SUPPLEMENTAL MATERIAL

Table S1. Hazard ratios (95% confidence intervals) for the association between Δ pulse pressure categories (Reference: ≥-5 to <5 mmHg) and all-cause mortality using time-varying Cox regression analyses without imputation of missing covariates

Δ Pulse pressure (mmHg)	**All-cause death hazard ratios (95% confidence intervals)**		
	Minimally SBP adjusted (n=98,577)	**SBP & Case-mix adjusted (n=62,162)**	**SBP & Case-mix & MICS adjusted (n=57,681)**
<-25	1.26 (1.18-1.34)	1.06 (0.97-1.16)	1.13 (1.01-1.27)
≥-25 to <-15	1.00 (0.94-1.06)	0.93 (0.86-1.01)	1.03 (0.93-1.14)
≥-15 to <-5	0.95 (0.90-0.99)	0.92 (0.86-0.99)	1.00 (0.91-1.08)
≥-5 to <5	Reference	Reference	Reference
5 to <15	1.13 (1.08-1.19)	1.04 (0.98-1.12)	1.03 (0.95-1.12)
15 to <25	1.30 (1.23-1.37)	1.23 (1.13-1.33)	1.16 (1.05-1.28)
≥25	1.27 (1.18-1.35)	1.20 (1.09-1.32)	1.17 (1.04-1.32)
Δ Pulse pressure (mmHg)	**Minimally MAP adjusted (n=98,577)**	**MAP & Case-mix adjusted (n=62,162)**	**MAP & Case-mix & MICS adjusted (n=57,681)**
<-25	0.98 (0.92-1.04)	0.86 (0.79-0.94)	0.98 (0.88-1.10)
≥-25 to <-15	0.88 (0.83-0.93)	0.83 (0.77-0.90)	0.95 (0.86-1.06)
≥-15 to <-5	0.90 (0.85-0.94)	0.88 (0.82-0.94)	0.96 (0.88-1.05)
≥-5 to <5	Reference	Reference	Reference
5 to <15	1.17 (1.11-1.22)	1.08 (1.01-1.15)	1.05 (0.97-1.15)
15 to <25	1.37 (1.29-1.44)	1.30 (1.20-1.40)	1.20 (1.09-1.33)
≥25	1.39 (1.30-1.49)	1.33 (1.21-1.46)	1.25 (1.11-1.41)

Note: Minimally adjusted model included adjustment for entry calendar quarter, and pre-dialysis SBP or pre-dialysis MAP. Case-mix adjusted for covariates in the minimally adjusted model plus ultrafiltration percentage, age, sex, race/ethnicity, presence of diabetes mellitus, 9 pre-existing comorbidities, history of tobacco smoking, dialysis duration categories, primary insurance, types of vascular access, and dialysis dose as indicated by single pool Kt/V. Case-mix & MICS adjusted for all case-mix covariates plus body mass index, serum levels of albumin, creatinine, total iron-binding capacity, ferritin, calcium, phosphorus, bicarbonate, hemoglobin, blood white blood cells, and lymphocyte percentage.

Abbreviations: SBP, systolic blood pressure; MAP, mean arterial blood pressure; MICS, malnutrition-inflammation complex syndrome.

Table S2. Hazard ratios (95% confidence intervals) for the association between Δ pulse pressure categories (Reference: ≥-5 to <5 mmHg) and all-cause mortality using time-varying Cox regression analyses with inclusion of outliers (<1st and >99th percentiles) of Δ pulse pressure

Δ Pulse pressure (mmHg)	All-cause death hazard ratios (95% confidence intervals)		
	Minimally SBP adjusted (n=99,044)	**SBP & Case-mix adjusted (n=99,044)**	**SBP & Case-mix & MICS adjusted (n=99,044)**
<-25	1.31 (1.23-1.39)	1.16 (1.09-1.23)	1.26 (1.18-1.34)
≥-25 to <-15	1.00 (0.94-1.06)	0.94 (0.89-1.00)	1.03 (0.98-1.10)
≥-15 to <-5	0.94 (0.90-0.99)	0.93 (0.89-0.98)	1.01 (0.96-1.06)
≥-5 to <5	Reference	Reference	Reference
5 to <15	1.13 (1.08-1.19)	1.11 (1.06-1.16)	1.06 (1.01-1.11)
15 to <25	1.30 (1.23-1.38)	1.25 (1.19-1.33)	1.18 (1.11-1.24)
≥25	1.30 (1.22-1.38)	1.22 (1.15-1.30)	1.19 (1.12-1.26)
Δ Pulse pressure (mmHg)	**Minimally MAP adjusted (n=99,044)**	**MAP & Case-mix adjusted (n=99,044)**	**MAP & Case-mix & MICS adjusted (n=99,044)**
<-25	1.00 (0.95-1.06)	0.92 (0.87-0.98)	1.06 (1.00-1.12)
≥-25 to <-15	0.88 (0.83-0.93)	0.84 (0.80-0.89)	0.95 (0.90-1.01)
≥-15 to <-5	0.90 (0.85-0.94)	0.89 (0.84-0.93)	0.97 (0.92-1.01)
≥-5 to <5	Reference	Reference	Reference
5 to <15	1.17 (1.12-1.23)	1.15 (1.10-1.20)	1.09 (1.04-1.14)
15 to <25	1.37 (1.30-1.45)	1.33 (1.26-1.41)	1.23 (1.16-1.30)
≥25	1.46 (1.37-1.55)	1.39 (1.31-1.48)	1.30 (1.23-1.38)

Note: Minimally adjusted model included adjustment for entry calendar quarter, and pre-dialysis SBP or pre-dialysis MAP. Case-mix adjusted for covariates in the minimally adjusted model plus ultrafiltration percentage, age, sex, race/ethnicity, presence of diabetes mellitus, 9 pre-existing comorbidities, history of tobacco smoking, dialysis duration categories, primary insurance, types of vascular access, and dialysis dose as indicated by single pool Kt/V. Case-mix & MICS adjusted for all case-mix covariates plus body mass index, serum levels of albumin, creatinine, total iron-binding capacity, ferritin, calcium, phosphorus, bicarbonate, hemoglobin, blood white blood cells, and lymphocyte percentage.

Abbreviations: SBP, systolic blood pressure; MAP, mean arterial blood pressure; MICS, malnutrition-inflammation complex syndrome.

Figure Legend

Figure S1: Algorithm of study cohort creation.

Abbreviations: HD, hemodialysis; PP, pulse pressure.

Figure S2: SBP adjusted (A) and MAP adjusted (B) log hazard ratio (solid lines) and 95% confidence interval (dashed lines) of all-cause mortality associated with change in pulse pressure during hemodialysis using time-varying Cox regression analyses in 98,577 hemodialysis patients for case-mix adjusted models.

Case-mix adjusted models included adjustment for entry calendar quarter, pre-dialysis SBP (A) or pre-dialysis MAP (B), ultrafiltration percentage, age, sex, race/ethnicity, presence of diabetes mellitus, 9 pre-existing comorbidities, history of tobacco smoking, dialysis duration categories, primary insurance, types of vascular access, and dialysis dose as indicated by single pool Kt/V.

Abbreviations: SBP, systolic blood pressure; MAP, mean arterial blood pressure..

Figure S3: Association between change in pulse pressure during hemodialysis and cardiovascular mortality in 98,577 hemodialysis patients: (A) SBP & case-mix & MICS adjusted and (B) MAP & case-mix & MICS adjusted models. The solid lines and dashed lines represent log hazard ratio and 95% confidence interval, respectively.

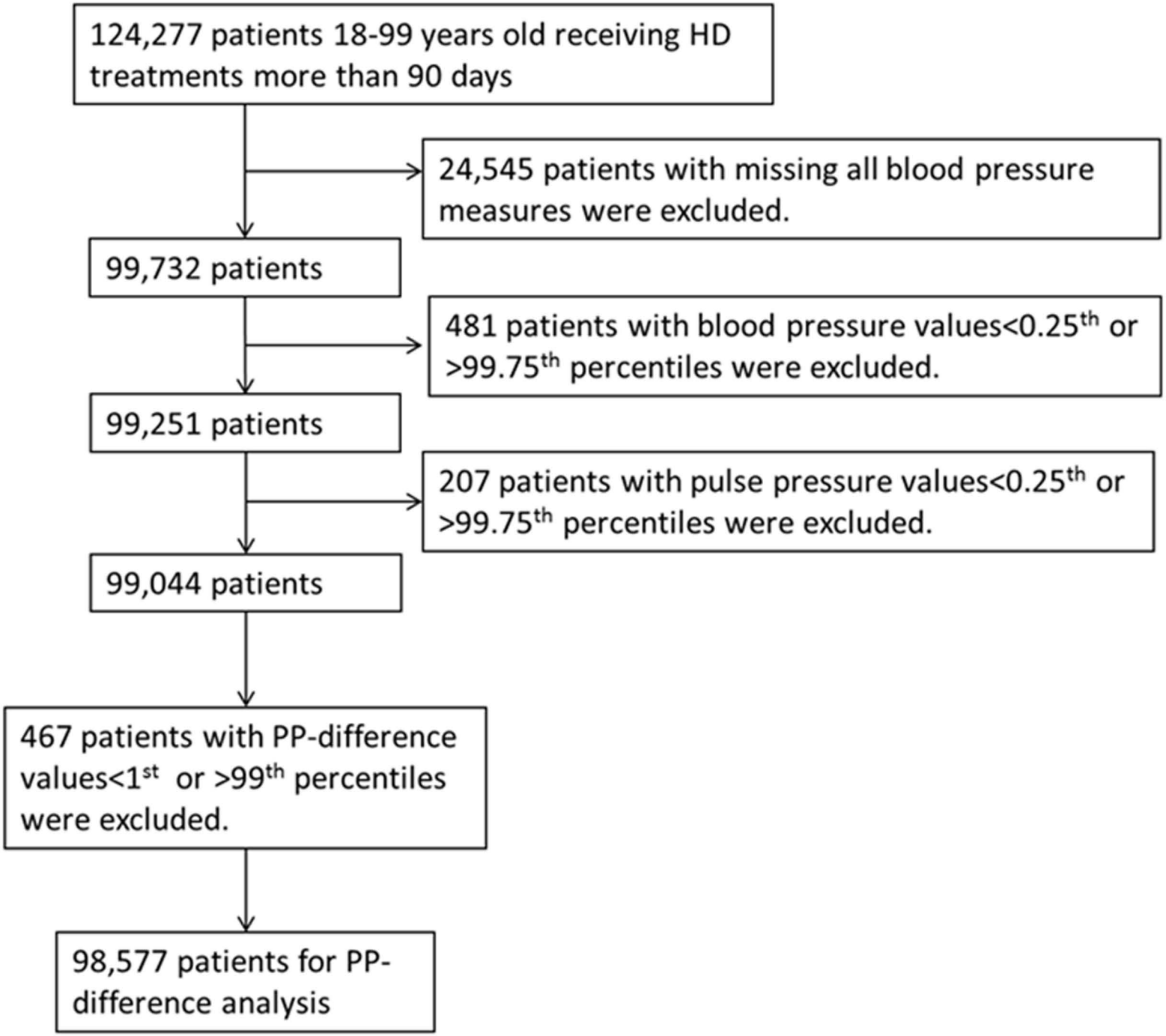
The models were adjusted for entry calendar quarter, pre-dialysis SBP (A) or pre-dialysis MAP (B), ultrafiltration percentage, age, sex, race/ethnicity, presence of diabetes mellitus, 9 pre-existing comorbidities, history of tobacco smoking, dialysis duration categories, primary insurance, types of vascular access, dialysis dose as indicated by single pool Kt/V, body mass index, serum levels of albumin, creatinine, total iron-binding capacity, ferritin, calcium, phosphorus, bicarbonate, hemoglobin, blood white blood cells, and lymphocyte percentage.

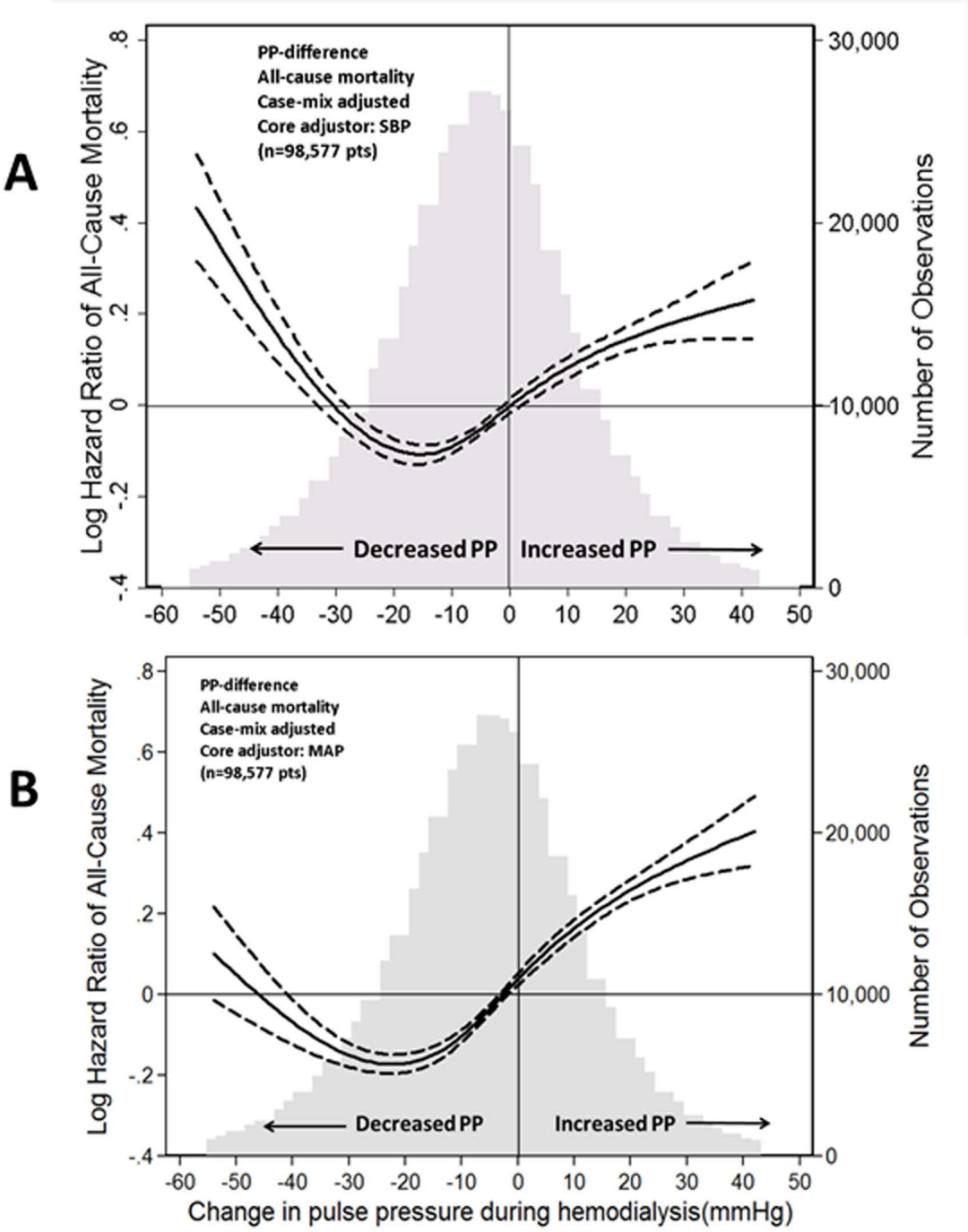
Abbreviations: SBP, systolic blood pressure; MAP, mean arterial blood pressure; MICS, malnutrition-inflammation complex syndrome.

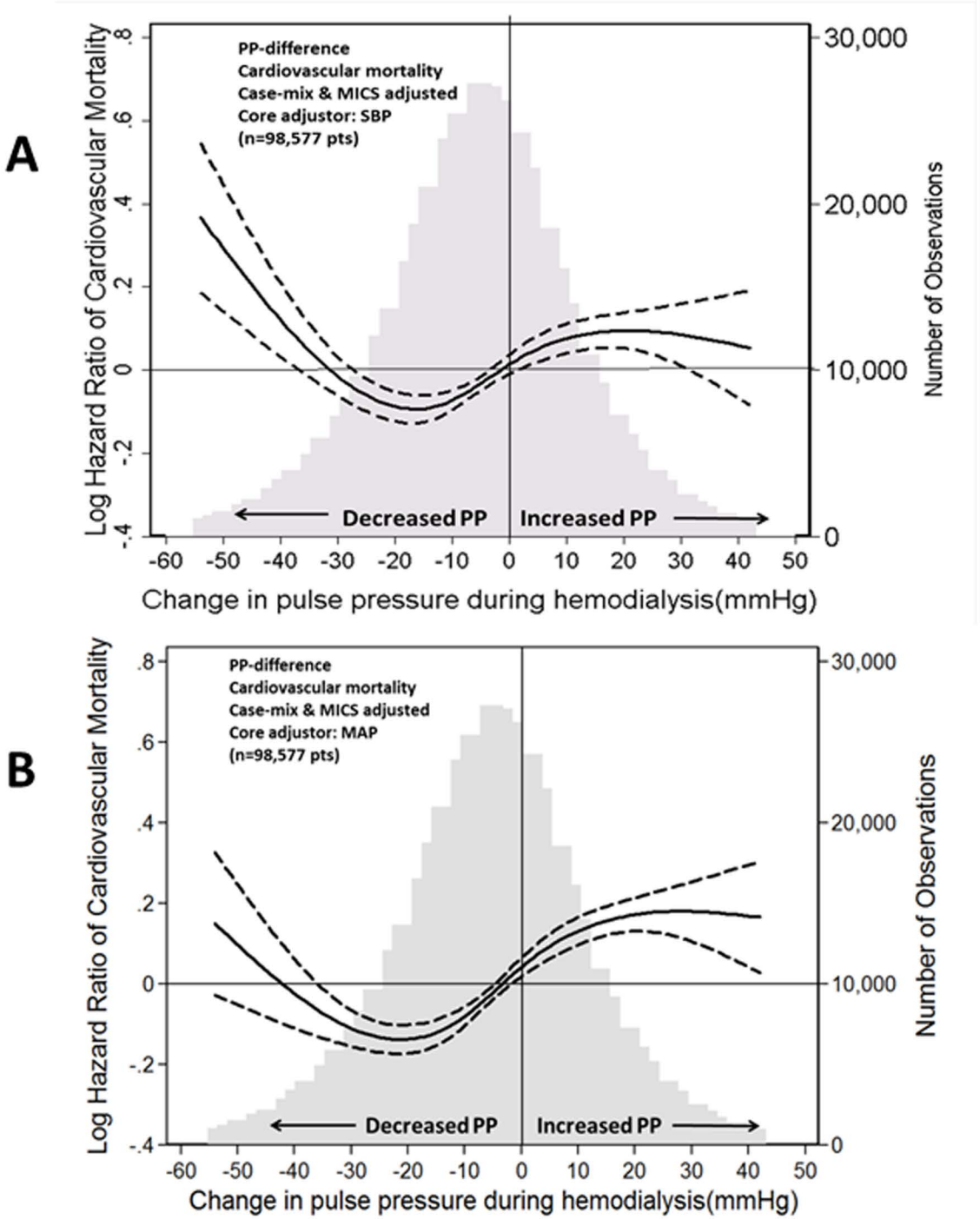
Figure S4: Adjusted log hazard ratio (solid lines) and 95% confidence interval (dashed lines) of all-cause mortality associated with change in pulse pressure during hemodialysis using time-varying Cox regression analyses in 98,577 hemodialysis patients in the two separate models: (A) pre-dialysis pulse pressure & case-mix & MICS adjusted and (B) post-dialysis pulse pressure & case-mix & MICS adjusted models.

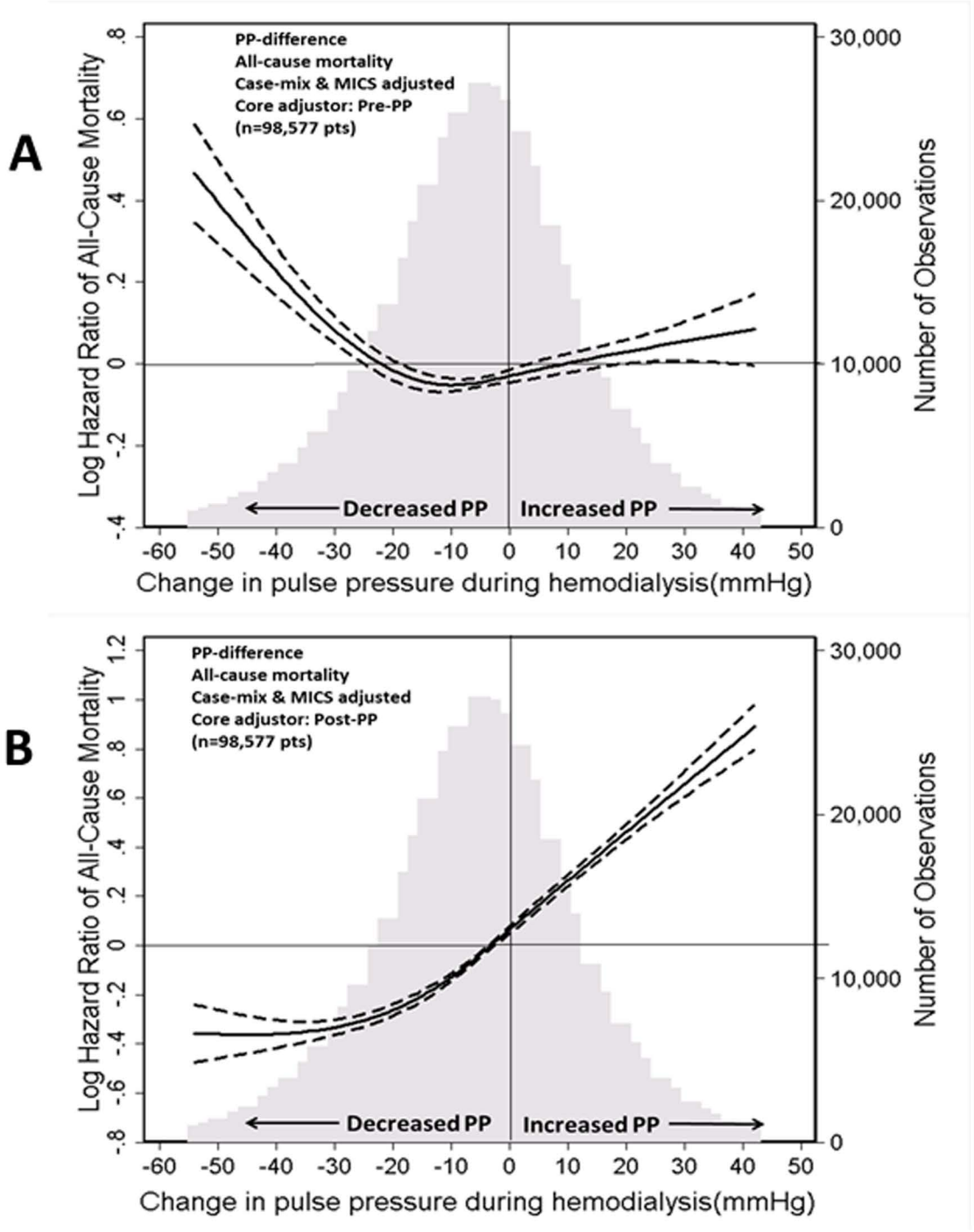
In addition to pre-dialysis pulse pressure (A) or post-dialysis pulse pressure (B), each model was adjusted for entry calendar quarter, ultrafiltration percentage, age, sex, race/ethnicity, presence of diabetes mellitus, 9 pre-existing comorbidities, history of tobacco smoking, dialysis duration categories, primary insurance, types of vascular access, dialysis dose as indicated by single pool Kt/V, body mass index, serum levels of albumin, creatinine, total iron-binding capacity, ferritin, calcium, phosphorus, bicarbonate, hemoglobin, blood white blood cells, and lymphocyte percentage.

Abbreviations: MICS, malnutrition-inflammation complex syndrome.


124,277 patients 18-99 years old receiving HD treatments more than 90 days
24,545 patients with missing all blood pressure measures were excluded.
99,732 patients
481 patients with blood pressure values<0.25th or >99.75th percentiles were excluded.
99,251 patients
207 patients with pulse pressure values<0.25th or >99.75th percentiles were excluded.
99,044 patients
467 patients with PP-difference values<1st or >99th percentiles were excluded.
98,577 patients for PP-difference analysis


A
PP-difference
All-cause mortality
Case-mix adjusted
Core adjustor: SBP
(n=98,577 pts)
Log Hazard Ratio of All-Cause Mortality
Number of Observations
Decreased PP
Increased PP
B
PP-difference
All-cause mortality
Case-mix adjusted
Core adjustor: MAP
(n=98,577 pts)
Log Hazard Ratio of All-Cause Mortality
Number of Observations
Decreased PP
Increased PP
Change in pulse pressure during hemodialysis(mmHg)


A
PP-difference
Cardiovascular mortality
Case-mix & MICS adjusted
Core adjustor: SBP
(n=98,577 pts)
Log Hazard Ratio of Cardiovascular Mortality
Number of Observations
Decreased PP
Increased PP
Change in pulse pressure during hemodialysis(mmHg)
B
PP-difference
Cardiovascular mortality
Case-mix & MICS adjusted
Core adjustor: MAP
(n=98,577 pts)
Log Hazard Ratio of Cardiovascular Mortality
Number of Observations
Decreased PP
Increased PP
Change in pulse pressure during hemodialysis(mmHg)


A
PP-difference
All-cause mortality
Case-mix & MICS adjusted
Core adjustor: Pre-PP
(n=98,577 pts)
Log Hazard Ratio of All-Cause Mortality
Number of Observations
Decreased PP
Increased PP
Change in pulse pressure during hemodialysis(mmHg)
B
PP-difference
All-cause mortality
Case-mix & MICS adjusted
Core adjustor: Post-PP
(n=98,577 pts)
Log Hazard Ratio of All-Cause Mortality
Number of Observations
Decreased PP
Increased PP
Change in pulse pressure during hemodialysis(mmHg)