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Cardiovascular-kidney-metabolic syndrome and reproductive factors in postmenopausal Chinese and United States women: a cross-sectional analysis of two national survey cohorts

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Abstract

Background

Whether female reproductive history is associated with cardiovascular-kidney-metabolic (CKM) syndrome staging and cardiometabolic multimorbidity, and whether such associations differ between populations, is unclear. We examined age at menarche, parity, and age at first birth in relation to these outcomes in two national cohorts of postmenopausal women in China and the United States.

Methods

We analyzed 3,876 women in China postmenopausal at the 2011 examination and 4,357 naturally postmenopausal United States women. Using harmonized definitions, including a modified CKM staging based on the American Heart Association framework, we estimated prevalence ratios (PRs) by modified Poisson regression for CKM stage ≥ 2 (primary), CKM stage ≥ 3, and cardiometabolic multimorbidity, and tested whether PRs differed between cohorts.

Results

Later menarche was associated with lower CKM stage ≥ 2 prevalence in both cohorts (China PR 0.985/year [95% CI 0.974–0.996]; United States 0.982 [0.969–0.995]), but survived correction in the United States only. Later age at first birth was associated with lower CKM stage ≥ 2 prevalence in the United States (0.991 [0.985–0.996]) but not in China (0.997 [0.992–1.003]). For multimorbidity, later menarche was associated with lower prevalence in the United States (0.919 [0.873–0.967], survived correction), whereas age at first birth showed only a nominal association in China (0.967 [0.940–0.994], not surviving correction). Parity was not associated with any outcome.

Conclusions

Later menarche was associated with lower CKM stage ≥ 2 prevalence in both cohorts, with similar magnitude, although this survived correction in the United States only; later age at first birth was associated with lower prevalence in the United States only. For multimorbidity, only later menarche in the United States survived correction. Parity was not associated with any outcome, and no cross-cohort difference survived correction. In these cross-sectional analyses, reproductive history appears to be a life-course marker of modest effect size, warranting prospective evaluation rather than causal or clinical use.

Background

Cardiovascular-kidney-metabolic (CKM) syndrome, formalized by the American Heart Association, describes the pathophysiological links among metabolic risk factors, chronic kidney disease, and cardiovascular disease [1, 2]. Its staging framework (stages 0 through 4) enables systematic risk stratification, and advanced stages carry substantially elevated mortality [3].

Postmenopausal women are at disproportionately elevated cardiometabolic risk. This is largely attributed to estrogen withdrawal, which accelerates dyslipidemia, insulin resistance, and central adiposity [4, 5]. Because reproductive events can shape lifetime hormonal exposure patterns, they may in turn influence cardiometabolic health in later life.

Female reproductive factors, including the timing of menarche, parity, and age at first birth, have been implicated in cardiovascular-metabolic outcomes. Earlier menarche has been associated with higher all-cause mortality [6], higher parity with cardiovascular disease [7], and younger age at first birth with elevated cardiovascular risk [8]. These associations often persist beyond traditional risk factors [9, 10]. Yet the available evidence rests almost entirely on single populations. Whether

these associations, and their magnitude within the integrated CKM framework, differ between populations with different reproductive patterns and health-system contexts remains unknown.

An association observed in a single country may reflect that country's particular socioeconomic, behavioral, or healthcare structure. This gap therefore warrants attention: only by comparing cohorts from different contexts can we determine whether these associations are generalizable. Comparing two national survey cohorts that differ in reproductive distributions, socioeconomic structure, and health systems allows the difference between their associations to be estimated directly [11]. We therefore evaluated, using harmonized definitions, the associations of age at menarche, parity, and age at first birth with three cardiometabolic outcomes among postmenopausal women in two national survey cohorts, one in China and one in the United States. The outcomes were CKM stage ≥ 2 (the primary outcome), CKM stage ≥ 3, and cardiometabolic multimorbidity, and we tested cross-cohort heterogeneity directly.

Methods

Study design and populations

This was a cross-population comparison of female reproductive history and cardiometabolic-kidney health in two national survey cohorts of postmenopausal women. The first cohort was drawn from the China Health and Retirement Longitudinal Study (CHARLS) [12], an ongoing survey of community-dwelling adults aged 45 years or older across 28 provinces; the baseline physical examination and venous blood biomarkers were obtained in 2011. Ages at menarche and menopause were self-reported in the health module of the main survey, and the most recent valid report across the 2011, 2013, 2015, and 2018 interviews was used. Parity was the number of biological live births recorded in the birth histories of the 2014 Life History Survey; for the 391 women without a usable birth history, it was taken from the household roster. Age at first birth was derived from the same birth histories (biological children only). Women were classified as postmenopausal when at least 12 months had elapsed since the last menstrual period. Because the biomarkers and outcomes were measured in 2011, the analytic sample was restricted to women whose recalled age at menopause was not later than their age at the 2011 examination, so that menopausal status was already attained when the outcomes were measured. Of the 9,228 women at baseline, we excluded those without a 2011 venous blood sample (2,884), those who were not postmenopausal or did not report an age at menopause (2,101), those without a recorded age at the 2011 examination (39), and those whose menopause occurred after the 2011 examination (328), leaving 3,876 women (Fig. 1). Estimates for this cohort were unweighted because the analytic sample did not correspond to the original sampling frame. The age at menopause came from the 2011 interview for 3,411 of these women and from a later interview for 465 (12.0%). For the 397 of them without a valid 2011 report, inclusion depended on participation in a later wave; for the remaining 68, a later report superseded a valid 2011 one.

Table 2
Cross-cohort prevalence ratios for reproductive exposures and cardiometabolic outcomes: China (CHARLS) versus United States (NHANES).

Outcome	Exposure	CHARLS PR (95% CI)	n	NHANES PR (95% CI)	n	Ratio of PRs (95% CI)	P for heterogeneity	FDR-adjusted q
Panel A. Prespecified multiplicity family: CKM stage ≥ 2 (primary outcome) and cardiometabolic multimorbidity								
CKM ≥ 2	Age at menarche (years)	0.985 [0.974, 0.996]	3449	0.982 [0.969, 0.995]	3786	0.997 [0.979, 1.015]	0.744	0.887
CKM ≥ 2	Parity (births, capped at 5)	0.996 [0.981, 1.012]	3864	0.985 [0.964, 1.006]	3379	0.989 [0.963, 1.015]	0.397	0.595
CKM ≥ 2	Age at first birth (years)	0.997 [0.992, 1.003]	3405	0.991 [0.985, 0.996]	2985	0.993 [0.985, 1.001]	0.104	0.220
CMM ≥ 2	Age at menarche (years)	0.976 [0.936, 1.017]	3362	0.919 [0.873, 0.967]	3786	0.942 [0.882, 1.005]	0.072	0.220
CMM ≥ 2	Parity (births, capped at 5)	1.004 [0.932, 1.081]	3757	1.012 [0.937, 1.092]	3379	1.008 [0.906, 1.121]	0.887	0.887
CMM ≥ 2	Age at first birth (years)	0.967 [0.940, 0.994]	3311	0.999 [0.970, 1.029]	2985	1.033 [0.993, 1.076]	0.110	0.220
Panel B. CKM stage ≥ 3 (secondary outcome, outside the multiplicity family)								
CKM ≥ 3	Age at menarche (years)	0.961 [0.927, 0.997]	3449	0.940 [0.901, 0.982]	3786	0.978 [0.924, 1.035]	0.445	–
CKM ≥ 3	Parity (births, capped at 5)	0.986 [0.914, 1.063]	3864	1.006 [0.938, 1.079]	3379	1.021 [0.921, 1.132]	0.697	–
CKM ≥ 3	Age at first birth (years)	0.975 [0.950, 1.0004]	3405	1.007 [0.983, 1.032]	2985	1.033 [0.997, 1.070]	0.074	–
Panel C. Categorical parity (reference = one birth; nulliparous women excluded)								
CKM ≥ 2	Parity 2 vs 1 birth	0.975 [0.896, 1.060]	3812	0.989 [0.915, 1.070]	3369	1.015 [0.905, 1.138]	0.803	–
CKM ≥ 2	Parity 3–4 vs 1 birth	0.960 [0.883, 1.044]	3812	0.983 [0.902, 1.071]	3369	1.023 [0.907, 1.154]	0.707	–
CKM ≥ 2	Parity ≥ 5 vs 1 birth	0.978 [0.897, 1.067]	3812	0.940 [0.860, 1.027]	3369	0.961 [0.849, 1.088]	0.528	–
CMM ≥ 2	Parity 2 vs 1 birth	1.133 [0.793, 1.618]	3707	1.103 [0.806, 1.508]	3369	0.973 [0.606, 1.564]	0.911	–
CMM ≥ 2	Parity 3–4 vs 1 birth	1.306 [0.896, 1.905]	3707	0.889 [0.628, 1.260]	3369	0.681 [0.407, 1.138]	0.142	–

Outcome	Exposure	CHARLS PR (95% CI)	n	NHANES PR (95% CI)	n	Ratio of PRs (95% CI)	P for heterogeneity	FDR-adjusted q
CMM ≥ 2	Parity ≥ 5 vs 1 birth	1.136 [0.763, 1.691]	3707	1.136 [0.826, 1.561]	3369	1.000 [0.601, 1.664]	> 0.99	–

Footnote 1. PR = prevalence ratio estimated by modified Poisson regression with robust variance. Model 1 covariates differed by cohort. NHANES: age, age², race/ethnicity, education, family income-to-poverty ratio, smoking, alcohol use, and survey cycle; CHARLS: age, age², urban/rural residence, education, marital status, smoking, and alcohol use. Each reproductive exposure was modeled separately. Estimates with a covariate set common to both cohorts are given in Additional file 1: Table S11.

Footnote 2. Ratio of PRs = United States PR divided by China PR (the exponentiated difference in log PRs), with its 95% CI; P for heterogeneity is from the two-sided Wald test of that difference, using the standard errors from each cohort's model.

Footnote 3. Panel C excludes nulliparous women owing to sparse cells and near-separation; the reference category is one birth.

Footnote 4. CHARLS sample: Chinese women who were already postmenopausal at the CHARLS 2011 examination (recalled age at menopause not later than age at that examination); age is age at the 2011 examination and variances are county-level cluster-robust. NHANES sample: naturally postmenopausal women in the United States (NHANES 2007–2018, 6 cycles). Sample sizes vary by exposure (complete cases).

Footnote 5. CKM = cardiovascular-kidney-metabolic syndrome, staged with a modified staging based on the American Heart Association framework and applied identically in both cohorts (Additional file 1: Table S3). CMM = cardiometabolic multimorbidity, ≥ 2 of three self-reported cardiometabolic domains (cardiovascular, kidney, and metabolic).

Footnote 6. FDR-adjusted q = Benjamini-Hochberg false-discovery-rate q-value across the six cross-cohort heterogeneity tests in Panel A (Panels B and C are outside this family and are shown as '–'). Per-cohort prevalence ratios with nominal P values and q-values for the same family are reported in Additional file 1: Table S13.

The second cohort comprised naturally postmenopausal women aged 45 years or older from six consecutive cycles of the National Health and Nutrition Examination Survey (NHANES) of the United States, spanning 2007–2018. Women with surgical or other non-natural menopause were excluded, leaving 4,357 women for the primary analysis. The survey's complex design was applied by pooling mobile examination center weights across the six cycles (the two-year weight divided by six) with the corresponding strata and primary sampling units [13]. All NHANES estimates were survey-weighted to the United States population.

Reproductive exposures

Three reproductive exposures were harmonized across cohorts: age at menarche (years), parity, and age at first birth (years, among parous women; Additional file 1: Table S1). Because parity was higher in China than in the United States, it was modeled as the number of live births with five or more coded as five. This count was entered continuously in the primary specification (per additional live birth) and as categories (one, two, three to four, and five or more births). Nulliparous women were few and were excluded from the categorical analysis because of sparse cells and model near-separation; an alternative collapsed coding is reported in Additional file 1: Table S2.

Outcomes and cross-cohort harmonization

CKM syndrome was staged with a modified version of the framework of the 2023 American Heart Association presidential advisory and scientific statement [1, 2], which classifies individuals into stages 0 through 4; the criteria and their data sources in each cohort are detailed in Additional file 1: Table S3, and component prevalences in Table S4. Stage 1 denoted excess adiposity (body-mass index ≥ 25 kg/m² or waist circumference ≥ 88 cm, the same cutpoints in both cohorts) or prediabetes; stage 2, hypertension, diabetes, triglycerides ≥ 135 mg/dL, or an estimated glomerular filtration rate (eGFR) of 45–59 mL/min/1.73 m²; stage 3, an eGFR below 45 mL/min/1.73 m²; and stage 4, clinical cardiovascular disease (self-

reported heart disease or stroke) together with at least one stage 1–3 criterion. Diabetes was defined in both cohorts as HbA1c ≥ 6.5%, fasting glucose ≥ 126 mg/dL, or a self-reported diagnosis. Because the urinary albumin-to-creatinine ratio was unavailable in one cohort, kidney criteria used eGFR alone, computed with the 2021 race-free CKD-EPI creatinine equation [14], and no 10-year cardiovascular risk equation was used. Women with albuminuria alone may therefore have been assigned a lower stage, and stage 3 is a simplified phenotype. A component that was not measured was counted as not met. The primary outcome was CKM stage 2 or higher; CKM stage 3 or higher was a secondary outcome. Cardiometabolic multimorbidity was defined in both cohorts from self-reported physician diagnoses spanning at least two of three domains: cardiovascular (heart disease or stroke), kidney (kidney disease), and metabolic (hypertension, diabetes, or dyslipidemia). It was analyzed together with CKM stage ≥ 2 in the multiplicity-controlled family described below.

Covariates

The crude model (Model 0) was unadjusted. The primary adjusted model (Model 1) included, for NHANES, age, age-squared, race and ethnicity, education, the family income-to-poverty ratio, smoking, alcohol use, and survey cycle. For CHARLS, it included age at the 2011 examination, its square, and five covariates measured at the same 2011 wave and taken from the Harmonized CHARLS data file: urban or rural residence, educational attainment (no primary schooling; primary or middle school; high school or above), marital status (currently married or partnered versus not), ever smoking, and any alcohol use in the past year. Covariate versions carried in later waves were not used: their availability is determined by participation in those waves, so adjusting for them would both use information recorded after the outcome and restrict the complete-case sample to women who remained in the study years later. To avoid conditioning on potential mediators, body-mass index and counts of chronic disease were not included in the primary model. Because several adult covariates may lie downstream of reproductive history, Model 1 should be read as an adjusted association model rather than a minimally sufficient causal adjustment set. A conceptual directed acyclic graph (Additional file 2: Figure S1) summarizes the assumed structure. It shows the adjustment covariates in Model 1; upstream factors that were not adjusted directly (birth cohort, captured by the adjustment for age and, in the United States, survey cycle; early-life socioeconomic position, which was not included); and the adult adiposity and metabolic intermediates treated as mediators and therefore not adjusted. Each reproductive exposure was modeled separately; simultaneous (mutual) adjustment for the other reproductive variables was reserved for sensitivity analysis. Because the two Model 1 covariate sets differ, a common core model adjusted both cohorts for the same constructs only (age, age squared, education, smoking, and alcohol use) and was used to repeat the cross-cohort comparison. Age at menopause, hypertension treatment, and body-mass index were added to Model 1 as sensitivity layers in the United States cohort.

Statistical analysis

Prevalence ratios (PRs) with 95% confidence intervals, the primary effect measure given the high prevalence of the outcomes, were estimated by modified Poisson regression with robust variance [15]. For NHANES, models were fitted with survey-weighted generalized linear models. For CHARLS, models were fitted with Poisson generalized linear models and cluster-robust sandwich variance with counties as clusters (149 clusters, identified from the first five digits of the participant identifier). This accounts for within-county correlation arising from the multistage sampling design. The survey's own primary sampling units are villages and urban communities; clustering at that level instead (431 clusters) changed the standard errors by factors of 0.87 to 1.04, and a small-sample (CR2) correction at the county level gave similar intervals (Additional file 1: Table S5). In NHANES, triglycerides and fasting glucose were measured only in the morning fasting subsample. The primary analysis used the full examination sample with the mobile examination center weights and counted women without a measurement as not meeting the criterion. Of the 2,329 women without a triglyceride measurement, 459 were classified below stage 2 and would have moved to stage 2 or higher had their triglycerides been elevated. Two phenotypes address this dependency (Additional file 1: Table S6): a biochemical phenotype modeled in the fasting subsample with the fasting-subsample weights, and a phenotype without the fasting criteria on the full examination sample. Odds ratios from logistic regression and proportional-odds ratios for the ordinal CKM stage are reported in Additional file 1: Table S7. In all 18 primary

and secondary cells, the odds ratios agreed with the prevalence ratios in direction and in whether the 95% confidence interval excluded 1.0. Cross-population heterogeneity was assessed without individual-level pooling. For each exposure–outcome pair, the difference in log-prevalence-ratio coefficients between cohorts ($\Delta\beta = \beta_{NHANES} - \beta_{CHARLS}$) was tested with a two-sided Wald test, with the standard error of the difference taken as the square root of the summed cohort-specific squared standard errors. The ratio of prevalence ratios is reported as $\exp(\Delta\beta)$. Because the Model 1 covariate sets and the weighting differ between cohorts, this test compares two adjusted associations, each for its own target population, rather than testing effect modification by country. To address multiple comparisons within the prespecified primary set, the Benjamini-Hochberg false-discovery-rate procedure was applied separately to three families: the six primary association tests in each cohort (three exposures × CKM stage ≥ 2 and cardiometabolic multimorbidity) and the six cross-cohort heterogeneity tests. The q-values are reported alongside nominal p-values; the secondary CKM stage ≥ 3 outcome was not included in these families. Dose-response relations of age at menarche and age at first birth with CKM stage ≥ 2 were examined with restricted cubic splines with four knots at the 5th, 35th, 65th, and 95th percentiles of each cohort's distribution, with the cohort median as reference.

Sensitivity analyses

Sensitivity analyses comprised multiple imputation of missing covariates, E-values for unmeasured confounding [16], simultaneous adjustment for the other reproductive variables on a matched analytic subset, the common core covariate model, and alternative parity codings. Multiple imputation by chained equations (20 imputations) imputed only covariates, by predictive mean matching for continuous and logistic or polytomous regression for categorical variables. The imputation model included all Model 1 covariates, the three exposures, the two primary outcomes and, in NHANES, the survey weights, strata, and primary sampling units, which served as predictors but were not imputed. Each completed dataset was analyzed with the primary model, and estimates were combined on the log scale by Rubin's rules. Within the United States cohort, two richer CKM phenotypes, a biochemical phenotype in the fasting subsample and a phenotype without the fasting criteria on the full examination sample, added two stage 3 criteria: high predicted 10-year risk by the PREVENT equations [17] and the KDIGO grid of eGFR by albumin-to-creatinine ratio [18] (Additional file 1: Table S6). Within the Chinese cohort, a lenient-menopause layer added back the 328 women (7.8% of those otherwise eligible) whose recalled age at menopause was later than their age at the 2011 examination (Table S8). The age specification and the variance estimator were held fixed, so the two layers differ in menopause timing alone. A further layer reimposed two restrictions common in longitudinal analyses of CHARLS (a second venous blood sample in 2015, and the later-wave versions of the five covariates), singly and together (Table S9). Women with and without a usable 2014 birth history were compared on characteristics measured in 2011 (Table S10). For each sensitivity layer applied in both cohorts, the cross-cohort heterogeneity test was repeated within that layer, with the primary Model 1 carried as the reference row (Table S11). Benjamini-Hochberg q-values were computed within each layer for its six primary comparisons.

Ethical considerations

The CHARLS protocol was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015; biomarker collection IRB00001052-11014) and conducted in accordance with the Declaration of Helsinki. NHANES was approved by the National Center for Health Statistics Research Ethics Review Board (Protocols #2005-06, #2011-17, and #2018-01). All participants provided written informed consent. The present work was a secondary analysis of de-identified, publicly available data.

Reporting and software

The study was reported following the STROBE guideline for cross-sectional studies. Analyses were performed in R version 4.6.1 (R Foundation for Statistical Computing) with the survey, sandwich, mice, EValue, and MASS packages.

A generative artificial intelligence tool (Claude, Anthropic) was used solely to improve the language and readability of the manuscript text. It was not used for the study design, data curation, statistical analysis, interpretation of the results, or the generation of any scientific content, and all authors reviewed and take full responsibility for the final text.

Results

Participant characteristics differed in reproductive profile but showed similar cardiometabolic burden across cohorts

A total of 3,876 postmenopausal women from CHARLS (China; outcomes and examination in 2011, with reproductive exposures drawn from 2011–2018) and 4,357 naturally postmenopausal women from NHANES (the United States, 2007–2018) were included (Fig. 1). NHANES estimates were survey-weighted to the United States population (Additional file 1: Table S12 compares weighted and unweighted NHANES prevalences), whereas CHARLS estimates were unweighted.

Women in CHARLS were slightly younger at the 2011 examination (mean 61.8 [SD 8.2] vs 63.4 [SD 9.4] years) and had a higher reproductive burden than those in NHANES: mean parity was 3.1 (SD 1.3) versus 2.6 (SD 1.2) live births, and 22.5% versus 10.2% had five or more births. Age at menarche was later in CHARLS (16.3 [SD 2.0] vs 12.9 [SD 1.7] years). Mean age at first birth among parous women was similar (22.8 [SD 3.5] vs 23.5 [SD 5.1] years) (Table 1).

Table 1
Participant characteristics by cohort.

Characteristic	China (CHARLS)	United States (NHANES)
N (unweighted)	3876	4357
Age, years, mean (SD)	61.8 (8.2)	63.4 (9.4)
Education, China categories[a]		–
Below primary school completion	67.4%	–
Primary or middle school	27.0%	–
High school or above	5.6%	–
Education, United States categories[a]	–	
Less than high school	–	16.7%
High school or equivalent	–	53.8%
Some college or above	–	29.5%
Ever smoker, %	9.6%	40.2%
Current drinker, %[b]	12.0%	61.8%
Age at menarche, years, mean (SD)	16.3 (2.0)	12.9 (1.7)
Parity (capped at ≥ 5), mean (SD)	3.1 (1.3)	2.6 (1.2)
Parity category		
Parity 0	1.3%	0.3%
Parity 1	9.0%	18.1%
Parity 2	26.1%	36.1%
Parity 3–4	41.0%	35.3%
Parity ≥ 5	22.5%	10.2%
Age at first birth, years (parous only), mean (SD)	22.8 (3.5)	23.5 (5.1)
Urban residence, %[c]	37.0%	–
Race/ethnicity[c]	–	
Non-Hispanic White	–	73.3%
Non-Hispanic Black	–	9.3%
Mexican American	–	5.3%
Other Hispanic	–	5.0%
Other race	–	7.0%
Family income-to-poverty ratio, mean (SD)[c]	–	3.1 (1.6)
Currently married/partnered, %[c]	82.1%	–
BMI, kg/m², mean (SD)[d]	23.8 (4.0)	29.2 (7.2)

Characteristic	China (CHARLS)	United States (NHANES)
Waist circumference, cm, mean (SD)[d]	86.3 (10.4)	98.6 (15.6)
eGFR, mL/min/1.73 m², mean (SD)[d]	93.1 (14.0)	83.0 (19.1)
Hypertension, %[d]	57.3%	67.5%
Diabetes, %[d]	17.8%	19.0%
Clinical cardiovascular disease, %[d]	17.7%	11.1%
CKM stage distribution		
Stage 0	11.1%	6.2%
Stage 1	14.2%	17.7%
Stage 2	58.1%	62.6%
Stage 3	0.4%	2.4%
Stage 4	16.3%	11.0%
CKM stage ≥ 2, %	74.7%	76.0%
CKM stage ≥ 3, %	16.7%	13.4%
Cardiometabolic multimorbidity (≥ 2 domains), %	13.8%	12.6%
Values are mean (SD) or percentage, complete-case within each cohort (a woman missing a variable is excluded from that variable's denominator). China (CHARLS) values are unweighted; United States (NHANES) values are weighted with the examination weights pooled over six cycles. '–', not applicable (variable or category recorded in one cohort only).		
[a] Education was recorded in cohort-specific categories that are not directly comparable.		
[b] China, any alcohol use in the past year; United States, current drinker.		
[c] Model 1 covariate in one cohort only: residence and marital status in China; race and ethnicity and the income-to-poverty ratio in the United States.		
[d] Components of the modified CKM staging (definitions in Additional file 1: Table S3; prevalence of every component in Table S4). Hypertension and diabetes not recorded were counted as absent, as in the staging. eGFR, 2021 CKD-EPI creatinine equation.		
Missing values in China (n): smoking 12, alcohol 11, marital status 1, age at menarche 416, age at first birth (includes nulliparous women) 459, BMI 497, waist circumference (includes 61 values below 50 cm) 531, eGFR 70, clinical cardiovascular disease 19, cardiometabolic multimorbidity 117.		
Missing values in the United States (n): education 10, smoking 2, alcohol 10, income-to-poverty ratio 478, age at menarche 90, parity 527, age at first birth (includes nulliparous women) 957, BMI 66, waist circumference 240, eGFR 279.		
China (CHARLS): women who were postmenopausal at the 2011 examination (N = 3876). United States (NHANES): naturally postmenopausal women, 2007–2018 (N = 4357).		
BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CKM, cardiovascular-kidney-metabolic; eGFR, estimated glomerular filtration rate; SD, standard deviation.		

Cardiometabolic burden was comparable across cohorts. The prevalence of CKM stage ≥ 2 was 74.7% in CHARLS and 76.0% in NHANES; the corresponding prevalences were 16.7% and 13.4% for CKM stage ≥ 3, and 13.8% and 12.6% for cardiometabolic multimorbidity. Most women were at stage 2 in both cohorts (58.1% in CHARLS and 62.6% in NHANES; Additional file 2: Figure S2). Stage 3 was rare in China (0.4%, 14 women) compared with the United States (2.4%).

Consequently, of the 646 Chinese women at stage ≥ 3, only 14 were at stage 3 and the remaining 632 were at stage 4. Component prevalences are given in Additional file 1: Table S4.

Within the Chinese sample, the 391 women without a usable 2014 birth history were older (mean 63.5 vs 61.7 years), more often urban, and more often reported heart disease (21.6% vs 15.1%) than the remaining 3,485, but had a similar prevalence of CKM stage ≥ 2 (76.5% vs 74.5%; Additional file 1: Table S10). These differences suggest some selection bias, but the similar prevalence of CKM stage ≥ 2 argues against a major impact on the primary outcome.

Later menarche was associated with lower CKM stage ≥ 2 prevalence in both cohorts, and later first birth in the United States only

For CKM stage ≥ 2 (Model 1; Fig. 2, Table 2), later age at menarche was associated with a lower prevalence in both populations (China: PR 0.985 per year, 95% CI 0.974–0.996; United States: PR 0.982, 0.969–0.995). The two estimates were closely matched: the ratio of the United States to the China prevalence ratio was 0.997 (95% CI 0.979–1.015), the most closely matched pair of estimates in the study. Later age at first birth was associated with a lower prevalence in the United States (PR 0.991 per year, 0.985–0.996) but not in China (PR 0.997, 0.992–1.003), with a ratio of prevalence ratios of 0.993 (0.985–1.001). Parity was not associated with CKM stage ≥ 2 in either cohort (China: PR 0.996 per additional live birth, 0.981–1.012; United States: PR 0.985, 0.964–1.006; ratio 0.989, 0.963–1.015). In cross-cohort comparisons, the confidence interval of the ratio of prevalence ratios included 1.0 for all three exposures. After Benjamini-Hochberg correction within each cohort's six-test primary family (Additional file 1: Table S13), the associations of menarche ($q = 0.017$) and age at first birth ($q = 0.005$) with CKM stage ≥ 2 remained significant in the United States; in China, the menarche association was nominally significant but did not survive correction ($p = 0.010$, $q = 0.052$). Restricted cubic splines did not indicate nonlinearity (all tests of nonlinearity $p \geq 0.14$; Fig. 3). The overall spline test was significant for menarche in China ($p = 0.036$) and for age at first birth in the United States ($p = 0.002$), but not for menarche in the United States ($p = 0.055$) or age at first birth in China ($p = 0.221$). For menarche in the United States, the nonsignificant overall spline test likely reflects lower power of the flexible (spline) fit, since the linear Model 1 estimate was significant (PR 0.982, 0.969–0.995).

For cardiometabolic multimorbidity, menarche was associated in the United States and age at first birth in China, while parity was unrelated in both

For cardiometabolic multimorbidity (Fig. 2, Table 2), later age at menarche was associated with a lower prevalence in the United States (PR 0.919 per year, 0.873–0.967) and was in the same direction but not significant in China (PR 0.976, 0.936–1.017); the ratio of prevalence ratios was 0.942 (0.882–1.005). After within-cohort correction, this association remained significant in the United States ($q = 0.005$). Later age at first birth was associated with a lower prevalence in China (PR 0.967 per year, 0.940–0.994) but not in the United States (PR 0.999, 0.970–1.029), with a ratio of 1.033 (0.993–1.076); after within-cohort correction, this association in China was nominally significant but did not survive correction ($p = 0.017$, $q = 0.052$). Parity was not associated with multimorbidity in either cohort (China: PR 1.004 per additional live birth, 0.932–1.081; United States: PR 1.012, 0.937–1.092; ratio 1.008, 0.906–1.121). None of the six prespecified cross-cohort comparisons reached nominal significance (smallest Wald $p = 0.072$, for menarche and multimorbidity), and none was significant after Benjamini-Hochberg correction (smallest $q = 0.220$). Thus, the exposure associated with multimorbidity differed between cohorts: menarche in the United States and age at first birth in China, whereas parity was unrelated in both.

A categorical specification of parity yielded the same null result

When parity was modeled categorically, the results were unchanged (reference category: one birth; nulliparous women were excluded because of sparse numbers; Additional file 2: Figure S3B, Table 2). For multimorbidity in China, the prevalence ratios were 1.133 (0.793–1.618) for two births, 1.306 (0.896–1.905) for three to four births, and 1.136 (0.763–1.691) for five or more, with no apparent monotonic pattern (no formal trend test was performed); every confidence interval included 1.0. The corresponding United States estimates were 1.103 (0.806–1.508) for two births, 0.889 (0.628–1.260) for three to four births, and 1.136 (0.826–1.561) for five or more, and the between-cohort difference in each parity category did not reach

nominal significance (Wald p = 0.911, 0.142, and > 0.99). For CKM stage ≥ 2, categorical parity was likewise not associated in either cohort (Table 2).

Consistent with the primary outcome, later menarche was associated with a lower prevalence of the simplified advanced-CKM phenotype (stage ≥ 3) in both cohorts

For the simplified advanced-CKM phenotype (CKM stage ≥ 3; Table 2), later age at menarche was associated with a lower prevalence in both cohorts (China: PR 0.961, 0.927–0.997; United States: PR 0.940, 0.901–0.982), with a ratio of prevalence ratios of 0.978 (0.924–1.035). Neither parity (China: PR 0.986, 0.914–1.063; United States: PR 1.006, 0.938–1.079; ratio 1.021, 0.921–1.132) nor age at first birth (China: PR 0.975, 0.950–1.0004; United States: PR 1.007, 0.983–1.032; ratio 1.033, 0.997–1.070; Wald p = 0.074) was associated with CKM stage ≥ 3 in either cohort. Across all nine exposure–outcome pairs (three exposures × three outcomes), the two point estimates lay on the same side of 1.0 in seven, including all six primary pairs; the exceptions were parity and age at first birth with CKM stage ≥ 3, for which every confidence interval included 1.0.

Parity remained null across specifications, although longitudinal restrictions moved the estimate upward without reaching significance

Parity remained null across specifications. In China, parity was not associated with multimorbidity under any specification examined (Additional file 2: Figure S3A): unadjusted PR 0.944 (0.875–1.019), Model 1 PR 1.004 (0.932–1.081), Model 1 restricted to the mutual-adjustment subset PR 1.033 (0.940–1.136), mutually adjusted for the other reproductive exposures PR 0.991 (0.898–1.094), and under multiple imputation PR 1.004 (0.932–1.082). In the United States the unadjusted estimate (PR 1.098, 1.019–1.183) moved to the null after adjustment. Because the 2011-wave covariates were almost complete, multiple imputation and complete-case analysis were nearly identical in the Chinese cohort (largest relative change in any of the six primary prevalence ratios, 0.06%).

Longitudinal restrictions common in CHARLS analyses moved the Chinese parity estimate upward but not to significance (Additional file 1: Table S9): requiring a second venous blood sample in 2015 gave PR 1.058 (0.965–1.160), replacing the 2011-wave covariates with their later-wave versions gave PR 1.070 (0.967–1.185), and imposing both gave PR 1.073 (0.967–1.191). No configuration excluded 1.0. Both restrictions condition eligibility or the complete-case sample on survey participation after the outcome was measured, and neither was used in the primary analysis.

E-values for the associations whose confidence interval excluded 1.0 were modest (Additional file 1: Table S14). In China they were 1.14 (confidence limit 1.06) for menarche and CKM stage ≥ 2, 1.22 (1.08) for age at first birth and multimorbidity, and 1.24 (1.06) for menarche and CKM stage ≥ 3. In the United States they were 1.16 (1.07) and 1.11 (1.06) for menarche and age at first birth with CKM stage ≥ 2, 1.40 (1.22) for menarche and multimorbidity, and 1.32 (1.16) for menarche and CKM stage ≥ 3.

Other sensitivity analyses were consistent. Adding back the 328 women whose recalled age at menopause was later than their age at the 2011 examination (lenient-menopause layer, n = 4,204) changed no point estimate by more than 0.005 on the prevalence-ratio scale (Additional file 1: Table S8). Clustering the Chinese variance at the village or community level changed whether the confidence interval excluded 1.0 for one association, age at first birth with CKM stage ≥ 3 (0.975, 0.952–0.998; Additional file 1: Table S5). Odds ratios and ordinal models agreed with the prevalence ratios (Table S7), and the within-United-States phenotypes and covariate layers are reported in Table S6.

Repeating the cross-cohort comparison within each sensitivity layer applied to both cohorts (Additional file 1: Table S11), 3 of 36 comparisons had p < 0.05, where 1.8 would be expected under the null hypothesis if the tests were independent. Two were in the common core covariate model: age at first birth with CKM stage ≥ 2 (United States PR 0.989, China 0.998; ratio 0.991, 0.983–0.998; p = 0.018) and menarche with multimorbidity (0.909 versus 0.972; ratio 0.936, 0.876–0.999; p = 0.047). The third was menarche with multimorbidity under multiple imputation (ratio 0.934, 0.876–0.997; p = 0.039). None remained

significant after Benjamini-Hochberg correction within its layer (q = 0.108, 0.140, and 0.211), and in each case the association was stronger in the United States.

Discussion

In two national survey cohorts of postmenopausal women, one in China and one in the United States, we examined the associations of age at menarche, parity, and age at first birth with modified CKM syndrome staging and cardiometabolic multimorbidity. Later menarche was associated with a lower prevalence of CKM stage ≥ 2 in both populations, with nearly identical estimates (ratio of prevalence ratios 0.997, 95% CI 0.979–1.015). Later age at first birth was associated with a lower CKM stage ≥ 2 prevalence in the United States but not in China. Parity was not associated with any outcome in either cohort. For multimorbidity, the associated exposure differed between cohorts (menarche in the United States, age at first birth in China). None of the six prespecified cross-cohort comparisons reached nominal significance. When both cohorts were adjusted for the same covariates, two did, but neither survived correction. The absence of detected heterogeneity is not evidence of equivalence: no equivalence margin was specified, and the intervals for the ratios of prevalence ratios are compatible with modest differences. Nor does similarity between the two populations rule out biases that the surveys share, including recall of reproductive events decades later, selective survival to older age, and residual socioeconomic confounding.

The inverse association of later menarche with CKM stage ≥ 2, observed in both cohorts, is consistent with meta-analyses linking earlier menarche to higher risk of metabolic syndrome [19] and insulin resistance [20], and with cross-sectional analyses of CHARLS relating earlier menarche to higher blood pressure [21] and adverse lipid profiles [22]. The same direction and similar magnitude appeared in two populations with markedly different menarcheal-age distributions (mean 16.3 versus 12.9 years). The broadly linear pattern we observed contrasts with a meta-analysis of 29 studies in which the association was J-shaped and menarche at 16 years or older carried the highest cardiovascular risk [23]. A prospective study of 300,000 Chinese women suggests the shape may differ by birth cohort [24], although this does not reconcile the inverse direction we observed. Mendelian randomization evidence further suggests the menarche–cardiometabolic association is partly mediated by adiposity but retains an independent component [25]. The menarche association with CKM stage ≥ 2 survived false-discovery-rate correction in the United States but not in China, where it was nominally significant (q = 0.052).

Meta-analyses of parity and cardiovascular-metabolic disease [7, 26] and prior cohort evidence [27] report higher risk at higher parity. We did not reproduce this in either cohort: parity was unassociated with CKM stage ≥ 2, CKM stage ≥ 3, or multimorbidity in China and the United States alike, under both continuous and categorical specifications. In the Chinese cohort, reimposing two restrictions common in longitudinal analyses of CHARLS (a second blood sample four years later, or covariates recorded seven years after the outcome) moved the multimorbidity estimate upward (PR 1.058 to 1.073), although no configuration excluded 1.0. Both restrictions condition eligibility or the complete-case sample on survey participation after the outcome was measured, and both select on health. A British birth cohort similarly found no consistent relationship between number of children and coronary heart disease risk factors [28], and evidence linking higher parity to intermediate pathways is partial and largely attenuated after adjustment for cardiovascular risk factors [29]. We therefore read the parity result as a null with intervals wide enough to accommodate the modest effects reported elsewhere (for multimorbidity, upper confidence limits of 1.081 in China and 1.092 in the United States per additional live birth).

Later age at first birth was associated with a lower prevalence of CKM stage ≥ 2 in the United States but not in China (ratio of prevalence ratios 0.993, 0.985–1.001). This is the pair for which a cross-cohort difference is most plausible: the comparison was not significant under Model 1 (p = 0.104) but was nominally significant when both cohorts were adjusted for the same covariates (p = 0.018; q = 0.108 within that layer). The United States association accords with prospective evidence from the United Kingdom [8] and with a systematic review of age at first birth and later-life cardiovascular disease in which ten of the reviewed studies reported a positive association between early first birth and cardiovascular disease [30]. A weaker association in China could reflect greater attenuation by recall error: an error of the same absolute size dilutes an association more where the reported ages are less dispersed (SD 3.5 versus 5.1 years). It could also reflect differences in

what the age at first birth indexes socially in the two populations. Our data cannot distinguish these explanations. For multimorbidity the pattern was reversed, with an inverse association in China and none in the United States (ratio of prevalence ratios 1.033, 0.993–1.076).

Several features of the two settings may explain why the same reproductive exposures did not yield identical associations. First, the distributions of the exposures differed substantially: mean age at menarche was 16.3 years in China versus 12.9 years in the United States, and 22.5% of Chinese women had five or more births versus 10.2% of United States women. Where an exposure is shifted toward one end of its range, the same absolute change may map onto different underlying risk, and the shape of the association may differ even when the average direction is similar. Second, the two cohorts differ in the social meaning of reproductive timing. In China, earlier menarche and higher parity were common in older, rural, less educated generations, so these exposures may partly index socioeconomic disadvantage and limited access to care; in the United States, where menarche is earlier and parity lower, the same exposures may index different social and behavioral pathways. Third, the two health systems and treatment environments differ: widespread antihypertensive and lipid-lowering treatment in the United States may attenuate associations with measured risk factors, whereas lower treatment coverage in China may leave associations more visible. Fourth, the two cohorts differ in the covariates available and in the target populations: the United States estimates are survey-weighted to the national population, whereas the Chinese estimates are unweighted and restricted to women who were already postmenopausal in 2011, and surgical menopause could not be excluded in China. Finally, statistical power differed: the Chinese cohort had fewer women at advanced CKM stages (stage 3 was 0.4% versus 2.4% in the United States), so associations with stage ≥ 3 and cross-cohort comparisons involving it were less precisely estimated. These differences mean that the cross-cohort comparisons should be read as comparisons of two adjusted associations, each for its own target population, rather than as tests of effect modification by country. They also mean that the absence of a detected difference should not be interpreted as evidence that the underlying associations are identical.

Few studies have applied the CKM framework to reproductive history. A 2026 United States analysis linked pregnancy-related conditions to CKM stage ≥ 2 in younger women while finding grand multiparity not independently significant [31]. Our results complement that work by examining life-course exposures (menarche, parity, age at first birth) in postmenopausal women and by comparing the associations directly across two national survey cohorts. Two single-cohort analyses address the same question in each of our populations. In CHARLS, a cross-sectional study reported a nonlinear parity–CKM pattern with a nadir at two to three births, although neither flanking category differed significantly from the reference [32]; our null parity result is consistent with those category contrasts. In NHANES, age at first birth showed a U-shaped association with CKM syndrome, with the inverse association confined to ages below 24 years [33]; our spline analysis did not reproduce that curvature, possibly because we restricted to naturally postmenopausal women. Prospectively, reproductive factors have also been tied to cardiometabolic multimorbidity in the UK Biobank [34], and multi-cohort comparisons of reproductive factors and cardiometabolic outcomes have been reported [10, 35–38]. Because the staging definition, including an eGFR-based definition of advanced kidney involvement, was applied identically in both cohorts, CKM stage ≥ 3 could be analyzed as a secondary outcome. The menarche association was nominally significant in both cohorts at this stage as well, whereas neither parity nor age at first birth was associated with it in either cohort.

The study drew on two large, independent national survey cohorts (survey-weighted for the United States and unweighted for China, where the analytic subset no longer matched the original sampling frame), analyzed with harmonized exposure and outcome definitions and a common core covariate model, which allowed a formal cross-cohort heterogeneity test. Prevalence ratios were used throughout as directly interpretable effect measures, multiplicity was addressed by false-discovery-rate control, and a broad set of sensitivity analyses (multiple imputation, E-values, mutual adjustment on a matched subset, alternative parity codings, alternative CKM phenotypes, alternative variance estimators, and layers that reimpose restrictions common in longitudinal analyses) is reported in full.

This study has limitations. Both cohorts were cross-sectional, so causal inference is not possible. Reproductive history and several diagnoses were self-reported and subject to recall error [39]. In CHARLS, parity and age at first birth come from the

2014 Life History Survey, after the 2011 assessment of biomarkers and outcomes, and for 12.0% of the Chinese cohort the age at menopause that established eligibility came from an interview after 2011, so inclusion partly depended on survival to and participation in a later wave. The 391 women without a usable birth history, whose parity was taken from the household roster, were older, more often urban, and more often reported heart disease than the other women (Additional file 1: Table S10), and they do not contribute to the age-at-first-birth analyses. Eligibility required a 2011 venous blood sample, which is contemporaneous with the outcome but selects on attendance at the 2011 examination. Unlike the United States cohort, the Chinese cohort could not exclude surgical menopause, so the two target populations differ in this respect. The Model 1 covariate sets differed between cohorts: race and ethnicity, the family income-to-poverty ratio, and survey cycle were included only in the NHANES model, and urban or rural residence and marital status only in the CHARLS model. In the common core covariate model, which used the same covariates in both cohorts, two of the six comparisons were nominally significant, neither after correction, and both indicated a stronger association in the United States. The harmonized CKM stage ≥ 3 outcome was a simplified phenotype lacking albuminuria and risk-equation inputs. Its composition also differed between cohorts under common thresholds: in China it was almost entirely stage 4 (clinical cardiovascular disease), whereas the stage-3-only fraction was several times larger in the United States (0.4% versus 2.4%; Additional file 2: Figure S2). E-values indicated that the associations were vulnerable to moderate unmeasured confounding [16]. Several reproductive factors (breastfeeding, pregnancy complications, and contraceptive and hormone use) were not available in both cohorts. Finally, the associations were small on the absolute scale. Against a CKM stage ≥ 2 prevalence of about 75% in both cohorts, each additional year of later menarche corresponded to roughly one fewer affected woman per 100, and each additional year of later age at first birth to well under one.

Conclusions

Across two national survey cohorts of postmenopausal women, later menarche was associated with a lower prevalence of CKM stage ≥ 2 in both China and the United States, with estimates of similar size; only the United States estimate remained significant after false-discovery-rate correction. Later age at first birth was associated with CKM stage ≥ 2 in the United States only. Parity was not associated with cardiometabolic burden in either cohort. No cross-population difference survived correction for multiple testing. Reproductive history is a routinely available life-course marker; the effect sizes are modest, and prospective evaluation is warranted before clinical application.

Abbreviations

CHARLS
China Health and Retirement Longitudinal Study
CI
confidence interval
CKD
chronic kidney disease
CMM
cardiometabolic multimorbidity
CKD-EPI
Chronic Kidney Disease Epidemiology Collaboration
CKM
cardiovascular-kidney-metabolic
eGFR
estimated glomerular filtration rate
HbA1c
glycated hemoglobin
KDIGO

Kidney Disease:Improving Global Outcomes
NHANES
National Health and Nutrition Examination Survey
PR
prevalence ratio
SD
standard deviation
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology.

Declarations

Ethics approval and consent to participate

The CHARLS protocol was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015; biomarker collection IRB00001052-11014) and was conducted in accordance with the Declaration of Helsinki. NHANES was approved by the National Center for Health Statistics Research Ethics Review Board (Protocols #2005-06, #2011-17, and #2018-01). All participants of both surveys provided written informed consent. The present work was a secondary analysis of de-identified, publicly available data and did not require additional ethical approval.

Consent for publication

Not applicable. This study contains no data from any individual person in any form.

Competing interests

The authors declare that they have no competing interests.

Authors' information

Not applicable.

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Author Contribution

Chujie Chen, Yaqing Wen and Weiyue Huang contributed equally to this work and share first authorship. Zhen Zhang and Xiahong Lin are co-corresponding authors. Zhen Zhang, Chujie Chen and Xiahong Lin conceived and designed the study. Chujie Chen, Yaqing Wen, Weiyue Huang and Xinwei Huang curated the data and performed the cross-cohort harmonization. Chujie Chen and Zhen Zhang performed the statistical analysis. Weiyue Huang, Lili Yang and Xiahong Lin conducted the investigation. Yaqing Wen contributed the endocrinological interpretation of the results. Chujie Chen, Yaqing Wen and Zhen Zhang wrote the original draft. Zhen Zhang and Xiahong Lin supervised the study. All authors interpreted the results, critically revised the manuscript, and read and approved the final manuscript.

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Data Availability

The datasets analyzed during the current study are available in the China Health and Retirement Longitudinal Study repository, http://charls.pku.edu.cn, and in the National Health and Nutrition Examination Survey repository of the National Center for Health Statistics, United States Centers for Disease Control and Prevention, https://www.cdc.gov/nchs/nhanes. Both are de-identified, publicly available secondary data obtainable on registration. The analysis code supporting the conclusions of this article is available from the corresponding author on reasonable request.

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Figures

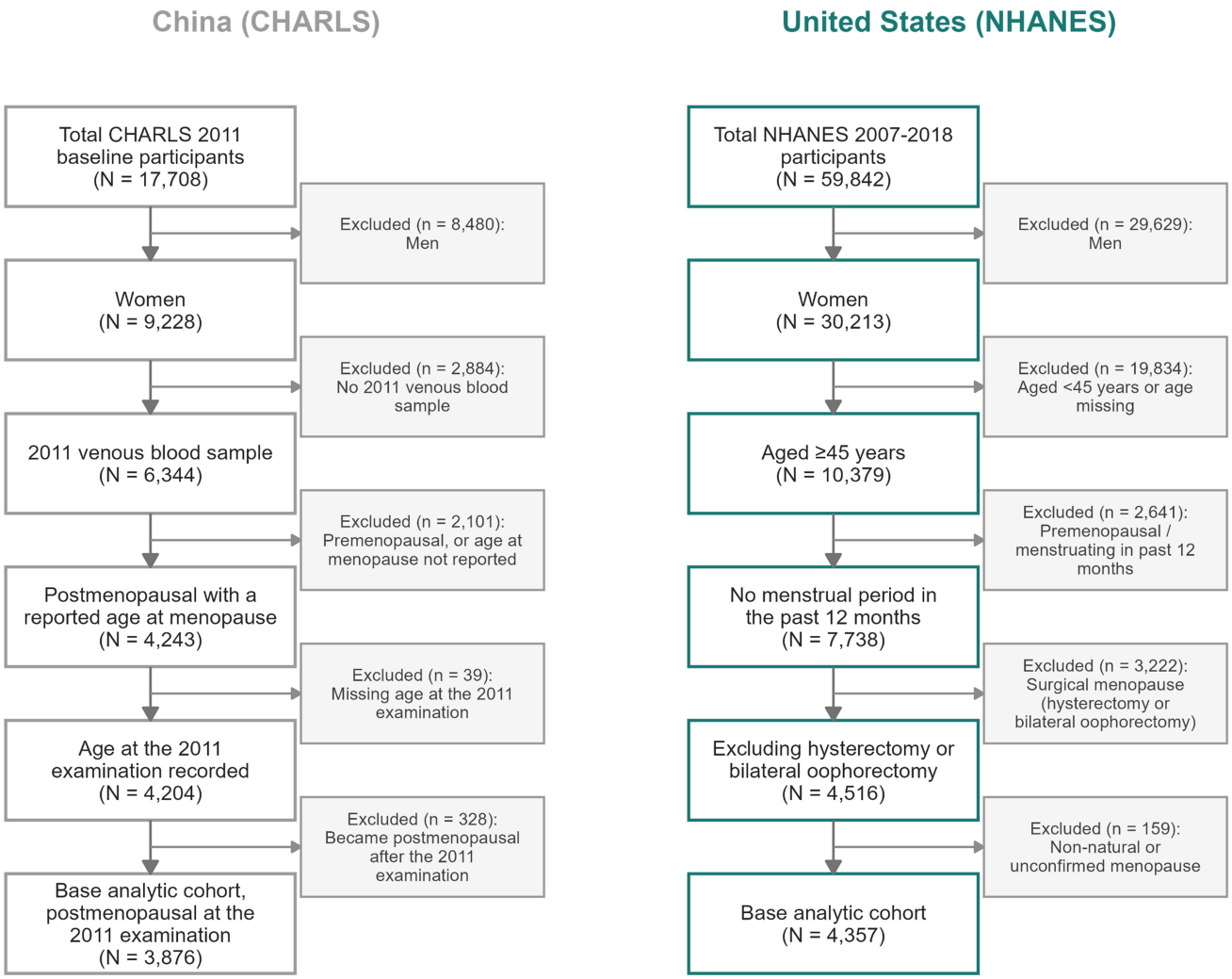


Figure 1

Participant selection. Two-cohort flow of participant selection with sequential exclusions. For the United States (NHANES, 2007–2018), the derivation proceeded from all participants through sex, age, menstrual status, and surgical- and non-natural-menopause exclusions to the analytic sample of 4,357 naturally postmenopausal women. For China (CHARLS), the derivation proceeded from the 17,708 participants of the 2011 baseline through sex (9,228 women), availability of a 2011 venous blood sample (6,344), postmenopausal status with a reported age at menopause (4,243), and a recorded age at the 2011 examination (4,204), to women already postmenopausal at the 2011 examination, giving the analytic sample of 3,876 women. Ages at menarche and menopause in CHARLS were self-reported in the main-survey interviews; parity and age at first birth were taken from the birth histories of the 2014 Life History Survey (parity from the household roster for the 391 women without a usable birth history). Postmenopausal status was defined as self-reported cessation of menstruation for ≥ 12 months; surgical menopause could not be excluded in the Chinese cohort. Model-specific complete-case sample sizes differed by exposure and covariate availability and are shown in Table 2.

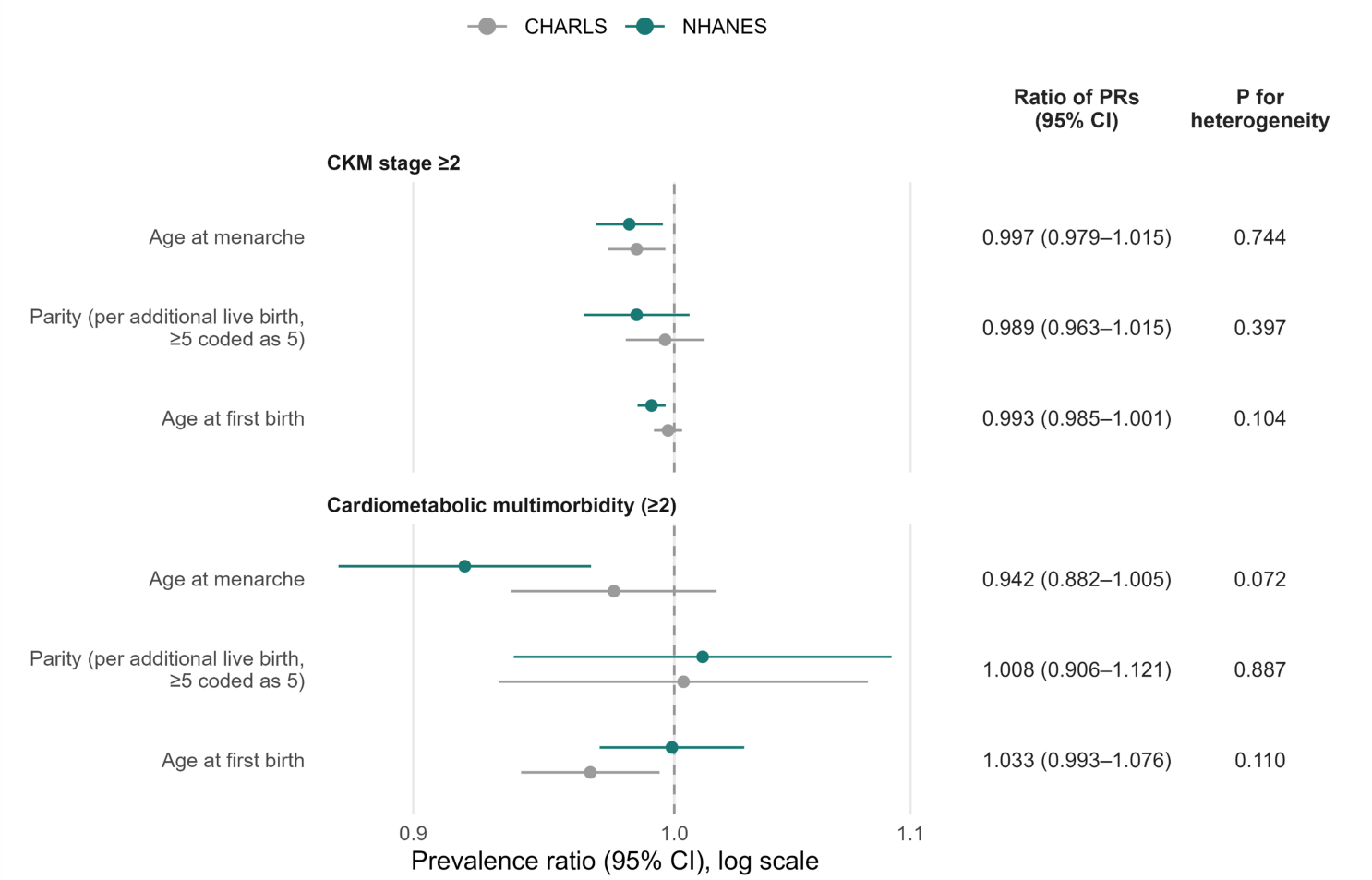


Figure 2

Cross-cohort prevalence ratios for reproductive exposures and cardiometabolic outcomes.

Prevalence ratios (95% confidence intervals) from modified Poisson regression (Model 1) for age at menarche (per year), parity (per additional live birth, with five or more births coded as five), and age at first birth (per year), in relation to CKM stage ≥2 and cardiometabolic multimorbidity, in China (CHARLS) and the United States (NHANES). Model 1 covariates differed by cohort (NHANES: age, age², race/ethnicity, education, family income-to-poverty ratio, smoking, alcohol use, and survey cycle; CHARLS: age, age², urban/rural residence, education, marital status, smoking, and alcohol use). The two rightmost columns show the ratio of the United States to the China prevalence ratio (95% confidence interval) and the P value of the Wald test of their difference. NHANES estimates are survey-weighted; CHARLS estimates are unweighted. Sample sizes: CHARLS n = 3,876; NHANES n = 4,357 (complete cases vary by exposure; see Table 2). The dashed vertical line marks the null (prevalence ratio = 1.0). CKM, cardiovascular-kidney-metabolic; CHARLS, China Health and Retirement Longitudinal Study; NHANES, National Health and Nutrition Examination Survey.

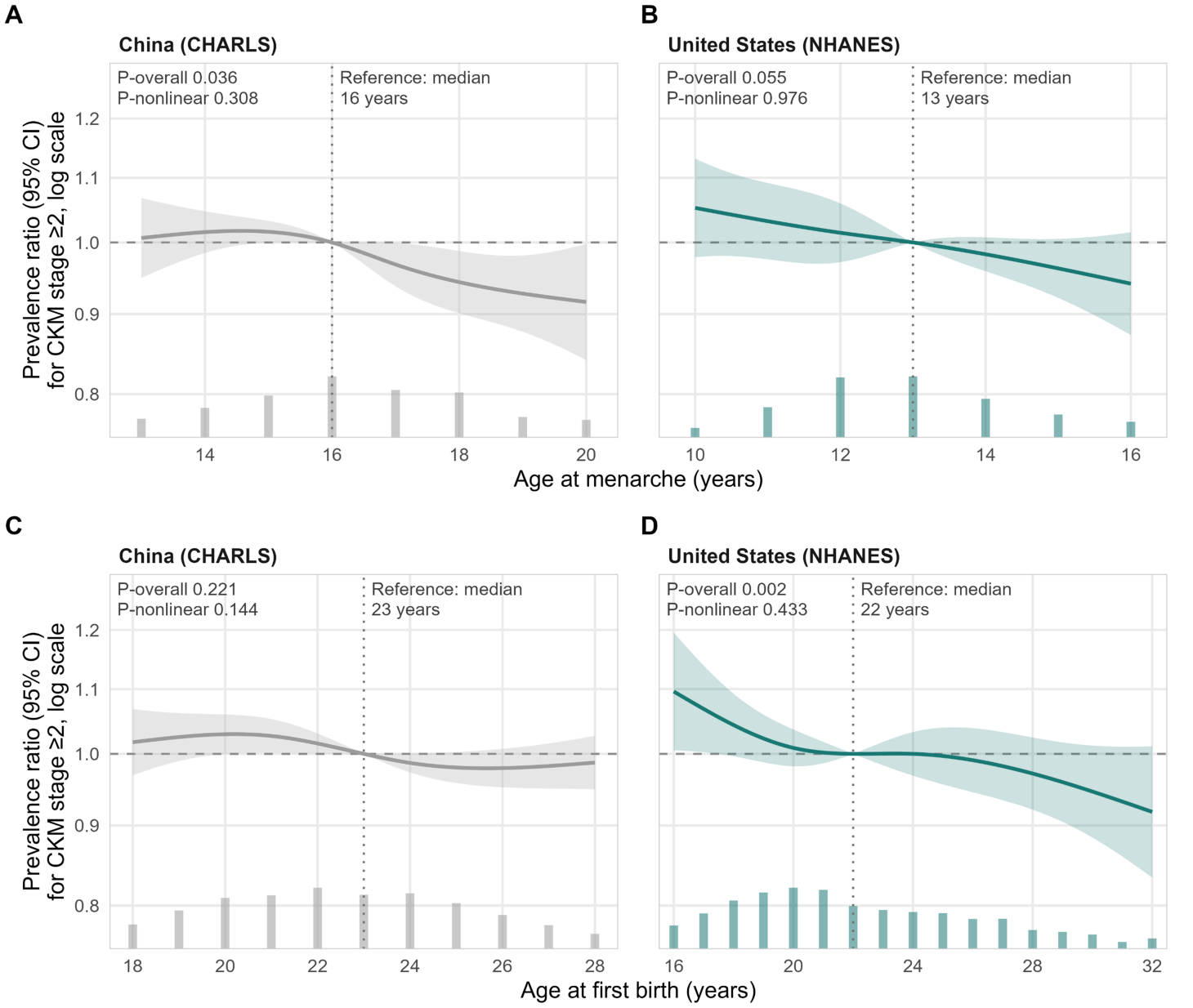


Figure 3

Dose-response splines for age at menarche and age at first birth with CKM stage ≥2.

Adjusted prevalence ratios (Model 1) with 95% confidence bands, on a logarithmic scale, for age at menarche in China (CHARLS; A) and the United States (NHANES; B) and for age at first birth in China (C) and the United States (D), relative to the cohort median (dotted vertical line: menarche 16 years in China and 13 years in the United States; age at first birth 23 years in China and 22 years in the United States). The restricted cubic splines had four knots at the 5th, 35th, 65th, and 95th percentiles (menarche 13, 16, 17, and 20 years in China and 10, 12, 13, and 16 years in the United States; age at first birth 18, 21, 24, and 28 years in China and 16, 20, 24, and 32 years in the United States). The spikes along the bottom of each panel show the distribution of the exposure (rug plot). P-overall and P-nonlinear are Wald tests for the overall spline and for nonlinearity, respectively. NHANES estimates are survey-weighted; CHARLS estimates are unweighted. Sample sizes: CHARLS n = 3,876; NHANES n = 4,357 (complete cases vary by exposure; see Table 2). The dashed horizontal line marks the null (prevalence ratio = 1.0). Confidence bands in the sparse tails should be interpreted with caution. CKM, cardiovascular-

kidney-metabolic; CHARLS, China Health and Retirement Longitudinal Study; NHANES, National Health and Nutrition Examination Survey.

Supplementary Files

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