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# Sonographic fatty liver and current gallstones among normal-weight adults at a Chinese health-check center: a cross-sectional study of 162,312 participants

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## Abstract

# Background

Sonographic fatty liver and gallstones share metabolic correlates, but contemporaneous organ-local estimates on both relative and absolute scales remain limited among normal-weight Chinese adults. We evaluated whether sonographic fatty liver was associated with current gallstones in this population.

# Methods

Project source documentation described health-check records collected from January 2020 through April 2025 at a tertiary hospital in Wenzhou, China. We linked examination-level records to raw item-level ultrasound reports and selected one index examination per identity-linked adult. Organ-local rules classified fatty liver and current gallstones from abdominal ultrasound reports; post-cholecystectomy, nonvisualized, ambiguous, conflicting, and inadequately visualized gallbladders without definite current-stone evidence were excluded. Normal weight was defined as body mass index (BMI) 18.5 to < 24.0 kg/m². Modified Poisson regression with robust variance estimated prevalence ratios (PRs), adjusting for age, sex, and within-range BMI.

# Results

Among 162,312 normal-weight adults, 30,458 (18.8%) had fatty liver and 6,702 (4.1%) had current gallstones. Observed gallstone prevalence was 6.5% with fatty liver and 3.6% without fatty liver. The adjusted PR was 1.20 (95% confidence interval [CI] 1.13–1.26). Covariate-standardized prevalence was 4.70% with fatty liver and 3.93% without fatty liver, an absolute difference of 0.77 percentage points (95% CI 0.54–1.01). There was no evidence of multiplicative interaction by age group (P = 0.168) or sex (P = 0.974). Across sensitivity analyses, adjusted PRs ranged from 1.15 to 1.24.

# Conclusions

Within the normal BMI range, sonographic fatty liver co-occurred with a modestly higher prevalence of current gallstones. Because both findings are available from the same routine examination, the result is relevant to their joint interpretation when already reported; it does not justify additional imaging and does not establish temporal order, causality, or future gallstone risk.

## Background

Gallstones are common worldwide and are often detected incidentally during abdominal ultrasonography. A recent systematic review of 115 studies estimated a pooled global prevalence of 6.1%, with substantial variation by age, sex, and region [1]. Gallstone formation reflects interacting

metabolic, biliary, genetic, and environmental factors [2]. In a nationwide Chinese health-screening study, gallbladder stones were the most frequent anatomic subtype and their prevalence increased markedly with age [3]. These features make routinely collected health-check data useful for studying how gallstones co-occur with other sonographic abnormalities.

Fatty liver and gallstones share correlates such as adiposity, dyslipidemia, altered glucose metabolism, and insulin resistance. A meta-analysis of 12 observational studies reported an association between gallstone disease and nonalcoholic fatty liver disease [4], and large cohort studies subsequently reported longitudinal associations in Korean [5] and Chinese [6] populations. However, terminology and estimands differ across those studies, while relative estimates alone do not convey the absolute difference in prevalence between contemporaneous ultrasound phenotypes.

Normal body weight does not exclude hepatic steatosis or metabolic heterogeneity. Nonobese and lean fatty-liver phenotypes are particularly relevant in Asian populations [7, 8]. A recent Korean health-screening study of 265,353 adults reported that fatty liver was associated with gallstones among nonobese and lean participants [7]. More recent US cross-sectional analyses reported associations using metabolic dysfunction-associated steatotic liver disease, controlled attenuation parameter-defined fatty liver, or the hepatic steatosis index [9–11]. However, these studies used self-reported physician-diagnosed gallstone history and/or composite steatosis definitions and did not target contemporaneous organ-local ultrasound findings in normal-weight Chinese adults. Important gaps remain: absolute prevalence differences are seldom standardized, repeated examinations may be mixed across time, and broad text searches can misclassify renal or bile-duct stones as gallbladder stones.

We therefore conducted a measurement-focused replication and extension by rebuilding an examination-consistent cohort with one selected examination per identity-linked adult and re-extracted organ-local ultrasound labels de novo. Our primary objective was to estimate the cross-sectional association between sonographic fatty liver and current gallstones among adults with normal weight by Chinese BMI criteria. We also quantified covariate-standardized absolute prevalence differences, examined age and sex heterogeneity, and tested robustness to index-examination selection, ultrasound-report restrictions, BMI source, and alternative normal-weight definitions.

## Methods

# 3.1 Study design and setting

This cross-sectional study used routine health-check data from the health examination center of Wenzhou People's Hospital, a tertiary hospital in Wenzhou, China. The integrated examination-level database contained 1,720,871 records, and the raw item-level table contained 136,258,384 result rows. All analyses were restricted to records made available in this fixed deidentified extract. Project source documentation recorded data collection from January 2020 through April 2025. The deidentified analytic extract did not retain calendar examination dates; consequently, the exact source period could not be

reconstructed from the available fields, and year-specific or longitudinal analyses were not possible. The study was reported with reference to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) extension [12, 13]. Patients and the public were not involved in the study design, analysis, or reporting.

## 3.2 Data sources, identity linkage, and index examination

Demographic, anthropometric, blood-pressure, and laboratory fields were drawn from the integrated health-check database. Hepatobiliary ultrasound reports and C-reactive protein (CRP) results were re-extracted from the raw item-level table using health-check identifiers. Personal identifiers were used only within the local linkage process and were not exported to analysis files.

Repeated examinations were linked conservatively. A Chinese resident identity number was accepted only after format, checksum, date-of-birth, and sex checks, then immediately converted to a Secure Hash Algorithm 256-bit (SHA-256) digest derived using a separately held linkage key. Records without a valid identity number were linked only through a unique name-sex-date-of-birth mapping; ambiguous records remained separate. One examination per linked adult was selected by a deterministic pseudo-random SHA-256 ranking independent of exposure, outcome, and laboratory completeness. Full linkage rules and quality counts are in Additional file 1.

## 3.3 Study population

Eligible records belonged to adults aged 18–100 years with valid sex and an eligible hepatobiliary ultrasound report. After index selection, we required an assessable liver parenchymal description and an observable current gallbladder. We excluded explicit post-cholecystectomy status, nonvisualized gallbladders, inadequately visualized gallbladders without definite current-stone evidence, ambiguous suspected stones, sludge, or debris without definite stones, and conflicting liver or gallbladder reports. The primary population comprised adults with BMI 18.5 to < 24.0 kg/m², the normal-weight range proposed by the Working Group on Obesity in China [14].

No a priori sample-size calculation was performed because the analysis used all eligible records in the fixed source extract; statistical precision was summarized using 95% confidence intervals.

## 3.4 Ultrasound exposure and outcome

The exposure was sonographic fatty liver. A report was positive when it contained a non-negated explicit diagnosis or a characteristic liver-parenchymal pattern, including diffusely increased or fine dense echogenicity with posterior attenuation or reduced vascular conspicuity. Names of quantitative measurement fields, including B-mode Ratio or an ultrasound-guided attenuation parameter (UGAP) 'fatty liver index', were not treated as diagnoses without a narrative diagnosis or characteristic parenchymal pattern; no device-specific index threshold was applied. A negative label required an assessable liver parenchymal description and no positive pattern. We use the term sonographic fatty liver rather than nonalcoholic fatty liver disease (NAFLD) or metabolic dysfunction-associated steatotic

liver disease (MASLD) because alcohol intake, viral hepatitis, medication exposure, and other etiologic exclusions were unavailable. Conventional ultrasound is well validated for moderate-to-severe steatosis, while performance for mild steatosis is less certain [15].

The outcome was current gallstones in an observable gallbladder. Positive evidence included a non-negated current stone term in the organ-local gallbladder section, a mobile echogenic focus or an echogenic focus with acoustic shadowing, or a wall-echo-shadow (WES) or packed-stone pattern. Organ boundaries prevented renal, intrahepatic-duct, or common-bile-duct findings from establishing gallbladder observability or current gallstones. Reports stating that the gallbladder was not visualized or was absent were unobservable; poorly visualized reports were unclassifiable unless they contained definite current stone evidence. Historical or postoperative stone terms alone were not treated as current gallstones. Tentative current-stone wording such as 'cannot be excluded' was retained as uncertain. Negated stones, fixed comet-tail artifacts, and isolated sludge were not classified as positive. When multiple eligible reports existed within an examination, evidence was aggregated separately for liver and gallbladder outcomes. Definite positive and negative evidence for the same outcome, and post-cholecystectomy status combined with current gallbladder evidence, were treated as conflicts and set to unclassifiable. Otherwise, definite positive evidence took precedence over tentative wording, and tentative wording precluded classification as negative. Report counts and conflicts were audited before cohort construction.

Rule implementation passed 33 fixed report-level regression tests and 12 fixed report-to-examination aggregation tests; scenarios and aggregation audits are reported in Additional file 1. These software tests verified implementation consistency but did not constitute independent clinician validation of report-text classification or rereading of source ultrasound images.

## 3.5 Body mass index and supporting covariates

BMI was taken from the reported examination value when available and otherwise calculated as measured weight in kilograms divided by measured height in meters squared. Implausible age, anthropometric, blood-pressure, and laboratory values were set to missing using predefined physiologic ranges detailed in Additional file 1. Age, sex, and continuous within-range BMI were the primary adjustment variables.

Supporting complete-case analyses additionally considered systolic and diastolic blood pressure, glycated hemoglobin, log-transformed triglycerides, high-density lipoprotein cholesterol, and uric acid. CRP was accepted only when the analyte name identified CRP or high-sensitivity CRP and the source unit was mg/L; high-sensitivity CRP was preferred when duplicate assay types were present. CRP entered supporting models as log(CRP + 0.1).

## 3.6 Statistical analysis

Characteristics were summarized as median [interquartile range] or number (percentage). Because current gallstones were not treated as a rare outcome, modified Poisson regression with the

heteroskedasticity-consistent HC0 sandwich variance estimator estimated prevalence ratios (PRs) and 95% confidence intervals (CIs) [16]. Model 0 was unadjusted; Model 1 adjusted for sex and age represented by a cubic B-spline basis with five degrees of freedom; and the primary Model 2 additionally adjusted for continuous BMI within the normal range.

Age, sex, and BMI were selected a priori because they strongly structure the prevalence of both ultrasound findings. Model 2 therefore estimates a conditional descriptive association comparing adults at the same age, sex, and position within the normal BMI range; it was not intended to estimate a causal total effect. Metabolic biomarkers were reserved for supporting analyses because their temporal relations to both cross-sectional findings were uncertain and their availability depended strongly on health-check package selection.

Model-based marginal prediction from Model 2 standardized gallstone prevalence to the observed age, sex, and BMI distribution under fatty-liver present and absent scenarios. Delta-method standard errors used the robust covariance matrix. Subgroup models were fitted by age (18–39, 40–59, and ≥ 60 years) and sex, with joint Wald tests for multiplicative interaction on the PR scale.

For context across the BMI distribution, we estimated observed prevalence in 2-kg/m² bands and an age- and sex-adjusted fatty-liver-by-BMI spline interaction. The displayed curve was limited to the overlapping 2.5th-97.5th percentile BMI support of both exposure groups (20.56–28.20 kg/m²). We also tested the interaction within BMI 18.5 to < 28.0 kg/m² to reduce sparse-tail influence.

Sensitivity analyses used the most metabolically complete examination, participants with only one eligible examination, examinations with one extracted ultrasound report, exclusion of globally poor-quality reports, relaxed liver-assessability criteria while retaining the primary current-gallbladder rules, reported BMI only, BMI recalculated from height and weight for everyone, an Asian lean threshold of BMI 18.5 to < 23.0 kg/m² to facilitate comparison with studies using that threshold, and the World Health Organization (WHO) normal-weight threshold of BMI 18.5 to < 25.0 kg/m². Ten alternative SHA-256 rankings assessed index-selection variability. A full-BMI inverse-probability-weighted analysis explored sensitivity to BMI availability [17]. A separate normal-weight analysis used stabilized inverse-probability weights for having fully assessable organ-local exposure and outcome labels among adults without post-cholecystectomy status; the observation model included nonlinear age, sex, and BMI. In a distinct exploratory analysis, we added adults with an unconflicted explicit post-cholecystectomy statement and defined an expanded outcome as either current gallstones or post-cholecystectomy status. Because the surgical indication was unavailable, this outcome was not interpreted as gallstone disease.

Additional post hoc diagnostics varied age and BMI functional forms, fitted log-binomial and logistic-standardization alternatives, tested a within-range fatty-liver-by-BMI spline interaction, and checked design rank, common support, and predicted probabilities. Full specifications are in Additional file 1; these checks were not used to select or redefine the primary model.

The primary model had complete age, sex, BMI, exposure, and outcome by design. Supporting laboratory models used complete cases without imputation because laboratory missingness was extensive and reflected health-check package selection. Tests were two-sided with alpha = 0.05; secondary interaction and sensitivity analyses were interpreted as robustness and heterogeneity assessments rather than separate confirmatory claims. Analyses used Python 3.9.6, pandas 2.2.3, NumPy 2.0.2, SciPy 1.13.1, statsmodels 0.14.6, patsy 1.0.2, and Matplotlib 3.9.4.

## Results

# 4.1 Cohort derivation

Of 1,720,871 examination records, 780,622 had a retained organ-local hepatobiliary ultrasound report (45.4%) and 776,586 were valid adult examinations that could be linked conservatively. These represented 374,443 adults; 163,785 had more than one eligible examination (maximum 18). After deterministic pseudo-random index selection, 11,283 adults had at least one ultrasound exclusion, leaving 363,160 with an assessable liver and active gallbladder. BMI was available for 300,017 (82.6%), of whom 162,312 were normal weight and comprised the primary population (Fig. 1). In the primary population, 107,913 (66.5%) index examinations contributed one eligible ultrasound report and 54,399 (33.5%) contributed two or three reports (Supplementary Table S11).

# 4.2 Characteristics of normal-weight adults

Among 162,312 normal-weight adults, 30,458 (18.8%) had sonographic fatty liver and 6,702 (4.1%) had current gallstones. Participants with fatty liver were older than those without fatty liver (median 52 versus 39 years), more often male (56.6% versus 42.1%), and had a higher median BMI within the normal range (22.7 versus 21.4 kg/m²). Available blood pressure and metabolic laboratory values were less favorable in the fatty-liver group, although individual laboratory variables had approximately 58%-72% missingness (Table 1 and Supplementary Table S3 in Additional file 1).

Table 1
Characteristics of normal-weight adults by fatty-liver status

| Characteristic | Overall | No fatty liver | Fatty liver | Missing, n (%) |
|---|---|---|---|---|
| N | 162312 | 131854 | 30458 | NA |
| Age, years | 41.0 [30.0–55.0] | 39.0 [29.0–53.0] | 52.0 [38.0–62.0] | 0 (0.0%) |
| Male sex | 72740 (44.8%) | 55491 (42.1%) | 17249 (56.6%) | 0 (0.0%) |
| Age group: 18–39 years | 77146 (47.5%) | 68559 (52.0%) | 8587 (28.2%) | 0 (0.0%) |
| Age group: 40–59 years | 54347 (33.5%) | 42156 (32.0%) | 12191 (40.0%) | 0 (0.0%) |
| Age group: ≥60 years | 30819 (19.0%) | 21139 (16.0%) | 9680 (31.8%) | 0 (0.0%) |
| BMI, kg/m² | 21.7 [20.4–22.8] | 21.4 [20.1–22.6] | 22.7 [21.8–23.4] | 0 (0.0%) |
| Current gallstones | 6702 (4.1%) | 4726 (3.6%) | 1976 (6.5%) | 0 (0.0%) |
| Systolic blood pressure, mmHg | 120 [109–132] | 118 [108–130] | 127 [116–140] | 93 (0.1%) |
| Diastolic blood pressure, mmHg | 71 [64–79] | 70 [64–78] | 76 [69–84] | 79 (< 0.1%) |
| HbA1c, % | 5.1 [4.8–5.5] | 5.1 [4.8–5.4] | 5.5 [5.1–5.8] | 112362 (69.2%) |
| Triglycerides, mmol/L | 1.07 [0.76–1.57] | 1.00 [0.72–1.42] | 1.70 [1.19–2.43] | 100506 (61.9%) |
| HDL-C, mmol/L | 1.52 [1.28–1.78] | 1.54 [1.30–1.80] | 1.39 [1.19–1.63] | 100507 (61.9%) |
| LDL-C, mmol/L | 2.50 [2.10–2.97] | 2.45 [2.06–2.89] | 2.85 [2.42–3.36] | 100506 (61.9%) |
| Uric acid, μmol/L | 294 [237–359] | 285 [232–349] | 341 [282–404] | 98537 (60.7%) |
| ALT, U/L | 16.0 [12.0–24.0] | 15.0 [11.0–22.0] | 24.0 [17.0–35.0] | 94344 (58.1%) |
| GGT, U/L | 18.0 [13.0–28.0] | 17.0 [13.0–25.0] | 28.0 [19.0–46.0] | 98535 (60.7%) |
| CRP, mg/L | 0.5 [0.3–1.1] | 0.5 [0.3-1.0] | 0.9 [0.5–1.7] | 98579 (60.7%) |

Values are median [interquartile range] or n (%). Percentages use nonmissing denominators. No between-group P values are shown because Table 1 is descriptive and the large sample would make clinically trivial differences statistically significant. ALT, alanine aminotransferase; BMI, body mass index; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NA, not applicable.

# 4.3 Primary association and absolute prevalence

Observed gallstone prevalence was 6.49% (1,976/30,458) among adults with fatty liver and 3.58% (4,726/131,854) among those without fatty liver (Fig. 3A). The crude PR was 1.81 (95% CI 1.72–1.90), which decreased to 1.26 (95% CI 1.20–1.33) after age and sex adjustment. In the primary age-, sex-, and within-range-BMI-adjusted model, the PR was 1.20 (95% CI 1.13–1.26; P < 0.001) (Table 2; Fig. 3C).

Table 2
Relative and absolute association between fatty liver and current gallstones

| Estimand | Adjustment or contrast | N | Estimate (95% CI) | P value |
|---|---|---|---|---|
| PR, Model 0 | Crude | 162312 | 1.81 (1.72–1.90) | < 0.001 |
| PR, Model 1 | Age and sex adjusted | 162312 | 1.26 (1.20–1.33) | < 0.001 |
| PR, Model 2 | Age, sex, and within-range BMI | 162312 | 1.20 (1.13–1.26) | < 0.001 |
| Standardized prevalence: no fatty liver | Primary Model 2 | 162312 | 3.93% (3.82%-4.04%) | NA |
| Standardized prevalence: fatty liver | Primary Model 2 | 162312 | 4.70% (4.50%-4.91%) | NA |
| Standardized absolute difference | Fatty liver minus no fatty liver | 162312 | 0.77 percentage points (0.54–1.01) | < 0.001 |

PRs compare sonographic fatty liver with no fatty liver and were estimated by modified Poisson regression with robust variance. Model 2 standardized prevalence to the observed age, sex, and within-range BMI distribution; 95% CIs used the robust covariance matrix and delta method. The analysis included 6702 current gallstone cases. Age was modeled with a five-degree-of-freedom B-spline; BMI was continuous within 18.5 to < 24.0 kg/m². BMI, body mass index; CI, confidence interval; NA, not applicable; PR, prevalence ratio.

After standardization to the observed covariate distribution, estimated gallstone prevalence was 4.70% (95% CI 4.50%-4.91%) with fatty liver and 3.93% (95% CI 3.82%-4.04%) without fatty liver. The adjusted absolute difference was 0.77 percentage points (95% CI 0.54–1.01) (Table 2; Fig. 3B; Supplementary Table S4).

# 4.4 Age and sex subgroups

Adjusted PRs were 1.41 (95% CI 1.18–1.69) at ages 18–39 years, 1.21 (95% CI 1.10–1.32) at ages 40–59 years, and 1.17 (95% CI 1.09–1.26) at ages ≥ 60 years. Figure 2 shows the corresponding descriptive age-specific prevalence pattern. However, there was no evidence of multiplicative interaction by age group (P = 0.168) or by continuous age (P = 0.512). Estimates were similar in women (PR 1.22, 95% CI 1.13–1.30) and men (PR 1.19, 95% CI 1.10–1.29), with no evidence of multiplicative interaction by sex (P = 0.974) (Table 3; Figs. 2 and 4).

Table 3
Association within normal-weight subgroups

| Grouping | Level | No fatty liver, n/N (%) | Fatty liver, n/N (%) | Adjusted PR (95% CI) | P value | P interaction |
|---|---|---|---|---|---|---|
| Overall | All | 4726/131854 (3.6%) | 1976/30458 (6.5%) | 1.20 (1.13–1.26) | < 0.001 | |
| Age group | 18–39 | 870/68559 (1.3%) | 166/8587 (1.9%) | 1.41 (1.18–1.69) | < 0.001 | 0.168 |
| Age group | 40–59 | 1764/42156 (4.2%) | 664/12191 (5.4%) | 1.21 (1.10–1.32) | < 0.001 | |
| Age group | ≥ 60 | 2092/21139 (9.9%) | 1146/9680 (11.8%) | 1.17 (1.09–1.26) | < 0.001 | |
| Sex | Female | 2927/76363 (3.8%) | 1121/13209 (8.5%) | 1.22 (1.13–1.30) | < 0.001 | 0.974 |
| Sex | Male | 1799/55491 (3.2%) | 855/17249 (5.0%) | 1.19 (1.10–1.29) | < 0.001 | |

Overall and age-stratified models adjusted for age, sex, and continuous within-range BMI as applicable; sex-stratified models adjusted for nonlinear age and continuous BMI. Interaction P values are joint Wald tests from models containing the relevant product terms and therefore assess multiplicative interaction on the PR scale, not additive interaction. BMI, body mass index; CI, confidence interval; PR, prevalence ratio.

# 4.5 Context across BMI and robustness analyses

In 300,017 adults across the full BMI distribution, the age-, sex-, and BMI-adjusted PR was 1.14 (95% CI 1.10–1.18), and standardized prevalence differed by 0.64 percentage points (95% CI 0.47–0.82). The overall multiplicative fatty-liver-by-BMI spline interaction was significant ($P < 0.001$), but the interaction within BMI 18.5 to < 28.0 kg/m² was not ($P = 0.108$). Observed high-BMI patterns therefore were treated as contextual heterogeneity rather than evidence of a protective effect (Supplementary Figure S1; Supplementary Table S9).

Normal-weight sensitivity estimates were directionally consistent: adjusted PRs ranged from 1.15 to 1.24 across alternative index examinations, report restrictions, and label definitions. Restriction to the 107,913 adults with one eligible ultrasound report yielded a PR of 1.24 (95% CI 1.16–1.33). Recalculation of BMI from measured height and weight yielded a PR of 1.20 (95% CI 1.14–1.26), and the Asian lean definition yielded a PR of 1.23 (95% CI 1.15–1.31). The WHO normal-weight definition yielded a PR of 1.20 (95% CI 1.14–1.25). Across ten alternative SHA-256 index rankings, PRs ranged from 1.148 to 1.197, and every confidence interval excluded 1.0 (Supplementary Figures S2-S3; Supplementary Tables S6-S7).

Among 164,579 normal-weight, non-post-cholecystectomy candidates, 2,267 (1.38%) were excluded because organ-local exposure or outcome labels were not fully assessable. Those excluded were older than selected participants (mean 58.45 versus 43.51 years). Stabilized inverse-probability weighting yielded a PR of 1.196 (95% CI 1.134–1.261), compared with 1.197 (95% CI 1.135–1.262) without weighting. Weights ranged from 0.989 to 1.157, with an effective sample size of 162,279. The full-BMI analysis weighted for BMI availability also remained numerically unchanged (PR 1.14, 95% CI 1.10–1.18). These analyses supported robustness under the modeled observation assumptions but could not exclude selection through unmeasured health-check-package factors (Supplementary Table S10).

The exploratory expanded-outcome analysis added 1,917 normal-weight adults with unconflicted explicit post-cholecystectomy status. Among 164,229 adults, 8,619 had current gallstones or post-cholecystectomy status; the adjusted PR was 1.30 (95% CI 1.24–1.36). This broader endpoint was used only to assess robustness to exclusion of postoperative anatomy and was not treated as evidence of previous gallstone surgery (Supplementary Table S14).

In post hoc model-form checks, adjusted or standardized PRs ranged from 1.19 to 1.22, and standardized absolute differences ranged from 0.76 to 0.85 percentage points; every corresponding confidence interval excluded the null. All model-based predicted prevalences remained between 0 and 1, and there was no evidence of a statistical fatty-liver-by-BMI interaction on the multiplicative PR scale across BMI 18.5 to < 24.0 kg/m² (P = 0.422) (Supplementary Table S13).

In selected laboratory-complete subsets, associations remained positive after additional metabolic and CRP adjustment. Although individual model covariates were missing in up to 69% of normal-weight adults, only 38,407 (23.7%) and 37,071 (22.8%) had all variables required for the metabolic and CRP models, respectively. Because these complete-case subsets differed from the primary cohort, the estimates were considered supporting only and were not used to infer mediation or attenuation (Supplementary Tables S3 and S5).

# Discussion

In this large health-check study, sonographic fatty liver was associated with a modestly higher prevalence of current gallstones among 162,312 adults whose BMI was within the Chinese normal-weight range. The crude difference was substantial, but much of it reflected the older age and higher within-range BMI of participants with fatty liver. After adjustment, the relative prevalence was 20% higher and the standardized absolute difference was 0.77 percentage points. Presenting both scales is important: the association was statistically precise and stable across the conducted sensitivity analyses, but its absolute magnitude was modest.

Our estimate is consistent with, but not directly interchangeable with, earlier evidence. Jaruvongvanich et al. reported a pooled odds ratio of 1.55 across observational studies [4]. A 2024 multicenter Chinese health-check analysis and updated meta-analysis likewise reported positive associations in broader populations [18]. Kim et al. recently reported an adjusted odds ratio of 1.20 in a lean Korean subgroup

[7]. Recent United States cross-sectional studies also reported positive associations using MASLD, controlled attenuation parameter-defined fatty liver, or the hepatic steatosis index [9–11], but their smaller samples, self-reported gallstone history, and broad BMI ranges addressed different estimands. Rather than presenting the association as a new etiologic discovery, our study provides a high-precision Chinese replication and measurement-focused extension: it targets normal-weight adults, aligns exposure and outcome within the same index examination, applies organ-local report phenotyping, and reports directly interpretable PRs alongside a standardized absolute prevalence difference. The similarity of the point estimate to the Korean lean estimate provides external consistency, although differing definitions and covariates prevent formal equivalence.

The attenuation from a crude PR of 1.81 to an adjusted PR of 1.20 underscores the importance of age and BMI structure. Fatty liver in the normal-weight group was concentrated among older adults and at the upper end of the normal BMI range. Nevertheless, the remaining association was stable when BMI was derived entirely from height and weight and when the WHO threshold was used. Earlier Asian ultrasound studies reported a positive association among Chinese adults younger than 50 years [19] and an association with moderate-to-severe but not mild fatty liver in a Taiwanese population [20]. In our data, point estimates were numerically higher among adults aged 18–39 years, but neither the categorical nor continuous multiplicative interaction test supported heterogeneity on the PR scale. The data therefore do not justify labeling the younger subgroup as a distinct early-onset phenotype. The final organ-local extraction did not yield a clinically validated steatosis grade, so we did not evaluate a severity-response pattern.

Several biologic pathways could contribute to co-occurrence. Hepatic lipid handling, insulin resistance, biliary cholesterol supersaturation, and gallbladder motility are relevant to cholesterol-stone formation [2, 21]. A 2026 Chinese dynamic health-examination cohort of 6,308 adults linked higher controlled attenuation parameter values with incident gallstone disease [22], but it did not target normal-weight adults and addressed a longitudinal rather than contemporaneous estimand. Normal BMI also does not measure visceral adiposity, ectopic fat, diet, or genetic susceptibility. However, our data cannot establish which pathway explains the observed association. The supporting laboratory-complete models were selected subsets and should not be interpreted as mediation analyses.

The supplementary full-BMI analysis adds an important caution. Relative associations appeared to diminish toward the high-BMI tail, producing a significant interaction across the entire distribution, whereas the interaction was not significant within the Chinese nonobese range. Sparse exposure overlap, differential ultrasound sensitivity, health-check selection, and residual confounding may all influence tail behavior. We therefore do not interpret the observed high-BMI pattern as evidence that obesity protects against gallstones. Instead, it reinforces the value of a focused normal-weight estimand with adequate overlap.

From a public-health and health-screening perspective, normal weight does not preclude coexisting sonographic liver and gallbladder abnormalities. The result supports more integrated interpretation of

liver and gallbladder findings that are already available from the same routine abdominal examination. It does not, by itself, justify additional imaging. Normal BMI alone should not be treated as evidence against coexisting sonographic abnormalities. However, our cross-sectional result does not by itself support new screening intervals, treatment thresholds, or prediction of future stones.

Strengths include the large normal-weight sample, identity-aware handling of repeated examinations, exposure-outcome alignment within one index examination, conservative organ-local ultrasound coding, a transparent audit of report-to-examination aggregation, direct PR estimation, standardized absolute prevalence differences, and extensive sensitivity analyses. Selection-weighted analyses for BMI availability and ultrasound assessability produced nearly unchanged estimates under their modeled observation assumptions. The deterministic pseudo-random index design reduced preferential selection of metabolically complete or disease-positive visits, and ten alternative rankings quantified the resulting variability.

Several limitations require emphasis. First, the cross-sectional design precludes temporal or causal inference. Second, this was a single-center health-check population and may not represent the general Chinese population or patients seeking care. Eligibility also depended on an assessable hepatobiliary ultrasound examination and, for the primary population, available BMI; only 45.4% of source examination records had a retained organ-local ultrasound report, and BMI was available for 82.6% of adults with assessable liver and gallbladder labels. Health-check package selection may therefore have introduced additional selection bias. Weighting for BMI availability and ultrasound assessability produced nearly unchanged estimates under modeled observation assumptions, but could not address unmeasured reasons for package or imaging selection. Because normal-weight status defined the target population, the estimate describes association within that selected BMI range and should not be generalized outside it or interpreted as an effect of normal weight. Third, project source documentation recorded data collection from January 2020 through April 2025, but the deidentified extract lacked calendar dates; therefore, the exact study period could not be recovered from analytic fields, and temporal changes in equipment, reporting, or health-check packages could not be examined. Fourth, diagnoses were derived from report text rather than image rereading; ultrasound is operator dependent, and its validation is strongest for moderate-to-severe rather than mild steatosis [15]; independent clinician validation of the report-text labels was not available. Approximately one-third of the primary cohort had more than one eligible report; although contradictory evidence was excluded and restriction to single-report examinations produced a consistent estimate, report aggregation remains another potential source of classification error. The final organ-local extraction did not yield a clinically validated steatosis severity grade, precluding severity-response analysis. Because exposure and outcome labels came from the same report, sonographer- or report-level recording practices could also induce correlated misclassification; examiner identifiers were unavailable, so its direction and magnitude could not be quantified. Fifth, alcohol use, viral hepatitis, medications, diet, waist circumference, body composition, parity, menopausal status, estrogen exposure, and family history were unavailable. We therefore could not diagnose NAFLD/MASLD or fully address residual confounding. Sixth, stone size, number, symptoms, gallbladder function, and cholecystectomy indication were unavailable. Accordingly, the

expanded postoperative-status analysis was interpreted only as a robustness check, not as a gallstone-disease endpoint. Seventh, most laboratory variables had substantial package-related missingness, limiting extended adjustment. Finally, conservative identity linkage may leave some repeat examinations unlinked or, rarely, join records with matching demographics.

## Conclusions

Among normal-weight adults undergoing health checks in China, sonographic fatty liver co-occurred with a modestly higher prevalence of current gallstones after adjustment for age, sex, and within-range BMI. We found no statistical evidence that the association differed by age group or sex on the multiplicative PR scale, and the estimate was robust to alternative examination, ultrasound, BMI-source, and normal-weight definitions. These findings characterize the joint occurrence of liver and gallbladder findings already available from routine ultrasonography; prospective and independently validated studies are needed before causal, prognostic, or screening inferences.

## Abbreviations

AI
artificial intelligence
ALT
alanine aminotransferase
BMI
body mass index
CI
confidence interval
CRP
C-reactive protein
GGT
gamma-glutamyl transferase
HbA1c
glycated hemoglobin
HC0
heteroskedasticity-consistent sandwich variance estimator
HDL-C
high-density lipoprotein cholesterol
LDL-C
low-density lipoprotein cholesterol
MASLD
metabolic dysfunction-associated steatotic liver disease
NAFLD
nonalcoholic fatty liver disease

PR
prevalence ratio
RECORD
REporting of studies Conducted using Observational Routinely-collected health Data
SHA-256
Secure Hash Algorithm 256-bit
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
UGAP
ultrasound-guided attenuation parameter
WES
wall-echo-shadow
WHO
World Health Organization.

## Declarations

### Ethics approval and consent to participate

This retrospective study involved human participants and was approved by the Wenzhou People's Hospital Ethics Committee under the same institutional approval as the related study from this health-check database. The study was conducted in accordance with the ethical standards of the institution and the principles outlined in the Declaration of Helsinki (1964) and its subsequent amendments. All experimental protocols were approved by the Human Ethics Committee of Wenzhou People's Hospital. Written informed consent was waived by the Human Ethics Committee of Wenzhou People's Hospital because of the retrospective nature of the study.

### Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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# Author Contribution

JX contributed to study conception and design, data curation, statistical analysis, visualization, and drafting of the manuscript. SL and ML contributed to data curation, clinical interpretation, and manuscript review. YH contributed to study conception, supervision, clinical interpretation, and critical revision. All authors contributed to the article and approved the submitted version.

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# Data Availability

All data generated for this study are included in the article. The data sets generated during the current study are available from the corresponding author on reasonable request.

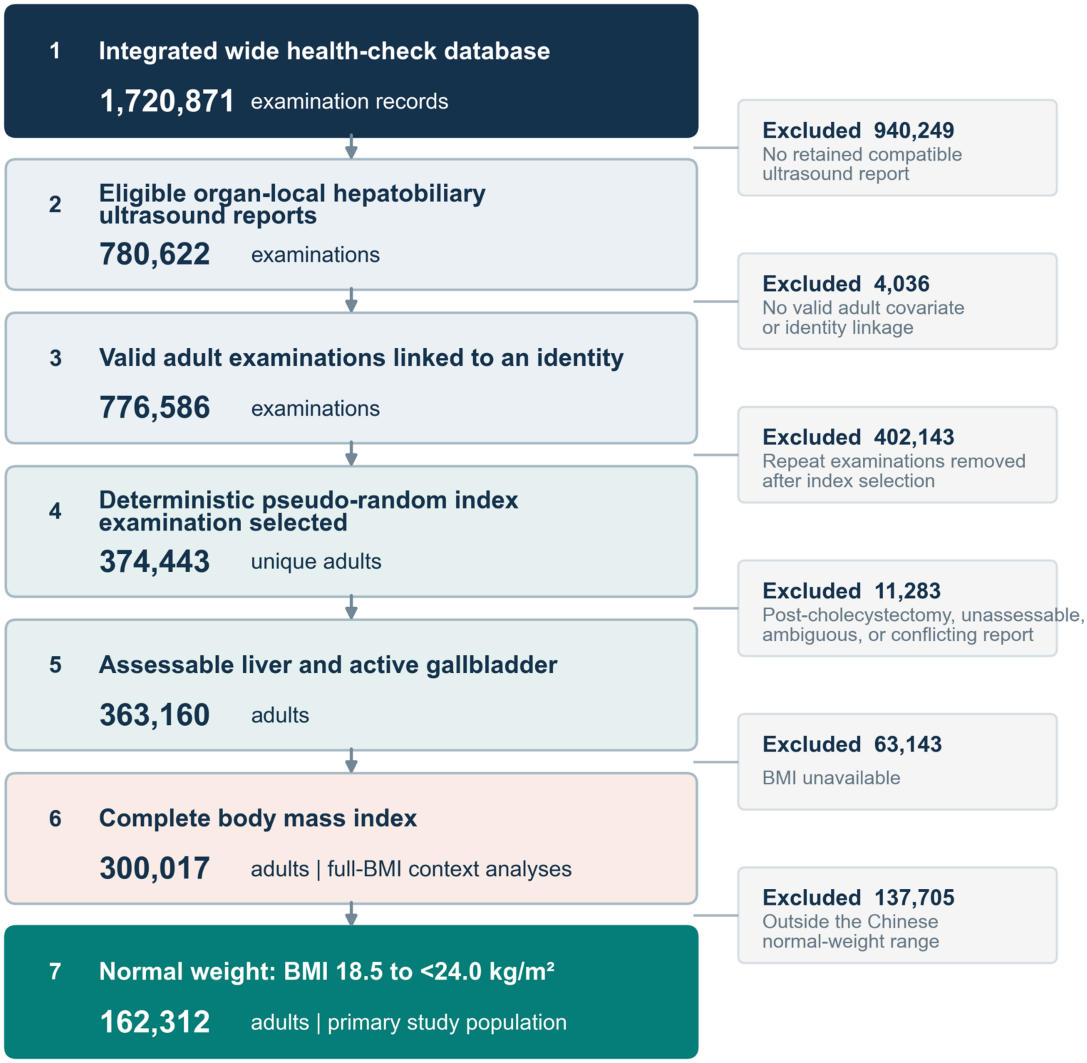
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# Figures




## Figure 1

**Derivation of the normal-weight study population.** Counts are examinations before and unique adults after index selection. One deterministic pseudo-random examination was retained per conservatively linked adult. Reasons for excluding 11,283 adults were post-cholecystectomy status; an unassessable liver or gallbladder; inadequate visualization without definite stones; ambiguous stones, sludge, or debris; or conflicting reports. BMI, body mass index.

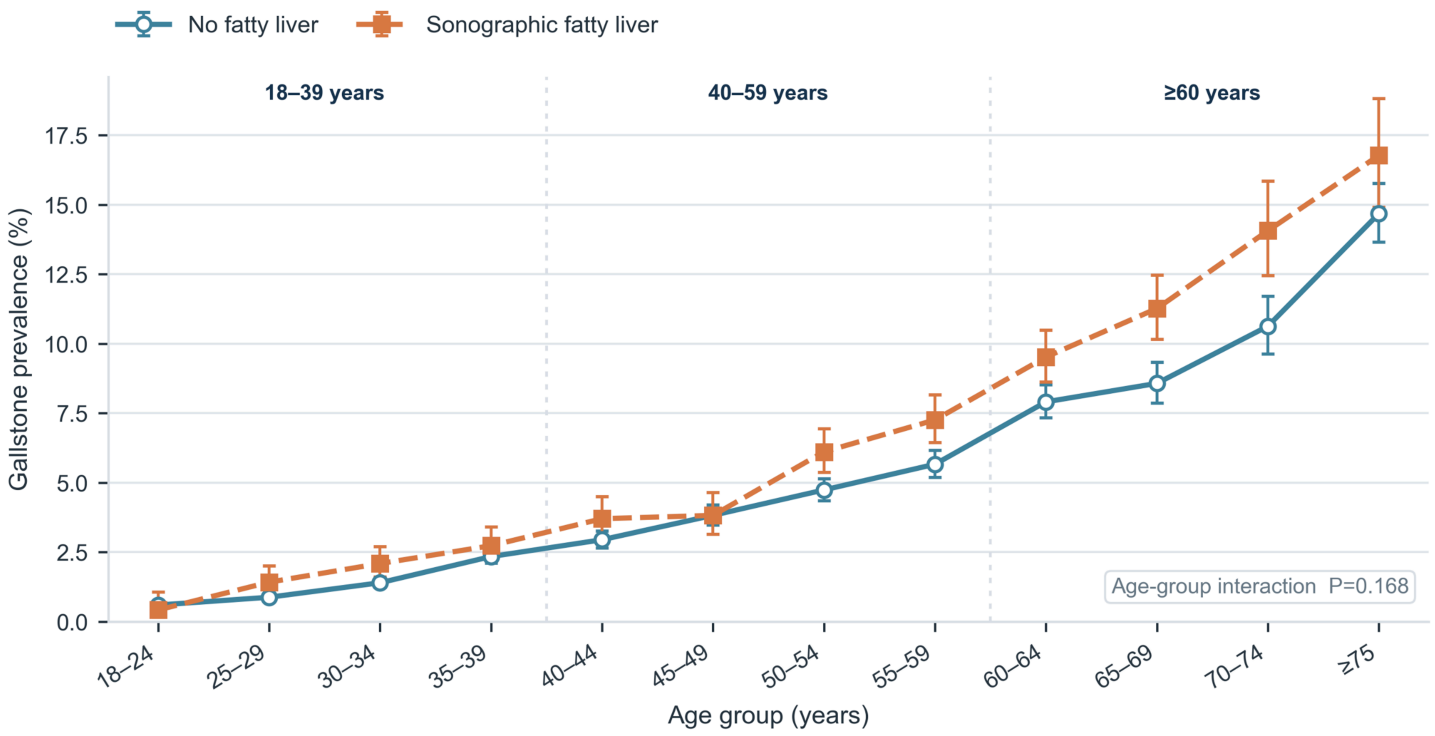
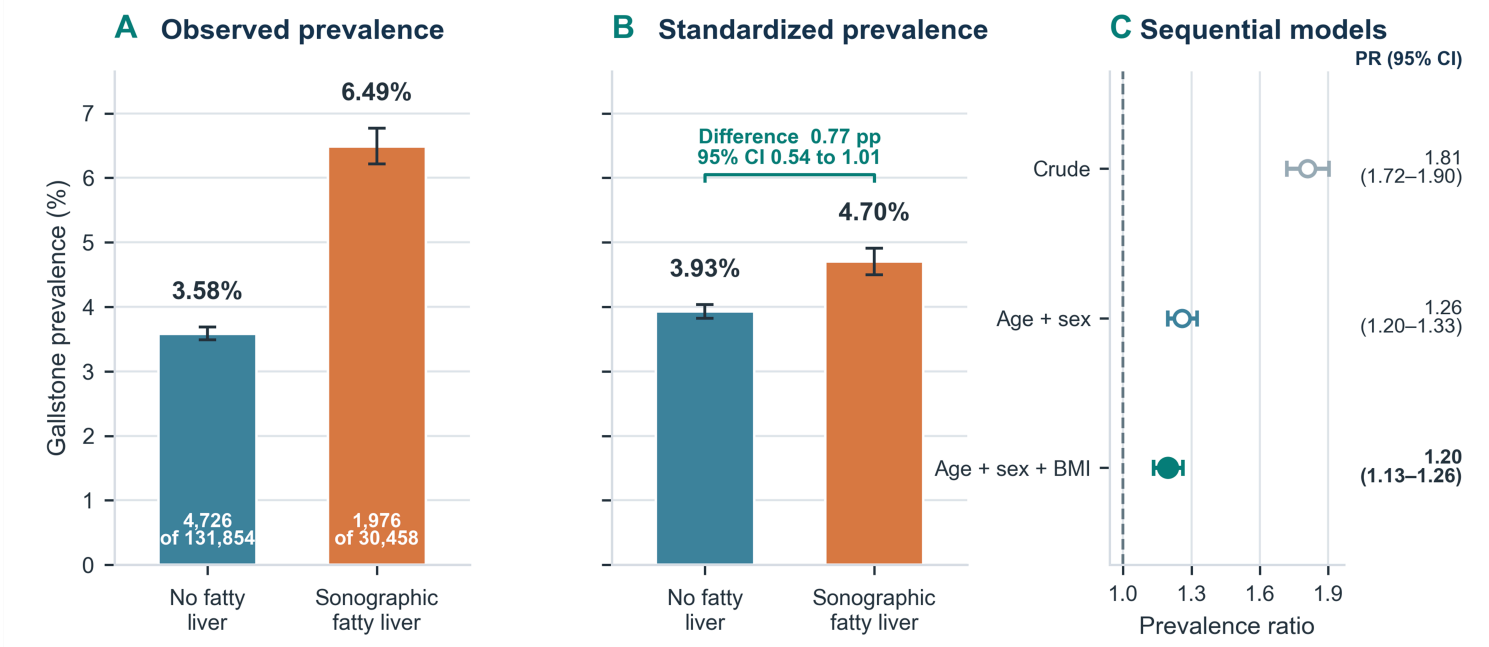



**Figure 2**

**Age-specific gallstone prevalence among normal-weight adults.** Lines show unadjusted prevalence and Wilson 95% confidence intervals by fatty-liver status in five-year age bands (75 years or older combined). Open circles with a solid line denote no fatty liver; filled squares with a dashed line denote sonographic fatty liver. P=0.168 is from the adjusted three-category age interaction on the multiplicative PR scale, not the plotted bands. Only four gallstone cases occurred among exposed adults aged 18-24 years; that estimate is imprecise.




## Figure 3

**Gallstone prevalence among normal-weight adults.** Panel A, observed prevalence; panel B, primary-model age-, sex-, and within-range-BMI-standardized prevalence with 95% confidence intervals; panel C, sequential modified Poisson prevalence ratios. Models included 162,312 adults and 6,702 current gallstone cases. BMI, body mass index; CI, confidence interval.

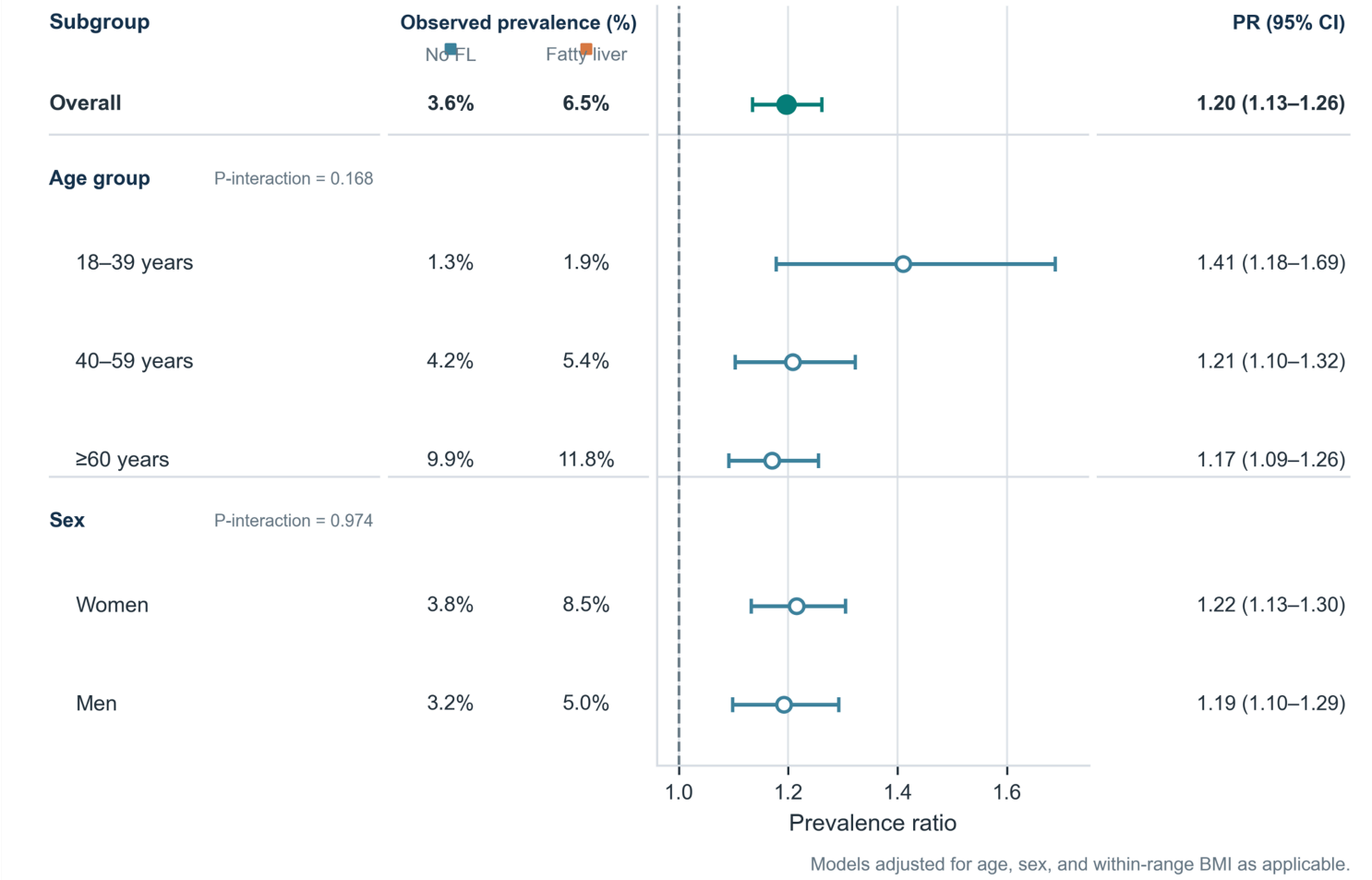



**Figure 4**

**Association within normal-weight subgroups.** Adjusted prevalence ratios and 95% confidence intervals are shown. Age-stratified models adjusted for continuous age, sex, and within-range BMI; sex-stratified models for nonlinear age and within-range BMI. Interaction P values are full-population joint Wald tests on the multiplicative PR scale; they do not test additive interaction. BMI, body mass index; CI, confidence interval.

# Supplementary Files

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- Additionalfile1SupplementaryMaterial.docx