

## Risk Benefit Analysis of Vaccines Versus Blood Clots

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Interim analysis from 4 trials (24,000 volunteers) in the United Kingdom, Brazil and South Africa showed that the AstraZeneca-Oxford University (AZ) vaccine had a Vaccine Efficacy (VE) of 60% in preventing COVID-19 in persons more than 18 years old. There were no reports of major AEFI (Adverse Effects Following Immunization) [1]

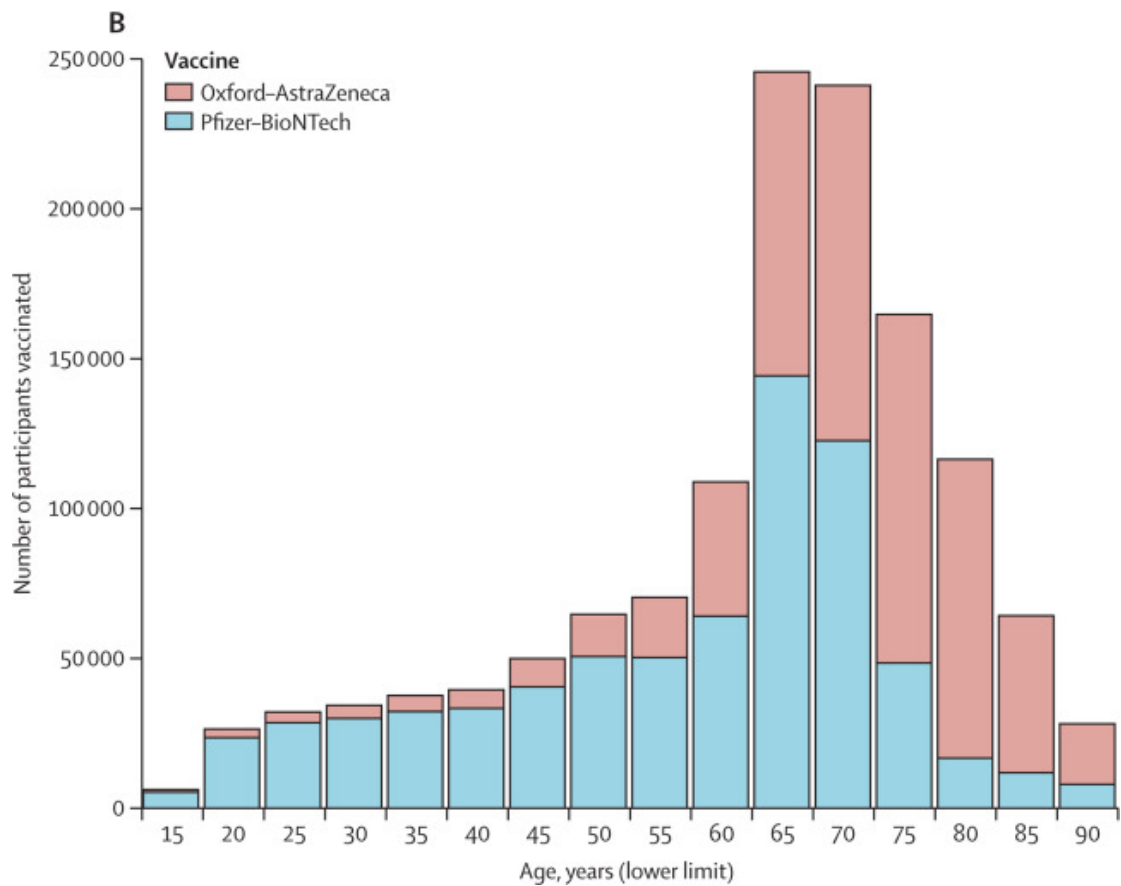
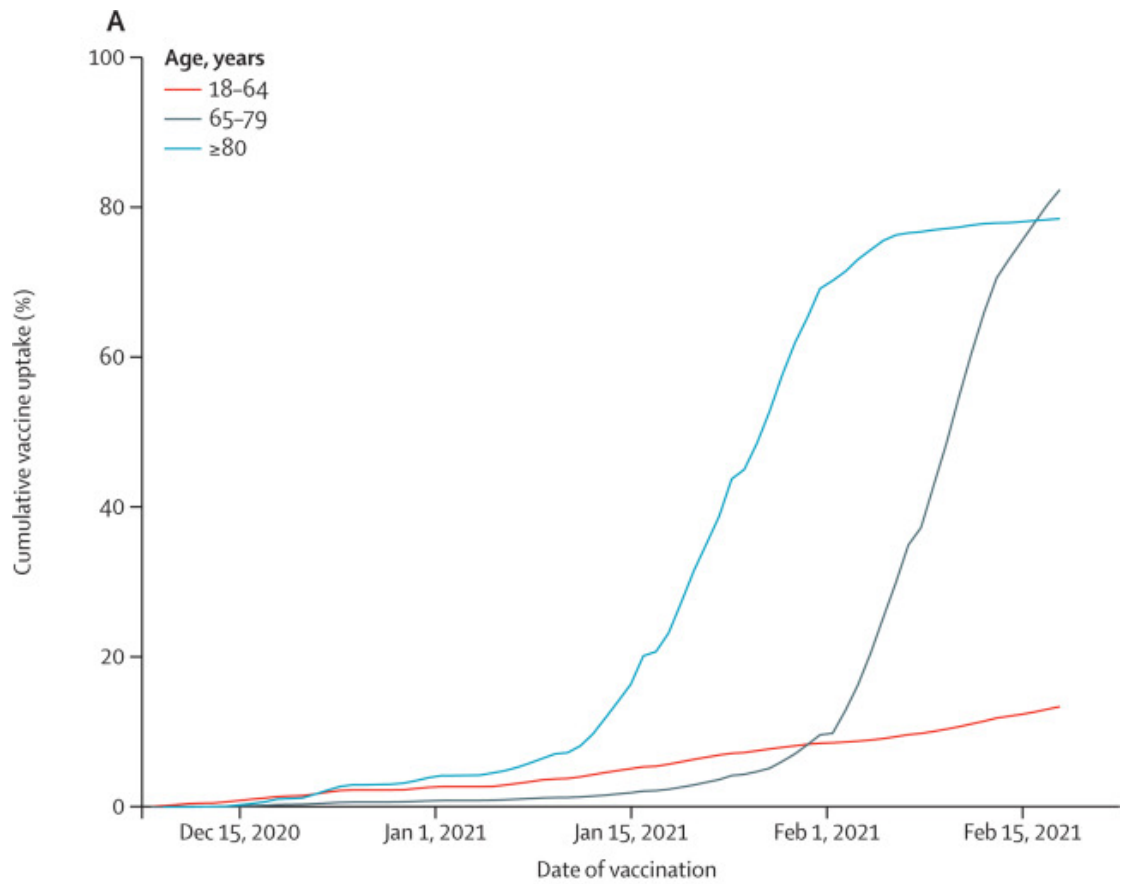
The US trial based on 32,449 participants in the US, Peru and Chile, showed that the AZ vaccine had a VE of 79% against symptomatic COVID and 100% against severe disease and hospitalization. Persons above 65 years old comprised 20% of the study population and showed VE of 79.9% against symptomatic COVID.

The study did not find any increased risk of blood clot events (thrombosis) in the vaccines group. [2]

These have now been confirmed in real world experience. First doses of either the Pfizer or AZ vaccines have been associated with a 90% reduction of COVID associated hospitalizations in Scotland. The rate of decline was most pronounced in those above 80 years old, who were the first to be vaccinated and mainly with the AZ vaccine as seen in Figure 1 [3]

Within 4 months of the swift vaccine rollout (Dec 2020 – Mar 2021), Public Health England estimated that 10,400 deaths have been prevented in persons above 60 years old in England [4]

FIGURE I: Rollout of the Pfizer and AZ vaccines in Scotland.



Following the reports of blood clots in AZ recipients, regulators in a few European countries suspended the use of the AZ vaccine in early March 2021. [5]. The European Medicines Agency (EMA) recommended its continued use, saying the benefits far outweighed the possible link to a rare clotting disorder with low platelets. [6]. Europe was then in the midst of another COVID wave, reporting more than 3,000 daily deaths.

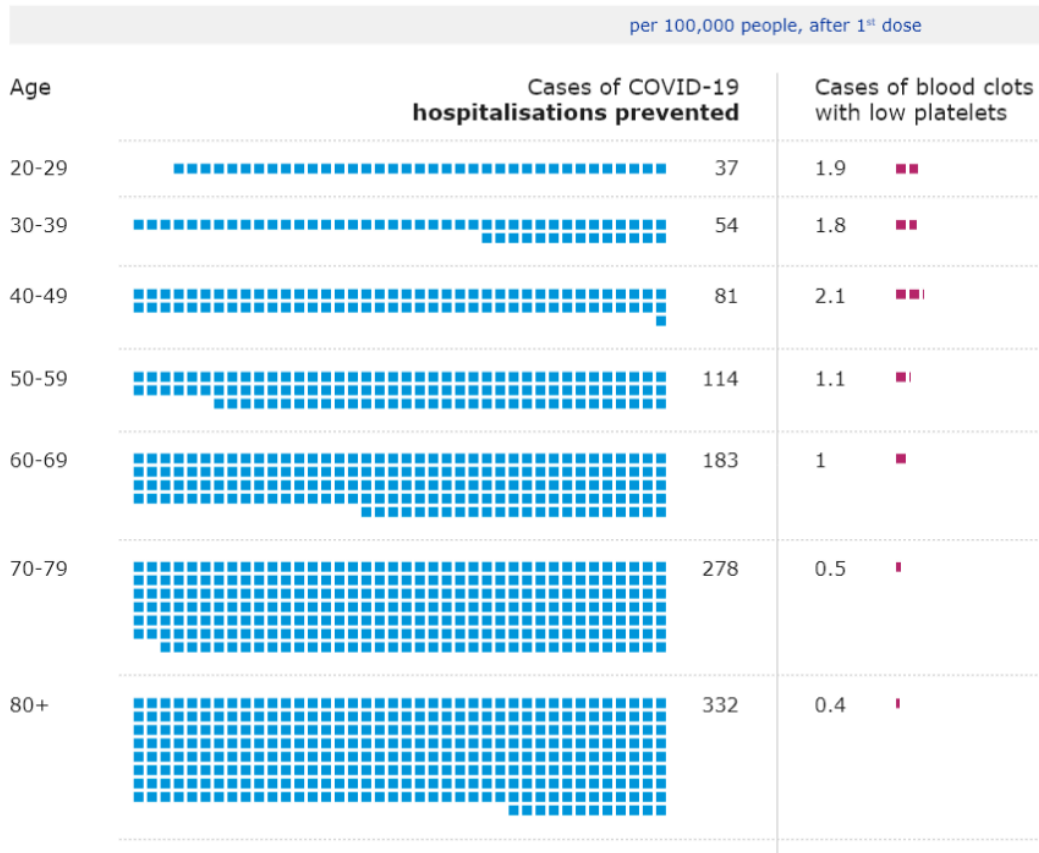
As one of 4 vaccines approved by the WHO for emergency use, the AZ vaccine is at the centre of the COVAX initiative for a major rollout of vaccine doses to 92 participating countries by the year end. [7,8]

Like the EMA, the WHO and the International Society on Thrombosis and Hemostasis recommended the continuing use of the AZ vaccines. [9]

The EMA has since analysed the data to balance the very rare risk of blood clots with the benefits for different age groups and COVID incidence rates. [10]

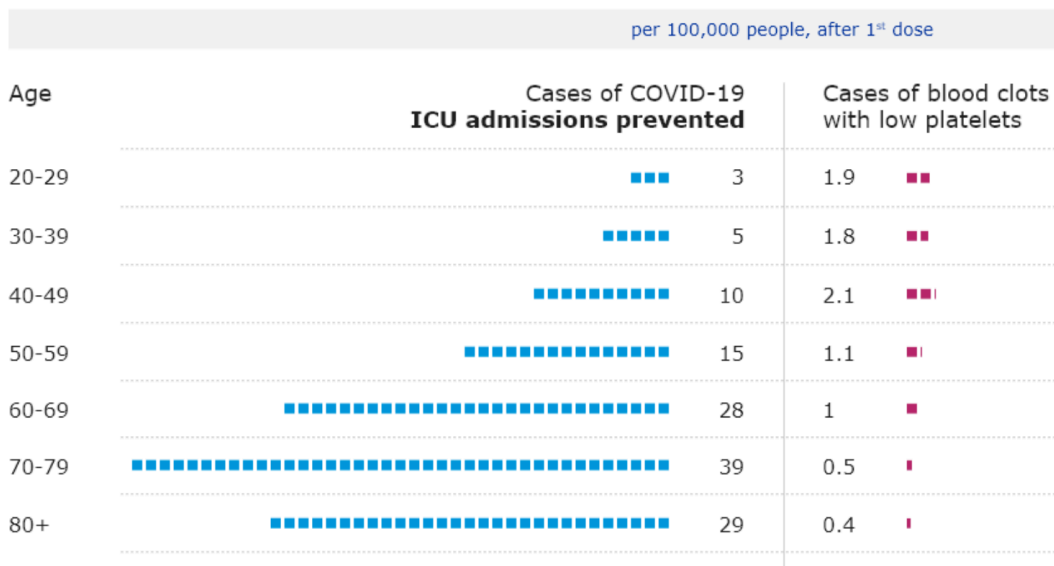
As at 20 April 2021, Malaysia's infections rate was 727 per 100,000. We therefore fall into the medium category (401-885 per 100,000 people). The following 3 tables from the EMA, illustrates the cases of hospitalizations/ICU admission and deaths prevented when compared with the cases of blood clots with low platelets (Thrombocytosis Thrombocytopenia Syndrome, TTS), per 100,000 people, after the first dose of the AZ vaccine in a Middle Infection Rate country. The risk is stratified according to the different age groups.

## Medium infection rate\*



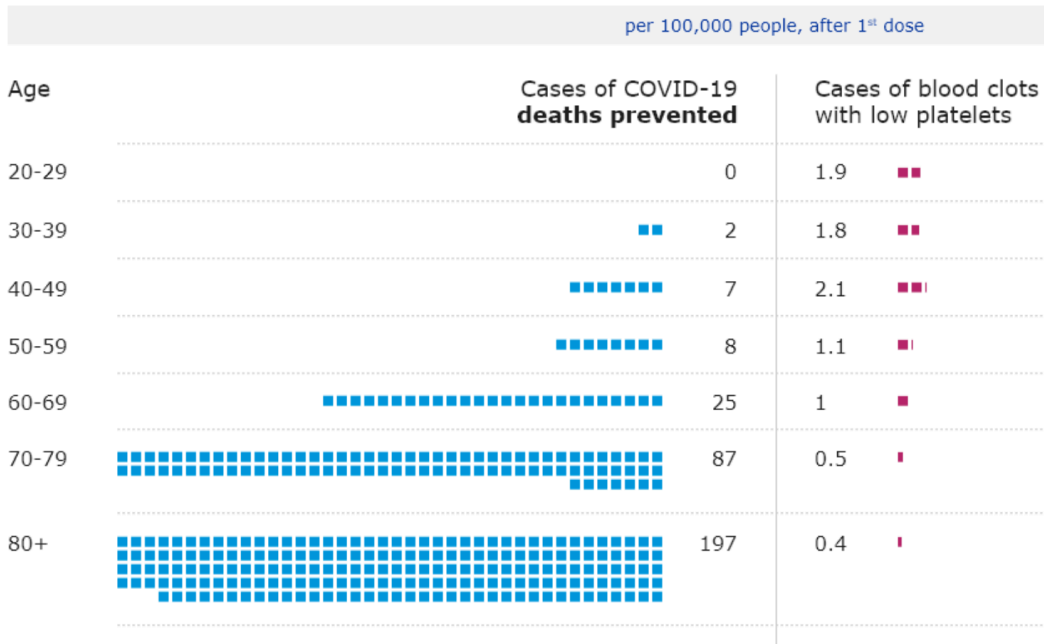
\* "Medium" exposure: using virus circulation for March 2021 (incidence 401/100,000 population)

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**Table I: Summary of cases per 100,000 persons after 1 dose of AZ vaccine in a MEDIUM Infection Rate Country**

Per 100,000 persons	Under 50 years	50-69 years	70+ years
Risk of blood clots	2	1	0.5
Hospitalizations prevented	57	149	305
ICU admissions prevented	6	21.5	34
Deaths prevented	3	16.5	142

From the above table I, it shows that the benefits of vaccination increases with increasing age and infection rates (see Table II)

The vaccine would very much benefit persons who are above 50 years old. For the 50-69 years old cohort, 16.5 lives/100,000 persons are saved from COVID deaths, 21.5/100,000 persons are spared ICU admissions, and 149/100,000 persons prevented from being admitted into hospitals. This contrasts with the risk of a blood clot occurring at a rate of 10 per million.

The benefits are even more amplified for those over 70 years of age, especially towards preventing 1420 deaths per million persons, and preventing 3050 hospital admissions per million persons. And the risk of TTS is halved at 5 per million persons.

If Malaysia (God Forbid) slips into a High Infection Rate country (886 per 100,000 people), which is not unlikely with the current and persistent upsurge in the daily cases, then the benefits of the AZ becomes even more pronounced as illustrated in Table II.

**Table II: Summary of cases per 100,000 persons after 1 dose of AZ vaccine in a HIGH Infection Rate Country**

Per 100,000 persons	Under 50 years	50-69 years	70+ years
Risk of blood clots	2	1	0.5
Hospitalizations prevented	89	266	893
ICU admissions prevented	10	39	94
Deaths prevented	4	30	453

The risk of being admitted to hospital and of dying from COVID in a 70 year old is 1786 and 906 times respectively, when compared to the risk of suffering from a blood clot.

We've also somewhat forgotten that COVID itself is associated with an increased risk of thromboembolism (TE). A meta-analysis of 42 studies showed that the overall venous TE rate was 21%. 1 in 3 had a TE event in the ICUs. The mortality rate among patients who developed TE was 74% higher.[11]

Unfortunately, the adverse effects of vaccines has occupied our conversations and claimed the attention of the public and media coverage, often with negative connotations which has much eroded confidence in vaccines.

Global agencies and national regulators have unequivocally stated that vaccines are powerful public health tools and all of the presently authorized COVID vaccines were highly effective in preventing hospitalization and were 100% protective against COVID associated deaths [12]

We must realize that we are not out of the woods. Since October 2020 we have been swept with the third COVID wave which has stubbornly refused to abate and in the past week has shown an upsurge in cases.

We are deeply embroiled in a pandemic situation and better late than never, we must accept and realize that apart from non-pharmaceutical interventions, ONLY a speedy and scaled up vaccine coverage will confer us the benefits of protecting our healthcare capacity and exit us from this ravaging pandemic.

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