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**Too short or too long reproductive span increases risk
of diabetes in postmenopausal women**

Is there an optimal amount of lifetime estrogen exposure for metabolic functioning?

CLEVELAND, Ohio (Wednesday, July 27, 2016)— Using data from the Women’s Health Initiative (WHI), a new study has found that women with reproductive-period durations of less than 30 years had a 37% increased risk of type 2 diabetes compared with women whose reproductive durations were somewhere in the middle (36 to 40 years). Researchers were surprised to learn that women with longer reproductive-period durations (45 years or more) were at a 23% higher risk than women with medium-length periods. These results are published online in *Menopause*, the journal of The North American Menopause Society.

“The Women’s Health Initiative provides a unique setting to evaluate the associations between reproductive characteristics and diabetes because of its large size, robust characterization of reproductive histories, long duration of follow-up, and ability to prospectively ascertain type 2 diabetes,” says JoAnn V. Pinkerton, MD, NCMP, Executive Director of The North American Menopause Society. The estimated overall prevalence of diabetes ranges from 5.8% to 12.9% (median, 8.4%) in US adults; therefore, an increased risk associated with reproductive characteristics could have significant clinical implications.

An analytic cohort of 124,379 postmenopausal women aged 50 to 79 years completed questionnaires on demographics, medical and family history, and various lifestyle factors such as physical activity. Height, weight, and waist circumference were measured and used to determine body mass index (BMI). Age of menarche and final menstrual period and history of irregular menses were garnered from questionnaires at baseline. Reproductive length was determined by subtracting age of menarche from the final menstrual period. Women were followed for a mean of 12.2 years. The primary outcome was a new diagnosis of diabetes; women with a previous diagnosis of diabetes were excluded from analyses.

Cox proportional hazards techniques were used to estimate unadjusted and age-adjusted associations between reproductive-period duration and diabetes incidence. The association between reproductive period and type 2 diabetes was U-shaped, with shorter and longer reproductive duration lengths associated with increased risk. In addition, those with the shortest and longest reproductive periods had higher BMIs and waist circumferences compared with those with midrange reproductive lengths. Women with shorter reproductive-period duration

were more likely to have undergone surgical menopause and more likely to be current or past users of hormone therapy.

The finding that earlier reproductive age was associated with diabetes was not surprising, because low estrogen negatively affects body fat distribution and fat accumulation, contributors to type 2 diabetes. A later age of menopause, however, with longer reproductive-period durations, has not previously been associated with increased risk. When the components of reproductive-period duration were examined separately, age at final menstrual period, not age at menarche, was associated with type 2 diabetes risk in a U-shaped pattern similar to the association with reproductive-period duration. Having more pregnancies, which would be associated with higher lifetime estrogen exposure, was found to further increase risk of type 2 diabetes. After full data adjustment, neither age at menarche or irregular cycles was found to be associated with a significantly increased risk of developing diabetes compared with women with regular cycles.

These results suggest that lifetime estrogen exposure may play a role in the development of type 2 diabetes, although any link to exogenous estrogen is unclear. Understanding who is at risk for type 2 diabetes is important because preventive measures such as weight loss, improved diet, and increased exercise can decrease risk. Reproductive period length and age of final menstrual period may be important factors to add to the risk pool when counseling women about their risk of diabetes and the need to make lifestyle changes.

“The finding that both shorter and longer reproductive durations were associated with risk of diabetes has important implications for women with early or late menopause as well as for those with *BRCA* gene mutations considering risk-reducing bilateral oophorectomy that would shorten their reproductive time,” says Dr. Pinkerton. “Given the high prevalence of diabetes in postmenopausal women, those with shorter and longer reproductive periods may benefit from lifestyle counseling. Future research should focus on ways to prevent type 2 diabetes in women at risk as they age.”

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Founded in 1989, The North American Menopause Society (NAMS) is North America’s leading nonprofit organization dedicated to promoting the health and quality of life of all women during midlife and beyond through an understanding of menopause and healthy aging. Its multidisciplinary membership of 2,000 leaders in the field—including clinical and basic science experts from medicine, nursing, sociology, psychology, nutrition, anthropology, epidemiology, pharmacy, and education—makes NAMS uniquely qualified to serve as the definitive resource for health professionals and the public for accurate, unbiased information about menopause and healthy aging. To learn more about NAMS, visit www.menopause.org.