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Presentation Title: Age-specific relative risks in steroid hormone pathway gene polymorphisms associated with breast cancer.

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Breast cancer is typically a late onset and complex disease with incidence rates increasing with age. Following early research on environmental causes of breast cancer, ever-improving genotyping technologies for single nucleotide polymorphisms (SNPs) has refocused attention on breast cancer genetics. Unlike environmental factors whose effects often vary with age, the penetrance of genetic polymorphisms has generally been assumed to confer a constant relative risk (RR) throughout life. Although this assumption has seldom been questioned, the current study demonstrates that RRs for certain SNPs exhibit breast cancer risk associations that vary with age. SNPs in 12 steroid hormone pathway genes were investigated for age-specific relative risk associations with breast cancer in a case-control study consisting of a discovery set (1,667 cases and 3,333 age-matched controls) and an independent validation set (526 cases and 1,057 controls). Significant age-related trends were identified and confirmed for SNPs in four genes associated with breast cancer risk. The C/C genotype of Cytochrome P450 XIB2 (CYP11B2) was associated with decreased risk at younger ages (30-44 years) but increased risk at older ages (55-69 years). The CG/CG genotype of UDP glycosyltransferase 1A7 (UGT1A7) was associated with increased risk at younger ages but decreased risk at older ages. Additionally, SNP associations in Cytochrome P450 19 (CYP19) and Progesterone receptor (PGR) were confined to middle-age (45-54 years). This discovery of age-specific relative risk associations could have profound implications for future etiological studies of breast cancer, as well as the use of SNP genotyping to accurately predict breast cancer risk in women.