

Clustering historical controls for a continuous outcome in a Bayesian Phase II vulvodynia trial design

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Vulvodynia

- Is defined as chronic vulvar pain with no apparent cause
- Is diagnosed by exclusion
 - physical exams rule out injury
 - swabs rule out infections
- A cotton swab test identifies locations of pain
 - often the vestibule
- Treatments are not generally effective, but can include
 - topical anesthetics
 - physical therapy
 - counseling
 - surgery removing the painful tissue

- Vulvar Vestibulitis Clinical Trial: Desipramine-Lidocaine (VVCT)
 - NICHD-funded RCT
 - 2 X 2 parallel design studying oral desipramine and topical lidocaine in local provoked vulvodynia sample
 - N=132, only 32 controls
 - 50% response in control group
- A Trial of Gabapentin in Vulvodynia: Biological Correlates of Response (GABAgroup)
 - NICHD-funded multicenter RCT
 - crossover design studying oral gabapentin in local provoked vulvodynia sample
 - 6 week followup
 - N=89, only 64 controls

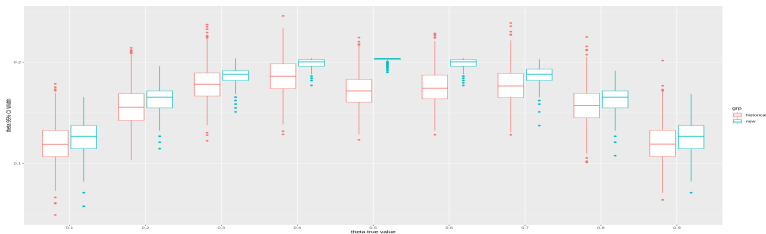
New design

- New science has brought mechanistic understanding
- There is a new targeted therapy currently going into a Phase 1B trial
- We are designing a new Phase 2 trial
 - control groups responds strongly to attention
 - recruitment is difficult and slow (GABA group recruited 230, 89 with any results, 66 completed interventions)
- We will use historical controls to reduce the randomization to control
- We will cluster controls using baseline and 4-week outcomes
- We will include historical controls with a weight equal to the probability of cluster membership

SAM: Self-adapting Mixture Prior to Dynamically Borrow Information from Historical Data in Clinical Trials

- What happens if we use Yang et al (2023)?
 - use mixture priors to incorporate historical data
 - weights determined from Bayes factors
 - priors are data-driven and self-adapting

$$\pi_{sam}(\theta) = w\pi_1(\theta) + (1 - w)\pi_0(\theta), \quad w \propto R = \frac{\rho(H_0)}{\rho(H_1)} BF$$



Thank you

- The URMV Vulvodynia Team
- NIH
 - R01 HD092334 Mechanisms of vulvodynia involving dysregulation of pro-resolving lipids
 - R01 HD108173 Transient Vanilloid Receptors and Vulvar Pain: New Therapeutic Targets for Vulvodynia
- You! Thank you for listening