Alastair J.J. Wood M.D.

Managing Director
Symphony Capital LLC
New York, NY
Emeritus Professor of Medicine
Vanderbilt University

Recurrent Issues at NDAC Meetings

- Interpretation of label comprehension studies
- Interpretation of actual use studies
- Potential use/misuse by “non target” populations

Interpretation of Label Comprehension Studies--Problems

- No predefined end point
  - What was the study goal?
- Frequently the data analysis seems to be a moving target
- No agreement on “passing grades”
- No agreement on “critical questions”
- No agreement on data analysis
  - Frequent post hoc merging of “similar” questions
    - Often appears to be retrospective polishing of data
    - Data manipulation is rampant

Interpretation of Actual Use Studies Problems

- Same issues as with label comprehension
- In addition
  - Do results from actual use trump comprehension or vice versa?
  - They often do not appear additive or even complementary
  - Should they have different goals?

Data Analysis

- Usual analysis standards should apply
  - Prespecify analysis plans
  - Prespecify “critical questions/outcomes”
  - Merging of outcomes must be prespecified
- Study goal(s) needs to be defined
  - Should explore how to best convey information (comparisons)
  - Not just how badly (or not) we did
- Standards for passing grades predefined
- Standard/strategy for low literacy predefined
- Need to be consequences of unacceptable outcome

Fundamental Problems

- Impression is that we just do a study and see how it comes out
  - Then try to justify the outcome
  - Then try to explain away poor outcomes
  - No consequences
- No comparator
  - So we never find the best (or better) approach
    - Just how this specific approach worked
    - Is there a better approach—never know
    - No iterative approach

Potential Use/Misuse by "Non Target" Populations

- Comes up every time
- Often entirely theoretical
  - "But what if this other group took it for XXX"?
  - "What if another group misunderstands?"
- Drugs do not usually have to be proved safe/effective in patients who should not be taking them
- Is there an acceptable/unacceptable level of risk in non indicated patients?
  - How do we know?
  - How would/could we know?

Conclusions

- Data analysis
  - Same rigor required as in other settings
    - Currently not seen
- Actual use/Comprehension studies
  - Expectations not defined
  - No comparisons so no learning/improvement
    - Should there be a control group in every study?
      - Versus say another accepted label to define difference in performance
      - Versus alternative information presentation

Non Target Groups

- We need data not conjecture
- Is potential harm different from lack of benefit?
- How does proven benefit to target group outweigh potential harm to non target group?
  - Does it?
  - Should it?
- Actual misuse versus potential misuse
- Is deliberate misuse different from misunderstanding?

- **We need to**
  - **Define standards to be met**
  - **Have expectations that these standards will be met**
  - **Consequences when standards are not met**