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Finding a way through the forest: A Biopsychosocial model of hot flashes

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We thank both Drs. Maas and Reame¹ for their commentaries on our recent publication *Abdominal adiposity and hot flashes among midlife women*.² They provide a thoughtful analysis and raise several important questions.

Dr. Maas notes the (albeit inconsistent^{3, 4}) links between hot flashes and elevated blood pressure in previous research, and questions whether differences in blood pressure may account for our observed associations between abdominal adiposity and hot flashes. In these SWAN Heart participants, after accounting for age, neither systolic blood pressure (SBP) nor diastolic blood pressure (DBP) was significantly associated with hot flashes (p 's > 0.25). Moreover, controlling for SBP and DBP in multivariable models with other covariates did not reduce observed associations between abdominal adiposity and hot flashes (total adiposity: OR=1.26, 95% CI: 1.02–1.57, p =0.04; subcutaneous adiposity: OR=1.28, 95% CI 1.03–1.60), p =0.03).

Dr. Reame observes that the relative distribution of visceral adipose tissue (VAT) versus subcutaneous adipose tissue (SAT) varied between the African American and White women in SWAN Heart, with proportionately more SAT versus VAT among the African American women. She notes that VAT is the more metabolically active type of fat, more strongly associated with risks such as diabetes than SAT (although not all SAT is so metabolically benign⁵). She indicates that we are silent on the paradox of these racial/ethnic differences in fat distribution, given that African American women are at increased risk for diseases such as diabetes. This is clearly an important issue. Given the focus of our publication on hot flashes, addressing racial/ethnic differences in fat distribution and metabolic risk was beyond the scope of our report. However, African American women are more likely to report hot flashes than White women.⁶ African American women also have proportionately more SAT than White women, that most strongly related to hot flashes.² We did not report but did examine whether racial differences in hot flashes were accounted by these racial differences in fat distribution. We found that the differences in hot flashes between African

American and White women were reduced by only 17% when accounting for differences in SAT. Racial differences in hot flashes may have a biological component, although the etiology of racial/ethnic health disparities is multifactorial, driven not only by biological differences, but by pronounced differences in social and economic conditions between groups.⁷ While not the focus of our publication, better understanding these racial/ethnic differences is an important area for future research.

Dr. Reame also points out that VAT is more easily lost with behavioral interventions than SAT. Preferential loss of VAT may be the case with modest or initial weight loss. Whether these losses impact hot flashes remains to be seen. However, considering women's health more broadly, with a majority of American adults overweight or obese⁸ and the substantial health risk associated with obesity, weight loss is clearly indicated for many. SWAN has taught us that women progressively gain weight,⁹ particularly fat,¹⁰ over midlife. Given that the postmenopause is a time of heightened cardiovascular risk, minimizing gains is important. Appropriately designed behavioral interventions are effective in achieving at least modest weight loss that can impact key metabolic parameters.¹¹ Maintaining these losses, as well as weight over time, is the challenge.

Dr. Reame cites our findings as “one more tree in the forest,” calling for a comprehensive model to integrate the diverse findings on hot flashes (from SWAN and elsewhere) and to guide future research. In short, we need a model to help us see the “forest,” rather than simply to describe one more tree. Such a model is important given the incomplete understanding of hot flashes etiology and dearth of effective and widely-accepted nonhormonal methods to manage hot flashes. We believe that the most appropriate model is a biopsychosocial one. As we present in the Figure below, biological, behavioral, psychological and social factors, interacting over time, all influence the occurrence and reporting of hot flashes.

For example, there are clearly biological correlates of hot flashes, with the most well-elucidated biological model a thermoregulatory one. According to this model, hot flashes represent heat dissipation events occurring in the context of altered thermoregulatory functioning of menopausal women.¹² There are also multiple other biological correlates of hot flashes, including (but not limited to) estrogen metabolism genetic polymorphisms,¹³ increases in FSH and decreases in estradiol occurring during menopause,¹⁴ and changes in neurotransmitters such as norepinephrine¹⁵ and possibly serotonin.¹⁶

However, behavioral, psychological, and social influences on hot flashes cannot be ignored. For example, smoking is a well-known risk factor related to hot flashes,⁶ and obesity, now identified as a risk factor for hot flashes^{2, 6, 17} clearly has a behavioral contribution.¹¹ Further, anxiety, even when assessed years prior to hot flashes, is a consistent predictor of hot flashes.⁶ Negative affect may be quite important to consider in the reporting of or perceived bother¹⁸ associated with hot flashes, particularly hot flashes reported but not detected physiologically.¹⁹ Finally, key social factors are related to hot flashes. Low socioeconomic status (SES) is a robust and consistent predictor of hot flashes,⁶ and SES is known to be related to many of the behavioral and psychological risk factors detailed above. Notably, in a recent report in *Menopause*, we show that women exposed to childhood abuse

or neglect were more likely to report hot flashes during the menopausal transition, an association persisting with adjustment for multiple confounding factors.²⁰

Thus, the predictors of hot flashes are multiple, including physiological, as well as social and psychological factors. Although yet to be fully elucidated, these factors likely operate in part through each other to impact health. Such a model implies that there may be multiple points of intervention to reduce hot flashes and improve the quality of life of midlife women. We hope that this model, as it is further elucidated, can provide a path through the forest, helping to guide and integrate future research on the etiology and treatment of menopausal hot flashes.

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Figure 1.
Biopsychosocial Model of Hot Flashes