Conclusions

- No one approach will work for every setting
- Good to remember all approaches involve subjectivity
- Specific endpoint + composites that summarize effect on multiple endpoints seems like a flexible and powerful combination

…

- A prior development of risk-benefit statistic and boundary is a useful decision tool but cannot be prescriptive

Comments

- Tension between suitability for a given trial and wide acceptability
- Optimum is in the eye of the beholder – sponsor/funder vs investigator vs DSMB
- Midcourse changes are very apt to meet resistance
- Whatever the basis of choosing the primary endpoint for monitoring, stick with it; explore alternative choices in final analysis
- If something very alarming occurs, the DSMB must bring in the other stakeholders, just as in the case of a recommendation to stop

A Framework for Risk-Benefit Evaluations in Biomedical Research

From Rid A and Wendler D (2011). *Kennedy Institute of Ethics Journal*

- Guidance for IRBs in judging whether the risk of harm to a patient exceeds the prospect of benefit
- No matter how much data there are, weighing harms against benefits is challenging
- "From a practical perspective … it is important to note that clinicians routinely make similar evaluations in the context of clinical care…. This suggests that [IRB members] should adopt an informed clinician's perspective to determine whether individual research interventions pose, or do not pose, net risks."

Similarity between IRBs and DSMBs

- IRBs and DSMBs have similar challenges in assessing the balance of harms and benefits, IRBs for every research intervention, DSMBs for a single intervention and a body of new data collected to inform the assessment.
- When it comes to addressing that balance, informed clinical judgment may be the best approach, but whose?