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## COVID-19 human challenge studies in the UK



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The Human Challenge Consortium consists of UK Government representatives and experts from the National Health Service (NHS), academia, and the private sector. The group has come together to explore the feasibility and ethics of human challenge trials that could potentially accelerate the development of vaccines to protect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

The first study phase, which could begin in January, 2021, aims to discover the smallest amount of virus it takes to cause the infection in up to 90 healthy young people, aged between 18 and 30 years, who are at the lowest risk of harm from COVID-19. The study will take place in the high-level isolation unit of the Royal Free Hospital, London, UK.

Later, a vaccine candidate that has been proven safe in clinical trials could be given to a group of healthy adults in this age range, who are then exposed to the virus in a controlled environment. They would then be closely monitored by medics and researchers to see if the vaccine is successful in preventing infection, as well as identifying any side effects.

The project, which will be granted £33 million of funding from the UK Government, was announced to UK media in a special media briefing at the UK Science Media Centre, based at the Wellcome Trust, London, UK. Addressing the briefing, Peter Openshaw, co-investigator on the study and an immunologist at Imperial College London (London, UK) said "Deliberately infecting volunteers with a known human pathogen is never undertaken lightly. However, such studies are enormously informative about a disease. It is really vital that we move as fast as possible towards getting effective vaccines and other treatments for COVID-19, and challenge studies have the potential to accelerate and de-risk the development of novel drugs and vaccines." Also

addressing the media briefing, lead researcher for the project Dr Chris Chiu, from Imperial College London, said "My team has been safely running human challenge studies with other respiratory viruses for over 10 years. No study is completely risk free, but the Human Challenge Programme partners will be working hard to ensure we make the risks as low as we possibly can."

However, some commentators have questioned both the timing and the ethical dilemmas presented by the study. Among the hundreds of COVID-19 vaccines being developed around the world, several candidates are already in the final stages of testing, and thus could provide definitive results and be approved before this challenge trial has even had the chance to begin. "Any studies involving the novel coronavirus will focus on those most likely to experience a mild infection— young healthy volunteers", says Jonathan Ball, Professor of Molecular Virology, University of Nottingham (Nottingham, UK). "Yet the people we need to protect against serious disease are more vulnerable older people, so what we learn from challenge studies might have limited wider relevance."

"The greatest concern about challenge studies is both the safety of the participants and the impact of a death on trust in science and medicine", says Professor Julian Savulescu (Director at Oxford Uehiro Centre for Practical Ethics, University of Oxford, Oxford, UK). "Despite their ethical justifiability, it is quite possible that the backlash against a death of a healthy volunteer might shut down or significantly retard the use of challenge studies, and perhaps vaccines in general. There is already a high level of hesitancy about vaccines around the world." However, he adds that in this worldwide pandemic emergency, time lost means lives lost, and thus there is a moral imperative to develop a safe and effective vaccine as soon as possible. "The chance of someone aged

20–30 years dying of COVID-19 is about the same as the annual risk of dying in a car accident. That is a reasonable risk to take, especially to save hundreds of thousands of lives. It is surprising challenge studies were not done sooner. Given the stakes, it is unethical not to do challenge studies."

Looking at comparisons with other global health emergencies past and present, Savulescu comments "Smallpox was eradicated by 1979 through vaccination, which was mandatory in many countries (parents were fined in the UK if they did not vaccinate their baby in time). In the face of that kind of emergency, research and control are moral imperatives, even involving compulsory vaccination. There is a moral imperative to prevent and treat any disease that causes suffering and death."

"Whether challenge trials have a role to play in COVID-19 vaccine development depends on country circumstances, and weighing of all the considerations by regulators, scientists, and ethicists," adds Anita Zaidi, director of the vaccine development, surveillance, and enteric and diarrhoeal diseases programs at the Bill & Melinda Gates Foundation (BMGF), Seattle, WA, USA. Zaidi confirmed that the BMGF is not currently funding any challenge trials for COVID-19 vaccines.

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