



## Invited Editorial

## Childhood predictors of age at natural menopause



Although the age of menopause and the symptoms that may arise in this period of a woman's life cycle have been studied, scant research has attempted to identify childhood factors that affect the timing of menopause's onset and the intensity of symptoms. However, the research that has been done has explored a range of potential markers, including age at menarche, childhood growth and body mass index (BMI), cognitive ability, parental influence, smoke exposure, genetics, factors related to birth, and history of physical and sexual abuse.

Regarding the prediction of menopausal onset, age at menarche does not appear to be a factor. Bjelland et al. looked at this association in a group of women in Norway, and concluded that there was no significant difference in age at menarche for any age at menopause [1]. However, even though age at menarche does not influence age at menopause, those with an earlier menarche, which may be related to growth rate and familial conflict, do have a longer reproductive time frame [1].

A girl's nutritional status may influence both age at menopause as well as, interestingly, age at menarche. Children who are not breastfed, who have poor early growth, and who are malnourished tend to experience an earlier menopause [2,3]. One study reported that women in a New Guinea population with a high rate of malnourishment, shorter height, and lower weight experienced menopause on average 4 years earlier than a similar population in New Guinea with adequate nourishment and growth markers [2]. This association seems to be restricted to childhood nourishment status, as no correlation has been reported between adult BMI and age at menopause [3]. It has been hypothesized that early malnourishment may affect the hypothalamic-pituitary-ovarian axis, leading to decreased ovulation and earlier menopause [3].

Cognitive ability, defined as either a specific score on an assessment or the length of time provided to the child in formal education, has also been assessed as a factor potentially affecting age at menopause. Some researchers, such as Kuh et al., using two cohort studies, noted that lower cognitive scores were associated with earlier menopause [4]. However, more than 50% of the studies in a 2011 review reported no relationship between cognitive ability and menopausal age [5].

Parents also may have an influence on when their female offspring will eventually become menopausal. A study based on the English Longitudinal Study of Aging reported that overprotection by both parents can lead to a shorter reproductive life span, with paternal overprotection more significantly associated than maternal overprotection [6]. Additionally, one study reported that

parental divorce before the age of 15 was associated with a twofold increased rate of early menopause [7].

Another environmental influence on age at menopause may be exposure to parental smoke. Tawfik et al., in a prospective analysis, proposed that prenatal smoke exposure can lead to early menopause by influencing the development of follicles and limiting the reproductive period even before birth [8]. Prenatal tobacco exposure as well as tobacco exposure as a woman approaches menopause seem to have the most obvious effects on the timing of menopause, that is, when follicles are at their newest and oldest [8].

A woman's mother's age at menopause appears to be a factor in her own age at menopause, as family and twin studies have reported that 30–85% of their participants' age at menopause was influenced by genetic factors [3]. Potential sources of heritability include polymorphisms on chromosomes 13, 19, 20, the estrogen receptor genes and TNF genes, as well as the FRAXE premutation found on the X chromosome [3,4].

The most predictive marker for timing of menopause, however, appears to be Antimüllerian hormone (AMH). Dolleman et al. reported that AMH is a much better predictor of age at menopause than mother's age, although the combination of these two factors may provide a fairly accurate age prediction [9].

The time of year of birth also may influence age at menopause. Cagnacci et al. reported an association between season of birth and timing of menopause, such that those born in March seem to have an earlier menopause than those born in October [10]. This may be due to environmental factors like temperature, photoperiod, diet modifications, and infections. Where a woman was born may be a factor as well. Mishra et al. used data from the Australian Longitudinal Study on Women's Health, surveying women born in Australia versus those living in Australia but born in Asia, at ages 45 to 50, and again two years later. Of interest, 26.7% of Asian-born women had already reached menopause, while only 12.2% of Australian-born women had undergone the transition over this two-year follow-up [11]. Additionally, the Asian-born menopausal women did not report vasomotor symptoms, although those Australian-born ones who were menopausal did report symptoms [11].

Regarding menopausal symptom severity and childhood factors, there are even less data than there are data predicting menopausal age. The limited research available suggests that childhood abuse may correlate with symptom severity. Carson et al. reported that women with a history of physical or sexual abuse have a 1.5–2 times greater risk of vasomotor sleep symptoms than those without this

history [12]. This association, however, was not noted in women who reported only emotional abuse.

Overall, the scant literature available suggests that childhood factors may indeed impact menopausal age and severity of menopausal symptoms, but definitive answers through prospective studies are lacking. Most studies available on this topic are retrospective, and, therefore, influenced by recall bias. Additionally, these studies tend to lack diversity in their study groups, and some data sets do not have the comprehensive information necessary for in-depth data analysis, as some of these surveys were conducted years before the research questions were formulated.

Factors influencing the age of menopause are assuming greater importance, as age at first pregnancy is trending later in a woman's reproductive life [13]. With further research that more definitively characterizes what childhood factors are of importance, interventions directed at modifying or anticipating them should help in improving health outcomes through the woman's reproductive years, the menopause transition, and beyond.

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### References

- [1] E.K. Bjelland, S. Hofvind, L. Byberg, A. Eskild, The relation of age at menarche with age at natural menopause: a population study of 336 788 women in Norway, *Hum. Reprod.* 33 (6) (2018) 1149–1157, <http://dx.doi.org/10.1093/humrep/dey078>.
- [2] G.D. Mishra, R. Cooper, S.E. Tom, D. Kuh, Early life circumstances and their impact on menarche and menopause, *Women's Heal* 5 (2) (2009) 175–190, <http://dx.doi.org/10.2217/17455057.5.2.175>.

- [3] E.B. Gold, The timing of the age at which natural menopause occurs, *Obstet. Gynecol. Clin. North Am.* 38 (3) (2011) 425–440, <http://dx.doi.org/10.1016/j.ogc.2011.05.002>.
- [4] D. Kuh, S. Butterworth, H. Kok, et al., Childhood cognitive ability and age at menopause: evidence from two cohort studies, *Menopause* 12 (4) (2005) 475–482, <http://dx.doi.org/10.1097/01.GME.0000153889.40119.4C>.
- [5] F.S. Canavez, G.L. Werneck, R.C.M. Parente, R.K. Celeste, E. Faerstein, The association between educational level and age at the menopause: a systematic review, *Arch. Gynecol. Obstet.* 283 (1) (2011) 83–90, <http://dx.doi.org/10.1007/s00404-009-1323-6>.
- [6] P. Demakakos, N. Pashayan, G. Chrousos, E. Linara-Demakakou, G.D. Mishra, Childhood experiences of parenting and age at menarche, age at menopause and duration of reproductive lifespan: evidence from the English Longitudinal Study of Ageing, *Maturitas* 122 (January) (2019) 66–72, <http://dx.doi.org/10.1016/j.maturitas.2019.01.010>.
- [7] R. Hardy, D. Kuh, Social and environmental conditions across the life course and age at menopause in a British birth cohort study, *BJOG Int. J. Obstet. Gynaecol.* 112 (3) (2005) 346–354, <http://dx.doi.org/10.1111/j.1471-0528.2004.00348.x>.
- [8] H. Tawfik, J. Kline, J. Jacobson, et al., Life course exposure to smoke and early menopause and menopausal transition, *Menopause* 22 (10) (2015) 1076–1083, <http://dx.doi.org/10.1097/GME.0000000000000444>.
- [9] M. Dölleman, M. Depmann, M.J.C. Eijkemans, et al., Anti-Müllerian hormone is a more accurate predictor of individual time to menopause than mother's age at menopause, *Hum. Reprod.* 29 (3) (2014) 584–591, <http://dx.doi.org/10.1093/humrep/det446>.
- [10] A. Cagnacci, F.S. Pansini, A. Bacchi-Modena, et al., Season of birth influences the timing of menopause, *Hum. Reprod.* 20 (8) (2005) 2190–2193, <http://dx.doi.org/10.1093/humrep/dei040>.
- [11] G. Mishra, C. Lee, W. Brown, A. Dobson, Menopausal transitions, symptoms and country of birth: the Australian Longitudinal Study on Women's Health, *Aust. N. Z. J. Public Health* 26 (6) (2002) 563–570, <http://dx.doi.org/10.1111/j.1467-842X.2002.tb00367.x>.
- [12] M.Y. Carson, R.C. Thurston, Childhood abuse and vasomotor symptoms among midlife women, *Menopause* 26 (10) (2019) 1, <http://dx.doi.org/10.1097/gme.0000000000001366>.
- [13] T.J. Mathews, B.E. Hamilton, Mean age of mothers is on the rise: United States, 2000–2014 key findings data from the national vital statistics system, *NCHS Data Brief* (232) (2016) <https://www.cdc.gov/nchs/data/databriefs/db232.pdf>.

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