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- Disclosure:
  - Employee of Sunovion Pharmaceuticals, Inc
- (Self) Disclosure:
  - I am not a statistician and do not fully understand the intricacies of Network Meta-Analysis

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The Good

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The Bad

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How Should Findings be Interpreted: Danger of the Horse Race

- Drugs may be limited by formulary decision makers and will be discouraged for use in practice
- What are clinicians to do in actual practice?
  - Should clinicians assume that certain drugs will have little probability of efficacy for their individual patients?
  - Should they switch to a more efficacious treatment?
- "Acceptability" in the real-world is not easily inferred from discontinuations in clinical trials
  - Trials typically have restrictive inclusion and exclusion which can make generalization of safety from trials to real-world patients somewhat difficult
  - Measures may not be optimal in clinical trials (ie. sexual dysfunction in initial trials with SSRIs)
- Efficacy is not always a singular construct
  - Systems pharmacology is informing how we develop drugs
  - As an industry, we may be moving towards developing drugs with broader spectrums of efficacy (ie. positive symptoms, negative symptoms, cognition)

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Moving from a Race to a Sandbox

- European and other regulatory agencies typically mandate active comparator studies for registration
  - These are often lengthy and costly, resulting in slowed development timelines
- Can we consider utilizing a NMA approach to registering a compound
  - If a compound falls within the pre-specified range of efficacy and acceptability to approved agents, can this preclude the need for a dedicated active comparator study?

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Meta-Analysis Ad Infinitum?

- Need to address how to best incorporate re-defined endophenotypes based on biomarkers and enrichment strategies that have and will continue to emerge?
  - Example:
    - Alzheimer's Disease:
      - Trials in the past were exclusively defined by clinical criteria (ie. probable AD, possible AD); likely that other dementias were unwittingly included in these trials
      - Current trials tend to use techniques to enrich and better define the population (ie. amyloid imaging), resulting in potentially more homogeneous populations
      - Is it appropriate to continue comparing effectiveness to earlier studies when we have substantially refined the criteria underlying the disease state?