# splitting alpha

stats methodologists meeting

18 June 2015

# Double-blind randomised placebo-controlled trial of daily vitamin D3 supplementation for the prevention of cancer and cardiovascular disease in older adults (Daily-D)

- PI: Professor Adrian Martineau, (*Barts and The London School of Medicine*)
- many fine Priment collaborators and others

# primary outcome measures

- The incidence of all-site cancers (time to first diagnosis)
- The incidence of cardiovascular disease (composite of time to first: acute myocardial infarction; cerebrovascular accident; revascularisation)
- N≈20,000

# P-value Interpretation and Alpha Allocation in Clinical Trials

L.A. Moye (Ann Epid 1998)

- “Conservative allocation of alpha has the advantage of being disciplined,prospectively identified, and unambiguous in its interpretation…
- …the population at large often bears the brunt of type I errors”

# Power Calculation

- outcome 1: alpha=2.2%
- outcome 2: alpha=2.8%

- what was the price for splitting alpha?
- had we picked a single primary, how much less need N have been?
- (*see co_primaries.xlsx*)

# Points

- increase in precision (i.e. drop in SE) with increase in N is subject to diminishing returns…
- …but drop in tail area (of a Normal distribution) is fast (~exp[-$x^2$])
- so, the ability to detect *real* effects remains sensitive to increases in N
- and the option of accommodating 'extra' endpoints by increasing N may well be practical