

OBJECTIVE

- •Transdermal (TD) estradiol (E2) gel is a commonly used menopausal hormone therapy (MHT).
- In research studies investigating gels, serum is often used to measure
 E2 levels, but the results only represent a moment in time during phle-botomy.
- •In contrast, urine may provide a representation of serum E2 levels over a 24-hour period, and it is non-invasive and easier to collect.
- The aim of this study was to evaluate a dried urine sampling method to determine if it may be a viable option for monitoring TD E2 gels.

DESIGN

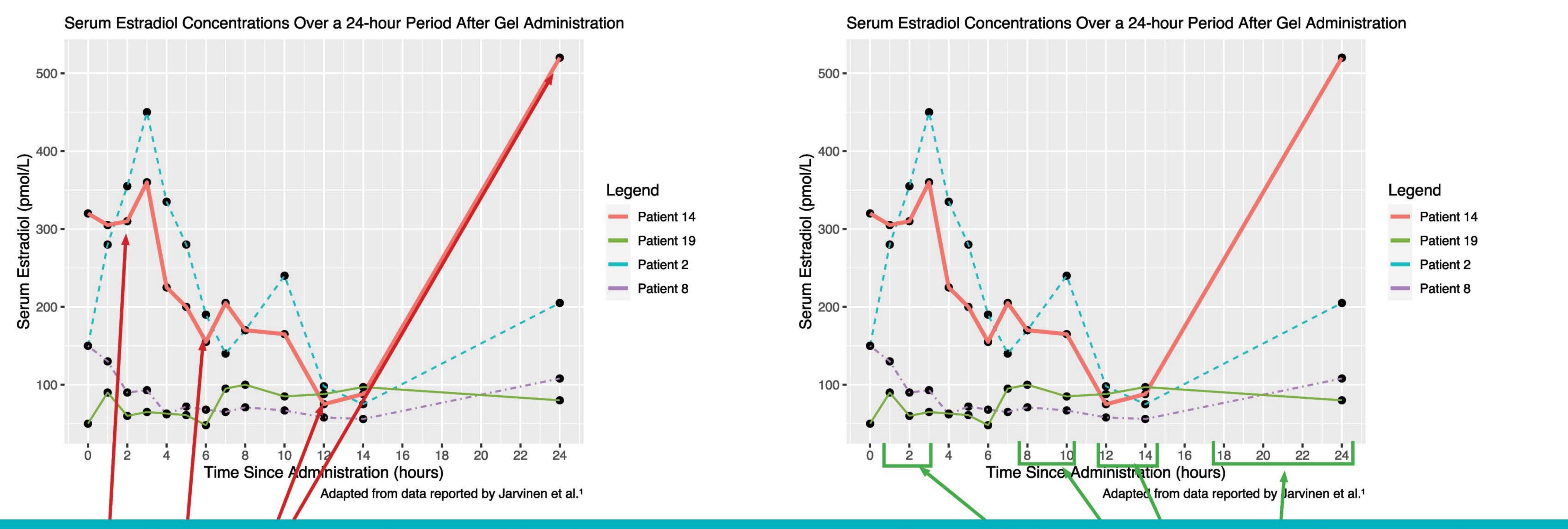
- This study utilized data from a retrospective observational study, Precision Analytical Retrospective Data Correlation (NCT04305093).
- The dataset from this larger study contained measures of multiple urinary markers obtained via a 4-spot dried urine sampling method.
- For this analysis, we used a subset of the data that included only the urinary E2 profiles of:
- Premenopausal women (n = 16308)
- Postmenopausal women not on menopausal hormone therapy (n = 17827)
- Postmenopausal women using TD E2 gel (n = 261)
- Urinary E2 was measured using gas chromatography/tandem mass spectrometry (GC-MS/MS) with a lower limit of quantification of 0.092 ng/mL.
- Doses were divided into 3 ranges:
- Low dose (0.25 mg, 0.26 mg, 0.375 mg, 0.5mg, and 0.52 mg)
- Mid-dose (0.75 mg and 1 mg)
- High dose (1.5 mg, 2.0 mg, 2.25 mg, and 3 mg)
- •The nonparametric Jonckheere-Terpstra (JT) trend test was used to assess for ordered differences across groups to determine if dose-proportional increases in urinary E2 were seen with increasing dose ranges of TD E2 gel.

MONITORING TRANSDERMAL ESTRADIOL GEL THERAPY WITH A VALIDATED DRIED URINE ASSAY

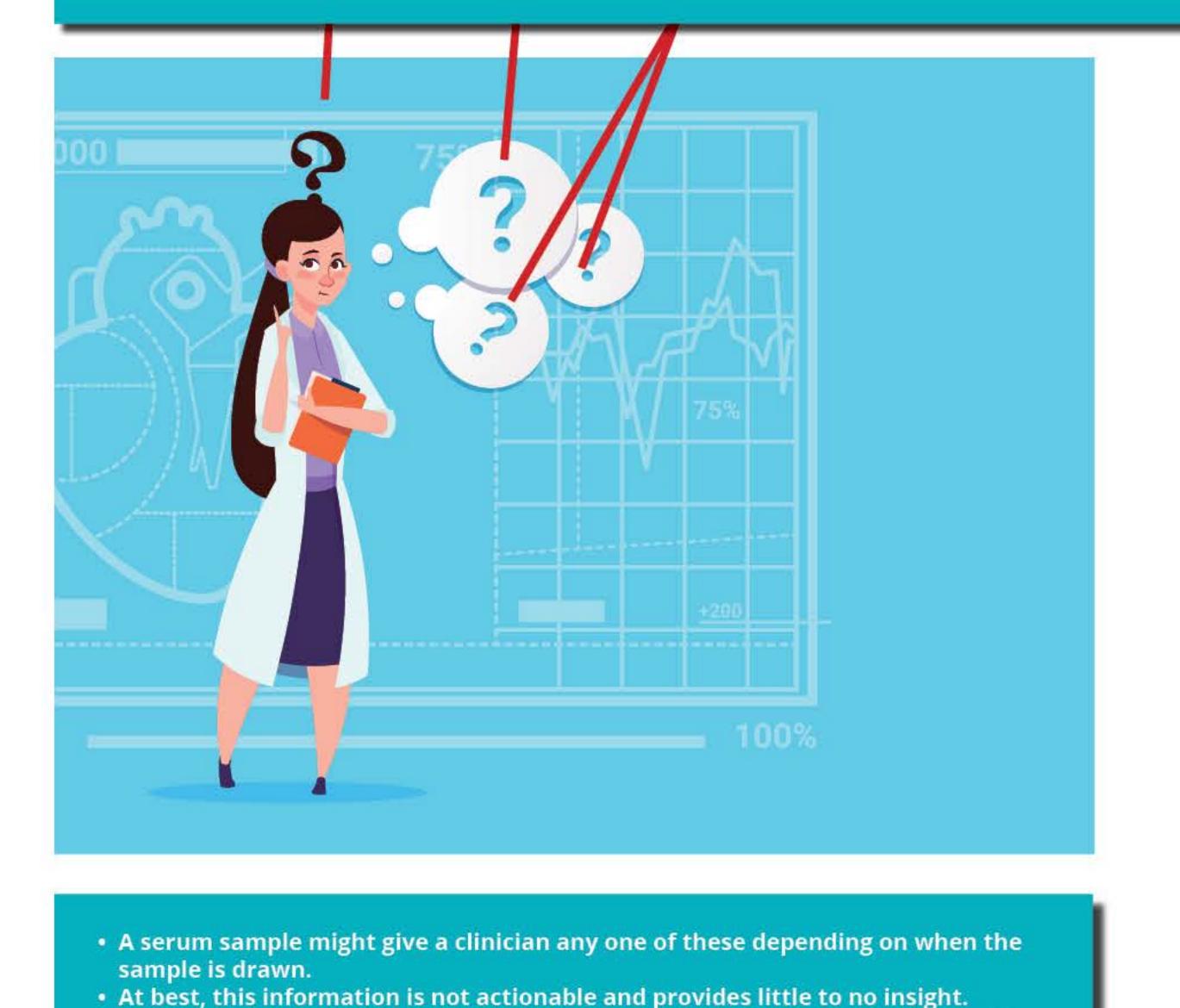
Mark Newman, MS¹; Doreen Saltiel, MD, JD^{1,2}; Bryan P. Mayfield, PharmD^{1,3}; Frank Stanczyk, PhD⁴

¹Precision Analytical, McMinnville, OR; ²Peak Health and Wellness, Asheville, NC; ³Texas Tech University Health Sciences Center Jerry H. Hodge School of Pharmacy, Lubbock, TX; ⁴University of California Keck School of Medicine, Los Angeles, CA

Pharmacokinetics of Transdermal Estradiol Gel in Serum



Does urine sampling provide a better representation of estradiol exposure compared to serum? (Serum only shows one moment in time)



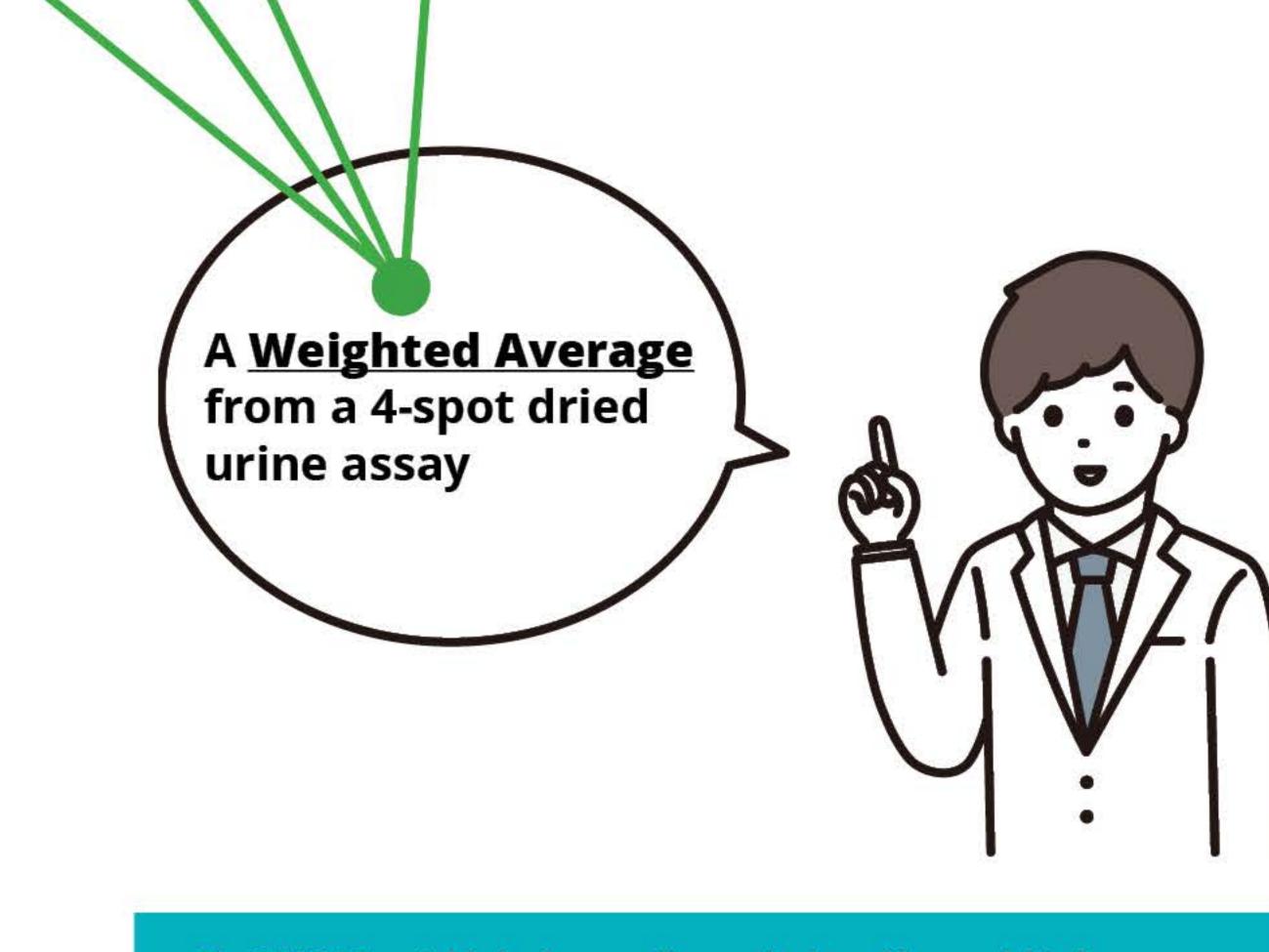
At worst, clinical decisions made using only one of these measurements could

lead to patient harm or insufficient clinical impact.

all estradiol exposure from MHT?

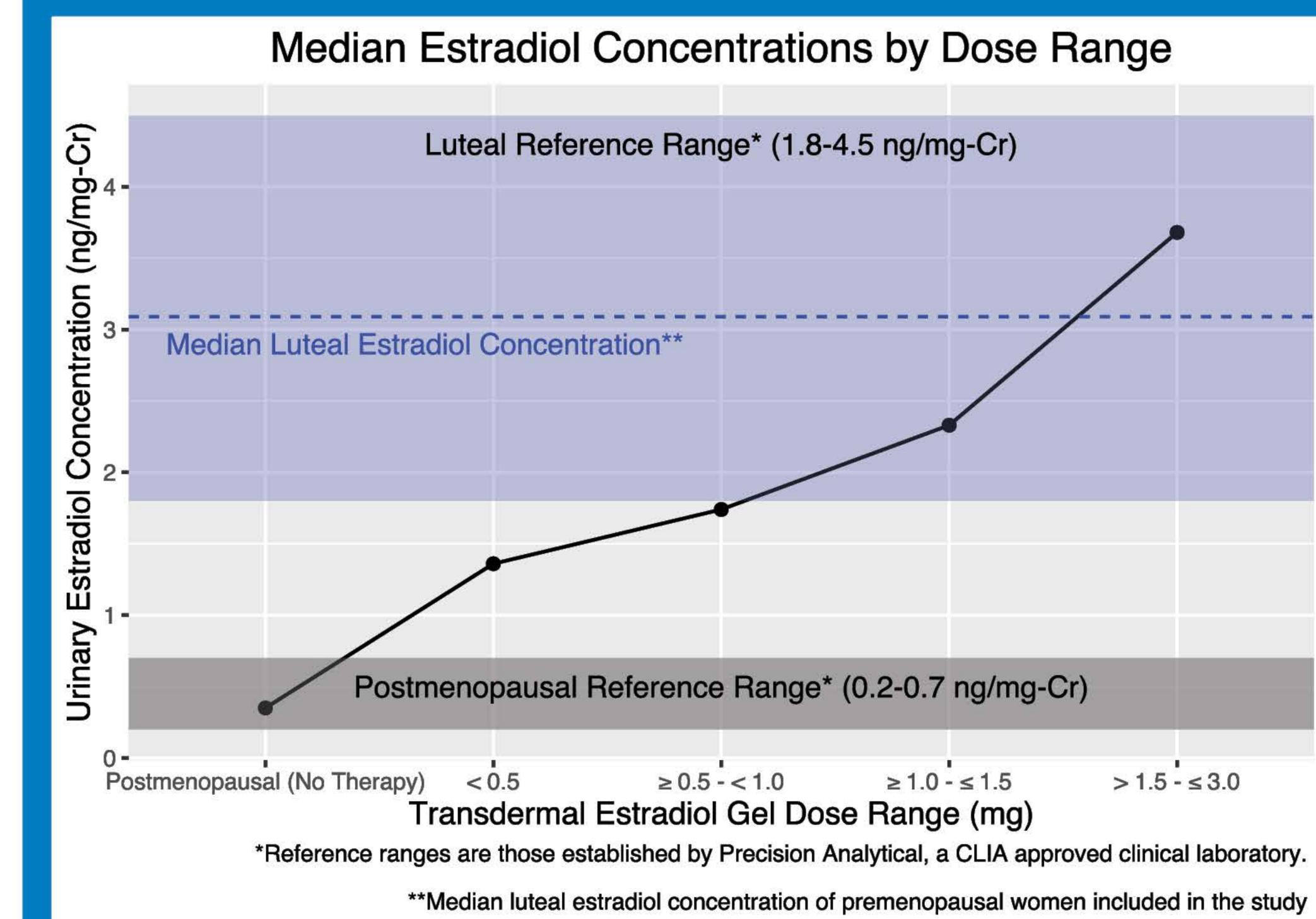
How does a researcher or clinician approximate over-

- A single serum measurement can be highly variable.
 Multiple serum measurements improve clinical insight but may not be practical in a research setting or a typical outpatient setting.
- A multi-spot dried urine collection with a weighted-average measurement may be the optimal solution.



The DUTCH 4-spot dried urine sampling method provides a weighted average of estradiol excretion that represents a ~10 - 14 hours portion of the day (compared to a single moment in time with serum).
 This provides a more accurate representation of estradiol exposure over the course of a day.

RESULTS



- Increasing dose ranges of TD E2 gel resulted in dose-proportional increases of median (IQR) concentrations of E2 which were:
- 0.35 ng/mg-Cr (0.20, 0.73) for women on no therapy
- 1.51 ng/mg-Cr (0.71,2.49) for women on low dose TD E2 gel
- 2.04 ng/mg-Cr (1.12, 3.63) for women on mid dose TD E2 gel
- 2.70 ng/mg-Cr (1.15, 5.20) for women on high dose TD E2 gel
- •A stepwise, dose-proportional, ordered trend existed for urinary E2 with each increase in dose of TD E2 gel (p = 0.001).

CONCLUSION

- •This large population-based study conducted using real-world data demonstrated that an assay performed with dried urine samples is a viable method of monitoring changes in women's urinary E2 profiles in response to MHT with differing dose ranges of TD E2 gels.
- These results suggest that the validated dried urine assay used in this study may provide an attractive alternative to serum for exploring not only the changes in the urinary E2 profile, but also the efficacy and effectiveness of TD E2 gels.

<u>Abbreviations</u>

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



1. Newman M, Pratt SM, Curran DA, Stanczyk FZ. Evaluating urinary estrogen and progesterone metabolites using dried filter paper samples and gas chromatography with tandem mass spectrometry (GC-MS/MS). BMC Chemistry. 2019;13(1):1-12. doi:10.1186/s13065-019-0539-1



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