002 - Motivating Examples

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Case study 1: Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2

Early phase COVID-19 vaccine trial[1]

Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial

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Summary

Background The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.

Methods We did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18–55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5×10^{10} viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. Humoral responses at baseline and following vaccination were assessed using a standardised total IgG ELISA against trimeric SARS-CoV-2 spike protein, a muliplexed immunoassay, three live SARS-CoV-2 neutralisation assays (a 50% plaque reduction neutralisation assay [$PRNT_{50}$]; a microneutralisation assay [MNA_{50}, MNA_{80}, and MNA_{90}]; and Marburg VN), and a pseudovirus neutralisation assay. Cellular responses were assessed using an ex-vivo interferon-γ enzyme-linked immunospot assay. The co-primary outcomes are to assess efficacy, as measured by cases of symptomatic virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were done by group allocation in participants who received the vaccine. Safety was assessed over 28 days after

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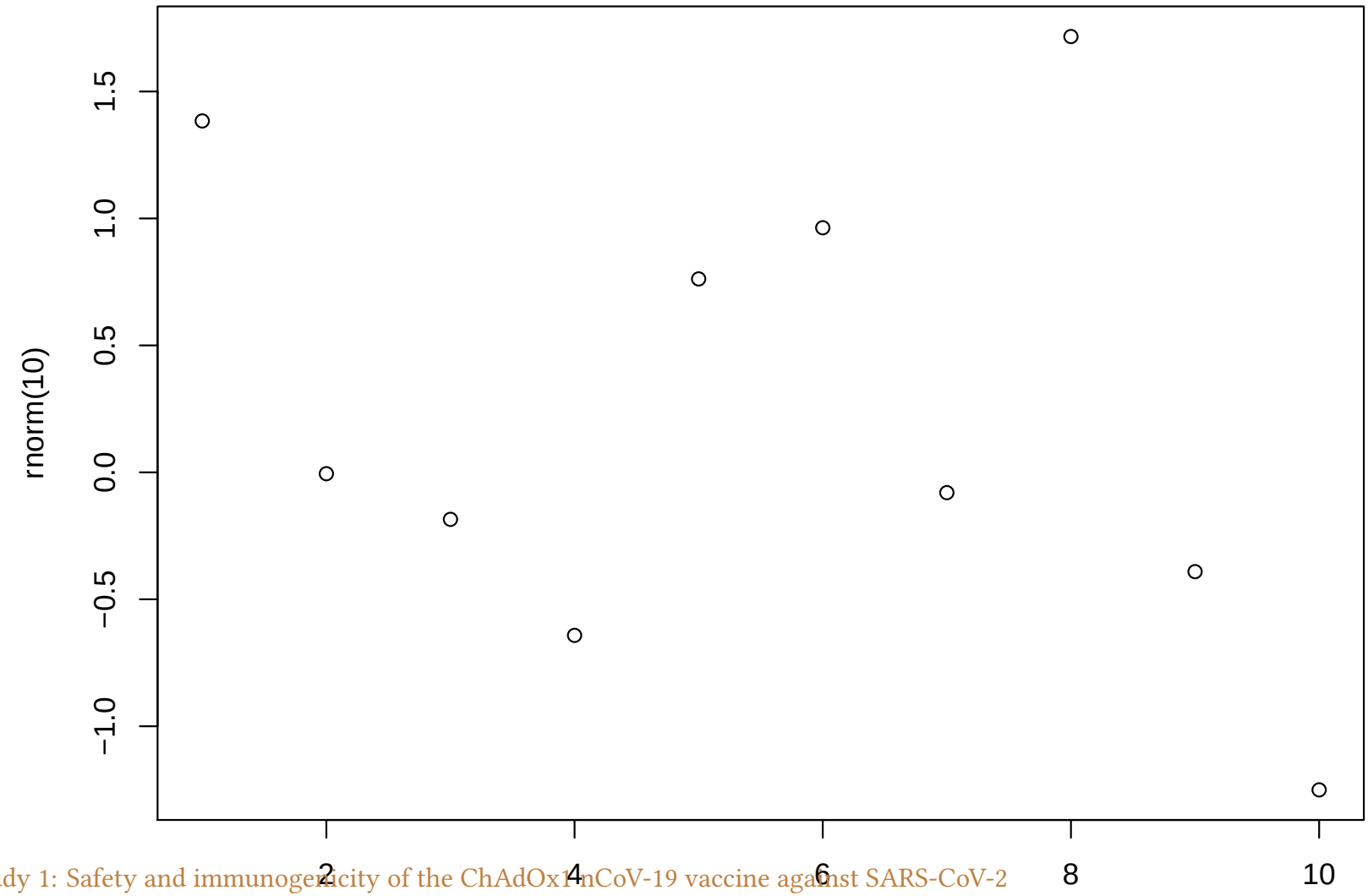
[1] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31604-4/fulltext

Phase 1/2 trial

- The focus in phase 1/2 trials is looking at what the vaccine does to the body and what the body does with the vaccine in *healthy* individuals
- Healthy adults aged 18-55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive **ChAdOx1 nCoV-19** at a dose of 5×10^{10} viral particles or **MenACWY** as a single intramuscular injection
- Between April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534)
- Convalescent plasma is collected from someone who has recovered from a virus. When a person is infected with a virus, their body starts making antibodies to fight it. It is believed these antibodies could be the key ingredient for a treatment to help others with the same virus.
- Safety was assessed over 28 days after vaccination

test

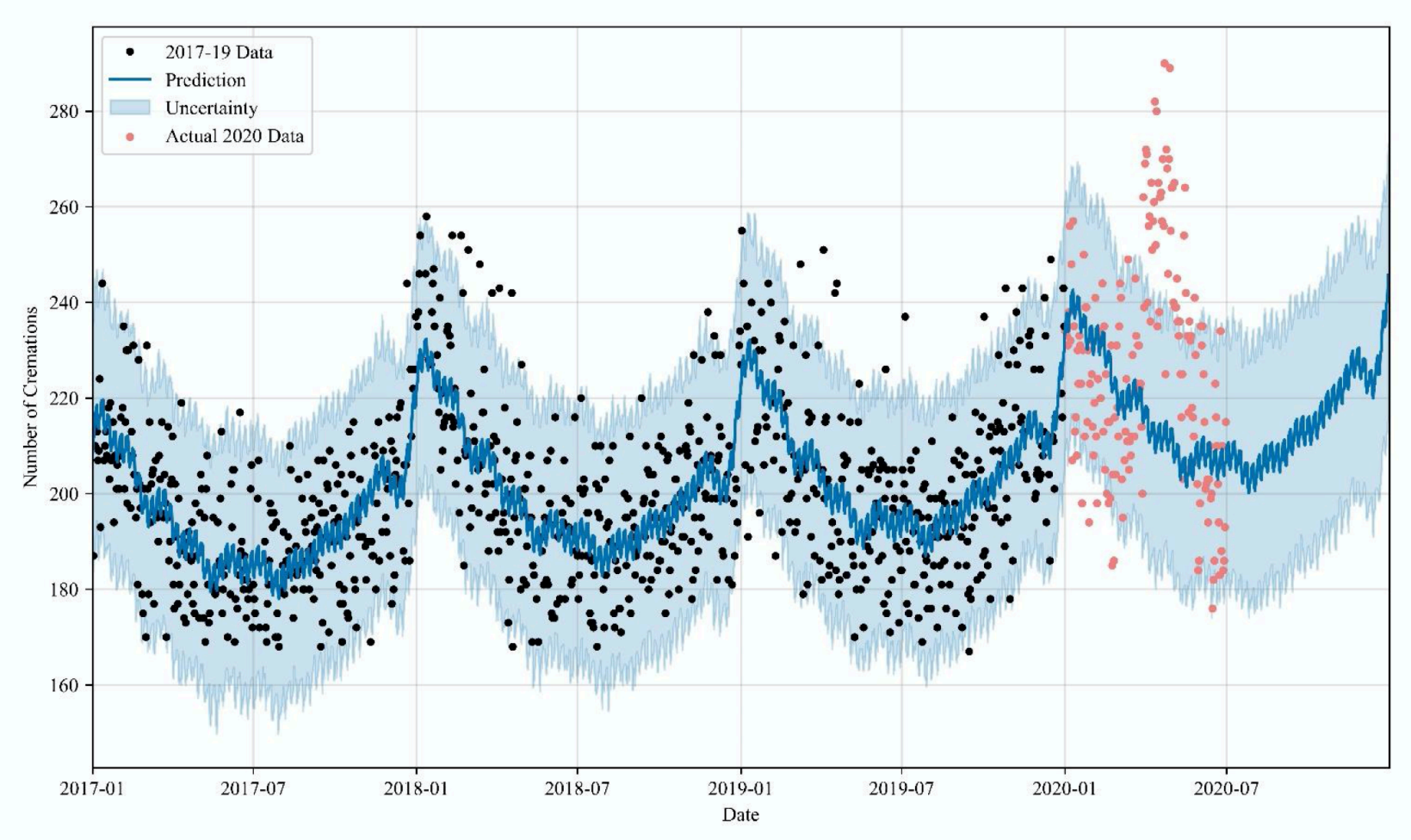
```
plot(rnorm(10))
```



tet

```
include_graphics2("http://www.biostat.mcgill.ca/hanley/statbook/OntarioCrematio
```

Figure 2: Weekly mortality rate from January 1, 2020 to May 31, 2020. The time series model is represented by the blue solid line and 95% confidence intervals in the shaded blue band.



sfs

```
ds=read.table("http://www.biostat.mcgill.ca/hanley/statbook/immunogenicityChAdO
str(ds)

## 'data.frame':^^I307 obs. of  2 variables:
##  $ RefIndexCategory             : Factor w/ 2 levels "Convalescent",..: 1 1 1
##  $ IgGResponse.log10.ElisaUnits: num  2.56 2.74 2.79 3.32 3.15 2.35 2.72 2.9

tail(ds)

##              RefIndexCategory IgGResponse.log10.ElisaUnits
## 302 Day28PostChAdOx1 nCoV-19                          1.99
## 303 Day28PostChAdOx1 nCoV-19                          1.99
## 304 Day28PostChAdOx1 nCoV-19                          2.42
## 305 Day28PostChAdOx1 nCoV-19                          2.46
## 306 Day28PostChAdOx1 nCoV-19                          2.42
## 307 Day28PostChAdOx1 nCoV-19                          1.17
```

Session Info

```
R version 3.6.2 (2019-12-12)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Pop!_OS 19.10

Matrix products: default
BLAS:   /usr/lib/x86_64-linux-gnu/openblas/libblas.so.3
LAPACK: /usr/lib/x86_64-linux-gnu/libopenblasp-r0.3.7.so

attached base packages:
[1] tools     stats     graphics  grDevices utils     datasets  methods
[8] base

other attached packages:
 [1] forcats_0.5.0      stringr_1.4.0      dplyr_1.0.2        purrr_0.3.4
 [5] readr_1.3.1        tidyr_1.1.2        tibble_3.0.3       ggplot2_3.3.2.9000
 [9] tidyverse_1.3.0    knitr_1.29

loaded via a namespace (and not attached):
 [1] Rcpp_1.0.4.6     highr_0.8        cellranger_1.1.0 pillar_1.4.6
 [5] compiler_3.6.2   dbplyr_1.4.2     jsonlite_1.7.0   lubridate_1.7.4
 [9] evaluate_0.14    lifecycle_0.2.0  gtable_0.3.0     pkgconfig_2.0.3
[13] rlang_0.4.7      reprex_0.3.0     cli_2.0.2        rstudioapi_0.11
[17] DBI_1.1.0        haven_2.3.1      xfun_0.16        withr_2.2.0
[21] xml2_1.3.0       httr_1.4.1       fs_1.3.2         generics_0.0.2
[25] vctrs_0.3.4      hms_0.5.3        grid_3.6.2       tidyselect_1.1.0
[29] glue_1.4.2       R6_2.4.1         fansi_0.4.1      readxl_1.3.1
[33] modelr_0.1.5     magrittr_1.5     backports_1.1.9  scales_1.1.1
[37] ellipsis_0.3.1   rvest_0.3.5      assertthat_0.2.1 colorspace_1.4-1
[41] stringi_1.4.6    munsell_0.5.0    broom_0.7.0      crayon_1.3.4
```