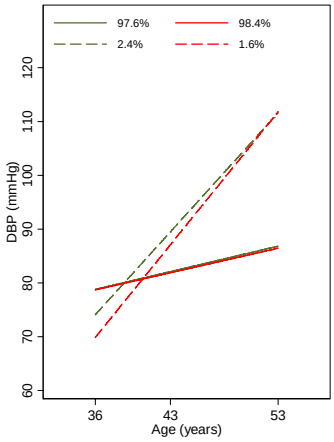
† Once an individual was known to be on treatment for high BP their trajectory was censored
‡ A constant of 10mmHg for SBP and 5mmHg for DBP was added to values observed on antihypertensive medication. These are the main models presented in the paper.
SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure;
Norm.: Normative class; Inc.: Increaser class; Dec.: Decreaser class

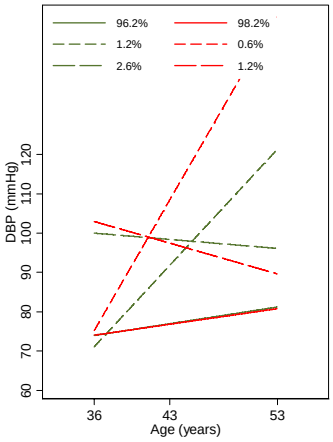
eTable 5: Class concordance in men between models generated from data where an individuals BP trajectory was censored at the point of first treatment for high BP and models that don't censor treated individuals.

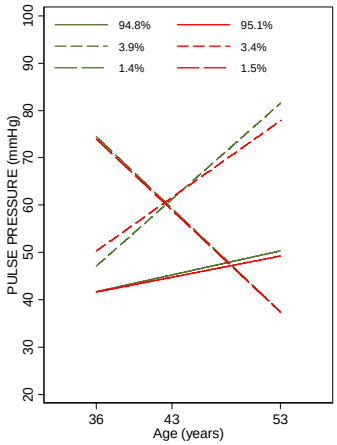
	Sensitivity models (treated BP censored)†								
	SBP			DBP			PP		
	Norm.	Inc.	High	Norm.	Inc.	High	Norm.	Inc.	High
Uncensored BP‡									
SBP n (%)									
Norm.	1652 (99.6)	7 (0.4)	0 (0)						
Inc.	49 (46.7)	56 (53.3)	0 (0)						
High	1 (7.1)	0 (0)	13 (92.9)						
DBP n (%)									
Norm.				1717 (99.7)	5 (0.3)	1 (0.1)			
Inc.				17 (81.0)	4 (19.1)	0 (0)			
High				12 (35.3)	2 (5.9)	20 (58.8)			
PP n (%)									
Norm.							1576 (95.6)	70 (4.2)	3 (0.2)
Inc.							41 (34.2)	79 (65.8)	0 (0)
High							1 (11.1)	0 (0)	8 (88.9)

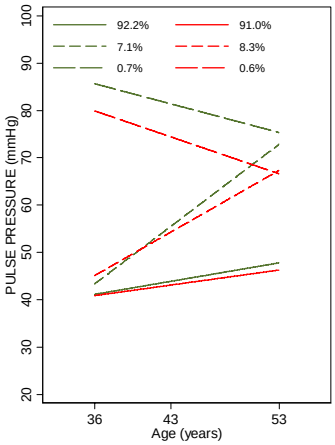
† Once an individual was known to be on treatment for high BP their trajectory was censored
‡ A constant of 10mmHg for SBP and 5mmHg for DBP was added to values observed on antihypertensive medication. These are the main models presented in the paper.
SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure;
Norm.: Normative class; Inc.: Increaser class;











eFigure 1. Latent trajectories of SBP, DBP and pulse pressure in men (left) and women (right) from treatment censored models (red lines) and the main models presented in the paper (green lines) (no censoring).

eTable 6. Reasons for the discordance in latent class groupings between the main models and treatment censored models. The number and percent of individuals who received treatment for high blood pressure (HypRx) and the number of observed data points (after censoring) by groups of individuals separated by their concordance between sets of models.

		HypRx(a)		Number of BP observations			
		Yes	P (b)	1	2	3	P(b)
Men:							
SBP	Concordant	8 (11.4)		6 (8.6)	24 (34.3)	40 (57.1)	
	Discordant 1	30 (100)	<0.001	10 (33.3)	20 (66.7)	0 (0)	<0.001
DBP	Concordant	0 (0)		2 (7.4)	4 (14.8)	21 (77.8)	
	Discordant 1	10 (66.7)	<0.001	2 (13.3)	9 (60.0)	4 (26.7)	0.004
PP	Concordant	5 (7.3)		6 (8.7)	23 (33.3)	40 (58.0)	
	Discordant 1	21 (95.5)	<0.001	9 (40.9)	12 (54.6)	1 (4.6)	<0.001
	Discordant 2	6 (30.0)	0.006	3 (15.0)	8 (40.0)	9 (45.0)	0.53
Women							
SBP	Concordant	14 (20.3)		9 (13.0)	27 (39.1)	33 (47.8)	
	Discordant 1	47 (94.0)	<0.001	16 (32.0)	31 (62.0)	3 (6.0)	<0.001
DBP	Concordant	12 (50.0)		6 (25.0)	13 (54.2)	5 (20.8)	
	Discordant 1	16 (55.2)	0.71	8 (27.6)	11 (37.9)	10 (34.5)	0.44
PP	Concordant	9 (10.3)		5 (5.88)	25 (28.7)	57 (65.5)	
	Discordant 1	42 (100.0)	<0.001	13 (31.0)	29 (69.1)	0 (0)	<0.001
	Discordant 2	9 (12.3)		2 (2.7)	19 (26.0)	52 (71.2)	0.69

(a) Received medication for hypertension from age 36 to 53 years

(b) Chi-squared test of general association with the concordant group

Concordant: among the non-Normative latent classes

Discordant 1: individuals classified as non-Normative in the main models but Normative in the censored models

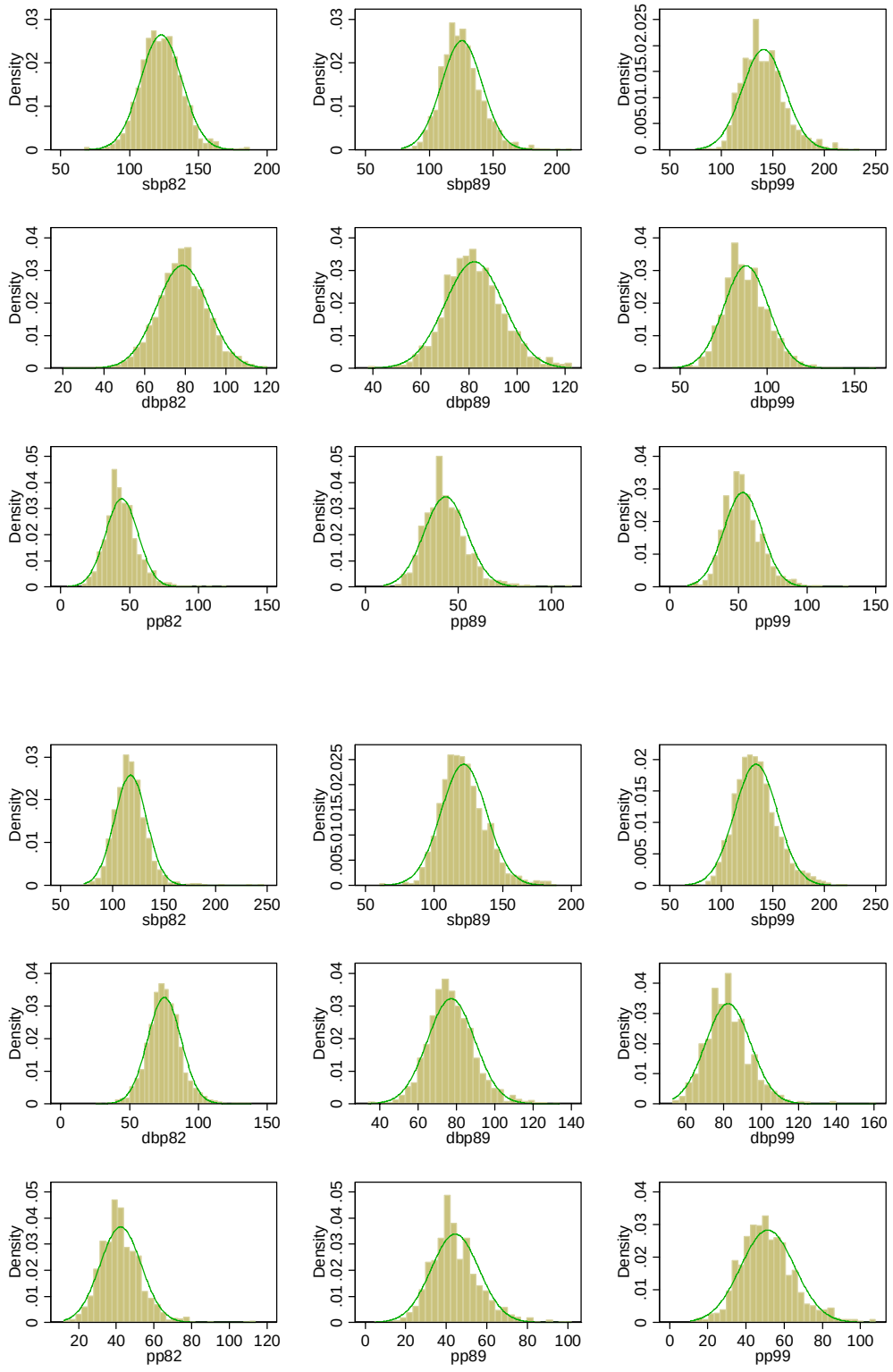
Discordant 2: individuals classified as Normative in the main models but non-Normative in the censored models

3 Distributions of blood pressure variables

eTable 7. Skewness and kurtosis of observed blood pressure data

		Men		Women	
	Age	Skewness	Kurtosis	Skewness	Kurtosis
SBP	36	0.304	3.88	1.26	9.26
	43	0.738	4.52	0.627	4.1
	53	0.753	4.07	0.587	3.65
DBP	36	-0.106	3.85	0.315	4.49
	43	0.3	3.53	0.466	4.3
	53	0.554	4.18	0.812	5.29
PP	36	0.86	5.52	1.06	7.22
	43	0.892	5.32	0.691	4.31
	53	0.724	4.46	0.584	3.82

SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure;



eFigure 2. Frequency histograms of the observed blood pressure data in men (top 3 rows) and women (bottom 3 rows) at each age.

4. Characteristics within each latent class from the main models in the paper.

eTable 8. Mean characteristics within each SBP trajectory class in men and women. Means are unadjusted.

	Men						*Women*							
		Normative		Increaser		P*		Normative		Increaser		High		P*
	N	Mean	95% CI	mean	95% CI		N	mean	95% CI	mean	95% CI	mean	95% CI	
Height and Weight (z-score)														
Birth weight	1834	0.05	0.00, 0.09	-0.16	-0.32, -0.01	0.028	1813	0.05	0.00, 0.10	-0.11	-0.29, 0.07	-0.36	-0.69, -0.03	0.029
Height age 7	1571	0.01	-0.04, 0.06	-0.24	-0.44, -0.03	0.027	1568	0.04	-0.02, 0.09	-0.30	-0.48, -0.12	-0.60	-1.02, -0.17	<0.001
BMI age 36	1632	0.00	-0.05, 0.05	0.30	0.12, 0.49	0.006	1647	-0.03	-0.08, 0.02,	0.38	0.18, 0.58	0.45	-0.12, 1.02	<0.001
Manual SEP (%):														
Childhood	1750	56.8	54.4, 59.2	67.0	57.8, 76.2	0.045	1714	57.9	55.5, 60.3	69.6	60.6, 78.6	62.5	40.6, 81.2	0.063
Adulthood	1826	41.2	38.8, 43.6	37.6	28.2, 47.0	0.48	1809	42.1	39.7, 44.5	46.7	37.3, 56.1	60.9	38.5, 80.2	0.147
Alcohol (%)														
Heavy drinking age 36‖	1195	36.1	33.2, 38.9	46.9	34.3, 59.8	0.081	1242	11.7	9.9, 13.6	16.7	8.9, 27.3	15.0	3.2, 37.9	0.43
Activity (non-work related) (%)														
Inactive	1642	31.0	28.7, 33.3	34.8	25.0, 45.7	0.45	1662	41.7	39.2, 44.1	46.5	36.4, 56.8	70.8	48.9, 87.3	0.01
Medication (%):														
Antihypertensive	1840	10.7	9.2, 12.1	40.4	30.9, 49.9	<0.001	1819	11.1	12.6	51.9	42.0, 61.6	75.0	53.3, 90.2	<0.001
Women only (%):														
OCP use (age 30-51)							1257	34.4	31.7, 37.1	39.0	28.0, 50.1	13.3	1.7, 40.5	0.161

CI: confidence interval, for small proportions (n<100) the CI's are exact from a binomial distribution
* F-test for continuous variables and chi-squared test of general association for categorical variables
§ 97.5% one-sided CI
‖ More than 21 units per week in men; more than 14 units per week in women (UK guidelines)

eTable 9. Mean characteristics within each DBP trajectory class in men and women. Means are unadjusted.

	Men						Women							
		Normative		Increaser		P*		Normative		Increaser		High		P*
	N	Mean	95% CI	mean	95% CI		N	mean	95% CI	mean	95% CI	mean	95% CI	
Height and Weight (z-score)														
Birth weight	1834	0.04	-0.01, 0.08	-0.11	-0.31, 0.09	0.31	1813	0.03	-0.01, 0.08	0.22	-0.27, 0.70	0.00	-0.29, 0.28	0.66
Height age 7	1571	0.00	-0.05, 0.05	-0.08	-0.41, 0.26	0.223	1568	0.02	-0.03, 0.07	-0.12	-0.62, 0.38	-0.29	-0.63, 0.05	0.12
BMI age 36	1632	0.01	-0.04, 0.06	0.21	-0.11, 0.52	0.228	1647	-0.02	-0.07, 0.03	0.72	0.29, 1.15	0.36	-0.01, 0.74	<0.001
Manual SEP (%):														
Childhood	1750	57.1	54.7, 59.5	69.0	52.9, 82.4	0.121	1714	58.3	55.9, 60.7	71.4	47.8, 88.7	65.2	49.8, 78.6	0.32
Adulthood	1826	41.0	38.6, 43.4	37.8	23.8, 53.4	0.66	1809	42.4	40.0, 44.8	52.4	29.8, 74.2	57.8	42.2, 72.3	0.08
Alcohol (%)														
Heavy drinking age 36‖	1195	37.0	34.2, 39.8	22.2	8.6, 42.3	0.115	1242	11.7	9.9, 13.6	28.6	8.4, 58.1	16.7	6.4, 32.8	0.109
Activity (non-work related) (%)														
Inactive	1642	31.3	29.0, 33.6	27.5	14.6, 43.9	0.61	1662	41.5	39.1, 43.9	55.0	31.2, 76.9	67.4	52.0, 80.5	0.001
Medication (%):														
Antihypertensive	1840	11.9	10.4, 13.4	28.9	16.4, 44.3	0.001	1819	12.5	10.9, 14.0	47.6	25.7, 70.2	68.8	53.7, 81.3	<0.001
Women only (%):														
OCP use (age 30-51)							1257	34.5	31.8, 37.2	43.8	19.8, 70.1	26.7	12.3, 45.9	0.492

CI: confidence interval, for small proportions or small samples (n<100) the CI's are exact from a binomial distribution
* F-test for continuous variables and chi-squared test of general association for categorical variables
§ 97.5% one-sided CI
‖ More than 21 units per week in men; more than 14 units per week in women (UK guidelines)

eTable 10. Mean characteristics within each PP trajectory class in men and women. Means are unadjusted.

	Men								Women							
		Normative		Increaser		Decreaser				Normative		Increaser		High		
	N	Mean	95% CI	mean	95% CI	mean	95% CI	P*	N	mean	95% CI	mean	95% CI	mean	95% CI	P*
Height and Weight (z-score)																
Birth weight	1834	0.05	0.00, 0.09	-0.21	-0.42, 0.00	-0.26	-0.60, 0.07	0.025	1813	0.05	0.00, 0.09	-0.13	-0.29, 0.04	0.33	-0.18, 0.85	0.076
Height age 7	1571	0.01	-0.04, 0.06	-0.24	-0.48, 0.00	-0.37	-0.78, 0.04	0.036	1568	0.03	-0.02, 0.08	-0.23	-0.39, -0.07	-0.36	-1.10, 0.37	0.012
BMI age 36	1632	0.01	-0.04, 0.06	0.25	0.03, 0.47	-0.37	-0.78, 0.04	0.033	1647	-0.03	-0.08, 0.02	0.26	0.08, 0.43	0.80	0.21, 1.39	<0.001
Manual SEP (%):																
Childhood	1750	57.1	54.7, 59.5	55.2	42.6, 67.4	80.0	59.3, 93.2	0.067	1714	58.1	55.7, 60.5	64.2	55.8, 72.6	83.3	51.6. 97.9	0.09
Adulthood	1826	40.7	38.3, 43.1	40.8	29.3, 53.2	62.5	40.6, 81.2	0.097	1809	42.4	40.0, 44.8	47.3	38.7, 55.9	72.7	39.0, 94.0	0.074
Alcohol (%)																
Heavy drinking age 36‖	1195	36.8	33.8, 39.4	35.4	22.2, 50.5	42.9	17.7, 71.1	0.9	1242	12.1	10.2, 13.9	11.3	5.3, 20.2	22.2	2.8, 60.0	0.63
Activity (non-work related) (%)																
Inactive	1642	30.7	28.4, 33.0	39.1	27.1, 52.1	45.8	25.6, 67.2	0.110	1662	41.8	39.3, 44.3	47.9	38.5, 57.3	63.6	30.8, 89.1	0.157
Medication (%):																
Antihypertensive	1840	11.2	9.7, 12.6	39.4	28.0, 51.7	12.0	2.5, 31.2	<0.001	1819	11.7	10.2, 13.3	44.6	35.9, 53.6	50.0	21.1, 78.9	<0.001
Women only (%):																
OCP use (age 30-51)									1257	34.0	31.3, 36.7	41.8	31.5, 52.6	12.5	0.3, 52.7	0.139

CI: confidence interval, for small proportions or small samples (n<100) the CI's are exact from a binomial distribution
* F-test for continuous variables and chi-squared test of general association for categorical variables
§ 97.5% one-sided CI
‖More than 21 units per week in men; more than 14 units per week in women (UK guidelines)