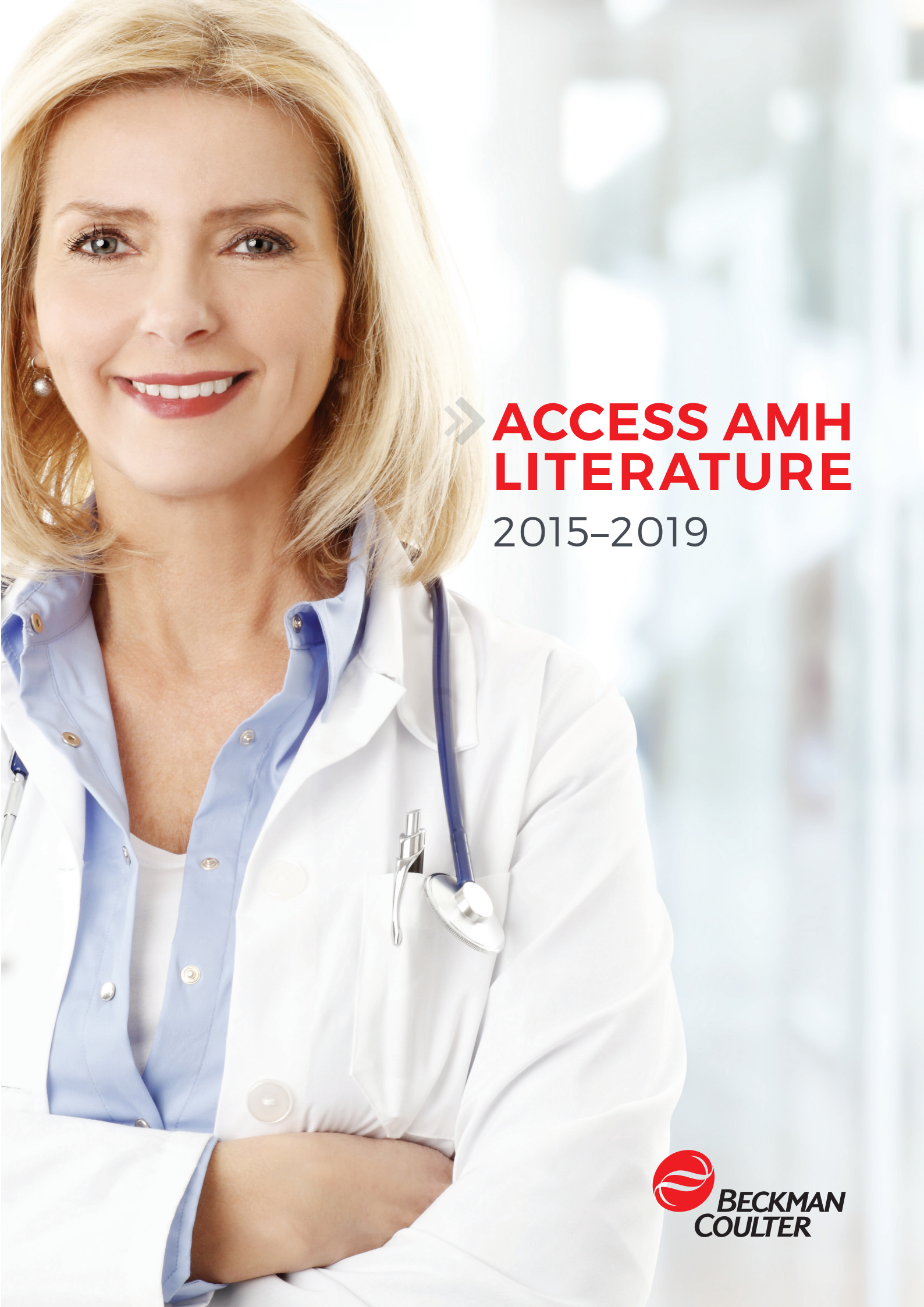


ACCESS AMH LITERATURE

2015–2019

BECKMAN COULTER

Table of contents

Performance Evaluation of Access AMH

Access AMH Method Comparisons

Access AMH in Clinical Practice

"The performance of the assays across numerous laboratories, and over a protracted timeframe, has been examined through the UK NEQAS published results. The automated assays show high quality performance figures over a broad concentration range, with exceptionally low variance figures, and they also yield very similar absolute concentration values."

Fleming R., et al. Human Fertility 2017
Jun. 8,1-5. doi: 10.1080/14647273.2017.1331298.

Performance characteristics of the Access AMH assay for the quantitative determination of anti-Müllerian hormone (AMH) levels on the Access family of automated immunoassay systems

Demirdjian G., Bord S., et al.

Clinical Biochemistry 2016;49:1267-1273.

Objectives: Anti-Müllerian hormone (AMH) measurement is useful as an aid in the evaluation of ovarian reserve. In the past, its conventional use was restricted by the low-throughput and variability of existing manual AMH assays. We developed the automated Access AMH assay for the quantitative determination of AMH levels on the Access family of immunoassay systems. The analytical performance of this new assay was evaluated.

Design and methods: Sensitivity, dilution linearity, assay imprecision, AMH sample stability, lot-to-lot comparison and correlation with AMH Gen II assay (Beckman Coulter, Inc.) were evaluated. Reference intervals for Access AMH were established in healthy females, males, newborns (≤60 days) and pediatric males classified by Tanner stages.

Results: The limit of blank and limit of detection were below 0.0077 and 0.0098 ng/mL, respectively. The limit of quantitation was 0.010 ng/mL. The total imprecision ranged from 2.4 to 5.2%. Linearity was observed up to 24 ng/mL. Sample storage at room temperature up to 48 h, at 2–8° C up to 7 days and at −20° C up to 15 months had no impact on measured AMH. The correlation study gave a coefficient between 0.99 and 1 and a regression slope between 0.89 and 0.92. Excellent lot-to-lot comparability was observed on controls and patient samples with a maximum bias of 3.7% between 2.81 and 15.03 ng/mL.

Conclusions: The fully automated Access AMH immunoassay demonstrates excellent analytical performance. As a consequence, the availability of this assay will represent a robust, fast and precise alternative to manual AMH assay testing.

A-040: A prospective multisite evaluation of the intra-menstrual cycle variability of anti-Müllerian hormone (AMH) using an automated AMH immunoassay

Shin S.S., Jones K.L., et al.

Clinical Chemistry 2015;61(S10):S13.

Background and Objective: Research studies indicate that AMH may be useful for evaluating response to controlled ovarian stimulation in women undergoing in vitro fertilization procedures. Published results for intra-menstrual cycle variability lack agreement. The purpose of this study is to determine whether or not AMH levels vary significantly across the normal menstrual cycle.

Methods: 24 apparently healthy women were prospectively enrolled from 2 sites with IRB-approved informed consent. Blood samples were collected 2 times per week throughout each complete menstrual cycle (21 to 35 days) starting with baseline (day 2 to 4). Eligibility criteria: ≥18 years to ≤45 years, both ovaries present, no polycystic ovary syndrome (PCOS), no history of ovarian surgery, no exposure to cytotoxic drugs or pelvic radiation therapy, no recent contraceptive use, and no other recent hormonal therapy. Serum samples were tested on the Beckman Coulter Access 2 immunoassay analyzer. Age-adjusted mixed-effects models were constructed to estimate intraclass correlation (ICC) and within-subject variability across the menstrual cycle.

Results: 191 specimens were collected from 24 women (mean age 35 years; range 24 to 45 years). Older age was significantly associated with lower mean AMH values (p-value = 0.004). There was no evidence of a linear trend in AMH levels across cycle days (p-value = 0.409). AMH showed more variability when AMH levels ≥3 ng/mL and less variability when AMH levels <3 ng/mL. The estimated ICC was 0.94 (95% confidence interval, 0.89–0.96), indicating that 6% of the overall variability in AMH was due to within-subject variability.

Conclusion: No trend in AMH results was observed throughout a normal menstrual cycle. Fluctuations in AMH results during the menstrual cycle accounted for only 6% of the overall variability.

T096: ACCESS® AMH immunoassay: performance of a new highly sensitive automated assay

Nicouleau L., Demirdjian G., et al.
Clin Chem Lab Med 2015;53S:s695.

Background-Aim: Anti-Müllerian hormone (AMH) measurement is useful as an aid in the evaluation of the ovarian reserve and in prediction of the outcome of assisted reproductive technology. A number of manual AMH enzyme linked immunosorbent assays (ELISA) are available to determine the AMH level in serum or plasma. However, with the development of automated assays that provide increased sensitivity and lower imprecision compared to ELISA, the use of AMH in routine clinical practice can be expanded. The aim of our study was to evaluate the performance of a new, fully automated AMH assay on the Access family of immunoassay systems.

Methods: Access AMH is a simultaneous one-step immunoenzymatic assay that uses two AMH-specific monoclonal antibodies in a sandwich format using serum or lithium heparin plasma. The Access AMH assay detects 140 kDa total AMH (cleaved and uncleaved) and does not bind to the other related members of transforming growth factor-β superfamily. Calibrators are prepared with recombinant human AMH. Twenty microliters of sample volume is needed and the quantitative result is available after approximately 40 minutes. Within run and total imprecision were calculated based on 4 serum samples. Method comparison was performed with the Beckman Coulter AMH Gen II assay in 104 patient sera and with the Ansh Labs and Immunotech AMH ELISA assays in 47 patient sera.

Results: The Access AMH assay was standardized against the Beckman Coulter AMH Gen II assay covering a measuring range from 0.02 to 24 ng/mL. The calibration curve and open vial calibrator stability are 31 and 90 days, respectively. Within run and total imprecision ranged from 1.5 to 1.7% and 3.0 to 3.1%, respectively. In this study, the limit of detection (LoD) was 0.0049 ng/mL and limit of quantitation (LoQ) was 0.010 ng/mL. Access AMH, when compared to the AMH Gen II, Ansh Labs, and Immunotech AMH ELISA kits yielded a correlation coefficient of 0.99, 0.99, and 1.00, and a slope of 0.91, 0.79, and 0.87, respectively.

Conclusion: The fully automated Access AMH immunoassay demonstrates excellent analytical performance. As a consequence, the availability of the fully automated Access AMH assay will represent a fast and precise alternative to manual AMH assay testing.

Assessment of complement interference in anti- Müllerian hormone (AMH) immunoassays

Turner K., Larson B., et al.
Am J Clin Pathol 2018;150:S159.

Anti-Müllerian hormone (AMH) is a dimeric glycoprotein produced by ovarian granulosa cells and used as a marker of ovarian reserve. Since 2011, the Beckman AMH Gen II assay has been widely used in research and clinical settings. This assay was reported to be affected by complement interference due to the binding of C1q to the capture antibody, resulting in C3 recruitment and activation of complement cascade. Steric hindrance from this complex prevents AMH binding, resulting in falsely lowered values in freshly drawn or freshly frozen samples. Introduction of a sample predilution step by the manufacturer prior to incubation with the capture antibody resolved the interference by preventing complement binding. Recently, automated high-throughput AMH immunoassays for Beckman Access and Roche Elecsys have been introduced. According to the 2017 CAP survey, 83% of labs that offer AMH testing use one of these automated platforms. Employing the same antibody pairs as the Gen II assay, these platforms may be susceptible to complement interference; however, no direct evaluation of complement interference has been published.

In this study, we assessed complement interference in the Beckman and Roche immunoassays. Spikerecovery experiments were performed in serum samples from females (>55 years old) with known C1q activity (n = 24). AMH recovery was compared to C1q activity in fresh and heat-inactivated samples. In samples with C1q activity within or above the reference interval (34–63 U/mL), complement interference in the Gen II assay was evident by a mean recovery of 41.0% (range, 28.1%-57.9%) followed by an increase in recovery to 77.0% (71.7%-84.2%) upon heat inactivation (P < .01). Complement inactivation was confirmed by measuring C1q activity. C1q activity was 60.3 U/mL (54.9–67.1 U/mL) before and 3.1 U/mL (0–12 U/mL) after heat inactivation (P < .01). Heat-inactivated recoveries corresponded with the recoveries seen in the Gen II assay with the predilution step, 71.6% (38.9%-81.5%) (P = .08). In samples with C1q activity below the reference interval, similar recoveries were observed with or without the predilution step with mean recoveries of 71.7% (67.5%-72.9%) and 77.7% (75.8%-77.7%), respectively (P = .07). In the Beckman and Roche assays, AMH recoveries were 111.0% (90.0%-125.0%) and 97.3% (74.6%-109.5%), respectively. Heat inactivation did not affect AMH recoveries significantly with post– heat inactivation recoveries of 93.3% (82.3%-99.9%, P < .01) for Beckman and 93.1% (83.6%- 107.3%, P = .2) for Roche.

Our study shows that C1q activity is responsible for AMH underrecovery on the Gen II assay when samples are not prediluted. Although there appears to be a C1q threshold for complement interference, the degree of underrecovery was independent of the level of complement activity once the activity was within the reference interval. Furthermore, we provide direct evidence that the automated Beckman and Roche AMH assays are not affected by complement interference despite using the same antibody pair as the Gen II assay.

Objective multicenter performance of the automated assays for AMH and estimation of established critical concentrations

Fleming R., Fairbairn C. & Gaudoin M.

Human Fertility. 2017 Jun 8:1-5. doi: 10.1080/14647273.2017.1331298.
[Epub ahead of print]

The measurement of AMH has now become widespread practice within the field of fertility treatment and research, despite technical issues with some of the original assays. The two new automated assays, with their potentially improved technical performance, require detailed examination and comparison under different conditions. In addition, the determination of categories of responses to ovarian stimulation, require re-evaluation for these new tests. The performance of the assays across numerous laboratories, and over a protracted timeframe, has been examined through the UK NEQAS published results. The automated assays show high quality performance figures over a broad concentration range, with exceptionally low variance figures, and they also yield very similar absolute concentration values. Critical response diagnostic concentrations have been re-evaluated by determination of age-related concentrations from within large population datasets.

Table. No difference between either the median concentration evaluations for the Elecsys and Access 2 assays, nor for the variance analysis between laboratories using the different automated assays from results from the objective multicenter UK NEQAS evaluation.

Assay	Median AMH (pmol/L)	Inter-laboratory variance (%) (mean)	Var low (mean)	Var high (mean)
Access 2	20.2	5.3	5.6	5.3
Elecsys	20.4	5.2	5.3	4.9

"The switching from manual to automatic assays for serum AMH measurement is on the way because of their better precision, lower limit of quantification and test duration."

Pigny P., et al. Fertility and Sterility. 105(4):1063-1069, 2016.

Comparative evaluation of three new commercial immunoassays for anti-Müllerian hormone measurement

Li H.W.R., Wong B.P.C., et al.
Human Reproduction 2016;31(12):2796-2802.

Study Design: How do the three new anti-Müllerian hormone (AMH) assay methods, manufactured by Beckman Coulter, Roche and Ansh Labs, compare with each other and with the Gen II assay?

Summary Answer: The three new AMH assays are well-correlated among themselves and with the Gen II assay, although differences in calibration do exist.

What is Known Already: The Gen II assay has been the mainstay method for AMH measurement in the past few years. Recently, a few new AMH measurement methods have come to the market.

Study Design, Size, Duration: This was a prospective assay evaluation performed on 178 human serum samples.

Participants/Materials, Setting, Methods: AMH concentration was measured in residual serum samples donated by female patients in a reproductive medicine center. The three new assay methods were tested in parallel and the numerical values obtained were compared among themselves and with those obtained by the Gen II assay. The assay stability upon different sample storage conditions, intra-assay and inter-assay precision, linearity and dilution recovery, and diagnostic performance for polycystic ovary syndrome (PCOS) of the three new AMH assay methods were also compared.

Main Results and the Role of Chance: AMH values measured by the Gen II kit and the three new assay methods have good correlations ($R > 0.9$ for all pairwise correlations). Values measured by the Ansh Labs assay were significantly higher, whereas those by the Roche assay were significantly lower, than those from the Gen II and Beckman-Coulter automated assays ($P < 0.05$). AMH values were significantly different when measured on the fresh and frozen–thawed serum sample (at −20° C and −80° C) for all three new methods ($P < 0.05$), but the magnitude of difference was very small with the Beckman Coulter automated assay and Roche assay. The intra-assay coefficients of variation (CVs) were 0.7–2.2%, 0.5–1.4%, and 1.4–5.4% for the Beckman Coulter automated, Roche and Ansh Labs assays, respectively. Their inter-assay CVs were 0.9–2.5%, 0.7–1.9%, and 6.2–13.5%, respectively. All three new assay methods showed acceptable linearity, and provided excellent discrimination of PCOS from controls.

Limitations, Reasons for Caution: The precision and dilution linearity experiments involved a small sample size, although these were not the primary outcome measures and have been properly evaluated in previous publications. The study was not designed or powered for determining diagnostic cutoff values.

Wider Implications of the Findings: The results demonstrate that the three new AMH assay methods are all valid methods to be adopted in the field of reproduction and are a basis for further work on their clinical application.

Performance of the two new fully automated anti-Müllerian hormone immunoassays compared with the clinical standard assay

Helden, J. V. and Weiskirchen R.

Human Reproduction 2015;30(8):1918-1926.

Study question: How do the two new fully automated anti-Müllerian hormone (AMH) assays released in September 2014 by two different diagnostic companies perform compared with the clinical standard assay, namely the AMH Gen II enzyme-linked immunosorbent assay (ELISA)?

Summary answer: Both fully automated AMH assays perform in a nearly identical fashion compared with the AMH Gen II assay, with a higher analytical sensitivity.

What is known already: Owing to the lack of standardization, the results of AMH ELISA assays are sometimes difficult to compare. The Beckman Coulter AMH Gen II assay became the clinical reference assay over the last few years. Two newly developed fully automated, highly sensitive AMH immunoassays, based on the AMH Gen II antibody composition have become available since September 2014.

Study design, size, duration: Previously characterized serum samples from 155 women were used to measure AMH with the three immunoassays, focusing on the aspect of predicting ovarian reserve.

Participants/materials, setting, methods: Samples from 94 women with an unfilled desire for a child diagnosed as infertile/subfertile, 29 samples women with polycystic ovary syndrome and 32 women approaching menopause were included in the study. The precision and the linearity in dilutions of the two new AMH assays were determined and the assay results were compared with the clinical reference (the modified version of the Beckman Coulter AMH Gen II assay) and to the antral follicle counts of the study participants. Cutoff values for the discrimination between each of two predefined groups were calculated using receiver operating characteristic analysis.

Main results and the role of chance: The performance evaluation of the fully automated AMH assays resulted in a within-run and intermediate precision of 0.9–1.9% and 2.5–6.5% with the one and 0.9–3.6% or 4.4–10.7% with the other immunoassay, respectively. Pearson's coefficient of correlation was 0.991 for the method comparison between both assays with a bias of 0.003ng/ml and a slope of 0.97. The discrimination of the new immunoassays between subfertile women and women approaching menopause was significantly better compared with the Beckman Coulter Gen II assay (87.5 versus 68.8%, P , 0.05).

Assessment of the Access AMH assay as an automated, high-performance replacement for the AMH Generation II manual ELISA

Pearson K., Long M., et al.

Reproductive Biology and Endocrinology 2016;14:8.

Background: The manual Generation II (Gen II) ELISA method used to measure anti-Müllerian Hormone (AMH) from Beckman Coulter has recently been superseded by a fully automated AMH immunoassay. The aim of this study was to evaluate the performance of the Access AMH assay and directly compare it to the modified Gen II ELISA method. A secondary aim was to verify that the fertile age-related AMH range previously established using the Gen II ELISA could be used to interpret results from the new automated Access assay.

Methods: The precision, stability, linearity, measurement range and detection limits were determined using recombinant AMH and patient serum samples. Different diluents and their effects on AMH concentration were compared. A correlation study was performed on patient samples to compare the Access AMH assay to the ELISA method on the Access 2 and DxI 800 analysers. The fertile AMH range was verified by comparing the 10th, 50th and 90th percentile values from both methods obtained from 489 natural conception pregnant women.

Results: The Access AMH assay showed good performance across the measuring range for both intra-assay (CV1.41–3.30 %) and inter-assay (CV 3.04–5.76 %) precision and acceptable sample stability. Dilution of the high concentration samples with the recommended diluent resulted in a small but significant downward shift in values. The assay was linear over the range of values recommended by the manufacturer, allowing for accurate reporting within the reported range. The two assay types were highly correlated (R2 = 0.9822 and 0.9832 for Access 2 and DxI 800, respectively), and the differences observed between the Access 2 and DxI 800 analysers were within clinically acceptable ranges, indicating that the methods are interchangeable. Furthermore, we demonstrated that results from the published reference range for the Gen II ELISA correlate with those from the automated Access AMH assay.

Conclusion: Here, we verified the published performance of the Access AMH assay and showed excellent correlation with the Gen II ELISA method. Moreover, we validated this correlation by confirming that the results from a fertile AMH reference range established using the preceding Gen II ELISA are interchangeable with the new automated Access AMH assay.

Two new automated, compared with two enzyme-linked immunosorbent, anti-Müllerian hormone assays

Nelson SM, Pastuszek E, et al.

Fertil Steril 2015;104(4):1016-1021.e6.

Objective: To compare new automated anti-Müllerian hormone (AMH) assay performance characteristics from the new automated Elecsys AMH (Roche; Elecsys) and Access AMH (Beckman Coulter; Access) assays with the existing AMH Gen II ELISA (enzyme-linked immunosorbent assay; Gen II; Beckman Coulter) and AMH ELISA (Ansh Labs) assays.

Patients: Patients referred for serum AMH measurement (n = 83) before start of in vitro fertilization cycle between September 2014 and October 2014.

Results: Intra-assay coefficients of variation were low; Ansh ≤9.0%; Gen II ≤5.8%; Access ≤10.7%; and Elecsys ≤2.8%. The Passing-Bablok regression equations (pmol/L) were y (Access) = 0.128 + (0.781 × Gen II); and y (Access) = 0.302 + (0.742 x Ansh). For y (Elecsys) = 0.087 + (0.729 x Gen II) and y (Elecsys) = 0.253 + (0.688 x Ansh Labs). For y (Elecsys) = 0.943 - (0.037 × Access). For all the assays, AMH exhibited a moderate positive correlation with AFC (r = 0.62–0.64); number of cumulus oocyte complexes (r = 0.60–0.64); and metaphase II oocytes (r = 0.48–0.50). Accuracy of pregnancy prediction, as determined by area under the receiver operating characteristic curve, was uniformly low for all assays (0.62–0.63).

Conclusions: The novel automated assays exhibit strong concordance in calibration, but derived values are substantially lower than those obtained from pre-existing assays, with assay-specific interpretation required for routine clinical use. These results highlight the need for an international standard of measurement of AMH.

Please see the following site for additional comments and insights into this publication
http://fertstertforum.com/nelsons-automated-manual-amh-assays/

Re: Two new automated, compared with two enzyme-linked immunosorbent, anti-Müllerian hormone assays.
By Nigel Groome BSc MSc (Birm) MSc PhD (Lond), Emeritus Professor

P-364 Validation of the Access AMH assay & its comparison with LabCorp Ultrasensitive assay

Younis A., Hawkins K.C., and Butler W.J.
Fertility and Sterility 2016;106 (3):e24.

Objective: AMH is the best currently available measure of ovarian reserve. In the USA, most fertility clinics get AMH values from LabCorp or specialty laboratory such as Ansh Labs. We are the first outpatient fertility laboratory to validate and implement the Beckman Coulter Access AMH assay in USA. The objective of this study was to evaluate the performance of the Access AMH assay using patient serum samples and directly compare results with LabCorp AMH levels.

Design: Prospective AMH assay evaluation in a fertility outpatient laboratory.

Material and Methods: Coefficients of variation, precision, stability, linearity, and inter-laboratory comparison were determined using recombinant AMH quality control and patient serum samples. Patients were consented and made aware that AMH assay will based on materials designed by manufacturer as research-use-only (RUO). Blood were collected for AMH on the day of the first office visit for fertility workup. Serum AMH level of 30 women (age 20–44 yrs) were assayed locally using Access 2 analyzer and at LabCorp using their ultrasensitive AMH assay. Inter-laboratory correlation study was performed on 75 patient samples in which AMH values were first obtained using a UniCell DXI analyzer at an independent outside laboratory (Pathology Associates Medical Laboratories, Spokane, WA). The serum samples were frozen and shipped in dry ice to our location where they were thawed and analyzed in Access 2 analyzer using similar reagent kit lots. All statistical evaluation was performed using SPSS.

Results: The Access AMH assay demonstrated excellent performance across the measuring range for both intra-assay and inter-assay coefficients of variation (2.1 % and 1.8 %, respectively). The assay was linear over the six ranges recommended by the manufacturer, and no strong bias was observed. AMH values ranged from 0.015 to 20.01ng/ml with the LabCorp and 0.011 to 25.40ng/ml with Access AMH. Values between fresh and frozen samples using Access AMH assay revealed no impact of sample freezing/storage. The Access AMH and LabCorp ultrasensitive assay types were highly correlated (R2=0.97, Slope0.96), and no statistical differences were observed between the two methods. Inter-laboratory comparison results showed that the two systems were statistically identical (R2=0.998 and 0.997 for Access 2 and UniCel DxI respectively).

Conclusions: We have validated and now routinely measure serum AMH levels in-house using the Access automated assay. Regression analysis demonstrates high correlation across the measuring range between the results obtained on two different analyzers located in different geographical locations. The findings of our correlation studies demonstrate strong agreement between the results generated by the Access AMH and LabCorp ultrasensitive assay indicating that the two methods are interchangeable.

T-069: Measurement of anti-Müllerian hormone by a new automated chemiluminescent immunoassay

Baraldi E., Roli L., et al.

Clin Chem Lab Med 2015;53S:s668.

Background-Aim: Anti-Müllerian hormone (AMH) is primarily used in the evaluation of ovarian reserve and to predict an infertile woman's response to controlled ovarian stimulation. Considering the wide use of AMH measurement in daily clinical practice and the large number of conditions in which it may be used, it is essential for the clinician to have accurate and reproducible results. Currently the most widely used method is enzyme linked immunoassay (ELISA) but this method has intrinsic limitations of sensitivity and of throughput. Recently a new automated chemiluminescent immunoassay method is available. As laboratory tests performed on automated platforms are more accurate and less time costing, we compared results of our traditional method ELISA with the new automated one.

Methods: A total of 107 archived serum samples from women with subfertility or reproductive endocrine disorders (aged from 22 to 52) were assayed using the AMH Gen II ELISA manual assay (Beckman Coulter) and Access AMH assay, a paramagnetic particle chemiluminescent immunoassay (Beckman Coulter) using the DxI 600 instrument . The samples covered a wide range of AMH concentrations (0.0–22 ng/ml).

Results: Total imprecision of the AMH Gen II ELISA and the Access AMH assays was ≤12.0 and ≤10.0%, respectively, over a range of concentrations from 0.16 to 22 ng/ml. The detection limit of the assays was 0.08 ng/ml and 0.02 ng/ml. For the AMH Gen II and the Access AMH assays, the median (interquartile range) was 1.51 (0.08–20.0) ng/ml and 1.03 (0.02–25.4) ng/ml, respectively (P<0.0001). The Passing-Bablok regression equation (in ng/ml) was: y (AMH Access) = -0.0195+0.7312 x (AMH Gen II ELISA) and the regression coefficient R=0.988.

Conclusion: AMH concentrations using the Access AMH assay are slightly lower than those from the AMH Gen II ELISA kit, but well correlated. The worldwide standardization of the assay is required and this study can facilitate a comparison between the old results and those which will be obtained in the future, using any of the two assays considered. Meanwhile, adapting clinical cutoffs from previously published works by direct conversion is not still recommended, but it is important a critical clinical evaluation together with other diagnostic and ecographic parameters.

T072: Anti-Müllerian hormone—immunoassay method comparison

Alves J., Manaças M., et al.
Clin Chem Lab Med 2015;53S:s671.

Background-Aim: Anti-Müllerian hormone (AMH) is a dimeric glycoprotein produced in the gonad exclusively. It is used as marker for assessing the ovarian reserve and as an initial predictor of ovarian response to gonadotropin stimulation. The National Institute for Health and Care Excellence (NICE-UK) recommends a 3-class approach when aiming at in vitro fertilization (IVF) ovarian gonadotrophin stimulation response prediction (Low <0,8 ng/mL; Moderate 0,8–3,6 ng/mL; High >3,6 ng/mL). The objective of this study was to evaluate the performance of two different AMH immunoassays (CLIA and ECLIA), and compare them with the long standing standardized ELISA method.

Methods: 78 patients were enrolled (convenience sample). Serum AMH levels were simultaneously assayed using three distinct analytical methods: ELISA (AMH Gen II ELISA, Beckman Coulter; Werfen Best® 2000), CLIA (Access AMH Paramagnetic-Particle CLIA Beckman Coulter; Beckman Coulter Access® 2) and ECLIA (Elecsys® AMH Roche; Roche Cobas® e411). SPSS® 20V software was used for statistical analysis.

Results: After removal of three outliers >15 ng/mL, the Correlation Coefficient showed a very strong positive correlation between ELISA/CLIA assays (R=0,977) (p<0,001)(Pearson's test)(y=0,93x), and between ELISA/ECLIA assays (R=0,980) (p<0,001) (Pearson's test)(y=0,81x–0,01). The Bland-Altman dispersion plot pointed that, despite the very strong correlation, the values obtained when using the ELISA assay were almost always higher than values obtained by CLIA or ECLIA. This difference was more obvious with the ELISA/ECLIA comparison. The Fleiss' test showed a strong class (three classes) agreement between ELISA/CLIA (κ=0,846)(p<0,001) and ELISA/ECLIA (κ=0,750)(p<0,001) which was stronger between ELISA/CLIA.

Conclusion: A strong correlation has been shown between the ELISA/CLIA and ELISA/ECLIA assays. When compared with the standardized ELISA assay, the CLIA assay had a better class agreement, when using the above described prognostic groups. Clinical studies should address the prognostic importance of class allocation and class inclusion cutoff values regarding AMH, since small interassay differences, in highly correlated assays, can mean different class allocation and different prognosis.

Multicenter evaluation of the Access AMH anti -Müllerian hormone assay for the prediction of antral follicle count and poor ovarian response to controlled ovarian stimulation

Baker V. L., Gracia C. et al.
Fertility and Sterility 2018;110(3):506-513.e3.

Objective: To evaluate a new fully automated anti-Müllerian hormone (AMH) assay for prediction of poor ovarian response (POR) to ovarian stimulation defined as four or fewer oocytes retrieved.

Design: Prospective cohort study.

Setting: Thirteen private and academic fertility centers in the United States.

Patients(s): A total of 178 women undergoing their first in vitro fertilization (IVF) cycle eligible for the study were consented and enrolled, with data available from 160 women for prediction of POR and 164 women for AMH correlation with antral follicle count (AFC).

Main Outcome Measure(s): Cutoff point for AMH that predicts POR. Correlation of AMH with AFC, and cutoff point for AMH that correlates with antral follicle count >15.

Result(s): The mean AMH among the poor responders was 0.74 ng/mL, compared with 3.20 ng/mL for normal to high responders. The AMH cutoff at 90% specificity for predicting POR with the use of the receiver operating characteristic (ROC) curve was 0.93 ng/mL, with an associated sensitivity of 74.1%. For prediction of POR, ROC analysis showed that AMH (area under the ROC curve [AUC] = 0.929) was significantly better than FSH (AUC = 0.615; P<.0001). AMH was positively correlated with AFC (Spearman rho = 0.756). The AMH at 90% sensitivity for AFC >15 was 1.75, with specificity of 59.1%.

Conclusion(s): A fully automated AMH assay can be a useful biomarker for predicting POR in IVF cycles. Because AMH cutoff points vary depending on the assay used, future studies should continue to calibrate test results to clinically important outcomes.

Multi-center clinical evaluation of the Access AMH assay to determine AMH levels in reproductive age women during normal menstrual cycles

Gracia C.R., Shin S. S., et al.

Journal of Assisted Reproduction and Genetics 2018;35:777 –783.

Background: AMH is widely used for assessing ovarian reserve, and it is particularly convenient, because it is thought to have minimal variability throughout the menstrual cycle. However, studies assessing the stability of AMH over the menstrual cycle have been conflicting.

Purpose: The purpose of this study is to determine whether AMH levels vary across the normal menstrual cycle.

Design: A multi-center, prospective cohort study conducted at three US centers.

Methods: Fifty females with regular menstrual cycles aged 18–45 underwent serial venipuncture every 3–5 days starting in the early follicular phase and lasting up to 10 collections. AMH was tested using the Access 2 immunoassay system.

Results: Age-adjusted mixed-effect models utilizing data from 384 samples from 50 subjects demonstrated a within subject standard deviation of 0.81 (95% CI 0.75–0.88) with a coefficient of variation of 23.8% across the menstrual cycle and between subject standard deviation of 2.56 (95% CI 2.13–3.21) with a coefficient of variation of 75.1%. Intra-class correlation (ICC) of AMH across the menstrual cycle was 0.91.

Conclusion: Overall, AMH levels, using the automated Access AMH assay, appear to be relatively stable across the menstrual cycle. Fluctuations, if any, appear to be small, and therefore, clinicians may advise patients to have AMH levels drawn at any time in the cycle.

"The Anti-Müllerian Hormone assay is a valuable test that we have incorporated at our fertility clinic in order to assess ovarian reserve. Measures of ovarian reserve such as AMH and antral follicle counts are helpful to predict an infertile woman's response to controlled ovarian stimulation. The Access AMH assay is a new automated AMH assay which has recently been FDA cleared for clinical use after a rigorous multi-center study. I anticipate that this automated platform will make this assay more widely available."

Dr. Clarisa R. Gracia, M.D.,
Director, Fertility Preservation
Associate Professor of Obstetrics and Gynecology
at the Hospital of the University of Pennsylvania

Pediatric anti-Müllerian hormone measurement: male and female reference intervals established using the automated Beckman Coulter Access AMH assay

Jopling H., Yates A., et al.

Endocrinology, Diabetes & Metabolism 2018;1(4):1-8.

Objective: Anti-Müllerian Hormone (AMH) concentration is high at birth in males, demonstrating the presence of functional testicular tissue in the prepubertal period, and acting as a useful marker in the investigation of pediatric reproductive disorders. AMH also provides a tool in the investigation of female virilization, premature ovarian failure and polycystic ovarian syndrome in childhood. Robust, assay- specific pediatric AMH reference intervals are therefore required for clinical interpretation of results.

The aim of this study was to derive age-specific AMH reference intervals for males and females aged 0- 18 years.

Design and Patients: Plasma samples were obtained from patients at Royal Manchester Children's Hospital and analyzed for AMH using the automated Beckman Coulter Access AMH Assay. Patients under investigation for pediatric reproductive or endocrine disorders were excluded from the study. Measurements: Seven hundred and two patient plasma samples (465 male, 237 female) were subject to AMH measurement, and results were analyzed in order to derive continuous and discrete reference intervals for the pediatric age range.

Results: Clear discrimination between male and female AMH results was evident in the prepubertal age range, with some overlap between the genders following pubertal onset.

Conclusions: We have derived age-related reference intervals for plasma AMH in the pediatric age range (0-18 years) using the automated Beckman Coulter Access AMH assay which will aid in the investigation of pediatric endocrine disorders such as disorders of sexual development.

P-388 Age stratified anti-Müllerian Hormone (AMH) reference range evaluation in polycystic ovary syndrome women at reproductive age using an automated AMH assay

Sun L., Retka S., et al.

Human Reproduction 2018;33 suppl 1: i318-i319.

Study design, size, duration: This study was a multi-center, prospective, cross-sectional study of 146 PCOS women enrolled from March 2016 to August 2016. The study used four geographically diverse sites in the United States.

Participants/materials, setting, methods: The study included PCOS women aged 18–45 years who met the Rotterdam criteria. The age stratified AMH reference ranges were established, and the difference of AMH distributions between age groups were further analyzed using the Kruskal-Wallis test. A comparison of PCOS reference ranges was made to age-matched healthy adult females. Serum samples were measured at a separate, single site using the Beckman Coulter Access 2 immunoassay system and the Access AMH assay.

Main results and the role of chance: Age stratified AMH reference ranges were established in 146 PCOS women with AMH levels ranging from 0.03 to 34.6 ng/mL. Age was categorized as 18-25 (n = 16), 26-30 (n = 51), 31-35 (n-41), 36-40 (n = 23), and 41-45 (n = 15) years. Median AMH levels categorized by age for PCOS women demonstrated a decreasing trend (7.11, 7.35, 6.77, 3.95 and 1.63 ng/mL, respectively) with increased age, but were statistically significantly higher than apparently healthy age-matched adult women. Overall, median AMH level for PCOS women was 3 times higher than apparently healthy adult women with a statistical significance (6.02 vs. 1.83 ng/mL, respectively, p-value<0.0001). Kruskal-Wallis test showed substantial difference in AMH distributions between the age groups (p-value = 0.0022) in PCOS women, and the Pearson's correlation analysis confirmed a negative relationship between AMH levels and age (r=-0.229, 95%CI=-0.379 – -0.069, p-value = 0.0054).

Wider implications of the findings: To our knowledge, this is the first study that established the age stratified AMH reference ranges using the automated AMH assay in PCOS women. AMH distributions in PCOS women differ significantly between age groups, questioning the use of one universal AMH threshold for PCOS women at all ages.

Table. Age stratified AMH (ng/mL) 95% reference ranges in PCOS women.

Age (Years)	N	AMH (ng/mL)		
		Median	2.5th Percentile	97.5th Percentile
18–25	16	7.11	0.03	16.2
26–30	51	7.35	0.79	31.24
31–35	41	6.77	0.5	18.26
36–40	23	3.95	0.04	11.5
41–45	15	1.63	0.03	24.6

Age-specific values of Access anti-Müllerian hormone immunoassay carried out on Japanese patients with infertility: a retrospective large-scale study

Segawa T., Omi K., et al.

BMC Women 's Health 2019;19(57):1 -6.

Background: The ovarian reserve in women is known to correlate with anti-Müllerian hormone (AMH) levels, and currently the latest, third-generation, fully-automated AMH immunoassays, such as Access and Cobas, are beginning to be used for measuring AMH levels. However, the age-specific reference values obtained for AMH levels have been based on samples from an American population, measured using first-generation immunoassays. In this study, we attempted to determine the age-specific AMH reference values based on a large set of samples taken from Japanese infertile women measured by Access so that they could be used by infertility centers treating Japanese patients and those with similar racial and life-style characteristics.

Methods: The study included 5483 Japanese patients who enrolled in infertility treatment programs at two in-vitro fertilization centers, Shimbashi YUME Clinic and Natural ART Clinic Nihombashi in Tokyo, and who had their serum AMH levels measured between December 2015 and November 2017 by Access. Each patient was represented only once in the study. The mean, median, and standard deviation values were obtained from the measured values for single-year intervals from 28 through 48 years of age (21 age groups in total). The 3D-fitted curve of age-specific mean and median values measured by Access was obtained by regression analysis.

Results: The mean and median values decreased with advancing age (mean: R2 = 0.9864; median: R2 = 0.9926). In all age groups, the mean values were higher than the median values; however, the differences between these values decreased with increasing age.

Conclusions: The age-specific AMH reference values measured by Access in this study may serve as a useful diagnostic marker in infertility centers, especially those treating Japanese patients or patients with similar characteristics.

P-570 Derivation of reference intervals (RIs) for Anti-Müllerian hormone (AMH), specific for Russian population, using automated Access AMH assay

Guzov I., Pecherina E., et al.
Fertility and Sterility 2019;34(suppl 1): i403.

Study design, size, duration: Following CLSI EP 28AC, 436 women and 24 men were recruited; women were further grouped by age. Pregnant women, women with polycystic ovary syndrome and women undergoing ovarian surgery were excluded. Antral follicle counts (AFCs) were defined as sum of follicles 2–10 mm in diameter in both ovaries. The women were divided into groups with non-detectable, low (<10) and normal (11-20) AFCs by transvaginal ultrasound (TVUS). The duration of the study was 1 year.

Participants/materials, setting, methods: 460 volunteers aged 18-60 years were recruited, AMH was measured on the Access 2 analyzer (Beckman Coulter, Inc.) at CIR Laboratories on peripheral blood collected without regard to menstrual cycle day. AFCs were assessed in women on days 1–4 of their menstrual cycles using TVUS (Medison Ultrasound Systems). A nonparametric analysis of RIs was carried out using Stata 11 statistical analysis software.

Main results and the role of chance: In the Russian population, women aged 26-30 and 31-35 years had median and upper limit (UL) values for AMH that were significantly higher than those provided by the manufacturer (median 3.38 vs. 2.27, 2.85 vs. 1.88; UL 11.03 vs. 7.37, 11.61 vs. 7.35, respectively). In comparison to a Brazilian study (Woloszynek, 2015), the median and UL in the Russian population were lower for women aged 18-30 years group (median 3.35 vs. 3.7, respectively). In women aged 41-45, >46 and men, RIs were consistent with those provided by the manufacturer. Significant negative correlation between AMH and age was shown in women over 35 (rp=-0.46). Correlation between AMH concentration and AFC in both ovaries was demonstrated (rp=0.64; 0.69), with significant differences noted between AMH levels in groups of the same age but with different AFCs (low vs. normal AFC, 1.15 vs. 2.6, respectively).

Wider implications of the findings: This study establishes Russian population-specific RIs for AMH using Beckman Coulter's Access AMH assay. These results reinforce the importance of obtaining population- specific reference intervals. Correlation among age, AMH concentration and antral follicle count (AFC) was estimated.

Anti-Mullerian Hormone (AMH) and Age – An Indian laboratory retrospective analysis

K K., Lyer S., et al.

Asian J of Health Sciences 2019;5(1):7

Introduction: Anti-Mullerian Hormone (AMH) is considered to be a sensitive biological indicator of the ovarian reserve among women. Produced by the granulosa cells in the ovary, AMH is also considered to be a good biochemical marker to time menopause, apart from being monitored during treatment of certain ovarian tumors. Our retrospective report is an attempt to study AMH levels across different age-groups between 18–50 years of age and present age-related changes in levels.

Methods: Serum AMH estimation was done in a total of 219,227 Asian Indian women using the chemiluminescent immunoassay technology.

Results: Our analysis of different age-groups with AMH levels detected a declining trend and a significant drop in levels was recorded between ages 19–20 years and 35–36 years of age at $p<0.05$.

Conclusion: Our report is an attempt to present age-effect on AMH levels in a pan-India cohort of Asian Indian women and analysis detected a negative correlation between age and AMH levels.

Age-independent anti-Müllerian hormone (AMH) standard deviation scores to estimate ovarian function

Helden J.V., Weiskirchen R.

European Journal of Obstetrics & Gynecology and Reproductive Biology 2017;213:64-70.

Objectives: To determine single-year age-specific anti-Müllerian hormone (AMH) standard deviation scores (SDS) for women associated to normal ovarian function and different ovarian disorders resulting in sub- or infertility.

Design and methods: Determination of particular year median and mean AMH values with standard deviations (SD), calculation of age-independent cutoff SDS for the discrimination between normal ovarian function and ovarian disorders.

Results: Single-year-specific median, mean, and SD values have been evaluated for the Beckman Coulter Access AMH immunoassay. While the decrease of both median and mean AMH values is strongly correlated with increasing age, calculated SDS values have been shown to be age independent with the differentiation between normal ovarian function measured as occurred ovulation with sufficient luteal activity compared with hyperandrogenemic cycle disorders or anovulation associated with high AMH values and reduced ovarian activity or insufficiency associated with low AMH, respectively.

Conclusion: These results will be helpful for the treatment of patients and the ventilation of the different reproductive options.

Relationship between anti-Müllerian hormone and antral follicle count across the menstrual cycle using the Beckman Coulter Access assay in comparison with Gen II manual assay

Schiffner J., Roos J., et al.

Clin Chem Lab Med 2017;55(7):1025-1033

Background: The study aim was to validate Beckman Coulter's fully automated Access immunoassay system (Beckman Coulter Access assay) for anti-Müllerian hormone (AMH) and compare it with Beckman Coulter's Modified Manual Generation II assay (Beckman Coulter Mod Gen II), with regard to cycle AMH fluctuations and antral follicle counts.

Methods: During one complete menstrual cycle, transvaginal ultrasound was performed on regularly menstruating women (n = 39; 18–40 years) every 2 days until the dominant ovarian follicle reached 16 mm, then daily until observed ovulation; blood samples were collected throughout the cycle. Number and size of antral follicles was determined and AMH levels measured using both assays.

Results: AMH levels measured by the Beckman Coulter Access assay vary over ovulatory menstrual cycles, with a statistically significant pre-ovulatory decrease from -5 to +2 days around objective ovulation. Mean luteal AMH levels were significantly lower (-7.99%) than mean follicular levels but increased again towards the end of the luteal phase. Antral follicle count can be estimated from AMH (ng/mL, Beckman Coulter Access assay) concentrations on any follicular phase day. Beckman Coulter Access assay-obtained AMH values are considerably lower compared with the Beckman Coulter Mod Gen II assay (-19% on average); conversion equation: Beckman Coulter Access AMH (ng/mL) = 0.85 [Beckman Coulter Mod Gen II AMH (ng/mL)]0.95.

Conclusions: AMH levels vary throughout the cycle, independently of assay utilized. A formula can be used to convert Beckman Coulter Access assay-obtained AMH levels to Beckman Coulter Mod Gen II values. The number of antral follicles can be consistently estimated from pre-ovulatory AMH levels using either assay.

New automated anti-Müllerian hormone assays are more reliable than the manual assay in patients with reduced antral follicle count

Tadros T., Tarasconi B., et al.
Fertil Steril 2016;106:1800-1806.

Objective: To compare the strength of the relationship between antral follicle count (AFC) and serum anti-Müllerian hormone (AMH) concentrations obtained with two automated and one manual AMH assays in three different AFC populations.

Patient(s): Frozen–thawed serum samples of 211 assisted conception candidates, aged 24–43 years.

Intervention(s): Serum AMH was measured using one manual (AMH Gen II) and two fully automated (Access AMH and Elecsys AMH) assays. Antral follicle count was performed under strictly standardized conditions and sorted into three groups according to tercile values: low AFC (3–12 follicles; n=73), intermediate AFC (13–20 follicles; n=65), and high AFC (21–84 follicles; n=73).

Main Outcome Measure(s): Strength of correlation between AMH levels and AFC.

Result(s): Overall, AMH levels were lower with Access AMH (-16%) and Elecsys AMH (-20%) than with AMH Gen II. Remarkably, the strength of correlations between AFC and circulating AMH levels was the same with the three assays (r=0.83). Yet in the low AFC group, serum AMH levels obtained by Access AMH and Elecsys AMH showed a stronger correlation with AFC (r=0.63 and r=0.65, respectively) than the AMH Gen II (r=0.52), a phenomenon that was not observed in the remaining AFC groups.

Conclusion(s): As compared with conventional AMH Gen II assay results, [1] serum AMH concentrations were -16% and -20% lower with Access AMH and Elecsys AMH, respectively; and [2] automated assays were more strongly correlated to AFC in the subset of patients with reduced follicle count.

Effect of long-term use of hormonal contraception on anti-Müllerian hormone secretion

Kucera R., Ulcova-Gallova Z., et al.

Gynecological Endocrinology 2015 Dec 11:1-3.

Abstract: Anti-Müllerian hormone (AMH) is an important factor associated with female fertility and the ovarian reserve. There are several past studies available concerning the influence of hormonal contraception (HC) on serum AMH levels. Recent studies have reported that AMH levels in women using HC can be about 30% lower compared to those not using HC. However, earlier studies showed no reduction in AMH levels in HC users. We decided to evaluate the effects of long-term HC use (mean duration of HC use: 11.4 years) on AMH levels in women. To exclude potential shorter and reversible decreasing effects of HC on fertility function, we decided to include women in the study who had stopped using HC 1 year before the AMH sample collection. We examined 105 women who used HC and 44 women who had never used HC. The median concentration of AMH in the group of long-term users of HC was 2.89 and 3.37 ng/ml in the group of women who had never used HC. We found no statistically significant difference (p=0.3261). In conclusion, we observed no negative impact of HC on the AMH serum levels. AMH can be used as an ovarian reserve marker for these women.

AMH serum levels were assayed using the chemiluminescent kit Access AMH (Beckman Coulter, Brea, CA). Measurements were performed using the UniCel DxI 800 (Beckman Coulter).

Comparative assessment of five serum anti-Müllerian hormone assays for the diagnosis of polycystic ovary syndrome

Pigny P., Girisse E., et al.

Fertility and Sterility 2016; 105(4):1063-1069.

Objective: To determine whether the different anti-Müllerian hormone (AMH) immunoassays on the market offer the same performance for the diagnosis of polycystic ovary syndrome (PCOS).

Design: A total of 95 serum AMH samples were retrospectively evaluated for a period of 3 months in the same laboratory.

Setting: Academic center laboratory.

Patient(s): Forty-eight control women with regular menses and no hyperandrogenism and 47 patients with classic PCOS (i.e., hyperandrogenism plus oligoanovulation) attending our department for infertility.

Intervention(s): None.

Main Outcome Measure(s): AMH measurement using five commercial assays. Method comparison and evaluation of the diagnostic performance by receiver operating characteristic analysis.

Result(s): Values obtained with Gen II and AL-105i ELISAs were similar to those provided by EAI AMH/MIS, whereas automatic assays generated lower values. A significant mean difference was observed between Access DxI (1.35 ng/mL) or Cobas (1.73 ng/mL) and EIA AMH/MIS ELISA. By ROC analysis each assay displayed similar efficiency for PCOS diagnosis. Sensitivities varied from 49% to 74% when setting the specificity at 92%. Cluster analysis run in the control group identified a subgroup of asymptomatic women with polycystic ovary morphology (PCOM). After exclusion of PCOM, the 95th percentile of controls was 4.2 ng/mL (30 pmol/L) with the automatic assays and 5.6 ng/mL (40 pmol/L) with the manual assays.

Conclusion(s): Performance of the different AMH assays for PCOS diagnosis is comparable, providing that different threshold values are used for manual and automatic assays. Measurement of serum AMH level appears as a robust tool for the definition of PCOM.

Salivary and serum androgens with anti-Müllarian hormone measurements for the diagnosis of polycystic ovarian syndrome

Sathyapalan T, Al-Qaissi A, et al.
Scientific Reports 2018;8:3795.

To determine the predictive value of a raised androgen level with an elevated anti-Müllerian hormone (AMH) for the diagnosis or exclusion of polycystic ovary syndrome (PCOS), a prospective cross-sectional study of 170 women (105 with PCOS type A and 65 normal) was undertaken. AMH was combined with one of, total serum testosterone (T); calculated free androgen index; salivary testosterone (salT); serum androstenedione (A); salivary androstenedione (salA). The diagnostic sensitivity and specificity of AMH (>35 pmol/l) alone for PCOS were 55% and 79% respectively. The diagnostic sensitivity and specificity of AMH (>35 pmol/l) with either an elevated T or raised FAI level for PCOS showed 100% specificity and a 100% positive predictive value. Conversely, diagnostic exclusion of PCOS was shown by an AMH <35 pmol/l with a normal T or FAI salivary testosterone giving 100% specificity and 100% positive predictive value. AMH with an elevated A or elevated salA level gave specificities of 87% and 94%, and positive predictive values 80% and 94%, respectively. Therefore, the combination of an AMH with a cut off of 35 pmol/l combined with a raised T and/or a FAI will confirm PCOS whilst a normal AMH with a normal T and/or FAI will exclude PCOS, thus addressing diagnostic uncertainty.

Technical and performance characteristics of anti-Müllerian hormone and antral follicle count as biomarkers of ovarian response

Iliodromiti S., Anderson R., et al.

Human Reproduction Update 2015;21(6):698-710.

Background: Stratified (individualized) medicine has been recognized as a key priority for policy makers and healthcare providers. The main principle of individualized care depends on utilizing patients' characteristics and biomarkers to predict prognosis, tailor intended treatment and predict treatment outcomes. In reproductive medicine a wide variety of biomarkers have been proposed as predictors of ovarian response; of these, anti-Müllerian hormone (AMH) and antral follicle count (AFC) are purported as exhibiting the most favourable analytical and performance characteristics. Previously AFC and AMH have been considered essentially interchangeable; however, recent trial data have questioned this postulation. The aim of this review is to present an analysis of the strengths and weaknesses of these biomarkers as predictors of ovarian response, using both physiological and technical perspectives.

Methods: We have conducted a systematic search of the most recent (to May 2014) relevant literature and summarized the existing evidence. Articles written in a language other than English without an available English translation were excluded.

Results: Both AMH values and AFC can be influenced by comparable technical, physiological and exogenous factors. AMH displays some variation within and between cycles, consistent with its physiological role in follicle development, and there are growing data on the impact of pharmacological treatments and pathological conditions but cycle-independent measurement is appropriate for clinical purposes. A range of issues with manual AMH assays may be resolving with the development of fully automated assays. Despite described standardization of its measurement technique, AFC is subject to marked inter- and intra-operator variability and the effects of external influences are likely to be comparable. Out with some highly specialist centres, the intracyclic variation in AFC requires its measurement between Day 2 and 4 of the cycle. Observational studies suggest comparable performance characteristics for AMH and AFC in predicting poor and high ovarian response, but recent RCTs suggest markedly better performance for AMH.

Conclusions: The performance characteristics of both AMH and AFC for the prediction of ovarian response to exogenous gonadotrophins have been inflated by single site observational cohorts, resulting in the viewpoint that AMH and AFC exhibit equivalent performance.

Evaluation of the multisite anti-Müllerian hormone (AMH) age related reference intervals on women with proven natural fertility using the Beckman Coulter Access immunoassay systems

Wyness SP, Denham DS, et al.
AACC poster 2016;S76.

Background: Anti-Müllerian hormone (AMH) is a naturally occurring hormone found in both males and females. Published literature suggests AMH has potential for evaluating the ovarian reserve in women of reproductive age and is known to vary by age. Beckman Coulter has developed an automated version of the AMH Gen II assay used on the Beckman Coulter Access 2 immunoassay analyzer. Age-specific reference intervals were evaluated.

Methods: 622 women with proven natural fertility were prospectively enrolled from three U.S. centers. All racial backgrounds were eligible. Subjects were ≥18 years of age, had regular menses (21–35 days) and both ovaries. Women with PCOS, previous ovarian surgery, exposure to cytotoxic drugs or pelvic radiation therapy, or recent contraceptive use were excluded. Serum samples were analyzed using the Beckman Coulter Access 2 Immunoassay Analyzer. Data were initially stratified to age ranges: 18–25, 26–30, 31–35, 36–40, 41–45, and ≥46 years. Outliers were removed using Tukey's method on Box-Cox transformed data. The robust method was used to estimate the 2.5th and 97.5th percentiles and their 90% confidence intervals.

Results: Reference intervals are reported in Table 1. Data groups 18–25 and 26–30 years were combined as the overlapping 90% confidence intervals suggested no difference between the two groups. AMH levels were age related, with values generally higher at younger ages, and decreasing with age. There was a wide range of AMH values observed within the reference intervals, especially in the younger groups.

Conclusion: This is the first report of AMH reference intervals using the Access 2 immunoassay analyzer. Results are consistent with published data and support that AMH concentrations in women generally decrease with age but with a wide range of values within the same age group.

P-3-790: Evaluation of two new anti-Müllerian hormone assays for the investigation of disorders of sexual development in neonates

Ho C.K.M. and Setoh J.W.S.

ESPE Abstracts 2015;84:P-3-790.

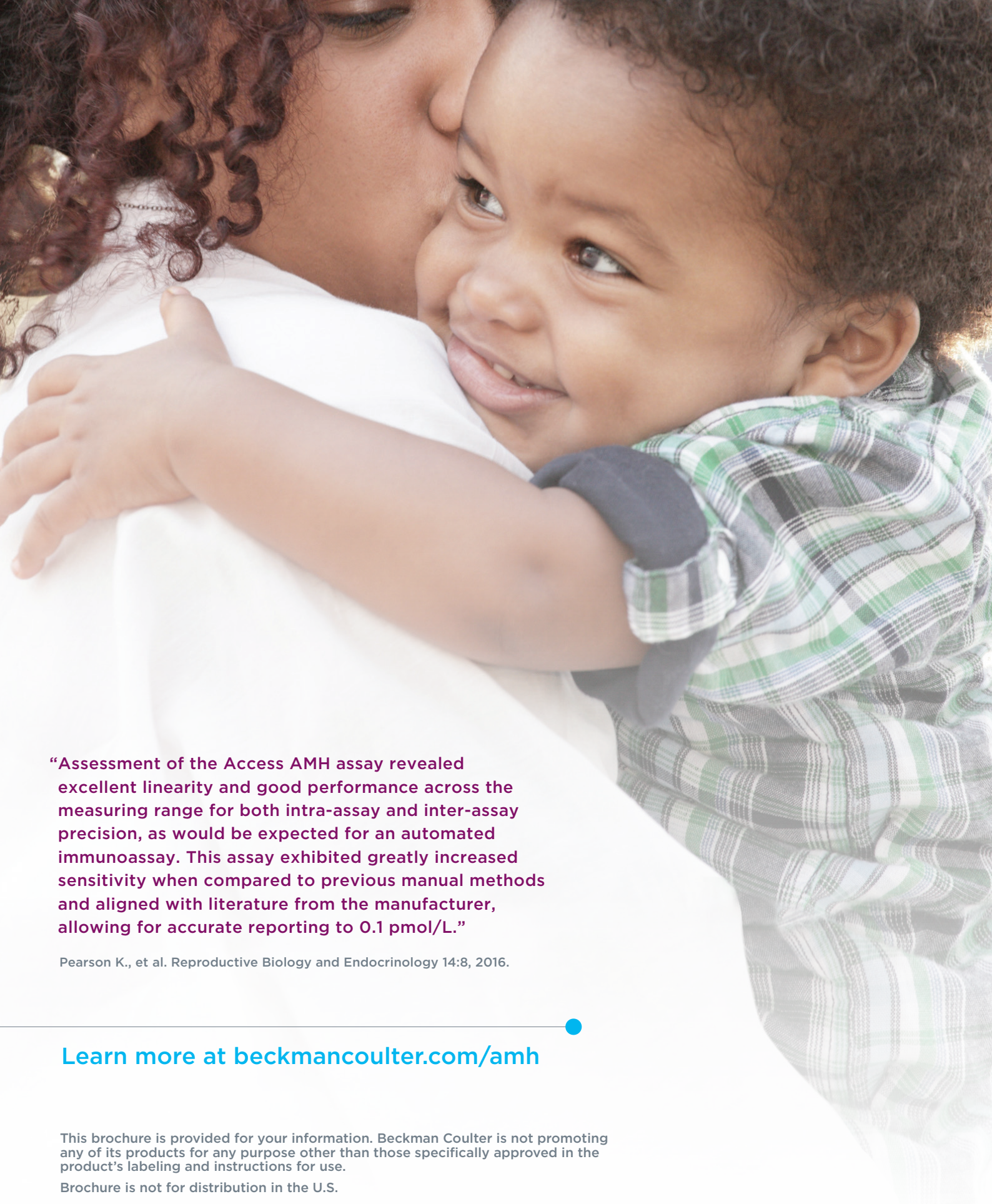
Background: Anti-Müllerian hormone (AMH) inhibits the in utero growth of the Müllerian structures in female fetuses. In neonates with suspected disorders of sexual development (DSDs), the presence of testicular tissues and functioning Sertoli cells can be investigated by testing for serum AMH concentration.

Objective: To evaluate the performance of two new AMH assays in a hospital laboratory.

Method: The technical performance of two new assays for AMH (Beckman Coulter and Roche) was evaluated and compared with each other using standard laboratory protocols. Serum AMH concentrations were also measured in 44 neonates with no suspected DSDs.

Results: AMH results generated by the two assays are highly comparable (Pearson correlation coefficient=0.966). Both assays were linear within their reportable ranges. Precision studies showed that coefficients of variation (CVs) at the limits of quantitation (LOQ) were <7%. In the female neonates (n=24; aged 0–29 days; mean age=5.9 days), AMH concentrations (Beckman Coulter assay) ranged from 0.02 to 2.28 ng/ml (mean±S.D., 0.22±0.47 ng/ml). In comparison, in the male neonates (n=20; aged 0–30 days; mean age=11.7 days), AMH concentrations ranged from 15.5 to 157.6 ng/ml (mean±S.D., 70.5±48.7 ng/ml).

Conclusion: There is no overlap between serum AMH concentrations in the two gender groups of neonates. All AMH concentrations measured in the male and female neonates fall within their respective reference intervals provided by one of the manufacturers (males <60 days, 15.1–266.6 ng/ml; females <60 days, 0.01–3.39 ng/ml). In conclusion, both AMH assays were analytically sensitive enough to be used in neonates, and differential AMH concentrations in male and female neonates render this test a useful tool for the investigation of DSDs.



"Assessment of the Access AMH assay revealed excellent linearity and good performance across the measuring range for both intra-assay and inter-assay precision, as would be expected for an automated immunoassay. This assay exhibited greatly increased sensitivity when compared to previous manual methods and aligned with literature from the manufacturer, allowing for accurate reporting to 0.1 pmol/L."

Pearson K., et al. Reproductive Biology and Endocrinology 14:8, 2016.

Learn more at beckmancoulter.com/amh

For Beckman Coulter's worldwide office locations and phone numbers, please visit www.beckmancoulter.com/contact

BR-241000

BECKMAN COULTER