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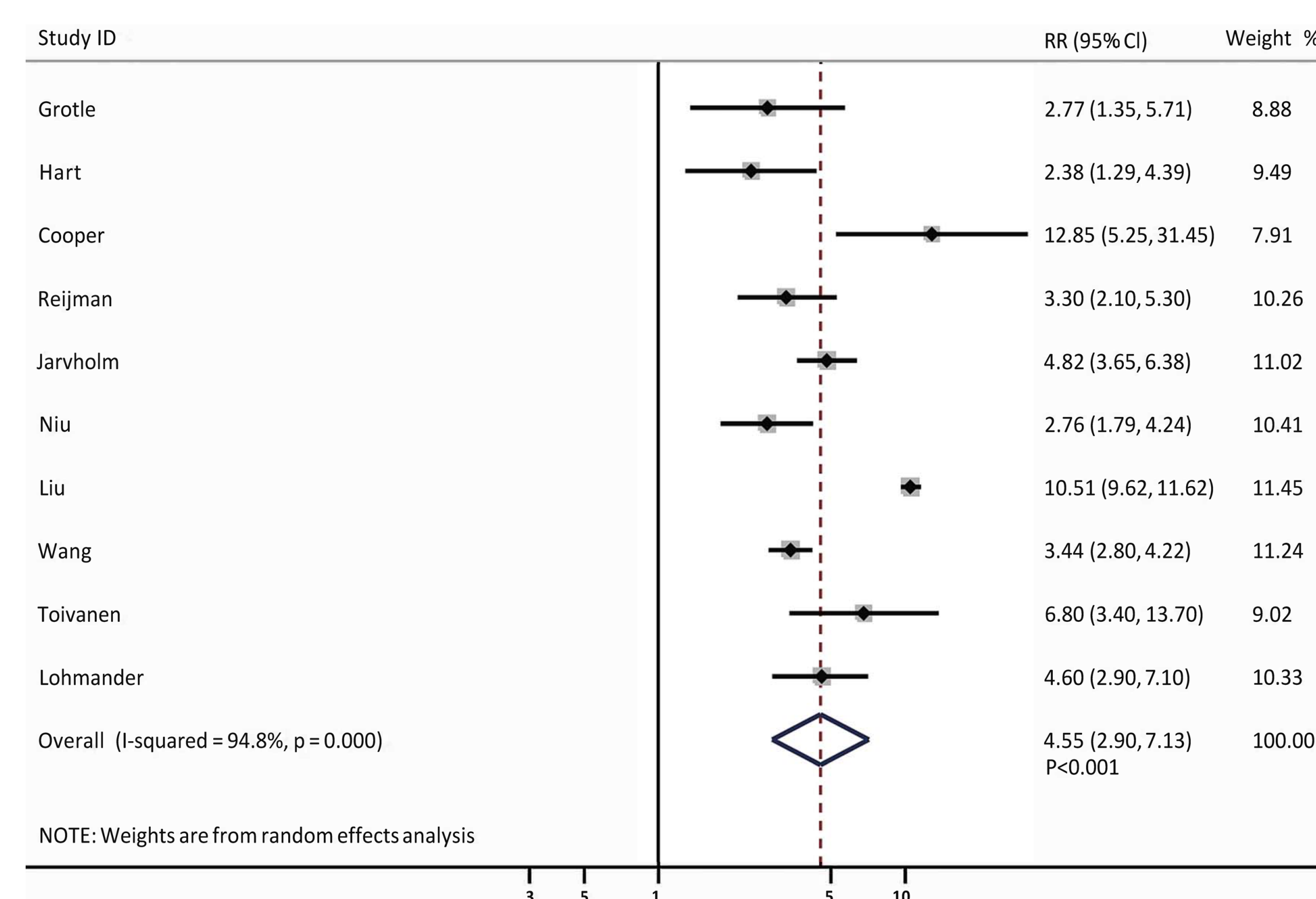
INTRODUCTION

- Currently, nearly 75% of Americans are overweight or obese, with approximately 42% considered obese^{1,2}
 - By 2050, 80% of U.S. adults (213M) will be overweight or obese²
- Obesity is a serious, chronic, multisystem disease that can contribute to the development of a myriad of comorbidities such as cancer, cardiovascular disease, chronic pain, dementia, diabetes, liver disease, and osteoarthritis (OA)³
- Obesity-related comorbidities are associated with considerable per patient direct costs (2025 USD):
 - Cancer: ~\$52,800 annually (initial phase)³
 - Dementia: ~\$49,000 annually⁵
 - Diabetes: ~\$13,600 annually⁶
 - Knee OA: ~\$7,700 (1st year)⁷
 - Nonalcoholic fatty liver disease (NAFLD) ~\$4,400 (1st year)⁸
- Anti-obesity medications (AOM; i.e., incretin mimetics) have the potential to prevent and/or help manage a diverse set of chronic health conditions that are associated with significant economic burden

KEY RESULTS: OBESITY IS ASSOCIATED WITH MULTIPLE CHRONIC COMORIBIDITIES, WITH RELATIVE RISK INCREASING UP TO 4.5X COMPARED TO NORMAL WEIGHT

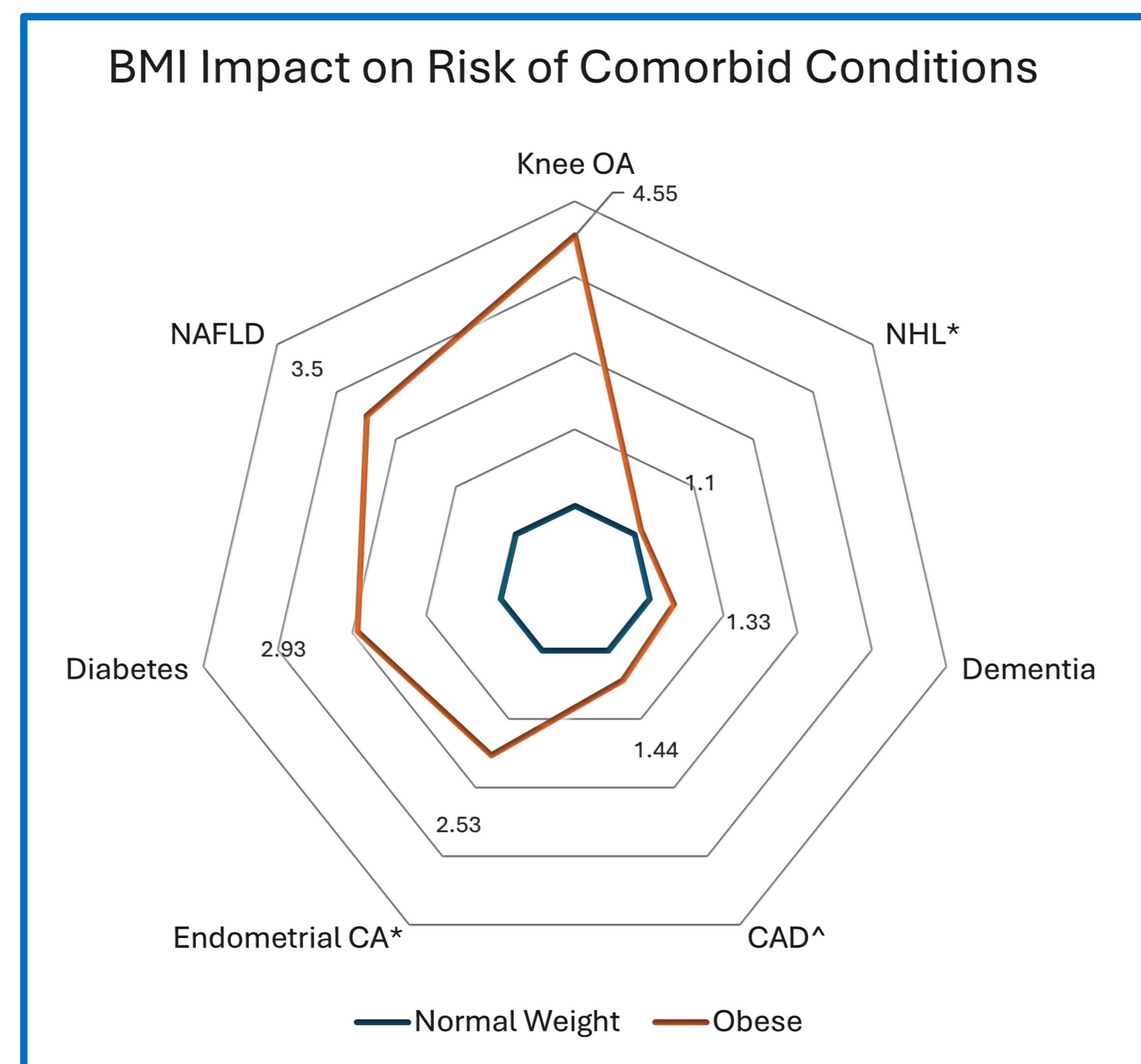
KNEE OSTEOARTHRITIS¹⁴ (14 studies)

- Overweight and obesity were significantly associated with higher knee OA risk
 - RR overweight: 2.45 (1.88, 3.20)
 - RR obese: 4.55 (2.90, 7.13)



NONALCOHOLIC FATTY LIVER DISEASE¹³ (21 studies)

- Compared with normal weight, obesity was associated with a 3.5-fold increased risk of developing NAFLD [RR 3.53 (2.48, 5.03) $P < 0.001$]
- Dose-dependent relationship between BMI and NAFLD risk; per 1-unit increase in BMI, RR 1.20 (1.14, 1.26) $P < 0.001$



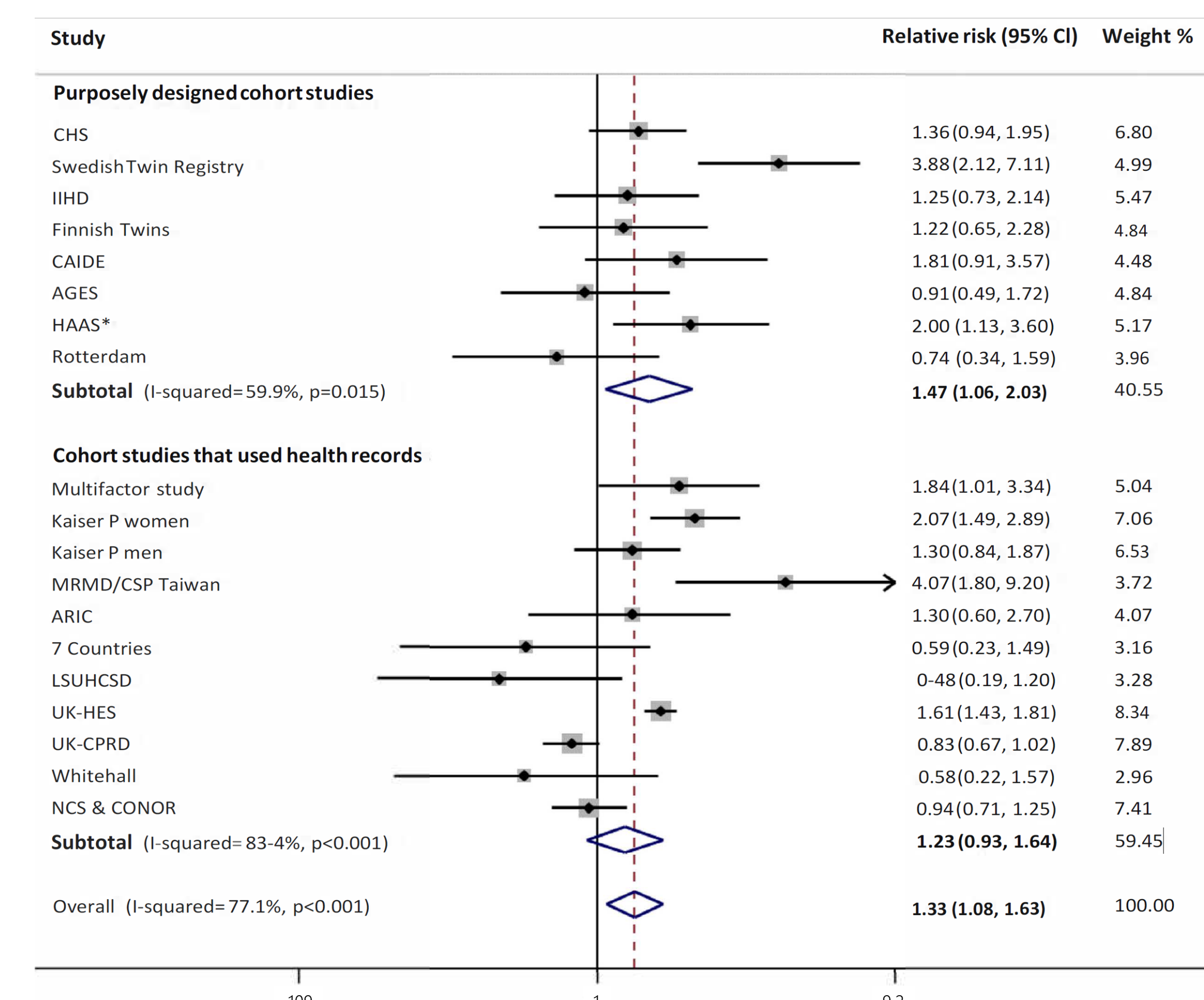
CA, cancer; CAD, coronary artery disease; NHL, non-Hodgkin lymphoma; NAFLD, nonalcoholic fatty liver disease; OA, osteoarthritis; SD, standard deviation.
*Based on a 2-SD increase (1-SD = 5 kg/m²) in BMI (~35 kg/m²).
*Represent range of risk ratios for 19 cancer types with significantly increased risk; BMI of 35 kg/m².

DIABETES¹⁰ (91 studies)

- Overall diabetes incidence among adults with overweight/obesity was 10.5 (9.3, 11.8) per 1000 person-years (PY) vs 2.7 (2.2, 3.3) for normal weight
 - Incidence increased from ~6 per 1000 PY in 1985 to 11 per 1000 PY between 1995 and 2000, and remained stable between 2000 and 2010
 - After 2010, diabetes incidence in overweight/obese spiked to 16.4 per 1000 PY compared to 5.6 per 1000 PY in normal weight adults
- Obesity is associated with almost 3 times the risk of diabetes compared to normal weight adults

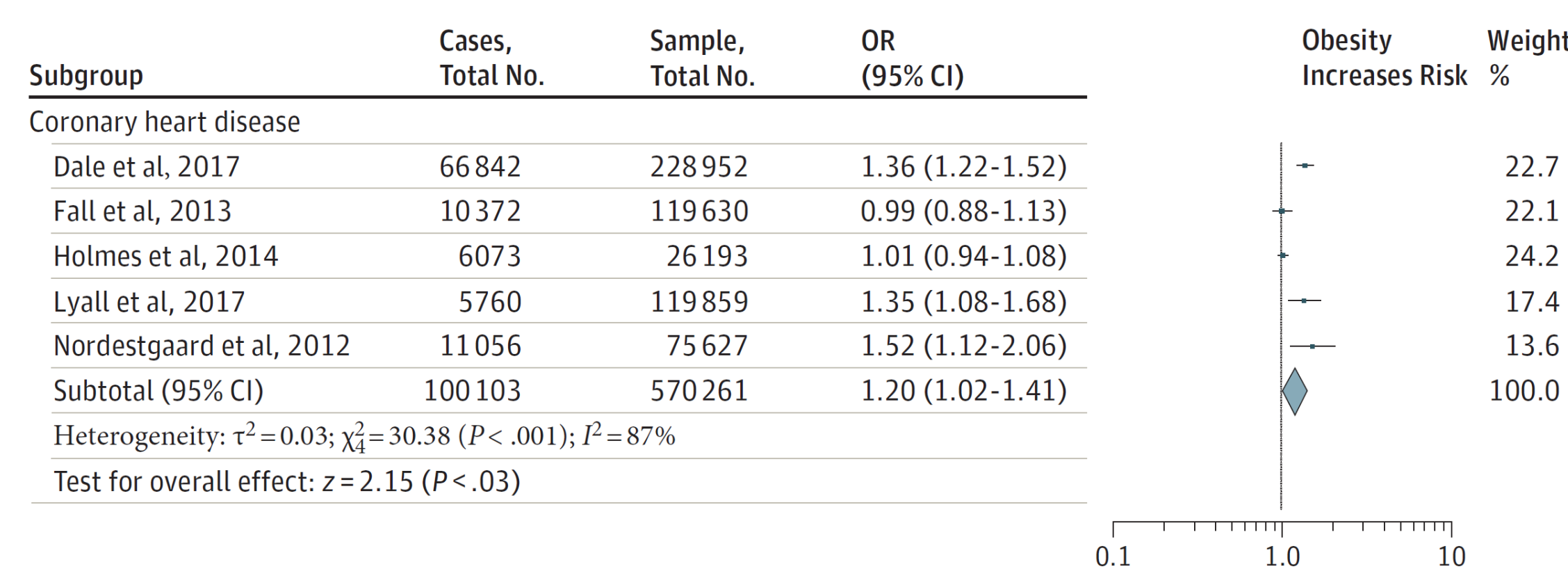
DEMENTIA¹¹ (19 studies)

- Midlife (35-65 years) obesity (BMI ≥ 30) was associated with dementia in late life (≥ 65 years)
- Risk of dementia with midlife obesity was 33% higher than no midlife obesity [RR 1.33 (1.08, 1.63)]



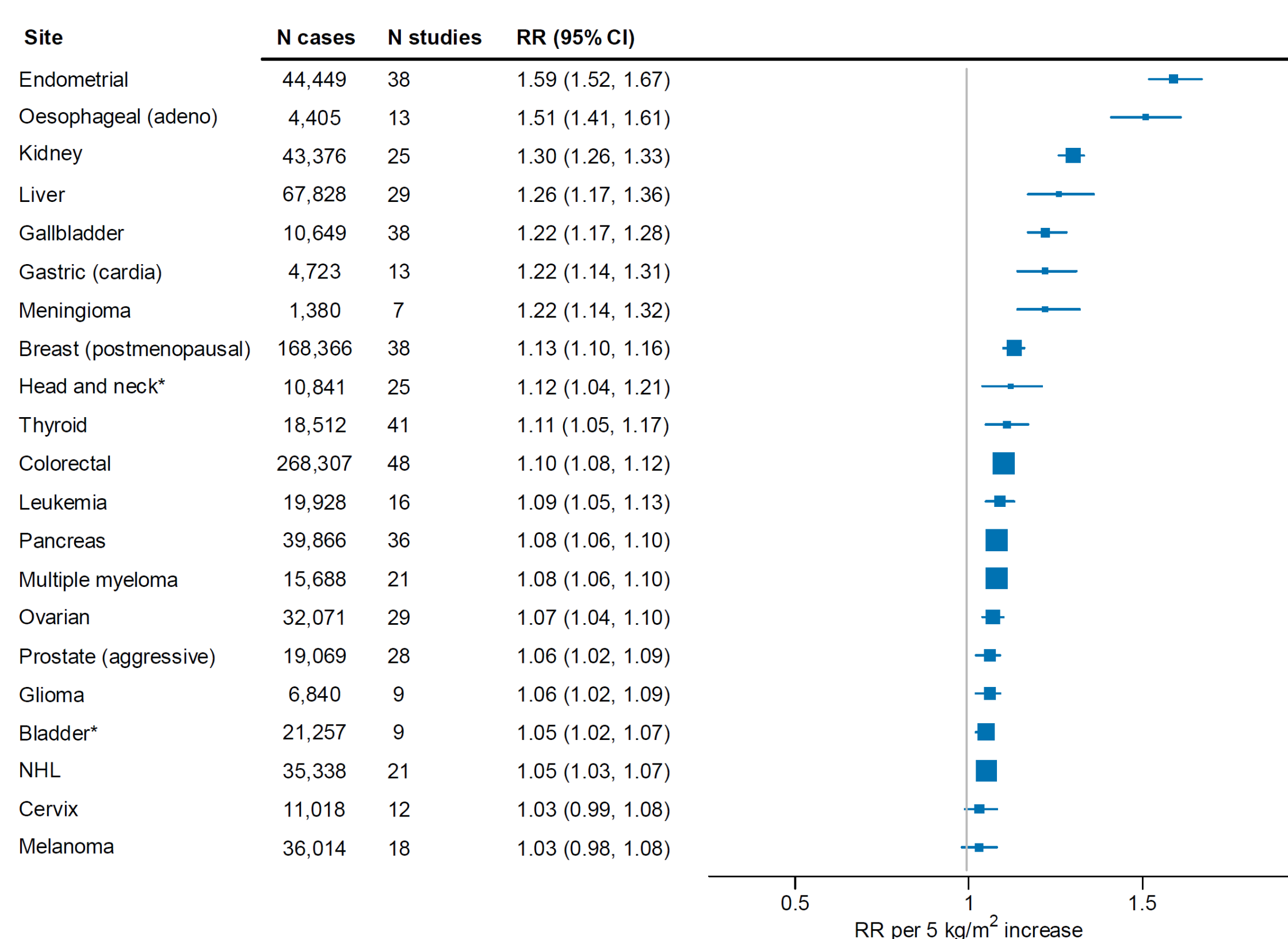
CORONARY ARTERY DISEASE¹² (5 studies)

- Meta-analysis, including Mendelian randomization studies to minimize bias between association of obesity and cardiovascular outcomes
- Each 1-SD increase in BMI increased the odds of CAD by 20%



CANCER⁹ (250 studies)

- Higher BMI was significantly associated with increased risk of 19 cancers
- RR (95% CI) per 5 kg/m² BMI increase, range:
 - 1.05 (1.03, 1.07) for non-Hodgkin lymphoma
 - 1.59 (1.52, 1.67) for endometrial cancer



OBJECTIVE

The objective of this study was to quantify the risk of obesity-related chronic comorbidities, including cancer, cardiovascular disease, dementia, diabetes, liver disease, and OA in adults

METHODS

- A narrative literature (i.e., systematic review, meta-analyses) review was conducted for publications that focus on the effect of obesity on related comorbidities (cancer, cardiovascular disease, dementia, diabetes, liver disease, and OA) in adults
- Publication dates between 2014 and 2024 were selected
- Non-English language articles were excluded
- Risk ratios (RR) are shown with 95% CI in parentheses
- RR greater than 1 fall to left of solid line in figures, red dashed lines indicate overall risk from analysis

CONCLUSIONS

- Obesity, a multisystem disease, is forecasted to increase globally by 68.3% by 2050²
- Obesity is associated with an increased risk of a myriad of chronic comorbidities secondary to mechanical stress, chronic inflammation, and metabolic impacts
- Reduction in BMI has been associated with improved health outcomes^{15, 16} and reduced healthcare costs¹⁷
- While lifestyle-based interventions alone have demonstrated limited success with weight loss, incretin mimetics present a potentially effective option to address obesity / overweight and associated chronic comorbid conditions
- Accounting for the reduced risk of chronic comorbidities associated with obesity will more accurately assess the potential clinical and economic value of novel AOMs
- Further research is needed to examine the relationship among obesity-related conditions and the impact of AOMs in the real-world

Disclosures

KC, MM, KM, SJ, and BL are employees of Viking Therapeutics, Inc.
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