Global Health Trials Discussion Forum:

Data Safety Monitoring Boards

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DSMB Discussion Topics

- **Why?** The Purpose of a DSMB?

- **When?** For which kinds of clinical trials?

- **How?** What should be in a DSMB Charter?

- **What?** Examples of DSMB recommendations?
Purpose of a DSMB

- How does a DSMB differ from routine safety monitoring?
When needed?

- In vivo artemether-lumefantrine therapeutic efficacy studies
- Phase 1 Bioequivalence study? E.g. FDC vs loose TB treatment (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol)
- Randomised controlled trial comparing SP with artesunate plus SP?
- Sulfadoxine-pyrimethamine (SP) Intermittent Preventive Treatment in pregnant women?
- Artemether-lumefantrine drug-drug interaction studies with nevirapine or protease inhibitor based antiretrovirals in HIV infected patients.
- OZ439-mefloquine drug-drug interaction study.
Key elements of DSMB Charter

- Who?
- How many?
- How often?
- What data?
- Unblinding?
DSMB recommendations

- Examples?
To stop a study early – risk:benefit
(10-fold increase between 1975 and 2005)

- **Harm:** ILLUMINATE – increased risk major cardiovascular events and death in torcetrapib group @ 18 months (n~5000).

- **Benefit:** pre-operative beta-blockade before vascular surgery showed 2/59 bisoprolol vs 8/53 control had major cardiovascular events

- **Futility:** ARDS Network found only 1% probability of showing superiority of higher vs lower PEEP in 2\textsuperscript{nd} interim analysis of 549 of planned 750 patients

- **New non-study information:** increased risk of major CVE with celecoxib in men with prostate cancer
Why is stopping trials early problematic?
Why is stopping trials early problematic?

- Effects of multiple testing and overestimation of treatment effects.
- Comprehensive assessment of treatment impact limited
  - Long term outcomes
  - Patient important outcomes
- Publication bias -> impact on guidelines
- Freezing effect: Tough to launch new trial on QN if study stopped early

POISE n=8000
- 30% decrease in non-fatal MI
- 33% increase in overall mortality
- 2-fold increased risk of stroke
Lessons learnt?