Does White Coat Hypertension End with Hypertension? A Systematic Review and Meta-Analysis

Abstract:

Background: Office blood pressure (BP) can be influenced by an alerting reaction to the clinical setting, giving rise to white-coat hypertension (WCH), long regarded as a benign phenotype. Whether WCH genuinely progresses to sustained hypertension remains debated. This review aimed to determine the pooled risk of progression from WCH to sustained hypertension and to explore the influence of diagnostic method, follow-up duration, and population characteristics on this risk.

Methods: Following PRISMA 2020 and Cochrane Handbook guidance, MEDLINE/PubMed, Web of Science, Scopus, CENTRAL, ScienceDirect, and ClinicalTrials.gov were searched from inception to 3 July 2026 for observational cohort studies classifying untreated participants as WCH or normotensive using paired office and out-of-office BP, with repeated assessment at follow-up. Risk of bias was assessed using the QUIPS tool. Random-effects meta-analysis pooled risk ratios (RR); adjusted odds ratios (OR) and hazard ratios (HR) were pooled separately by generic inverse variance.

Results: Twenty-four studies met inclusion criteria. Event-based pooling of 15 studies (8,297 participants) showed WCH was associated with significantly increased risk of progression to sustained hypertension versus normotension (RR 2.52, 95% CI 1.93–3.29; I^2=85%). Pooled adjusted estimates confirmed this association (RR 2.83, 95% CI 2.37–3.38; OR 2.60, 95% CI 2.13–3.17; HR 1.69, 95% CI 1.35–2.12), with low heterogeneity and no evidence of publication bias. Progression risk increased with follow-up duration and varied by diagnostic method and population setting.

Conclusion: WCH is not a benign office-only phenomenon but an intermediate-risk state that frequently progresses to sustained hypertension, supporting regular out-of-office BP monitoring and long-term surveillance.

Keywords

White-coat hypertension; Ambulatory blood pressure monitoring; Sustained hypertension; Systematic review and meta-analysis.

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Introduction

Hypertension remains the leading modifiable risk factor for cardiovascular disease and premature death worldwide, and its diagnosis has traditionally relied on blood pressure (BP) readings obtained in the clinic or office setting (1). However, office BP is a single, static snapshot that can be markedly influenced by an alerting reaction to the medical environment, and it correlates imperfectly with the BP levels a person experience during ordinary daily life (2, 3). Recognition of this discordance has driven the widespread adoption of out-of-office BP assessment, principally 24-hour ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM), which are now recommended by major guidelines as an integral step before a diagnosis of hypertension is confirmed (2, 4).

Comparison of office and out-of-office BP has identified four principal BP phenotypes: sustained normotension, sustained hypertension (SH), masked hypertension (normal office BP with elevated out-of-office BP), and white-coat hypertension (WCH), in which office BP is elevated while ambulatory or home BP remains within the normal range (3, 5). The European Society of Hypertension defines WCH as an office BP of at least 140/90 mmHg together with a mean 24-hour ABPM below 130/80 mmHg or a home BP below 135/85 mmHg in an untreated individual, whereas the American College of Cardiology/American Heart Association apply a lower office threshold of 130/80 mmHg with a concordant out-of-office cut-off, a discrepancy that itself contributes to inconsistent case ascertainment across studies (4, 5).

For many years WCH was regarded as a largely benign, anxiety-related phenomenon that carried little of the long-term risk associated with true hypertension, and clinical attention focused chiefly on avoiding unnecessary drug treatment (6, 7). This view has been challenged by a growing body of longitudinal evidence indicating that individuals with WCH occupy an intermediate risk position between normotension and SH, and that a substantial proportion goes on to develop sustained elevation of their out-of-office BP over time (7, 8).

Despite this accumulating evidence, the published literature on the natural history of WCH remains markedly heterogeneous(5, 9). Many existing systematic reviews and meta-analyses in this field have concentrated on cardiovascular events, mortality, or subclinical organ damage as the outcome of interest, rather than on the specific and clinically actionable question of whether, and to what extent, WCH itself evolves into SH on repeated BP assessment(10, 11).

Quantitative synthesis restricted to studies with repeated, out-of-office BP assessment and an explicit incident-hypertension outcome is therefore needed to consolidate the available longitudinal evidence, to derive an estimate of the risk of progression from WCH to SH relative to normotension, and to explore the extent to which this risk is modified by the diagnostic method used, the duration of follow-up, and the characteristics of the population studied. Clarifying this question has direct implications for surveillance strategies, since guidelines already recommend periodic reassessment of individuals with WCH. This systematic review and meta-analysis were therefore conducted to answer the question: does WCH end with hypertension?

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Methods

Methodology

The protocol of this systematic review and meta-analysis was registered at the International Prospective Register of Systematic Reviews (PROSPERO) (registration number:CRD420261449066) on July 12, 2026.

The conduction and reporting of this systematic review and meta-analysis followed the principles of the Cochrane Handbook for Systematic Reviews of Interventions, version 6, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (12, 13).

Research question

Among individuals identified with WCH on office and out-of-office BP assessment, what is the risk of progression to SH on repeated blood pressure assessment, and how does this risk vary according to the out-of-office diagnostic method used (ambulatory versus home blood pressure monitoring), the duration of follow-up, and other population characteristics?

Research aim

To systematically review and quantitatively synthesize the available longitudinal evidence on the risk of progression from WCH to SH, with attention to the diagnostic method used, the duration of follow-up, and relevant population and methodological factors.

Research objectives

Specifically, this study aimed to: (1) determine the pooled risk of progression to SH among individuals with WCH; (2) explore the influence of the out-of-office diagnostic method (ambulatory versus home blood pressure monitoring) on the estimated risk of progression; (3) evaluate the effect of the duration of follow-up on the cumulative incidence of progression; (4) assess whether the risk of progression differs between "true" and "partial" WCH, where such subclassification is reported; (5) investigate variation in progression risk across different population settings (community-based, occupational, hospital-based, and pediatric cohorts); and (6) evaluate the influence of potential effect modifiers and confounders, including age, sex, body mass index, and baseline blood pressure level, on the association between WCH and progression to SH.

Inclusion criteria

Types of studies

This systematic review considered observational studies with a longitudinal design, including prospective and retrospective cohort studies (community-based, occupational, hospital-based, and registry-based), that performed a baseline classification of participants as white-coat hypertensive or normotensive using paired office and out-of-office (ambulatory and/or home) blood pressure measurements, and that repeated blood pressure assessment at one or more follow-up time points to determine progression to SH.

Participants

The study population consisted of untreated children, adolescents, or adults classified with WCH at baseline (elevated office blood pressure with normal out-of-office blood pressure, by ambulatory and/or home monitoring). Studies of individuals already diagnosed with hypertension and receiving multiple antihypertensive drugs (i.e., white-coat effect superimposed on treated or resistant hypertension) were not eligible, as this represents a distinct clinical question from incident hypertension in a previously untreated, office-elevated group.

Intervention

The exposure of interest was baseline classification as WCH. The comparator, if any, was a baseline normotensive group, defined as normal office and out-of-office blood pressure. Studies were not required to use a single

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standardized definition of WCH or a uniform blood pressure threshold; any explicit, repeatable definition was eligible for inclusion provided that a subsequent reassessment of blood pressure status were reported.

Exclusion criteria

Studies were excluded if they did not include a repeat blood pressure assessment (i.e., cross-sectional or single-occasion ambulatory blood pressure monitoring studies). Studies were also excluded if the reported outcome was cardiac or non-cardiac complications, cardiovascular events, or hospitalization stratified by baseline blood pressure category, without a corresponding blood pressure reclassification outcome at follow-up. Studies of white-coat resistant hypertension (patients already diagnosed with hypertension and treated with three or more antihypertensive drugs whose office blood pressure remains elevated while ambulatory blood pressure is controlled) were excluded, as this addresses the reproducibility of controlled status on treatment rather than incident hypertension in a previously office-elevated, untreated group. Cross-sectional echocardiographic sub studies comparing target-organ damage across normotensive, white-coat, and SH groups at a single time point were excluded in the absence of a repeat blood pressure assessment. Narrative brief reviews, editorials, and letters to the editor commenting on primary studies without extractable cohort-level data of their own were excluded. Records that were inaccessible in full text, non-English-language publications, duplicate publications of the same cohort (in which case the most complete and non-overlapping dataset was retained), and oral presentations or conference materials without sufficient extractable data were also excluded.

Search strategy

Electronic searches

The following electronic databases were searched for eligible studies: MEDLINE/PubMed, Web of Science (WOS), Scopus, the Cochrane Central Register of Controlled Trials (CENTRAL)/Cochrane Library, ScienceDirect, and ClinicalTrials.gov. The reference lists of relevant articles and reviews were also searched manually for additional eligible studies. The search was set for all articles published in English from inception until 3rd July 2026.

The following search terms were used: ("White Coat Hypertension" OR "white coat hypertension" OR "white-coat hypertension "OR "white coat effect" OR "isolated clinic hypertension" OR "isolated office hypertension" OR "isolated clinical hypertension") AND ("Hypertension" OR "sustained hypertension" OR "established hypertension" OR "incident hypertension" OR "new-onset hypertension" OR "progression" OR "conversion" OR "transition" OR "develop*" OR "evolve*") AND ("Follow-Up Studies" OR "Longitudinal Studies" OR "Cohort Studies" OR "Prospective Studies" OR "follow-up" OR "longitudinal" OR "cohort" OR "prospective" OR "long-term").

Other resources

In addition to the electronic database searches, the first reviewer manually searched the reference lists of all retrieved articles, relevant reviews, and meta-analyses for other potentially eligible studies that were not retrieved by the electronic search.

Selection of studies

The first reviewer screened the retrieved reports for eligibility through title and abstract screening, followed by full-text screening. The second reviewer checked the retrieved studies, and discrepancies were resolved through discussion with a third reviewer.

Data extraction

The first reviewer carried out data extraction from the included studies using a standardized data sheet. The extracted data included: study ID (author, year), country, study design, study setting, sample size, number of WCH participants, comparison group, if any (normotension, masked hypertension, etc.), age (mean ± SD or median with

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IQR), sex distribution (% female), follow-up duration, diagnostic criteria for WCH (office BP threshold + ABPM/HBPM definition), BP measurement method (ABPM, HBPM, both), antihypertensive treatment at baseline, outcomes, and key results. The second reviewer independently checked all collected data for accuracy and completeness. Any disagreements between reviewers were resolved through discussion and, if necessary, arbitration by a third reviewer.

Measured outcomes

The primary outcome was progression from WCH to SH at follow-up, expressed as a relative risk (RR), odds ratio (OR), or hazard ratio (HR) with 95% confidence intervals, or as the incidence proportion of progression where comparative effect estimates were not reported.

Secondary outcomes included the influence of the out-of-office diagnostic method (ambulatory versus home blood pressure monitoring) on the risk of progression, the influence of the duration of follow-up on cumulative progression, differences in progression risk between true and partial WCH where reported, and the influence of confounding factors (e.g., age, sex, body mass index, and baseline blood pressure level) on the WCH–progression association, where such data were extractable.

Assessment of the risk of bias

Risk of bias was independently assessed using the Quality In Prognosis Studies (QUIPS) tool(14), which evaluates six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Each domain was rated as low, moderate, or high risk of bias, and an overall risk-of-bias judgment was assigned for each study. Disagreements were resolved through discussion until consensus was reached.

Data synthesis

Electronic database searches initially retrieved 2702records. After removing duplicates and screening titles and abstracts, 43full-text articles were assessed for eligibility, of which 24 studies(8, 9, 15-36)met all inclusion criteria and were included in this systematic review (Table 1). The remaining studies were excluded according to the pre-defined exclusion criteria, studies focusing on white-coat resistant hypertension (n=3), as this population is already on ≥3 antihypertensives and examines treatment reproducibility rather than progression from WCH. Cross-sectional echocardiographic sub studies evaluating left ventricular hypertrophy prevalence without repeat BP assessment were also removed (n=2), alongside single-occasion ABPM studies with no follow-up (n=3). Furthermore, 2 editorial commentaries were excluded due to lack of extractable primary data. Finally, we removedduplicate records (n=6),inaccessible full-text articles (n=2), and one non-English publication(Figure 1).

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Table 1: Summary of the included studies.

Anjum B, 2026 [sas15]s	**Study ID**
Retrospective single-center cohort study	**StudyDesign**
Canada	**Country**
Single tertiary pediatric heart-transplant center (Stollery Children's Hospital, Edmonton)	**Study setting**
33	**Sample size**
6	**Number of WCH participants**
Normotension (including well-controlled HTN); also compared with masked/sustained HTN	**Comparison group (Normotension, masked HTN, etc.)**
Median age at first ABPM 7.3 (IQR 5.3–10.4) years; median age at transplant 6.1 (IQR 2.4–10.1) years	**Age (mean ± SD or median with IQR)**
61% female (20/33)	**Sex distribution (% female)**
Serial ABPMs over study period (transplanted 2010–2023); median 0.7 (0.2–2.6) y post-transplant at first ABPM; longitudinal re-assessment thereafter	**Follow-up duration**
WCH = office/clinic BP >95th percentile (<13y) or ≥130/80 mmHg (≥13y) WITH normal ABPM (24h/awake/sleep) per 2022 AHA ABPM criteria and 2017 AAP office BP criteria	**Diagnostic criteria for WCH (Office BP threshold + ABPM/HBPM definition)**
Both (clinic BP + 24-h ABPM, Spacelabs OneTrak 90227)	**BP measurement method (ABPM, HBPM, both)**
79% (26/33) of whole cohort on ≥1 antihypertensive at first ABPM; among WCH subgroup not separately reported	**Antihypertensive treatment at baseline**
BP phenotype classification (normotensive/WCH/masked/sustained HTN); longitudinal transition on serial ABPM; LV mass/LVMi by echocardiography; clinical/demographic correlates	**Outcomes**
Retrospective cohort of 33 pediatric heart-transplant recipients with ≥1 post-transplant ABPM. At initial ABPM, 82% (27/33) were normotensive and 18% (6/33) hypertensive; of those with elevated clinic BP, 60% (6/10) had a normal ABPM (i.e., WCH). On longitudinal follow-up, 5 of the 6 WCH patients (83%) progressed to hypertension on a subsequent ABPM (3 of these developed isolated nocturnal hypertension), one had no further ABPM. Among the 21 sustained-normotensive patients, 43% (9/21) later developed hypertension. Median left ventricular mass was significantly higher in the masked/sustained-hypertensive group (160.9 g) than in WCH (54.4 g) or normotensive patients (66.9 g), p=0.032. No formal survival/regression analysis of predictors of WCH progression was performed given small sample size.	**Key Results**

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Chung C-M, 2014 [17]	Cacciolati C, 2013 [16]
Prospective longitudinal cohort study	Prospective community-based cohort study (Three-City Study, ancillary HBPM sub-study)
Taiwan	France
20 community pharmacies	Community-based (Three-City Study, Bordeaux center); home BP monitoring sub-study
1838	1481
460	198
Normotension (community pharmacy BP + home BP both normal); also masked HTN and sustained HTN	Normotension/controlled hypertension (office+home BP normal); also masked/home-uncontrolled HTN (MHT/HUHT)
Mean 66 ± 10 years	Mean 78.7 (SD 3.9) years (whole sample), all ≥73 years
62.6% female	65% female (whole sample)
1 year (BP reassessed every 4 months)	1 year
WCH = community pharmacy BP (CPBP) >140/90 mmHg with home BP (HBPM) daytime mean <135/85 mmHg	WCHT (untreated) = office BP ≥140/90 mmHg AND home BP (HBPM) <135/85 mmHg, no antihypertensive treatment; OUHT = same BP pattern but on treatment (ESH criteria)
Both (community pharmacy BP via validated OMRON M10-IT + home BP monitoring [HBPM])	Both (office BP by validated oscillometric device + home BP monitoring [HBPM], same OMRON M6 device for both)
Not reported/not restricted to untreated; general community sample ≥45 years	Stratified by treatment: untreated WCHT n=83 and treated (office-uncontrolled) OUHT n=113; 54% of whole sample on antihypertensive medication
Prevalence and predictors of WCH; 1-year incidence of progression to sustained hypertension	1-year risk of developing sustained hypertension (untreated) or uncontrolled hypertension (treated), by home BP monitoring
In 1838 community pharmacy attendees (mean age 66 years), 25% (460/1838) had WCH, 43% normotension, 31% sustained hypertension, and a small proportion masked hypertension. Patients with WCH were older and had higher BMI, waist-hip ratio, and higher office SBP/DBP than normotensives. Multivariable analysis identified age (OR 1.029), office SBP (OR 1.145) and office DBP (OR 1.080) as independent predictors of WCH. At 1-year follow-up, 10.2% (47/460) of WCH subjects had progressed to sustained hypertension compared with 2.1% (16/790) of normotensive subjects (OR 6.62, p<0.001), demonstrating that WCH is a significant risk factor for future sustained hypertension in a community setting.	Community-based cohort of 1481 individuals aged ≥73 years followed for 1 year with repeated office and home BP. Frequency of sustained/uncontrolled hypertension at 1 year was 13% among those with high office BP (WCHT/OUHT) and 26% among those with high home BP (MHT/HUHT), vs 5% among those with normal office and home BP. In untreated participants, WCHT carried a 4-fold increased risk of developing sustained hypertension versus normotension (fully adjusted OR 4.3, 95% CI 1.2–15.4, p=0.03), while masked hypertension (MHT) carried an even higher risk (OR 16.8, 95% CI 5.3–52.8, p<0.0001). Home systolic BP was the only variable independently predicting progression to sustained/uncontrolled hypertension in those with baseline WCHT/OUHT (OR 3.29 per SD, 95% CI 1.35–8.06, p=0.01); office BP level did not predict progression.

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Faria J, 2020 [19]	De la Sierra A, 2016 [18]
Prospective longitudinal observational cohort study	Retrospective analysis of a multicenter registry (Spanish ABPM Registry)
Portugal	Spain
3 hospitals in northern Portugal (Hospital Blood Pressure Units)	Multicenter (hypertension units contributing to the Spanish ABPM Registry)
899	839
399	205
Normotension (NT); treated WCHT also compared as intermediate group	Normotension, masked hypertension, sustained hypertension (all by combined office+24-h ABPM criteria)
NT 48 ± 14 y; untreated WCHT 51 ± 14 y; treated WCHT 51 ± 15 y	Not given as single overall figure; concordant-diagnosis subgroup 52.6 ± 13.9 y, non-concordant subgroup 53.9 ± 13.7 y
NT 52.9% female; untreated WCHT 50.1% female; treated WCHT 54.4% female	44% female (concordant 44.5%, non-concordant 43.6%)
Median 7.1 ± 1.9 years (range 0.9–10.1); assessed at baseline, 30–60 months, and 70–120 months	Median 3 months (IQR 0–13) between two assessments; sub-analyses for <1 month and >1 month (median 11, IQR 4–23 months) intervals
WCHT (untreated at baseline) = office BP ≥140/90 mmHg with 24-h ABP <130/80, daytime <135/85, AND night-time <120/70 mmHg (normal night-time BP required)	WCH = office BP ≥140/90 mmHg with normal 24-h ABP (<130/80 mmHg); parallel analysis using stricter criteria (normal 24-h, daytime AND night-time BP) also performed
Both (office BP, Omron M6 + 24-h ABPM, Spacelabs 90207) at 3 time points	Both (office BP + 24-h ABPM, Spacelabs 90207), all patients untreated at both assessments
Untreated WCHT (n=399) remained treatment-free throughout follow-up; treated WCHT (n=156) started antihypertensive therapy during follow-up at physician discretion; NT untreated	None, all patients untreated at first and second assessment (by inclusion criteria)
Cumulative incidence/transition to sustained ambulatory hypertension (SHT: daytime ≥135/85 and/or night-time ≥120/70) over long-term follow-up	Short-term and long-term reproducibility of hypertension phenotypes (normotension, WCH, masked HTN, sustained HTN) on repeat office+ABPM assessment
In 899 nondiabetic, cardiovascular-event-free subjects (344 normotensive, 399 untreated WCHT, 156 treated WCHT) followed a median of 7.1 years with repeated 24-h ABPM, untreated WCHT showed a significantly higher and faster progression to sustained hypertension than normotensives: at 30–60 months, 10.1% of untreated WCHT vs 3.8% of normotensives had progressed (2.7-fold higher); by end of follow-up, 16.5% vs 9.6% had progressed (1.7-fold higher), p<0.009 for both comparisons. Treated WCHT showed an intermediate progression rate (6.3% at 30–60 months, 13.6% at end of follow-up) and their office BP decreased over time (annual change −2.03 mmHg/year) whereas untreated WCHT office BP also decreased modestly but ambulatory (24-h/daytime/night-time) BP increased significantly faster than in normotensives and treated WCHT. Baseline systolic BP (office, 24-h, daytime, night-time) was significantly higher in those who progressed to SHT across all groups combined. No significant differences in cardiovascular event rates were found between groups (NT 4.7%, untreated WCHT 7%, treated WCHT 8%, p=0.188), though the study may have been underpowered for this outcome.	In 839 untreated patients from the Spanish ABPM Registry undergoing two office+24-h ABPM assessments (median interval 3 months), only sustained hypertension was highly reproducible (82.2%). WCH at the first assessment was reproducible in 55.6% at the second assessment, with 25.9% (53/205) of WCH patients switching to sustained hypertension (mover-stayer model estimate 27.4%). Reproducibility of WCH was strongly dependent on the interval between assessments: 89% when assessments were <1 month apart but only 42% when >1 month apart, with corresponding increases in the proportion progressing to sustained hypertension. No baseline clinical or demographic variable significantly predicted a switch to sustained hypertension among WCH patients (all comparisons p>0.05); a significant predictor (higher office diastolic BP) was found only for the masked-hypertension-to-sustained-hypertension transition.

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Li L, 2015 [21]	Flores L, 2006 [20]
Prospective observational cohort study	Prospective cohort study
China	Spain
Single center, Cardiovascular Center & Sleep Center, Beijing Tong Ren Hospital, Capital University of Medical Sciences	Single center, Diabetes Unit, Hospital ClíniciUniversitari, Barcelona
78	40
51	20
Healthy normotensive controls (age/BMI matched); internal comparison also made between WCH with and without OSA	Normotension (type 1 diabetic patients with similar age/disease duration)
Control 53±12 y; WCH (no OSA) 54±6 y; WCH+OSA 55±11 y	WCH 32.2 ± 7.8 y; normotensive 30.7 ± 8.1 y
11% female (control 12%, WCH 11%, WCH+OSA 11%; cohort 88–89% male)	WCH group 43% male (57% female); normotensive group 55% male (45% female)
26 months (office BP + ABPM repeated every 6.5 months)	5 years (clinical visits every 4 months; annual 24-h urine collection)
WCH = office BP ≥140/90 mmHg (mean of 3 readings, 2 visits) WITH mean daytime ABPM ≤135/85 mmHg, untreated at enrolment	WCH = office BP ≥140/90 mmHg with mean daytime ABP <135/85 mmHg (sensitivity analysis also performed using <130/80 mmHg cut-off)
Both (office BP + 24-h ABPM, Spacelabs 90207)	Both (office BP by mercury sphygmomanometer + 24-h ABPM, Spacelabs 90207)
None at enrolment (untreated); 3 patients who started CPAP during follow-up were censored/excluded; patients who started antihypertensive drugs had last pre-drug BP data used	None, all patients had normal urinary albumin excretion and no antihypertensive treatment at baseline/during follow-up
Development of sustained hypertension (office ≥140/90 + daytime ABPM >135/85); change in non-dipper SBP/DBP status; diurnal (daytime-nighttime) BP difference over follow-up	Development of microalbuminuria and/or sustained hypertension over 5 years in patients with type 1 diabetes
In this prospective study, 70 WCH patients underwent sleep testing and were followed with office BP and 24-h ABPM every 6.5 months for 26 months; 51 WCH patients (28 with OSA, 23 without) and 27 age/BMI-matched healthy controls completed follow-up and were analysed. WCH patients with OSA showed significantly higher daytime and night-time BP and a reduced diurnal SBP difference at study end compared with WCH-alone and control groups (all P<0.05), with a markedly higher rate of new non-dipper status (SBP 28.6%, DBP 32.1%) than the other two groups (P<0.01 for all comparisons). Sustained hypertension developed in 42.8% of WCH+OSA patients, compared with an intermediate rate in WCH-alone (13%) and a low rate in controls (~3.7%) (P<0.01), and was independently predicted by non-dipper status on 24-h ABPM (P<0.05) rather than by age, sex, AHI, or WCH status itself in multivariate analysis. The authors concluded that WCH may represent a prehypertensive state that can progress to sustained hypertension, an effect accelerated by co-existing OSA via non-dipping nocturnal BP patterns.	In a 5-year prospective study of 40 patients with type 1 diabetes mellitus (20 with WCH, 20 normotensive at baseline; 16 and 18 completed follow-up respectively), microalbuminuria developed in 4 WCH patients and sustained hypertension in 1 more, for a combined event rate of 31% (5/16) in the WCH group, versus 0% in the normotensive group (log-rank p<0.001). Kaplan–Meier analysis showed the relative risk of developing microalbuminuria/sustained hypertension was 25% higher in the WCH group, remaining significant after adjusting for baseline urinary albumin excretion. At baseline, WCH patients who later developed these hypertensive/renal events had significantly higher night-time systolic (119.4 vs 109.8 mmHg, p=0.04) and diastolic (73.2 vs 64.8 mmHg, p=0.04) ABPM values than those who did not, despite no differences in office BP or clinical characteristics, underscoring the prognostic value of nocturnal BP even within the WCH group.

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Mancia G, 2013 [22]	Mancia G, 2009 [8]
Prospective population-based cohort study (PAMELA); 16-year mortality follow-up with control 10-year mean repeat hypertension analysis WCH	Prospective population-based cohort study (PAMELA)
Italy	Italy
Population-based — residents of Monza (PAMELA cohort), outpatient sector of S. Gerardo Hospital	Population-based, residents of Monza (northeast outskirts of Milan), recruited via WHO-MONICA sampling frame
1589	1412
391	225 (office-vs-24h definition) / 177 (office-vs-home definition)
Normotension (office+24-h+home BP all normal, n=825); sustained hypertension (all 3 BPs elevated, n=373) as high-risk comparator; WCH further split into true WCH (n=164) and partial WCH (n=227)	True normotension (NT); masked hypertension (MHT) and true/sustained hypertension (SHT) also assessed as comparator/reference groups
Normotension 43.7±11.9 y; WCH (overall) 54.7±11.5 y; sustained hypertension 60.1±10.0 y; True WCH 51.6±11.5 y; Partial WCH 56.9±11.0 y	True NT 44.0±11.9 y; WCHT 53.3±11.2 y (office-vs-24h) / 50.3±10.4 y (office-vs-home); MHT 47.8±12.7 y
Normotension 60.1% female; WCH (overall) 47.8% female; sustained hyprtension 38.9% female; True WCH 49.4% female; Partial WCH 46.7% female (calculated as 100% – % mean reported)	True NT ~56.6% female; WCHT ~51% female (office-vs-24h) / ~48% female (office-vs-home); MHT ~39% female
Mortality: average 16 years (baseline 1991–1993 to September 2008); New-onset sustained hypertension: 10 years in a subgroup of 750 subjects free of sustained sustained hypertension at baseline	10 years (baseline 1990–1992, re-examination 2001–2002)
WCH = office BP ≥140/90 mmHg (untreated definition per guidelines) WITH normal 24-h ABPM (<125/79 mmHg) OR normal home BP (<132/83 mmHg); True WCH = both 24-h AND home BP normal; Partial WCH = only 1 of the 2 out-of-office BPs normal (the other elevated); subjects with normal office but elevated out-of-office BP (masked hypertension) excluded from analysis	WCHT = office BP ≥140/90 mmHg WITH 24-h ambulatory BP <125/79 mmHg OR home BP <132/83 mmHg (untreated at baseline); parallel definitions using office-vs-24h and office-vs-home BP
Both (office BP [mercury sphygmomanometer, 3 readings] + 24-h ABPM [Spacelabs 90207] + home BP [2 readings, Philips HP 5331])	Both (office BP + 24-h ABPM [Spacelabs 90207] + home BP)
4.3% (normotension), 27.2% (WCH overall: 22.0% true WCH, 31.0% partial WCH), 41.8% (sustained hypertension) on antihypertensive drugs at baseline; key analyses repeated after excluding treated subjects, with similar results	216 subjects on antihypertensive drugs at first visit; analyses repeated after excluding treated subjects (sensitivity n=497) with similar results
Cardiovascular and all-cause mortality over 16-year follow-up (Cox proportional hazards; unadjusted, age/sex-adjusted, and fully adjusted for glucose, cholesterol, smoking, prior CV events, antihypertensive treatment, BMI), including separately for true vs partial WCH; 10-year incidence and relative risk of new-onset sustained hypertension (office+home+24-h all elevated) in normotension, true WCH, and partial WCH (modified Poisson regression, age/sex/BMI-adjusted)	Development of new-onset sustained hypertension (SHT, elevated both office and out-of-office BP) at 10-year follow-up; age/sex-adjusted odds ratios; 10-year change in office/ambulatory systolic BP and pulse pressure
In 2051 PAMELA population participants (1589 analyzed after excluding masked hypertension), WCH, diagnosed as in clinical practice by an elevated office BP with a normal 24-h or home BP, had a prevalence of 24.6% and, over an average 16-year follow-up, showed a progressively higher CV and all-cause mortality than normotensives, with fully adjusted HR of 2.04 (CV mortality, 95% CI 0.87–4.78, P=0.099) and 1.50 (all-cause mortality, 95% CI 1.03–2.18, P=0.034), compared with 2.94 and 1.47 respectively for sustained hypertension. When the WCH group was split by home and 24-h ABPM normality, true WCH (both out-of-office BPs normal, 41.9% of WCH) showed no significant increase in fully adjusted CV (HR 0.67, 95% CI 0.14–3.18) or all-cause mortality (HR 1.35, 95% CI 0.81–2.23) versus normotensives, whereas partial WCH (only 1 out-of-office BP normal, 58.1% of WCH) showed a markedly and significantly increased risk for both CV mortality (HR 2.76, 95% CI 1.16–6.59, P=0.022) and all-cause mortality (HR 1.58, 95% CI 1.05–2.38, P=0.027); results were similar after excluding treated subjects. In multivariable analysis, independent predictors of mortality in the WCH group included office SBP, age, prior CV events, smoking, BMI, antihypertensive treatment, and (for all-cause mortality) sex and home DBP. Over 10 years in 750 subjects free of sustained hypertension at baseline, both true WCH (age/sex/BMI-adjusted RR 2.89, 95% CI 1.95–4.32, P<0.0001) and partial WCH (RR 2.58, 95% CI 1.77–3.77, P<0.0001) showed a significantly increased risk of developing new-onset sustained hypertension compared with normotensives (9.9% NT vs 35.5% true WCH vs 45.5% partial WCH at 10 years). The authors concluded that WCH as usually diagnosed in clinical practice is not clinically innocent, but that within the WCH population two very different long-term mortality-risk groups coexist (true WCH, indistinguishable in mortality risk from normotension, vs partial WCH, whose mortality risk approaches that of sustained hypertension), and that measuring both ambulatory and home BP is needed to distinguish them, even though both true and partial WCH carry an increased risk of progressing to sustained hypertension.	In 1412 subjects from the PAMELA population followed for 10 years, 54.1% were normotensive, 16.1% WCHT, 8.9% MHT, and 20.9% SHT at baseline. At follow-up, new-onset SHT developed in 42.6% of WCHT (office-vs-24h definition) and 43.9% of WCHT (office-vs-home definition), compared with 18.2% and 13.3% of true normotensives, respectively; MHT also showed a substantially elevated conversion rate (47.1% and 40.4%). Age- and sex-adjusted odds ratios for developing SHT versus true normotension were 2.51 (95% CI 1.79–3.54, P<0.0001) for WCHT by office-vs-24h BP and 3.81 (95% CI 2.57–5.64, P<0.0001) by office-vs-home BP, with no significant difference in risk between WCHT and MHT (P=0.372 and P=0.398). Findings were essentially unchanged after excluding treated subjects (OR 3.25 [2.08–5.07] and 3.69 [2.17–6.28]). Over the 10 years, WCHT and MHT subjects showed significantly greater increases in systolic BP and pulse pressure than true normotensives, while diastolic BP increases were similar or smaller, and office/ambulatory/home BP values, together with age and metabolic variables (serum glucose, BMI), were independent predictors of new-onset SHT. The authors concluded that WCHT and MHT

UNDER PEER REVIEW

Miyashita Y, 2022 [25]	Márquez Contreras E, 2001 [24]	Mancia G, 2022 [23]
Retrospective longitudinal cohort study (Pediatric Nephrology Research Consortium, 11 centers)	Prospective cohort study	Prospective population-based cohort study (PAMELA), longitudinal follow-up with
USA	Spain	Italy
11 pediatric nephrology referral centers across the USA (Pediatric Nephrology Research Consortium)	Primary care health center (Centro de Salud La Orden, Huelva)	Population-based, residents of Monza, Italy (PAMELA cohort)
89	82	1423
89	41	397 (276 without OD+ 121 with baseline OD)
No external normotensive comparator; internal comparison between 'stable WCH' (n=71, hypertensive clinic BP at nephrology visit) and 'intermittent WCH' (n=18, normal clinic BP at	Normotension (untreated volunteers)	Normotensive subjects without and with baseline OD; sustained hypertensive subjects without and with baseline OD served as high-risk comparators
Median 13.9 years (73/89 aged 12–17 y; 16/89 <12 y)	Overall 52.2 ± 10.7 y; WCH group 53 ± 10.5 y; normotensive group 51.4 ± 10.9 y	N without OD 42.4±11.5 y; WCH without OD 52.5±11.3 y; sustained hypertension without OD 58.0±9.7 y (older with baseline OD in each group)
22% female (78% male)	Overall 63.4% female; WCH group 61% female; normotensive group 65.9% female	N without OD 56.6% female; WCH without OD 42% female; sustained hypertension without OD 34.8% female
Median 14 months (IQR 12–22) between initial and follow-up ABPM	1 year (ABPM repeated at baseline, 6 months, 12 months)	Median 29 years (IQR 23–30) for mortality; 10 years for new-onset sustained hypertension/masked hypertension and new-onset OD sub-analysis
WCH = hypertensive clinic BP with normal ABPM (mean wake and sleep systolic/diastolic BP <95th percentile for sex/height, BP loads all <25%) per AHA pediatric ABPM statement	WCH = ≥3 clinic BP readings (mercury sphygmomanometer) >140/90 mmHg AND ABPM daytime (08:00–23:00) mean <135/85 mmHg, untreated; Normotension = clinic BP <140/90 with same ABPM criterion	WCH = office SBP ≥140 mmHg or DBP ≥90 mmHg WITH 24-h ambulatory BP <130/80 mmHg or home BP <135/85 mmHg; no baseline echocardiographic LVH and no reduced eGFR defined the 'without OD' subgroup
Both (clinic BP + ABPM; Spacelabs models 90207/90217/90227)	Both (office BP by mercury sphygmomanometer + 24-h ABPM, Spacelabs 90207)	Both (office BP + 24-h ABPM [Spacelab 90207] + home BP) plus echocardiography and eGFR for OD
None, patients on antihypertensive medication at either ABPM were excluded (except stable-dose stimulant medication for ADHD)	None, both groups untreated at baseline and throughout follow-up; no participant started antihypertensive medication prior to ABPM	1.8% of normotensive-no-OD, 19.2% of WCH-no-OD, and 29.6% of sustained hypertension-no-OD on antihypertensive drugs at baseline; adjusted for in mortality models
Progression at follow-up ABPM to an abnormal phenotype (ambulatory hypertension or ambulatory prehypertension) vs remaining normal; predictors of progression	Incidence of sustained hypertension (by ABPM) at 6 and 12 months	Cardiovascular and all-cause mortality over 29-year median follow-up; 10-year incidence/risk of new-onset sustained hypertension or masked hypertension; 10-year incidence/risk of new-onset cardiac (LVH) or renal (eGFR<60) OD
In this multicenter retrospective cohort of 89 children/adolescents (median age 13.9 y, 78% male) diagnosed with WCH on initial ABPM and re-tested a median of 14 months later, 61% progressed to an abnormal ABPM phenotype: 23% (20/89) to frank ambulatory hypertension (65% of these isolated sleep-hypertension) and 38% (34/89) to ambulatory prehypertension; only 39% (35/89) remained normal. Age 12–17 years and 'stable' WCH (hypertensive clinic BP specifically at the pediatric nephrology visit, present in 80% of the cohort) were associated with greater progression to prehypertension/hypertension (Fisher exact P=0.04 and P=0.03). In multivariable models, a baseline wake systolic BP index ≥0.9 was significantly associated with higher odds of progressing to ambulatory hypertension (OR 3.07, 95% CI 1.02–9.23) and to hypertension-or-prehypertension combined (OR 4.37, 95% CI 1.35–14.15); baseline 'stable' WCH also independently predicted progression to hypertension-or-prehypertension (OR 6.67, 95% CI 1.67–25.00). Baseline BMI z-score/obesity did not predict progression. The authors concluded that the majority of children with WCH progress to an abnormal ABPM phenotype within just over a year, supporting existing pediatric guideline recommendations for routine follow-up ABPM in 1–2 years.	Prospective cohort of 82 untreated adults (41 with WCH, 41 normotensive) followed with repeated ABPM. Incidence of sustained hypertension at 6 months was 19.0% (8/41) in the WCH group vs 4.8% (2/41) in normotensives (RR 3.8, 95% CI 0.86–16.9, p=0.052); at 12 months, incidence was 46.3% (19/41) in the WCH group vs 9.8% (4/41) in normotensives (RR 4.63, 95% CI 1.7–12.4, p=0.001). The two groups did not differ in age, sex, BMI, cardiovascular risk group, or comorbidities. Incidence of hypertension increased with increasing initial diurnal diastolic ABPM values in both groups. The authors concluded WCH may represent a prehypertensive state.	In 1423 subjects followed for a median of 29 years (165 cardiovascular and 526 all-cause deaths), OD prevalence rose progressively from normotensive (10.6%) to WCH (30.5%) to sustained hypertensive (43.8%). After full adjustment, WCH without OD carried a cardiovascular mortality risk twice that of normotensives without OD (HR 2.0, 95% CI 1.1–3.6, P=0.02) and an all-cause mortality HR of 1.2 (0.9–1.5); risks were higher again in sustained hypertension without OD (HR 2.7 and 1.5) and highest in all groups with baseline OD. In a nested 10-year sub-analysis, WCH without OD had a substantially greater risk of progressing to new-onset sustained hypertension or masked hypertension than normotensives without OD (fully adjusted OR 2.4, 95% CI 1.6–3.7, P<0.0001; incidence 34.1% vs 14.9%), with an even greater risk in WCH with baseline OD versus normotensives with OD (OR 3.5, 95% CI 1.8–6.5, P=0.0001; incidence 41.5% vs 20.8%). WCH also carried a significantly greater 10-year risk of developing new cardiac or renal organ damage than normotensives (fully adjusted OR 1.7, 95% CI 1.1–2.6, P=0.0198; 41.2% vs 18.5% incidence), a risk comparable in magnitude to that of sustained hypertension (OR 1.7, 0.9–3.3). The authors concluded that, even without baseline organ damage, WCH is not a clinically innocent condition, given its independently increased long-term mortality and its marked propensity to progress to sustained hypertension and organ damage within a

UNDER PEER REVIEW

Palatini P, 2023 [27]	Obrycki L, 2024 [26]
Prospective cohort study (HARVEST)	Conference abstract; retrospective longitudinal follow-up cohort
Italy	Poland (with collaboration from Canada)
17 hypertension units, northeast Italy (multicenter)	Department of Nephrology, Kidney Transplantation and Hypertension, Children's Memorial Health Institute, Warsaw, Poland (pediatric/young-adult hypertension referral center)
1096	27
228	27
Normotensive (office and 24h BP both normal at 3-month assessment, n=132); also compared with masked hypertension (n=195) and sustained hypertension (n=610)	Within-group comparison only (subjects who developed sustained hypertension vs those who normalized/maintained WCH); no separate concurrent normotensive control group reported
Mean 33.0±8.6 years at entry (BMI 25.4±3.5 kg/m2)	Diagnosed with WCH at 14.5±2.5 years (adolescence); re-evaluated as young adults after follow-up (implied current age ~22-23 years)
27.3% female (72.7% male)	Not reported
Mean 17.4 years (survival analysis, N=1050); reproducibility assessed at 3 months	8.3±1.2 years
WCH = office BP ≥140/90 mmHg AND average 24-h ABPM <130/80 mmHg, untreated; assessed at baseline and again at 3 months. Stable WCH = WCH criteria met at both assessments (n=76); Unstable WCH = WCH criteria met at only one of the two assessments (n=83, combining those who reverted from/to WCH)	WCH = elevated office BP with normal ABPM
Both (office BP [auscultatory, mean of 6 readings over 2 visits] + 24-h ABPM [A&D TM2420 or SpaceLabs 90207])	Both (office BP + ABPM; also central SBP, augmentation pressure, carotid IMT, LV mass index, pulse wave velocity)
None, all HARVEST participants untreated at baseline and for ≥3 months (never previously treated for hypertension)	Not reported; presumed untreated at WCH diagnosis (consistent with WCH definition)
Reproducibility of WCH (weighted kappa) over 3 months; long-term (17.4-year) risk of established hypertension needing antihypertensive treatment (multivariable Cox regression) by baseline/3-month BP phenotype	Development of sustained hypertension; hypertension-mediated OD (LVH, cIMT, PWV, LVMi); lipid/metabolic parameters
In 1096 untreated HARVEST participants with stage 1 hypertension at entry, baseline WCH (20.8% of the cohort, n=228) was confirmed at 3-month reassessment in only 33.3% of cases; 31.6% became normotensive, 8.8% masked hypertensive, and 26.3% sustained hypertensive. WCH reproducibility (weighted kappa) was fair (0.27, 95%CI 0.20–0.37), reflecting poor agreement for office hypertension (kappa 0.14) versus moderate agreement for ambulatory hypertension (kappa 0.47). In long-term follow-up of 1050 participants (mean 17.4 years), 80.5% overall developed established hypertension requiring treatment. In multivariable Cox regression (adjusted for age, sex, BMI, smoking, alcohol, coffee use, physical activity), unstable WCH (present at only one of the two assessments) was NOT a significant predictor of future hypertension (p=0.86 at baseline, p=0.16 at 3 months). In contrast, stable WCH (present at both baseline and 3 months, n=76) carried a significantly increased risk compared with normotensives (HR 1.50, 95%CI 1.06–2.13, p=0.022), a risk level similar to masked hypertension (HR 1.35, 95%CI 1.02–1.80) and sustained hypertension (HR 1.52, 95%CI 1.19–1.95). The authors conclude WCH has limited reproducibility and should be diagnosed using two separate sets of office and ambulatory BP measurements; only reproducible ('stable') WCH carries meaningful long-term hypertension risk.	27 adolescents diagnosed with WCH (mean age 14.5±2.5y) underwent full diagnostic work-up (anthropometry, biochemistry, office BP, ABPM, central SBP/augmentation pressure, cIMT, LVMi, PWV) and were re-evaluated after 8.3±1.2 years. At diagnosis, LVH was present in 11%, increased cIMT in 11%, and increased PWV in 70%. At re-evaluation, 20/27 (74%) had normalized BP or maintained WCH status, while 7/27 (26%) had progressed to sustained hypertension. Waist circumference, total/LDL-cholesterol, fasting glycemia, central SBP, PWV, cIMT, and LVMi all increased in both the normalized/WCH and SH groups over follow-up, with no significant between-group difference except LVMi, which was significantly higher at follow-up in those who developed sustained hypertension (p=0.001). At re-evaluation, LVH was diagnosed in 15% of those who normalized/maintained WCH vs 29% of those with SH, and increased PWV in 20% vs 29% respectively. Patients who normalized/maintained WCH had had lower LDL-cholesterol at initial WCH diagnosis than those who progressed to sustained hypertension (85±27 vs 103±30 mg/dL; p<0.05). The authors conclude that adolescents with WCH remain at risk of developing sustained hypertension and hypertension-mediated OD and should be closely monitored; lipid disorders may be an additional risk marker.

UNDER PEER REVIEW

Rao S, 2024 [29]	Polonia JJ, 2005 [28]
Prospective observational cohort study	Prospective longitudinal cohort study (extension/follow-up of previous cohort)
United Arab Emirates	Portugal
Department of Cardiology outpatient care centre, Unicare Medical Centre, Burjuman, Dubai, UAE	Single center, Unidade de Hipertensão e Risco Cardiovascular, Hospital Pedro Hispano, Matosinhos / Faculdade de Medicina do Porto
32	118
32	79
Within-group comparison only (subjects who developed sustained hypertension at 1 year, n=7, vs those who remained normotensive, n=25); no separate concurrent normotensive control cohort	Normotension (n=39); WCH subdivided into treated and untreated subgroups during follow-up
Normotensive (remained WCH/normalized) group 42.24±9.45 years; Hypertensive (progressed) group 39.14±8.82 years (p=0.44, NS)	Baseline: Normotension 43.4±2.6 y; WCH-treated 45.9±2.5 y; WCH-untreated 49±2.1 y
18.75% female overall (6/32); Normotensive group 4/25 female (16%); Hypertensive group 2/7 female (29%)	Normotension 23/16 F/M (59% female); WCH-treated 20/14 (59% female); WCH-untreated 28/17 (62% female)
12 months (reassessed at 6 and 12 months)	Mean 7.4 years total (intermediate ABPM at 35±3 months [Normotension] / 49±4 months [WCH]; final ABPM at 86±4 months [Normotension] / 88–92±4–5 months [WCH])
WCH = 3 serial office BP measurements over 4 weeks ≥140/90 mmHg AND normal 24-h ABPM (24h <130/80, daytime <135/85, night-time <120/70 mmHg)	WCH = untreated clinic/office BP ≥140/90 mmHg (systolic <175 and/or diastolic <105) WITH mean awake ABPM <130/85 mmHg (90th percentile of healthy volunteers), no other major CV risk factors, normal ECG/echo; Normotension = clinic BP <140/90 mmHg with same ABPM criterion
Both (office BP + 24-h ABPM via TRISMED monitor); plus echocardiography (E/A ratio, E-wave deceleration time, E/E' ratio, LV ejection fraction)	Both (office/clinic BP + 24–26 h ABPM, Spacelabs 90207, validated against mercury manometer)
None, all WCH subjects managed with lifestyle modification only, no antihypertensive medication during follow-up	None at baseline (all 118 subjects untreated at entry, per inclusion criteria); during follow-up 36 WCH subjects started antihypertensive treatment (WCH-treated) while 43 remained untreated
Progression to sustained hypertension (needing medication) at 12 months; correlation of baseline echocardiographic left ventricular diastolic parameters (E/A, E-deceleration time, E/E') with progression	Progressive change in casual and 24-h ABPM values over ~7.4-year follow-up; development of ambulatory hypertension (daytime BP >130/85 mmHg); incidence of first cardiovascular events
Among 129 consecutive subjects referred for elevated office BP and evaluated by 24-h ABPM, 32 (24.8%) were diagnosed with WCH and followed prospectively for 12 months. At 1 year, 25/32 (78.12%) remained normotensive and 7/32 (21.88%) progressed to sustained hypertension requiring medication. Baseline clinical characteristics (age, BMI, fasting glucose, LDL-cholesterol) did not differ significantly between those who progressed and those who did not, although ejection fraction was slightly lower in the eventual hypertensive group (65.14±2.74% vs 69.4±4.49%, p=0.02). Mitral E/A ratio and E-wave deceleration time showed no significant correlation with progression to hypertension. However, the E/E' ratio (a marker of LV filling pressure) showed a significant positive correlation with 12-month systolic BP in the hypertensive group (R=0.77, p=0.04), a correlation that was weak and non-significant at 6 months (R=0.33, p=0.46) and non-significant throughout in the normotensive group. The authors conclude that echocardiographic E/E' ratio may serve as an early predictor of progression from WCH to sustained hypertension, while conventional diastolic indices (E/A, deceleration time) do not.	In this 7.4-year (mean) follow-up extension of a previous cohort, 39 normotensive and 79 white-coat hypertensive (36 treated, 43 untreated after baseline) subjects, all initially free of major cardiovascular risk factors, underwent repeated 24-h ABPM. Twenty-four-hour ABPM systolic/diastolic BP rose progressively and similarly in all three groups (Normotension +4.9/2.1 mmHg; WCH-treated +5.0/1.2 mmHg; WCH-untreated +5.4/3.2 mmHg over follow-up; annual increases of 0.66–0.74/0.31–0.39 mmHg/year, not significantly different between groups). In contrast, casual/office BP rose in Normotension (+5.7/3.9 mmHg) but fell in both WCH-treated (–7.8/5.2 mmHg) and WCH-untreated (–4.9/1.1 mmHg) groups over the same period. Development of ambulatory hypertension (daytime BP >130/85 mmHg) at the end of follow-up occurred in 15.4% (6/39) of Normotension, 22.7% (8/36) of WCH-treated, and 26.1% (11/43) of WCH-untreated subjects (NS, p>0.25). Only 3 first cardiovascular events were recorded, all in WCH subjects (3% of 101 contactable WCH subjects) versus none in the 70 contactable Normotension subjects. The authors concluded that, when selected under strict low-risk criteria (no other major CV risk factors, no baseline organ damage, restrictive ABPM cut-points <130/85 mmHg), WCH, whether treated or untreated, shows a similar rate of ABPM progression and

UNDER PEER REVIEW

Satoh M, 2023 [9]	Santos Moreira C, 2010 [30]
Prospective cohort study (Ohasama Study)	Prospective single-arm cohort study (conference abstract; no
Japan	Portugal
Community-based, rural town of Ohasama, Iwate Prefecture (general population)	Single center, Department of Medicine, Faculty of Medicine of Lisbon
153	92
23	92
Normotension (n=113 at baseline); also compared with masked hypertension (n=8) and sustained hypertension (n=9) at baseline	None, single-arm cohort of WCH patients only; internal comparison is WCH patients who remained WCH vs those who converted to sustained 'hypertensive dipper' status over time
Mean 64.4±5.8 years at baseline (68.4±5.8 years at 4-year visit)	WCH (remaining) 54.9±9.2 y; converted to hypertension dipper 55.1±8.4 y (no significant difference)
77.1% female (22.9% male)	Approximately 57–61% female in the subgroups reported (WCH remaining 57% female; converted-to-Hypertension dipper 61%
4 years (single follow-up interval)	5 years, with annual ABPM and clinical reassessment
WCH = home BP <135/85 mmHg AND office BP ≥140/90 mmHg, untreated; Normotension = home BP<135/85 and office BP<140/90; Masked Hypertension = home BP≥135/85 and office BP<140/90; Sustained Hypertension = both ≥ thresholds	WCH with dipper profile on ABPM (specific numeric office BP/ABPM)
Both (home BP via Omron HEM-747ICN/HEM7080IC, self-measured over 4 weeks + office BP via Omron HEM-907/HEM-9000AI, measured twice at a local medical center)	Both (clinic BP + ABPM, annual reassessment)
None, only participants untreated with antihypertensive drugs at BOTH baseline and the 4-year visit were included (n=153 of 970 consented; 437 already treated at baseline were excluded, 84 more	Not reported in abstract (population implicitly untreated, consistent with WCH definition)
4-year reproducibility of white-coat hypertension/hypertension phenotype (kappa, ICC) as categorical and continuous (white-coat effect) variables; transition rates between phenotypes	Conversion from WCH to sustained hypertensive ('hypertensive dipper') status over 5 years of annual follow-up
In 153 untreated participants from the general Ohasama population followed for 4 years, 23 (15.0%) had WCH at baseline. At the 4-year visit, only 11/23 (47.8%) still had WCH, while 4/23 (17.4%) had become normotensive and 8/23 (34.8%) had progressed to sustained hypertension (0% became masked hypertensive). Overall agreement between baseline and 4-year hypertension phenotype was minimal (kappa=0.36, 95%CI 0.25–0.48). The white-coat effect (office-home BP difference) treated as a continuous variable showed only moderate correlation between baseline and 4-year values (r=0.41 systolic, r=0.40 diastolic), with intraclass correlation coefficients of only ~0.40–0.41 for the white-coat effect, versus much higher reproducibility for home BP alone (ICC 0.74–0.80) than office BP alone (ICC 0.64–0.67). Change in the white-coat effect was mainly driven by fluctuation in office BP rather than home BP. Among normotensives at baseline, 5/113 (4.4%) progressed to sustained hypertension over 4 years, compared with 8/23 (34.8%) of baseline WCH. The authors conclude that the white-coat effect and WCH phenotype are not reproducible over the long term in a general untreated population, that this variability is mainly attributable to office BP fluctuation, and that home and office BP should be measured repeatedly/regularly rather than relying on a single assessment.	In this single-arm abstract-only cohort of 91–92 patients with white-coat hypertension and a dipper ABPM profile followed annually for 5 years, the proportion remaining classified as WCH fell steadily while the proportion converting to sustained ('hypertensive dipper') status rose progressively: from 81 WCH/10 Hypertension dipper after year 1 (11% cumulative conversion), to 69/21 (13.5%) after year 2, 61/29 (11.6%) after year 3, 49/39 (16.4%) after year 4, and 35/51 (24.4% incremental, 55% cumulative) after year 5. No significant baseline differences in age, sex, BMI, hypertension duration, smoking, or sleep time distinguished those who remained WCH from those who converted to sustained hypertension. The authors concluded that roughly half of WCH patients progress to sustained hypertension within 5 years, arguing against considering WCH an innocent condition and instead framing it as an early stage in the development of hypertension. No normotensive comparator group was included, so no between-group effect estimate (HR/OR) is derivable from this study.

UNDER PEER REVIEW

Stolarz-Skrzypek K, 2022 [32]	Sivén SS, 2016 [31]
Prospective pooled cohort analysis of 5 population-based cohorts (IDACO)	Prospective population-based cohort study (Finn-Home study)
Multi-national (IDACO consortium; 5 population-based cohorts, countries not individually specified in abstract)	Finland
Population-based cohorts contributing ambulatory and conventional BP data to the IDACO database	Nationwide population-based sample; home BP measurement sub-study (Finn-Home) nested within the Health 2000/Health 2011 national health examination surveys
749	944
64	142
Normotension (n=575, 76.8%); masked hypertension (MH, n=110, 14.7%) also compared	Normotension (n=528); masked hypertension (n=63) also compared; 211 with sustained hypertension at baseline excluded from progression analysis
Not separately reported for WCH in the abstract; masked hypertension subgroup older than normotensives (50 vs 45 years, P<0.01)	Mean 54.1 ± 7.4 years (whole cohort, untreated at baseline); WCH treated subgroup 55.3 ± 7.8 years; Normotension subgroup 52.8 ± 6.8 years
Not separately reported for WCH in the abstract; masked hypertension more frequently male than normotensives (59.9% vs 31.5%, P<0.01)	45.7% male overall (i.e., 54.3% female); WCH treated subgroup 51.4% male (48.6% female)
Median 9.7 years	11.0 ± 0.1 years (mean)
Conventional/office BP (CBP) ≥140/90 mmHg AND daytime ABPM <135/85 mmHg; untreated at baseline	Office BP ≥140/90 mmHg AND home BP <135/85 mmHg (mean of 28 self-measurements over 7 days, twice daily); untreated at baseline
Both (ABPM + conventional/office BP)	Both (office BP: mercury sphygmomanometer, 2 readings; home BP: validated automatic oscillometric device [Omron HEM-722C at baseline 2000, HEM-7211-E at follow-up 2011], 28 measurements over 7 days)
None, excluded subjects on BP-lowering treatment at baseline (n=252) and those with untreated sustained hypertension at baseline (n=80)	None, antihypertensive drug treatment at baseline was an exclusion criterion (n=239 excluded)
Progression to sustained hypertension over median 9.7-year follow-up (264 incident cases among 749 analyzed); HR adjusted for cohort, sex, age, BMI, smoking, drinking	Progression to sustained hypertension (sustained hypertension: office BP ≥140/90 mmHg AND home BP ≥135/85 mmHg, or new antihypertensive treatment) over 11-year follow-up; multivariable-adjusted relative risk; nonfatal cardiovascular events
In a pooled analysis of 1081 individuals from 5 IDACO population-based cohorts with both office and ambulatory BP at baseline and follow-up (after excluding those on BP-lowering treatment or with untreated sustained hypertension, leaving 749 analyzed), 8.5% had WCH and 14.7% had masked hypertension at baseline. Over a median follow-up of 9.7 years there were 264 incident cases of sustained hypertension. In multivariable-adjusted analyses (cohort, sex, age, BMI, smoking, drinking), both masked hypertension (HR 2.23, 95% CI 1.57–3.17) and WCH (HR 1.84, 95% CI 1.37–2.47) significantly increased the risk of progression to sustained hypertension compared with normotensive subjects. The authors noted this observed risk elevation might partly reflect more frequent initiation of antihypertensive therapy in the WCH/masked hypertension groups rather than a pure BP-driven effect.	In this nationwide unselected Finnish sample (n=944, mean follow-up 11.0 years), progression to sustained hypertension increased from normotension (18.2%) to WCHT, 52.1% and masked hypertension (73.0%), P<0.0001. In multivariable log-binomial regression (adjusted for sex, age, smoking, BMI, diabetes, hypercholesterolemia), the relative risk of progressing to sustained hypertension versus normotension was 2.8 (95% CI 2.2–3.6, P<0.0001) for WCH treated and 3.8 (95% CI 2.9–5.0, P<0.0001) for masked hypertension. Risk of progression increased steadily with baseline home BP category (P-trend<0.0001). Nonfatal cardiovascular events during follow-up were also more frequent in WCH treated (10.4%) and masked hypertension (16.4%) than in normotension (2.4%). The authors concluded WCH treated and masked hypertension are prehypertensive states warranting active follow-up and lifestyle counselling.

UNDER PEER REVIEW IN BMJ

Toyama H, 2008 [34]	Strandberg TE, 2000 [33]
Prospective cohort study (4-year targeted screening	Prospective occupational cohort study (Helsinki
Japan	Finland
Tohoku University Health Center, Sendai (targeted hypertension screening at annual university general health check-up)	Occupational health cohort of businessmen and executives in Helsinki
87	536
72	18
Essential hypertension students (n=15); male students undergoing the 2006 regular check-up used as reference/control group (n=8,102)	Normotensive (n=259); also mildly hypertensive (n=150) and persistently hypertensive (n=109) comparator groups
WCH (whole group) 21.7±2.36 y; Essential hypertension 21.4±2.35 y; male control students (2006) 21.5±2.6 y; (subset with ≥2 years follow-up: consistent WCH	Baseline (1974–75) mean age by group: normotensive 46±4 y, mildly hypertensive 47±4 y, persistently hypertensive 48±4 y, white-coat
100% male (all WCH and Essential hypertension students identified were male, consistent with prior	0% female (cohort restricted to male businessmen/executives)
4 consecutive school years (2003–2006); WCH students re-screened annually, with 38/72 WCH students completing ≥2 consecutive years of follow-up (up to 3 years for a subset of 7)	21 years
WCH = casual/office BP ≥140/90 mmHg on 3 sequential screening measurements (1st, 2nd [1 month later], 3rd [by physician after ≥30-min rest]) WITH home BP (self-measured mornings, >7 measurements over >2 weeks using validated automatic device) <135/85 mmHg	White-coat hypertension defined per Muscholl et al. cut-points using nurse- vs physician-measured BP as a surrogate for out-of-office/in-office discordance (nurse SBP/DBP <140/90 mmHg AND physician SBP/DBP ≥160/95 mmHg). NOTE: this is NOT an ABPM/HBPM-based definition, nurse-measured
Both (casual/office BP via automatic device at health check-up + home BP self-monitoring)	Neither ABPM nor HBPM, clinic-based comparison of nurse-measured BP vs physician-measured BP (both by mercury sphygmomanometer after 5–10 min rest)
None, all students untreated; those with confirmed high home BP (≥135/85 mmHg) were referred to university hospital and separately diagnosed as essential hypertension or secondary hypertension	None, cohort was free of regular medication and serious disease at baseline (1974)
Annual re-classification of WCH status (transient vs consistent WCH) on repeat casual BP screening; progression of home BP to hypertensive levels; comparison of pulse rate and BP-pulse rate correlation between WCH and essential hypertension students	21-year all-cause and cardiovascular mortality; development of drug-treated hypertension during follow-up
Over 4 consecutive years of targeted screening (12,000–17,000 students screened per year), 72 WCH and 15 essential hypertension students (all male) were identified via 3 sequential casual BP measurements plus home BP monitoring. None of the WCH students developed home BP at hypertensive levels during their time at university. Among 38 WCH students followed for ≥2 years, 26 (68%) showed normal casual BP the following year ("transient WCH") while 12 (32%) again showed high casual BP with normal home BP ("consistent WCH"); home BP values in the consistent-WCH group remained essentially unchanged on repeat annual screening and none of these students were subsequently diagnosed with essential hypertension. Casual BP, and BMI were significantly higher in both WCH and essential hypertension students than in male controls, with no significant difference between WCH and essential hypertension on these parameters; genetic background (hypertension in parents) was markedly more common in essential hypertension (86.7%) and WCH (52.7%) than controls (10.1%). WCH students had a significantly higher pulse rate than controls, but pulse rate could not fully differentiate WCH from essential hypertension; systolic/diastolic BP correlated with pulse rate in essential hypertension students but this correlation was essentially absent in WCH students. The authors concluded that young-onset WCH rarely progresses to essential hypertension during the (typically 4-year) period of university enrollment, that longer follow-up after graduation is needed to	In this 21-year prospective study of 536 initially healthy Finnish businessmen, 18 men were classified as WCH using nurse- vs physician-measured BP discordance. Mortality was significantly higher in the WCH group (33.3%) than in the normotensive group (9.5%, P=0.0005); the multivariable-adjusted relative risk of death was 3.3 (95% CI 1.2–7.6) and of cardiovascular death 4.1 (95% CI 1.03–16.1) compared with normotensives. Development of drug-treated hypertension during 21-year follow-up was also more common in WCH (27.8%) than normotensives (13.4%, P<0.0001 across groups). A large white-coat effect (>30 mmHg physician-minus-nurse SBP difference, n=37) independently predicted mortality (adjusted RR 2.2, 95% CI 1.1–4.2). The authors concluded WCH/effect is not an innocent phenomenon and tends to co-exist with metabolic risk factors.

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Westerståhl M, 2017 [36]	Ugajin T, 2005 [35]										
Prospective cohort follow-up study (re-examination of [illegible])	Prospective population-based cohort study (Ohasama Study)										
Sweden	Japan										
Community/school-based cohort of Swedish schoolchildren originally screened for WCH, re-examined in young adulthood (Karolinska Institutet/University Hospital)	Community-based, Ohasama town, Iwate Prefecture (population-based home BP measurement project)										
30	777										
30	128										
None external, within-cohort reclassification at follow-up into normotension (n=23) vs sustained hypertension (n=7); no separate normotensive control arm followed in parallel	Sustained normotension (n=649)										
22.1 (IQR 20.5–23.8) years at follow-up; normotension subgroup 22.4 (21.6–23.9) years; sustained hypertension subgroup 20.9 (20–22.3) years	Mean 56.0 ± 8.7 years (whole cohort); WCH 57.0 ± 9.5 years; normotension 55.8 ± 8.5 years (P=0.13)										
63.3% female (19/30); normotension 65.2% female (15/23); sustained hypertension 57.1% female (4/7)	34.0% male overall (i.e., 66.0% female); WCH 42.2% male vs normotension 32.4% male (P=0.03)										
Median 9.3 (IQR 8.0–9.8) years since childhood WCH diagnosis	Mean 8.2 ± 2.0 years (8-year follow-up)										
Childhood diagnosis: casual/office SBP and/or DBP >95th height-/sex-adjusted percentile on 3 separate visits AND normal ABPM (mean systolic/diastolic BP during awake and sleep periods ≤95th adjusted percentile). Follow-up sustained hypertension defined per 2013 ESH/ESC ABPM thresholds: ≥130 and/or ≥80 mmHg for 24-hour; ≥135 and/or ≥85 mmHg	Office/screening BP ≥140/90 mmHg AND home BP <135/85 mmHg (mean of all self-measurements, mean 23.2 [SD 6.8] measurements over 4 weeks at baseline), untreated										
Both (casual/office BP + 24-hour ABPM) at both childhood baseline and young-adult follow-up	Both (home BP: semiautomatic oscillometric device [HEM401C, Omron], morning measurements over 4 weeks; office/screening BP: fully automatic device [USM-700F, UEDA Electronic Works] via Korotkoff sound technique, annual health check-up)										
Not explicitly stated, pediatric/young-adult population, presumed untreated at baseline diagnosis	None, excluded n=582 regularly using antihypertensive medication and n=235 with home hypertension at baseline										
Progression from childhood WCH to sustained hypertension in young adulthood; cardiovascular status including PWV, cIMT, LVM/LVMI, LVH	Development of home hypertension (progression to home BP ≥135/85 mmHg or start of antihypertensive medication) over 8-year follow-up; multivariable logistic regression for risk factors										
In this prospective re-examination of 30 young adults (56 originally identified as having childhood WCH out of 1470 Swedish schoolchildren screened; 18 declined and 8 were lost to follow-up) after a median 9.3-year follow-up, 7 of 30 (23.3%) had progressed to sustained hypertension while 23 (76.7%) remained normotensive. Ambulatory BP, PWV, and cIMT values were all significantly higher in the sustained hypertension group than in the normotension group (e.g., 24-hour systolic BP 133.0 vs 121.0 mmHg, P=0.0011; PWV 7.8 vs 6.6 m/s, P=0.007; carotid IMT 0.5–0.6 vs 0.5 mm, P=0.002), though PWV and cIMT remained within the normal reference range, suggesting early, subclinical hypertensive vascular changes. Two normotension and two sustained hypertension participants had LVH. The authors concluded that childhood WCH can progress to sustained hypertension in young adulthood and that affected children warrant follow-up for early detection and management of hypertension.	In this 8-year follow-up study of 777 Japanese residents of Ohasama aged ≥40 years (128 with WCH, 649 with sustained normotension, all untreated and without home hypertension at baseline), 46.9% of WCH subjects versus 22.2% of normotension subjects developed home hypertension (P<0.001). The adjusted odds ratio for WCH to progress to home hypertension was 2.86 (95% CI 1.90–4.31, P<0.001), independent of baseline home BP levels and other confounders (age, sex, smoking, obesity, family history of hypertension, hypercholesterolemia, diabetes). The elevated risk was consistent whether hypertension was defined by home BP threshold or by start of antihypertensive treatment, and was observed even in subjects with baseline home BP within the completely normal range (threshold as low as 108/58 mmHg). The authors concluded WCH represents a transitional condition toward hypertension outside medical settings and may carry a poor cardiovascular prognosis.										

WCH (white-coat hypertension), ABPM (ambulatory blood pressure monitoring), HBPM (home blood pressure monitoring), HTN (hypertension), LV (left ventricular), LVMi (left ventricular mass index), AHA (American Heart Association), AAP (American Academy of Pediatrics), MHT (masked hypertension), OUHT (office-uncontrolled hypertension), ESH (European Society of Hypertension), CPBP (community pharmacy blood pressure), SHT (sustained hypertension), OSA (obstructive sleep apnea), CPAP (continuous positive airway pressure), BMI (body mass index), AHI (apnea-hypopnea index), PAMELA (PressioniArterioseMonitorate E Loro Associazioni), MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease), HR (hazard ratio), RR (relative risk), OR (odds ratio), CI (confidence interval), CV (cardiovascular), OD (organ damage), eGFR (estimated glomerular filtration rate), LVH (left ventricular hypertrophy), SBP (systolic blood pressure), DBP (diastolic blood pressure), IMT (intima-media thickness), cIMT (carotid intima-media thickness), PWV (pulse wave velocity), HARVEST (Hypertension and Ambulatory Recording Venetia Study), E/E' (ratio of early diastolic transmitral flow velocity to early diastolic tissue velocity), IDACO (International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes), CBP (conventional blood pressure), ESC (European Society of Cardiology), and ICC (intraclass correlation coefficient).

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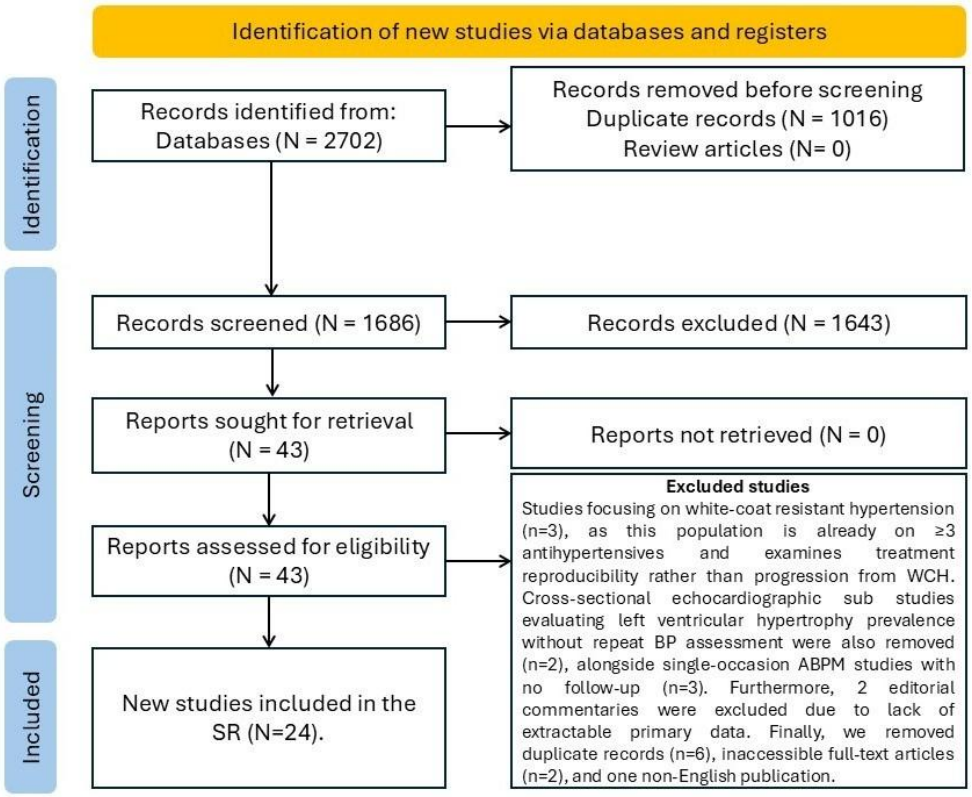


Figure 1: PRISMA flow chart. WCH; white coat hypertension, ABPM; ambulatory blood pressure monitoring.

Statistical analysis

Statistical analyses were performed using a random-effects model for the primary pairwise meta-analysis to account for anticipated clinical and methodological heterogeneity across studies. Effect estimates were expressed as RRs with corresponding 95% confidence intervals (CIs). Adjusted effect estimates reported by the included studies (RRs, ORs, and HRs) were pooled separately using the generic inverse variance method after logarithmic transformation of the effect estimates and calculation of their standard errors. Statistical heterogeneity was assessed using Cochran's Q test and the I^2 statistic. Publication bias was evaluated by visual inspection of funnel plots and Egger's regression test when sufficient studies were available. Sensitivity analyses were performed using a leave-one-out approach, whereby each study was sequentially omitted to evaluate the robustness of the pooled estimates and to identify potential sources of heterogeneity. Statistical significance was defined as a two-sided $p< 0.05$.

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Results

Study and Population Characteristics

Twenty-four studies (8, 9, 15-36)met the inclusion criteria, comprising prospective and retrospective cohorts published between 2000 and 2026 and originating from Europe, Asia, North America, and the Middle East, with one multinational pooled cohort analysis(32)· Study settings were heterogeneous, encompassing community- and population-based surveys (8, 9, 16, 17, 22, 23, 31, 35), hospital- and hypertension-unit-based cohorts (18-21, 24, 27-30), an occupational cohort of Finnish businessmen (33), and five pediatric or young-adult cohorts(15, 25, 26, 34, 36)· Sample sizes ranged from 27 to 1838 participants, and the number of individuals with WCH per study ranged from 6 to 460· Follow-up duration varied widely, from 3 months to a median of 29 years· WCH was diagnosed using ABPM alone, HBPM alone, or both modalities in combination, against a range of office blood pressure thresholds and out-of-office cut-points, reflecting substantial methodological heterogeneity across the diagnostic definitions applied.

Pooled Risk of Progression to SH

Across the 15 studies (8, 9, 16-24, 28, 31, 33, 35)reporting a comparative estimate of progression risk in individuals with WCH relative to normotensive controls, the direction of association was consistently positive, although the magnitude varied considerably with population, definition, and follow-up length· Adjusted risk estimates for progression to SH in WCH versus normotension ranged from approximately 1·5- to nearly 7-fold· The largest population-based cohorts reported HRs or ORs in the range of 1·5-3·8 (8, 27, 31, 32, 35), while smaller clinic-based or shorter-duration cohorts reported considerably higher RRs, up to 6·6-fold (17) and 4·6-fold(24)· Crude progression proportions among WCH participants ranged from 10·2% at one year(17) to over 50% at five to eight years(30, 35), against comparator progression proportions of 2-22% in normotensive groups over similar intervals· Two studies were notable exceptions to this pattern: Polonia(28), in a strictly low-risk cohort free of other cardiovascular risk factors, found no significant excess of ambulatory hypertension in WCH relative to normotension, and Toyama (34), in a cohort of young, healthy university students followed for only four years, observed no progression to essential hypertension in the WCH group· These discordant findings are considered further under population setting and follow-up duration.The narrative pattern across studies nonetheless supports a consistent, if heterogeneous, increase in the risk of progression to SH among individuals with WCH.

Influence of the Out-of-Office Diagnostic Method on Estimated Progression Risk

Fourteen studies diagnosed WCH using ABPM, seven using HBPM, and several applied both modalities either in parallel or in combination to define subcategories of WCH· Direct within-cohort comparison was possible in the PAMELA study(8), in which WCH defined against 24-hour ABPM carried an age- and sex-adjusted ORs for new-onset SH of 2·51 (95% CI 1·79-3·54), whereas the same population classified using home blood pressure yielded a higher OR of 3·81 (95% CI 2·57-5·64), suggesting that home-based diagnosis identified a somewhat higher-risk subgroup than ambulatory-based diagnosis within an identical source population· Studies relying exclusively on HBPM for WCH diagnosis in community settings(17, 31, 35) reported some of the higher progression estimates in the dataset (odds/relative risks of 2·9-6·6), while ABPM-based hospital and registry cohorts(18, 19, 27) reported comparatively more moderate, though still significant, associations (HRs of 1·5-1·8)· Studies combining both ABPM and HBPM to require concordant normality on both measures(22, 23) generally produced more conservative or attenuated risk estimates, consistent with a more specific, lower-risk phenotype when both out-of-office measures were required to be normal· Overall, the pattern across studies suggests that the choice of out-of-office diagnostic method is not interchangeable: HBPM-based definitions tended to yield somewhat higher estimated progression risk than ABPM-based definitions, while dual-modality definitions produced more conservative estimates, likely reflecting differences in the sensitivity and specificity of each method for detecting genuinely elevated ambulatory pressure.

Effect of Follow-Up Duration on Cumulative Incidence of Progression

A clear duration-dependent gradient in cumulative progression was evident both within and across studies· Within the same cohort, De la Sierra(18)demonstrated that the proportion of WCH participants who converted to SH rose sharply with the interval between assessments, from a low conversion rate when the two BP assessments were less

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than one month apart to a substantially higher conversion rate when the interval exceeded one month (median 11 months)· Similarly, Márquez Contreras(24) reported a rise in cumulative incidence of SH in WCH from 19·0% at six months to 46·3% at twelve months, and Santos Moreira(30) documented a progressive increase in cumulative conversion to sustained ("hypertensive dipper") status from approximately 11% after one year to approximately 55% after five years of annual reassessment· Longer-term cohorts corroborated this pattern at a population level: Faria(19) reported progression rising from 10·1% at 30-60 months to 16·5% by a median of 7·1 years, while the longest-duration cohorts (Mancia(22, 23); Palatini(27)), spanning 16 to 29 years, reported the highest cumulative burden of established hypertension, with the majority of the overall HARVEST cohort (80·5%) eventually requiring antihypertensive treatment· Conversely, the shortest-duration cohort in the dataset, Toyama(34), which followed young university students for only four years, observed no progression to essential hypertension, and the pediatric cohort of Anjum(15), despite reporting a high proportion of progression, did so over a comparatively short and highly variable interval in a very small sample· Taken together, these findings indicate that cumulative incidence of progression from WCH to SH increases with the length of follow-up, and that studies with short observation periods (particularly under one to two years) are likely to underestimate the true long-term risk.

Progression Risk in "True" versus "Partial" White-Coat Hypertension

Only one study in this review formally subclassified WCH according to concordance between ABPM and HBPM (Mancia(22))· In this analysis, "true" WCH (both 24-hour ambulatory and home blood pressure normal) carried a 10-year age-, sex-, and BMI-adjusted relative risk of new-onset SH of 2·89 (95% CI 1·95-4·32), while "partial" WCH (only one of the two out-of-office measures normal) carried a similarly elevated RR of 2·58 (95% CI 1·77-3·77), with 10-year cumulative incidences of 35·5% and 45·5%, respectively, compared with 9·9% among normotensives· Notably, this concordance-based distinction was more informative for long-term mortality than for progression risk: over a mean 16-year follow-up, true WCH showed no significant excess of cardiovascular or all-cause mortality relative to normotension, whereas partial WCH carried a significantly increased risk of both cardiovascular mortality (HR 2·76, 95% CI 1·16-6·59) and all-cause mortality (HR 1·58, 95% CI 1·05-2·38)· A conceptually related, though not identical, subclassification based on temporal reproducibility rather than measurement concordance was reported by Palatini (27), in which "stable" WCH (confirmed on both baseline and three-month reassessment) carried a significantly increased long-term risk of established hypertension (HR 1·50, 95% CI 1·06-2·13), whereas "unstable" WCH (present at only one of the two assessments) was not significantly associated with future hypertension· Together, these findings suggest that both concordance-based ("true" versus "partial") and reproducibility-based subclassification of WCH may identify subgroups with differing long-term prognostic implications, although this distinction was reported in only a minority of the included studies and warrants further investigation.

Variation in Progression Risk Across Population Settings

Progression risk varied appreciably according to the population setting in which WCH was ascertained· In community- and population-based cohorts, progression proportions at extended follow-up were substantial, ranging from approximately 35-46% at ten years in the PAMELA cohort(8, 22, 23) to 46·9% at eight years (Ugajin(35)) and 52·1% at eleven years (Sivén(31))· Hospital- and hypertension-unit-based cohorts showed a broadly similar direction of effect but somewhat more heterogeneous magnitude, ranging from a non-significant excess in a strictly low-risk hospital cohort (Polonia (28)) to markedly elevated risk in registry- and clinic-based samples(18, 19, 27, 29)· The single occupational cohort (Strandberg(33)), though defined using a non-ABPM/HBPM surrogate for white-coat effect, showed a substantially higher rate of drug-treated hypertension at 21 years in white-coat hypertensive men (27·8%) compared with normotensive colleagues (13·4%), alongside markedly increased all-cause and cardiovascular mortality· Pediatric and young-adult cohorts generally showed higher short- to medium-term progression proportions than adult cohorts followed over comparable or even longer intervals: 61% of children progressed to an abnormal ambulatory phenotype within a median of 14 months in a multicenter nephrology cohort (Miyashita(25)), and progression proportions of 23-26% were observed within approximately 8-9 years in other pediatric or young-adult cohorts (Obrycki(26); Westerståhl(36)), notwithstanding the markedly higher figure in the very small heart-transplant cohort (Anjum(15))· The university-based screening cohort of otherwise healthy young men (Toyama(34)) was a clear outlier, with no progression to essential hypertension over

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four years, suggesting that setting-related differences in baseline cardiovascular risk, age, and comorbidity burden substantially modify the observed rate of progression independent of the WCH diagnosis itself·

Effect Modifiers and Confounders: Age, Sex, Body Mass Index, and Baseline Blood Pressure

Several studies examined candidate effect modifiers and confounders of the association between WCH and progression, with baseline out-of-office blood pressure level emerging as the most consistent independent predictor· In Cacciolati(16), home systolic blood pressure independently predicted progression to sustained or uncontrolled hypertension (OR 3·29 per standard deviation), whereas office blood pressure did not· Faria (19) similarly found that baseline systolic blood pressure, whether measured in-office or ambulatorily, was significantly higher among those who subsequently progressed, and Miyashita(25) identified a baseline wake systolic blood pressure index of 0·9 or higher as an independent predictor of progression to ambulatory hypertension (OR 3·07, 95% CI 1·02-9·23)· By contrast, De la Sierra(18) found that no baseline clinical or demographic variable, including age, sex, or blood pressure level, significantly predicted conversion from WCH to SH, in marked contrast to the masked-hypertension subgroup in the same cohort, where higher office diastolic blood pressure did predict progression· Age showed an inconsistent role: it was associated with progression in the pediatric cohort of Miyashita(25), where participants aged 12-17 years were more likely to progress than younger children, and was retained as a significant independent predictor of WCH prevalence, alongside office blood pressure, in Chung(17), but did not emerge as an independent predictor of longitudinal progression in most adult cohorts once adjusted analyses were performed· Sex distribution differed between WCH and comparator groups in some cohorts (for example, a higher proportion of men among WCH participants in Ugajin(35)), but sex was generally handled as an adjustment covariate rather than identified as an independent effect modifier of progression risk· Body mass index was consistently higher among individuals with WCH than normotensive comparators at baseline (Chung(17)) and was retained as an independent predictor of new-onset SH in multivariable models (Mancia(8)), yet did not predict progression in the pediatric cohort of Miyashita(25), where baseline BMI z-score and obesity status were not significant· Taken together, these findings indicate that baseline blood pressure level, particularly out-of-office blood pressure, is the most robust and reproducible predictor of progression from WCH to SH across settings, whereas age, sex, and body mass index show more setting- and population-specific effects that are less consistently replicated across studies.

Meta analysis results

Overall pooled risk (event-based meta-analysis)

A total of 15 studies (8, 9, 16-24, 28, 31, 33, 35)comprising 8,297 participants (2,456 with WCH and 5,841 normotensive controls) were included in the pooled analysis. White-coat hypertension was associated with a significantly increased risk of progression to SH compared with normotensive individuals (RR = 2.52, 95% CI: 1.93–3.29; $p < 0.001$). Considerable between-study heterogeneity was observed ($I^2 = 85\%$), that was best removed by exclusion of Mancia (with organ damage)(23) **(Figure 2A)**. No evidence of publication bias was detected based on funnel plot inspection or Egger's regression test (intercept = 1.20, 95% CI: −1.16 to 3.55; $p = 0.336$).

Generic inverse variance analysis (Risk Ratio)

A total of 4 studies (22, 24, 31, 33)were pooled using the generic inverse variance method. The analysis demonstrated that WCH was associated with a significantly increased risk of progression to SH compared with normotensive controls (RR = 2.83, 95% CI: 2.37–3.38; $p < 0.001$). A fixed-effect model was applied, and no statistical heterogeneity was observed ($I^2 = 0\%$; Q $p = 0.88$), **(Figure 2B)**. Funnel plot assessment and Egger's regression test showed no evidence of publication bias (intercept = 0.70, 95% CI: −0.23 to 1.63; $p = 0.237$).

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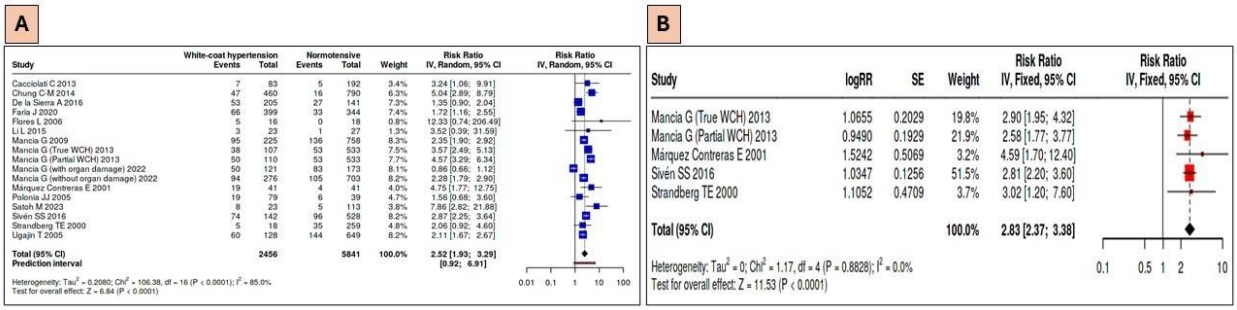


Figure 2: A) Forest plot of the pooled risk ratio comparing the risk of progression to sustained hypertension in individuals with white-coat hypertension versus normotensive controls. B) Forest plot of the generic inverse variance meta-analysis of adjusted risk ratios for the association between white-coat hypertension and progression to sustained hypertension.

Generic inverse variance analysis (Odds Ratio)

A total of 5 studies (8, 16, 21, 23, 35)were included in the generic inverse variance analysis of adjusted ORs. White-coat hypertension was associated with significantly higher odds of developing SH than normotensive controls (OR = 2.60, 95% CI: 2.13–3.17; p < 0. 001). A fixed-effect model was used, and no heterogeneity was detected (I^2 = 0%; Q p = 0.62), **(Figure 3A)**. There was also no evidence of publication bias according to funnel plot inspection and Egger's regression test (intercept = 0.31, 95% CI: −1.75 to 2.37; p = 0.783).

Generic inverse variance analysis (Hazard Ratio)

A total of 2 studies (27, 32)were pooled in the generic inverse variance analysis of adjusted HRs. White-coat hypertension was associated with a significantly increased hazard of progression to SH compared with normotensive individuals (HR = 1.69, 95% CI: 1.35–2.12; p < 0. 001). A fixed-effect model was used, and no heterogeneity was observed (I^2 = 0%; Q p = 0.39)**(Figure 3B)**.

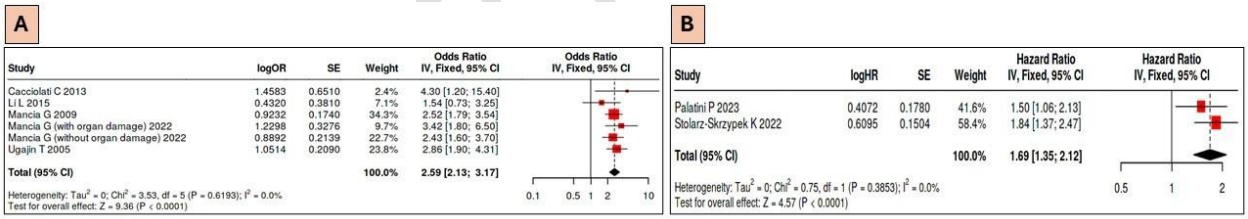


Figure 3: A) Forest plot of the generic inverse variance meta-analysis of adjusted ORs for the association between white-coat hypertension and progression to sustained hypertension. B) Forest plot of the generic inverse variance meta-analysis of adjusted HRs for the association between white-coat hypertension and progression to sustained hypertension.

Risk of Bias assessment

Among the 24 included cohort studies, the overall methodological quality was generally good according to the QUIPS tool. Most large prospective cohorts were judged to have a low risk of bias, particularly in the domains of prognostic factor measurement, outcome measurement, and statistical analysis. Moderate risk of bias was primarily attributed to limited reporting of participant attrition, incomplete adjustment for potential confounders, and small sample sizes in several single-center studies. Two studies were judged to be at high risk of bias because of substantial concerns regarding confounding and limited statistical adjustment. No study was considered at high risk for outcome measurement, reflecting the objective ascertainment of sustained hypertension using standardized office and ambulatory blood pressure measurements**(Figures 4A and B).**

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Figure 4: A) Summary plot of the overall risk of bias across all included studies according to the Quality In Prognosis Studies (QUIPS) tool.B)Traffic-light plot of the risk of bias assessment of the included studies according QUIPS tool.

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Discussion

White-coat hypertension is not a benign office-only phenomenon, but a heterogeneous intermediate phenotype with a consistent tendency to progress toward SH over time (32, 37, 38). This interpretation is also consistent with the broader outcome literature, in which WCH generally carries lower risk than SH but often exceeds true normotension, particularly in untreated or higher-risk populations (6, 39, 40). Interpretation The observed association is most plausibly explained by WCH representing early blood pressure dysregulation rather than isolated measurement artifact (32, 37, 40). Longitudinal population data show that baseline WCH independently predicts later SH after adjustment for age, sex, body mass index, smoking, and alcohol intake (32, 37). The prognostic gradient appears to be driven more by baseline out-of office blood pressure than by office pressure alone, as increasing home blood pressure category predicts conversion and higher ambulatory or home systolic burden identifies those most likely to progress (37, 41, 42). This interpretation is biologically coherent because WCH clusters with metabolic and vascular abnormalities that are intermediate between normotension and SH. Population studies have linked WCH to impaired insulin sensitivity, higher glucose, increased heart rate, dyslipidemia, arterial stiffness, coronary calcium, and carotid atherosclerotic burden (43, 44). In children and adolescents, target-organ findings are less consistent, but left ventricular mass, carotid thickness, and endothelial function often appear intermediate between normal blood pressure and established hypertension (42). Heterogeneity The marked between-study heterogeneity is expected because WCH is definition-sensitive (45). Even modest changes in ambulatory thresholds alter prognosis: a stricter definition using 24-hour blood pressure below 125/75 mmHg identifies a low-risk group, whereas the broader threshold below 130/80 mmHg captures participants with higher long-term cardiovascular and mortality risk (45). Variation in whether treated individuals, masked hypertension in the reference group, or participants with prior organ damage are included further shifts apparent risk (45). Diagnostic modality is another major source of variation because ambulatory and home monitoring do not identify interchangeable phenotypes (21, 46). Home monitoring has high specificity but limited sensitivity for WCH relative to ambulatory monitoring, and disagreement between methods remains substantial even when both are protocolized. This supports interpreting home blood pressure-based and ambulatory blood pressure-based estimates separately rather than assuming equivalence (41, 46, 47).

Population Differences Population context also modifies prognosis. In untreated adults, excess cardiovascular risk is most apparent in older participants and those with higher baseline cardiovascular or kidney risk, whereas low-risk WCH often resembles matched normotension (6, 38). Age is especially important because the prevalence of WCH rises sharply across the life course, increasing from 2.2% in younger adults to 19.5% in those aged 70 years or older in participant-level analyses (40). The phenotype also differs by sex and clinical context. Female sex is a reproducible predictor in adult screening and population studies (48, 49), whereas adolescent cohorts have reported the opposite pattern, with higher odds in males and a positive association with body mass index (50). High-stress screening environments can greatly inflate apparent office hypertension, as shown by a medical personnel cohort in which 80% of those with elevated clinic blood pressure had WCH on subsequent home monitoring (48). Implications and Limitations These findings justify longitudinal surveillance rather than reassurance alone, because WCH is often unstable and may convert with time (38, 42). ABPM remains the preferred method for initial phenotype confirmation in untreated adults, while HBPM is useful for repeated long-term follow-up when applied with validated devices and standardized technique (33, 41, 47). Earlier diagnostic comparisons similarly support using home monitoring as a screening or complementary tool, with ambulatory monitoring reserved for confirmation when classification is uncertain (46, 51). Several limitations should be acknowledged here. First, part of the excess progression signal may reflect treatment initiation during follow-up, especially when drug-treated hypertension is incorporated into outcome definitions (32, 37). Second, reproducibility is incomplete, particularly in younger low-risk populations, indicating that a single baseline classification may misclassify transient white-coat responses (38). Third, emerging prediction models based on office blood pressure, body mass index, sex, cholesterol, homocysteine, and heart rate may improve triage, but they do not replace out of office confirmation (52). Overall, WCH is best framed as a heterogeneous precursor state whose progression risk depends on diagnostic definition, monitoring method, baseline out-of-office pressure, underlying cardiovascular risk, and duration of observation.

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Limitations

Several limitations should be acknowledged. First, the included evidence was derived exclusively from observational cohort studies, making the findings susceptible to residual confounding despite multivariable adjustment in many analyses. Second, heterogeneity across studies may be attributable to differences in follow-up duration, definitions of WCH and SH, ABPM protocols, and outcome ascertainment. Third, treatment initiation during follow-up may have influenced progression estimates, particularly in studies that incorporated drug-treated hypertension into the outcome definition. Finally, the reproducibility of WCH is imperfect, especially among younger and lower-risk individuals, and a single baseline assessment may misclassify transient white-coat responses.

Conclusion

White-coat hypertension is associated with a substantially increased risk of progression to SH compared with normotension. The primary pooled analysis demonstrated more than a twofold increased risk (RR = 2.52, 95% CI: 1.93–3.29; $p < 0.001$). This association remained significant after adjustment for potential confounders, with pooled RRs (RR = 2.83, 95% CI: 2.37–3.38; $p < 0.001$), ORs (OR = 2.60, 95% CI: 2.13–3.17; $p < 0.001$), and HRs (HR = 1.69, 95% CI: 1.35–2.12; $p < 0.001$). These findings indicate that WCH is not a benign condition and support regular out-of-office blood pressure monitoring and long-term follow-up to facilitate early detection of progression to SH.

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