

Age at Menopause in Women Participating in the Postmenopausal Estrogen/Progestins Interventions (PEPI) Trial: An Example of Bias Introduced by Selection Criteria

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Abstract: Our objective is to illustrate the bias introduced in assessing factors associated with age at menopause when the population sample has been selected using restricted criteria, i.e. number of years since menopause, by using a cross-sectional analysis of baseline data from a population-based randomized clinical trial. The participants were women who participated in the Postmenopausal Estrogen/Progestins Intervention (PEPI) trial, had not had a hysterectomy, were between 45 and 64 years old, and were menopausal for at least 1 but not greater than 10 years. The outcome measures were self-reported age at menopause and factors thought to be associated with it, including smoking, alcohol use, oral contraceptive use, number of pregnancies, education, income, body mass index, waist-hip ratio, thigh girth, and systolic and diastolic blood pressures. At entry, the mean age of the 601 women was 56.2 years. Mean age at menopause was 51.0 years. Chronologic (current) age was strongly correlated with age at menopause ($r = 0.74$, $p = 0.0001$). In bivariate analyses, factors associated with younger age at menopause were ever-use of cigarettes, former oral contraceptive use, and higher thigh girth; factors associated with later age at menopause were greater number of pregnancies, higher waist-hip ratio, and higher systolic blood pressure. After stratification by 5-year age intervals, these associations were no longer statistically significant. Because of restricted sampling, an artificial association was observed between chronologic age and age at time of menopause. This artifact made it difficult to distinguish between factors associated with chronologic age and those that may be independently associated with menopause. Failure to recognize this bias could lead to erroneous conclusions.

Key Words: Sampling bias -- Randomized clinical trial -- Risk factors -- Ovary -- Ovarian aging.