META-ANALYSIS

Fang et al: Body weight and BMI variability in dementia

Body weight and BMI variability linked to dementia risk: A meta-analysis

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ABSTRACT

Emerging evidence suggests that fluctuations in body weight (BW) or body mass index (BMI), independent of average levels, may influence dementia risk. However, the association between intra-individual variability in BW or BMI and incident dementia remains unclear. This meta-analysis aimed to clarify this relationship. A systematic search of PubMed, Embase, and Web of Science was conducted through March 25, 2025, to identify longitudinal observational studies reporting dementia outcomes in relation to BW or BMI variability. Relative risks (RRs) comparing the highest versus lowest variability categories were pooled using a random-effects model. Subgroup and sensitivity analyses were performed to explore heterogeneity and assess the robustness of the results. Nine cohort studies (10 datasets; 4,232,666 participants) were included. Overall, high BW or BMI variability was associated with a significantly increased risk of dementia (RR = 1.36, 95% CI: 1.27–1.46; $p < 0.001$; I² = 84%). The association was consistent for both BW (RR = 1.45) and BMI (RR = 1.34) variability. Subgroup analyses showed stronger associations in prospective studies than in retrospective ones, and in studies that did not adjust for baseline BW/BMI compared to those that did (p for subgroup difference < 0.05). Associations remained robust in sensitivity analyses and across dementia subtypes, including Alzheimer's disease and vascular dementia. No significant publication bias was detected (Egger's test, $p = 0.22$). In conclusion, greater intra-individual variability in BW or BMI may be independently associated with increased dementia risk. These findings underscore the importance of maintaining weight stability in mid-to-late life as a potential preventive strategy for dementia.

KEYWORDS: Body weight; Variability; Dementia; Alzheimer's disease; Risk factor.

INTRODUCTION

Dementia is a progressive neurodegenerative syndrome characterized by cognitive decline, functional impairment, and loss of independence (1, 2). Currently, over 55 million individuals worldwide are living with dementia, a figure projected to triple by 2050 due to population aging. Alzheimer's disease (AD) and vascular dementia (VD) are the two most prevalent subtypes, collectively accounting for the majority of cases (3-5). Despite advancements in symptomatic treatments and recent efforts toward disease-modifying therapies, dementia remains incurable, imposing a significant burden on patients, families, and healthcare systems (5). Given the limited effectiveness of existing treatments, identifying modifiable risk factors for early prevention and intervention has become a major public health priority (6, 7). Established risk factors for dementia include age, genetics (e.g., APOE ε4), cardiovascular disease, and lifestyle factors; however, many cases remain unexplained, highlighting the need to investigate novel predictors (8).

In recent years, increasing attention has been directed toward the role of intra-individual variability in body composition—BW and BMI—as potential indicators of health instability (9). Variability in BW or BMI is typically quantified using statistical metrics such as standard deviation (SD), coefficient of variation (CV), average successive variability (ASV), or variability independent of the mean (VIM), derived from serial measurements over time (10). Unlike static values of BW or BMI, which are well-documented in their associations with various chronic diseases, variability reflects dynamic physiological and behavioral changes (9, 10). Previous studies have linked fluctuations in BW or BMI to increased risks of mortality, cardiovascular events, and metabolic disturbances, potentially mediated by mechanisms such as chronic inflammation, autonomic dysregulation, and impaired homeostasis (11-13).

The potential relationship between BW/BMI variability and cognitive dysfunction or dementia has recently emerged as a focal point of research (14). Fluctuations in BW may indicate underlying frailty, neuroendocrine disruption, or nutritional instability—all factors implicated in cognitive decline (15, 16). However, existing studies on this topic have yielded inconsistent findings, and the strength and direction of the association remain unclear (17-25). Furthermore, variability in measurement methods, study populations, and dementia outcomes has contributed to heterogeneity in results. Therefore, this study aims to perform a meta-

analysis to systematically evaluate the association between intra-individual variability in BW or BMI and the risk of incident dementia.

MATERIAL AND METHODS

This meta-analysis was conducted in accordance with the PRISMA 2020 statement (26, 27) and the Cochrane Handbook for Systematic Reviews (28), which guided the development of the protocol, data collection, statistical synthesis, and reporting. The protocol has been prospectively registered in the PROSPERO database under the identifier CRD420251043561.

Database search

To identify studies relevant to this meta-analysis, we searched PubMed, Embase, and Web of Science databases using an extensive array of search terms, including: (1) "body weight" OR "body mass index" OR "BMI"; (2) "variation" OR "variability" OR "fluctuation" OR "oscillation" OR "fluctuate"; (3) "dementia" OR "Alzheimer" OR "Alzheimer's" OR "cognitive decline" OR "cognitive impairment" OR "cognitive dysfunction" OR "cognition"; and (4) "prospective" OR "prospectively" OR "longitudinal" OR "incident" OR "incidence" OR "risk" OR "followed" OR "follow-up" OR "cohort". The literature search was limited to studies involving human participants and included only full-length, peer-reviewed articles published in English. To ensure comprehensive coverage, the reference lists of relevant original and review articles were also manually screened for additional eligible studies. The search spanned from the inception of each database through March 25, 2025, with detailed search strategies provided in **Supplemental File 1**.

Study selection

The inclusion criteria were structured according to the PICOS framework:

Population (P): Adults aged 18 years or older without dementia at baseline.

Exposure (I): High intra-individual variability in BW or BMI, as defined by original studies employing quantitative measures. Exposure classification adhered to the original cutoffs established in each study.

Comparison (C): Individuals exhibiting low BW or BMI variability at baseline.

Outcome (O): Incident cases of all-cause dementia, AD, or VD during follow-up, with diagnostic definitions and validation methods consistent with those utilized in the respective studies.

Study design (S): Longitudinal observational studies, encompassing cohort studies, nested case-control designs, and post-hoc analyses of clinical trials.

Exclusion criteria comprised reviews, editorials, meta-analyses, preclinical studies, and studies that included participants with dementia at baseline, lacked a defined measure of BW or BMI variability, or did not report incident dementia outcomes. In instances of overlapping populations, the study with the largest and most comprehensive dataset was selected for inclusion.

Study quality evaluation and data collection

The literature search, study selection, quality assessment, and data extraction were conducted independently by two reviewers, with any disagreements resolved through discussion with the corresponding author. Study quality was assessed using the Newcastle–Ottawa Scale (NOS), which evaluates three domains: participant selection, control for confounding, and outcome assessment (29). The NOS assigns scores ranging from 1 to 9, with higher scores indicating superior quality; studies scoring 7 or above were classified as high quality. Extracted data encompassed study-level information (first author, publication year, country, and study design), participant characteristics (source population, number of subjects, mean age, and sex), methods of measuring body weight or BMI variability (number and timing of measurements, variability metrics, and cutoffs used), follow-up duration, dementia diagnosis methods, types of dementia outcomes reported (all-cause, Alzheimer's disease, or vascular dementia), number of incident dementia cases, and covariates adjusted for in the association analyses.

Statistical analyses

The association between BW or BMI variability and the risk of dementia was assessed by pooling relative risks (RRs) and their corresponding 95% confidence intervals (CIs). This analysis compared individuals in the highest and lowest categories of BW/BMI variability at baseline. The estimates were directly extracted from the original studies without converting continuous measures (e.g., per-standard deviation hazard ratios) into categorical contrasts.

Consequently, no transformation methods were applied. When necessary, RRs and their standard errors were calculated from reported 95% CIs or *p* values, followed by log transformation to stabilize variance and normalize the distribution. (28).

Between-study heterogeneity was evaluated using the Cochrane Q test and the I² statistic, with thresholds of < 25%, 25–75%, and > 75% interpreted as low, moderate, and high heterogeneity, respectively. (30). A random-effects model was employed to accommodate expected variation across studies. (28). In addition, we performedAdditionally, sensitivity analyses were conducted using the Hartung–Knapp–Sidik–Jonkman (HKSJ) method with restricted maximum likelihood (REML) estimation to assess the robustness of the results under a more conservative variance estimator. Sensitivity analyses also involved sequentially omitting each study to evaluate the stability of the pooled estimates.

Subgroup analyses were performed to explore the influence of study-level characteristics, including the type of variability assessed (BW vs. BMI), dementia outcomes (Alzheimer's disease or vascular dementia), study design (prospective versus retrospective), baseline age group (≥ 60 years versus ≥ 40 years), proportion of male participants, follow-up duration, method of dementia validation (clinical diagnosis, ICD coding, or self/proxy report), and whether baseline BW/BMI was adjusted for in the analysis. Median values of continuous variables were used to establish subgroup cutoffs. Publication bias was assessed through visual inspection of funnel plots and formally tested using Egger's regression test (6). Atest, with a *p* value < 0.05 indicating statistical significance. All statistical analyses were conducted using RevMan (version 5.1; Cochrane Collaboration, Oxford, UK) and Stata (version 12.0; Stata Corporation, College Station, TX, USA).

RESULTS

Study retrieval

The study selection process is depicted in **Figure 1**. Initially, 1,001 potentially relevant records were identified through database searches and citation screening. Following the removal of 389 duplicates, 612 records remained for title and abstract screening, resulting in the exclusion of 588 articles that did not align with the objectives of the meta-analysis. The full texts of the remaining 24 articles were independently assessed by two reviewers, which

led to the exclusion of 15 studies for the reasons detailed in **Figure 1**. Ultimately, nine studies met the inclusion criteria and were incorporated into the quantitative synthesis (17-25).

Overview of the study characteristics

Table 1 presents a summary of the characteristics of the nine studies included in this meta-analysis, published between 2013 and 2024, and conducted in Israel, South Korea, the United States, and Australia. All studies are longitudinal cohorts, comprising six prospective (17, 18, 20, 22, 24, 25) and three retrospective (19, 21, 23), encompassing a total of 4,232,666 participants. The study populations included middle-aged to older adults, with mean ages ranging from 44.3 to 74.6 years, and the proportion of male participants varied from 43.3% to 100%. Intra-individual variability in BW (17, 19, 22, 23) or BMI (18, 20, 21, 24, 25) was assessed using statistical parameters such as SD, CV, ASV, and VIM. The number and timing of repeated BW/BMI measurements varied from three to nine time points over periods of two to sixteen years, with comparisons typically made between the highest and lowest variability categories, such as quintiles (20), quartiles (17-19, 21-24), and tertiles (25). All studies reported incident dementia outcomes, including all-cause dementia in seven studies (17-20, 22, 23, 25), AD in six studies (18, 19, 21-24), and VD in three studies (18, 19, 23). Dementia diagnoses were validated using various methods, including clinical assessments (17, 20, 24, 25), ICD-10 codes accompanied by medication records or structured cognitive tests (18, 19, 21, 23), and self/proxy physician reports (22). Follow-up durations ranged from 2.7 to 36 years, with outcome ascertainment aligned with each study's protocol. Most studies adjusted for a comprehensive set of covariates, including age, sex, education, and comorbidities; however, three studies did not account for baseline BW or BMI, potentially influencing the observed associations (22, 24, 25). As illustrated in **Table 2**, the Newcastle-Ottawa Scale (NOS) scores ranged from 6 to 9, indicating moderate to high methodological quality. Notably, three studies achieved the maximum score of 9 stars (17, 24, 25), three studies scored 8 stars (18, 20, 22), and three studies scored either 7 (19, 23) or 6 (21) stars, primarily due to limitations in follow-up duration or outcome ascertainment.

Association between variability of BW/BMI and dementia risk

Since one of the included studies (21) reported outcomes for men and women separately, these datasets were independently incorporated into the meta-analysis, resulting in a total of 10 datasets available for quantitative analysis. Pooled analysis using a random-effects model

revealed that individuals exhibiting the highest variability in BW or BMI had a significantly elevated risk of developing dementia compared to those with the lowest variability (RR = 1.36, 95% CI: 1.27–1.46; $p < 0.001$; **Figure 2A**), with substantial heterogeneity observed across studies ($I^2 = 84\%$). Furthermore, a sensitivity analysis employing the HKSJ method with restricted maximum likelihood (REML) estimation yielded consistent results (RR = 1.37; 95% CI: 1.24–1.52; $p < 0.001$; $I^2 = 87\%$; **Supplemental Figure 1**).

To assess the robustness of the pooled results, a sensitivity analysis was performed by sequentially omitting each included study. The overall association between high variability in BW or BMI and dementia risk remained statistically significant across all iterations, with pooled RRs ranging from 1.34 to 1.40, all with $p < 0.001$ (**Table 3**). The I^2 values varied between 58% and 86%, indicating persistent heterogeneity without substantially altering the direction or magnitude of the effect. Notably, the sensitivity analysis limited to studies of good quality (NOS ≥ 7) (17-20, 22-25) demonstrated similar results (RR = 1.42; 95% CI: 1.30–1.55; $p < 0.001$; $I^2 = 87\%$).

Additionally, subgroup analyses by exposure type revealed consistent associations for both BW variability (RR = 1.45; 95% CI: 1.23–1.70; $I^2 = 76\%$) and BMI variability (RR = 1.34; 95% CI: 1.22–1.48; $I^2 = 62\%$), with no significant difference between subgroups ($p = 0.43$; **Figure 2B**). Stratification by dementia subtype indicated that higher variability was associated with an increased risk of both AD (RR = 1.32; 95% CI: 1.27–1.38; $I^2 = 45\%$) and VD (RR = 1.40; 95% CI: 1.23–1.59; $I^2 = 83\%$), with no significant subgroup difference ($p = 0.41$; **Figure 2C**).

Further subgroup analyses indicated a stronger association in prospective studies (RR = 1.51; 95% CI: 1.35–1.68; $I^2 = 29\%$) compared to retrospective studies (RR = 1.27; 95% CI: 1.20–1.34; $I^2 = 40\%$), with a significant subgroup difference ($p = 0.005$; **Figure 3A**). Comparable associations were observed in participants aged ≥ 60 years (RR = 1.39; 95% CI: 1.22–1.58; $I^2 = 67\%$) and those aged ≥ 40 years (RR = 1.36; 95% CI: 1.23–1.51; $I^2 = 93\%$; p for subgroup difference = 0.79; **Figure 3B**), as well as in studies with < 55% men (RR = 1.43; 95% CI: 1.30–1.56) compared to those with ≥ 55% men (RR = 1.29; 95% CI: 1.18–1.41; p for subgroup difference = 0.11; **Figure 4A**). The association remained consistent across studies with shorter (< 7 years; RR = 1.37) and longer (≥ 7 years; RR = 1.42) follow-up durations (p for subgroup difference = 0.73; **Figure 4B**). Studies utilizing clinical evaluations for dementia diagnosis exhibited a similar association (RR = 1.52; 95% CI: 1.30–1.77; $I^2 = 0\%$) compared

to those relying on ICD codes or self/proxy reports (RR = 1.33; 95% CI: 1.23–1.44; I² = 90%; p for subgroup difference = 0.15; **Figure 5A**). However, the association was significantly stronger in studies that did not adjust for baseline BW or BMI (RR = 1.66; 95% CI: 1.32–2.10) compared to those that did (RR = 1.32; 95% CI: 1.23–1.42; p for subgroup difference = 0.04; **Figure 5B**).

Publication bias

The funnel plots evaluating the relationship between body weight or BMI variability and dementia risk are illustrated in **Figure 6**. A visual inspection of these plots reveals a symmetrical distribution, suggesting a minimal likelihood of publication bias. This finding is further corroborated by Egger's regression test, which produced a non-significant result (p = 0.22).

DISCUSSION

This meta-analysis presents the most current and comprehensive evidence regarding the relationship between intra-individual variability in BW or BMI and the risk of developing incident dementia. Our findings, derived from nine longitudinal cohort studies involving over 4.2 million participants, indicate that increased variability in BW or BMI significantly correlates with a heightened risk of dementia onset. This association was consistent across various dementia subtypes, including AD and VD, and remained robust through numerous subgroup and sensitivity analyses.

The clinical significance of these findings is underscored by the consistency of the observed associations across diverse populations, study designs, and adjustment strategies. Subgroup analyses based on exposure type revealed similar effect sizes for variability in BW and BMI, indicating their interchangeable roles in predicting dementia risk. Notably, even in studies that adjusted for baseline BW or BMI, the association, while attenuated, remained statistically significant. This suggests that the predictive value of weight variability is independent of an individual's static body composition and reflects more complex underlying physiological or behavioral instability. Research by Liang et al. (32) and Aiken-Morgan et al. (33) supports this interpretation, demonstrating that variability in BMI, rather than baseline BMI alone, is more strongly associated with cognitive decline and the onset of mild cognitive impairment (MCI) in older adults.

Several pathophysiological mechanisms may elucidate the observed relationship between BW/BMI variability and dementia. First, fluctuations in weight may indicate underlying metabolic dysregulation, including impaired glucose tolerance, insulin resistance, and dyslipidemia—factors well-documented as risk contributors to cognitive decline (34, 35). Second, BW/BMI variability has been correlated with chronic systemic inflammation (36) and altered adipokine signaling (37), both of which can lead to neuroinflammation and dysfunction of the blood-brain barrier. Third, weight fluctuations might signal sarcopenia, malnutrition, or early frailty—conditions associated with neuronal loss and cognitive impairment (38-40). Notably, Zhou et al. found that greater variability in cardiometabolic and inflammatory markers, including BMI, was independently linked to accelerated cognitive decline in memory and verbal fluency performance over time (41). Similarly, Kang et al. demonstrated that increased BMI variability correlated with heightened amyloid-β deposition in non-demented individuals, suggesting a potential connection between body composition instability and early AD pathology (42). Furthermore, the study by Liang et al. (2022) indicated that greater BMI variability predicted faster cognitive decline, even when controlling for mean BMI, highlighting a unique biological pathway through which variability, rather than obesity per se, influences cognition (32). Our meta-analysis reinforced that the association between BW/BMI variability and dementia was significantly stronger in studies that did not adjust for baseline BW or BMI, although the effect remained statistically significant even in adjusted analyses. This disparity may reflect residual confounding by absolute weight status in the unadjusted subgroup, where individuals with greater variability may also exhibit higher or lower baseline weights, both of which are established risk factors for cognitive decline.

Interpretation of subgroup analyses provides additional insights. The stronger association observed in prospective studies compared to retrospective ones likely reflects improved temporal alignment between exposure and outcome measurement, thereby reducing recall bias and enhancing causal inference (43). However, it is essential to recognize that early prodromal stages of cognitive decline, such as MCI or subjective cognitive decline, may already be present during the exposure period and influence lifestyle factors, including nutrition and weight regulation (44). For example, in the extensive study by Lee et al. (18), while dementia diagnoses were made post-variability assessment, early cognitive changes might have remained undetected due to the limitations of administrative databases, complicating causality interpretations. Although associations were observed across various

age strata and sex distributions, these characteristics did not significantly alter the effect, suggesting that BW/BMI variability serves as a broadly applicable risk marker. The consistency of results across subgroups defined by follow-up duration and dementia diagnosis methods (e.g., clinical evaluations versus ICD codes or proxy reports) supports the robustness and generalizability of these findings. However, the consistency of associations across AD and VD may also reflect a common endpoint—cognitive decline—rather than a shared etiological mechanism. It is plausible that subtle, preclinical cognitive changes may have already begun to impact daily functioning, appetite, and self-care behaviors, resulting in weight fluctuations independent of dementia subtype (45). This interpretation underscores the necessity of considering reverse causality in evaluating these findings. Moreover, the observed heterogeneity ($I^2 = 84\%$) suggests that methodological differences, such as variations in defining variability (e.g., standard deviation versus coefficient of variation versus variability independent of the mean), the number and timing of BW/BMI measurements, and the statistical models employed, may contribute to differential estimates and warrant exploration in future individual patient data meta-analyses. Additionally, although three included studies (22, 24, 25) were conducted in Western populations, the majority of the sample was derived from East Asian health-insurance cohorts. Ethnic, lifestyle, and healthcare system differences may influence body weight dynamics, access to preventive care, and dementia diagnosis methods. Therefore, caution is advised when generalizing these findings to other regions, particularly where sociocultural and medical practices differ significantly.

This meta-analysis presents several notable strengths. It exclusively includes cohort studies with longitudinal follow-up, thereby minimizing the risk of reverse causality. The large sample size enhances statistical power to detect moderate associations and conduct meaningful subgroup analyses. All included studies employed multivariable-adjusted models, and sensitivity analyses confirmed the stability of results across various study exclusions. Our extensive literature search and rigorous quality assessment using the NOS further bolster the credibility of the findings.

However, several limitations should be acknowledged. First, the heterogeneity among studies was moderate to high, likely attributable to variations in populations, definitions of exposure, and assessments of outcomes. Second, the metrics used to quantify BW/BMI variability were not standardized across studies, which limits comparability and complicates the establishment

of clinically actionable thresholds. To our knowledge, an optimal protocol and parameter to accurately reflect the severity of BW variability remain undetermined. Our subgroup analysis based on BW and BMI variability yielded consistent results. Third, although all studies adjusted for key confounders, residual confounding from unmeasured factors (e.g., diet, depression, physical activity, or frailty) cannot be ruled out. Fourth, the reliance on study-level rather than individual-level data precluded exploration of nuanced dose-response relationships or potential non-linear effects. Additionally, the studies did not differentiate between unidirectional changes (i.e., sustained weight loss or gain) and bidirectional fluctuations (i.e., weight cycling), which may have distinct physiological and clinical implications. For instance, weight loss may indicate frailty or malnutrition, while weight gain may signal underlying metabolic dysregulation (46). Therefore, while our findings suggest that weight instability is associated with an increased risk of dementia, further research is warranted to clarify whether the direction of weight change influences this relationship. In addition, the temporal distribution of weight variability—whether fluctuations occurred rapidly over a short interval or gradually across a longer period—was not consistently reported among studies. This limitation hinders our ability to assess whether short-term instability poses a greater risk than long-term trends. Understanding the timing and clustering of variability may refine surveillance strategies and inform the timing of interventions aimed at stabilizing weight.

Furthermore, although all included studies utilized cohort designs, the possibility of reverse causality cannot be entirely excluded. Dementia has a prolonged preclinical phase, during which subtle cognitive decline may already impact appetite regulation, nutrition, or daily functioning, potentially contributing to body weight variability prior to formal diagnosis (47).Moreover, although temporality was generally ensured by study design, causality cannot be definitively established due to the observational nature of the evidence. Finally, while Egger's test did not indicate significant publication bias, this finding should be interpreted with caution, given the limited power of asymmetry tests when applied to a small number of studies.

Despite these limitations, our findings carry significant clinical and public health implications. Monitoring BW/BMI variability over time may serve as a simple, non-invasive, and cost-effective tool for identifying individuals at higher risk of dementia, particularly in mid to late life. While guidelines traditionally emphasize achieving a healthy weight, our results suggest

that maintaining weight stability may be equally crucial for preserving cognitive health(48). These findings support the incorporation of longitudinal weight trends into dementia risk models and highlight the potential utility of personalized weight management strategies for cognitive aging prevention. Further studies are warranted to elucidate the importance of maintaining weight stability on cognitive function.

CONCLUSION

In conclusion, this meta-analysis demonstrates that greater intra-individual variability in body weight or BMI may be independently associated with a higher risk of developing dementia. Given the observational nature of the included studies and the possibility of residual confounding, the overall certainty of the evidence should be considered low to moderate.These findings support the hypothesis that weight instability reflects underlying physiological disturbances that may contribute to neurodegeneration. Future research should aim to clarify causal pathways, define optimal variability thresholds, and evaluate whether interventions targeting weight stability can mitigate dementia risk.

REFERENCES

1. Wang C, Song P, Niu Y. The management of dementia worldwide: A review on policy practices, clinical guidelines, end-of-life care, and challenge along with aging population. Biosci Trends. 2022;16(2):119-29.

2. Watt JA, Porter J, Tavilsup P, Chowdhury M, Hatch S, Ismail Z, et al. Guideline Recommendations on Behavioral and Psychological Symptoms of Dementia: A Systematic Review. J Am Med Dir Assoc. 2024;25(5):837-46 e21.

3. 2024 Alzheimer's disease facts and figures. Alzheimers Dement. 2024;20(5):3708-821.

4. Shin JH. Dementia Epidemiology Fact Sheet 2022. Ann Rehabil Med. 2022;46(2):53-9.

5. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health. 2022;7(2):e105-e25.

6. Passeri E, Elkhoury K, Morsink M, Broersen K, Linder M, Tamayol A, et al. Alzheimer's Disease: Treatment Strategies and Their Limitations. Int J Mol Sci. 2022;23(22).

7. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020;396(10248):413-46.

8. López-Antón R. Recent Advances in Alzheimer's Disease Research: From Biomarkers to Therapeutic Frontiers. Biomedicines. 2024;12(12).

9. Lowe MR, Benson L, Singh S. Individual differences in within-subject weight variability: There's a signal in the noise. Physiol Behav. 2020;226:113112.

10. Prattichizzo F, Frigé C, La Grotta R, Ceriello A. Weight variability and diabetes complications. Diabetes Res Clin Pract. 2023;199:110646.

11. Huang S, Shi K, Ren Y, Wang J, Yan WF, Qian WL, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78.

12. Massey RJ, Siddiqui MK, Pearson ER, Dawed AY. Weight variability and cardiovascular outcomes: a systematic review and meta-analysis. Cardiovasc Diabetol. 2023;22(1):5.

13. Bhadada SK, Malhotra B, Shetty AJ. Body Weight Variability and Cardiovascular Health in Diabetes. J Clin Endocrinol Metab. 2023;108(2):e19-e20.

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14.   Lee YH. Body Weight Variability: A Marker for Increased Risk or a Causative Factor for Dementia? J Obes Metab Syndr. 2021;30(3):191-3.

15.   Eymundsdottir H, Ramel A, Geirsdottir OG, Skuladottir SS, Gudmundsson LS, Jonsson PV, et al. Body weight changes and longitudinal associations with cognitive decline among community-dwelling older adults. Alzheimers Dement (Amst). 2021;13(1):e12163.

16.   Zonneveld MH, Noordam R, Sabayan B, Stott DJ, Mooijaart SP, Blauw GJ, et al. Weight loss, visit-to-visit body weight variability and cognitive function in older individuals. Age Ageing. 2023;52(1).

17.   Ravona R, Schnaider-Beeri M, Goldbourt U. Body weight variability in midlife and risk for dementia in old age. Neurology. 2013;80(18):1677-83.

18.   Lee SH, Han K, Cho H, Park YM, Kwon HS, Kang G, et al. Variability in metabolic parameters and risk of dementia: a nationwide population-based study. Alzheimers Res Ther. 2018;10(1):110.

19.   Roh E, Hwang SY, Kim JA, Lee YB, Hong SH, Kim NH, et al. Body Weight Variability Increases Dementia Risk Among Older Adults: A Nationwide Population-Based Cohort Study. Front Endocrinol (Lausanne). 2020;11:291.

20.   Bae EM, Park SM. Association between Variations in Body Mass Index and Cognitive Function in Older Korean Adults. J Obes Metab Syndr. 2021;30(3):271-8.

21.   Kang SY, Kim YJ, Jang W, Son KY, Park HS, Kim YS. Body mass index trajectories and the risk for Alzheimer's disease among older adults. Sci Rep. 2021;11(1):3087.

22.   Chen H, Zhou T, Guo J, Ji JS, Huang L, Xu W, et al. Association of Long-Term Body Weight Variability With Dementia: A Prospective Study. J Gerontol A Biol Sci Med Sci. 2022;77(10):2116-22.

23.   Park KY, Nam GE, Han K, Hwang HS. Body weight variability and the risk of dementia in patients with type 2 diabetes mellitus: A nationwide cohort study in Korea. Diabetes Res Clin Pract. 2022;190:110015.

24.   Wang RT, Sun Z, Tan CC, Tan L, Xu W. Dynamic Features of Body Mass Index in Late Life Predict Cognitive Trajectories and Alzheimer's Disease: A Longitudinal Study. J Alzheimers Dis. 2024;100(4):1365-78.

25.   Wu Z, Owen A, Woods RL, Cribb L, Alharbi T, Zhou Z, et al. Associations of body habitus and its changes with incident dementia in older adults. J Am Geriatr Soc. 2024;72(4):1023-34.

26.   Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

27.   Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.

28.   Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. The Cochrane Collaboration. 2021;www.training.cochrane.org/handbook.

29.   Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2010;http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

30.   Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58.

31.   Rover C, Knapp G, Friede T. Hartung-Knapp-Sidik-Jonkman approach and its modification for random-effects meta-analysis with few studies. BMC Med Res Methodol. 2015;15:99.

32.   Liang F, Fu J, Moore JB, Zhang X, Xu Y, Qiu N, et al. Body Mass Index, Waist Circumference, and Cognitive Decline Among Chinese Older Adults: A Nationwide Retrospective Cohort Study. Front Aging Neurosci. 2022;14:737532.

33.   Aiken-Morgan AT, Capuano AW, Wilson RS, Barnes LL. Changes in Body Mass Index and Incident Mild Cognitive Impairment Among African American Older Adults. J Gerontol A Biol Sci Med Sci. 2024;79(3).

34.   Zhang H, Tamakoshi K, Yatsuya H, Murata C, Wada K, Otsuka R, et al. Long-term body weight fluctuation is associated with metabolic syndrome independent of current body mass index among Japanese men. Circ J. 2005;69(1):13-8.

35.   Lee JS, Kawakubo K, Kobayashi Y, Mori K, Kasihara H, Tamura M. Effects of ten year body weight variability on cardiovascular risk factors in Japanese middle-aged men and women. Int J Obes Relat Metab Disord. 2001;25(7):1063-7.

36.   Tamakoshi K, Yatsuya H, Kondo T, Ishikawa M, Zhang H, Murata C, et al. Long-term body weight variability is associated with elevated C-reactive protein independent of current body mass index among Japanese men. Int J Obes Relat Metab Disord. 2003;27(9):1059-65.

37.   van Baak MA, Mariman ECM. Mechanisms of weight regain after weight loss - the role of adipose tissue. Nat Rev Endocrinol. 2019;15(5):274-87.

38.   Chen A, Ren L, Min S, Li P, Wei K, Cao J, et al. Analysis of the relationship between body habitus and frailty of community adults in Chongqing: a cross-sectional survey study. Front Public Health. 2023;11:1189173.

39.   Hettiarachchi J, Verstraeten LMG, Pacifico J, Reijnierse EM, Meskers CGM, Maier AB. Body Weight and Composition Changes in Geriatric Rehabilitation Are Dependent on Sarcopenia and Malnutrition: RESORT. J Am Med Dir Assoc. 2024;25(8):105030.

40.   McMenamin KJ, Harris TB, Baker JF. Weight variability, physical functioning and incident disability in older adults. J Cachexia Sarcopenia Muscle. 2023;14(4):1648-56.

41.   Zhou R, Liu HM, Li FR, Yu JR, Yuan ZL, Zheng JZ, et al. Variability in Cardiometabolic and Inflammatory Parameters and Cognitive Decline. Am J Prev Med. 2021;61(4):e181-e9.

42.   Kang SH, Kim JH, Chang Y, Cheon BK, Choe YS, Jang H, et al. Independent effect of body mass index variation on amyloid-β positivity. Front Aging Neurosci. 2022;14:924550.

43.   Euser AM, Zoccali C, Jager KJ, Dekker FW. Cohort studies: prospective versus retrospective. Nephron Clin Pract. 2009;113(3):c214-7.

44.   Dominguez LJ, Veronese N, Vernuccio L, Catanese G, Inzerillo F, Salemi G, et al. Nutrition, Physical Activity, and Other Lifestyle Factors in the Prevention of Cognitive Decline and Dementia. Nutrients. 2021;13(11).

45.   Morrow CB, Leoutsakos J, Yan H, Onyike C, Kamath V. Weight Change and Neuropsychiatric Symptoms in Alzheimer's Disease and Frontotemporal Dementia: Associations with Cognitive Decline. J Alzheimers Dis Rep. 2023;7(1):767-74.

46.   Crow RS, Petersen CL, Cook SB, Stevens CJ, Titus AJ, Mackenzie TA, et al. Reported Weight Change in Older Adults and Presence of Frailty. J Frailty Aging. 2020;9(2):74-81.

47.   Franx BAA, Arnoldussen IAC, Kiliaan AJ, Gustafson DR. Weight Loss in Patients with Dementia: Considering the Potential Impact of Pharmacotherapy. Drugs Aging. 2017;34(6):425-36.

48.   Kivimäki M, Luukkonen R, Batty GD, Ferrie JE, Pentti J, Nyberg ST, et al. Body mass index and risk of dementia: Analysis of individual-level data from 1.3 million individuals. Alzheimers Dement. 2018;14(5):601-9.

TABLES AND FIGURES WITH LEGENDS

Table 1. Characteristics of the included studies

Study	Country	Study design	Population characteristics	No. of subjects	Mean age (years)	Men (%)	Times and durations for determining BW/BMI variability	Parameters for evaluating BW/BMI variability	Cutoff for evaluating BW/BMI variability	Follow-up duration (years)	Dementia outcome reported	Outcome validation	No. of patients with dementia	Variables adjusted
Ravona et al., 2013	Israel	PC	Apparently healthy men aged 40–70 years	1620	44.3	100	BW measured at 3 time points in 5 years	SD-BW	Q4:Q1	36	Overall dementia	TICS-m telephone screening and in-person neurologist/ psychiatrist assessment using DSM-	307	Age, SES, height, DM, baseline weight, BP, cholesterol, smoking, physical activity, dietary intake, and

Study	Country	Design	Population	N	Age	% Female	BW assessment	Index	Comparison	Follow-up (years)	Outcome	Ascertainment	Cases	Adjustments
												IV criteria		intentional dieting
Lee et al., 2018	South Korea	PC	General population aged ≥45 years without history of hypertension, DM, or dyslipidemia	293081 6	54.4	50.9	BW measure d ≥3 times between 2005 and index year	CV-BMI	Q4:Q1	5.5	Overall dementi a, AD, and VD	ICD-10 codes and prescription of dementia medications	32901 (AD: 24486, VD: 3629)	Age, sex, smoking, alcohol consumption, physical activity, income, baseline BMI, BP, glucose, and TC
Roh et al., 2020	South Korea	RC	Older adults aged ≥ 67 years	19987	73.1	60.2	BW measure d ≥3 times in 4 years	VIM-BW	Q4:Q1	6.5	Overall dementi a, AD, and VD	ICD codes with documented cognitive decline	1592 (AD: 1217, VD: 304)	Age, sex, BMI at baseline, smoking, alcohol, exercise, income, DM, hypertension, dyslipidemia, IHD, and

														cerebrovascular disease
Bae et al., 2021	South Korea	PC	Adults aged ≥45 years with normal cognitive function at baseline	3477	NR	53.7	BW measured at 3 time points in 4 years	ASV-BMI	Q5:Q1	10	Overall dementia	K-MMSE ≤17	NR	Age, sex, marital status, education, income, health insurance, region, smoking, alcohol, physical activity, comorbidities, depression, and BMI at baseline
Kang et al., 2021	South Korea	RC	Adults aged ≥60 years	45076	NR	51.7	BW measured at 3 time points in 5 years	ASV-BMI	Q4:Q1	2.7	AD	ICD-10 codes, prescription of anti-dementia drugs, and	4055	Age, sex, insurance premium, BMI at baseline, smoking, alcohol,

Study	Country	Design	Population	N	Age		BW measurement	Exposure	Comparison	Follow-up	Outcome	Outcome ascertainment	Cases	Covariates
												documentation of cognitive dysfunction		physical activity, hypertension, DM, and dyslipidemia
Park et al., 2022	South Korea	RC	Adults aged ≥40 years with T2DM and no prior dementia	1206764	59.4	62.5	BW measured ≥3 times in 5 years	VIM-BW	Q4:Q1	7.9	Overall dementia, AD, and VD	ICD-10 codes and prescription of dementia medications	162615 (AD: 65169, VD: 18705)	Age, sex, smoking, alcohol, exercise, income, hypertension, dyslipidemia, insulin use, number of oral antidiabetics, DM duration, baseline BW
Chen et al., 2022	USA	PC	Adults aged ≥70 years, cognitively intact	5547	71.1	43.3	BW measured at 9 time	CV-BW	Q4:Q1	6.8	Overall dementia and AD	Self/proxy report of physician-diagnosed	427 (AD: 201)	Age, sex, race, education, income, smoking,

Study	Country	Design	Population	N	Age	%	Exposure	BMI measure	Comparison	Follow-up	Outcome	Diagnostic criteria	Cases	Adjustments
							points in 16 years				dementia			alcohol, exercise, weight change over 16 years, and comorbidities
Wang et al., 2024	USA	PC	Non-demented adults aged ≥65 years	542	74.6	57	BW measured at 5 time points in 4 years	SD-BMI	Q4:Q1	8	AD	NINCDS-ADRDA clinical diagnostic criteria	285	Age, sex, education, APOE ε4 status, baseline cognitive status, hypertension, DM, smoking, and intracranial volume
Wu et al., 2024	Australia and USA	PC	Community-dwelling individuals aged ≥65 years,	18837	NR	44	BW measured at 3 time points in	SD-BMI	T3:T1	6.3	Overall dementia	DSM-IV criteria	844	Age, sex, education, ethnicity, living situation, smoking,

		cognitively intact and free of major illness at baseline				2 years							alcohol, hypertension, DM, dyslipidemia, depression, pulse pressure, TG, and APOE ε4

PC, prospective cohort;RC, retrospective cohort;BW, body weight;BMI, body mass index;SD, standard deviation;CV, coefficient of variation;VIM, variability independent of the mean;ASV, average successive variability;Q1, first quartile;Q4, fourth quartile;Q5, fifth quintile;T1, first tertile;T3, third tertile;AD, Alzheimer's disease;VD, vascular dementia;DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition;ICD-10, International Classification of Diseases, Tenth Revision;TICS-m, modified Telephone Interview for Cognitive Status;MMSE, Mini-Mental State Examination;K-MMSE, Korean Mini-Mental State Examination;CDR, Clinical Dementia Rating;GDS, Global Deterioration Scale;NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association;SES, socioeconomic status;DM, diabetes mellitus;BP, blood pressure;TC, total cholesterol;IHD, ischemic heart disease;TG, triglycerides;APOE ε4, apolipoprotein E epsilon 4 allele;NR, not reported.

Table 2. Study quality evaluation via the Newcastle-Ottawa Scale

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age and sex	Control for other confounding factors	Assessment of outcome	Enough long follow-up duration	Adequacy of follow-up of cohorts	Total
Ravona et al., 2013	1	1	1	1	1	1	1	1	1	9
Lee et al., 2018	1	1	1	1	1	1	0	1	1	8
Roh et al., 2020	0	1	1	1	1	1	0	1	1	7
Bae et al., 2021	1	1	1	1	1	1	1	1	1	8
Kang et al., 2021	0	1	1	1	1	1	0	0	1	6
Park et al., 2022	0	1	1	1	1	1	0	1	1	7
Chen et al., 2022	1	1	1	1	1	1	0	1	1	8

Wang et al., 2024	1	1	1	1	1	1	1	1	9
Wu et al., 2024	1	1	1	1	1	1	1	1	9

Table 3. Sensitivity analyses

	RR for the association between BW or BMI variability and the risk of dementia			
Dataset omitted	RR [95% CI]	p for effect	I^2	p for Cochrane Q test
Ravona et al., 2013	1.35 [1.26, 1.46]	< 0.001	85%	< 0.001
Lee et al., 2018	1.35 [1.25, 1.47]	< 0.001	61%	0.009
Roh et al., 2020	1.36 [1.26, 1.47]	< 0.001	86%	< 0.001
Bae et al., 2021	1.36 [1.26, 1.46]	< 0.001	86%	< 0.001
Kang et al., 2021 men	1.40 [1.30, 1.51]	< 0.001	85%	< 0.001
Kang et al., 2021 women	1.37 [1.27, 1.49]	< 0.001	86%	< 0.001
Park et al., 2022	1.39 [1.28, 1.51]	< 0.001	58%	0.01
Chen et al., 2022	1.34 [1.25, 1.43]	< 0.001	83%	< 0.001
Wang et al., 2024	1.35 [1.26, 1.46]	< 0.001	85%	< 0.001
Wu et al., 2024	1.36 [1.26, 1.46]	< 0.001	86%	< 0.001

RR: Relative risk; BW: Body weight; BMI: Body mass index; CI: confidence interval.
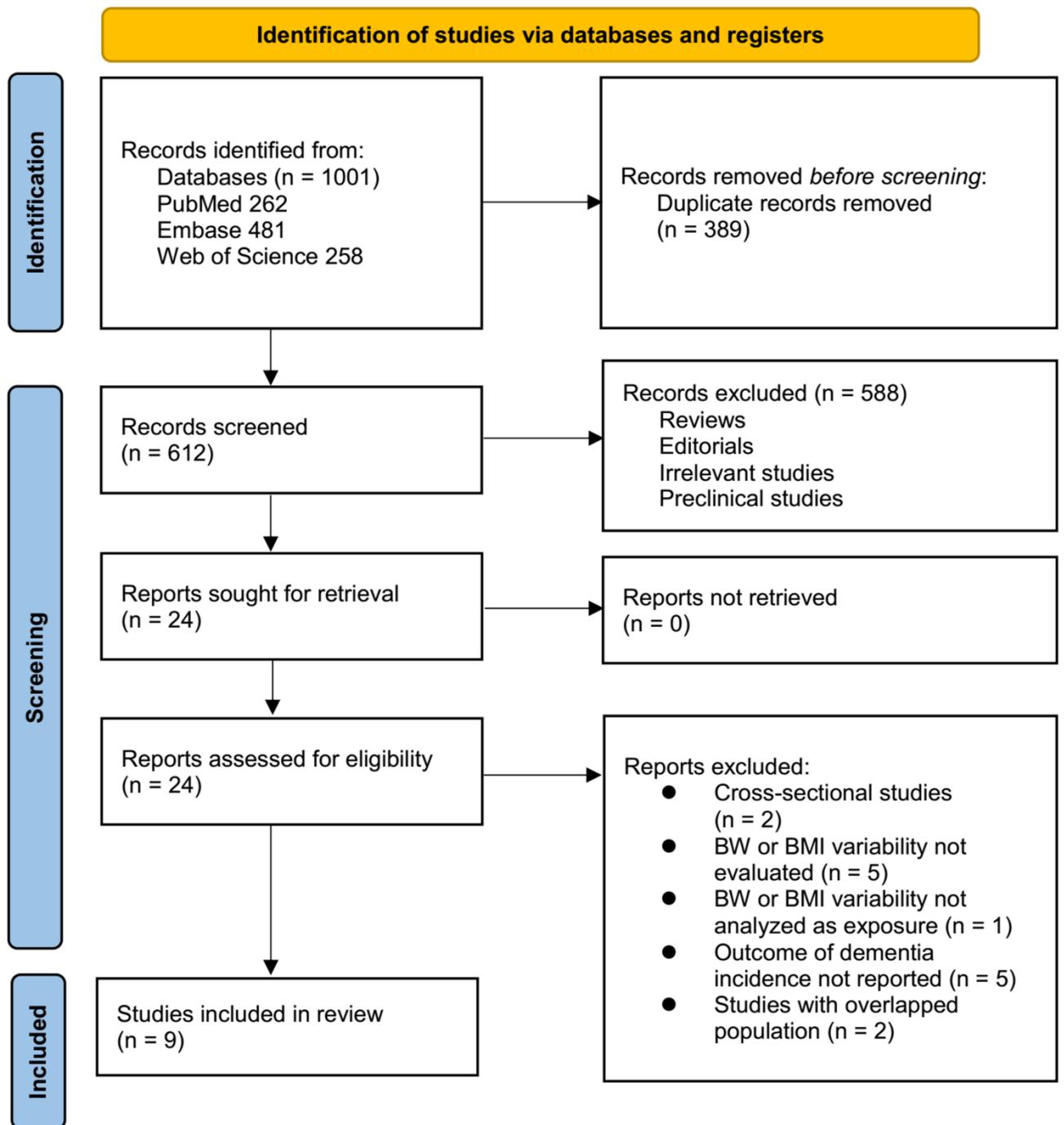
Figure 1. Flow diagram of study selection.

A total of 1,001 records were initially identified through database searches and citation screening. After removing 389 duplicates, 612 records were screened based on title and abstract, of which 588 were excluded for not meeting the eligibility criteria. The full texts of

the remaining 24 articles were reviewed in detail, resulting in the exclusion of 15 studies for reasons specified in the diagram. Ultimately, nine studies were included in the final quantitative synthesis.

A

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Total (95% CI)			100.0%	1.36 [1.27, 1.46]

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)

B

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.2.1 BW variability				
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Subtotal (95% CI)			41.2%	1.45 [1.23, 1.70]

Heterogeneity: Tau² = 0.02; Chi² = 12.47, df = 3 (P = 0.006); I² = 76%
Test for overall effect: Z = 4.45 (P < 0.00001)

1.2.2 BMI variability				
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Subtotal (95% CI)			58.8%	1.34 [1.22, 1.48]

Heterogeneity: Tau² = 0.01; Chi² = 13.05, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 5.98 (P < 0.00001)

Total (95% CI)			100.0%	1.36 [1.27, 1.46]

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)
Test for subgroup differences: Chi² = 0.61, df = 1 (P = 0.43), I² = 0%

C

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.3.1 AD				
Lee et al., 2018	0.3074847	0.01876596	21.3%	1.36 [1.31, 1.41]
Roh et al., 2020	0.18232156	0.16035935	1.5%	1.20 [0.88, 1.64]
Kang et al., 2021 men	0.12221763	0.06752361	6.7%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	8.6%	1.31 [1.17, 1.46]
Park et al., 2022	0.28517894	0.01151032	24.1%	1.33 [1.30, 1.36]
Chen et al., 2022	0.60976557	0.23770961	0.7%	1.84 [1.15, 2.93]
Wang et al., 2024	0.56531381	0.23694502	0.7%	1.76 [1.11, 2.80]
Subtotal (95% CI)			63.6%	1.32 [1.27, 1.38]

Heterogeneity: Tau² = 0.00; Chi² = 10.90, df = 6 (P = 0.09); I² = 45%
Test for overall effect: Z = 13.05 (P < 0.00001)

1.3.2 VD				
Lee et al., 2018	0.41210965	0.04712605	10.8%	1.51 [1.38, 1.66]
Roh et al., 2020	0.37843644	0.08347268	4.8%	1.46 [1.24, 1.72]
Park et al., 2022	0.24686008	0.01993999	20.8%	1.28 [1.23, 1.33]
Subtotal (95% CI)			36.4%	1.40 [1.23, 1.59]

Heterogeneity: Tau² = 0.01; Chi² = 11.98, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 5.19 (P < 0.00001)

Total (95% CI)			100.0%	1.34 [1.29, 1.39]

Heterogeneity: Tau² = 0.00; Chi² = 23.18, df = 9 (P = 0.006); I² = 61%
Test for overall effect: Z = 14.36 (P < 0.00001)
Test for subgroup differences: Chi² = 0.67, df = 1 (P = 0.41), I² = 0%

Figure 2. Forest plot of the association between body weight or BMI variability and risk of dementia.

(A) Pooled analysis comparing the highest versus lowest variability categories shows that greater intra-individual variability in BW or BMI is significantly associated with increased dementia risk;

(B) Subgroup analysis by type of exposure (BW vs. BMI variability);

(C) Subgroup analysis by type of dementia (AD vs. VD).

A

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 Prospective				
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Subtotal (95% CI)			**40.2%**	**1.51 [1.35, 1.68]**

Heterogeneity: Tau² = 0.01; Chi² = 6.99, df = 5 (P = 0.22); I² = 29%
Test for overall effect: Z = 7.50 (P < 0.00001)

1.4.2 Retrospective				
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Subtotal (95% CI)			**59.8%**	**1.27 [1.20, 1.34]**

Heterogeneity: Tau² = 0.00; Chi² = 4.97, df = 3 (P = 0.17); I² = 40%
Test for overall effect: Z = 8.25 (P < 0.00001)

Total (95% CI)			**100.0%**	**1.36 [1.27, 1.46]**

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)
Test for subgroup differences: Chi² = 7.98, df = 1 (P = 0.005), I² = 87.5%

B

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.5.1 Only subjects ≥ 60 years				
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Subtotal (95% CI)			**53.3%**	**1.39 [1.22, 1.58]**

Heterogeneity: Tau² = 0.02; Chi² = 15.26, df = 5 (P = 0.009); I² = 67%
Test for overall effect: Z = 5.01 (P < 0.00001)

1.5.2 Subjects ≥ 40 years				
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Subtotal (95% CI)			**46.7%**	**1.36 [1.23, 1.51]**

Heterogeneity: Tau² = 0.01; Chi² = 40.51, df = 3 (P < 0.00001); I² = 93%
Test for overall effect: Z = 5.77 (P < 0.00001)

Total (95% CI)			**100.0%**	**1.36 [1.27, 1.46]**

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)
Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%

Figure 3. Subgroup analyses of the association between BW/BMI variability and dementia risk.

(A) Stratified by study design (prospective vs. retrospective);

(B) Stratified by baseline age of the study population (≥ 60 years vs. ≥ 40 years).

A

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
1.6.1 Men < 55%					
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]	
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]	
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]	
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]	
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]	
Subtotal (95% CI)			48.6%	1.43 [1.30, 1.56]	

Heterogeneity: Tau² = 0.00; Chi² = 7.56, df = 4 (P = 0.11); I² = 47%
Test for overall effect: Z = 7.74 (P < 0.00001)

1.6.2 Men ⩾ 55%					
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]	
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]	
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]	
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]	
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]	
Subtotal (95% CI)			51.4%	1.29 [1.18, 1.41]	

Heterogeneity: Tau² = 0.00; Chi² = 8.14, df = 4 (P = 0.09); I² = 51%
Test for overall effect: Z = 5.51 (P < 0.00001)

Total (95% CI)			100.0%	1.36 [1.27, 1.46]	

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)
Test for subgroup differences: Chi² = 2.55, df = 1 (P = 0.11), I² = 60.8%

0.5 0.7 1 1.5 2

B

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
1.7.1 Followed < 7 years					
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]	
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]	
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]	
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]	
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]	
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]	
Subtotal (95% CI)			71.8%	1.37 [1.25, 1.50]	

Heterogeneity: Tau² = 0.01; Chi² = 16.98, df = 5 (P = 0.005); I² = 71%
Test for overall effect: Z = 6.72 (P < 0.00001)

1.7.2 Followed ⩾ 7 years					
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]	
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]	
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]	
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]	
Subtotal (95% CI)			28.2%	1.42 [1.17, 1.72]	

Heterogeneity: Tau² = 0.02; Chi² = 4.94, df = 3 (P = 0.18); I² = 39%
Test for overall effect: Z = 3.58 (P = 0.0003)

Total (95% CI)			100.0%	1.36 [1.27, 1.46]	

Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 8.40 (P < 0.00001)
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² = 0%

0.5 0.7 1 1.5 2

Figure 4. Subgroup analyses of the association between BW/BMI variability and dementia risk.

(A) Stratified by the proportion of male participants (<55% vs. ⩾55%);

(B) Stratified by follow-up duration (<7 years vs. ⩾7 years).

A

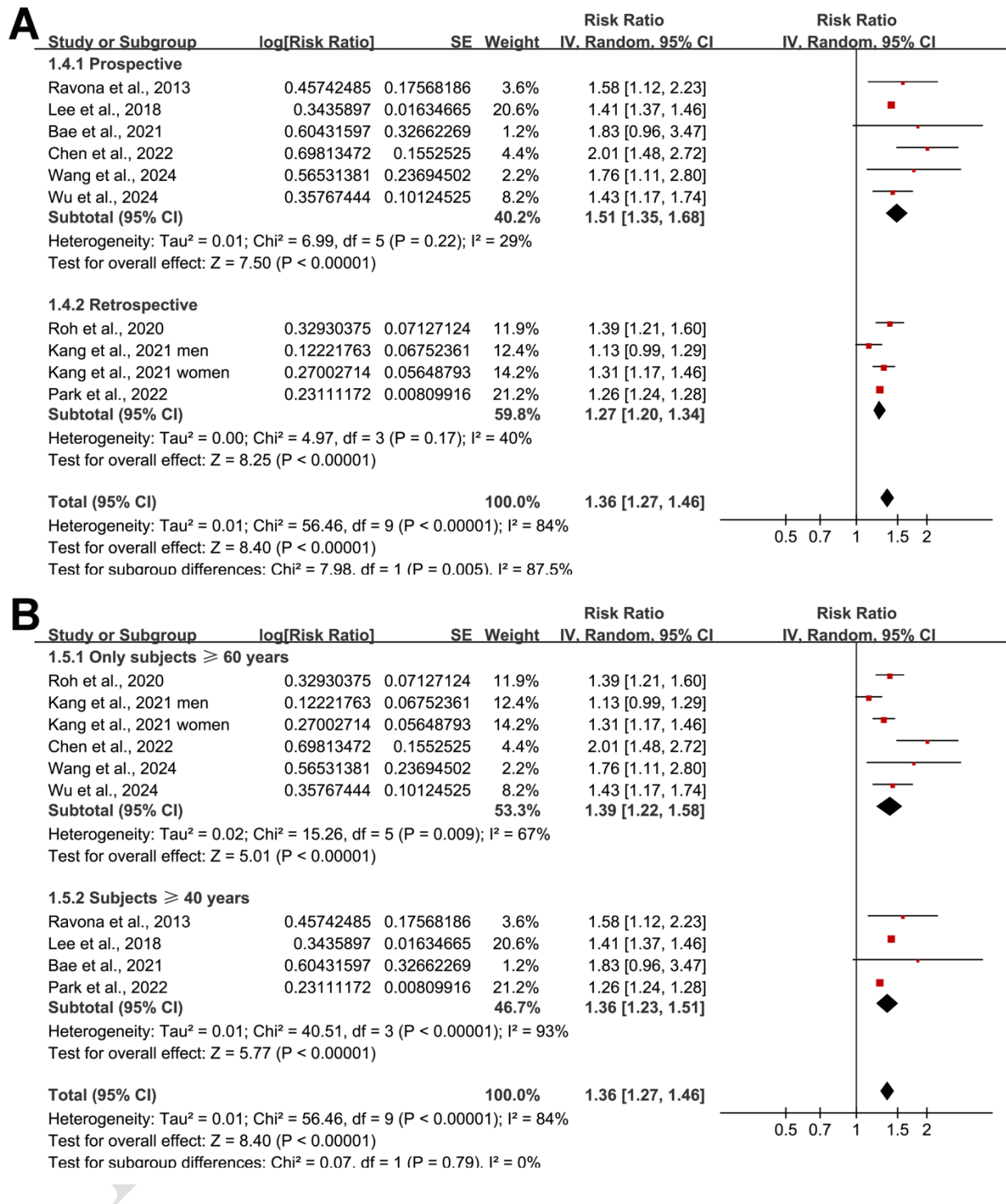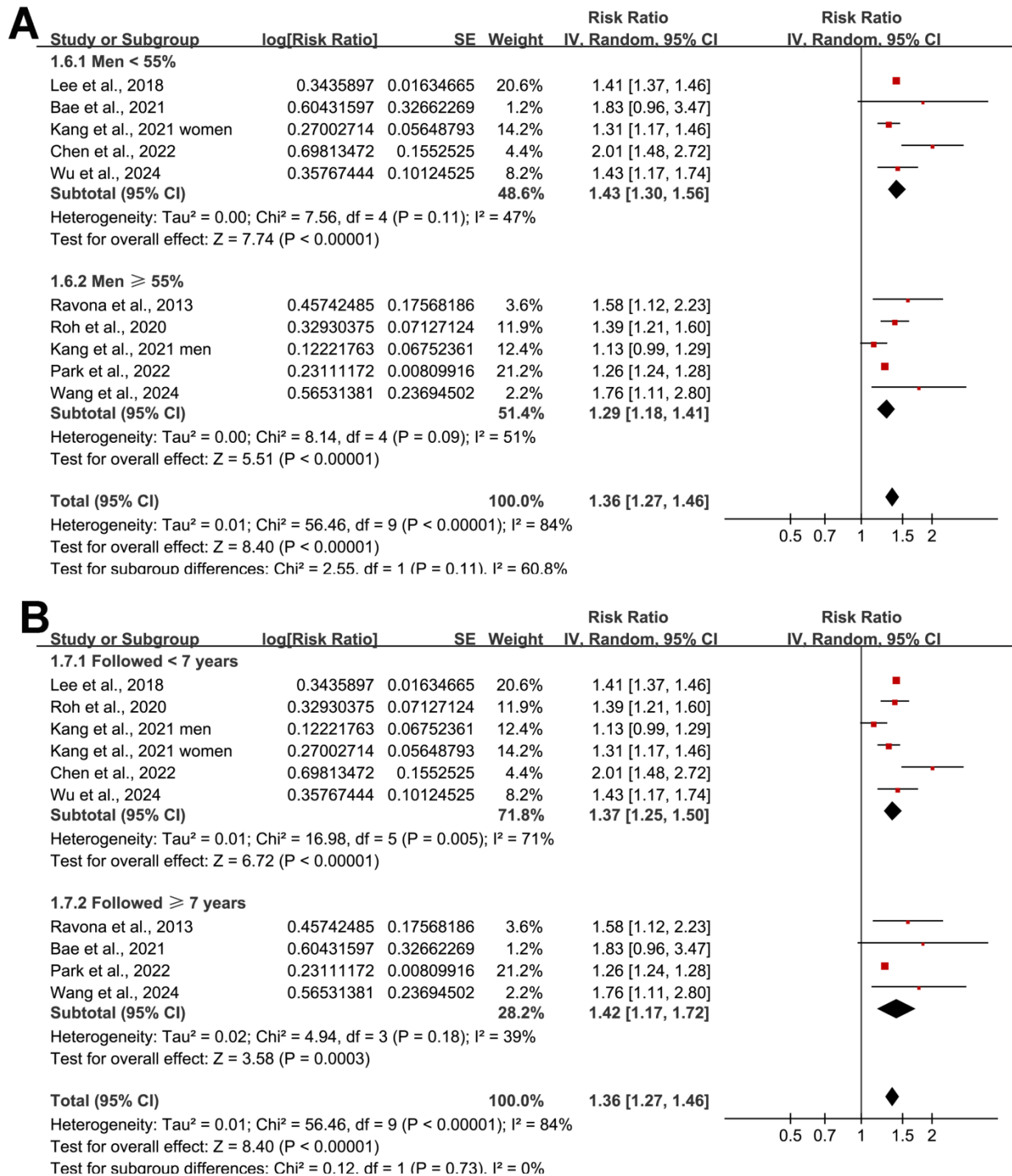| Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.8.1 Clinical evaluation				
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Subtotal (95% CI)			**15.2%**	**1.52 [1.30, 1.77]**
Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 3 (P = 0.77); I² = 0%				
Test for overall effect: Z = 5.22 (P < 0.00001)				
1.8.2 ICD codes or self/proxy reported				
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Subtotal (95% CI)			**84.8%**	**1.33 [1.23, 1.44]**
Heterogeneity: Tau² = 0.01; Chi² = 51.21, df = 5 (P < 0.00001); I² = 90%				
Test for overall effect: Z = 7.17 (P < 0.00001)				
Total (95% CI)			**100.0%**	**1.36 [1.27, 1.46]**
Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%				
Test for overall effect: Z = 8.40 (P < 0.00001)				
Test for subgroup differences: Chi² = 2.10, df = 1 (P = 0.15), I² = 52.3%				

0.5 0.7 1 1.5 2

B

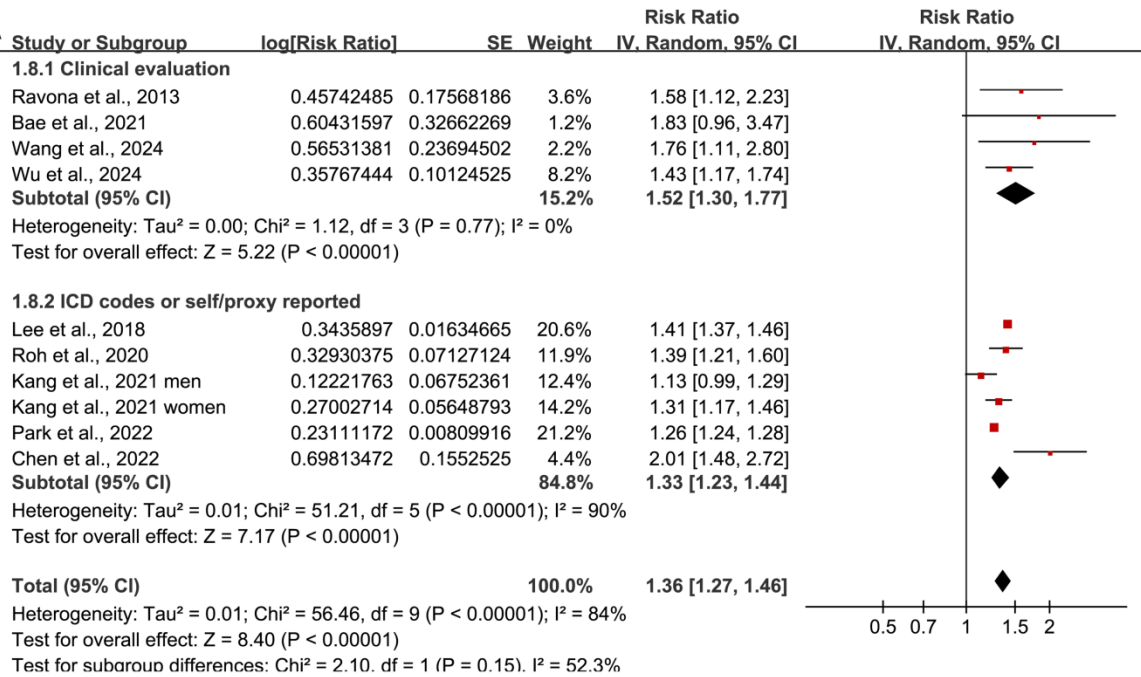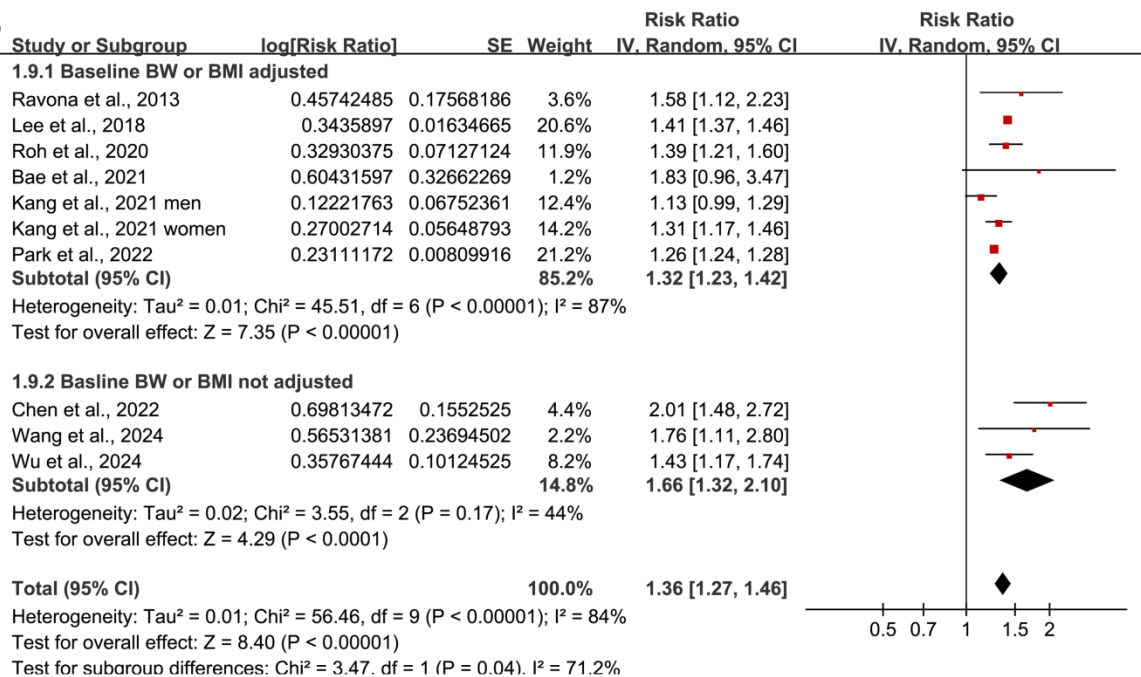| Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.9.1 Baseline BW or BMI adjusted				
Ravona et al., 2013	0.45742485	0.17568186	3.6%	1.58 [1.12, 2.23]
Lee et al., 2018	0.3435897	0.01634665	20.6%	1.41 [1.37, 1.46]
Roh et al., 2020	0.32930375	0.07127124	11.9%	1.39 [1.21, 1.60]
Bae et al., 2021	0.60431597	0.32662269	1.2%	1.83 [0.96, 3.47]
Kang et al., 2021 men	0.12221763	0.06752361	12.4%	1.13 [0.99, 1.29]
Kang et al., 2021 women	0.27002714	0.05648793	14.2%	1.31 [1.17, 1.46]
Park et al., 2022	0.23111172	0.00809916	21.2%	1.26 [1.24, 1.28]
Subtotal (95% CI)			**85.2%**	**1.32 [1.23, 1.42]**
Heterogeneity: Tau² = 0.01; Chi² = 45.51, df = 6 (P < 0.00001); I² = 87%				
Test for overall effect: Z = 7.35 (P < 0.00001)				
1.9.2 Basline BW or BMI not adjusted				
Chen et al., 2022	0.69813472	0.1552525	4.4%	2.01 [1.48, 2.72]
Wang et al., 2024	0.56531381	0.23694502	2.2%	1.76 [1.11, 2.80]
Wu et al., 2024	0.35767444	0.10124525	8.2%	1.43 [1.17, 1.74]
Subtotal (95% CI)			**14.8%**	**1.66 [1.32, 2.10]**
Heterogeneity: Tau² = 0.02; Chi² = 3.55, df = 2 (P = 0.17); I² = 44%				
Test for overall effect: Z = 4.29 (P < 0.0001)				
Total (95% CI)			**100.0%**	**1.36 [1.27, 1.46]**
Heterogeneity: Tau² = 0.01; Chi² = 56.46, df = 9 (P < 0.00001); I² = 84%				
Test for overall effect: Z = 8.40 (P < 0.00001)				
Test for subgroup differences: Chi² = 3.47, df = 1 (P = 0.04), I² = 71.2%				

0.5 0.7 1 1.5 2

Figure 5. Subgroup analyses by methodological characteristics.

(A) Stratified by method of dementia diagnosis (clinical assessment vs. ICD codes or self/proxy report);

(B) Stratified by whether baseline body weight or BMI was adjusted in the analysis.

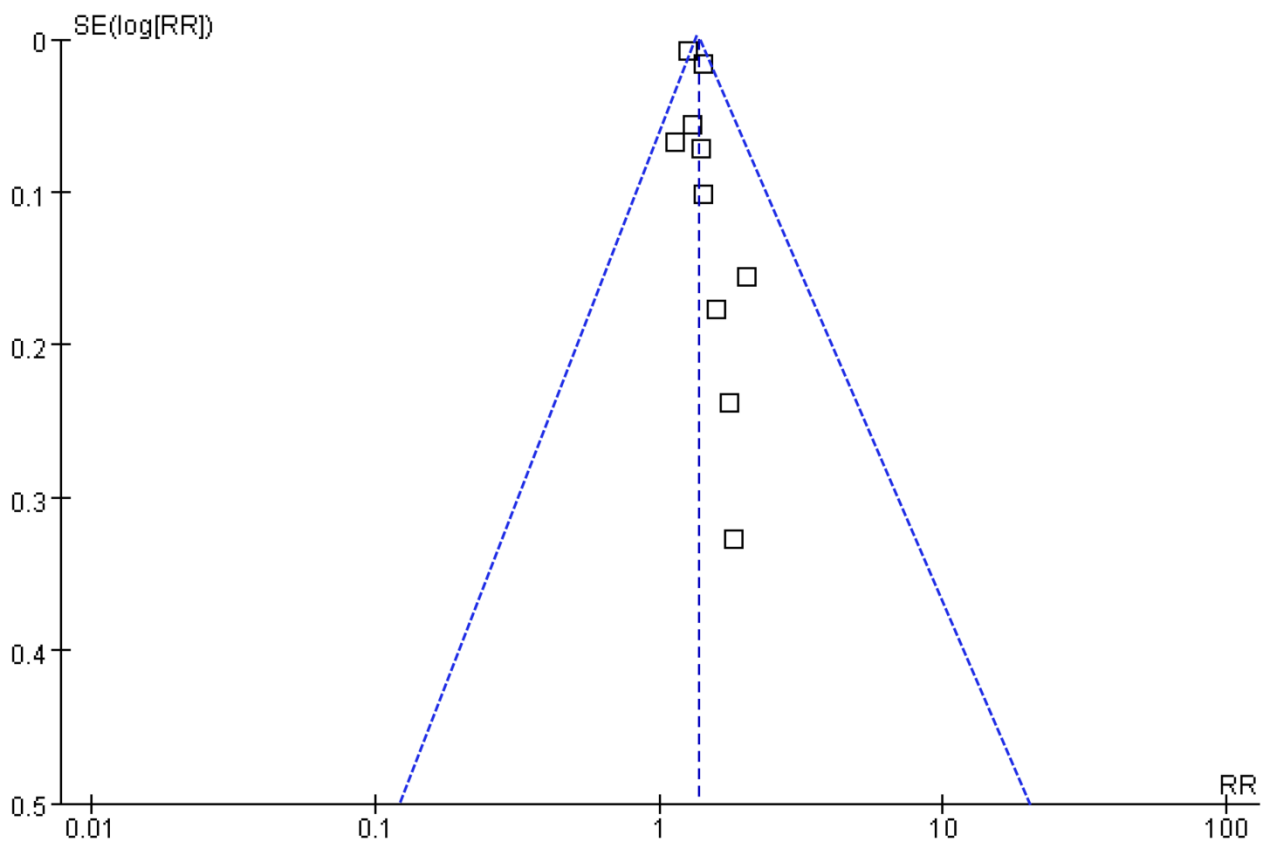A stronger association was observed in studies that did not adjust for baseline BW/BMI.

Figure 6. Funnel plot assessing publication bias.

Funnel plot of studies evaluating the association between BW/BMI variability and dementia risk. Visual symmetry suggests low risk of publication bias, supported by Egger's regression test ($p = 0.22$).

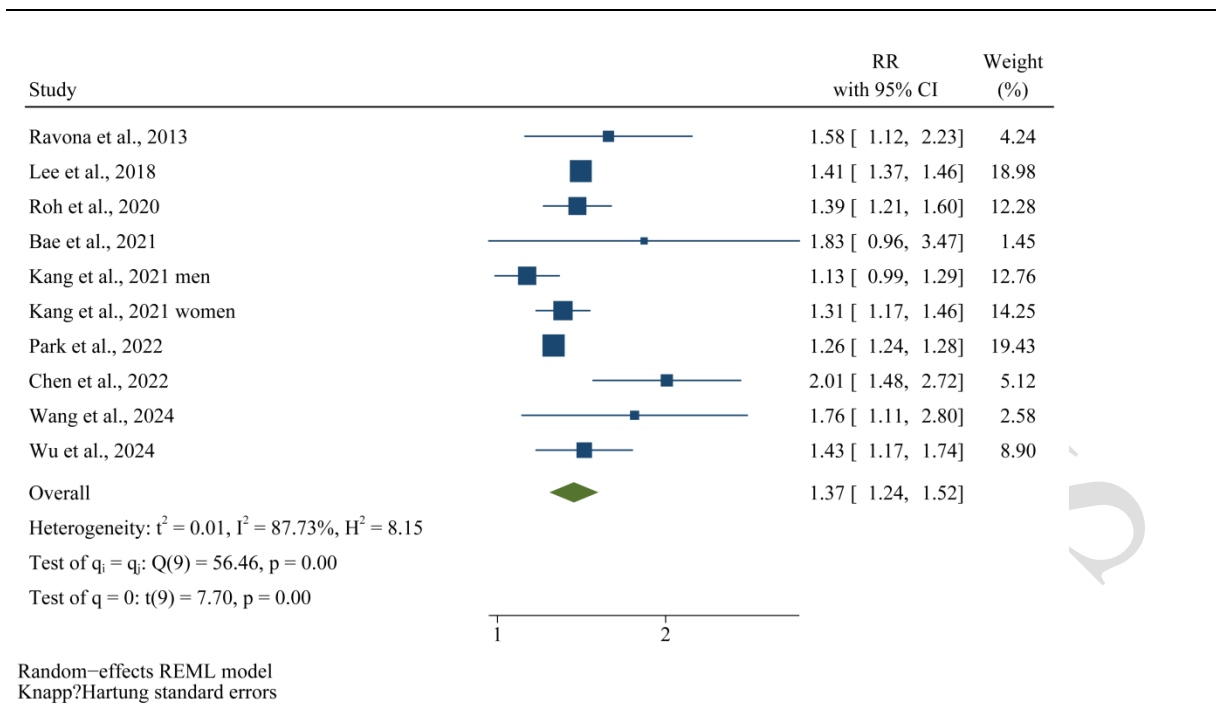**Supplemental File 1 Detailed search strategy for each database**

PubMed

("Body Weight"[Mesh] OR "Body Mass Index"[Mesh] OR "body weight" OR "body mass index" OR BMI) AND ("Variability" OR "variation" OR "fluctuation" OR "oscillation" OR "fluctuate") AND ("Dementia"[Mesh] OR "Alzheimer Disease"[Mesh] OR dementia OR Alzheimer OR "Alzheimer's" OR "cognitive decline" OR "cognitive impairment" OR "cognitive dysfunction" OR cognition) AND ("Prospective Studies"[Mesh] OR prospective OR prospectively OR longitudinal OR incident OR incidence OR risk OR followed OR "follow-up" OR cohort)

Embase

('body weight'/exp OR 'body mass index'/exp OR 'body weight' OR 'body mass index' OR BMI) AND ('variability' OR 'variation' OR 'fluctuation' OR 'oscillation' OR 'fluctuate') AND ('dementia'/exp OR 'Alzheimer disease'/exp OR dementia OR Alzheimer OR "Alzheimer's" OR 'cognitive decline' OR 'cognitive impairment' OR 'cognitive dysfunction' OR cognition) AND ('prospective study'/exp OR prospective OR prospectively OR longitudinal OR incident OR incidence OR risk OR followed OR 'follow-up' OR cohort)

Web of Science

TS=("body weight" OR "body mass index" OR BMI) AND TS=("variation" OR "variability" OR "fluctuation" OR "oscillation" OR "fluctuate") AND TS=("dementia" OR "Alzheimer" OR "Alzheimer's" OR "cognitive decline" OR "cognitive impairment" OR "cognitive dysfunction" OR "cognition") AND TS=("prospective" OR "prospectively" OR "longitudinal" OR "incident" OR "incidence" OR "risk" OR "followed" OR "follow-up" OR "cohort")

Study		RR with 95% CI	Weight (%)
Ravona et al., 2013		1.58 [1.12, 2.23]	4.24
Lee et al., 2018		1.41 [1.37, 1.46]	18.98
Roh et al., 2020		1.39 [1.21, 1.60]	12.28
Bae et al., 2021		1.83 [0.96, 3.47]	1.45
Kang et al., 2021 men		1.13 [0.99, 1.29]	12.76
Kang et al., 2021 women		1.31 [1.17, 1.46]	14.25
Park et al., 2022		1.26 [1.24, 1.28]	19.43
Chen et al., 2022		2.01 [1.48, 2.72]	5.12
Wang et al., 2024		1.76 [1.11, 2.80]	2.58
Wu et al., 2024		1.43 [1.17, 1.74]	8.90
Overall		1.37 [1.24, 1.52]	

Heterogeneity: $t^2 = 0.01$, $I^2 = 87.73\%$, $H^2 = 8.15$

Test of $q_i = q_j$: Q(9) = 56.46, p = 0.00

Test of q = 0: t(9) = 7.70, p = 0.00

Random−effects REML model
Knapp?Hartung standard errors

Supplemental Figure 1. Forest plots for the sensitivity analysis using the HKSJmethod with REML estimation.

The figure presents a sensitivity analysis of the association between high variability in body weight or BMI and risk of dementia. Using the HKSJ method with REML estimation, the pooled risk ratio was 1.37 (95% CI: 1.24–1.52; $p < 0.001$), with substantial heterogeneity across studies ($I^2 = 87\%$), confirming the robustness of the main findings.

HKSJ: Hartung-Knapp-Sidik-Jonkman; REML: Restricted Maximum Likelihood; BMI: Body Mass Index; CI: Confidence Interval; RR: Risk Ratio; I^2: I-squared (measure of heterogeneity).

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