Twitter Thread by Dr. Tory Eisenlohr-Moul, PhD ■■■■



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Want to include the menstrual cycle in your scientific work, but aren't sure how to do it? My lab (@katjaschmalen) have just published an article on best practices for observational studies of the cycle! Thread below! ■

Despite decades of research on the menstrual cycle, empirical studies have not adopted consistent methods for operationalizing the menstrual cycle, resulting in confusion in the literature and limited possibilities to conduct systematic reviews and meta-analyses.

Below, I summarize this "how to" article, and relay some of the key points!

PARTICIPANTS: All participants should be naturally-cycling people with ovaries (remember that they are not necessarily "women"! ■■■■■ ■).

We provide a Reproductive Status Questionnaire with rules for identifying naturally-cycling people (current function of the sexual organs and hormonal/other medications that stop the cycle).

APPENDIX 1: Reproductive Status Questionnaire for Menstrual Cycle Studies

REPRODUCTIVE STATUS QUESTIONNAIRE This questionnaire is meant to help the study team understand your current reproductive functioning		***NOTE FOR RESEARCH TEAM:***
(0) What is your age (in years)?		
(1) How do you describe your gender identity? Please select ONE.		
○ female/woman	comment:	
○ male/man	comment:	
○ nonbinary	comment:	
○ genderfluid	comment:	
○ other	comment:	
(2) What pronouns do you use? Please select ONE.		*It has been proven useful to make a corresponding note on front of participant binder to make sure to always address the participant correctly.*
○ he		
○ she		
○ other	comment:	
(3) What was your assigned sex at birth? Please select ONE.		
○ female	comment:	
○ intersex	comment:	
○ male	comment:	
(4) First, since we are interested in knowing the kinds of hormones your body is making, will you tell us which reproductive organs you currently have? Please select ONE.		

We also highlight that individual differences in biological and behavioral response to the cycle are the norm, not the exception-- epidemiologic and experimental work highlights that only a minority show significant changes (eg., #PMDD #PME, #hormonesensitivity). ■■■■

One sampling option is to take a case-control approach, recruiting both a control group (no cyclical sx) and a clinical group of hormone-sensitive people w cyclical sx (using daily ratings and algorithms, e.g., C-PASS: https://t.co/8GkEb17Hn6)

If a dimensional approach is desired (e.g., no groups), the sample should be large enough to detect and model between-person moderators of within-person cyclical change (e.g., https://t.co/6r1PyWkp50)

When taking the latter approach, it might be useful to over-recruit based on factors associated with hormone sensitivity, such as stress/trauma and poor executive functioning; reviewed in https://t.co/NzJNV41qun

STUDY DESIGN: Don't default to "typical" cycle phases. Identify a hypothesized mechanism (usually hormone/metabolite effects on the brain, but could also be cognitive/behavioral) and select lab visit timing based on the hypothesis. Daily ratings encouraged. ■

Given that people differ in their vulnerability to cyclical hormone changes, we recommend that studies focusing on the cycle use a repeated-measures design-- this is the only way to detect and model who is experiencing cyclical changes, and who is not. ■

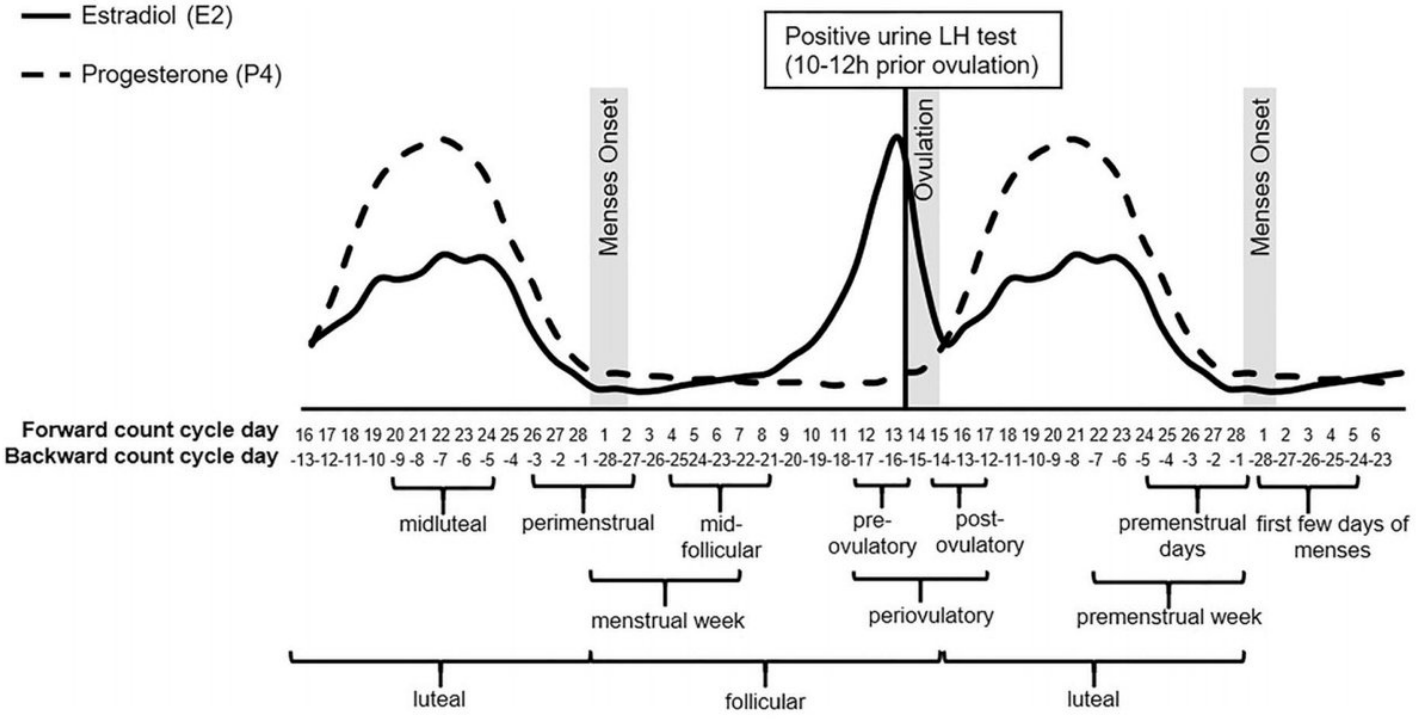
A repeated-measures design should be used because it allows us to model the within-person effects of cycle phase (or cyclical hormones) as a function of between-person risk factors (stress/trauma, EF)-- that is, we can model predictors of #hormonesensitivity! ■■

In cross-sectional studies where the cycle is not the primary variable of interest (but its effect on the primary outcome should be controlled), we recommend timing assessments to one cycle phase chosen based on the question at hand (not always the mid-follicular phase). ■

MEASUREMENT OF THE CYCLE: In the article, we demonstrate how to measure menstrual bleeding dates, the preovulatory LH surge in urine, cyclical changes in basal body temperature (BBT), and ovarian hormones and associated substances (e.g., E2, P4, ALLO).

We explain how to select your biomarkers (basal body temp, salivary or blood or urinary hormones) based on your hypothesis and study design. ■

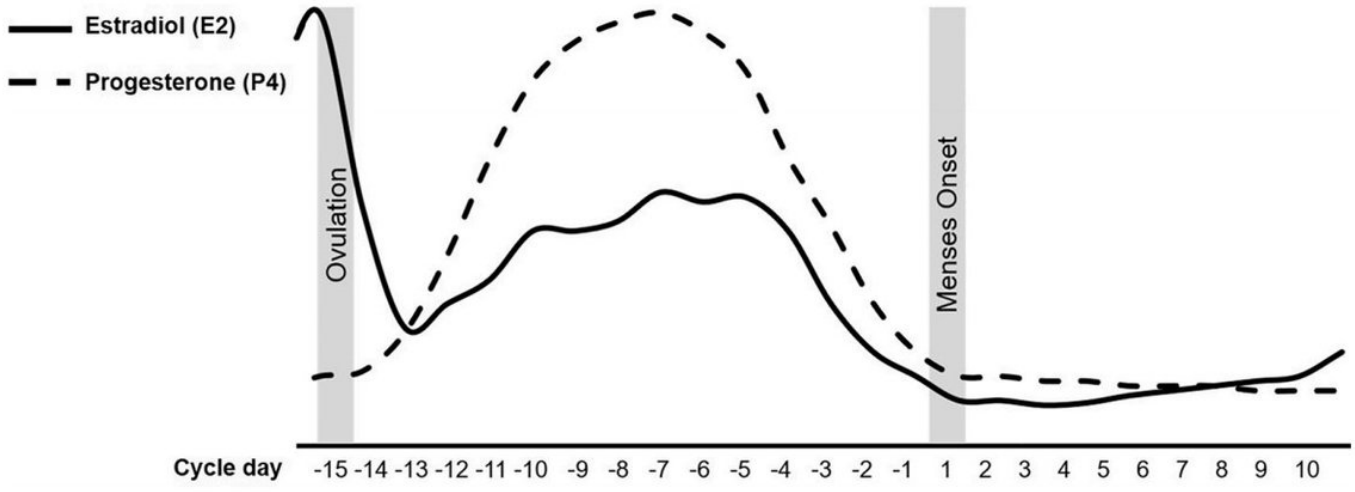
We also provide algorithms for coding cycle day and phase. For each phase, we describe the hormonal events occurring during that phase, and indicate best practices for coding and validating them using counting (relative to menses onset) and biological measures.



We introduce an additional PERI-menstrual phase approach given that E2 and P4 show rapid withdrawal perimenstrually (between cycle days -3 and +3) and not in the whole week before onset of menses (i.e., days -7 to -1, premenstrual phase).

This is also critical given that epidemiologic studies show that the average peak symptom expression among hormone-sensitive people occurs in the perimenstrual--not the premenstrual-- phase. See https://t.co/F1VH77IE9I.

STATISTICS AND VISUALIZATION: We include recommendations for modeling menstrual cycle effects, including guidelines on how to visualize cycle effects, how to carry out categorical phase contrasts, and how to carry out daily modeling with lagged/concurrent hormone levels.



This statistical section ends with approaches to modeling between-person differences in cyclical change which can be top-down and hypothesis-driven (e.g., multilevel growth models with a cross-level interaction) or bottom-up and data-driven (e.g., longitudinal mixture models).

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Finally, when interpreting cycle results remember that cyclical hormone effects often operate on a time lag, in which outcomes are not caused by the hormonal events on the same day, but rather by hormonal events that occurred up to two weeks ago.

■ https://t.co/PxHSmdNhaV

In conclusion, we hope that this paper can help to provide a uniform set of tools and vocabulary that allows future observational menstrual cycle studies to choose and document their approach in a well-informed and standardized manner.

We believe that following these recommendations will help make menstrual cycle studies more meaningful and replicable, allow for more rapid accumulation of knowledge, and facilitate meta-analysis.

Bonus point--> Dear men: it is *not* sexist to study the menstrual cycle if you do it right and acknowledge/model individual differences in #hormonesensitivity as a clinically-relevant phenomenon. Join us in feminist cycle science! ■■■■■■

Check out the article here! https://t.co/IHD7E4fLN7