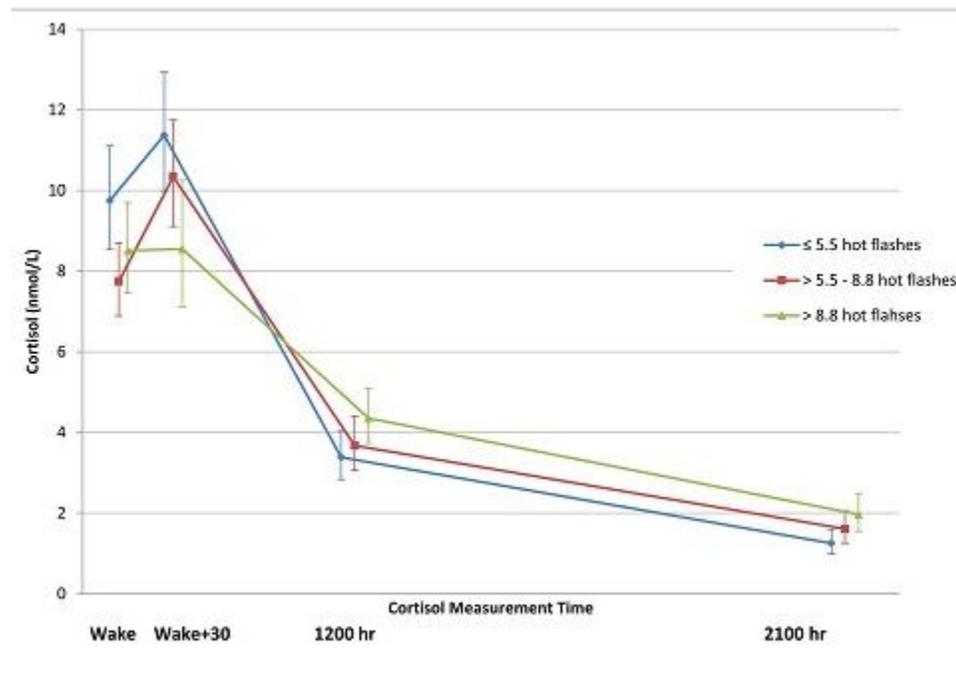


Hot flashes keeping you awake at night? Blame the cortisol.

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Geometric mean salivary cortisol concentrations in 306 women over time, by mean daily hot flash frequency tertiles. N=103, < 5.5 mean daily hot flashes; N=103, 5.5-8.8 mean daily hot flashes; and N=100, > 8.8 mean daily hot flashes.

Image provided by Dr. Susan Reed.

Acute stress is associated with an abrupt rise in cortisol, a glucocorticoid hormone released from the adrenal gland. In healthy adults, cortisol concentrations rise abruptly within thirty minutes of awakening (cortisol awakening response), and diminish throughout the day with the lowest concentrations in the evening. Blunted cortisol responses, as indicated by diminished awakening response or a lower diurnal (daily) variation/concentration, likely reflect chronic illnesses or stressors, while increased evening cortisol can accompany chronic stress, insomnia, and sleep disturbances.

Diurnal salivary cortisol patterns in healthy adults are well established but have not been studied in menopausal or post-menopausal women with hot flashes. Cortisol patterns in women bothered by hot flashes may vary from those not experiencing hot flashes for a couple reasons: 1) hot flashes associate with stress and anxiety and 2) estrogen, a sex hormone that fluctuates during menopause, may affect cortisol secretion.

To address this question, Drs. Susan Reed, Katherine Guthrie, and colleagues examined daily salivary cortisol concentrations and patterns in midlife women with hot flashes. Specifically, the researchers sought to evaluate the potential differences in cortisol by hot flash frequency and the factors that might influence cortisol concentrations and patterns in these women. The results from their study have been recently published in *Clinical Endocrinology*.

The study included 306 women (ages 40-62) randomized to a behavioral intervention (e.g. yoga, meditation, tai chi) for hot flashes, from the Menopausal Strategies: Finding Lasting Answers to Symptoms and Health (MsFlash) network. Salivary cortisol was collected for 2 consecutive days prior to randomization during the weeks of baseline hot flash data collection. Each day, 4 time points were collected: awakening, 30 minutes post-awakening, early afternoon, and bedtime. Participants recorded the timing and presence of alcohol, caffeine, nicotine, intense physical activity, and eating within 2 hours of cortisol collection. Using this cortisol data the researchers calculated 3 measures: 1) estimated daytime cortisol exposure (area under the curve or AUC); 2) awakening cortisol response; and 3) diurnal variation. These particular measures have been shown to be abnormal in other populations with chronic stress, illness, and sleep disturbances.

Women on average had 7.6 (SD = 3.9) hot flashes per day. Higher baseline hot flash frequency was associated with lower age, higher diastolic blood pressure, and higher hot flash severity. The mean daily cortisol values for all women, averaged over the 2 days, followed a normal diurnal pattern. The median percent cortisol rise from awakening was 18%. While this rise did not differ by hot flash frequency, in normal healthy adults cortisol values typically rise 50-100% after awakening. Using repeated measures linear models, the researchers found that women with the greatest frequency of hot flashes had the lowest cortisol concentrations at 30 minutes post-awakening ($P = 0.003$) and the highest concentrations in early afternoon ($P = 0.02$). This finding supports the hypothesis that women with greater hot flash frequency display a different pattern of cortisol compared to women with few hot flashes. However, the researchers found no evidence that women with more reported stress and anxiety had increased hot flashes and thus altered cortisol patterns. A small number of women reported high stress and anxiety in this study, which may contribute to this null association.

Dr. Reed describes the public health implications of these findings, "a greater frequency of moderate to severe hot flashes in midlife women may be associated with subtle abnormalities in free cortisol concentrations in a pattern consistent with chronic sleep disturbance. More than 80% of US women report hot flashes and the majority rate them as moderate to severe, so the potential magnitude of the impact of our findings is not inconsequential. Individuals with chronic sleep disturbance have greater health risks – the long term health consequence of chronic frequent hot flashes and aberrant

cortisol patterns may have an adverse effect on the health of women experiencing hot flashes at menopause. It will be important to confirm our findings in larger populations. Many factors can affect cortisol measurements.

[Reed SD, Newton KM, Larson JC, Booth-LaForce C, Woods NF, Landis CA, Tolentino E, Carpenter JS, Freeman EW, Joffe H, Anawalt BD, Guthrie KA](#). 2015. Daily salivary cortisol patterns in midlife women with hot flashes. *Clinical endocrinology*. doi: 10.1111/cen.12995. [Epub ahead of print]

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