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LETTER

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# Two Randomized Controlled Trials of Bacillus Calmette-Guérin Vaccination to reduce absenteeism among health care workers and hospital admission by elderly persons during the COVID-19 pandemic: A structured summary of the study protocols for two randomised controlled trials

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## Abstract

**Objectives:** The objectives of these two separate trials are: (1) to reduce health care workers (HCWs) absenteeism; and (2) to reduce hospital admission among the elderly during the COVID-19 pandemic through BCG vaccination.

**Trial design:** Two separate multi-centre placebo-controlled parallel group randomized trials

**Participants:** (1) Health care personnel working in the hospital or ambulance service where they will take care of patients with the COVID-19 infection and (2) elderly  $\geq 60$  years. The HCW trial is being undertaken in 9 hospitals. The elderly trial is being undertaken in locations in the community in Nijmegen, Utrecht, and Veghel, in the Netherlands, using senior citizen organisations to facilitate recruitment.

**Intervention and comparator:** For both trials the intervention group will be randomized to vaccination with 0.1 ml of the licensed BCG vaccine (Danish strain 1331, SSI, Denmark, equivalent to 0.075 mg attenuated *M. bovis*). The placebo group consists of 0.1 ml 0.9% NaCl, which is the same amount, and has the same colour and appearance as the suspended BCG vaccine.

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**Main outcomes:** (1) Number of days of unplanned work absenteeism in HCWs for any reason which can be continuously measured on a bi-weekly basis, and (2) the cumulative incidence of hospital admission due to documented COVID-19.

**Randomisation:** Participants will be randomized to BCG vaccine or placebo (1:1) centrally using a computer-based system, stratified by study centre.

**Blinding (masking):** Subjects, investigators, physicians and outcome assessors are blinded for the intervention. Only the pharmacist assistant that prepares- and research personnel that administers- study medicines are unblinded.

**Numbers to be randomised (sample size):** (1) The sample size for the first trial is N=1500 HCWs randomised 1:1 to either BCG vaccine (n=750) and placebo (n=750) and (2) The sample size for the second trial is N=1600 elderly persons randomised to BCG vaccine (n=800) and the placebo group (n=800).

**Trial Status:** HCW: version 4.0, 24-04-2020. Recruitment began 25-03-2020 and was completed on the 23-04-2020. Elderly: version 3.0, 04-04-2020. Recruitment began 16-04-2020 and is ongoing.

**Trial registration:** The HCWs trial was registered 31-03-2020 at [clinicaltrials.gov](https://clinicaltrials.gov) (identifier: NCT04328441) and registered 20-03-2020 at the Dutch Trial Registry ([trialregister.nl](https://trialregister.nl), identifier Trial NL8477). The elderly trial was registered 22-04-2020 at the Dutch trial registry with number NL8547.

**Full protocol:** The full protocols will be attached as additional files, accessible from the Trials website (Additional file 1). In the interest in expediting dissemination of this material, the familiar formatting has been eliminated; this Letter serves as a summary of the key elements of the full protocol.

**Keywords:** COVID-19, Randomised controlled trial, protocol, BCG-vaccine, Health-Care Workers, Elderly

## Supplementary information

Supplementary information accompanies this paper at <https://doi.org/10.1186/s13063-020-04389-w>.

**Additional file 1.** Full study protocol.

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## Authors' contributions

The whole study team was involved in the design and conduct of this trial. The first version of the protocol manuscript was written by Thijs ten Doesschate and corrections to this draft were made by all study team members.

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The funding for these investigator-initiated studies for the BCG injections and the design of the eCRF and the mobile application came from the

UMCU and Radboudumc. The participating centers contributed without financial compensation. The authors received no external funding to prepare this trial protocol and summary.

## Availability of data and materials

The investigators from the UMC Utrecht will have access to the final trial dataset of the HCWs trial and the investigators from the Radboudumc will have access to the final trial dataset of the Elderly trial. For the HCWs trial the full dataset will be made available with online electronic Case Report Form (eCRF) ResearchOnline, and for the Elderly trial with Castor.

## Ethics approval and consent to participate

The HCWs trial was approved on 17-03-2020 by the medical ethics committee of the UMCU with reference number RJ/avd/20/010396. The elderly trial was approved on 9-04-2020 by the medical ethics committee of the Radboudumc with reference number 2020-6347. Local approval was given by all participating centres. Written informed consent to participate in this study was obtained from all participants. For both studies, the ethics committees assessed that the study possesses a negligible risk for subjects.

## Consent for publication

Written informed consent for the publication of these details has been obtained from all participants.

## Competing interests

The authors declare that they have no competing interests.

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