The Longitudinal Relation Between Pulse Pressure and Age in Middle-aged and Older Adults: The ARIC Study

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Background

- Pulse pressure (PP) is a surrogate of increased arterial stiffness and is associated with adverse cardiovascular (CV) prognosis.
- Previous observational studies show PP increases with age, because of a continuous rise in SBP and leveling or decrease in DBP.
- Gender differences are observed in PP trajectory with aging.

Objective

To assess:

- The magnitude and shape of the association between PP, SBP and DBP with age, in a middle-aged and older population free of CHD and treatment with anti-hypertensive medication.
- If the association between blood pressure measures and age differ in men and women.
- If cardiovascular disease risk factors confound the association between BP and age.

Methods

ARIC STUDY

- Prospective multi-center study of CVD etiology.
- Biracial population-sample of middle-aged men and women.
- Ages 45 - 64 years at baseline
- Field centers: Forsyth County, NC,
  Jackson, MS (Blacks only)
  Northwestern suburbs of Minneapolis, MN.
  Washington County, MD.
- The response rate was 46% in Jackson, MS and approximately 65% in the other three communities, resulting in a total sample size of 15,792

Methods

- Baseline:
  Home interview (1987 - 1989) to assess: demographics, health behaviors, and medical history.
  Clinic visit: CV risk factors, prevalent CVD, and subclinical CVD indices

- Follow-up: every 3 years for a total of 4 visits.

Methods

Hierarchical order for exclusion criteria for current analysis:

- Prevalent CHD (verified at each visit) (n=1,986)
- Anti-hypertensive medication listed in any visit or untreated hypertension (n=4,167)
- Missing values in variables in multivariate model (n=79)

A total of 9,544 participants (level 1 observations), having 27,611 level 2 outcomes were included in the final analysis

Methods

Blood Pressure Technique:

- Random zero sphygmomanometer.
- DBP…..fifth Korotkoff sound.
- Three BP measurements were taken at each visit, and the average of the last two readings was used in the analysis.
- PP = SBP-DBP
- MAP= DBP+PP/3

Methods

STATISTICAL METHODS:

- Longitudinal data analysis using random effects regression models.
- All analysis was stratified by gender.
- Random error components.
- Use of first order autoregressive-error (AR1) to account for within-individual residual correlation.

Methods

The analysis was performed in two-stage process:

- Serial data obtained at each visit (SBP, DBP and PP) were fitted to longitudinal models using piece-wise linear splines on age (B-splines).
- Based on the patterns of trajectory of these associations, we fitted a quadratic term on age for each BP parameter.
- Likelihood ratio test and the Akaike Information criteria (AIC) were used to select the best models, as well as a general measure of adequacy of fit of specific models

Methods

Statistical Models:

- PP pressure, SBP and DBP were modeled independently as growth curves.
- Time variable: age centered on 55 years.
- Age and age^2 were treated as random slopes.
- COVARIATES: Gender, race, SES (education level), diabetes, current smoker, BMI, total cholesterol/HDL ratio (the latter two included as deviation from their respectively mean).

Results

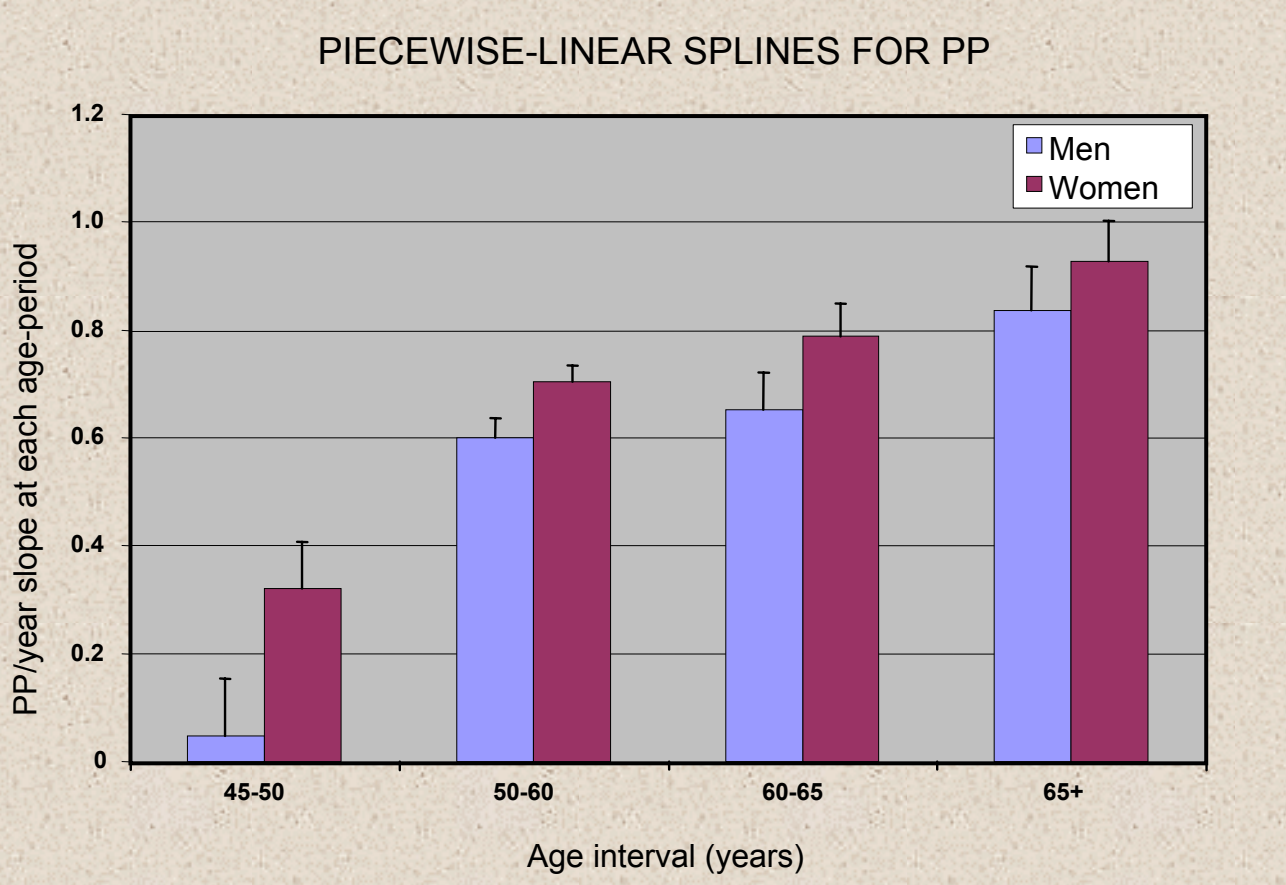
TABLE 1. Crossectional means for BP parameters

	Visits	N	SBP	DBP	PP
Men	1	3100	114	71	42.8
	2	3045	114	70	43.7
	3	2673	116	70	46.1
	4	2290	118	69	48.3
Women	1	4114	110	68	42.7
	2	4047	111	67	44.2
	3	3551	114	67	46.7
	4	2983	117	67	50.0

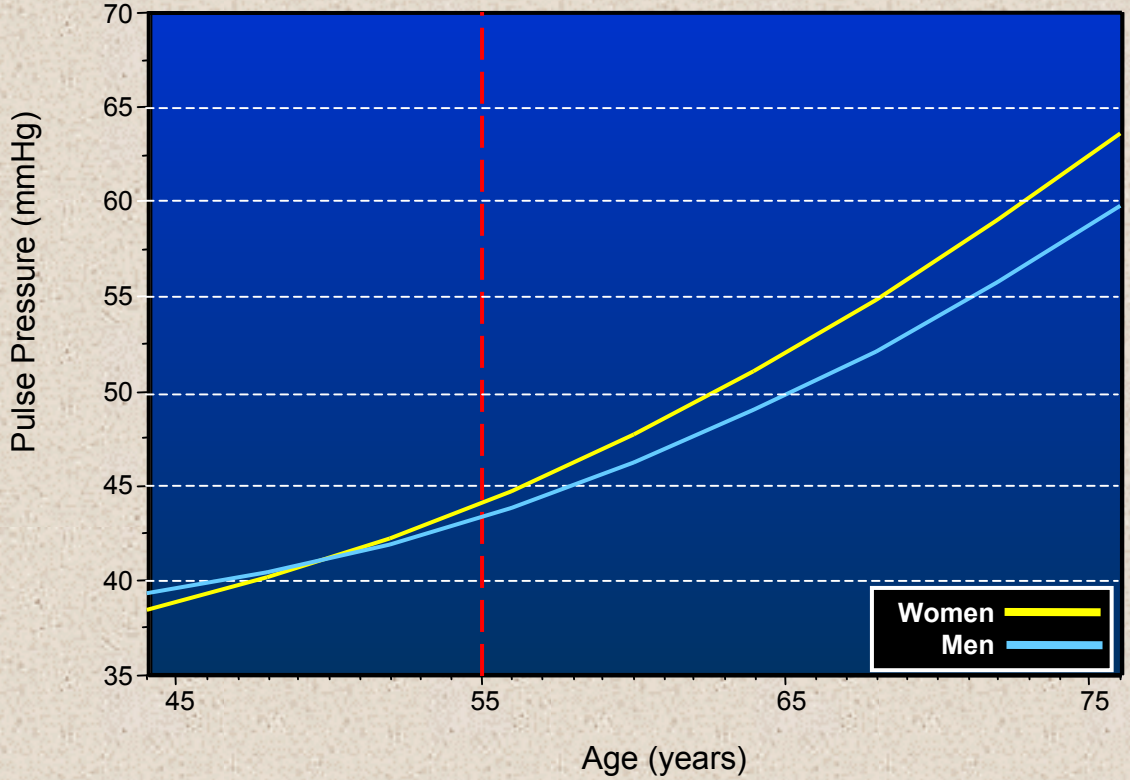
AR1 Models for PP, SBP and DBP

	PP			SBP			DBP		
Parameter	**Estimate**		**Std Err**	**Estimate**		**Std Err**	**Estimate**		**Std Err**
Const	44.31	*	0.22	116.47	*	0.30	72.22	*	0.17
Gender	0.86	*	0.22	-2.95	*	0.30	-3.82	*	0.17
Age_55	0.64	*	0.02	0.54	*	0.03	-0.11	*	0.02
(Age_55)^2	0.02	*	0.00	0.02	*	0.00	-0.01	*	0.00
Gender*age_55	0.17	*	0.03	0.25	*	0.03	0.07	*	0.02
Diabetes	2.12	*	0.27	0.70	**	0.34	-1.19	*	0.21
Cursmk	0.79	*	0.21	-0.85	*	0.26	-1.68	*	0.16
BMI	0.38	*	0.02	0.79	*	0.03	0.38	*	0.02
Black	1.17	*	0.28	6.00	*	0.38	4.80	*	0.22
Educ_level>3	-1.45	*	0.21	-1.35	*	0.28	0.07		0.16
Tch/hdl	-0.11		0.07	0.72	*	0.09	0.82	*	0.06

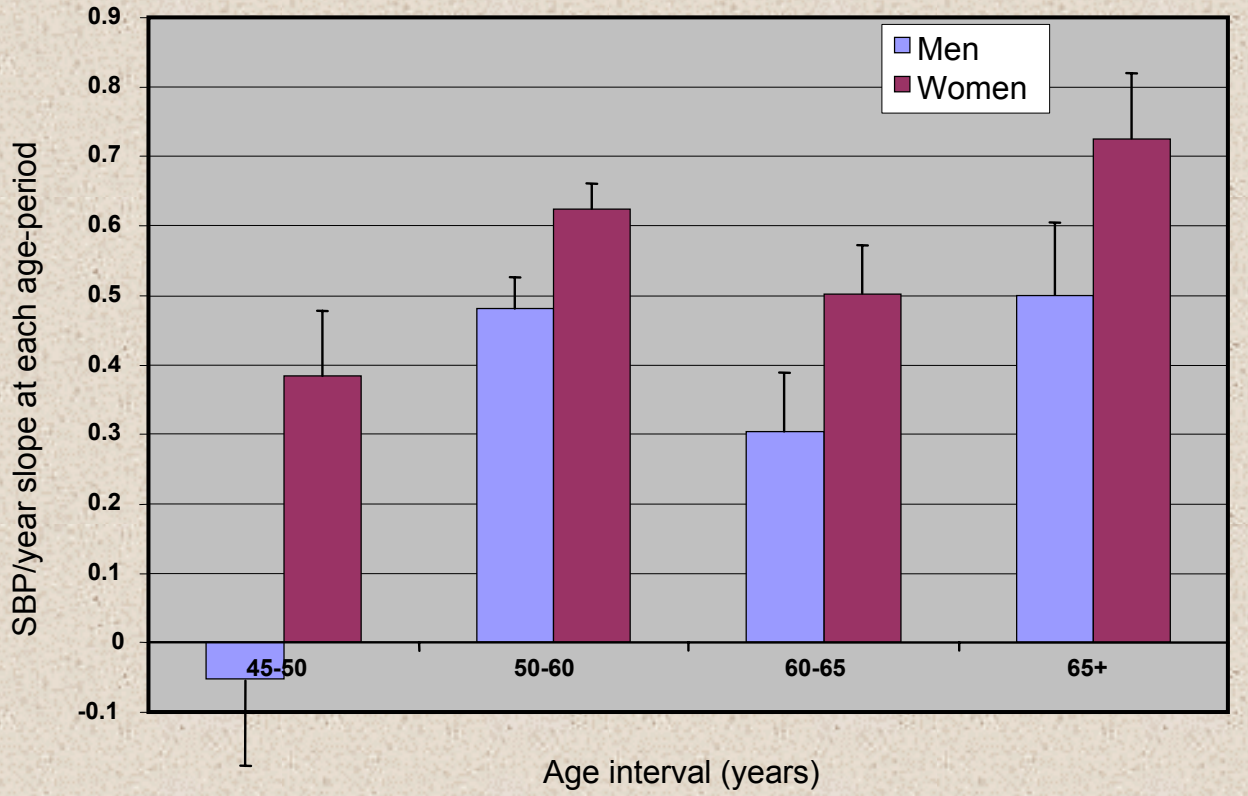
Significance: ''=5%; '*'=1%.**

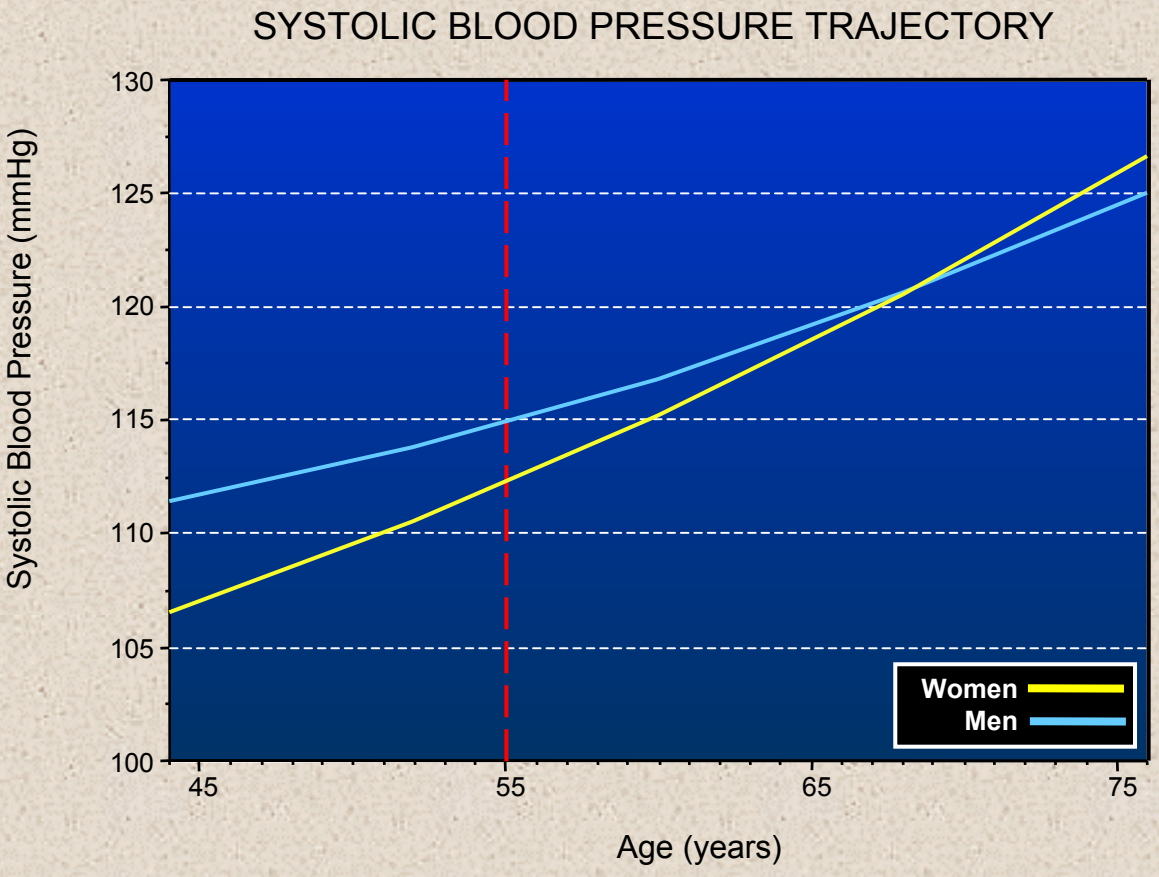

PIECEWISE-LINEAR SPLINES FOR PP
1.2
1.0
0.8
0.6
0.4
0.2
0
PP/year slope at each age-period
Men
Women
45-50
50-60
60-65
65+
Age interval (years)

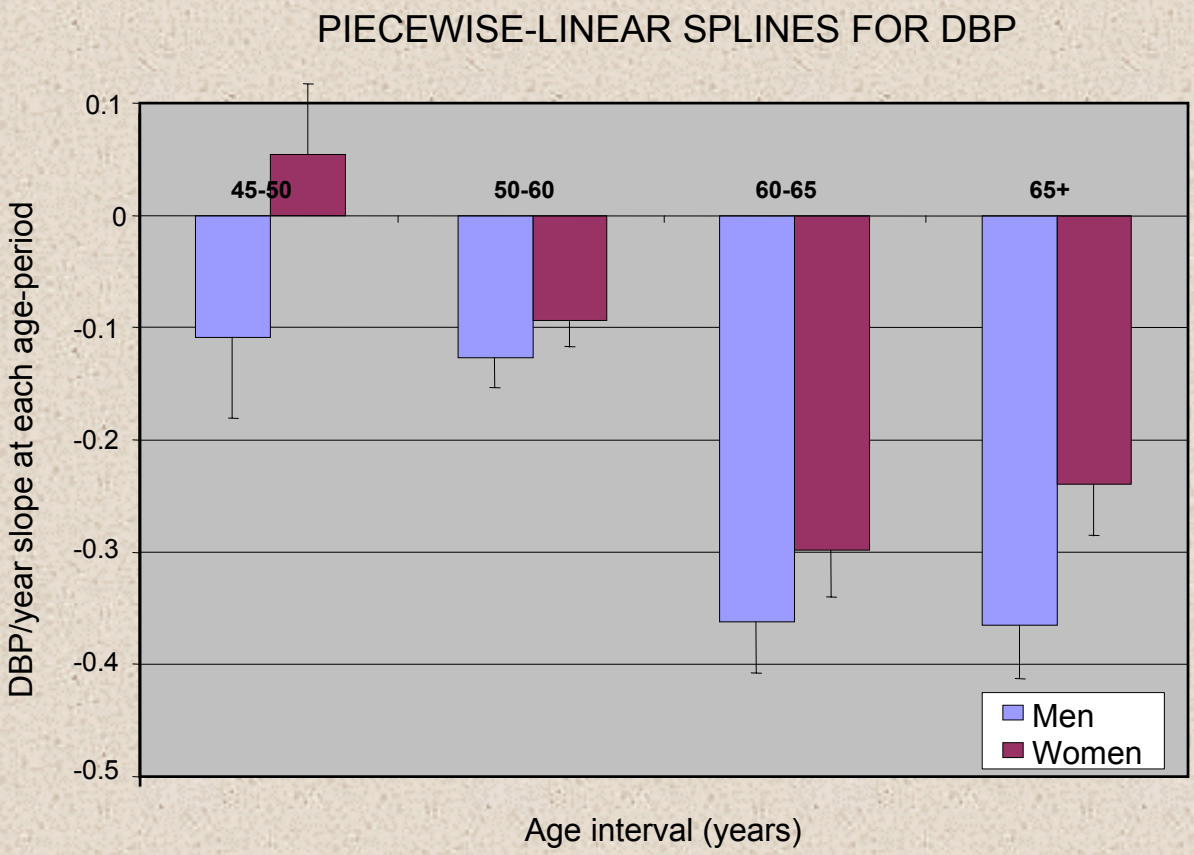
PULSE PRESSURE TRAJECTORY

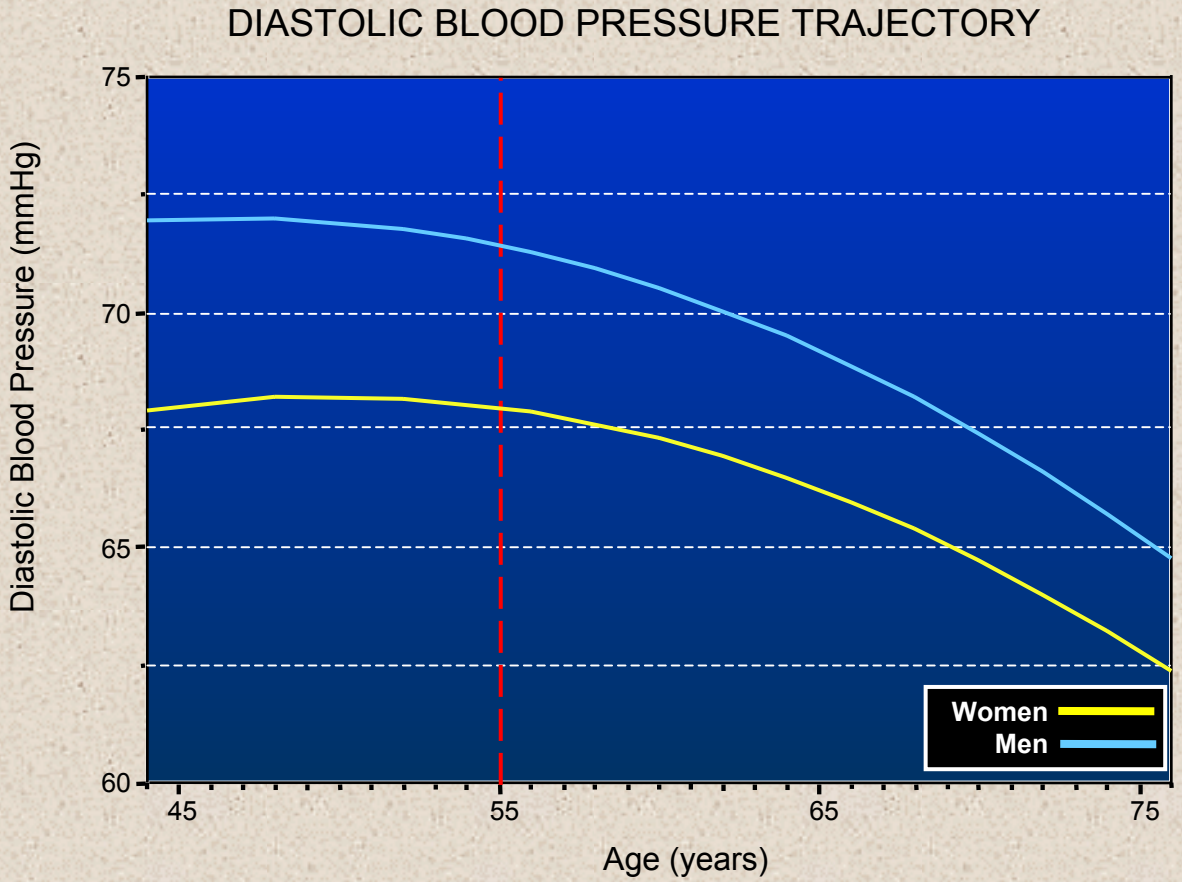


PIECEWISE-LINEAR SPLINES FOR SBP

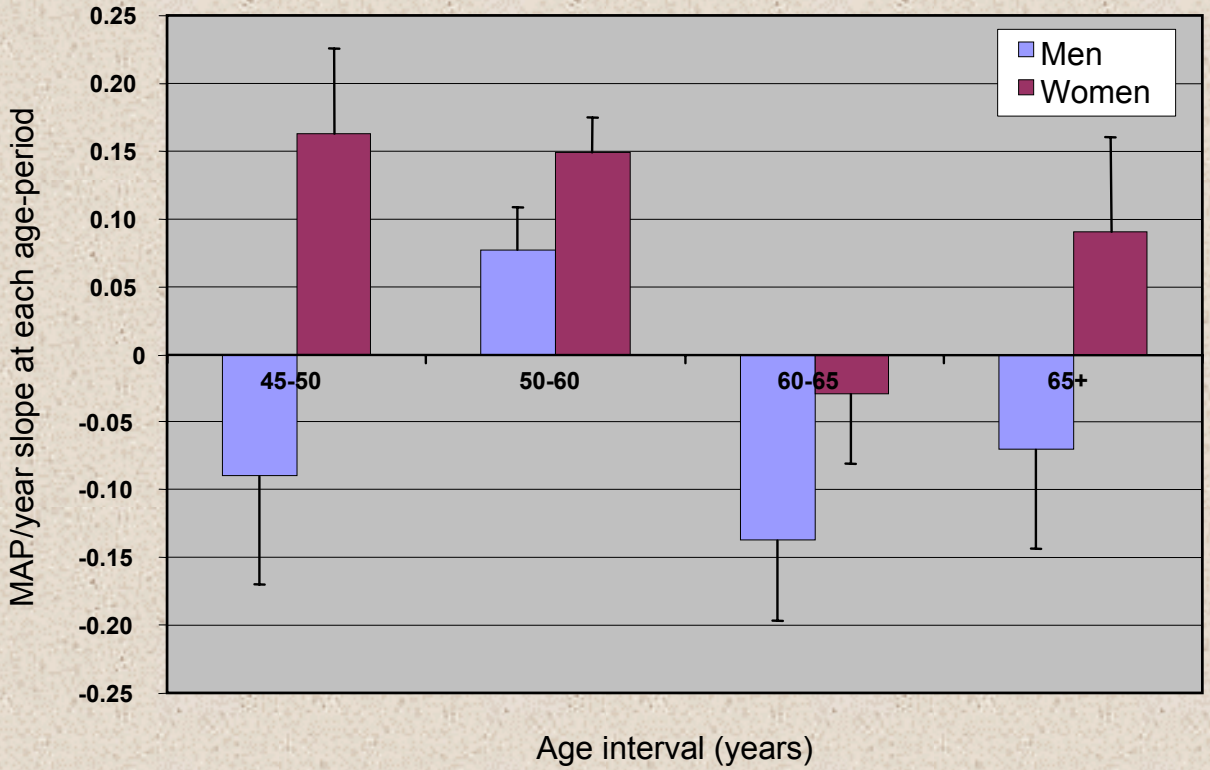



SYSTOLIC BLOOD PRESSURE TRAJECTORY
Systolic Blood Pressure (mmHg)
130
125
120
115
110
105
100
45
55
65
75
Age (years)
Women
Men

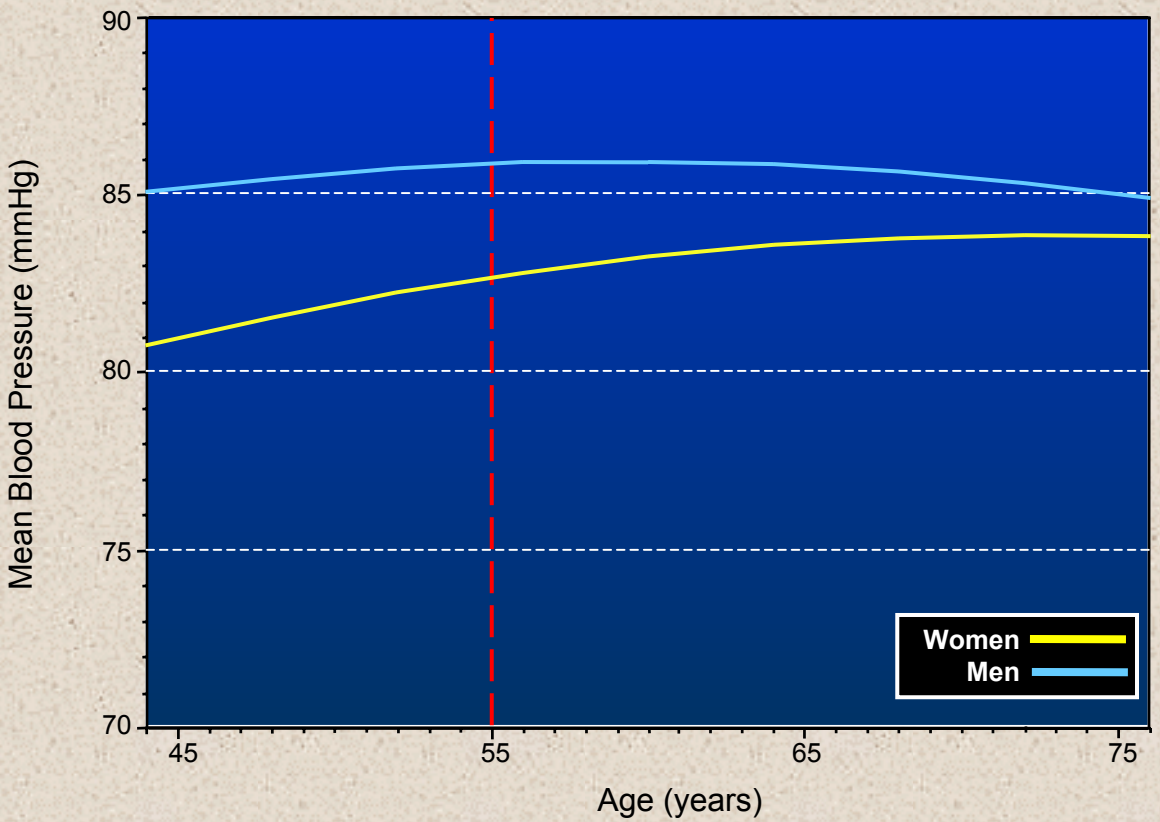

PIECEWISE-LINEAR SPLINES FOR DBP
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
DBP/year slope at each age-period
45-50
50-60
60-65
65+
Men
Women
Age interval (years)


DIASTOLIC BLOOD PRESSURE TRAJECTORY
Diastolic Blood Pressure (mmHg)
75
70
65
60
45
55
65
75
Age (years)
Women
Men

PIECEWISE-LINEAR SPLINES FOR MAP



MEAN BLOOD PRESSURE TRAJECTORY



Limitations

- We assume missingness is complete at random (MCAR) in our cohort.
- By excluding prevalent CHD and participants on anti-hypertensive medication, our results cannot be generalized to a general population.

PATTERN OF MISSING VISITS

	Women		Men	
Visits	Freq	%	Freq	%
..II	4	0.09	4	0.12
.I.I	7	0.16	1	0.03
.II.	10	0.23	9	0.26
.III	46	1.04	49	1.43
I..I	26	0.59	12	0.35
I.I.	31	0.70	24	0.70
I.II	67	1.51	39	1.14
II..	383	8.65	336	9.84
II.I	88	1.99	69	2.02
III.	427	9.65	339	9.92
IIII	3337	75.40	2534	74.18

Conclusions

1) The association between PP and age, in middle aged and elderly subjects, is best described as a positive and curvilinear trajectory (quadratic term fitted on age), for both men and women

2) This association was independent of race, smoking, diabetes, hypertension, BMI, total cholesterol/HDL ratio and education level.

3) The gender-age interaction points to a higher rate of increase in PP in women compared with men.
Net effect: women start with lower PP (at age 45) and by age 51 overcame values for men, causing that difference to widen with age.