

Reproductive history and risk of type 2 diabetes mellitus in postmenopausal women: findings from the Women's Health Initiative

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Abstract

Objective: The aim of the study was to understand the association between women's reproductive history and their risk of developing type 2 diabetes. We hypothesized that characteristics signifying lower cumulative endogenous estrogen exposure would be associated with increased risk.

Methods: Prospective cohort analysis of 124,379 postmenopausal women aged 50 to 79 years from the Women's Health Initiative (WHI). We determined age of menarche and final menstrual period, and history of irregular menses from questionnaires at baseline, and calculated reproductive length from age of menarche and final menstrual period. Presence of new onset type 2 diabetes was from self-report. Using multivariable Cox proportional hazards models, we assessed associations between reproductive variables and incidence of type 2 diabetes.

Results: In age-adjusted models, women with the shortest (<30 y) reproductive periods had a 37% (95% CI, 30-45) greater risk of developing type 2 diabetes than women with medium-length reproductive periods (36-40 y). Women with the longest (45+ y) reproductive periods had a 23% (95% CI, 12-37) higher risk than women with medium-length periods. These associations were attenuated after full adjustment (HR 1.07 [1.01, 1.14] for shortest and HR 1.09 [0.99, 1.22] for longest, compared with medium duration). Those with a final menstrual period before age 45 and after age 55 had an increased risk of diabetes (HR 1.04; 95% CI, 0.99-1.09 and HR 1.08; 95% CI, 1.01-1.14, respectively) compared to those with age of final menstrual period between 46 and 55 years. Timing of menarche and cycle regularity was not associated with risk after full adjustment.

Conclusions: Reproductive history may be associated with type 2 diabetes risk. Women with shorter and longer reproductive periods may benefit from lifestyle counseling to prevent type 2 diabetes.

Key Words: Cycle regularity – Diabetes – Menarche – Menopause – Reproductive risk duration.

In animal models, oophorectomy leads to visceral obesity and development of metabolic syndrome.¹ In vitro, estrogens have been shown to have metabolic actions on skeletal muscle, pancreas, adipose tissue, and the central nervous system.¹ In particular, low levels of estrogen tend to

adversely affect body fat distribution and accumulation, appetite, energy expenditure, insulin secretion, and glucose homeostasis,^{1,2} and these are critical contributors to the development of type 2 diabetes. In humans, however, exogenous estrogen has been associated with the reversal of these symptoms,

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of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

The full list of WHI investigators is available online at <http://www.whi.org/researchers/SitePages/Write%20a%20Paper.aspx>.

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