Research and published case studies using Mira

Collaborative Research and Clinical Trials

Duquesne University

Study Focus: Menstrual cycle data comparison in individuals with/without PCOS.

Goal: Identify common hormone patterns and enhance PCOS diagnostics.

Johns Hopkins University

Study Focus: Statistical analysis to refine Mira's algorithms.

Goal: Improve data accuracy and algorithm performance.

University of British Columbia

Study Focus: Validation of Mira's results with ultrasound and blood tests.

Goal: Ensure accuracy of Mira's readings.

University of Melbourne

Study Focus: Sex hormones' associations with metabolism, immune, and cardiovascular systems.

Goal: Explore impacts in post-viral syndrome individuals.

Icahn School of Medicine at Mount Sinai Hospital

Study Focus: Cortisol, sex hormones, and long COVID symptoms.

Goal: Investigate hormonal influences on long COVID.

Athletica

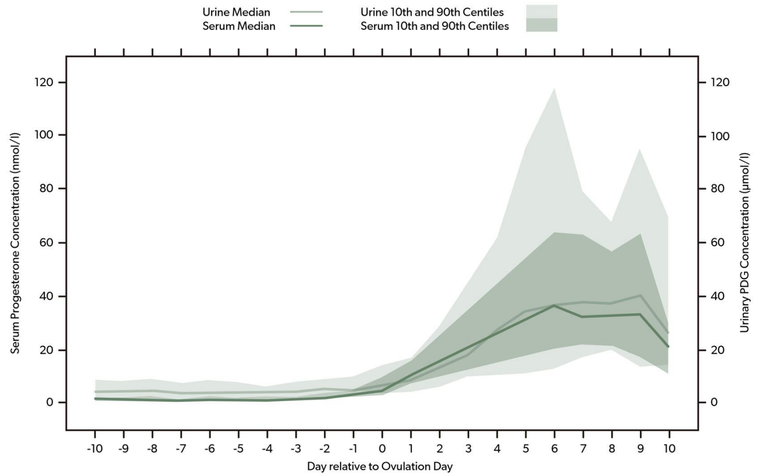
Study Focus: Effects of training load on menstrual cycle and ovulation.

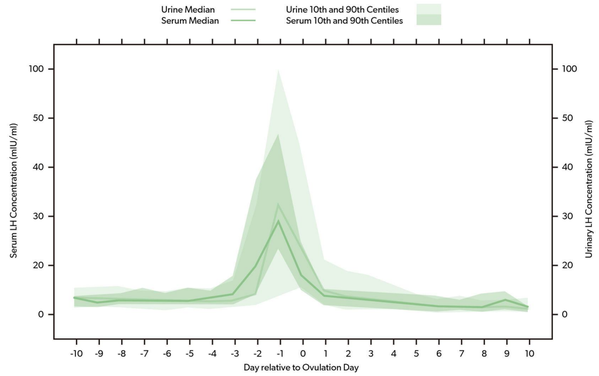
Goal: Understand exercise impacts on menstrual and reproductive health.

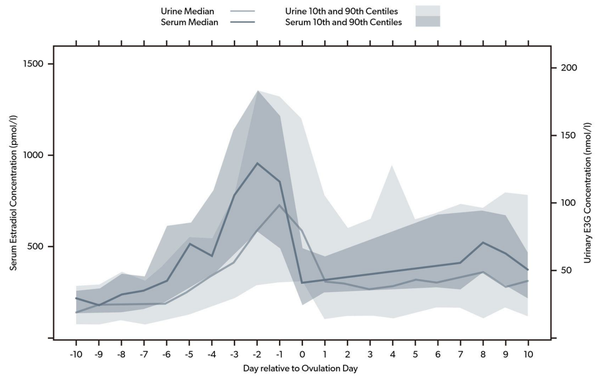
Research studies comparing hormone levels in urine and serum

Comparison of urinary and serum reproductive hormones referenced to true ovulation (n=40)

Urinary and serum reproductive hormones showed excellent agreement and may be used interchangeably. The beginning of the surge in serum and urinary LH was an excellent predictor of ovulation. The rise in progesterone and P3G above baseline was a consistent marker of luteinisation confirming ovulation. Both LH and progesterone surges delivered clear, sharp signals in all volunteers, allowing reliable detection and confirmation of ovulation.







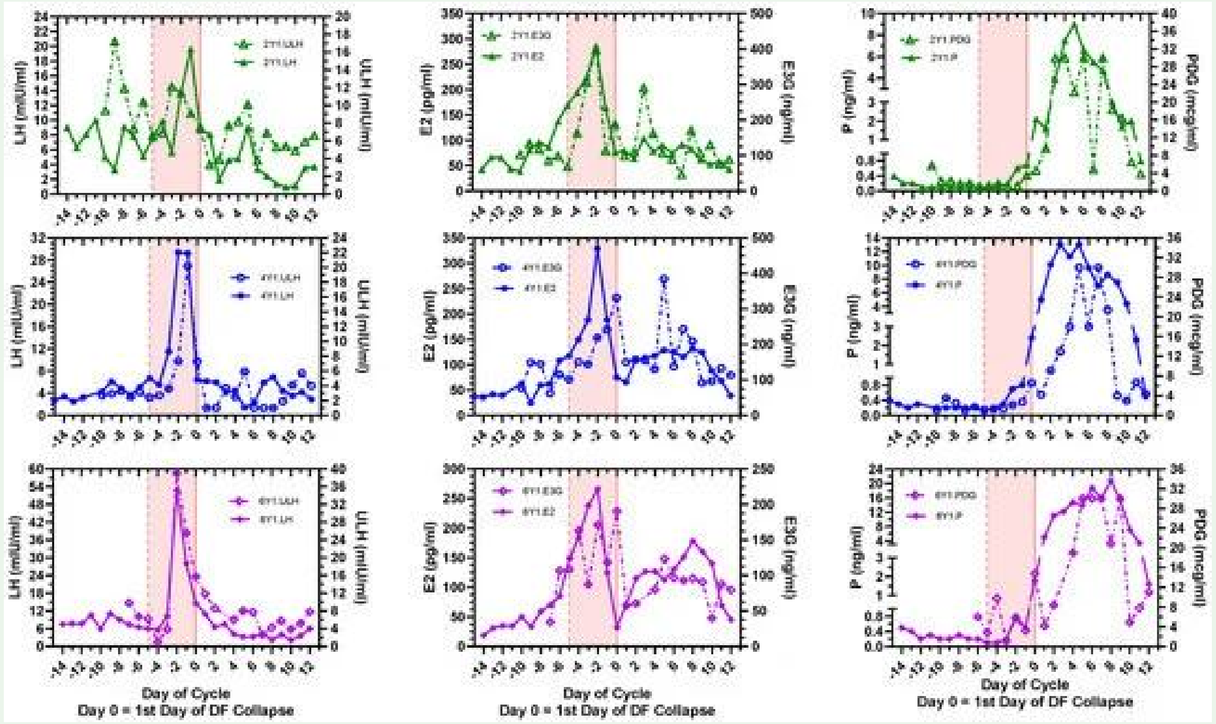
Roos J, Johnson S, Weddell S, Godehardt E, Schiffner J, Freundl G, et al. Monitoring the menstrual cycle: Comparison of urinary and serum reproductive hormones referenced to true ovulation. Eur J Contracept Reprod Health Care. 2015;20(6):438-50. Epub 2015/05/29. doi: 10.3109/13625187.2015.1048331. PubMed PMID: 26018113.

Comparison of Day-Specific Serum LH, Estradiol, and Progesterone with Mira Monitor Urinary LH, Estrone-3-glucuronide, and Pregnanediol-3-glucuronide Levels in Ovulatory Cycles

Conclusions:

The Area Under the Curve algorithm with (E2, P) or (E3G, PDG), showed that both serum and MiraTM hormone measurements could pinpoint the 24 h interval of ovulation and transition to the luteal phase.

The AUC (E3G, PDG) algorithm should be applicable to existing urinary hormone monitors. Serum E2 and P have promise as improved biomarkers for timing the major events during the menstrual cycle.

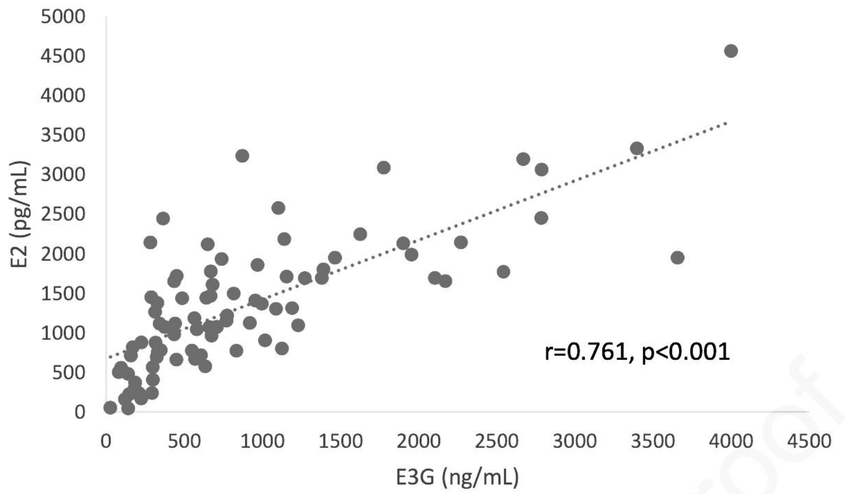


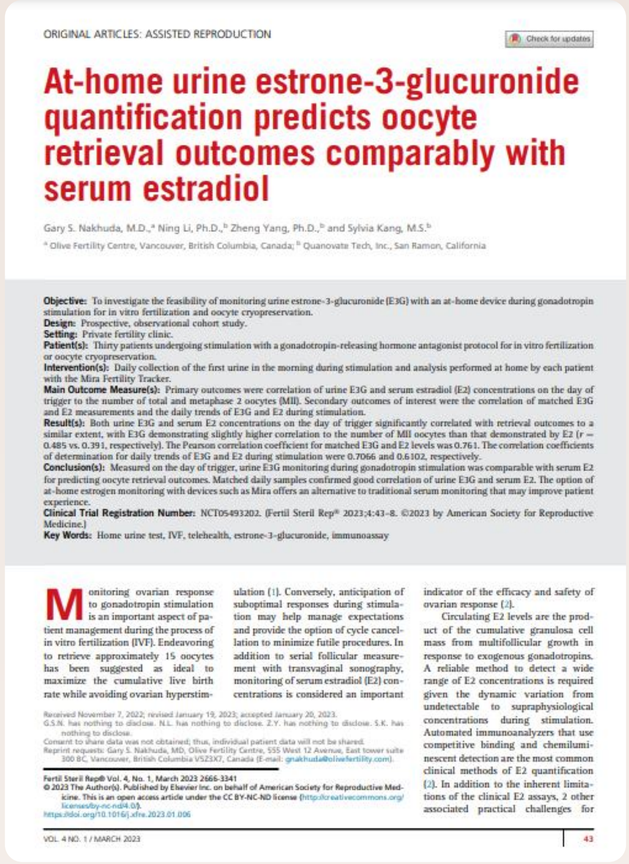
Comparison of Day-Specific Serum LH, Estradiol, and Progesterone with MiraTM Monitor Urinary LH, Estrone-3-glucuronide, and Pregnanediol-3-glucuronide Levels in Ovulatory Cycles by Stephen J. Usala, David D. Vineyard, Maria Kastis, A. Alexandre Trindade and Harvinder Singh Gill.

At-home urine estrone-3-glucuronide quantification predicts oocyte retrieval outcomes comparably to serum estradiol

Summary:

Urine E3G monitoring is comparable to serum E2 for predicting retrieval outcomes and offers a viable at-home alternative to traditional serum monitoring, potentially enhancing patient experience.





ORIGINAL ARTICLES: ASSISTED REPRODUCTION

Check for updates

At-home urine estrone-3-glucuronide quantification predicts oocyte retrieval outcomes comparably with serum estradiol

Gary S. Nakhuda, M.D.,[a] Ning Li, Ph.D.,[b] Zheng Yang, Ph.D.,[b] and Sylvia Kang, M.S.[b]

[a] Olive Fertility Centre, Vancouver, British Columbia, Canada; [b] Quanovate Tech, Inc., San Ramon, California

Objective: To investigate the feasibility of monitoring urine estrone-3-glucuronide (E3G) with an at-home device during gonadotropin stimulation for in vitro fertilization and oocyte cryopreservation.
Design: Prospective, observational cohort study.
Setting: Private fertility clinic.
Patient(s): Thirty patients undergoing stimulation with a gonadotropin-releasing hormone antagonist protocol for in vitro fertilization or oocyte cryopreservation.
Intervention(s): Daily collection of the first urine in the morning during stimulation and analysis performed at home by each patient with the Mira Fertility Tracker.
Main Outcome Measure(s): Primary outcomes were correlation of urine E3G and serum estradiol (E2) concentrations on the day of trigger to the number of total and metaphase 2 oocytes (MII). Secondary outcomes of interest were the correlation of matched E3G and E2 measurements and the daily trends of E3G and E2 during stimulation.
Result(s): Both urine E3G and serum E2 concentrations on the day of trigger significantly correlated with retrieval outcomes to a similar extent, with E3G demonstrating slightly higher correlation to the number of MII oocytes than that demonstrated by E2 ($r = 0.485$ vs. 0.391, respectively). The Pearson correlation coefficient for matched E3G and E2 levels was 0.761. The correlation coefficients of determination for daily trends of E3G and E2 during stimulation were 0.7066 and 0.6102, respectively.
Conclusion(s): Measured on the day of trigger, urine E3G monitoring during gonadotropin stimulation was comparable with serum E2 for predicting oocyte retrieval outcomes. Matched daily samples confirmed good correlation of urine E3G and serum E2. The option of at-home estrogen monitoring with devices such as Mira offers an alternative to traditional serum monitoring that may improve patient experience.
Clinical Trial Registration Number: NCT05493202. (Fertil Steril Rep® 2023;4:43–8. ©2023 by American Society for Reproductive Medicine.)
Key Words: Home urine test, IVF, telehealth, estrone-3-glucuronide, immunoassay

Monitoring ovarian response to gonadotropin stimulation is an important aspect of patient management during the process of in vitro fertilization (IVF). Endeavoring to retrieve approximately 15 oocytes has been suggested as ideal to maximize the cumulative live birth rate while avoiding ovarian hyperstimulation (1). Conversely, anticipation of suboptimal responses during stimulation may help manage expectations and provide the option of cycle cancellation to minimize futile procedures. In addition to serial follicular measurement with transvaginal sonography, monitoring of serum estradiol (E2) concentrations is considered an important indicator of the efficacy and safety of ovarian response (2).

Circulating E2 levels are the product of the cumulative granulosa cell mass from multifollicular growth in response to exogenous gonadotropins. A reliable method to detect a wide range of E2 concentrations is required given the dynamic variation from undetectable to supraphysiological concentrations during stimulation. Automated immunoanalyzers that use competitive binding and chemiluminescent detection are the most common clinical methods of E2 quantification (2). In addition to the inherent limitations of the clinical E2 assays, 2 other associated practical challenges for

Received November 7, 2022; revised January 19, 2023; accepted January 20, 2023.
G.S.N. has nothing to disclose. N.L. has nothing to disclose. Z.Y. has nothing to disclose. S.K. has nothing to disclose.
Consent to share data was not obtained; thus, individual patient data will not be shared.
Reprint requests: Gary S. Nakhuda, MD, Olive Fertility Centre, 555 West 12 Avenue, East tower suite 300 BC, Vancouver, British Columbia V5Z3X7, Canada (E-mail: gnakhuda@oliveifertility.com).

Fertil Steril Rep® Vol. 4, No. 1, March 2023 2666-3341

https://doi.org/10.1016/j.xfre.2023.01.006

Key Findings:

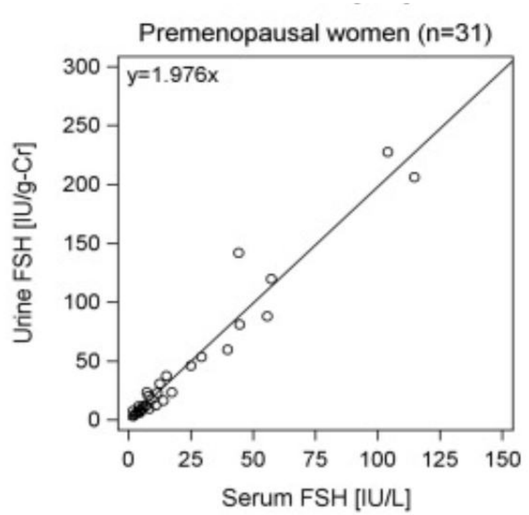
Urine E3G levels, measured by the Mira Fertility Plus® analyzer, and serum E2 concentrations on the day of trigger both show significant correlation with oocyte retrieval outcomes. E3G demonstrated a slightly higher correlation with the number of M2 oocytes ($r = 0.485$) compared to E2 ($r = 0.391$). The Pearson correlation coefficient between matched E3G and E2 levels was 0.761 ($p<.001$). The determination coefficients for daily trends during stimulation were 0.7066 for E3G and 0.6102 for E2.

Nakhuda GS, Li N, Yang Z, Kang S, At-home urine estrone-3-glucuronide quantification predicts oocyte retrieval outcomes comparably to serum estradiol., F&S Reports (2023), doi: https://doi.org/10.1016/j.xfre.2023.01.006.

Urine estrone-3-glucuronide (E3G) assay: is there any place during ovarian stimulation for IVF cycles?

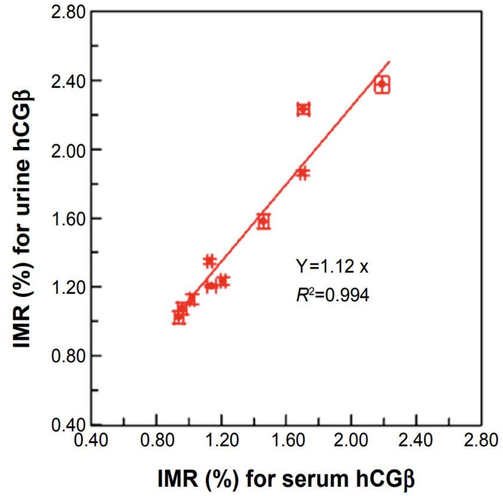
Association between FSH levels in urine and serum in premenopausal women

Urine FSH strongly correlated with FSH in serum in premenopausal (R^2 = 0.98) women.



Quantitative analysis of total β-subunit of hCG concentration in urine

An excellent correlation of total hCGβ IMR signals between urine and serum was noted (R^2=0.994).

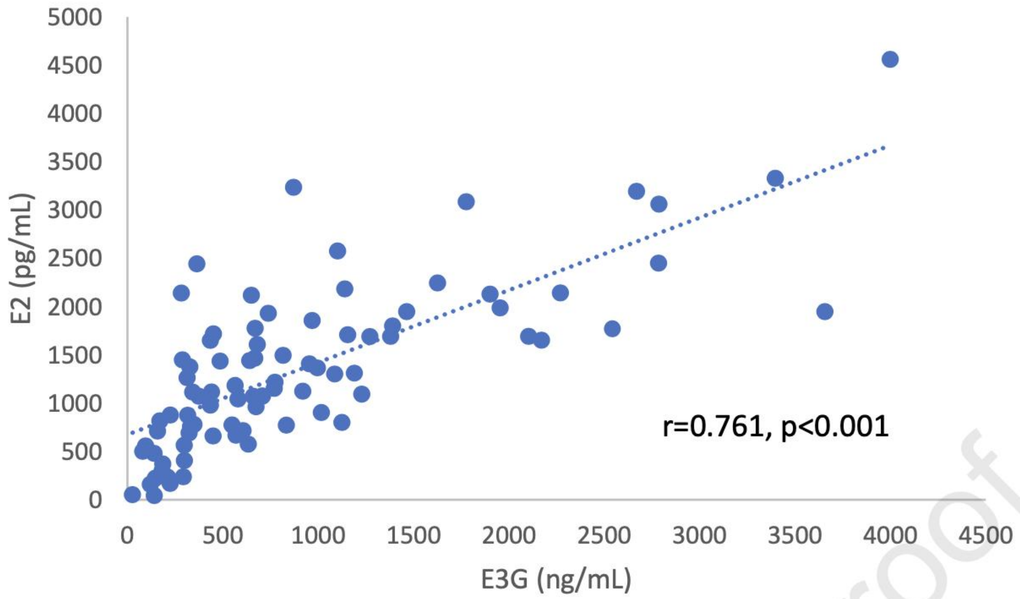


Yoko Onizuka, Kazue Nagai, Yuki Ideno, Association between FSH, E1, and E2 levels in urine and serum in premenopausal and postmenopausal women, Clinical Biochemistry, Volume 73 (2019), pp. 105-108;
Chen-Yu Chen, Yuh-Ming Hwu, Chie-Pein Chen, Quantitative analysis of total β-subunit of human chorionic gonadotropin concentration in urine by immunomagnetic reduction to assist in the diagnosis of ectopic pregnancy, Int J Nanomedicine (2015)10:2475-83. doi: 10.2147/IJN.S81201. eCollection 2015.

At-home urine estrone-3-glucuronide quantification predicts oocyte retrieval outcomes comparably to serum estradiol.

Key Findings:

Both urine E3G (measured by fluorescent immunoassay Mira Fertility Plus® analyzer) and serum E2 concentrations on day of trigger significantly correlated with retrieval outcomes to a similar extent, with E3G demonstrating slightly higher correlation to the number of M2 oocytes compared to E2 ($r = 0.485$ vs 0.391, respectively). The Pearson correlation coefficient for matched E3G and E2 levels was 0.761 ($p<.001$). The correlations of determination for daily trend of E3G and E2 during stimulation were 0.7066 and 0.6102, respectively. Measured on the day of trigger, urine E3G monitoring during gonadotropin stimulation is comparable to serum E2 for predicting oocyte retrieval outcomes. Matched daily samples confirm good correlation of urine E3G and serum E2. The option of at-home estrogen monitoring with devices such as Mira offers an alternative to traditional serum monitoring that may improve the patient experience.

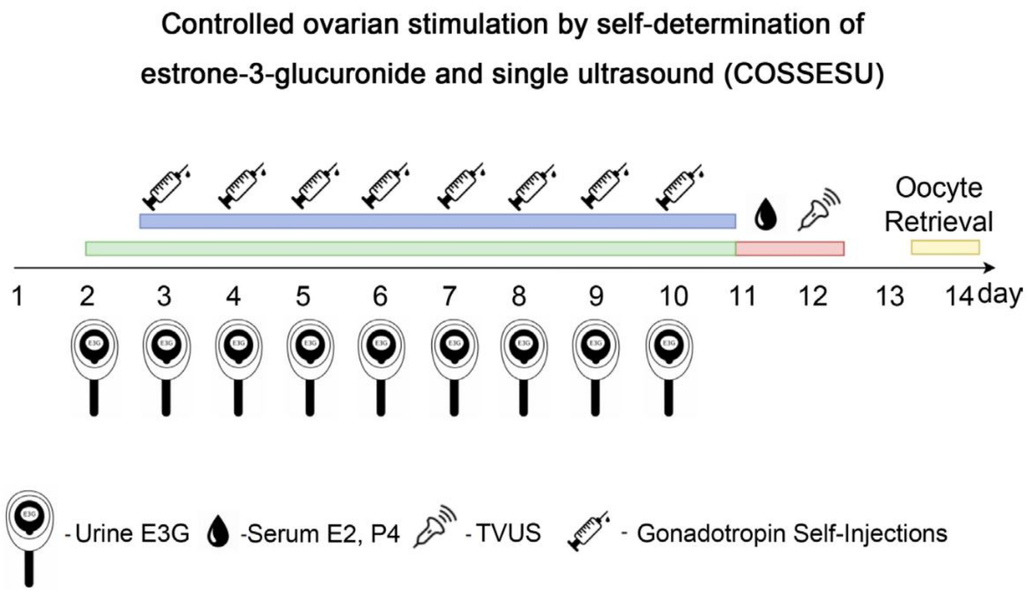


Nakhuda GS, Li N, Yang Z, Kang S, At-home urine estrone-3-glucuronide quantification predicts oocyte retrieval outcomes comparably to serum estradiol., F&S Reports (2023), doi: https://doi.org/10.1016/j.xfre.2023.01.006.

Urine estrone–3-glucuronide (E3G) assay: is there any place during ovarian stimulation for IVF cycles?

Key Findings:

Serum E2 values were assessed routinely, while E3G values were measured and validated using a fluorescent immunoassay Mira Fertility Plus® analyzer. The urine E3G of the assay was validated for intra and inter-assay variability with a coefficient of variation of < 20%. It was also validated for analytical and functional sensitivity and sample stability. Linear regression of serum E2 and E3G values of 56 early morning urine samples who had evaluated between days 4 and 13 of the menstruation cycle provided an r = 0,81. Urine E3G values also correlated to follicle growth. Patient survey results showed that urine sampling was the preferred method of analysis. Urine E3G testing correlates well to serum E2 assessment in COH. Urine E3G assay provides an alternative to serum-based assessment.



I Vladimirov, V Martin, T Desislava, P–670 Urine estrone–3-glucuronide (E3G) assay: is there any place during ovarian stimulation for IVF cycles?, Human Reproduction, Volume 36, Issue Supplement_1, July 2021, deab130.669, https://doi.org/10.1093/humrep/deab130.669;

Vladimirov, I. , Vladimirov, M. and Tacheva, D. (2021) A New Protocol for Controlled Ovarian Stimulation Monitoring by Self-Determination of Estrone-3-Glucuronide and Single Ultrasound (COSSESU). Open Journal of Obstetrics and Gynecology, 11, 1217-1228. doi: 10.4236/ojog.2021.119115.

Viability of home monitoring of estrone-3-glucuronide (E3G) urine levels in controlled ovarian stimulation: A pilot study

Key Findings:

The average female age was 32,1 years (±4.4), BMI 22,9 kg/m2 (±4,3), AMH 3,9 ng/ml (±2,7), stimulation days 10,1 (±1,2), collected oocytes 12,6 (±8,5), MII oocytes 10,8 (±7,9), fertilization rate 83,4% (±22,7), blastocyst formation 66,9% (±28,6), good quality blastocysts 31,1% (±16,6).

The log-linear mixed effect model (LLMM) estimation produced reasonable estimates of 49% average day-to-day growth rates (slope fixed effect), with one standard deviation (SD) range of 25% to 77% across patients (SD of the slope random effect).

Moreover, there was a comparatively high correlation of 0.76 between the individual growth rates of E3G estimated over days 3-6 (the slope random effects of the LLMM model) and the E3G levels at day 10. In this way, the estimated slope random effects appear to have a prognostic value and may potentially have therapeutic implications, for example, adjustment of the stimulation dose. Moreover, the Spearman correlation between Estradiol and E3G was 0.83

After analyzing interviews and questionnaires, patients evaluated the applied method as easy and convenient, with 97% of them preferring OS monitoring to be performed in this manner compared to the standard method, which includes regular ultrasound examinations and determination of serum hormone levels.

I.K. Vladimirov, D. Tacheva, I. Gatev, M. Rangelova, M. Vladimirov, **Viability of home monitoring of estrone-3-glucuronide (E3G) urine levels in controlled ovarian stimulation: A pilot study,** SBALAGRM-SOFIA, IVF unit, Sofia University "St.Kliment Ohridski", Cytology- Histology and Embryology.
https://www.eshre.eu/ESHRE2023/Programme/Searchable#!abstractdetails/0000721100

Mira vs. Laboratory Readers

Quantifiable Concentration Ranges

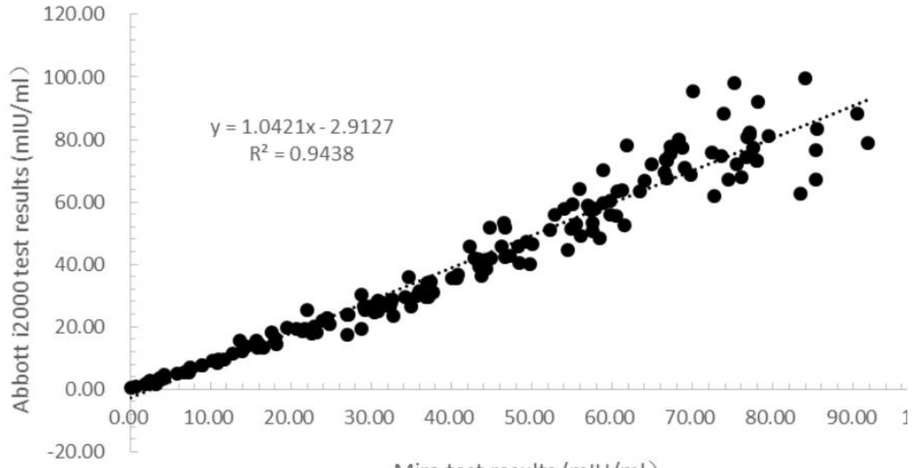
Dynamic range of Mira Tests

Hormone changes during Menstrual cycle	LH	E2 or E3G	Progesterone or PdG
Serum	0-200 mIU/ml	0-2000 pg/ml	0-20 ng/ml
Urine	0-200 mIU/ml	0-4000 ng/ml	0-15 µg/ml
Mira test	0-400 mIU/ml, customizable to 0-1000 mIU/ml	0-640 ng/ml, customizable to 0-4000 ng/ml	0-30 µg/ml

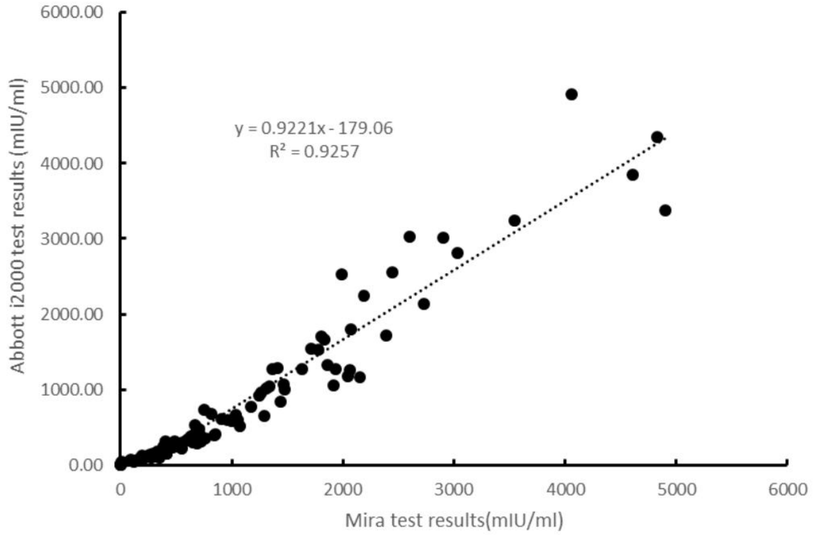
Mira's technology is based on the immunofluorescence method with accuracy equivalent to laboratory readers

The Mira LH and hCG measurements strongly correlated with Abbott ARCHITECT i2000SR. A good linear correlation (R^2>0.9) was displayed by The Mira Analyzer and Abbott ARCHITECT i2000SR for both LH (R^2=0.944; slope=1.042) and hCG (R^2=0.926; slope=0.922)*.

LH



hCG



* Under editor's review

Additional Research involving Mira

Oscillations of estradiol and gonadotropins are a missing link to solving the mystery of mono-ovulation in humans

Key Findings:

The research explores the patterns of the urinary metabolite of estradiol (E3G) across the menstrual cycle. It finds that, unlike the luteal phase where E3G levels remain relatively stable, E3G concentrations in the follicular phase fluctuate significantly. This fluctuation is not a linear increase but varies within a broad range. The study suggests that this pattern reflects the complex interplay between gonadotropins, which stimulate follicular development, and the ovarian production of estradiol. The findings highlight the dynamic hormonal relationships that govern the follicular phase, in contrast to the more consistent hormonal behavior observed during the luteal phase.

INKLINGS

Oscillations of estradiol and gonadotropins are a missing link to solving the mystery of mono-ovulation in humans

Regulation of follicular development leading to mono-ovulation remains one of the unsolved mysteries of human reproduction. The current working hypothesis in part postulates that as multiple follicles grow, they produce estradiol, which exerts continued negative feedback on the follicle-stimulating hormone (FSH) synthesis. As the availability of FSH declines to a threshold sufficient to sustain the development of only a single follicle (with the higher number of FSH receptors), it becomes dominant, destined to be the only one that will eventually ovulate. Other factors, including Inhibin B and the pulsatile nature of FSH, also may have a role, as may local factors, such as bone morphogenetic protein 15 and some other peptides, in follicular competition in primates. However, in humans, there is compelling evidence that the mono-ovulation conundrum must be explained at the systemic level. Indirect evidence for systemic influence stems from the observation that when negative feedback on FSH is blocked with a low dose of clomiphene citrate, a woman with two ovaries develops the same number of follicles as a woman with one ovary (Diamond et al. [1]). The concept of a systemic level of regulation subsequently has been strengthened by the direct demonstration that the ovulation side in women is random, and is not influenced by prior ovulation, or any other local factors (Ecochard and Gougeon [2]).

The weakest point of the current paradigm is a supposition that a random level of cumulative E2 production by the cohort of follicles can assure the precision of FSH suppression that would produce single dominant follicle development. If this was the only mechanism for the selection of the dominant follicle, a woman with no exogenous stimulation often would have no dominant follicle at all, and follicle is assured, and how the reduction from two leading follicles to one is achieved.

As we already stated, a linear slope for FSH suppression is not sufficient to assure mono-ovulation. However, is it really gradual? Recently, two California startups, Quanovate Tech, Inc. (Pleasonton, CA) and Inito, Inc. (Palo Alto, CA) have developed a once a day home test for quantitatively sampling estrone-3-glucuronide (E3G) in urine, which has been shown to correlate well with serum estradiol (Roos et al. [4]). This provides a rare insight into the daily profiles of reproductive hormones of normally menstruating women. When reviewing those hormonal profiles, we noticed that there is no linear rise of urinary E3G. Instead, E3G oscillates within a wide range of concentrations throughout the follicular phase, with a frequency of approximately 2 days (Fig. 1A, 1B). These oscillations are unlikely to be attributed to the pituitary pulses of FSH because the observed FSH frequency is days and not hours.

While the amplitude of the urine E2 profile may be affected by fluid intake and urine density, the frequency of the peaks would not be. Further, the consistency of the duration of observed oscillations, approximately 48 hours, from patient to patient, makes the possibility that we are looking at an artifact very unlikely. This periodicity disappears after ovulation (Fig. 1A), indicating that it is specific for the follicular phase.

We propose that these oscillations reflect a more complex relationship between ovarian estrogens and pituitary gonadotropins than counter-directed linear slopes as is currently held. We believe that the underlying mechanism of these oscillations likely involves the downregulation of gonadotropins by rising E2, which in its turn downregulates E2's own production by granulosa. This lowered E2 allows gonadotropin levels in the circulation to rise, pushing E2 production back up, which will again suppress gonadotropins, creating the observed oscillation pattern. Unlike linear slopes, these oscillations create not one, but multiple opportunities for the "surviving of the fittest" follicle. It also gua-

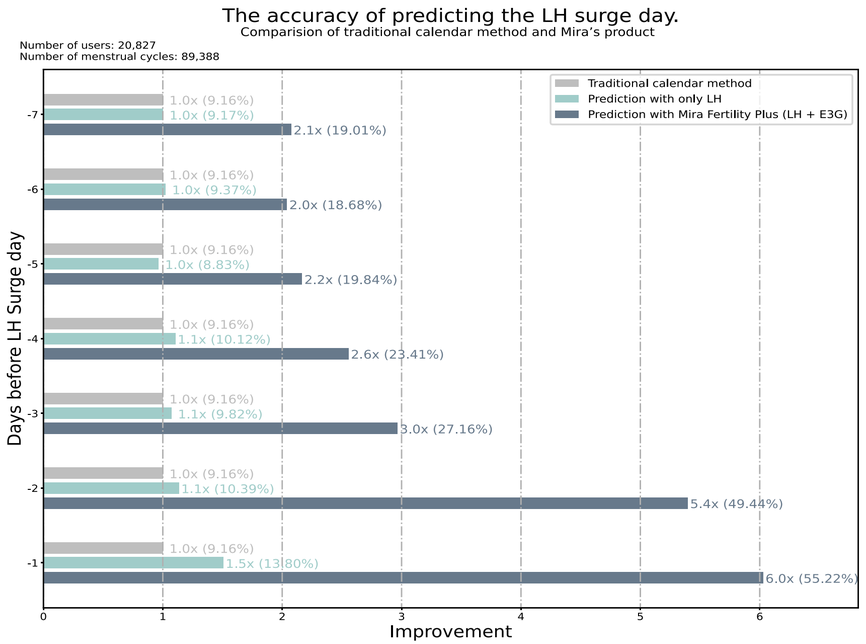
Dozortsev DI, Pellicer A, Diamond MP. Oscillations of estradiol and gonadotropins are a missing link to solving the mystery of mono-ovulation in humans. Fertil Steril. 2021 Sep;116(3):630-632. doi: 10.1016/j.fertnstert.2021.05.107. Epub 2021 Jul 22. PMID: 34303510.

Intelligent algorithms combined with a device that detects luteinizing hormone and E3G levels can significantly improve the prediction accuracy of ovulation day

Key Findings:

The accuracy of predicting the LH surge day was compared among three solutions: the traditional calendar method, using LH hormone only, and using both LH and E3G hormones together. Calculated in a retrospective analysis, from 1 to 7 days before the actual LH surge day.

Optimized with more than 7M data points and 600K+ menstrual cycles, the Mira algorithm is 6X more accurate than traditional calendar method and 5X more accurate than traditional ovulation prediction solutions offered over the counter.



Yang Z, Kang S, Li N, INTELLIGENT ALGORITHM COMBINED WITH DE-VICE THAT DETECTS LUTEINIZING HORMONELEVELS CAN IMPROVE THE PREDICTION ACCU-RACY OF OVULATION DAY, FERTILITY & STERILITY, VOLUME 114, ISSUE 3, SUPPLEMENT, E407, SEPTEMBER 2020

Establishing a Gold Standard for Quantitative Menstrual Cycle Monitoring

Ongoing study (will be published in May ‘25):

Background and Objectives: The Quantum Menstrual Health Monitoring Study will measure four key reproductive hormones in the urine (follicle-stimulating hormone, FSH; estrone-3-glucuronide, E13G; luteinizing hormone, LH; and pregnanediol glucuronide, PDG) to characterize patterns that predict and confirm ovulation, referenced to serum hormones and the gold standard of the ultrasound day of ovulation in participants with regular cycles. These normal cycles will provide a reference for comparison to irregular cycles in subjects with polycystic ovarian syndrome (PCOS) and athletes.

Hypothesis: The Mira monitor quantitative urine hormone pattern will accurately correlate with serum hormonal levels and will predict (with LH) and confirm (with PDG) the ultrasound day of ovulation in those with regular cycles as well as those with irregular cycles.

Rationale: Once the ultrasound validation is complete, tools like the Mira monitor with a customized app may become a new standard for at-home and remote clinical monitoring of the menstrual cycle without having to use labor-intensive follicular-tracking ultrasound or follow serum hormone changes.

Conclusions: Precision monitoring of the menstrual cycle is expected to impact individuals who want to increase their menstrual health literacy and guide decisions about fertility.

medicina

MDPI

Protocol

Establishing a Gold Standard for Quantitative Menstrual Cycle Monitoring

Thomas Bouchard [1,2,*], Paul Yong [1] and Patricia Doyle-Baker [3]

[1] Department of Obstetrics & Gynecology, University of British Columbia, Vancouver, BC V6Z 2K8, Canada; pyong@cw.bc.ca
[2] Department of Family Medicine, University of Calgary, Calgary, AB T3H 0N9, Canada
[3] Faculty of Kinesiology, University of Calgary, Calgary, AB T2N 1N4, Canada; pdoyleba@ucalgary.ca
* Correspondence: tbouchar@student.ubc.ca or tbouchar@ucalgary.ca

Abstract: *Background and Objectives:* The Quantum Menstrual Health Monitoring Study will measure four key reproductive hormones in the urine (follicle-stimulating hormone, FSH; estrone-3-glucuronide, $E_1$3G; luteinizing hormone, LH; and pregnanediol glucuronide, PDG) to characterize patterns that predict and confirm ovulation, referenced to serum hormones and the gold standard of the ultrasound day of ovulation in participants with regular cycles. These normal cycles will provide a reference for comparison to irregular cycles in subjects with polycystic ovarian syndrome (PCOS) and athletes. *Materials and Methods:* Participants will track their menstrual cycles for 3 months and be provided with an at-home urine hormone monitor (Mira monitor) to predict ovulation. The day of ovulation will be confirmed with serial ultrasounds completed in a community clinic. Urine results will be compared to serum hormone values. Other markers of menstrual health, such as bleeding patterns and temperature changes, will be determined using a customized app. Three groups will be recruited. Group 1 will include those with consistent regular cycle lengths (between 24–38 days), and will be compared to two groups with irregular cycle lengths (with increased cycle length variability and longer cycles). Group 2 will include those with polycystic ovarian syndrome (PCOS) with irregular cycles and Group 3 will include individuals participating in high levels of exercise with irregular cycles. *Hypothesis:* The Mira monitor quantitative urine hormone pattern will accurately correlate with serum hormonal levels and will predict (with LH) and confirm (with PDG) the ultrasound day of ovulation in those with regular cycles as well as those with irregular

check for updates

Bouchard, T., Yong, P., & Doyle-Baker, P. (2023). Establishing a Gold Standard for Quantitative Menstrual Cycle Monitoring. Medicina, 59(9), 1513. https://doi.org/10.3390/medicina59091513

Using Quantitative Hormonal Fertility Monitors to Evaluate the Luteal Phase: Proof of Concept Case Study

Key Findings:

By utilizing at-home hormone monitoring, such as Mira, women can track their individual cycle variations, moving beyond the traditional assumption of a standard 28-day cycle with ovulation on day 14. This personalized approach allows for more accurate identification of cycle abnormalities and enables healthcare providers to tailor treatments to each woman's unique needs. The study highlights the three distinct processes of the luteal phase—luteinization, progestation, and luteolysis—and demonstrates how quantitative hormone tracking can help diagnose luteal phase deficiencies, anovulation, and optimize fertility treatments. Further validation of fertility monitors like Mira is necessary through larger clinical trials to confirm their reliability in supporting these clinical insights.

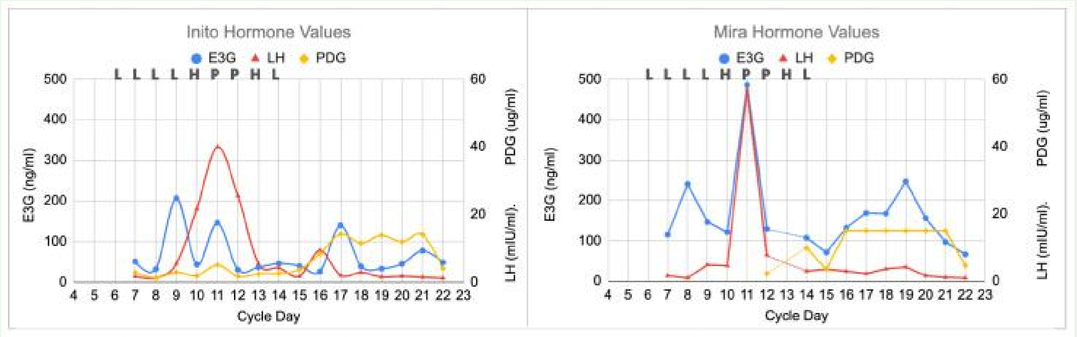


Figure 1: Normal cycle showing all three monitors with agreement on the peak day, with the highest LH value on that day (cycle day 11). The ClearBlue results (L = Low, H = High, and P = Peak) are shown above each graph on the respective days. The estimated day of ovulation was day 12 (day after LH peak). The luteal phase was 13 days (cycle length of 25 days). PDG initially rose on day 16 on the Inito monitor and on day 14 on the Mira monitor.

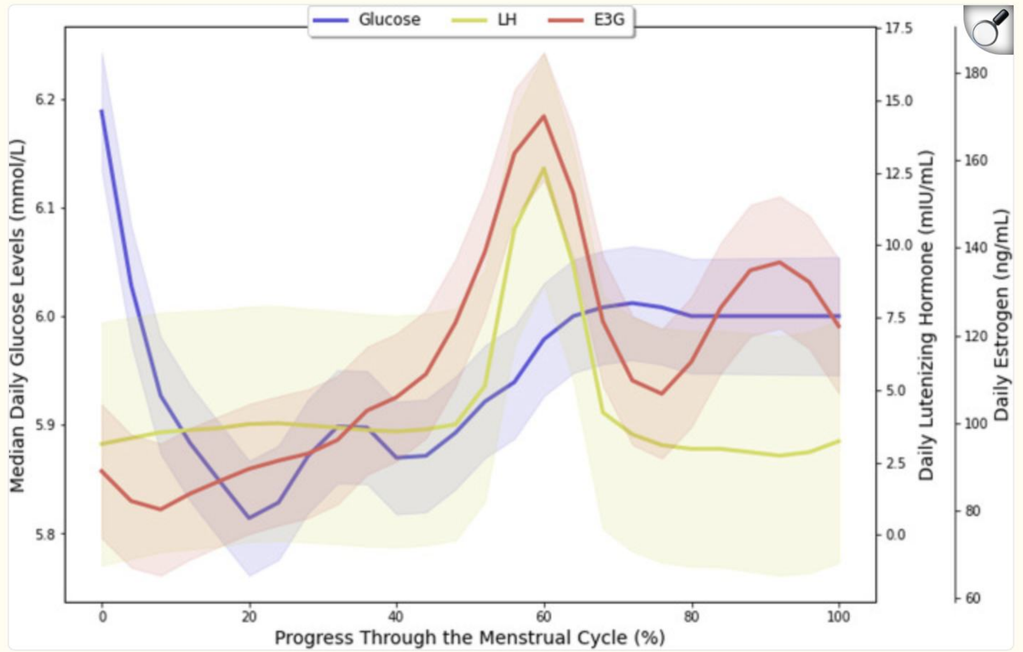
Bouchard TP. Using Quantitative Hormonal Fertility Monitors to Evaluate the Luteal Phase: Proof of Concept Case Study. Medicina (Kaunas). 2023 Jan 10;59(1):140. doi: 10.3390/medicina59010140. PMID: 36676764; PMCID: PMC9866173.

Blood glucose variance measured by continuous glucose monitors across the menstrual cycle

Conclusions:

“In this study, we identified significant associations between blood glucose and the individuals’ menstrual cycles. We observed a biphasic pattern across the menstrual cycle where daily median glucose levels peaked during the luteal phase and declined during the late-follicular phase. The increase in glucose levels from the late-follicular phase to the luteal phase was also robust to a number of confounders, including step count, estrogen, food cravings, fatigue, and sleep issues.

Our results serve as a basis for conversations on the interpretation of glucose levels with respect to menstrual health. Individuals who anticipate adjusting their behaviors (e.g., diet and sleep) based on their glucose variation may need to consider how menstruation influences their interpretation of this data. For example, those who have higher glucose levels while experiencing stronger food cravings might contemplate different symptom management strategies depending on how far along they are in their menstrual cycle.”



Blood glucose variance measured by continuous glucose monitors across the menstrual cycle by Georgianna Lin, Rumsha Siddiqui, Zixiong Lin, Joanna M Blodgett, Shwetak N Patel, Khai N Truong, Alex Mariakakis.

Case Reports from Women Using a Quantitative Hormone Monitor to Track the Perimenopause Transition

Conclusions:

Tracking fertility during Perimenopause with a quantitative hormonal device is a novel idea. A quantitative hormone monitor allows for the exact measurements of hormones in a woman's cycles and can give more accurate results of cycle patterns, especially as she ages. This study of women in perimenopause has revealed certain cycle characteristics unique to this period, which include cycles with delayed LH surges, quick rises in E3G toward the LH surge, low E3G and LH levels in a cycle, double LH surges in one cycle with corresponding FSH elevation during the highest LH surge, continuous high levels of E3G and LH throughout the cycle, and low PdG levels after an LH surge.

Figure 10. Variable cycle with MIRA: 49 yo with late LH peak, no PdG rise, and a 29-day cycle.

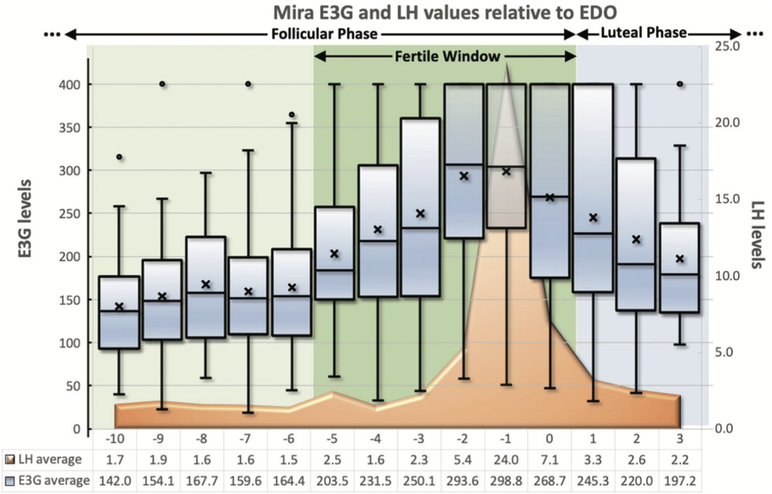
Case Reports from Women Using a Quantitative Hormone Monitor to Track the Perimenopause Transition
by Maria Meyers, Richard Jerome Fehring and Mary Schneider.

Mira used for fertility awareness based methods

Quantitative Versus Qualitative Estrogen and Luteinizing Hormone Testing for Personal Fertility Monitoring (Natural Family Planning — Marquette Method)

Key Findings:

The study established that due to the quantitative measurement of LH the peaks that indicates the most fertile period of the menstrual cycle by Mira monitor throughout 3 menstrual cycles, only 2% of LH peaks have been missed in comparison to 5% of peaks missed when using qualitative measurement with ClearBlue Fertility Monitor.



	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0	1	2	3
LH average	1.7	1.9	1.6	1.6	1.5	2.5	1.6	2.3	5.4	24.0	7.1	3.3	2.6	2.2
E3G average	142.0	154.1	167.7	159.6	164.4	203.5	231.5	250.1	293.6	298.8	268.7	245.3	220.0	197.2

Figure 5. Quantitative Mira levels of E3G (in ng/ml, blue box-and-whisker plots) and LH (in ng/ml, orange mean daily values). The Mira EDO (day 0) was defined as the day after the peak LH day, which is why the LH surge is noted on day -1. LH and E3G mean values are shown in the table below, with peak E3G at 298.8ng/ml and peak LH at 24.0 mIU/ml. E3G values were represented with 25-75 percentile boxplots with min/max whiskers (excluding outliers), The (x) represents the average (mean) for the day, and the horizontal line represents the median for values in the range. The Follicular Phase is defined from the first day of the menstrual period up to and including the day of ovulation. The Fertile Window is defined as the 6-day interval from 5 days before (-5) up to and including the estimated day of ovulation (EDO = 0). The Luteal phase is defined as the day after EDO until the past day of the menstrual cycle.

Thomas P. Bouchard, Richard J. Fehring & Qiyan Mu (2021) Quantitative versus qualitative estrogen and luteinizing hormone testing for personal fertility monitoring, Expert Review of Molecular Diagnostics, 21:12,1349-1360, DOI: 10.1080/14737159.2021.2000393

Quantitative versus qualitative estrogen and luteinizing hormone testing for personal fertility monitoring

Key Findings:

In this preliminary trial, the Mira monitor was shown to be effective at delineating the fertile window and ovulation. We demonstrated the feasibility of applying the Marquette Method algorithm with the use of the Mira monitor. Satisfaction differences between the two monitors did not reach statistical significance. We anticipate that quantitative fertility monitoring will give couples and health-care providers new and unprecedented insights into the menstrual cycle and fertility.

Bouchard TP, Fehring RJ, Mu Q. Quantitative versus qualitative estrogen and luteinizing hormone testing for personal fertility monitoring. Expert Rev Mol Diagn. 2021 Dec;21(12):1349-1360. doi: 10.1080/14737159.2021.2000393. Epub 2021 Dec 3. PMID: 34714210.

Using Quantitative Hormone Monitoring to Identify the Postpartum Return of Fertility

Conclusions:

In Cycle 0, higher thresholds of LH are required to trigger ovulation, so a higher thresh- old of LH (i.e., LH < 15), along with a more conservative E3G threshold (i.e., E3G < 100) to reflect the average E3G levels within the fertile window of Cycles 0–6 postpartum (Table 3), could be used in Cycle 0 for avoiding pregnancy (Table 6). This protocol will be the basis of a larger effectiveness study using the Mira Analyzer for avoiding pregnancy postpartum.

Table 3. Estrone-3-glucuronide (E3G) values in ng/mL for days leading up to estimated day of ovulation (EDO = 0).

	−6	−5	−4	−3	−2	−1	0	1
Cycle 0 (n = 10)	89 ± 58	105 ± 41	117 ± 63	159 ± 101	216 ± 132	255 ± 103	177 ± 176	129 ± 51
Cycle 1 (n = 10)	133 ± 162	142 ± 125	126 ± 73	148 ± 71	161 ± 76	155 ± 71	239 ± 180	236 ± 190
Cycle 2 (n = 8)	95 ± 55	111 ± 80	129 ± 62	119 ± 50	165 ± 60	216 ± 113	251 ± 191	300 ± 242
Cycle 3 (n = 8)	127 ± 76	110 ± 71	157 ± 97	190 ± 64	284 ± 142	207 ± 81	296 ± 189	197 ± 136
Cycle 4 (n = 5)	100 ± 58	88 ± 64	137 ± 33	133 ± 79	181 ± 106	212 ± 108	252 ± 229	167 ± 65
Cycle 5 (n = 4)	190 ± 170	166 ± 172	138 ± 89	135 ± 117	186 ± 88	232 ± 118	367 ± 108	128 ± 84
Cycle 6 (n = 2)	162 ± 73	116 ± 78	227 ± 249	106 ± 71	199 ± 88	294 ± 143	331 ± 83	175 ± 94

Table 6. Revised Cycle 0 protocol with updated thresholds based on the current pilot data. This is based on users testing daily.

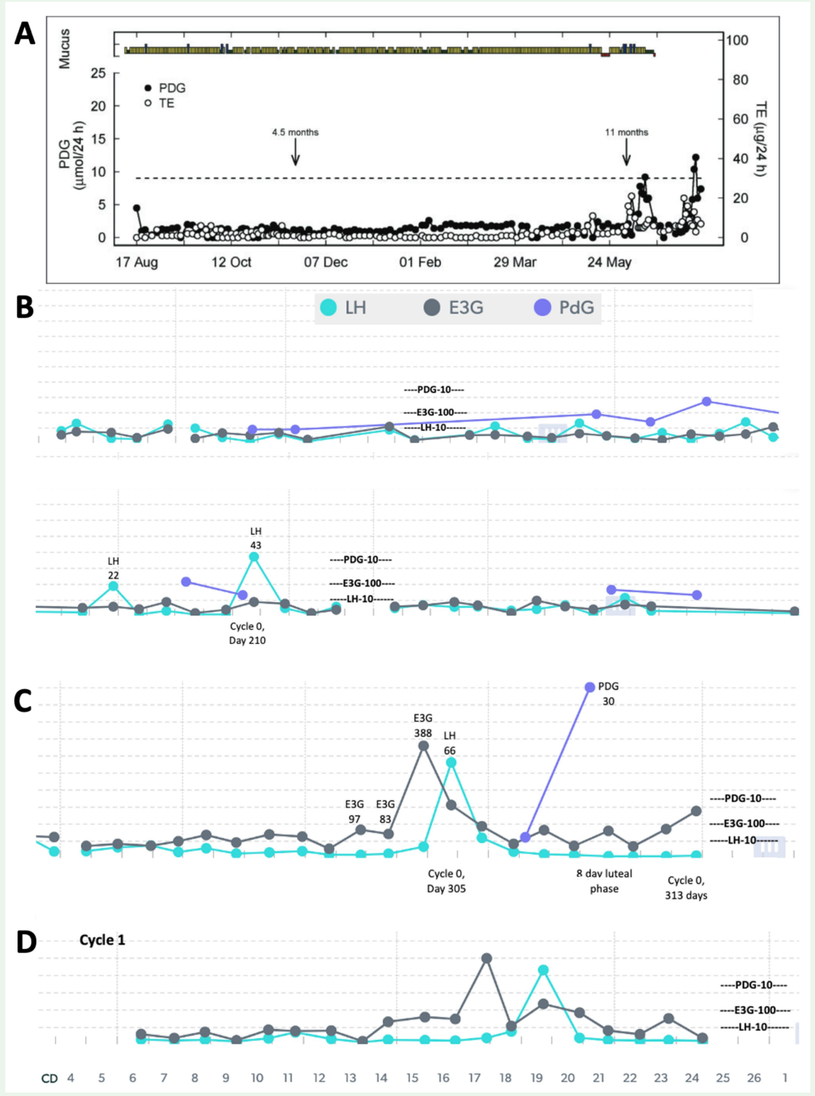
	Available Day for Intercourse?
If E3G is <100 today and yesterday AND If LH is <15 today and the last 4 days	Yes
If E3G is ≥100 today or yesterday	No
If LH is ≥15 today or the last 4 days	No

Using Quantitative Hormone Monitoring to Identify the Postpartum Return of Fertility by Thomas P. Bouchard, Katherine Schweinsberg, Amanda Smith and Mary Schneider.

Using Quantitative Hormone Monitoring to Identify the Postpartum Return of Fertility

Key Findings:

Higher LH thresholds in Cycle 0 suggest a decreased responsiveness of the ovaries to LH stimulation from the pituitary. This study replicates postpartum hormone patterns from a previous study. Larger studies are planned to evaluate the effectiveness for avoiding pregnancy using the Mira Analyzer in the postpartum return of fertility.



Bouchard, T. P., Schweinsberg, K., Smith, A., & Schneider, M. (2023). Using Quantitative Hormone Monitoring to Identify the Postpartum Return of Fertility. Medicina, 59(11), 2008. https://doi.org/10.3390/medicina59112008