#AHA24

IMPACT OF LONG-TERM BLOOD PRESSURE VARIABILITY ON ADVERSE CARDIOVASCULAR OUTCOMES IN HIGH- AND LOW-RISK POPULATIONS

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Disclosures

Presenter: Lynne Krohn

Conflict	Disclosure
Employee and stockholder	Alnylam Pharmaceuticals

Methods

Background:

- Hypertension is a major preventable risk factor for CV disease.[1]
- Evidence suggests that in addition to BP levels, BP consistency is a key determinant of clinical outcomes.[2]

Aim:

Investigate the role of long-term SBP consistency, as observed in real-world clinical settings, in predicting adverse CV and renal outcomes.

- Endpoints: 4-point MACE[a], renal failure, all-cause mortality

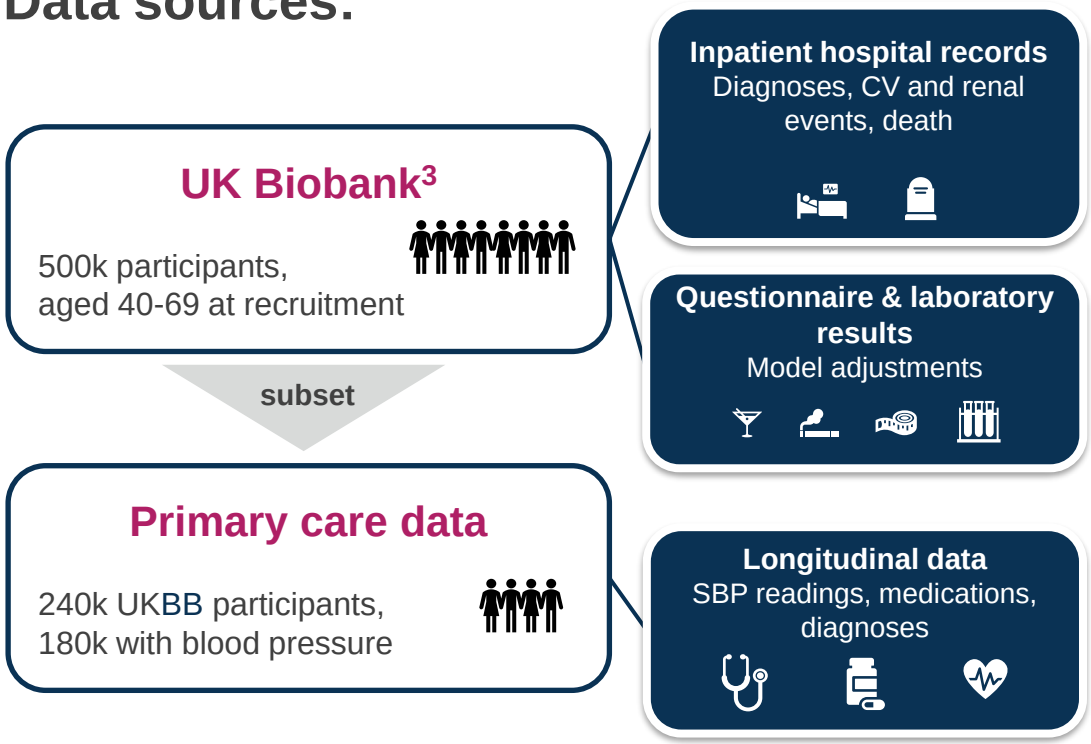
Populations:

- Diagnosed hypertension (N=39,816)
- Diagnosed chronic kidney disease (N=8,062)
- Neither of these diagnoses (N=17,702)

Model adjustments:

- Age, sex, chronic comorbidities[b], smoking and drinking behaviors, BMI, LDL cholesterol, SBP collection technical features

Data sources:



Longitudinal SBP data collection

Inclusion criteria: 4+ consecutive readings within 1 year of the last.

SBP data collection and event follow-up spanned 6.5 +/- 3.6 (SD) years on average with 115 +/- 45 days between each read.

This research has been conducted using the UK Biobank Applications 26041 and 65851.

BMI, body mass index; BP, blood pressure; CV, cardiovascular; LDL, low-density lipoprotein; MACE, major adverse cardiac event; SBP, systolic BP; SD, standard deviation; UKBB, United Kingdom Biobank.

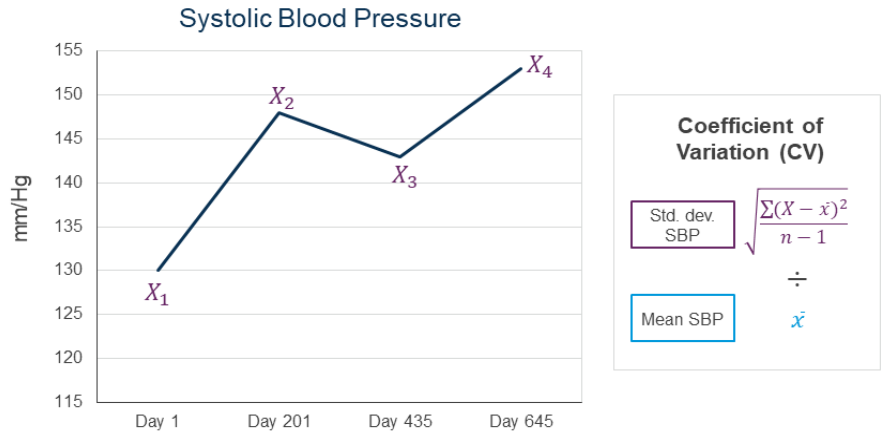
[a]4-point MACE: CV death, non-fatal myocardial infarction, non-fatal stroke, unstable angina requiring hospitalization. [b]Includes coronary artery disease, peripheral vascular disease, diabetes.

1. Fuchs, F. *et al*. High Blood Pressure and Cardiovascular Disease. *Hypertension* 2020 Feb;75(2):285-292. 2. Rosei, E. *et al*. How important is blood pressure variability? *Eur Heart J Suppl* 2020 Apr 6;22(Suppl E):E1–E6. 3. Allen, N. *et al.* UK Biobank: Current status and what it means for epidemiology. *Health Policy and Technology* 2012;**1**:123-126.

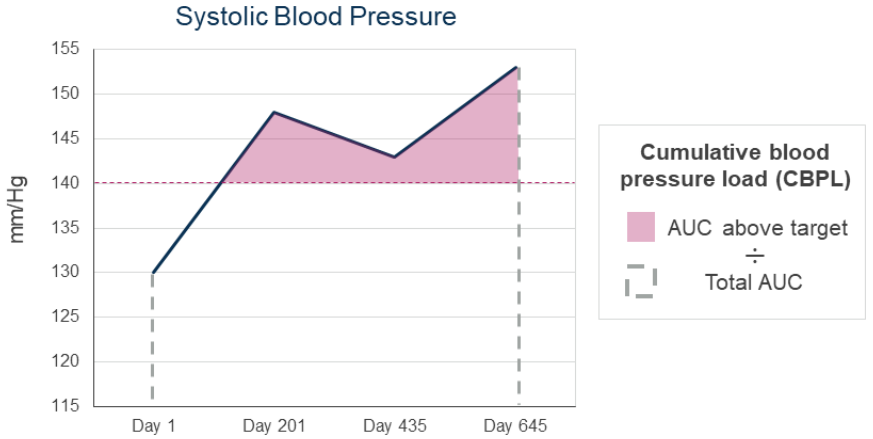
Capturing Multiple Aspects of the Consistency of SBP Control

Long-term Variability and Sustained Hypertension

Long-term blood pressure variability (LT-BPV)[1]
The overall variability between visit-to-visit blood pressure readings independent of mean SBP level



Cumulative blood pressure load (CBPL)[2]
The proportion of time a patient spent above a target SBP and the magnitude of that elevation



Statistics

Adjusted Cox regression to estimate hazard ratios in two ways:

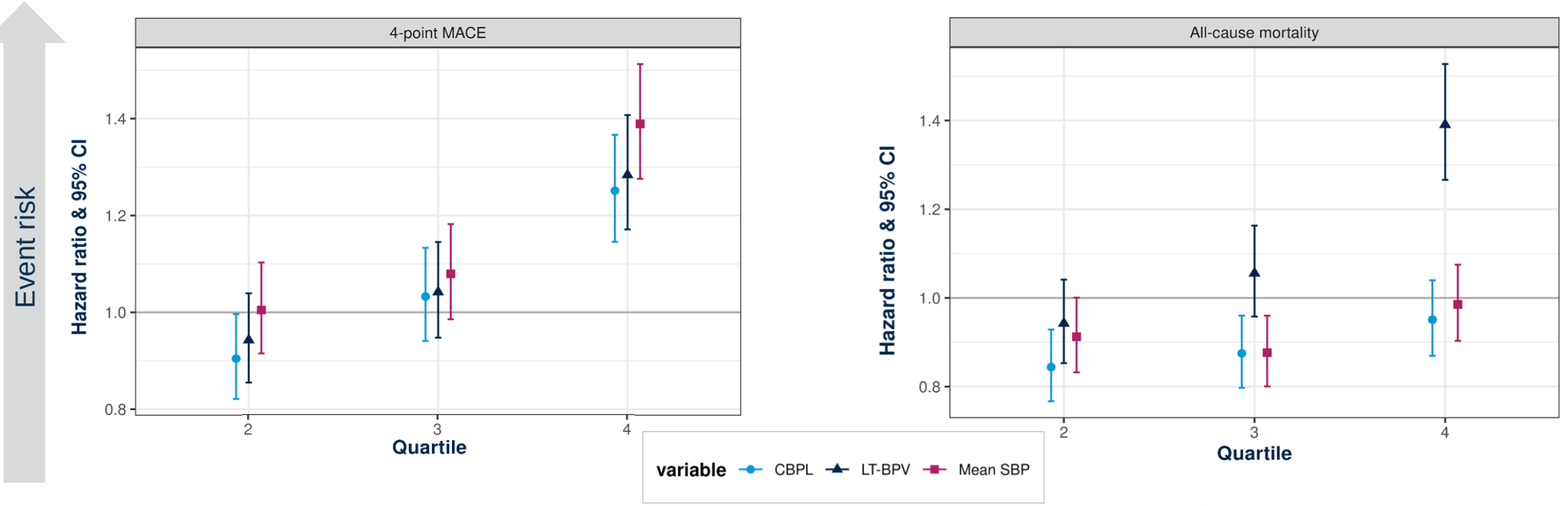
1. Per-quartile increase (Q2–4 compared to Q1)
2. Per-SD increase (continuous IRNT measurement)

Time to event or censor was calculated from first date of diagnosis (HTN and CKD populations) or first SBP read (population without these diagnoses).

AUC, area under the curve. CKD, chronic kidney disease; HTN, Hypertension; IRNT, inverse-rank normal transformed; Q, quartile; SBP, systolic blood pressure; SD, standard deviation.

1. Mancia, G., *et al.* Visit-to-visit blood pressure variability, carotid atherosclerosis, and cardiovascular events in the European Lacidipine Study on Atherosclerosis. *Circulation* 2012:**126**:569-578. 2. Wang, N. *et al.* Cumulative systolic blood pressure load and cardiovascular risk in patients with diabetes. *Journal of the American College of Cardiology* 2022;**80**:1147-1155.

Inconsistent SBP Control is Associated with MACE and Mortality in Those with Diagnosed Hypertension



LT-BPV and CBPL are associated with progression from hypertension diagnosis to MACE ($p<1.2^{E-10}$).

Only LT-BPV is associated with all-cause mortality ($p=9.1^{E-17}$).

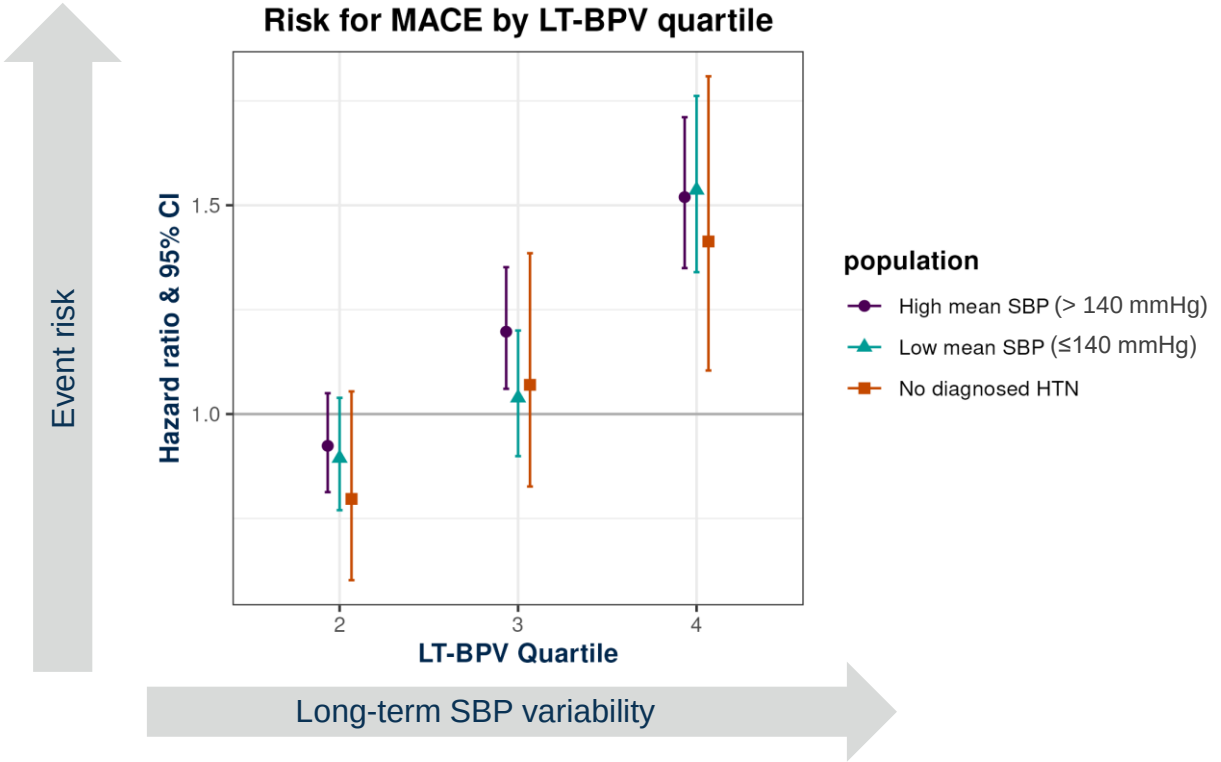
CBPL, cumulative blood pressure load; CI, confidence interval; LT-BPV, long-term blood pressure variability; MACE, major adverse cardiac event; SBP, systolic blood pressure.

Long-term SBP Variability is the Strongest Predictor of Adverse Outcomes in Populations with Lower Cardiovascular Risk

Non-hypertensive

No HTN diagnosis and mean SBP ≤140 mmHg

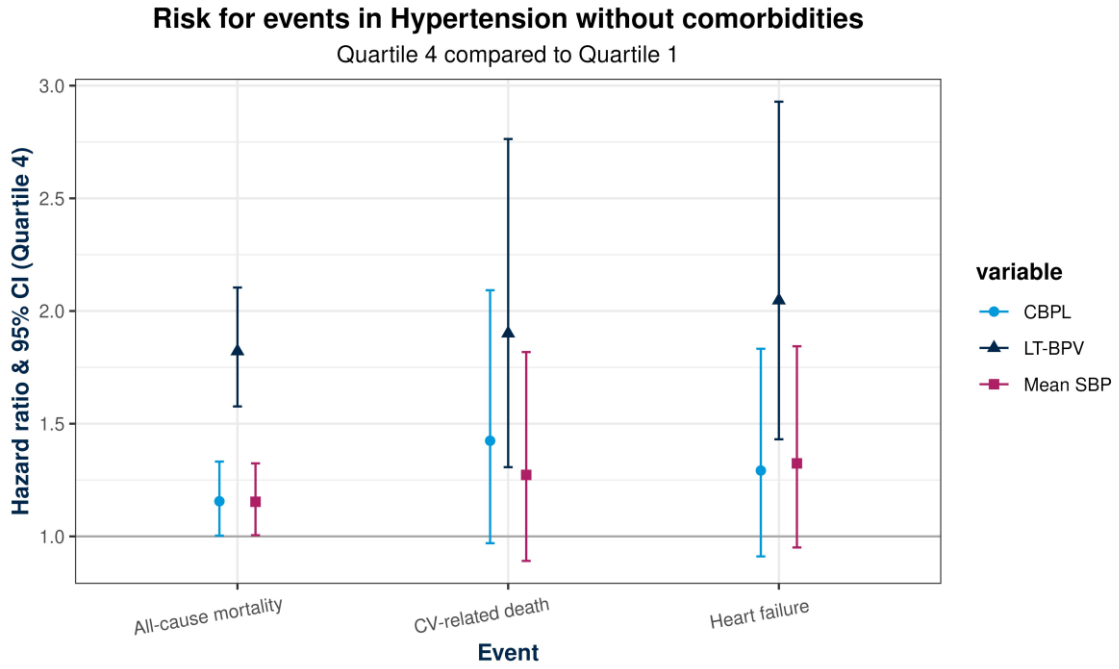
Only LT-BPV is associated with increased risk for MACE and all-cause mortality ($p<3.3^{E-16}$).



Lower-risk hypertensive

Diagnosed HTN without chronic comorbidities[a]

LT-BPV is the only significant predictor of all-cause mortality, CV-related death, and heart failure hospitalization (CBPL and mean SBP p>0.05).



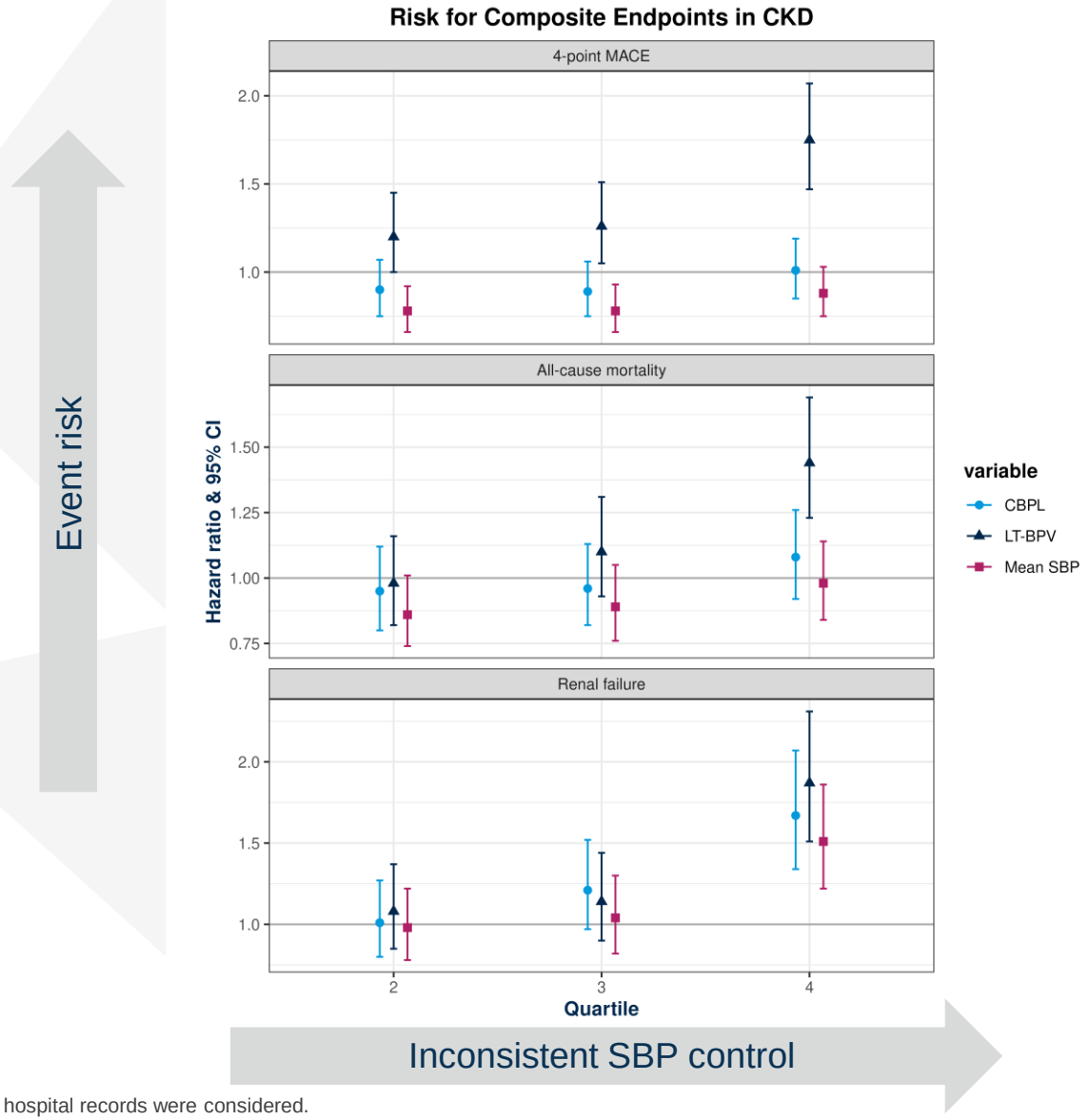
[a]No diagnoses for coronary artery disease, peripheral vascular disease, diabetes, or chronic kidney disease in primary care or hospital records (N=23,263).

CBPL, cumulative blood pressure load; CI, confidence interval; LT-BPV, long-term blood pressure variability; MACE, major adverse cardiac event; SBP, systolic blood pressure.

In Chronic Kidney Disease, Only LT-BPV Predicts Both Renal and Cardiovascular Outcomes

Only LT-BPV predicts progression from CKD diagnosis[a] to MACE and all-cause mortality ($p<2.9^{E-07}$).

LT-BPV, CBPL, and mean SBP are similarly associated with progression from CKD diagnosis to renal failure ($p<8.4^{E-05}$).



[a]Only participants with a first-recorded CKD diagnosis at stage 3 or below were included. Both primary care and hospital records were considered.

CBPL, cumulative blood pressure load; CI, confidence interval; CKD, chronic kidney disease; LT-BPV, long-term blood pressure variability; MACE, major adverse cardiac event; SBP, systolic blood pressure.

Summary and Conclusions

- This study examined long-term SBP variability (LT-BPV) and cumulative blood pressure load (CBPL) effects on event risks in a real-world, population-level analysis with SBP measurements spanning over 5 years on average.
- LT-BPV was the most consistent predictor of 4-point MACE[a], all-cause mortality, and CV-related death across populations, including “low risk” subsets.
- Both measurements predicted progression from CKD to renal failure, with similar association strength to mean SBP.

Conclusions:

- LT-BPV may capture CV risks in populations that would normally be overlooked if considering only BP levels.
- Antihypertensive therapies addressing both BP level and continuous control would likely maximize adverse outcome protection.

Thank you

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We are grateful for the opportunity to present our work and for your attention.

ukbiobank

We thank the participants and researchers of UK Biobank for creating an open-access resource.

paradigm4

Data management and analytics were performed using the REVEAL/SciDB translational analytics platform from Paradigm4.

UCL

We thank Dr. Bryan Williams for providing his expertise to help design and interpret this study.

[a]4-point MACE: CV death, non-fatal myocardial infarction, non-fatal stroke, unstable angina requiring hospitalization

CBPL, cumulative blood pressure load; CKD, chronic kidney disease; CV, cardiovascular; LT-BPV, long-term blood pressure variability; MACE, major adverse cardiac event; SBP, systolic blood pressure.