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From Data to Normogram: Modeling the Cubic Decline of AMH Beyond Fixed Cut-Offs in 15,000 Canadian Women

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INTRODUCTION

Anti-Müllerian Hormone (AMH) levels are increasingly recognized as the gold standard biomarker to evaluate ovarian reserve due to their stability throughout the menstrual cycle and predictive value in reproductive health. AMH declines naturally with age and is widely used in fertility assessments, IVF planning, and diagnosis of ovarian disorders. However, detailed age-specific percentiles and decline rates—particularly at clinically critical thresholds such as <1.0 ng/mL—remain underexplored.

AIM

This study seeks to characterize the natural, age-related decline of AMH across the reproductive lifespan in a large, representative Canadian cohort. By establishing robust, age-stratified reference values, the study aims to provide a clearer understanding of normative AMH trajectories. Furthermore, advanced predictive models will be developed to estimate ovarian reserve dynamics. Together, these outputs will support more precise clinical decision-making in reproductive medicine, improving individualized fertility counseling, assisted reproduction planning, and the early identification of abnormal ovarian aging patterns.

METHOD

A retrospective analysis was conducted on AMH test results from 15,119 women aged 18–49.

All AMH measurements were performed using the Beckman Coulter Access AMH assay on the Access 2 automated immunoassay analyzer, a validated platform widely used in clinical laboratories.

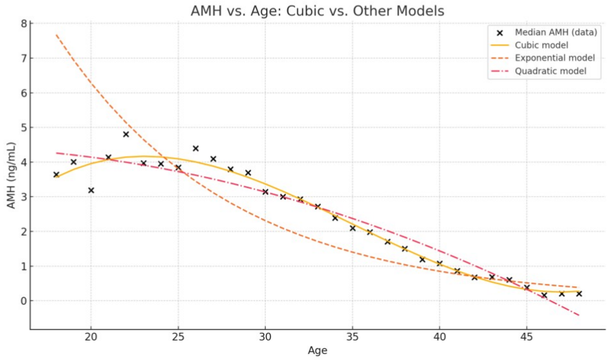
Data were grouped by age to calculate central tendencies (mean, median), dispersion (SD), and population percentiles (P5–P95). Decline rates were assessed annually and by grouped intervals. Predictive models—including exponential, quadratic, and cubic regressions—were fitted to mean AMH values. Model performance was evaluated using R^2 and Akaike information criterion (AIC).

RESULTS

AMH levels showed a progressive, age-related decline, with substantial interindividual variability.

The median AMH declined from 3.65 ng/mL at age 18 to 0.16 ng/mL by age 49, reflecting a near-complete depletion of ovarian reserve across the reproductive lifespan.

Three statistical models were fitted to mean AMH values across age: exponential decay model, quadratic model and cubic model.



The cubic polynomial $AMH = -13.81 + 1.863 \times Age - 0.0602 \cdot Age^2 + 0.000573 \cdot Age^3$ (R^2=0.982, AIC=7.11) outperformed all other models, capturing both the gradual early decline and the rapid fall observed after age 35.

Model	R^2 Score	AIC	Formula
Exponential	0,488	25,394	AMH = 40.08 * exp(-0.083 * Age)
Quadratic	0,952	36,023	AMH = 5.02 + 0.108 * Age - 0.0045 * Age^2
Cubic	0,982	7,112	AMH = -12.39 + 1.851 * Age - 0.0598 * Age^2 + 0.000558 * Age^3

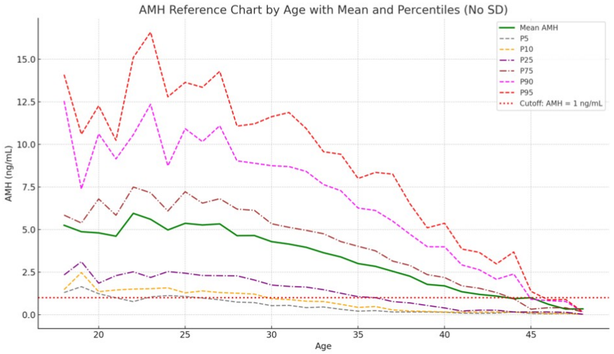
AMH Reference Values by 5-Year Age Bands (ng/mL)

Age Group	Median	Mean	N	Reference Interval (P5–P95)	Central Range (P25–P75)
18–24	4,06	5,24	430	1.06 – 13.75	2.39 – 6.56
25–29	3,92	4,95	2219	0.83 – 12.34	2.23 – 6.45
30–34	2,82	3,86	4972	0.45 – 10.61	1.54 – 4.87
35–39	1,72	2,52	5098	0.19 – 7.32	0.83 – 3.28
40–44	0,86	1,38	2291	0.11 – 4.22	0.29 – 1.74
45–49	0,29	0,76	100	0.06 – 1.09	0.15 – 0.35

Grouped age analysis confirmed that:

between ages 20–30, the decline was gradual (~0.09 ng/mL/year); from 30–40, the pace steepened (~0.15–0.20 ng/mL/year); after age 40, the majority of patients fell below 1.0 ng/mL by age 45.

To further quantify interindividual variation, we examined percentile ranges across age: at age 25, the P5–P95 range was 1.07–13.64 ng/mL, at age 35, this narrowed to 0.21–8.00 ng/mL, by age 45, the range was reduced to 0.16–3.69 ng/mL and at age 49, nearly all values fell at or below 0.16 ng/mL.



CONCLUSIONS

The cubic trajectory of AMH decline highlights the inadequacy of fixed cutoffs across ages and reinforces the value of age-specific interpretation. The findings support the integration of percentile-based tools and dynamic models into routine fertility care. AMH remains superior to other markers due to its direct association with follicular pool size and its age-sensitive variability.

AMH declines with age in a nonlinear, cubic fashion, with a marked acceleration after age 35. This large-scale population study—measured using the Beckman Coulter Access AMH assay—provides robust evidence and a predictive framework to guide age-specific interpretation of AMH in reproductive medicine.

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