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Endogenous Hormone Levels, Mammographic Density, and Subsequent Risk of Breast Cancer in Postmenopausal Women

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Background: Mammographic density and circulating sex hormones are two well-confirmed predictors of breast cancer risk. Whether mammographic density reflects levels of endogenous sex hormones is unclear. We examined whether these predictors are independently associated with breast cancer risk in a prospective study.

Methods: We conducted a nested case-control study within the Nurses' Health Study cohort of 253 case subjects with breast cancer and 520 control subjects. All participants were postmenopausal women who were not using postmenopausal hormones at the time of both blood collection and mammography. Plasma levels of estradiol, free estradiol, testosterone, and free testosterone were evaluated. Mammographic density was assessed by use of computer-assisted analysis of mammograms. Logistic regression models that were adjusted for matching variables and potential confounders were used to calculate relative risks (RRs) and 95% confidence intervals (CIs). All statistical tests

were two-sided.

Results: Levels of circulating sex steroids and mammographic density were both statistically significantly and independently associated with breast cancer risk. The relative risk of breast cancer associated with mammographic density (RR for highest quartile compared with lowest quartile = 3.8, 95% CI = 2.2 to 6.6; $P_{\text{trend}} < .001$) changed little when the analysis was adjusted for circulating estradiol (RR = 3.9, 95% CI = 2.2 to 6.9; $P_{\text{trend}} < .001$) or circulating t