

## RE: Weight Gain After Breast Cancer Diagnosis and All-Cause Mortality: Systematic Review and Meta-Analysis

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In the meta-analysis by Playdon et al. (1) in the Journal, the authors conclude,

“Weight gain after diagnosis of breast cancer is associated with higher all-cause mortality rates compared with maintaining body weight. Adverse effects are greater for weight gains of 10.0% or higher.” We believe this is a misleading oversimplification meant to align with the authors’ a priori definition of weight gain ( $\geq 5.0\%$  body weight) that does not accurately reflect the data. By the authors’ own presentation of the analysis stratified by level of weight gain (Figure 3), there is clear evidence of heterogeneity of the overall effect for moderate compared with high weight gain ( $P = .009$ ), with the increase in risk of death limited to those who gained more than 10% of their pre-diagnosis weight. Neither our individual studies nor the current meta-analysis showed any increase in mortality risk associated with moderate weight gain (hazard ratio = 0.97, 0.86 to 1.11). Thus, the implication that all levels of weight gain impact mortality may lead the casual reader or the popular press coverage read by women or providers to erroneously conclude that even modest changes in weight increase risk of death after a breast cancer diagnosis.

Additional methodological limitations further make these results difficult to interpret. Importantly, a substantial source of qualitative heterogeneity was largely ignored—time since diagnosis. For example, in the Long Island Breast Cancer Study cohort, mortality risk according to weight gain varied substantially according to the timing of weight gain, with an attenuation of the association of weight gain after two years postdiagnosis (2). The median weight assessment in studies analyzed by Playdon et al. was 1.5 years from diagnosis. If stratified by timing of weight gain, a different picture may have emerged.

The authors also pooled estimates from studies that used exposure measures beyond percent weight change, including absolute weight change, change relative to the median weight change, or

percent body mass index change. For an adult woman who weighs the US average of 75.6kg (166.2 pounds [3]), a 5% weight change equals 3.8kg gained. In the methods used to harmonize the Collaborative Women’s Longevity Study (CWLS) (4), weight gain of more than 2kg was analyzed as “moderate” weight gain; although in the example above, those in the 2 to 3.7kg range (4.4–8.2 lbs) should ideally be classified as weight stable. The harmonization of diverse exposure metrics could result in misclassification, particularly at the thresholds for moderate and high weight gain.

The topic of postdiagnosis weight gain and its effect on mortality has been, and continues to be, of great interest. Systematic reviews of the literature may be useful in the qualitative synthesis of results and to evaluate the current state of the science. However, quantitative summaries (meta-analyses) must be conducted and interpreted carefully in order to be meaningful. Quantitative measures of heterogeneity, while useful, cannot substitute for an appreciation of differences in study designs and exposure categorizations. Pooled measures of effect are warranted only when the reader can be assured that the combined estimate is meaningful and the included studies are sufficiently homogeneous.

### References

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