Contraceptive-specific antimüllerian hormone values in reproductive-age women: a population study of 42,684 women

Scott M. Nelson, M.D.,[a,b,c] Benjamin J. Ewing, M.S.,[d] Piotr S. Gromski, Ph.D.,[a] and Sharon F. Briggs, Ph.D.[d]

[a] School of Medicine, University of Glasgow, Glasgow, United Kingdom; [b] NIHR Bristol Biomedical Research Centre, Bristol, United Kingdom; [c] The Fertility Partnership, Oxford, United Kingdom; and [d] Modern Fertility, San Francisco, California

Objective: To determine how the contraceptive-specific serum antimüllerian hormone (AMH) levels compare across ages and percentiles in a reproductive-age cohort.
Design: Cross-sectional analysis of a prospectively recruited cohort.
Setting: Community.
Patient(s): This study included US-based women of reproductive age who purchased a fertility hormone test and consented to participate in research between May 2018 and November 2021. At the time of hormone testing, participants were users of various contraceptives (combined oral contraceptive [n = 6,850], progestin-only pill [n = 465], hormonal [n = 4,867] or copper [n = 1,268] intrauterine device, implant [n = 834], vaginal ring [n = 886]) or women with regular menstrual cycles (n = 27,514).
Intervention(s): Contraceptive use.
Main Outcome Measure(s): Age and contraceptive-specific estimates of AMH.
Result(s): There were contraceptive-specific effects on AMH with effect estimates ranging from 0.83 (95% confidence interval [CI], 0.82–0.85) (17% lower) for the combined oral contraceptive pill to no effect (1.00; 95% CI, 0.98–1.03) for the hormonal intrauterine device. We did not observe age-specific differences in suppression. However, there were differential suppressive effects of the contraceptive method across AMH percentiles, with the greatest effect at lower percentiles and least effect at higher percentiles. For example, for women taking the combined oral contraceptive pill, the AMH level was 32% lower at the 10th percentile (coefficient, 0.68; 95% CI, 0.65–0.71), 19% lower at the 50th percentile (coefficient, 0.81; 95% CI, 0.79–0.84), and 5% lower at the 90th percentile (coefficient, 0.95; 95% CI, 0.92–0.98), with other forms of contraception showing similar discordances.
Conclusion(s): These findings reinforce the body of literature that shows that hormonal contraceptives have different impacts on the AMH levels at a population level. These results add to this literature that these effects are not consistent; instead, the greatest impact occurs at the lower AMH percentiles. However, these contraceptive-dependent differences are small compared with the known biological variability in ovarian reserve at any given age. These reference values enable robust assessment of an individual's ovarian reserve relative to their peers without requiring cessation or potentially invasive removal of contraception. (Fertil Steril® 2023;119:1069-77. ©2023 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: AMH, contraception, combined oral contraceptive pill, hormonal IUD

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Reprint requests: Scott M. Nelson, M.D., School of Medicine, University of Glasgow, New Lister Building, Glasgow G31 2ER, United Kingdom (E-mail: Scott.Nelson@glasgow.ac.uk).

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Changes in global social structures and demographic transition have contributed to the increased prevalence of delayed childbearing and the widespread use of contraception (1, 2). As such, more people are proactively seeking information regarding their ovarian reserve and potential reproductive window while using different modes of contraception (3–6). The antimüllerian hormone (AMH) is increasingly recognized as the best currently available biomarker of the functional ovarian reserve, reflecting its associations with primordial follicle counts (7) and

treatment outcomes such as the ovarian response (8, 9). However, similar to other common measures of ovarian reserve, AMH has been shown to be impacted by some contraceptive methods (5, 10–18).

Early studies were inconsistent in quantifying the impact of contraceptives on AMH, with some suggesting a reduction and others suggesting no effect. The largest study to date (n = 27,125) has reported more precise estimates on the mean impact of a diverse set of contraceptives, with combined methods (combined oral contraceptive and vaginal ring) having the largest effect and locally acting methods (hormonal and copper intrauterine device [IUD]) having limited to no impact (15). Furthermore, analysis of the Study of Environment, Lifestyle, and Fibroids (SELF) cohort (n = 1,693 African American women) demonstrated that although AMH was reduced with all hormonal contraception types, the cumulative duration of hormonal contraceptive was not appreciably associated with the degree of reduction in the AMH levels (19). Although the contraceptive-associated reductions in the AMH levels are known to be temporary and reversible (19, 20), the time required for return to baseline is variable and contraceptive mode specific with some methods (e.g., medroxyprogesterone acetate injection) taking up to 12 months (19).

At present, it is still unclear whether the apparent suppression of AMH by some modes of contraception is consistent across all reproductive ages. Furthermore, are all women affected equally, or are women on the diverse AMH percentiles differentially affected by a specific mode of contraception? Can a clinically useful interpretation of AMH be made while on contraceptives, or should patients be asked to pause their contraception to obtain a more reliable AMH value while perhaps risking an unintended pregnancy? To answer these questions, we aimed to assess the contraceptive method–specific AMH reference values across reproductive ages and AMH levels in a large US population. Therefore, our objective was to enable women on any specific form of contraception to be able to assess their own AMH relative to more appropriate comparisons: first, to their peers making a similar choice of contraception and, second, to women not using these modes of contraception.

MATERIALS AND METHODS

Study Design and Participants

Study participants purchased a fertility hormone test from Modern Fertility (San Francisco, CA) between May 2018 and November 2021 and consented to research. The consent rate is approximately 65%. Participants were between the ages of 21 and 45 years. Those who were not using hormonal contraceptives were excluded if they self-reported an irregular cycle defined as <21 or >35 days. Participants who had a previous diagnosis of gonadal disorder/dysfunction, previous premature ovarian insufficiency, polycystic ovary syndrome, endometriosis, pelvic surgery, or known previous or current endocrine or metabolic disorders were excluded (Supplemental Fig. 1, available online).

Contraceptive type was self-reported and included combined oral contraceptive pill (COCP), progestin-only pill (POP), hormonal IUD, copper IUD, implant, vaginal ring, depot medroxyprogesterone injection, or patch. Baseline demographic data was self-reported via online questionnaire and included height, weight, smoking status, race/ethnicity, previous births, age of maternal menopause, and age at menarche. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants self-identified as American Indian or Alaskan, white, black or African American, Hispanic or Latino, Asian, Native Hawaiian or Pacific Islander, or "other." Individuals who self-identified as more than 1 race/ethnicity were considered of multirace/multiethnicity.

All participants provided informed consent to participate in the research with all data deidentified before analysis. This study was approved by the Western Institutional Review Board (protocol number 20180443), an ethics committee that ensures that proper research consent and methodology are followed.

AMH Measurement

Participants who used a copper IUD or no contraceptive were instructed to collect their sample on the third day of their menstrual cycle (range, days 2–4). Participants who used a hormonal IUD or POP who reported regular menstrual cycles were also instructed to collect on day 3. All other participants were instructed to collect on any day of their menstrual cycle.

Blood samples were collected by means of one of the following methods depending on the participants' preference: dried blood spot collection card processed by US Specialty Labs (San Diego, CA) or venipuncture processed at Quest Diagnostics (Secaucus, NJ). Both laboratories used Access AMH immunoassay by Beckman Coulter (Brea, CA) that has a reportable measuring range of 0.08–24 ng/mL, limit of detection of $\leq$0.02 ng/mL, and limit of quantitation of $\leq$0.08 ng/mL (21). All samples were analyzed continuously throughout the study period. For the dried blood spot samples, 4 large drops of blood were collected on serum separator cards. After drying completely, the cards were mailed to the laboratory for processing. Coefficient of variation varied from 3.3% to 4.5% as previously reported (22). Because previous study has demonstrated that AMH levels are stable only for up to 14 days, any samples received after the 14-day window were not processed, and a new sample was collected (23). Validation studies suggest excellent concordance between dried blood spot and venipuncture sampling for AMH ($r > 0.97$) and no statistically significant bias, suggesting that the AMH values from these 2 methods can be used and interpreted interchangeably (22, 23).

For the analysis, values below the assay limit of quantitation (henceforth below quantifiable limit [BQL]) were replaced by the assay upper limit of quantitation (0.079 ng/mL). We handled BQL replacement by also replacing values with 0.0001 ng/mL to determine the robustness of our selected approach because any true estimate would lie between these 2 extremes. After the BQL values were recoded, all AMH values were natural log-transformed to reduce skew and allow for normality assumptions to be met in the quantile additive regression.

Statistical Analysis

Patient characteristics were described using mean and standard deviation for continuous variables and frequencies and percentages for nominal variables. The overall, age-adjusted effect of contraception type on AMH was estimated by a general additive model.

The AMH percentiles were derived using smooth additive quantile regression (via the qgam package), which allows for well-calibrated inference about the conditional quantiles and automatic estimation of the smoothing parameters (24). The smoothing function allows the effect of age on AMH to vary; the quantile models estimate separate age smoothing by birth control type. The model uses its own distribution, called ELF distribution, which is an extension of the log-f distribution. The effect estimates reflect the Bayesian nonparametric quantile regression modeling outcomes. Exponentiated effects indicate the relative multiplicative difference between the response (birth control type) and reference (no birth control), which can be interpreted as the percentage change in the AMH values. Because qgam does not assume that the outcomes are binomial, the output is neither a risk ratio nor odd ratio. Additionally, we performed an adjusted additive quantile regression analysis including BMI, race, education, and smoking habits as covariates and an unadjusted additive quantile regression for participants with complete covariate information only.

All analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria), and all code files are shown in the Supplemental Materials.

We report the results for 5 empirical percentiles—10th, 25th, 50th, 75th, and 90th—and the estimated median AMH and confidence interval (CI) across birth control types for the ages of 20, 25, 30, 35, 40, and 45 years. Nomogram tables were also constructed.

RESULTS

A total of 42,684 subjects met the inclusion criteria, with 15,170 using 6 different modes of contraception and 27,514 with regular menstrual cycles not using any form of contraception (Supplemental Fig. 1). Overall participants were aged 31.4 ± 4.6 years, white, college educated, and nonsmokers with mean BMI and AMH level of 26.3 ± 6.5 kg/m^2 and 3.4 ± 2.7 ng/mL, respectively (Table 1). The COCP was the most common form of contraception used by 45.2% of participants with contraceptives, with the hormonal IUD used by 31.3%. The other methods were substantially less frequently used (copper IUD, 8.4%; vaginal ring, 5.8%; implant, 5.5%; and POP, 3.0%). We did not include depot medroxyprogesterone injection or patch in our results because of small sample sizes. Participants who used contraception methods were slightly younger than their nonuser counterparts, with those who chose the implant exhibiting the youngest mean age (Table 1 and Supplemental Fig. 2). Other characteristics, including age at menarche, number of previous births, and age at maternal menopause, were not substantially different across contraceptive types or between users and nonusers (Table 1).

We first calculated age-adjusted effect estimates for the difference in the AMH levels by contraceptive type (Table 2). At all ages, the COCP was associated with lower AMH levels (age adjusted, 17% lower; coefficient, 0.83; 95% CI, 0.82–0.85) (Table 2 and Fig. 1). Similarly, the use of the vaginal ring was associated with lower AMH levels (coefficient, 0.84; 95% CI, 0.80–0.89). For progestin-only–derived contraceptive methods, the greatest differences in the AMH values were observed in women who chose the implant (coefficient, 0.85; 95% CI, 0.81–0.90), with the POP (coefficient, 0.89; 95% CI, 0.83–0.96) exhibiting minor differences. For intrauterine contraceptive methods, both the hormonal IUD (coefficient, 1.00; 95% CI, 0.98–1.03) and copper IUD (coefficient, 1.06; 95% CI, 01.01–1.11) were not associated with lower AMH levels across the age ranges (Table 2 and Fig. 1). Estimates were similar but with wider CIs in the unadjusted complete case analysis.

We then investigated the effects of contraceptive use across ages at median AMH levels (Supplemental Table 1 and Fig. 1). These results show remarkable consistency in the contraceptive effect across age ranges. The data are particularly well illustrated by the COCP, where we observed statistically significant and consistently lower AMH levels, and hormonal IUD, where we noted a complete overlap not only of the confidence internals but also of the point estimates themselves (Fig. 1). The 95% CI was wider where there were fewer data points—at the lower and upper age bounds and in contraceptive types with smaller sample sizes (Supplemental Fig. 2). We additionally performed 2 sensitivity analyses. In the first, we modified our approach for handling BQL values. In the second, we adjusted for BMI, race, education, and smoking habits (Supplemental Fig. 4). Because the adjusted analysis requires all covariate data to be present, our sample size for this analysis was approximately half the unadjusted analysis (n = 20,444). Neither analysis changed the interpretation of the results.

We then turned our analysis to determine the effect of contraceptive use across AMH percentiles. We found that unlike age, there were large differences in the suppressive effects of contraceptives on the basis of AMH percentile, with the greatest impact on the lowest percentiles and the least impact at the higher percentiles (Supplemental Table 2 and Fig. 2). For example, the estimated median for the COCP was 19% lower (coefficient, 0.81; 95% CI, 0.79–0.84); however, at the 10th percentile, the estimate was 32% lower (coefficient, 0.68; 95% CI, 0.65–0.71), and at the 90th percentile, it was 5% lower (coefficient, 0.95; 95% CI, 0.92–0.98). Similar differential associations with AMH were observed for the vaginal ring, implant, and POP (Fig. 2). The hormonal IUD estimates did not significantly differ from those of the no contraceptive group regardless of the percentile; however, point estimate differences were observed matching this trend (Supplemental Table 2 and Fig. 2). The exemplar use of these contraceptive-specific reference ranges is shown for the age of 30 years in Supplemental Table 2, where the predicted 10th, 25th, 50th, 75th, and 90th percentiles and corresponding 95% CIs are shown for each mode of contraception.

Finally, we combined analyses by comparing both across ages and across percentiles (Supplemental Table 3 and

TABLE 1

Baseline characteristics stratified by mode of contraception.

Variable	Overall n = 42,684	No BC n = 27,514	Copper IUD n = 1,268	Hormonal IUD n = 4,867	Implant n=834	Progestin-only pill n = 465	Combined oral contraceptives n = 6,850	Vaginal ring n = 886
Age (y)	31.4 (4.6)	32.1 (4.7)	30.8 (4.1)	30.1 (3.9)	28.8 (3.8)	30.7 (4.4)	29.9 (4)	30.9 (3.8)
AMH (ng/mL)	3.4 (2.7)	3.4 (2.6)	3.6 (2.4)	3.8 (2.9)	3.6 (2.9)	3.4 (2.8)	3.4 (2.9)	3.3 (3)
BMI (kg/m^2)	26.3 (6.5)	26.7 (6.8)	24.9 (5.3)	25.7 (6.0)	26.9 (6.6)	27.2 (7.3)	25.3 (5.7)	25.9 (5.5)
Age of menarche	12.5 (1.6)	12.5 (1.6)	12.5 (1.5)	12.6 (1.6)	12.6 (1.6)	12.5 (1.7)	12.6 (1.6)	12.6 (1.6)
% unsure	544 (1.3%)	385 (1.4%)	7 (0.6%)	56 (1.2%)	11 (1.3%)	5 (1.1%)	75 (1.1%)	5 (0.6%)
Maternal age of menopause	50.8 (5.5)	50.8 (5.5)	51 (5.2)	50.9 (5.6)	50 (5.6)	50.8 (5.5)	50.8 (5.2)	50.8 (5.4)
% has not reached menopause	3,793 (8.9%)	2,383 (8.7%)	94 (7.4%)	444 (9.1%)	113 (13.5%)	42 (9%)	645 (9.4%)	72 (8.1%)
% unsure	8,945 (21%)	5,939 (21.6%)	245 (19.3%)	942 (19.4%)	154 (18.5%)	93 (20%)	1,415 (20.7%)	157 (17.7%)
Sample collection method (% dried blood spot)	41,219 (96.6%)	26,509 (96.4%)	1,223 (96.5%)	4,739 (97.4%)	813 (97.5%)	446 (95.9%)	6,633 (96.8%)	856 (96.6%)
Education								
High school or less	622 (2.7%)	506 (3.4%)	5 (0.7%)	26 (1%)	18 (3.9%)	8 (3.3%)	54 (1.6%)	5 (1.1%)
Some college	2,996 (13.1%)	2,304 (15.5%)	55 (7.7%)	208 (8%)	60 (13.1%)	30 (12.2%)	311 (8.9%)	28 (6.2%)
Completed college	11,117 (48.6%)	7,075 (47.5%)	364 (50.8%)	1,308 (50.3%)	229 (50.1%)	117 (47.6%)	1,787 (51.3%)	237 (52.5%)
Attended advanced degree	8,125 (35.5%)	5,022 (33.7%)	293 (40.9%)	1,059 (40.7%)	150 (32.8%)	91 (37%)	1,329 (38.2%)	181 (40.1%)
No. of missing	19,824	12,607	551	2,266	377	219	3,369	435
Race/ethnicity								
White	17,712 (75.2%)	11,285 (73.5%)	587 (79.3%)	2,145 (79.9%)	331 (72.6%)	175 (69.4%)	2,833 (79%)	356 (74.9%)
Hispanic/Latino	1,455 (6.2%)	1,076 (7%)	25 (3.4%)	108 (4%)	28 (6.1%)	13 (5.2%)	176 (4.9%)	29 (6.1%)
Asian	1,044 (4.4%)	676 (4.4%)	28 (3.8%)	108 (4%)	18 (3.9%)	14 (5.6%)	175 (4.9%)	25 (5.3%)
Black	877 (3.7%)	697 (4.5%)	12 (1.6%)	43 (1.6%)	16 (3.5%)	16 (6.3%)	78 (2.2%)	15 (3.2%)
Multiracial	2,175 (9.2%)	1,410 (9.2%)	79 (10.7%)	256 (9.5%)	57 (12.5%)	32 (12.7%)	295 (8.2%)	46 (9.7%)
Other	286 (1.2%)	212 (1.4%)	9 (1.2%)	25 (0.9%)	6 (1.3%)	2 (0.8%)	28 (0.8%)	4 (0.8%)
No. of missing	19,135	12,158	528	2,182	378	213	3,265	411
% with any previous births	3,091 (15.1%)	2,621 (18.8%)	65 (10.6%)	189 (8.8%)	28 (7.5%)	27 (13%)	139 (4.9%)	22 (6%)
Current smoking habits								
Nonsmokers	31,327 (90.3%)	20,169 (89.3%)	976 (90.5%)	3,561 (91.7%)	578 (90.7%)	331 (87.8%)	5,040 (93.5%)	672 (92.4%)
Smokers	3,354 (9.7%)	2,415 (10.7%)	103 (9.5%)	323 (8.3%)	59 (9.3%)	46 (12.2%)	353 (6.5%)	55 (7.6%)
No. of missing	8,003	4,930	189	983	197	88	1,457	159

Note: Values are mean (standard deviation) for continuous variables and frequency (percent) for nominal variables. AMH = antimüllerian hormone; BC = birth control; BMI = body mass index; IUD = intrauterine device.

Nelson. Contraceptive-specific AMH values. Fertil Steril 2023.

TABLE 2

Predicted estimates of effect on each mode of contraception on antimüllerian hormone and confidence intervals, controlling for age, derived by generalized additive models.

Contraceptive type	Estimate	5th confidence interval	95th confidence interval
Copper IUD	1.06	1.01	1.11
Hormonal IUD	1.01	0.98	1.03
Implant	0.85	0.81	0.90
Progestin-only pill	0.89	0.83	0.96
COCP	0.84	0.81	0.90
Vaginal ring	0.84	0.80	0.89

COCP = combined oral contraceptive pill; IUD = intrauterine device.

Nelson. Contraceptive-specific AMH values. Fertil Steril 2023.

Supplemental Fig. 3). The discordant effects on absolute levels across the percentiles were present at all ages, with widening CI at the upper percentiles of AMH for all modes of contraception. At the age of 30 years, where we had the greatest precision, comparing the estimate and CI of the controls with those of the COCP group showed that the CI overlapped at the 90th percentile (controls, 7.33 ng/mL; 95% CI, 7.17–7.50, vs. COCP, 7.18 ng/mL; 95% CI, 6.91–7.46) but approximately 14.7% lower at the 50th percentile (controls, 3.26 ng/mL; 95% CI, 3.19–3.34, vs. COCP, 2.78 ng/mL; 95% CI, 2.68–2.90) and then approximately 26% lower at the 10th percentile (controls, 1.22 ng/mL; 95% CI, 1.17–1.26, vs. COCP, 0.90 ng/mL; 95% CI, 0.85–0.96) (Supplemental Table 3). Similar percentile-specific effects were observed for the other modes of hormonal contraception. It is important to note that these findings are presented in relative differences rather than absolute differences. In some cases, differences in relative effects do not reflect differences in absolute effects (Supplemental Table 3; comparing COCP absolute differences across percentiles at the age of 30 years). However, this is not true across all ages and percentiles (Supplemental Table 1 and Fig. 2).

DISCUSSION

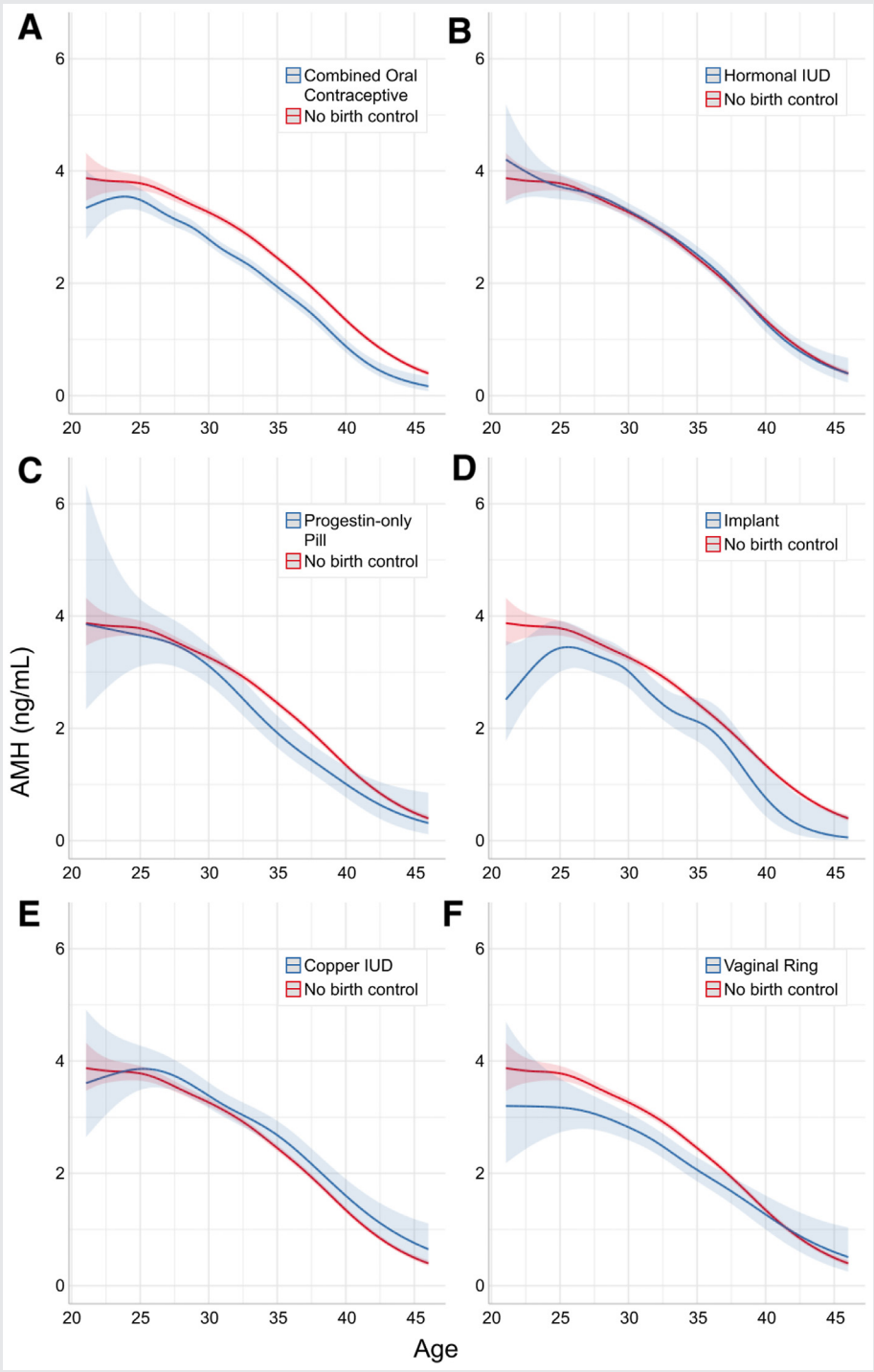
In this large population of reproductive-age women with no personal history of endocrine or surgical factors that may impact ovarian reserve, we have derived the contraceptive-specific reference values for AMH. We demonstrate that the AMH level was lower in women using the COCP, ring, POP and implant than in those who were not using contraceptives. For these 4 modes of contraception, women in the lower percentiles of AMH displayed potentially even lower AMH levels than their peers with higher AMH levels. No suppressive effect was observed for either the hormonal or copper IUD. Collectively, these data facilitate women and clinicians to accurately interpret AMH relative to age-matched peers using a similar mode of contraception without the inconvenience of having to discontinue contraception, allow for a washout period, and then reanalyze AMH. This is particularly relevant for women with long-acting reversible contraception, where invasive procedures would be required for the cessation of contraception.

The lower AMH levels in women who choose hormonal-based contraceptives are consistent with their known variable suppressive effects on pituitary gonadotropins resulting in inhibition of follicle development and ovulation (25, 26). Both the currently available COCPs and the combined contraceptive vaginal ring are effective in inhibiting folliculogenesis, whereas the POP and hormonal IUD are less effective (26). The degree of follicular activity remaining depends on the type and dose of steroids used, administration regimen, route of administration, user compliance, and individual responsiveness of the woman taking the hormones (27, 28). This contraceptive-specific effect on follicle populations will translate to the circulating AMH levels because follicles 5–8 mm in size make the greatest contribution (approximately 60%) to the circulating AMH levels, with a lesser contribution from follicles with a size of >8 mm (15%–20%) or <5 mm (20%–25%) (29). Thus, contraceptive methods that affect later stages of follicular growth are less likely to impact on the circulating AMH levels. This relationship of follicle size to the AMH levels may also partially explain our observed percentile effect. Those women with the greatest number of small follicles (on the higher percentiles) exhibit the lowest contraception-related difference in the AMH level as antral follicles are in themselves self-limiting in absolute number (30). This is in comparison with women with only a few follicles where the inhibition of the critical stages of antral development would have a more profound effect on the circulating AMH levels (29).

Our effect estimates are consistent with many of the previous observational studies using cross-sectional and longitudinal designs (5, 10–19, 31–33). In fact, our observation of percentile-specific effects may explain some of the heterogeneity in the previous published literature. Within a cohort enriched for individuals with low AMH, effect estimates may be exaggerated and vice versa if enriched for high AMH values. Our participants serve as a helpful reference point for the general population. Individuals who choose specific forms of contraception may differ from women who choose an alternative form, and this is unlikely to be completely adjusted for even in multivariable analyses because of the potential for significant unmeasured confounding. For example, women with dysmenorrhea may wish to use a hormonal form of contraception rather than the copper IUD to reduce the impact of menstrual cyclicity on their quality of life (34). However, these same women may have undiagnosed endometriosis adversely impacting on their ovarian reserve with the only manifestation being dysmenorrhea (35). The ability to interpret AMH relative to similar contraceptive users may minimize the risk of unmeasured confounding driven by contraceptive type choice.

From a clinical perspective, the lack of a negative association of AMH with a copper IUD or hormonal IUD in situ would suggest that removal would have no effect on AMH. In contrast, for patients using alternative hormonal forms of contraception, where an association with lower AMH levels was observed, several months of cessation may be required for the functional ovarian reserve to be fully restored (20). This effect may be particularly relevant for women on the lowest percentiles, particularly because women with a high

FIGURE 1



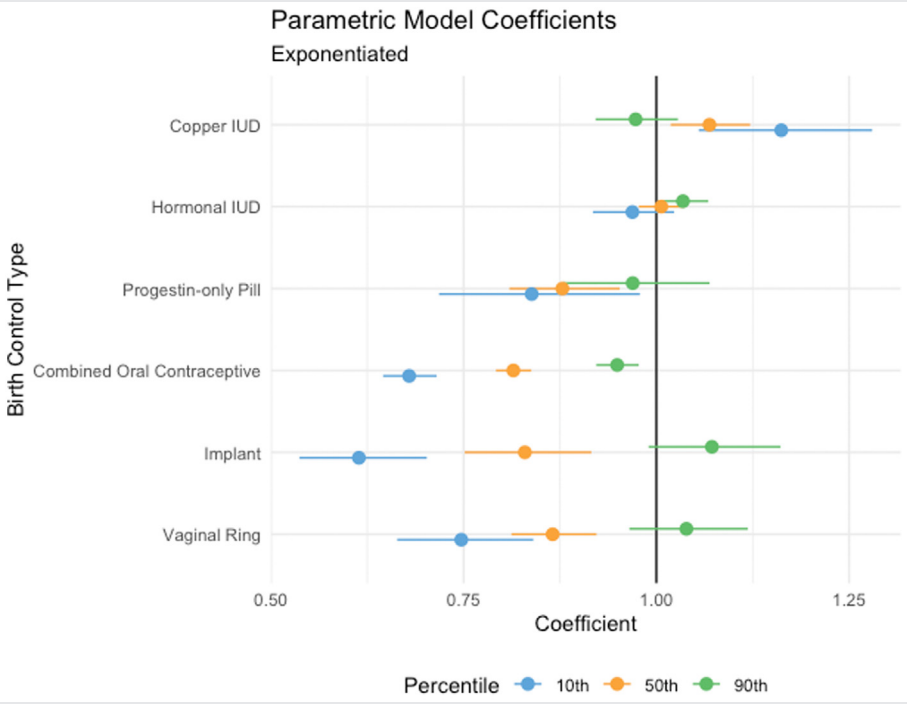
Median contraceptive-specific antimüllerian hormone (AMH) levels compared with those of controls who were not using contraceptives. The estimates were derived from smooth additive quantile regression models. The dark lines indicate the point estimates for the 50th percentile; the shaded regions indicate the 95% confidence intervals of the 50th percentile. Blue, contraceptive users; red, controls who were not using contraceptives. IUD = intrauterine device.

Nelson. Contraceptive-specific AMH values. Fertil Steril 2023.

AMH percentile will continue to have a high AMH level even on cessation of their chosen mode of contraception (e.g., the COCP).

Although our study has a number of strengths, including its size, selection of women with regular menstrual cycles, and no relevant medical history as the reference population,

FIGURE 2



Suppressive effects of contraceptives across antimüllerian hormone (AMH) percentiles. The exponentiated parametric model coefficients were shown for the 10th (blue), 50th (orange), and 90th (green) AMH percentiles. The results could be interpreted as the percentage change in the AMH values with no birth control as the reference group. For hormonal contraceptive methods, effects were largest at the 10th percentile. The circles indicate the point estimates; the horizontal lines indicate the 95% confidence intervals. IUD = intrauterine device.

Nelson. Contraceptive-specific AMH values. Fertil Steril 2023.

we do acknowledge several limitations. The participants were all customers of Modern Fertility, and therefore, there may be selection bias, particularly with respect to socioeconomic position and environmental, lifestyle, reproductive, or early childhood factors that may impact on AMH. However, the AMH values determined for the reference population are similar to the values published by Beckman Coulter in their package inserts, with their values derived from 620 apparently healthy women aged 18–45 years, suggesting that our participants are generally reflective of similar women (21). We have used a multiethnic population, and therefore, although a more homogenous ethnic cohort may give slightly different point estimates, our findings are more generalizable than several studies that have solely recruited from fertility clinics. We do not have specific contraceptive brands, and we acknowledge that different forms of steroid hormones within a contraceptive type may have differential effects that would be warranted in studies of adequate size. Similarly, we do not have the duration of contraceptive use for the study population. We acknowledge that women may choose different modes of contraception on the basis of personal preference or underlying pathologies. We were unable to provide estimates on depot medroxyprogesterone injection or patch modes of contraception because of the small sample size. We have used home testing and variable day of testing; however, we have previously shown the strong correlations with early follicular testing and that cycle day is not a significant determinant of the AMH levels (22, 23), reinforcing the convenience of being able to perform measurements on any day in women with oligomenorrhea or amenorrhea secondary to their contraceptive choice. Lastly, we have undertaken cross-sectional analysis, and the associations observed may not be casual and acknowledge the potential for unmeasured confounding.

In conclusion, our analyses of the AMH reference ranges for the 6 most common forms of contraception enable women and their clinicians to understand their functional ovarian reserve relative to their peers and women not using hormonal contraception without having to discontinue contraception and the associated risks. We believe that these data may be used in place of discontinuing contraceptives to obtain useful information about ovarian reserve, thus limiting the potential of adverse outcomes associated with the lack of contraception. Further longitudinal studies in different populations will enable more accurate estimation of the long-term impacts of different modes on contraception on the functional ovarian reserve.

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Valores de hormona antimülleriana anticonceptivo específicas en mujeres en edad reproductiva: población estudiada de 42684 mujeres.

Objetivo: Determinar cómo es el nivel en suero de hormona antimülleriana (AHM) anticonceptivo específico a través de las edades y los percentiles en una cohorte en edad reproductiva.

Diseño: Análisis transversal de cohorte reclutada prospectivamente.

Ajustes: comunidad.

Paciente(s): Este estudio incluye mujeres con base en US en edad reproductiva quienes compraron un test hormonal de fertilidad y consintieron participar en la investigación entre Mayo de 2018 y Noviembre de 2021. En el tiempo de testeo hormonal, las participantes eran usuarias de varios anticonceptivos (anticonceptivos orales combinados [n= 6,850], píldora de progesterona sola [n= 465], dispositivos intrauterinos hormonal [n= 4,867], o de cobre [n= 1,268], implantes [n= 834], anillo vaginal [n= 886] o mujeres con ciclos menstruales regulares [27,514].

Intervención(es): uso de anticonceptivos.

Principal(es) medida(s) de resultado(s): Edad y estimaciones específicas anticonceptivas de AHM.

Resultado(s): Hubo efectos específicos de los anticonceptivos en AHM con el rango del efecto estimado desde 0.83 (95% intervalo de confianza [CI], 0.82 – 0.85) (17% más bajo) para las píldoras anticonceptivas orales combinadas hasta los dispositivos intrauterinos en donde no hubo efectos (1.00; 95% CI, 0.98 – 1.03). No observamos diferencias específicas en la edad de la supresión. Sin embargo, hubo efectos de supresión diferentes de los anticonceptivos a través de los percentiles de AHM, con el mayor efecto en los bajos y el menor efecto en los altos. Por ejemplo, para mujeres tomando las píldoras anticonceptivas combinadas, el nivel de AHM fue de 32% más baja en el percentil 10 (coeficiente, 0.68; 95% CI, 0.65-0.71), 19% más bajo en el percentil 50 (coeficiente, 0.81; 95% CI, 0.79-0.84), y 5% más bajo en el percentil 90 (coeficiente, 0.95; 95% CI, 0.92-0.98), con otras formas de anticoncepción mostraron similares discordancias.

Conclusión(es): Estos hallazgos refuerzan los de la literatura que muestran que anticonceptivos hormonales tienen diferentes impactos en los niveles de AHM de la población. Estos resultados se suman a dicha literatura en que estos efectos no son consistentes, en cambio, el impacto mayor ocurre en los percentiles más bajos de AHM. Sin embargo, estas diferencias dependientes de los anticonceptivos son pequeñas comparadas con la conocida variabilidad biológica en la reserva ovárica a cualquier edad. Estos valores de referencia permiten un asesoramiento robusto de la reserva ovárica individual relativa de las compañeras sin requerir cese o potencial remoción invasiva de la anticoncepción.