Tang X, Liu G, et al. Obesity and risk of hip fracture in adults: a meta-analysis of prospective cohort studies. PLoS One. 2013 Apr 12;8(4):e55077.

Design: systematic review and meta-analysis of prospective cohort studies

Purpose of study: to estimate the association between obesity and risk of hip fracture from the available published prospective cohort studies

Brief summary of methods and findings:

- Because the meta-analysis is done on observational studies and there is no "intervention" under consideration, the only considerations are patient population, comparison, and outcome
- Population: adults at risk of hip fracture, presumably drawn from the general population of the countries in which the studies were conducted
    - Separate analyses were done when possible in men and in women
- Comparison: obesity versus non-obesity
    - For the majority of studies, obesity was defined as a BMI of 30 or greater, although this was not a selection criterion for study inclusion
- Outcomes: Hip fracture
    - Osteoporotic fractures were presumably the primary outcome of interest, but this was not a criterion for study selection
- Study types: prospective cohort studies only

Study selection:

- Search was conducted in PubMed and in EMBASE through May 6 of 2012
- Two authors independently conducted the study selection and data extraction, assessing quality with the Newcastle Ottawa scale for observational studies
    - The Newcastle Ottawa scale rates cohort studies on representativeness of the exposed cohort in the community, on selection of the non-exposed cohort being drawn from the same community as the exposed cohort, on ascertainment of exposure (highest score from secure records such as medical records), demonstration that the outcome of interest was not present at the start of the study, on assessment of outcome (independent blind assessment is the best), long enough followup for outcomes to occur, adequacy of followup of cohorts, and on comparability of the exposed and non-exposed cohorts (must be matched in the design and/or confounders must be adjusted for in the analysis)
- The common measure of association between obesity and hip fracture was the relative risk (RR) with its 95% confidence interval (95% CI)

Results:

- 23 full-text papers were initially included for the analysis, and after exclusion of 10 studies for not meeting all inclusion criteria, 15 studies were selected for the meta-analysis, with a total of 3,126,313 subjects
- Mean length of followup ranged from 1 to 16.4 years, and the size of the cohorts ranged from 3050 to 1,039,878
- There was substantial heterogeneity among the studies, but a significantly decreased risk for hip fracture was seen in the meta-analysis which took the heterogeneity into account
    - The RR for all included studies was 0.66 with 95% CI from 0.57 to 0.77, indicating that the risk of hip fracture for obese people is about 66% that of non-obese people, a relative risk reduction of one third
    - A subgroup analysis was done for the studies which adjusted for such factors as age, physical activity, diabetes, smoking, alcohol intake, and oral steroid use
        - For this adjusted analysis the RR was 0.48 with 95% CI from 0.39 to 0.58, indicating that when potential confounders are adjusted for, the risk reduction associated with obesity is greater than for the unadjusted analysis, and that the risk of hip fracture in obese persons is about half that of nonobese persons
- Subgroup analyses for men and for women both showed significantly reduced risk of hip fracture (RR of 0.54 for men and 0.70 for women)
- There was no obvious publication bias in the included studies; the size of the risk reduction in a particular did not seem to affect the likelihood that the study would be published or not published

Authors' conclusions:

- Obesity significantly reduces the risk of hip fracture in adults, and is probably a protective factor of hip fracture
- This may be related to increased bone mineral density associated with increasing BMI

Comments:

- Although the studies were not randomized trials, the prospective cohort design is suitable for estimating the association between potentially protective or adverse risk factors and health outcomes in settings in which patients cannot be randomized
- Although there was substantial heterogeneity in the estimate of the relative risks, it is clear from Figure 2, for the analyses of the adjusted RR, that all of the studies show a substantial reduction in the risk of hip fracture, and the heterogeneity arises from differences in the magnitude of the risk reduction, not from its presence or absence
- Even though there are potential risks of bias from confounders in cohort studies, the number of subjects, in excess of 13 million, and the substantial reduction in risk

which the pooled analysis yields, mean that confounding is extremely unlikely to account for the RR seen

- In the “study characteristics” paragraph of the Results section, there is an apparent error, where the authors state that the size of the cohorts ranged from 3050 to 9006; the largest study had over one million subjects
- One potential confounder not accounted for was race; African-American women tend to have higher BMI than white women, and their risk of osteoporotic fracture is also lower; however, if this had been adjusted for, it is likely that only a small change would have been seen in the pooled RR of hip fracture

Assessment: High quality meta-analysis with strong evidence that in adults at risk of hip fracture, obesity, defined as a BMI of 30 or greater, is associated with a substantial reduction in the risk of hip fracture compared to non-obese persons

Reference:

The Newcastle-Ottawa scale for case-control studies is online at
http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf