



Maximizing the clinical utility of antimüllerian hormone testing in women's health

Benjamin Leader^a and Valerie L. Baker^b

Purpose of review

To provide an update on the latest clinical applications of serum antimüllerian hormone (AMH) testing with practical approaches to mitigate the impact of significant variability in AMH results.

Recent findings

Recent studies continue to demonstrate that AMH is the best single serum test for ovarian response management with, at most, a weak-to-moderate age-independent association with live-birth rate and time to conception. Data confirm serum AMH levels improve menopause prediction, monitoring of ovarian damage, and identification of women at risk for several ovary-related disorders such as polycystic ovary syndrome and premature or primary ovarian insufficiency. However, it is now recognized that serum AMH results can have dramatic variability due to common, biologic fluctuations within some individuals, use of hormonal contraceptives or other medications, certain surgical procedures, specimen treatment, assay changes, and laboratory calibration differences. Practical guidelines are provided to minimize the impact of variability in AMH results and maximize the accuracy of clinical decision-making.

Summary

AMH is an ovarian biomarker of central importance which improves the clinical management of women's health. However, with the simultaneous rapid expansion of AMH clinical applications and recognition of variability in AMH results, consensus regarding the clinical cutpoints is increasingly difficult. Therefore, a careful approach to AMH measurement and interpretation in clinical care is essential.

Keywords

AMH, menopause, ovarian reserve, polycystic ovarian syndrome, premature ovarian failure

INTRODUCTION: ANTIMÜLLERIAN HORMONE, OVARIAN RESERVE, AND WOMEN'S HEALTH

Appropriate assessment of ovarian reserve with serum antimüllerian hormone (AMH) testing has the potential to improve the medical care provided to women in a variety of ways [1[•],2,3]. However, ovarian reserve assessment, the quantitative and qualitative characterization of a woman's supply of oocytes, is exceptionally complicated to approach because of the lack of consensus in terminology, differences in clinical study designs, and variability in testing methodology in clinical research [4^{••}]. Ovarian reserve assessment has been difficult to obtain in routine clinical practice as no biomarker with sufficient clinical accuracy has been easily available. Rapidly increasing numbers of clinical publications confirm serum AMH as a clinically useful, widely available, primarily quantitative, measure of ovarian reserve that is more accurate than serum follicle-stimulating hormone (FSH) alone. AMH is a powerful clinical biomarker that

helps improve the management of infertility treatment, planning of future pregnancy, menopause prediction, monitoring of ovarian damage from medications and procedures, and detection of ovary-related diseases such as polycystic ovary syndrome (PCOS) and premature or primary ovarian insufficiency (POI; Fig. 1).

^aClinical Research Division, ReproSource, Inc, Woburn, Massachusetts and ^bDivision of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, California, USA

Correspondence to Benjamin Leader, MD, PhD, Director of Clinical Research, ReproSource, Inc, 300 Tradecenter, Suite 6540, Woburn, MA 01801, USA. Tel: +1 781 937 8893; fax: +1 781 935 3068; e-mail: leader@reprosource.com

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KEY POINTS

- AMH has emerged as the single best blood marker for assessing the quantitative aspects of ovarian reserve and managing ovarian stimulation.
- Some studies continue to demonstrate a helpful, age-independent association of AMH with qualitative aspects of ovarian reserve such as egg quality, live birth rate, or time to conception, but this association is weak to moderate at best.
- Clinical studies now support expanded clinical applications of serum AMH testing such as prediction of menopause onset, monitoring of ovarian effects of medication and surgical procedures, and evaluating the risk of a variety of disorders such as PCOS, POI, POF, or autoimmunity.
- Caution is required when interpreting a single AMH measurement because biological fluctuation, surgical procedures, medications (e.g. contraceptives), and laboratory methodology can frequently lead to dramatic changes in AMH results within individuals.
- Recommended steps to account for variability in AMH results include using a single AMH testing source calibrated to clinical outcomes; informing patients about potential variability; and including medical history and other ovarian markers (e.g. antral follicle count and/or serum FSH) in ovarian reserve assessment.

However, it is now clearly important for clinicians to understand that serum AMH results can be misleading if appropriate steps are not taken to account for sources of variability in serum AMH results in clinical practice and ensure patients understand that information from AMH testing is directional, not definitive. Key practical steps are provided here for consideration to help ensure the appropriate use of AMH testing in clinical practice.

ANTIMÜLLERIAN HORMONE BIOLOGY AND PHYSIOLOGY

At the cellular level, AMH is thought to restrict the growth of ovarian follicles in response to serum FSH and also inhibit estradiol (E2) secretion [1[•],2]. AMH is produced by the granulosa cells surrounding each oocyte in the developing follicles, with rapid reduction in both *AMH* gene and protein expression observed in follicles reaching 8mm and above in diameter [5[•]]. The decline in AMH expression in larger follicles appears to be because of, at least in part, a reduction in the *AMH* gene promoter activity through E2 receptor beta [6]. One study demonstrates that reduced AMH levels, averaged from large follicles retrieved during in-vitro fertilization

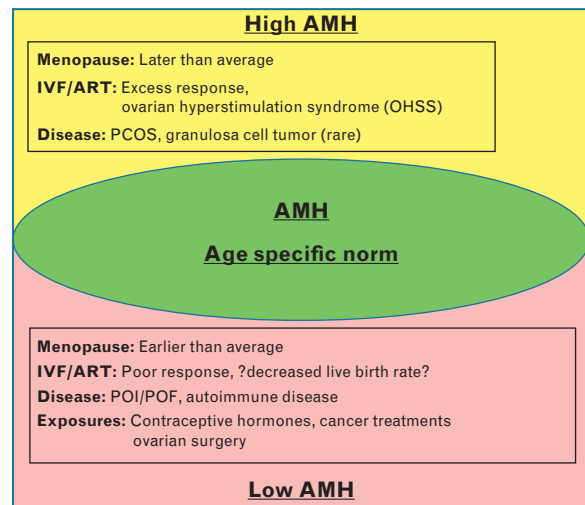


FIGURE 1. Age-specific AMH and associated conditions. Displayed at the top (yellow) are conditions associated with high age-specific AMH. At the bottom (pink), conditions associated with low age-specific AMH are listed. AMH, antimüllerian hormone; PCOS, polycystic ovary syndrome; POI, premature/primary ovarian insufficiency; POF, premature ovarian failure.

(IVF), were associated with higher IVF success rates [7], suggesting this follicular AMH reduction is a desired physiologic process.

Using population average serum AMH levels (Fig. 2), the literature appears to agree that values decline yearly at a fairly consistent rate after 25 years of age until below the clinical detection limit by 50 years of age [8,9^{••},10,11,12^{••},13]. However, the pattern of rise prior to age 25 has conflicting representation in the literature, with one study showing peaks and troughs [14] and another showing a gradual rise from birth to 15 years of age then decline [15^{••}] (Fig. 2). Therefore, clinicians should currently be more cautious about interpreting the rates of change in serum AMH in women below 25 years of age. Additionally, there are few data available to determine whether the pattern of decline in AMH values within an individual woman matches the pattern in the population average.

OOCYTE QUANTITY AND QUALITY, FERTILITY TREATMENT, AND NATURAL FERTILITY

It is well established that AMH testing effectively improves the management of ovarian stimulation in assisted reproductive technology (ART) therapy by identifying women likely to respond either poorly (with cycle cancellation/low oocyte yield) or excessively [with ovarian hyperstimulation syndrome (OHSS)/high oocyte yield] [1[•]]. Recent research has targeted developing specific ovarian stimulation

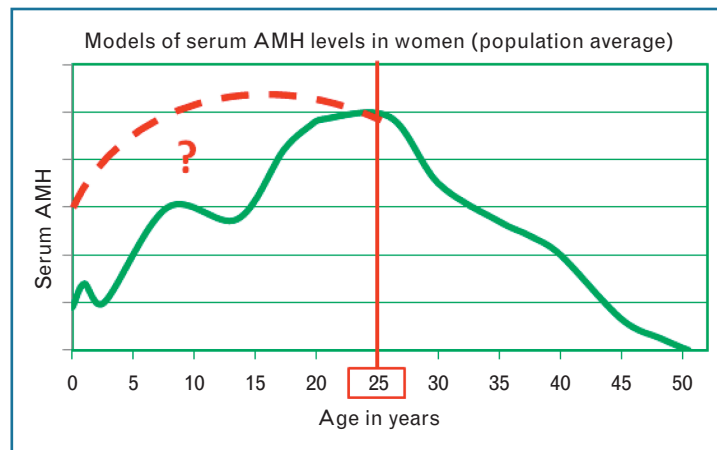


FIGURE 2. Population average serum AMH levels during a woman's lifetime. A model of a population average serum AMH level in women, plotted by year of life in green, demonstrates the rising serum AMH with two peaks and troughs prior to maximal value at 25 years of age followed by an almost linear decline (specific AMH values are not included on the Y-axis to avoid potential misapplication of laboratory-specific values). Although the literature generally agrees with the pattern of decline after 25 years of age, conflicting patterns of rise are described at younger ages (red dashed line and question mark). Caution is required with clinical interpretation of serum AMH in women below 25 years of age until further studies are reported. Further study is also required to determine how the pattern of decline in serum AMH within individuals relates to the decline of the population average display the same pattern of decline as demonstrated by the population average. AMH, antimüllerian hormone. Reproduced with permission [14].

protocols individualized by AMH results [16^{••},17[•]]. Other recent studies focus on refining information such as demonstrating that an AMH value from a single point in time will remain predictive for approximately 12 months [18], how certain stimulation protocols affect different patient phenotypes such as PCOS vs. low responders [19^{••},20], and prospectively demonstrating that application of AMH testing can improve expectation management and possibly treatment costs [21].

The value of serum AMH, independent of age, to predict live-birth rate or oocyte quality has remained controversial, with some studies continuing to show no association, whereas other studies demonstrate a small but useful association [22[•],23–28,29^{••}]. This controversy may be due in part to differences in AMH testing methodology and study design masking the association with serum AMH and oocyte quality. Ultimately, as a recent meta-analysis concludes, it is probable that AMH has an association with oocyte quality, but this association is likely weak to moderate at best independent of a woman's age [30^{••}]. AMH may best improve the oocyte quality prediction when incorporated in a multivariate, algorithmic approach [29^{••}]. However, as there continues to be evidence that live births are possible with very low AMH levels, AMH values alone should not be used to withhold care [31[•]].

In terms of natural fertility or time to conception, recent reports demonstrate conflicting data

[32,33,34[•]], which perhaps may be because of small sample sizes or AMH only being helpful when below a certain threshold or in a certain population of patients. Currently, however, the available data suggest that serum AMH levels in isolation cannot be used to counsel a patient whether or not natural conception is possible.

MENOPAUSE

Menopause is complex and no single test currently can definitively predict the onset with a high degree of accuracy. However, independent studies from a variety of sources for over a decade demonstrate serum AMH improves the prediction of menopause [1[•]]. Serum AMH was recently added as a marker for menopausal staging because it declines much earlier than other signs of menopause such as increasing serum FSH or irregular menses [35[•]]. Recently, serum AMH was shown to improve the prediction of menopause onset more than maternal age [36[•]]. Furthermore, different models using AMH to predict a higher chance of early or late onset of menopause relative to the expected average have now been cross-validated [37^{••}].

There are a number of variables which, if combined with serum AMH algorithmically, may increase the accuracy of menopause predictions. For example, one cross-sectional study of 2635 women demonstrated that for women with serum AMH in

the lower 5th percentile for their age, expected age of menopause was 43.4 years of age for obese, non-smokers versus 37.6 in thin women who smoked [38[■]]. In women with serum AMH in the upper 95th percentile for age, predicted age of menopause increased considerably but was again affected by body weight and smoking status (55.1 years of age in obese, nonsmokers versus 52.4 years of age in underweight smokers). Ethnicity also may influence serum AMH [39]. Interestingly, a recent study in 44 Japanese women demonstrated after AMH became undetectable, menopause onset was within 3 years [40], instead of 5 years shown by a study of large U.S. and European populations [41], although the study design and assay performance may contribute to these observational differences.

Although the relationship of AMH to the timing of menopause onset is highly statistically significant in the studies cited, the confidence intervals related to the predicted age of menopause remain wide at present. Thus, currently the present clinical interpretation is qualitative: women with a serum AMH very low or very high for their age are more likely to go into menopause earlier or later than average, respectively. Notably, for women with very low age-specific serum AMH who are not ready to attempt conception naturally or with donor sperm, oocyte cryopreservation, no longer considered experimental [42[■]], is now available as an alternative to help ensure the future ability to have children. Although serum AMH testing clearly provides helpful directional information in decision making, prior to ordering AMH testing, a clinician should consider verifying whether their patient considers qualitative information sufficiently meaningful to use.

POLYCYSTIC OVARY SYNDROME

The relationship of AMH with PCOS is complicated by the diagnosis itself being subject to a debate primarily centered, ironically, over whether polycystic ovaries are included (Rotterdam criteria) or are not included [National Institutes of Health (NIH) criteria] in the diagnosis of the disorder. Numerous studies demonstrate that PCOS is significantly associated with elevated serum AMH both with the NIH criteria [43[■],44[■]] and with the Rotterdam criteria [44[■],45[■],46[■],47–49]. One study demonstrated that in women presenting for fertility evaluation with serum AMH elevated, high, and very high, the frequency of PCOS diagnosis was 51.6% ($n=84$), 97% ($n=30$), and 100% ($n=20$), respectively [50[■]]. As serum AMH correlates well with the polycystic appearance of ovaries on ultrasound,

several studies are proposing to set thresholds by AMH as an alternative to ultrasound [44[■],46[■],48]. Recent evidence in 463 PCOS women suggests that serum AMH may provide insight into the subphenotypes of PCOS with higher serum AMH predicting longer menstrual cycle length, higher luteinizing hormone (LH) levels, and hirsutism [51[■]]. Clearly, markedly elevated age-specific AMH correlates with the clinical diagnosis and severity of PCOS and may eventually be adopted as a diagnostic criteria for PCOS.

DIMINISHED OVARIAN RESERVE, PREMATURE OR PRIMARY OVARIAN INSUFFICIENCY, AND PREMATURE OVARIAN FAILURE

Not surprisingly, numerous studies demonstrate serum AMH is dramatically lower in women symptomatic from ovarian insufficiency [47,52[■],53,54], although one study shows that serum LH levels may be better at identifying the onset of menstrual irregularities [55]. It seems unlikely that defects in the AMH molecule itself are a concern as a cause of POI as suggested by a recent study of 211 idiopathic POI women and 233 controls, which demonstrated no identifiable genetic differences in the AMH or the AMH receptor genes [56]. An area of current controversy is whether serum AMH has a clinically useful association with the number of CGG repeats in the fragile X gene, *FMR1*, which is known to have 55 or greater CGG repeats much more frequently in women with POI than normal controls [52[■],57]. An association of repeat length and serum AMH in women with fertility issues has been described by primarily one group [58–62], but this was not observed in another recent study of women not selected for fertility issues [63].

As AMH is clearly the earliest and most accurate serum biomarker reflecting decline in the quantitative aspects of ovarian reserve, it may be the earliest clinical means of detecting women likely to develop diminished ovarian reserve (DOR), POI, or premature ovarian failure (POF) prior to becoming symptomatic [52[■]]. In fact, a recent U.S. study of 5354 women presenting to fertility centers from 30 different states demonstrated that in women with reassuring early follicular serum FSH, serum AMH values concerning for low ovarian reserve were identified in 20% of women under 35 years of age and in over 30% of women by 40 years of age (Fig. 3) [12[■]]. Therefore, serum AMH testing can be an important means to identify many patients in routine practice at risk for an accelerated decline in ovarian reserve.

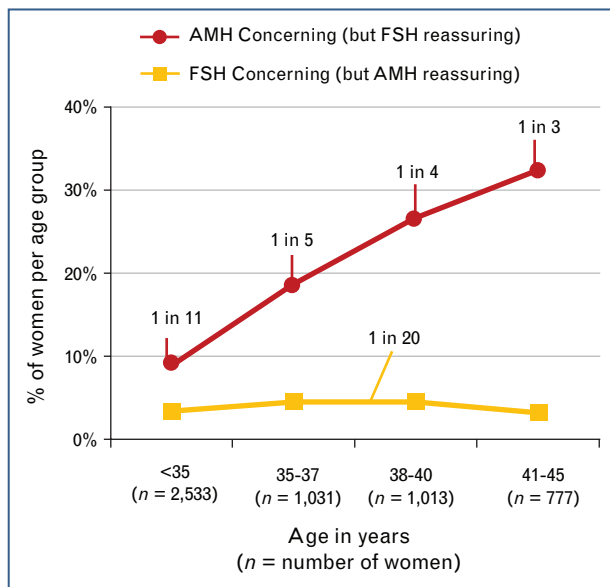


FIGURE 3. Frequency of discordance by age of serum FSH and AMH during estradiol-confirmed menstrual cycle days 2–4 in 5354 women from U.S. fertility centers. Discordance was defined when one test was ‘concerning’ and the other test was ‘reassuring’. Cutpoints for serum AMH were less than 0.8 ng/ml (concerning) and at least 0.8 ng/ml (reassuring), and for serum FSH were at least 10 IU/l (concerning) and less than 10 IU/l (reassuring). Y-axis displays the frequency of discordance of women in each of four age groups shown the X-axis. Note: AMH values are not standardized across laboratories. These data using cutpoints were calibrated to number of oocytes retrieved through ovarian stimulation and are specific to Ref. [12^{***}]. AMH, antimüllerian hormone; FSH, follicle-stimulating hormone. Modified with permission [12^{***}].

ASSOCIATION WITH OTHER DISORDERS: AUTOIMMUNITY, GRANULOSA CELL TUMORS, AND ENDOMETRIOSIS

Substantial evidence from a number of sources demonstrates serum AMH levels are associated with other diseases. For example, AMH is significantly lower in autoimmune disorders [64] such as lupus [65^{***},66] and Crohn’s disease [67^{*}]. Elevated AMH levels can also be useful in postmenopausal women as a strong indicator of granulosa cell tumors (GCTs) and for monitoring for the recurrence of GCTs, though in asymptomatic, premenopausal women, elevated AMH is too nonspecific for clinical utility as a screening test for these tumors [68,69]. The understanding of AMH and endometriosis continue to develop, with a recent report indicating AMH may actually play a role in endometriosis [70]. Although some consider endometrioma removal as important for improving fertility [71], clear evidence demonstrates serum AMH is lowered by ovarian surgeries

such as removing cysts and endometriomas [72^{*}, 73^{***},74–76].

MONITORING OVARIAN DAMAGE WITH MEDICAL THERAPIES AND SURGICAL PROCEDURES

Medical and surgical treatments are now being assessed and monitored for ovarian damage by utilization of ovarian reserve markers such as AMH. Numerous cancer therapy publications have demonstrated the dramatic effects of various chemotherapeutics in reducing serum AMH levels. Some of these studies have demonstrated that AMH testing can improve treatment selection by identifying which therapies are most toxic to the ovary and which patients are most at risk for postchemotherapy ovarian insufficiency [77^{*},78^{***}, 79–84]. Furthermore, numerous reports are confirming that after some ovarian-related surgeries such as removal of benign cysts and endometriomas, significant reductions in AMH are observed which may persist [72^{*},73^{***},74–76] with a recent study demonstrating similar reductions with benign cysts and endometriomas and more severe reductions with bilateral procedures [85]. Interestingly, one report shows only transient reductions in AMH in 22 PCOS patients undergoing the more minor procedure of ovarian puncture [86]. Given this data, a clinician and patient must carefully consider the possible negative impact of common ovarian surgeries on ovarian reserve. The ability of serum AMH levels to indicate and predict damage to the ovary confirm it is important to measure serum AMH before and after medical and surgical treatments to help plan treatment approaches, counsel the patient, and monitor ovarian reserve status.

ALGORITHMS AND MULTIVARIATE COMBINATIONS OF TESTS WITH ANTIMÜLLERIAN HORMONE

Multivariate, algorithmic approaches allow optimization of combinations of clinical variables to predict outcome. The reality is clinicians, if not provided with a validated algorithm, are forced in daily practice to weigh AMH with the provided variables such as age, BMI, medical history, antral follicle count (AFC), and serum FSH to the best of their ability without the benefit of mathematical optimization and large datasets. A number of recent studies demonstrate benefit by combining AMH with other variables in predicting the outcomes such as menopause [37^{***},38^{*}], live birth [33], or response to ovarian stimulation protocols in ART [29^{***},87]. However, other studies have not found

benefit in combining multiple tests, including a recent study combining 28 databases [88[•]]. It should be noted that the differences in AMH assay materials and laboratory performance make combining different AMH datasets complex and likely would reduce the associations with AMH and outcome. Therefore, although a multivariate approach is likely to dramatically improve the accuracy of decision making, it will require minimization of variability in AMH assay, laboratory performance, patient population definition, and study design.

THE CHALLENGE OF VARIABILITY IN ANTIMÜLLERIAN HORMONE RESULTS: BIOLOGY, EXPOSURE, AND LABORATORY

Perhaps the most important clinical advance in the medical literature related to AMH is the recent recognition of the significant variability in AMH results which must be taken into account for appropriate interpretation in clinical care. As described below, there are now three recognized sources for this variability (Fig. 4): biological fluctuation within certain individuals; exposure to medications (such as contraceptive hormones) and certain ovarian surgeries; and laboratory-specific AMH values as each laboratory provides its own value ranges and calibration. That said, the variability should be contextualized with the fact that AMH is still the best available serum marker of quantitative aspects of

ovarian reserve. The practical steps outlined below mitigate the issues of variability.

BIOLOGICAL FLUCTUATION IN SERUM ANTIMÜLLERIAN HORMONE VALUES

One of the most attractive aspects of serum AMH measurements, unlike serum FSH testing, is the lack of large changes in the average values at the population level during the menstrual cycle [89]. However, this led to the misconception that individuals do not show any fluctuation across the menstrual cycle. Fluctuation in serum AMH levels can be clearly observed by examining the graphs in previous studies which display individual patient data [89,90]. A recent study measuring AMH multiple times with the same menstrual cycle of 44 normally cycling healthy women demonstrated AMH values (ng/ml) within four individuals (9%) ranging approximately: 0.4–1.9, 1.9–4.2, 0.4–1.4, and 2.3–4.4 [91^{••}]. In another study, seven of 12 women re-measured during the same menstrual cycle were clinically reclassified [92[•]]. Therefore, the clinician should avoid using AMH as the only marker of ovarian reserve, counsel patients that occasionally results can fluctuate, and consider re-testing if the AMH value is not consistent with the clinical picture.

EXPOSURE TO CONTRACEPTIVE MEDICATIONS, PREGNANCY, METHOTREXATE, AND DEHYDROEPIANDROSTERONE

Another attractive aspect of serum AMH measurements is that they are not affected by contraceptive medications to the same degree as serum FSH, which propagated the unfortunate misunderstanding that AMH was not affected by contraceptives. Numerous studies have now confirmed that hormonal contraceptives often lower serum AMH [93–96]. A well designed prospective study of 44 women demonstrated serum AMH was lowered by an average of approximately 30% within two menstrual cycles of starting the contraceptive regardless of the route [97^{••}]. This was expected as other scenarios which disrupt the hormonal milieu (such as pregnancy) affect serum AMH levels. One study of 554 women in pregnancy demonstrated an approximately 50% lowering of serum AMH with each trimester and recovery after delivery [98^{••}]. The limited recent data on methotrexate use do not demonstrate an effect on serum AMH [99], consistent with the prior observations [100]. A number of fertility centers administer dehydroepiandrosterone (DHEA) to poor responders to ovarian stimulation in order to

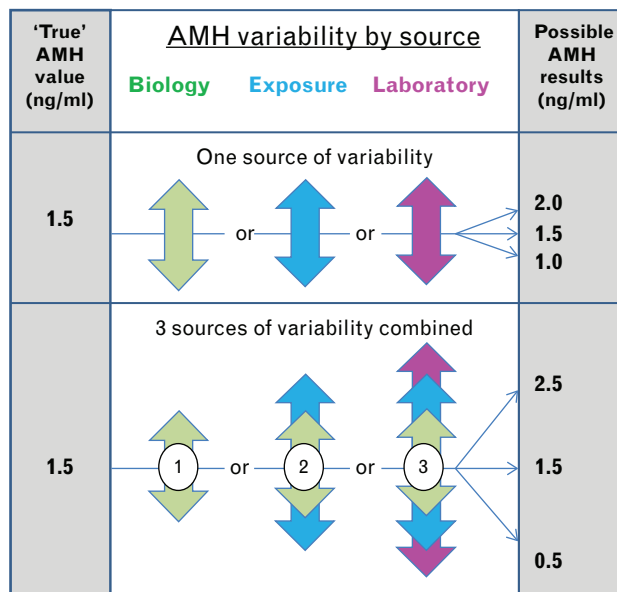


FIGURE 4. Variability by source possibly affecting a reported AMH result. Upper panel demonstrates the potential effect of a single source variable. Lower panel demonstrates how multiple sources of variability can be additive. AMH, antimüllerian hormone. Reproduced with permission from [3].

improve AMH values and follicular responsiveness [101]; however, the number of treated patients is small and poorly controlled, and in sum, current data do not support a clear effect by this medication [102,103].

ANTIMÜLLERIAN HORMONE ASSAYS: VALUES ARE LABORATORY SPECIFIC

The major challenge for the clinician attempting to apply serum AMH values to clinical care is the fact that each laboratory provides their own value ranges which may be clinically significantly different. Currently, there is no international reference standard for AMH measurement. A major recent advance for improved patient care is simply the recognition in the clinical literature that AMH values are currently laboratory specific and generally cannot be ‘mixed and matched’ [98,104–110]. Previously, clinicians were misguided into thinking they could simply apply the values they received locally using reported cutpoints in AMH studies done elsewhere. This is largely because of the mistaken assumptions propagated in the clinical literature such as: high correlations between AMH assays meant results were interchangeable between laboratories with simple factoring; there is only one kit (i.e. the Beckman Gen II AMH assay) in use when in fact there are several kits in use; and laboratories using the same kit would supply the same numerical result. In fact, virtually every study comparing different AMH assay systems provides different conversion methods, none of which are simple factoring but usually involve linear equations [104–108,110]. Currently, no fewer than four kits are commercially available [111,112], with more on the way. Current publications describe the findings from seven different AMH kits used over

the last 3–5 years. In addition, the Beckman Gen II assay itself has undergone two major methodology changes within 18 months (Beckman Product Notifications November 2012 and June 2013) [113], and not surprisingly, a systematic shift in calibration of the assay has just been reported in a cohort of 10 981 patients [98]. Furthermore, when 10 laboratories using the same Beckman Gen II assay were compared, there was a 40% variation in the values obtained [109]. In addition, specimen handling protocols affect the serum AMH values [107]. It is also critical to understand how a laboratory calibrates their clinical cutpoints by patient population and clinical outcome; otherwise, accurate interpretation of the result will be difficult.

A critical, additional mistake likely to be made in the future is concluding that FDA clearance of an AMH assay or production of an international standard will mean laboratories will report the same absolute value or calibrate clinical cutpoints the same way. FSH testing provides a recent history lesson demonstrating that this is not true. In fact, current FSH testing remains so controversial that no universally defined cutpoints are agreed upon despite multiple FDA cleared platforms and international reference standards [48]. Fortunately, to overcome this challenge, a clinician can follow a few practical steps outlined below.

PRACTICAL METHODS TO MINIMIZE THE VARIABILITY IN ANTIMÜLLERIAN HORMONE RESULTS AND MAXIMIZE THE CLINICAL UTILITY

Although the challenges facing the clinician applying laboratory results from ovarian testing such as AMH can seem daunting, by following a few

Table 1. Checklist to maximize the clinical utility of serum AMH testing

1. Use one laboratory, calibrated to outcomes	Avoid ‘mixing and matching’ AMH values from different laboratories and identify a reliable, single source for testing which both calibrates the results to the clinical outcomes of interest and commits to updating the clinician if calibration of the results changes.
2. Utilize more than one ovarian reserve test	Avoid using a single serum AMH measurement alone to assess ovarian reserve, and incorporate other markers such as antral follicle count (AFC) and/or early follicular phase serum FSH.
3. Identify exposures	Identify whether the patient has taken medications (e.g. hormonal contraceptives and chemotherapy) or had surgery (ovarian cyst or endometrioma removal) that affects the AMH levels.
4. Counsel patient	Prior to testing, verify the patient understands the directional nature of the information being provided by AMH testing, and that, in a subset of women, the test result may change substantially with biologic fluctuations.
5. Consider retesting	If testing results lead to life-changing decisions or if the results are inconsistent with the clinical scenario, consider retesting.

Many improvements to the management of women’s health are possible through appropriate AMH testing. However, variability in AMH results can lead to clinically significant variability in AMH results, making careful approach to the interpretation essential. With the above simple steps, a clinician can rapidly minimize the risks for incorrect interpretation.
AMH, antimüllerian hormone; FSH, follicle stimulating hormone.

practical steps in a checklist format, a clinician can overcome these challenges (Table 1). First and foremost, do not 'mix and match' the AMH values from different laboratories, but identify a reliable, single source of AMH testing which calibrates its testing to the clinical outcomes of interest and commits to updating the clinician should any changes occur in the calibration of the results. Medical insurance companies can present a challenge by restricting the testing services to a laboratory with which a clinician has no familiarity, but a clinician now has numerous publications as outlined in this review to demonstrate the medical risks this restrictive practice poses. Second, avoid using a serum AMH measurement alone to assess ovarian reserve, but incorporate other markers such as AFC and early follicular phase serum FSH. Third, identify whether the patient has a medical condition, has taken medications (e.g. hormonal contraceptive or chemotherapy), or had ovarian surgeries (e.g. cyst or endometrioma removal) that affect the AMH levels. Fourth, counsel the patient prior to testing about the qualitative nature of the information and that a single test result may change substantially in a certain subset of individuals because of biological fluctuations. Fifth, consider retesting if AMH results are clinically inconsistent, or if, based upon the testing results, life-changing decisions are to be made.

CONCLUSION

Hundreds of clinical studies confirm that adding serum AMH testing to a complete ovarian assessment provides a powerful tool to help provide better healthcare for women. The benefits of this testing can optimize fertility treatments; help lead to earlier diagnoses of PCOS, POI, POF, and certain autoimmune conditions; provide the opportunity for better planning for procreation and menopause; and allow for better medical decision-making by monitoring ovarian damage from exposures to medical or surgical therapies. Although challenges with variability in AMH results make the provided practical steps a prerequisite for appropriate interpretation of the testing, the clinical benefits of testing more than justify this additional effort.

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Conflicts of interest

B.L. – *ReproSource, Inc*; V.L.B. – *no relevant conflicts of interest.*

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- of special interest
- of outstanding interest

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