

Anticipatory Counseling Regarding Ovarian-Factor Fertility Decline

This Committee Statement was developed by the American College of Obstetricians & Gynecologists' Committee on Clinical Consensus–Gynecology in collaboration with Nancy Sokkary, MD, and Danielle Carter, MD.

Fertility, or the capacity to produce a child, declines with age as the ovaries undergo a natural decrease in follicle count related to oocyte atresia. However, patients significantly overestimate the likelihood of pregnancy at all ages. It is important that health care professionals educate patients regarding the natural decline in ovarian reserve and quality of egg follicles throughout their reproductive lifespans. Patients who are interested in becoming pregnant also should be educated on non–age-related factors that may accelerate ovarian decline to optimize and more completely understand their reproductive health and family-building opportunities. Despite the existence of resources on ovarian decline and non–age-related factors affecting fertility, more evidence-based resources on ovarian decline are needed for both patients and health care professionals.

SUMMARY OF RECOMMENDATIONS AND CONCLUSIONS

On the basis of the principles outlined in this Committee Statement, the American College of Obstetricians & Gynecologists (ACOG) makes the following recommendations and conclusions:

- **Obstetrician–gynecologists are encouraged to counsel their patients about ovarian decline as part of routine care, with open communication that honors patient concerns and family-building goals.**
- **Obstetrician–gynecologists should advocate for greater, accessible, evidence-based resources on ovarian decline for both health care professionals and patients.**
- **It is important that obstetrician–gynecologists and other reproductive health care professionals are aware of the variety of non–age-related factors that may contribute to ovarian decline as they counsel their patients.**

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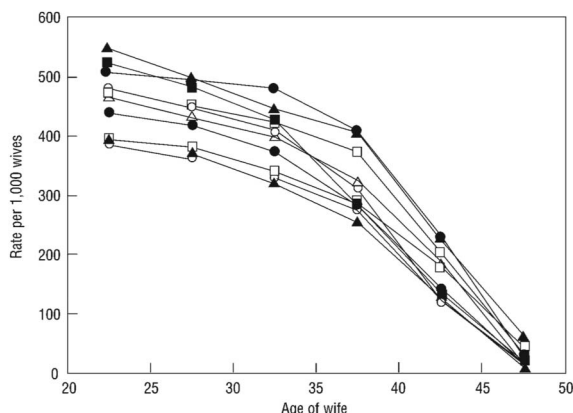


Fig. 1. Marital fertility rates by 5-year age groups. The ten populations (in descending order at age 20–24 years) are Hutterites, marriages in 1921–1930 (▲); Geneva bourgeoisie, husbands born in 1600–1649 (■); Canada, marriages in 1700–1730 (●); Normandy marriages in 1760–90 (○); Hutterites, marriages before 1921 (□); Tunis, marriages of Europeans 1840–1859 (Δ); Normandy, marriages in 1674–1742 (●); Norway, marriages in 1874–1876 (□); Iran, village marriages in 1940–1950 (▲); Geneva bourgeoisie, husbands born before 1600 (○). From Menken J, Trussell J, Larsen U. Age and fertility. *Science* 1986;233:1389–94. Reprinted with permission from AAAS.

BACKGROUND

Fertility, or the capacity to produce a child, declines with age due to both quality and quantity of oocytes. Ovaries undergo a natural decrease in follicle count related to oocyte atresia. The maximum number of oocytes is 6–7 million at 20 weeks of gestation in the female fetus. The number of oocytes decreases to approximately 1–2 million at birth; 300,000–500,000 at puberty; 25,000 at age 37 years; and 1,000 at age 51 years, the average age of menopause in the United States (1–3). Ovarian reserve refers to the number of oocytes within the ovaries, which can be measured, although to an imperfect extent. With age, the quality of eggs also declines due to cellular and molecular changes (4), thus increasing rates of aneuploidy and spontaneous abortion and consequently affecting an individual's ability to become pregnant (5). There is not, however, a standardized method to measure the quality of eggs. Additionally, there are several factors that can accelerate the decline of ovarian function outside of chronologic aging.

The majority of understanding of natural fertility rates comes from historical data (Fig. 1). A study from 1982 evaluating success with donor sperm insemination demonstrated that the pregnancy rate with up to 12 months of insemination cycles decreased from 74% for individuals younger than age 31 years, to 62% for those aged 31–35 years, and 54% for those older than age 35 years. The

pregnancy rate per cycle was noted to be higher for women younger than age 35 years compared with those older than 35 years (6).

The American Society for Reproductive Medicine (ASRM) defines *infertility* as the inability to achieve a successful pregnancy based on the combination of an individual's medical, sexual, and reproductive history, among other factors, such that they require medical intervention to achieve a successful pregnancy (7). Because of the age-related decrease in fertility and increase in pregnancy loss, the ASRM recommends consultation with a reproductive specialist in patients having regular, unprotected intercourse and without any known etiology for either partner suggestive of impaired reproductive ability when the female partner is aged (8):

- 35 years or younger: after 1 year of unsuccessfully attempting to conceive.
- 36–40 years: after 6 months of unsuccessfully attempting to conceive.
- Older than 40 years: immediately.

For individuals planning to delay childbearing, referral to a reproductive endocrinologist still should be considered. Evaluating egg quantity, such as through measurement of anti-müllerian hormone (AMH), may be a useful, albeit imperfect, predictor of ovarian reserve (9).

Although advances in assisted reproductive technology (ART), including oocyte cryopreservation, have expanded options for family building and have changed approaches to fertility, not all patients have equal access to, are good candidates for, or are aware of the true efficacy of ART. Many patients seeking ART have a false sense of security in the ability of ART to compensate for natural fertility decline (10).

Multiple studies indicate that patients significantly overestimate the likelihood of pregnancy at all ages and are not aware of the rate of fertility decline with age (10). In a focus group of men and women who self-identified as having low to average levels of knowledge about fertility, most overestimated the reproductive lifespan and fertile window (11). Another cross-sectional study of women aged 18–29 years demonstrated that, although 44% of participants had discussed fertility-related topics with their health care professionals, only 22% could identify the age of marked fertility decline, the fertile period, and that the ovaries did not continuously produce new eggs (12).

Although fertility awareness generally increases with education level (13), the overall limited awareness of reproductive aging persisted among undergraduate students, graduate students, and even medical residents (14–16). In fact, obstetrics and gynecology residents were no more likely to answer fertility or oocyte-preservation knowledge questions correctly compared with residents



in other specialties (16). In the aforementioned study of graduate students, more than 50% overestimated in vitro fertilization success rates (15).

As such, educating patients regarding a natural decline in ovarian reserve and the quantity and quality of follicles is important. Individuals with ovaries who may be interested in pregnancy also should be educated on non-age-related factors (discussed later in this document) that may accelerate ovarian decline to optimize and more completely understand their reproductive health and family-building opportunities. It is equally important for health care professionals to counsel their patients on their fertility throughout their reproductive lifespans. At the same time, it is important that reproductive health care professionals acknowledge that not all patients may desire pregnancy or be interested in family building and adjust their counseling as appropriate.

Presence of leiomyomas, history of tubal disease or pelvic infection, and endometriosis all can affect fertility but are beyond the scope of this document. Information on the effects of these conditions on fertility may be found in the ASRM Committee Opinion, "Fertility Evaluation of Infertile Women" (<https://www.asrm.org/practice-guidance/practice-committee-documents/fertility-evaluation-of-infertile-women-a-committee-opinion-2021/>).

This Committee Statement has been updated from Committee Opinion No. 589, *Female Age-Related Fertility Decline*. This revision includes more up-to-date data, expands on factors that may accelerate a decline in ovarian reserve and negatively affect egg quality, emphasizes inclusivity of family building to all patients interested in pursuing pregnancy, and focuses on the importance of counseling. This document serves as a resource for reproductive health professionals to counsel their patients on fertility decline due to ovarian aging and other factors that may contribute to ovarian decline.

COUNSELING

Current Trends in Counseling

Obstetrician–gynecologists are encouraged to counsel their patients about ovarian decline as part of routine care, with open communication that honors patient concerns and family-building goals.

A significant amount of literature exists for health care professionals regarding natural fertility and prepregnancy counseling, as well as specific counseling surrounding ART and oocyte preservation (8, 17, 18). However, there is a paucity of literature and resources, both clinical and patient facing, regarding the most effective methods and timing for counseling patients about their own fertility decline (19). In a cross-sectional study of physicians by ACOG, only 27.6% of respondents stated that they

frequently counsel women aged 18–34 years regarding reproductive aging. That number increased to 75.8% in women aged 35–44 years, even though 82.8% of respondents identified that these conversations were important to have and to have earlier in the reproductive lifespan, especially as a growing percentage of the population is choosing to delay childbearing (20). According to the Centers for Disease Control and Prevention, the average age of the birthing parent for their first child was 27.5 years in 2023, up from 25.4 years in 2010 (21).

Health care professionals also should consider the diversity of family-building preferences, including patients who may not desire pregnancy or children. Same-sex couples and gender-diverse individuals inherently have the same ovarian decline with age but may have additional risk factors or be candidates for ART.

From a patient perspective, there is agreement that counseling can come from obstetrician–gynecologists or primary care clinicians (11). Fertility awareness is greater in patients who have sought medical attention for fertility concerns from a primary care clinician or obstetrician–gynecologist already, suggesting that this conversation is often patient initiated and, therefore, delayed, with 52.9% of patients experiencing 1 year of infertility before seeking medical advice (13).

Patient-Forward Approach to Education on Ovarian Decline

Obstetrician–gynecologists should advocate for greater, accessible, evidence-based resources on ovarian decline for both health care professionals and patients.

Online educational content and social media are important sources of information for patients. These informational outlets have significant potential to improve knowledge about age-related fertility decline and treatments (11, 22), because 73% of adult women in the United States use social media (23). Further, in a survey of fertility clinic patients, 79.9% felt that their use of social media benefitted their patient experience (23).

However, the quality of this information may be of particular concern for health care professionals, especially with the rise of misinformation on social media. ACOG recognizes the potential harm misinformation online can have on patients and clinicians and has developed a resource page to combat misinformation in obstetric and gynecologic health care (see the Resources section below). A study about fertility education and social media found that only 10% of posts were by physicians and 1% by professional organizations (24). There also has been an increase in information within advertisements posted by creators with the potential for profit; 72.2% of these videos featured non-evidence-based information (25). Despite these limitations, social media will remain a popular resource for patients seeking



medical information, and physicians have an opportunity to provide widespread, accessible education with an evidence-based social media presence (24).

Women's health and reproductive health organizations, such as ACOG, the ASRM, and the Society for Women's Health Research, have physician and patient-facing resources regarding fertility and ovarian decline, but most are focused on patients who already have reached the age of expected ovarian decline or are not on readily accessible platforms. Health care professionals are therefore encouraged to incorporate conversations and evidence-based, patient-forward resources about reproductive life planning at visits with patients throughout their reproductive lifespans, not only when concerns surrounding fertility arise, whether initiated by the patient or the physician. A list of known, accessible, and evidence-based resources on fertility and ovarian decline are included in the Resources section. However, more resources on ovarian decline are needed for both patients and health care professionals. As part of educating and counseling patients, health care professionals should have an awareness and knowledge of the several factors outside of age that may contribute to ovarian decline. These factors are discussed in detail in the next section, including specific guidance on counseling where applicable.

NON-AGE-RELATED FACTORS AFFECTING OVARIAN FUNCTION

It is important that obstetrician–gynecologists and other reproductive health care professionals are aware of the variety of non–age-related factors that may contribute to ovarian decline as they counsel their patients.

A diverse array of non–age-related factors, ranging from inherited anomalies to environmental exposures, may affect the ovaries by diverse mechanisms. Some of these genetic, iatrogenic, and environmental factors are discussed in further detail later in the document. However, in many cases, the exact implications of these non–age-related influences are not yet known or have conflicting data in previous studies. Box 1 lists factors that may affect ovarian function, with limited or conflicting data. The number of factors that potentially affect the ovaries and the lack of conclusive data warrant further investigation and a supportive approach to patient counseling. The effects of these factors on pregnancy itself is covered in ACOG Committee Opinion No. 762, *Prepregnancy Counseling*.

Genetic

Familial and genetic factors are known to influence the age of menopause, and knowledge regarding genetic effects on ovarian decline specifically has expanded tremendously. Certain genetic disorders, such as fragile X premutation and Turner syndrome, are clearly associ-

Box 1. Factors Possibly Affecting Ovarian Function

Autoimmune diseases (26–30)

- Thyroid disease*
- Addison's disease
- Diabetes*
- Rheumatoid arthritis†
- Crohn's disease†
- Myasthenia gravis†
- Systemic lupus erythematosus†
- Multiple sclerosis

Sickle cell anemia†

Endometriosis (31–34)*

Testosterone for gendering-affirming care (35, 36)†

Alcohol consumption†‡

Endocrine Disruptors (37)§

- Perfluoroalkyl substances (38)
- 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (39)
- Bisphenol-A (BPA) (39, 40)
- Phthalates (41)
- Parabens

*Strong association.

†Weak association.

‡Conflicting evidence.

§Available evidence suggests causation and warrants further investigation.

ated with a decrease in ovarian reserve and with primary ovarian insufficiency (42).

There is a rapidly growing body of evidence regarding additional specific gene mutations that contribute to diminished ovarian reserve, with more than 50 genes implicated in primary ovarian insufficiency and 29% of women with primary ovarian insufficiency having variants in whole-exome sequencing (43–45). A family history of primary ovarian insufficiency, particularly among first-degree relatives such as siblings, poses a significant risk for primary ovarian insufficiency (46). Routine genetic screening to evaluate for risk of ovarian decline in patients at low to average risk is not recommended.

Iatrogenic

Several necessary iatrogenic interventions result in diminished ovarian reserve, including pelvic radiation and oophorotoxic chemotherapeutic agents (refer to ACOG Committee Opinion No. 747, *Gynecologic Issues in*



Children and Adolescent Cancer Patients and Survivors). Unilateral oophorectomy will diminish ovarian reserve, but partial oophorectomy and cystectomy also may have implications, because they can negatively affect the microenvironment and adnexal blood supply (47).

Exposures

Substance use and environmental exposures also may affect ovarian function. This area often garners media attention and patient interest, but many potential risk factors are not yet well understood. The Women's Health Initiative Study found an increase in infertility and a younger age of menopause among women who smoked or were exposed to high levels of secondhand smoke compared with women in a control group. This has been a consistent finding (48). An ASRM Committee Opinion states that extremes of body mass index (BMI), smoking, high caffeine, and mercury exposure all may increase infertility rates, which does not necessarily reflect ovarian reserve alone (8).

Conflicting data exist regarding the effect of alcohol consumption on ovaries and fertility. One systematic review found no association with low AMH levels and alcohol consumption. Most studies included in the review were primarily comparing consumers of alcohol with nonconsumers and did not delineate amount of consumption (49). A large cross-sectional study found a significantly lower AMH level among women who reported consuming alcohol (48). The ASRM recommends avoiding more than two drinks per day while attempting to become pregnant and notes limited data regarding moderate alcohol consumption affecting fertility (8).

Endocrine disruptors are synthetic chemicals found in both the environment and common household products (48). Both mainstream media and scientific journals have increased their focus on endocrine disruptors because of their ubiquity in everyday life and preliminary data suggesting that exposure likely leads to ovarian function decline. Patient concerns should be validated and evolving recommendations shared. A list of common endocrine disruptors can be found in Box 1, and an overview of pesticides and ways for patients to minimize exposure can be found on the Centers for Disease Control and Prevention's website (About Pesticides and Reproductive Health). This is a rapidly expanding area of research that both clinicians and patients should be encouraged to evaluate continually.

CONCLUSION

Reproductive health care professionals are encouraged to counsel their patients regarding ovarian decline and family building throughout their reproductive lifespans. Many individuals do not understand the implications of decreasing ovarian reserve, or they overestimate their ability to become pregnant. Patient education on fertility

and non-age-related factors affecting ovarian function may be further complicated or misunderstood due to the rise of medical misinformation on social media. Obstetrician-gynecologists and other reproductive health care professionals, therefore, should not wait to initiate reproductive life-planning discussions until patients raise concerns about their fertility and treatment options.

Although there are no specific guidelines addressing counseling on ovarian decline, it should be acknowledged that many factors in addition to age may contribute to an individual's ovarian function. At present, specific genetic anomalies, environmental factors, medical treatments, and systemic illnesses are known to result in a decrease in ovarian reserve and egg quality. However, there are more factors that are not yet fully understood in terms of their effect on ovarian function. Navigating these risks can be overwhelming for patients and health care professionals. For that reason, it is important to have an open and ongoing dialogue about family building between health care professionals and their patients who are pursuing pregnancy. It is also imperative to continue the study of ovarian decline and create appropriate, evidence-based, and accessible clinician and patient resources.

RESOURCES

American College of Obstetricians & Gynecologists

- Expert View: Reproductive Life Planning: A Tool to Shape Your Future
- FAQs: Having a Baby After Age 35: How Aging Affects Fertility and Pregnancy
- Combating Misinformation

American Society for Reproductive Medicine

- ReproductiveFacts.org
- Optimizing natural fertility: a committee opinion

Society for Women's Health Research

- Women's Resource Guide to Fertility Health Care
- Clinician Resource Guide to Fertility Health Care

Use of Language

The American College of Obstetricians & Gynecologists recognizes and supports the gender diversity of all patients who seek obstetric and gynecologic care. In original portions of this document, authors seek to use gender-inclusive language or gender-neutral language. When describing research findings, this document uses gender terminology reported by investigators. To review ACOG's policy on inclusive language, see <https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language>.



REFERENCES

1. Baker TG. A quantitative and cytological study of germ cells in human ovaries. *Proc R Soc Lond B Biol Sci* 1963;158:417–33. doi: 10.1098/rspb.1963.0055
2. Block E. Quantitative morphological investigations of the follicular system in women; variations at different ages. *Acta Anat (Basel)* 1952;14:108–23. doi: 10.1159/000140595
3. Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in mid-life: implications for forecasting menopause. *Hum Reprod* 1992;7:1342–6. doi: 10.1093/oxfordjournals.humrep.a137570
4. Moghadam AR, Moghadam MT, Hemadi M, Saki G. Oocyte quality system and aging. *JBRA Assist Reprod* 2022;26:105–22. doi: 10.5935/1518-0557.20210026
5. Franasiak JM, Forman EJ, Hong KH, Werner MD, Upham KM, Treff NR, et al. The nature of aneuploidy with increasing age of the female partner: a review of 15,169 consecutive trophectoderm biopsies evaluated with comprehensive chromosomal screening. *Fertil Steril* 2014;101:656–63.e1. doi: 10.1016/j.fertnstert.2013.11.004
6. Schwartz D, Mayaux MJ. Female fecundity as a function of age: results of artificial insemination in 2193 nulliparous women with azoospermic husbands. *Federation CECOS. N Engl J Med* 1982;306:404–6. doi: 10.1056/NEJM198202183060706
7. Practice Committee of the American Society for Reproductive Medicine. Definition of infertility: a committee opinion. *Fertil Steril* 2023;120:1170. doi: 10.1016/S0015-0282(23)01971-4
8. Practice Committee of the American Society for Reproductive Medicine, Practice Committee of the Society for Reproductive Endocrinology and Infertility; Penzias A, Azziz R, Bendikson K, Falcone T, et al. Optimizing natural fertility: a committee opinion. *Fertil Steril* 2022;117:53–63. doi: 10.1016/j.fertnstert.2021.10.007
9. The use of antimüllerian hormone in women not seeking fertility care. ACOG Committee Opinion No. 773. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2019;133:e274–8. doi: 10.1097/AOG.0000000000003162
10. Johnson J, Tough S. No-271-delayed child-bearing. *J Obstet Gynaecol Can* 2017;39:e500–15. doi: 10.1016/j.jogc.2017.09.007
11. Hammarberg K, Zosel R, Comoy C, Robertson S, Holden C, Deeks M, et al. Fertility-related knowledge and information-seeking behaviour among people of reproductive age: a qualitative study. *Hum Fertil (Camb)* 2017;20:88–95. doi: 10.1080/14647273.2016.1245447
12. Fowler CI, Koo HP, Richmond AD, Creel D, Asman K. U.S. women's knowledge of reproductive biology. *Womens Health Issues* 2023;33:54–66. doi: 10.1016/j.whi.2022.05.004
13. Swift BE, Liu KE. The effect of age, ethnicity, and level of education on fertility awareness and duration of infertility. *J Obstet Gynaecol Can* 2014;36:990–6. doi: 10.1016/S1701-2163(15)30412-6
14. Okine R, Hughes LM, Smith G, Bonus ML, Feinberg EC, Bernardi LA. Undergraduate students have low fertility knowledge and high anxiety regarding future fertility: an opportunity for education. *Heliyon* 2023;9:e14623. doi: 10.1016/j.heliyon.2023.e14623
15. Bernardi LA, Luck M, Kyweluk MA, Feinberg EC. Knowledge gaps in the understanding of fertility among non-medical graduate students. *F S Rep* 2020;1:177–85. doi: 10.1016/j.xfre.2020.08.002
16. Tsai S, Truong T, Eaton JL. Fertility awareness and attitudes among resident physicians across different specialties. *J Assist Reprod Genet* 2022;39:655–61. doi: 10.1007/s10815-022-02425-z
17. Prepregnancy counseling. ACOG Committee Opinion No. 762. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2019;133:e78–89. doi: 10.1097/AOG.0000000000003013
18. Saumet J, Petropanagos A, Buzaglio K, McMahon E, Warraich G, Mahutte N. No. 356-egg freezing for age-related fertility decline. *J Obstet Gynaecol Can* 2018;40:356–68. doi: 10.1016/j.jogc.2017.08.004
19. García D, Rodríguez A, Vassena R. Actions to increase knowledge about age-related fertility decline in women. *Eur J Contracept Reprod Health Care* 2018;23:371–8. doi: 10.1080/13625187.2018.1526895
20. Fritz R, Klugman S, Lieman H, Schulkin J, Taouk L, Castleberry N, et al. Counseling patients on reproductive aging and elective fertility preservation—a survey of obstetricians and gynecologists' experience, approach, and knowledge. *J Assist Reprod Genet* 2018;35:1613–21. doi: 10.1007/s10815-018-1273-7
21. Osterman MJ, Hamilton BE, Martin JA, Driscoll AK, Valenzuela CP. Births: final data for 2023. *Natl Vital Stat Rep* 2025;74:1–87. doi: 10.15620/cdc/175204
22. Herzberger EH, Sun B, Engel O, Wolf Y, Herzberger S, Kimhy RB, et al. How effective is digital educational content in shaping fertility awareness? An interventional, cross-sectional study. *J Assist Reprod Genet* 2022;39:2335–41. doi: 10.1007/s10815-022-02590-1
23. Blakemore JK, Bayer AH, Smith MB, Grifo JA. Infertility influencers: an analysis of information and influence in the fertility webspace. *J Assist Reprod Genet* 2020;37:1371–8. doi: 10.1007/s10815-020-01799-2
24. Peyser A, Goldstein L, Mullin C, Goldman RH. Fertility education: what's trending on Instagram. *Fertil Res Pract* 2021;7:3–6. doi: 10.1186/s40738-021-00095-6
25. Jahnke H, Henrich N, Salem W, Shah N. Evaluating the evidence base for TikTok videos on strategies for becoming pregnant. *O G Open* 2024;1:e1–3. doi: 10.1097/og9.0000000000000038
26. Szeliga A, Calik-Ksepka A, Maciejewska-Jeske M, Grymowicz M, Smolarczyk K, Kostrzak A, et al. Autoimmune diseases in patients with premature ovarian insufficiency—our current state of knowledge. *Int J Mol Sci* 2021;22:2594. doi: 10.3390/ijms22052594
27. Vogt EC, Breivik L, Røyrvik EC, Grytaas M, Husebye ES, Øksnes M. Primary ovarian insufficiency in women with Addison's disease. *J Clin Endocrinol Metab* 2021;106:e2656–63. doi: 10.1210/clinem/dgab140
28. Sadeghpour N, Mirmosayyeb O, Bjørklund G, Shaygannejad V. Is fertility affected in women of childbearing age with multiple sclerosis or neuromyelitis optica spectrum disorder? *J Mol Neurosci* 2020;70:1829–35. doi: 10.1007/s12031-020-01576-x
29. Wang R, Lv Y, Dou T, Yang Q, Yu C, Guan Q. Autoimmune thyroid disease and ovarian hypofunction: a review of literature. *J Ovarian Res* 2024;17:125. doi: 10.1186/s13048-024-01451-y
30. Oktem O, Guzel Y, Aksoy S, Aydin E, Urman B. Ovarian function and reproductive outcomes of female patients with systemic lupus erythematosus and the strategies to preserve their fertility. *Obstet Gynecol Surv* 2015;70:196–210. doi: 10.1097/OGX.0000000000000160
31. Shah DK. Diminished ovarian reserve and endometriosis: insult upon injury. *Semin Reprod Med* 2013;31:144–9. doi: 10.1055/s-0032-1333479
32. Tan Z, Gong X, Wang CC, Zhang T, Huang J. Diminished ovarian reserve in endometriosis: insights from in vitro, in vivo, and human studies—a systematic review. *Int J Mol Sci* 2023;24:15967. doi: 10.3390/ijms242115967
33. Feferkorn I, Suarathana E, Kigloo HN, Abow-Mohamed I, Golyari Y, Tulandi T. Combined effects of age and endometriosis on



- ovarian reserve in women with infertility. *Int J Gynaecol Obstet* 2023;161:129–36. doi: 10.1002/ijgo.14519
34. Tan Z, Gong X, Li Y, Hung SW, Huang J, Wang CC, et al. Impacts of endometrioma on ovarian aging from basic science to clinical management. *Front Endocrinol (Lausanne)* 2023;13:1073261. doi: 10.3389/fendo.2022.1073261
 35. Moravek MB, Kinnear HM, George J, Batchelor J, Shikanov A, Padmanabhan V, et al. Impact of exogenous testosterone on reproduction in transgender men. *Endocrinology* 2020;161:bqaa014. doi: 10.1210/endo/bqaa014
 36. Adeleye AJ, Cedars MI, Smith J, Mok-Lin E. Ovarian stimulation for fertility preservation or family building in a cohort of transgender men. *J Assist Reprod Genet* 2019;36:2155–61. doi: 10.1007/s10815-019-01558-y
 37. Ding T, Yan W, Zhou T, Shen W, Wang T, Li M, et al. Endocrine disrupting chemicals impact on ovarian aging: evidence from epidemiological and experimental evidence. *Environ Pollut* 2022;305:119269. doi: 10.1016/j.envpol.2022.119269
 38. Ding N, Harlow SD, Randolph JFJ, Loch-Caruso R, Park SK. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their effects on the ovary. *Hum Reprod Update* 2020;26:724–52. doi: 10.1093/humupd/dmaa018
 39. Patel S, Zhou C, Rattan S, Flaws JA. Effects of endocrine-disrupting chemicals on the ovary. *Biol Reprod* 2015;93:20. doi: 10.1095/biolreprod.115.130336
 40. Bloom MS, Mok-Lin E, Fujimoto VY. Bisphenol A and ovarian steroidogenesis. *Fertil Steril* 2016;106:857–63. doi: 10.1016/j.fertnstert.2016.08.021
 41. Evangelinakis N, Geladari EV, Geladari CV, Kontogeorgi A, Papaioannou G, Peppas M, et al. The influence of environmental factors on premature ovarian insufficiency and ovarian aging. *Maturitas* 2024;179:107871. doi: 10.1016/j.maturitas.2023.107871
 42. Cameron-Pimblett A, La Rosa C, King TFJ, Davies MC, Conway GS. The Turner syndrome life course project: karyotype-phenotype analyses across the lifespan. *Clin Endocrinol (Oxf)* 2017;87:532–8. doi: 10.1111/cen.13394
 43. Li N, Xu W, Liu H, Zhou R, Zou S, Wang S, et al. Whole exome sequencing reveals novel variants associated with diminished ovarian reserve in young women. *Front Genet* 2023;14:1154067. doi: 10.3389/fgene.2023.1154067
 44. Qin Y, Jiao X, Simpson JL, Chen Z. Genetics of primary ovarian insufficiency: new developments and opportunities. *Hum Reprod Update* 2015;21:787–808. doi: 10.1093/humupd/dmv036
 45. Heddar A, Ogur C, Da Costa S, Braham I, Billaud-Rist L, Findikli N, et al. Genetic landscape of a large cohort of Primary Ovarian Insufficiency: New genes and pathways and implications for personalized medicine. *EBioMedicine*. 2022;84:104246. doi: 10.1016/j.ebiom.2022.104246
 46. Guideline Development Group on Premature Ovarian Insufficiency. Premature ovarian insufficiency (POI). Accessed July 22, 2025. <https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency>
 47. Wang Y, Yuan Y, Meng D, Liu X, Gao Y, Wang F, et al. Effects of environmental, social and surgical factors on ovarian reserve: Implications for age-relative female fertility. *Int J Gynaecol Obstet*. 2021;154:451–8. doi: 10.1002/ijgo.13567
 48. Hyland A, Piazza K, Hovey KM, Tindle HA, Manson JE, Messina C, et al. Associations between lifetime tobacco exposure with infertility and age at natural menopause: the Women's Health Initiative Observational Study. *Tob Control* 2016;25:706–14. doi: 10.1136/tobaccocontrol-2015-052510
 49. Werner L, van der Schouw YT, de Kat AC. A systematic review of the association between modifiable lifestyle factors and circulating anti-Müllerian hormone. *Hum Reprod Update* 2024;30:262–308. doi: 10.1093/humupd/dmae004

CONFLICT OF INTEREST STATEMENT

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Anticipatory counseling regarding ovarian-factor fertility decline. Committee Statement No. 22. American College of Obstetricians & Gynecologists. *Obstet Gynecol* 2025;146:e98–e104.

