#### Title

# Impact of timing of antihypertensive treatment on mortality: An observational study from the Spanish Ambulatory Blood Pressure Monitoring Registry

#### **Abstract**

Background and aims: Whether bedtime versus morning administration of antihypertensive therapy is beneficial on outcomes is controversial. We evaluated the risk of total and cardiovascular mortality in a very large observational cohort of treated hypertensive patients, according to the timing of their usual treatment administration (morning versus evening). Methods: Vital status and cause of death were obtained from death certificates of 28 406 treated hypertensive patients (mean age 62 years, 53% male individuals), enrolled in the Spanish Ambulatory Blood Pressure Monitoring (ABPM) Registry between 2004 and 2014. Among the 28 406 patients, most (86%) received their medication exclusively in the morning; whilst 13% were treated exclusively in the evening or at bedtime. Follow-up was for a median of 9.7 years and 4345 deaths occurred, of which 1478 were cardiovascular deaths.Results:Using Cox-models adjusted for clinical confounders and 24-h SBP, and compared with patients treated in the morning (reference group), all-cause mortality [hazard ratio 1.01; 95% CI 0.93-1.09) and cardiovascular mortality (hazard ratio 1.04; 95% CI 0.91-1.19) was not significantly different in those receiving evening medication dosing. The results were consistent in all the subgroups of patients analysed. Conclusion: In this very large observational study, morning versus bedtime dosing of antihypertensive medication made no difference to the subsequent risk of all-cause or cardiovascular mortality. These findings are in accordance with results from a recent randomized controlled trial and do not support the hypothesis of a specific beneficial effect of night-time antihypertensive treatment dosing on risk of all-cause or cardiovascular death. © 2024 Lippincott Williams and Wilkins. All rights reserved.

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Antihypertensive Agents; Blood Pressure; Blood Pressure Monitoring, Ambulatory; Circadian Rhythm; Female; Humans; Hypertension; Male; Middle Aged; Registries; alpha adrenergic receptor blocking agent; angiotensin receptor antagonist; antihypertensive agent; beta adrenergic receptor blocking agent; calcium channel blocking agent; dipeptidyl carboxypeptidase inhibitor; diuretic agent; antihypertensive agent; adult; all cause mortality; antihypertensive therapy; Article; blood pressure measurement; cardiovascular mortality; cause of death registry; clinical outcome; cohort analysis; controlled study; death certificate; evening dosage; female; follow up; human; hypertension; hypertensive patient; ICD-10; major clinical study; male; middle aged; morning dosage; observational study; resistant hypertension; time to treatment; white coat hypertension; blood pressure; blood pressure monitoring; circadian rhythm; physiology; procedures; register

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