Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

An acute-on-chronic health crisis in Gaza

The Palestinian Gaza Strip is a 365 km² piece of land on the eastern coast of the Mediterranean, inhabited by more than 2 million Palestinians. This open-air enclave has been under siege for the past 14 years, which has left the health system jeopardised by limited resources, failing equipment, and many essential drugs in dangerously low supply. This grim situation was worsened by the arrival of the COVID-19 pandemic, threatening health services with collapse. Beginning on May 9, 2021, the Israeli Government and Hamas launched a military offensive against one another, the severity of which for the Gaza Strip is believed to be the worst since 2014.[1]

The background to this situation is important. There has been increasing tension in Israeli-occupied Palestinian East Jerusalem, with Palestinian families living in the Sheikh Jarrah neighbourhood fighting a legal struggle against their eviction.[2] Tensions grew further at the beginning of the Muslim holy month of Ramadan, with Israel blocking Palestinian gatherings, and with Palestinian worshippers calling for the removal of Israeli police from the al-Aqsa mosque, one of the three holiest sites of Islam where Palestinians pray during Ramadan. In the early morning of May 10, 2021, Israeli forces entered the al-Aqsa mosque while people were praying, with Palestinians injured by rubber bullets and tear gas.[3,4]

In the Gaza Strip, Hamas responded by firing rockets into Israel. Israel responded with strikes by fighter jets and attack helicopters on military targets, which also, and inevitably, included densely populated civilian areas. As of May 18, 2021, Israeli attacks are ongoing, and the Palestinian Ministry of Health has reported at least 212 Palestinians killed, including 36 women and 61 children, and about 1500 Palestinians wounded.[5,6] Hamas rockets have killed ten Israelis, including two children, and wounded at least 300 Israelis.[6] Hospital emergency departments in Gaza are unable to cope with critical medical conditions, including severe hypovolemic shock, penetrating head, chest, and abdominal injuries, burns, blast injures, and severe lacerated and fragmented lower limbs. The continuous attacks on dense Gaza urban settings have not only led to the deaths and injuries of civilians but have also left hundreds of people homeless.

We call upon world leaders to intervene for an immediate de-escalation of attacks by both the Israeli Government and Hamas and to end the violence, protect civilians from political violence in the Gaza Strip and the West Bank, and protect civilians in Israel. We also call for renewed international action to deliver justice, freedom, and self-determination for Palestinians.

We declare no competing interests.

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Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data

There is significant international interest in heterologous prime-boost COVID-19 vaccination to mitigate against supply shocks or shortages that might otherwise reduce the speed of vaccine roll-out. Additionally, in light of changing recommendations regarding use of the ChAdOx1 nCoV-19 (ChAd) COVID-19 vaccine (Vaxzevria, AstraZeneca), several countries are now advising that individuals previously primed with this vaccine should now receive an alternative vaccine as their second dose, most commonly mRNA vaccines such as the BNT162b2 (BNT) COVID-19 vaccine (Comirnaty, Pfizer–BioNTech), administered in a heterologous prime-boost schedule.[1–3] To date there are no data on the immunogenicity, reactogenicity, or safety of such schedules. Com-COV (ISRCTN 69254139) is a UK multicentre, participant-masked, randomised heterologous prime-boost COVID-19 vaccination study comparing all four prime-boost permutations of the ChAd and BNT vaccines both at 28-day and 84-day prime-boost intervals. Participants are 50 years and older with no or mild-to-moderate, well controlled comorbidity and were recruited across eight sites. The protocol is available online.

Following consultation with the study trial steering committee, here we present the initial reactogenicity and safety data, ahead of the primary immunological outcome, which is projected to be available in June, 2021. Reactogenicity data presented here consist of self-reported solicited local and systemic symptoms collected in the 7 days after both prime and boost vaccination in participants randomised to receive vaccines at 28-day intervals. Haematology and biochemistry safety monitoring blood results are also reported from the immunology cohort

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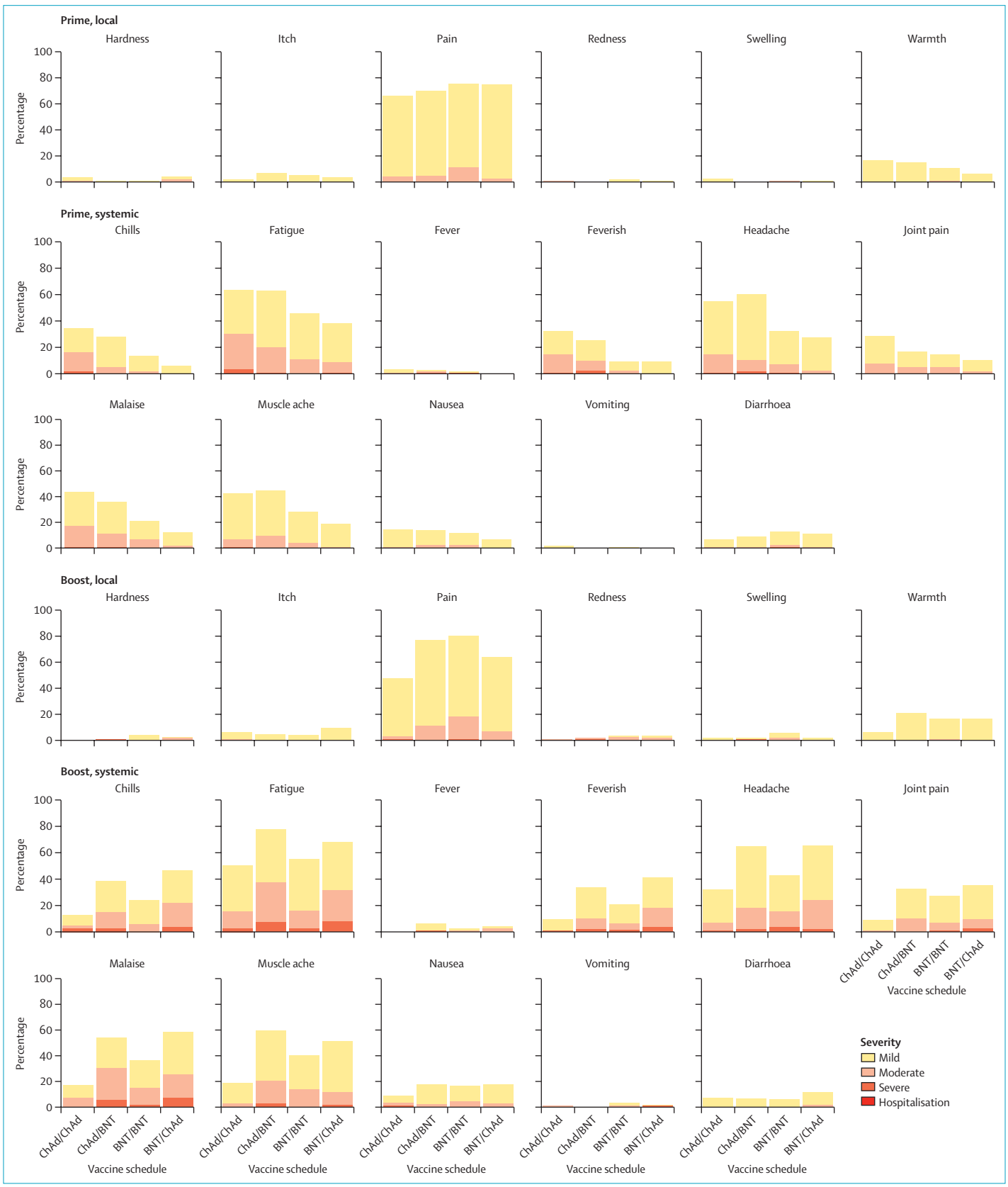
Prime, local
Hardness
Itch
Pain
Redness
Swelling
Warmth
Prime, systemic
Chills
Fatigue
Fever
Feverish
Headache
Joint pain
Malaise
Muscle ache
Nausea
Vomiting
Diarrhoea
Boost, local
Hardness
Itch
Pain
Redness
Swelling
Warmth
Boost, systemic
Chills
Fatigue
Fever
Feverish
Headache
Joint pain
Malaise
Muscle ache
Nausea
Vomiting
Diarrhoea
Percentage
0
20
40
60
80
100
ChAd/ChAd
ChAd/BNT
BNT/BNT
BNT/ChAd
Vaccine schedule
Severity
Mild
Moderate
Severe
Hospitalisation

(100 participants with additional visits), at baseline (before the prime dose), at day 28 (before the boost dose) and 7 days post-boost, graded according to a modified US Food and Drug Administration toxicity scale (appendix). All analyses are descriptive, as the study was not powered for reactogenicity, with endpoints reported as frequencies and percentages, together with absolute differences between heterologous and homologous vaccine schedules and corresponding 95% CIs.

Recruitment commenced on Feb 11, 2021, and was completed on Feb 26, 2021, with 830 participants enrolled and randomised from 978 screened (the CONSORT flow diagram is available in the appendix). 463 participants were randomly assigned to the four groups with a 28-day prime-boost interval, and 367 participants randomised to groups with an 84-day prime-boost interval. All 463 participants in the 28-day prime-boost interval group received their prime vaccine, and 461 participants received their boost vaccine. Among the 463 participants, the median age was 57 years (range 50–69), 212 (46%) participants were female, and 117 (25%) from ethnic minorities, with baseline characteristics well balanced across study groups. In groups with homologous vaccine schedules, systemic reactogenicity was greater after the prime dose in the ChAd group, and after the boost dose in the BNT group (figure).

Both heterologous vaccine schedules induced greater systemic reactogenicity following the boost dose than their homologous counterparts, with feverishness reported by 37 (34%) of 110 recipients of ChAd for prime and BNT for boost compared with 11 (10%) of 112 recipients of ChAd for both prime and boost (difference 24%, 95% CI 13–35%). Feverishness was reported by 47 (41%) of 114 recipients of BNT for prime and ChAd for boost, compared with 24 (21%) of 112 recipients of BNT for both prime and boost (difference 21%, 95% CI 8–33%). Similar increases were observed for chills, fatigue, headache, joint pain, malaise, and muscle ache (figure; appendix). There were no hospitalisations due to solicited symptoms, and most of this increase in reactogenicity was observed in the 48 h after immunisation (appendix).

Participants were advised that paracetamol might reduce vaccine side-effects but were not actively counselled to medicate prophylactically. Paracetamol use in the 48 h post-boost vaccine was reported by 40 (36%) of 112 recipients of ChAd for both prime and boost, 63 (57%) of 110 recipients of ChAd for prime and BNT for boost, 48 (41%) of 117 recipients of BNT for both prime and boost, and 68 (60%) of 114 recipients of BNT for prime and ChAd for boost, thereby mirroring the reactogenicity pattern.

Haematology and biochemistry profiles were similar between heterologous and homologous vaccine schedules, with all laboratory adverse events of grade 2 severity or less in the heterologous vaccine schedule, and no thrombocytopenia in any group at day 7 post-boost (appendix).

In this interim safety analysis, we found an increase in systemic reactogenicity after the boost dose reported by participants in heterologous vaccine schedules in comparison to homologous vaccine schedules, and this was accompanied by increased paracetamol usage. Of note, these data were obtained in participants aged 50 years and older, and reactogenicity might be higher in younger age groups[4,5] for whom a mixed vaccination schedule is being advocated in Germany, France, Sweden, Norway, and Denmark among those who have received a ChAd prime dose, in light of concerns regarding thrombotic thrombocytopenia after the first dose of ChAd.[6]

Pending availability of a more complete safety dataset and immunogenicity results for heterologous prime-boost schedules (to be reported shortly), these data suggest that the two heterologous vaccine schedules in this trial might have some short-term disadvantages. Routine prophylactic use of paracetamol after immunisation could help mitigate these[7] and is being studied in Com-COV participants receiving prime and boost vaccines at 12-week intervals. Regardless, it is reassuring that all reactogenicity symptoms were short lived, and there were no concerns from the limited haematology and biochemistry data available. Further studies evaluating heterologous prime-boost schedules, incorporating vaccines manufactured by Moderna and Novavax, are ongoing, and are crucial to informing the appropriateness of mixed COVID-19 vaccine schedules.

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See **Online** for appendix

***Figure*: Severity of solicited local and systemic reactions in days 0–7 after vaccination with ChAdOx1 nCoV-19 (ChAd) or BNT162b2 (BNT), by prime and boost vaccination and by vaccination group, as self-reported in participant electronic diaries**

ChAd/ChAd denotes a ChAd vaccine for prime and boost doses. ChAd/BNT denotes a ChAd vaccine for prime dose and a BNT vaccine for boost dose. BNT/BNT denotes a BNT vaccine for prime and boost doses. BNT/ChAd denotes a BNT for prime dose and a ChAd vaccine for boost dose. The severity presented is the participant's highest severity across 7 days after vaccination for each solicited adverse event. Fever was categorised as mild (38·0°C to <38·5°C), moderate (38·5°C to <39°C), or severe (≥39·0°C). Feverish was a self-reported feeling of feverishness. For systemic symptoms, grading was classified as mild (easily tolerated with no limitation on normal activity), moderate (some limitation of daily activity), and severe (unable to perform normal daily activity).

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For more on **vaccine doses administered** see https://ourworldindata.org/covid-vaccinations

See **Online** for appendix

For more on **COVAX** see https://www.who.int/initiatives/act-accelerator/about

A global compact to counter vaccine nationalism

Vaccine nationalism threatens to turn the triumph of science to give the world vaccines against COVID-19 into tragedy. The success of several initiatives, many funded by taxpayers, to rapidly develop and test several safe and effective vaccines has been nothing short of spectacular. The social promise of SARS-CoV-2 vaccines was to reduce the underlying inequalities by race, ethnicity, and geography that COVID-19 has both made visible and amplified.[1] Yet, most of the billion vaccine doses administered have been in high-income countries (HICs), with most low-income and middle-income countries (LMICs) left behind (appendix). WHO and Gavi, the Vaccine Alliance have created COVAX to finance SARS-Cov-2 vaccines for LMICs, yet supply of vaccines is still short and coming from only a few companies. India's mostly uncontrolled second viral wave threatens exports of vaccines promised to many countries. The US Government suspending its objections to COVID-19 vaccine patents could help. However, the priority is to produce sufficient quantities on an urgent basis to provide global coverage.

Aspirations to return to some sense of normality might well remain wishful thinking until most adults globally are vaccinated. How do we do that? We propose an integrated three-pillar global vaccine compact to expand vaccine supply and counter vaccine nationalism.

Global vaccine production capacity in non-pandemic times is too small and too concentrated in a handful of pharmaceutical companies.[2] The first pillar of our proposed compact would be for countries to adopt the idea of a fully immunised adult, and launch national adult vaccination programmes. Using the US Disease Control Priorities Cost Model,[3] we estimate that the total cost of routine annual influenza vaccination, 5-yearly pneumococcal vaccines, HPV vaccines for adolescent girls, and tetanus for expectant mothers (including HICs) could be US$34 billion annually. National governments would need to pay for adult programmes, aided by an expanded mandate for Gavi. Per year, an average of about 1·1 vaccines for 5 billion adults might save one million lives from the targeted diseases. Existing live attenuated vaccines have shown action against multiple pathogens, although COVID-19 trials remain to be done.[4] These vaccines might prove to be valuable additions to adult vaccination schedules in some circumstances. Analogously, preliminary data in preprint suggest that annual influenza vaccination reduces the risk of influenza pandemics and perhaps even COVID-19 infection.[5] Should SARS-CoV-2 vaccination need to be seasonal, adult vaccination programmes establish a delivery platform. Moreover, the world might well be entering the era where major zoonotic diseases are not events that happen once a century but once a decade. Thanks to the Bill & Melinda Gates Foundation and others, the world has endorsed universal access to life-saving vaccines for each of the 125 million children born annually. Adult and child vaccination programmes provide a cost-effective platform to prepare for future pandemics. A far larger market enables dispersed production, incentivises more companies to enter the market, and spurs innovation in vaccine design and delivery.

Next, uninterrupted supply of life-saving vaccines cannot be left only to market forces, or worse—insular political decisions. The second pillar we propose is a global vaccine manufacturing compact housed in less populous countries with good scientific and training infrastructure, a respect for legal contracts, and a reputation for fair play. Canada, Norway, Singapore, and Switzerland are possibilities, as might be several others—some of which are in Africa. The manufacturing compact would produce vaccines in the billions, far in excess of domestic demand. The compact would negotiate licences with vaccine producers but have as its core business model the sale of vaccines very near cost price. An independent governance model using professional business or civil service could counter political interference or cronyism. The facilities can learn from the successful Serum Institute of India, which helps vaccinate many of the world's children at low cost, and from Brazil's Fiocruz public partnership.[6] We estimate such a manufacturing pillar would cost about $4 billion to start (with variable running costs that can be priced into sales). It can proceed quickly. The UK was