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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Subgroup analysis

A posting from Astra Zeneca (19 November 2020) indicated that interim results from their phase II/III COV002 trial of AZD1222 (NCT04516746) demonstrated lower local and systemic reactions in older adults (≥56-69 years and ≥70 years) than in younger adults (≥18-55 years) and generated similar robust immune responses against the SARS-CoV-2.

Do you believe the finding is reproducible and if not, what would it take to convince you?

The registration lists five primary outcome measures and 14 secondary outcome measures, none of which relate to age of recipients. Also there is no evidence randomizations were stratified by age.

Trialists perform dozens of subgroup analyses to determine if it is reasonable to regard treatment effects as homogeneous across baseline subgroups. Such analyses have bearing on conclusions reached. Evidence of qualitative or quantitative treatment by baseline characteristic interaction obligate trialists to temper conclusions accordingly.

Subgroup analyses morphs to data dredging if results from such analyses are used to identify "significant" differences without regard to the number of analyses performed and when differences are presented as if the result of clinical insight.

Your thoughts?