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Hormone Replacement Therapy (HRT) and Its Impact on the All-Cause Mortality of UK Women: A Matched Cohort Study 1984-2017

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Abstract: Although Hormone Replacement Therapy (HRT) is an effective treatment in ameliorating menopausal symptoms, it has mixed effects on different health outcomes, increasing, for instance, the risk of breast cancer. Because of this, many symptomatic women are left untreated. Untreated menopausal symptoms may result in other health issues, which eventually put an extra burden and costs to the health care system. All-cause mortality analysis may explain the net benefits and risks of the HRT therapy. However, it received far less attention in HRT studies. This study investigated the impact of HRT on all-cause mortality using electronically recorded primary care data from The Health Improvement Network (THIN) that broadly represents the female population in the United Kingdom (UK). The study entry date for this study was the record of the first HRT prescription from 1984, and patients were followed up until death or transfer to another GP practice or study end date, which was January 2017. 112,354 HRT users (cases) were matched with 245,320 non-users by age at HRT initiation and general practice (GP). The hazards of all-cause mortality associated with HRT were estimated by a parametric Weibull-Cox model adjusting for a wide range of important medical, lifestyle, and socio-demographic factors. The multilevel multiple imputation techniques were used to deal with missing data. This study found that during 32 years of follow-up, combined HRT reduced the hazard ratio (HR) of all-cause mortality by 9% (HR: 0.91; 95% Confidence Interval, 0.88-0.94) in women of age between 46 to 65 at first treatment compared to the non-users of the same age. Age-specific mortality analyses found that combined HRT decreased mortality by 13% (HR: 0.87; 95% CI, 0.82-0.92), 12% (HR: 0.88; 95% CI, 0.82-0.93), and 8% (HR: 0.92; 95% CI, 0.85-0.98), in 51 to 55, 56 to 60, and 61 to 65 age group at first treatment, respectively. There was no association between estrogen-only HRT and women's all-cause mortality. The findings from this study may help to inform the choices of women at menopause and to further educate the clinicians and resource planners.

Keywords: hormone replacement therapy, multiple imputations, primary care data, the health improvement network (THIN)

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