Comparing Urinary Estrogen Profiles of Women on Transdermal Estradiol Patches, Gels, or Creams

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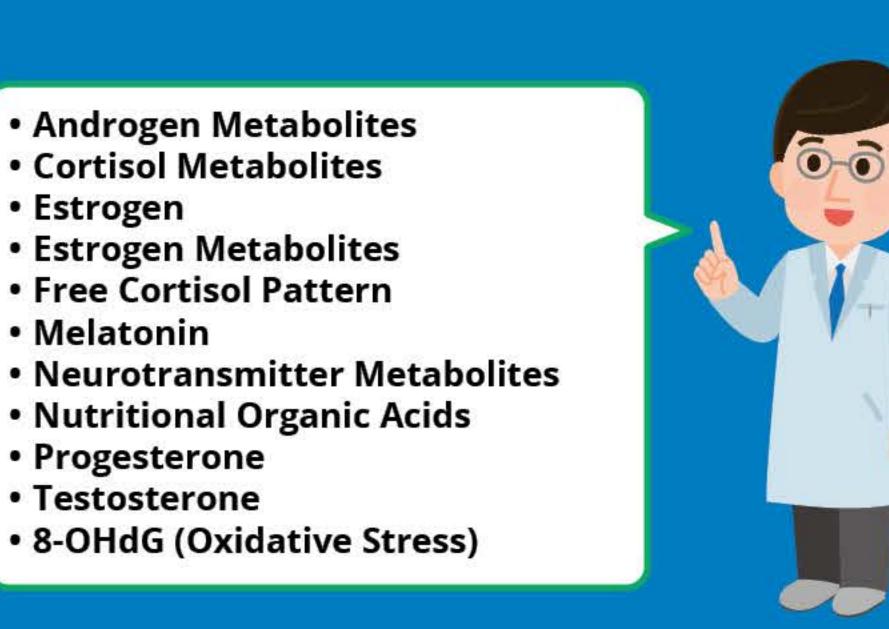
OBJECTIVE

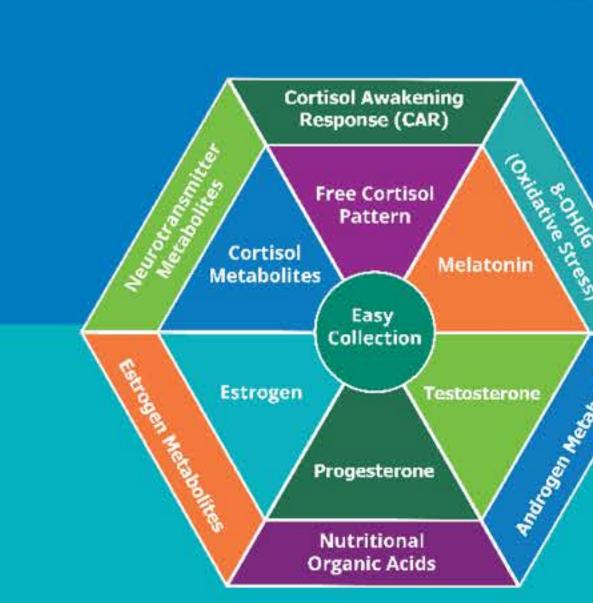
- Transdermal (TD) E2 patches and gels are the most commonly used types of TD E2 formulations; however, some providers choose to treat select patients with compounded E2 creams.
- A need exists to understand the comparative effects of these 3 different TD delivery systems given their complex and differing pharmacokinetics and the lack of data to support the efficacy of compounded E2 products.
- E2 levels are most often measured in serum, but these values may not be the most accurate, especially since creams and gels show significant variation in E2 levels throughout the day, and serum only represents 1 moment in time.
- In contrast, urinary E2 levels may provide a representation of serum E2 concentrations over a 24-hour period.
- The aim of this study was to compare the effects of increasing doses of TD E2 patches, gels, and creams on urinary E2 concentrations in postmenopausal women.

DESIGN

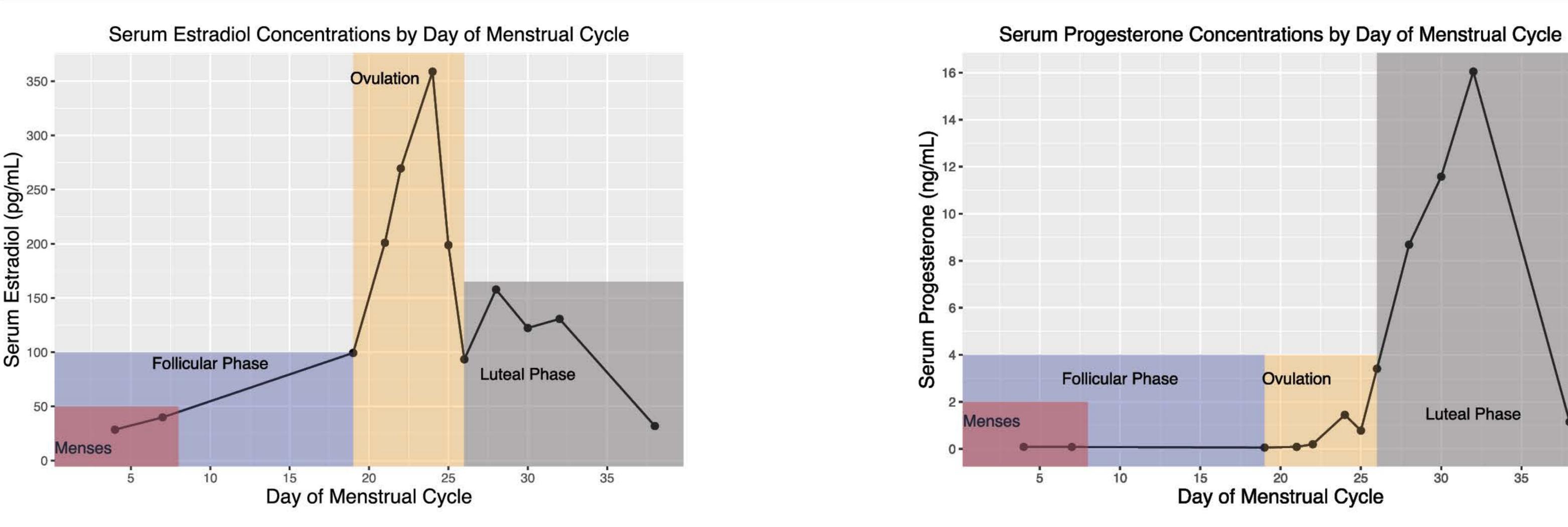
- This study utilized data from a retrospective observational study, Precision Analytical Retrospective Data Correlation (NCT04305093).
- The dataset from this larger study contained multiple urinary markers obtained via
 a 4-spot dried urine sampling method measured using gas chromatography/tandem
 mass spectrometry (GC-MS/MS) with a lower limit of quantification of 0.092 ng/mg for
 E2.
- For this analysis, we used a subset of the dataset that included only the urinary E2 profiles of premenopausal women, postmenopausal women not on MHT, and postmenopausal women using TD E2 patches, gels, or creams, which were divided into 3 dose range categories to facilitate comparison.
- Comparisons between groups were made by Kruskal-Wallis 1-way ANOVA and the nonparametric Jonckheere-Terpstra (JT) trend test.





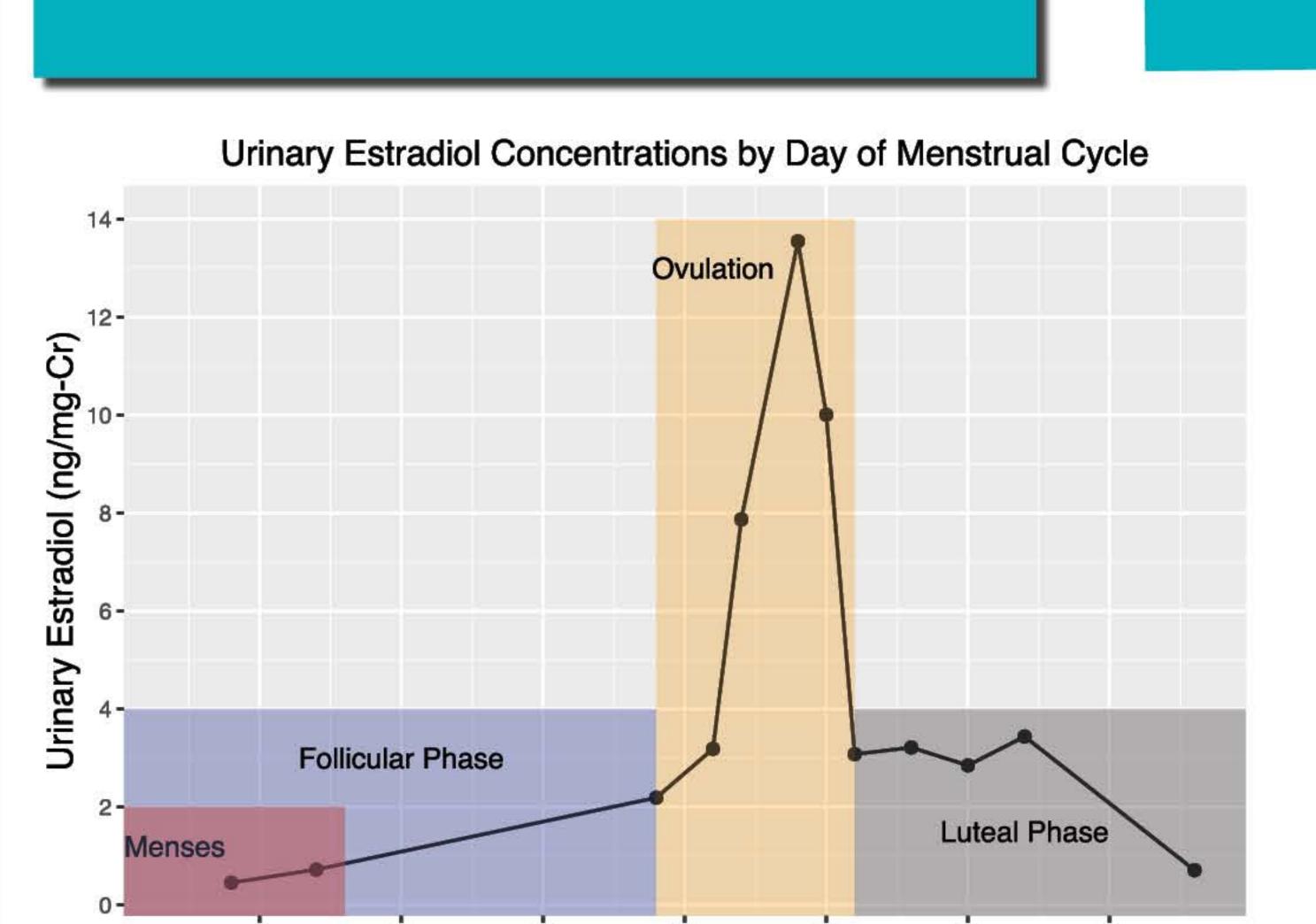


Assay Validation How do dried urine results compare to serum results?



• In a previous study,¹ estradiol measurements obtained via serum sampling were compared to measurements obtained from dried urine.

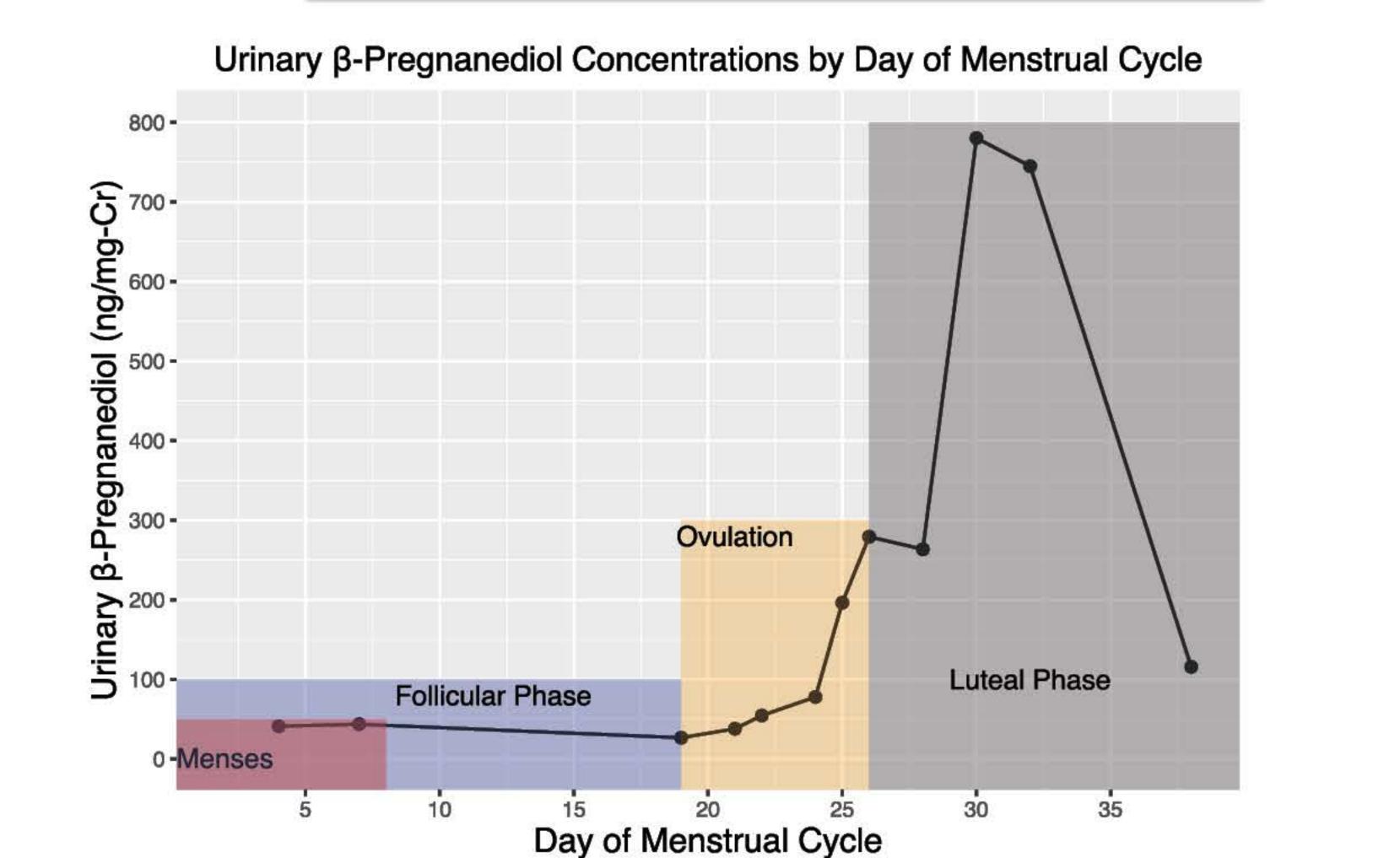
 measurements obtained from dried urine.
 Urinary estradiol concentrations followed the same pattern as results obtained from serum with similar timing of peaks and troughs.¹



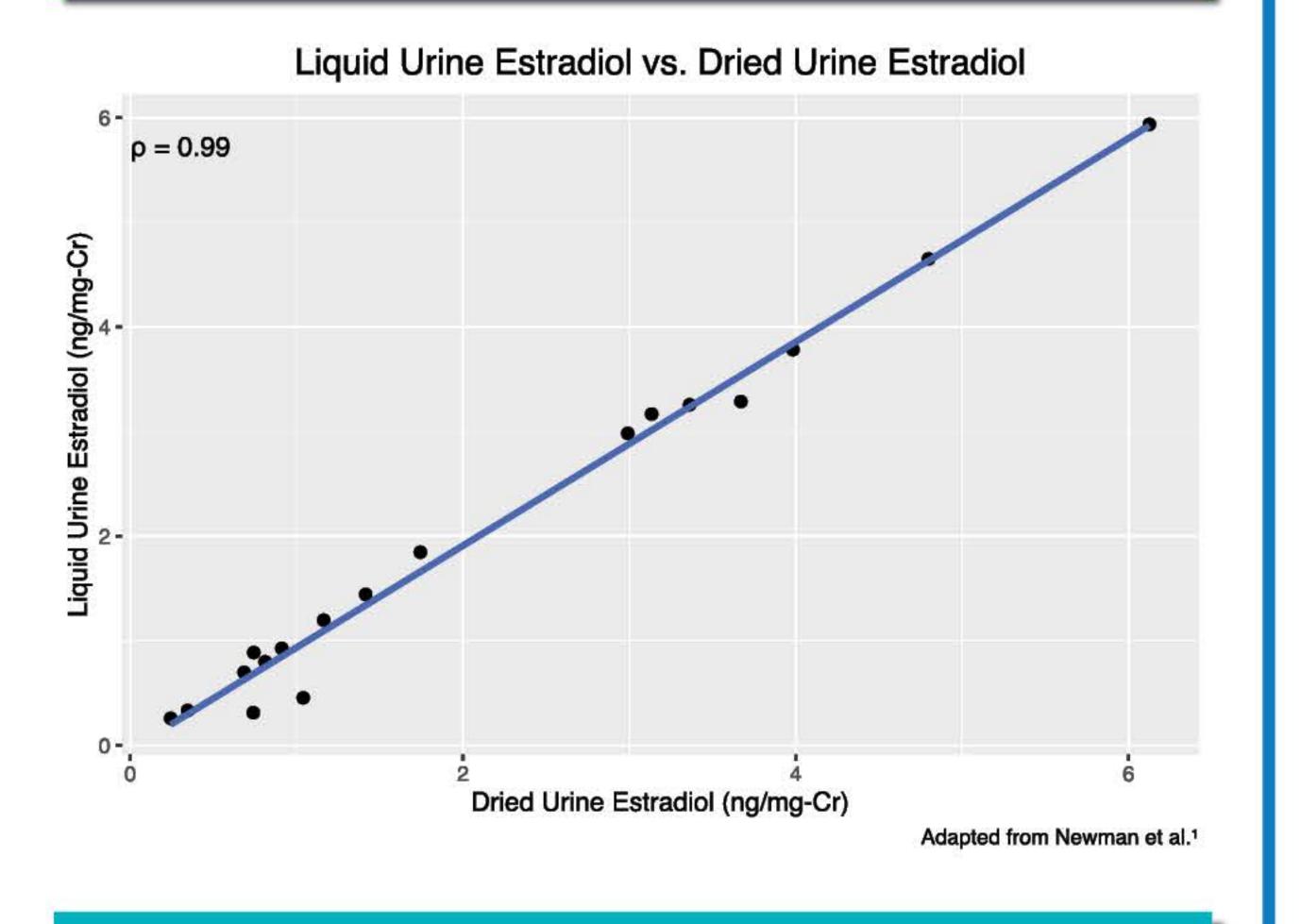
Day of Menstrual Cycle

In the same previous study,¹ serum progesterone levels were also compared to the equivalent biomarker in urine, β-pregnanediol.
 Urinary β-pregnanediol concentrations also fol-

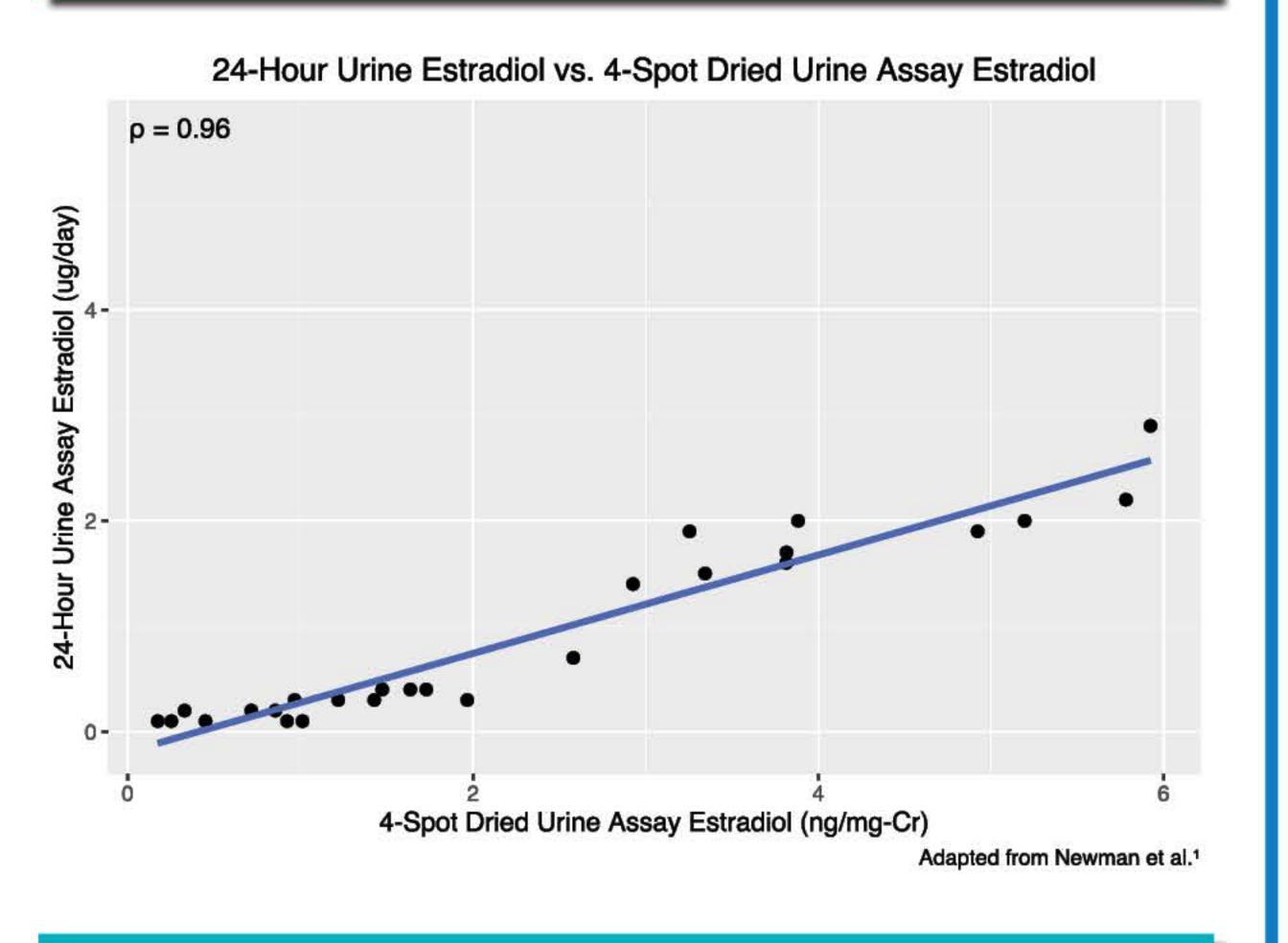
• Urinary β-pregnanediol concentrations also followed the same pattern as results obtained from serum with similar timings of peaks and troughs.¹



What about liquid urine vs. dried urine?



- No difference was found between analyzing liquid urine or dried urine samples from filter paper.¹
- Results from dried urine samples and liquid urine samples demonstrated excellent agreement.¹

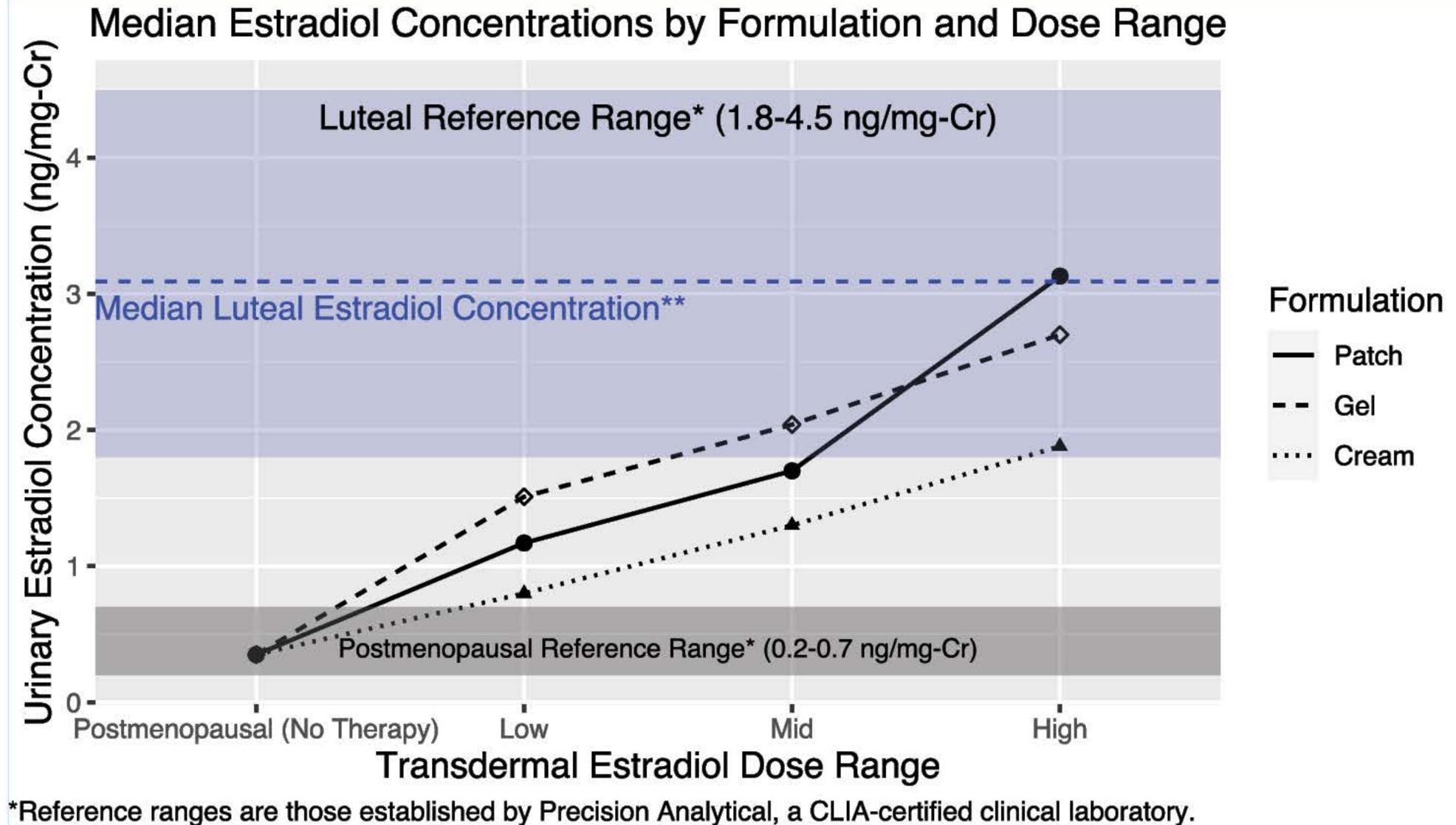


 Using a 4-spot collection technique is equivalent to doing a complete 24-hour urine collection as evaluated by intraclass correlations.¹

RESULTS

- Analysis of the data demonstrated that for patients in the patch and gel groups, E2 concentrations were similar within the defined dose ranges and the E2 concentrations for each of the 2 formulations showed an ordered trend with dose-proportional increases (P<0.0001 for patches and P=0.001 for gel).
- E2 concentrations for patients using creams also showed an ordered trend for dose-proportional increases (P<0.0001); however, the concentrations were lower than those observed with patches and gels in the same dose ranges.

How do gels, patches, and creams compare?



ence ranges are those established by i recision Analytical, a CLIA-certified clinical laboratory.

**Median luteal estradiol concentration of premenopausal women included in the study.

The respective dose ranges (mg) for the estradiol cream, gel, and patch were: Low: 0.25-0.5 (cream), 0.25-0.5 (gel), 0.025-0.0375 (patch) Mid: 0.75-1.25 (cream), 0.75-1.0 (gel), 0.05 (patch High: 1.5-3.0 (cream), 1.5-3.0 (gel), 0.075-0.1 (patch)

CONCLUSIONS

- Our results demonstrated the differences in urinary E2 profile changes in response to increasing doses of E2 patches, gels, and creams.
- These results suggest that the validated dried urine assay used in this study may provide an attractive alternative or complement to serum when monitoring TD E2 therapy.
- Future studies utilizing this assay may help illuminate the degree to which these measurements correlate with clinical improvement, which could lead to improved precision and personalization of MHT.



<u>Abbreviations</u>

- DUTCH: Dried Urine Test for Comprehensive Hormones
- DUTCH: Dried Urine Test for Comprehensive Hormones
 E2: Estradiol
- MHT: Menopausal Hormone Therapy
 TD: Transdormal
- TD: Transdermal
 GC MS/MS: Gas Chromatography Tandom Mass Spostrometry
- GC-MS/MS: Gas Chromatography-Tandem Mass Spectrometry
 IQR: Interquartile Range

References 1. Newman M, Pratt SM, Curran DA, Stanczyk F

Urine

