[1] Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand

[2] Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK

david.skegg@otago.ac.nz

Cite this as: *BMJ* 2020;371:m4918
http://dx.doi.org/10.1136/bmj.m4918
Published: 23 December 2020

COVID-19: LATE STAGE VACCINE CANDIDATES

Unwarranted optimism about vaccine efficacy

David Skegg,[1] Neil Pearce[2]

Interim results from phase III trials of the vaccine developed by the University of Oxford and AstraZeneca were announced through press releases on 23 November. Much has been made of an apparent difference in efficacy between the intended regimen (two full doses of the vaccine) and another regimen (a half dose followed by a full dose). Whereas the efficacy in people given the planned combination was found to be 62%, that in the second group was 90%. Immunologists have suggested possible mechanisms to explain why starting with a reduced dose might be more effective.[1] Their theories have fuelled hopes that 90% effectiveness could be achieved in vaccination programmes.

There has been far too little acknowledgment that chance is a likely explanation for the different results between the two groups. In clinical studies, subgroup analyses must always be treated with caution—especially when there was no prior hypothesis that an intervention would be more effective in one subgroup. About a quarter of the vaccinated participants received an initial lower dose of vaccine because of an error in preparation, not because anyone suggested that this regimen would be superior. From the numbers released, it is clear that the difference in results between the two groups could have occurred by chance (and would be marginal in terms of conventional criteria for statistical significance). It is also concerning that the two groups appeared to have different age distributions, as well as different distributions across participating countries.

The notion that a serendipitous error might have led to the discovery of a more effective regimen is appealing. Unless there is further evidence from clinical trials, however, it would be wise to assume that the only reliable estimate of efficacy comes from the full dataset—that is, 70%.

Competing interests: None declared.

1 Mahase E. Covid-19: What do we know about the late stage vaccine candidates? *BMJ* 2020;371:m4576. doi: 10.1136/bmj.m4576 pmid: 33234507