

Biomarker-Calibrated Measurements Reinforce Importance of Diet and Exercise

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Common advice for lowering disease risk is to exercise regularly and eat a well-balanced diet. Due to measurement error, however, it can be difficult for researchers to get accurate measurements of these factors for evaluating the associations between energy balance and disease risk. To increase the accuracy of these measurements, biomarker data can be utilized to calibrate self-reported energy intake and expenditure. In a recent report in the *American Journal of Epidemiology*, Drs. Cheng Zheng and Ross Prentice and colleagues in the Public Health Sciences Division evaluated the association between such biomarker-calibrated measurements and disease risk. These analyses demonstrated that the risks for each of cardiovascular disease, cancer, and diabetes were raised by increases in energy consumption and lowered by increases in energy expenditure.

To assess these associations, the investigators utilized data available from the Women's Health Initiative (WHI). To calculate the biomarker-calibrated measurements, the authors combined self-reported questionnaire data on diet and exercise with objective laboratory measurements of energy intake and expenditure. Total energy consumption was measured using a doubly labeled water biomarker assessment. This technique replaces water molecules with non-radioactive isotopes, and then measures the metabolic rate of clearance after consumption. Total activity-related energy expenditure was calculated by taking this biomarker-based estimate of total energy consumption and subtracting resting energy expenditure, as measured by indirect calorimetry. Importantly, body mass index measurements were included in the calibration equations to provide information on long term energy intake, output, and balance.

These biomarker-calibrated exposures were then evaluated for their impact on disease risk within WHI. For most of the diseases assessed, a twenty percent increase in total energy consumption was associated with significantly higher risk, while a twenty percent increase in activity-related energy expenditure was associated with significantly lower risk (see figure). Said senior author Dr. Prentice, "this work strongly suggests that diet and activity patterns over the lifespan may be major drivers of total and site-specific cancers, major cardiovascular diseases, and especially diabetes, among women in the WHI cohort study."

In contrast to these strong results, corresponding estimated hazard ratios using only the self-report measures of energy and activity showed little or no association with these diseases. This demonstrates the importance of using objective biomarker measures to correct self-reported assessments of these variables for measurement error. Said Prentice, "these findings can be expected to reinvigorate the diet/physical activity and chronic disease research agenda." Given these results, "biomarkers are sorely needed for additional aspects of diet (such as specific nutrients and foods) and activity (such as intensity and duration categories)."

Following up on their success at calibrating variables for energy and activity, the authors are planning to next apply this biomarker-calibration approach to other exposure measurements. Said Dr. Prentice, "working with several PHS colleagues, including Johanna Lampe, Marian Neuhouser, Lesley Tinker and Shirley Beresford, we have recently completed a feeding study among 153 WHI women in the Seattle area for the purpose of new nutritional biomarker development. The idea here is to use blood and urine measures to explain variation in the intake of foods or nutrients that were provided to women during their two-week feeding period. The most promising analyses so far involve the use of these specimens to derive both targeted and global metabolomic profiles. These profiles are developed in the laboratory of our colleague Dan Raftery, who is based in the UW Medical School. Preliminary analyses suggest that both blood and urine may be needed for reliable intake assessment, with additional implications for the conduct of future cohort studies that aim to contribute to the vitally important nutrition and physical activity research area."

Other PHS investigators contributing to this project were Drs. Lesley Tinker, Marian Neuhouser, Shirley Beresford, and Chongzhi Di.

[Zheng C, Beresford SA, Van Horn L, Tinker LF, Thomson CA, Neuhouser ML, Di C, Manson JE, Mossavar-Rahmani Y, Seguin R, Manini T, LaCroix AZ, Prentice RL.](#) 2014. Simultaneous association of total energy consumption and activity-related energy expenditure with risks of cardiovascular disease, cancer, and diabetes among postmenopausal women. *Am J Epidemiol.* pii: kwu152. Epub ahead of print.

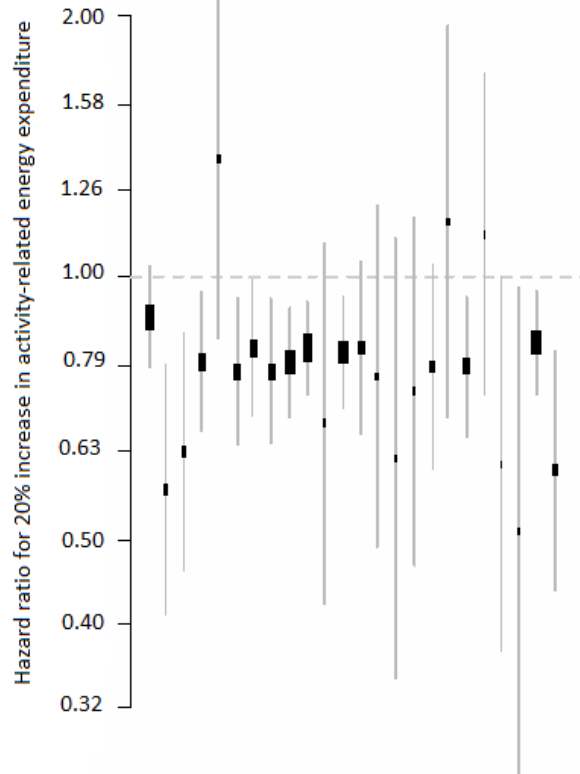
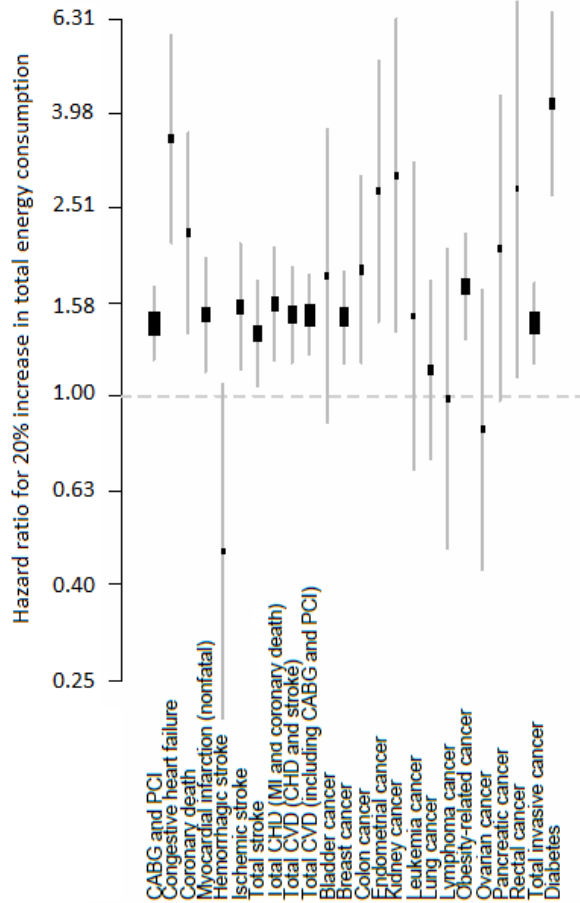


Image provided by Dr. Cheng Zheng

Plot of hazard ratios and 95% confidence intervals for the association between various diseases and 20% increases in biomarker-calibrated total energy consumption (top) or activity-related energy expenditure (bottom).