



Multiple Modes of Administration and Data Capture: Statistical Issues

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Use of mixed modes

- ⊙ Mixed modes produces statistical issues
 - ⊙ Understanding impact on trial outcomes
 - Licensing
 - 2ndary uses – economics
 - ⊙ Other study designs
 - ⊙ Establishing degree of equivalence



Promise of ePRO

- Improvements in reliability/ accuracy of data
- Avoidance of problems with back filling/ forward filling
- Improved adherence to study protocol
- More accurate study data
 - Smaller trials?
- But ePRO development may take longer than P&P
- Replacing P&P diaries with ePRO mid study could affect trial data

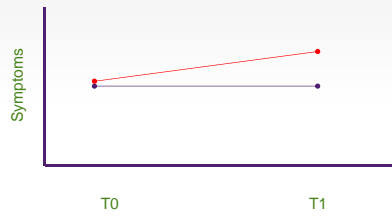


Random error/ systematic error

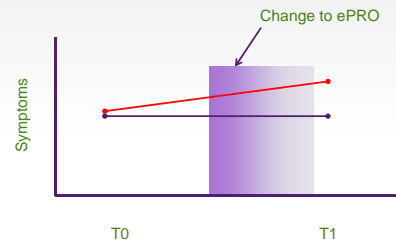
- One way to consider impact is in terms of random and systematic error
- If an eDiary stops working switching to P&P is a source of random error
 - Reduces chance of finding sig diffs
 - If infrequent event then risk is low
- If a trial is designed such that all patients will be switched to ePRO after 3 months – systematic error
 - May increase risk of misinterpreting data
 - Risk here is quite high
- If patients choose ePRO or P&P then this may be systematic error
 - Mid trial



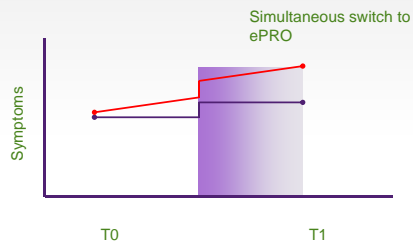
Collection of PRO data



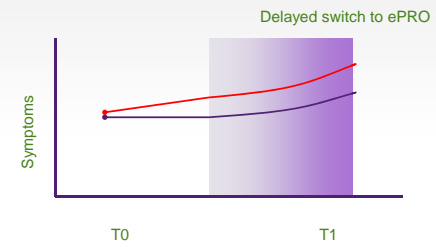
Systematic change to ePRO

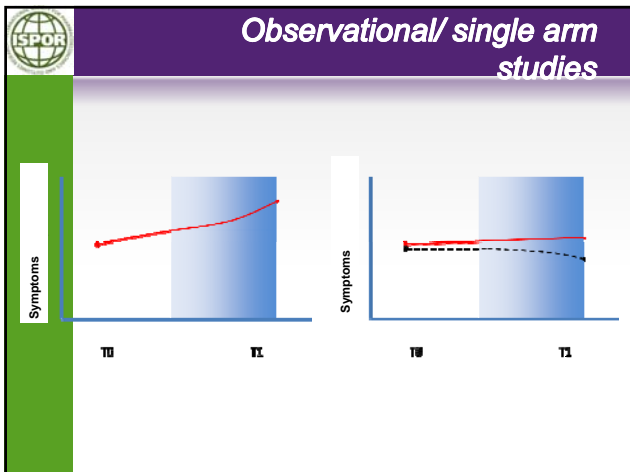


Simultaneous switch



Slow adoption





- Systematic switching to ePRO**
- Effects shown are exaggerated probably
 - But mid-study adoption has potential to cause problems with the data
 - Changing mid study could also affect other issues
 - Higher drop out rates in placebo (due to no efficacy) might interact to inflate Rx vs. Placebo difference

- Mixed modes or missing data?**
- ePROs will have technical problems
 - Device failure
 - What is best method for handling this?
 - If rate is low then switch to P&P diary
 - This should be a random error
 - Better to avoid missing data
 - Explore impact with sensitivity analyses?
 - Imputation has a limited or no role
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- The image shows a vertical stack of traffic signs. At the top is a red octagonal stop sign with the word 'STOP' in white. Below it are four circular signs with red borders and black symbols: a left-turn arrow, a right-turn arrow, a U-turn arrow, and a straight-ahead arrow, all with red slashes over them, indicating 'no' for each maneuver.

- What if the trial is underway?**
- Explore whether mode predicts PRO
 - Explore differential item functioning between ePRO and P&P
 - Does variability differ between modes?
 - Does adherence differ between modes?