Cohort study into COVID-19 vaccine effectiveness (COVE study)

Collaboration RIVM, UMC Utrecht, Julius Clinical

Agenda

- Study team / division of tasks
- METC protocol
  - Objectives / endpoints
  - Study design
  - Study population
  - Sample size
- Timeline
- Action points

Study team / division of tasks

Tasks	RIVM	UMC Utrecht	Julius Clinical
Sponsor/opdrachtgever	X		
Protocol writing	X	X	X
Data collection/logistics			X
Data analysis	X (PhD)		
Data reporting	X (PhD)		
Project management	x (5.1.2e)		X
…			

Primary objective

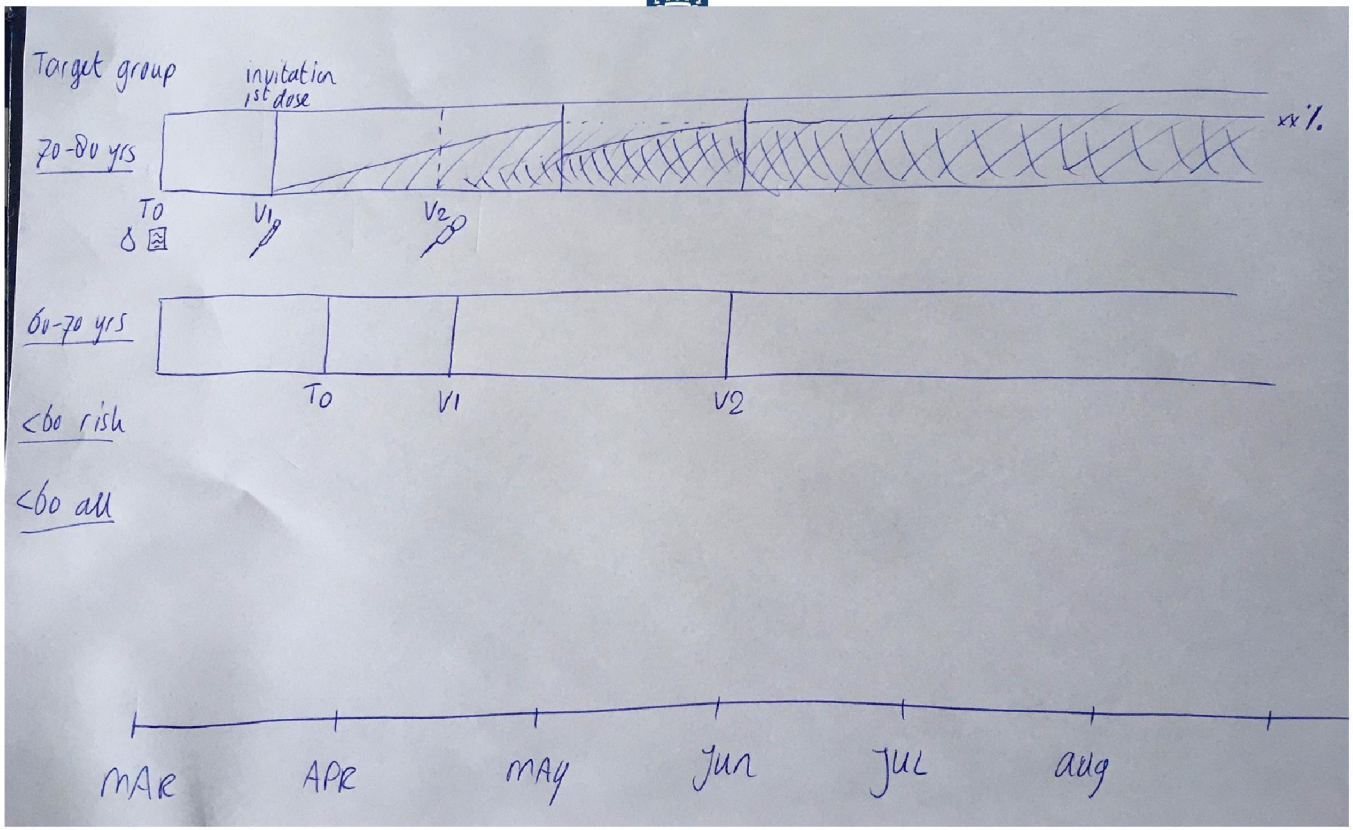
- To estimate product-specific VE of COVID-19 vaccines used in the Dutch national vaccination program against laboratory-confirmed SARS-CoV-2 infection at 12 months by age and medical risk groups
  - Include symptoms in end point? Or just according to testing policy?
  - Include positive tests based on population based screening, as now happening in geographic areas in NL?
  - Or 6 months?

Secondary objectives

- Product-specific VE against severe COVID-19 (hosp. and death)
- Product-specific VE by time since vaccination and nr doses
- Relative VE of different vaccines (in primary objective?)
- Monitoring (long-term) adverse events following immunization (definition, Lareb?)
- (Immunogenicity / immunologic parameters → substudy)
- (Regular (self) testing to detect asymptomatic infections → substudy)

Study design

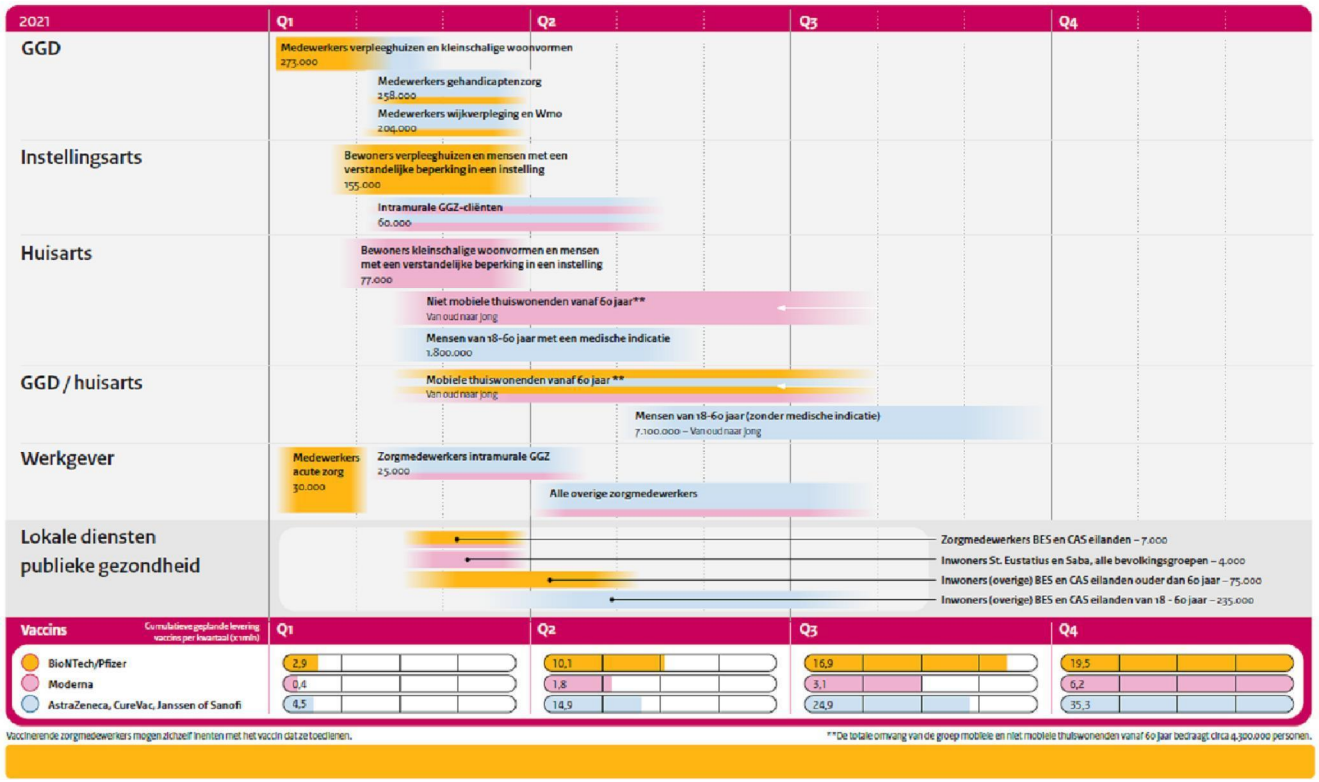
- Prospective observational cohort study
- Inclusion participants preferably at least 2-4 weeks before invitation COVID-19 vaccine
- COVID-19 vaccination given according to prioritization national vaccination program, not as part of the study
- Participants can contribute unvaccinated as well as vaccinated time (time varying exposure)
- Recruitment through BRP (stratified by age group and geographic region?) or through GP if sampling on medical risk group


Target group
invitation 1st dose
70-80 yrs
xx %
T0
V1
V2
60-70 yrs
T0
V1
V2
<60 risk
<60 all
MAR
APR
MAY
Jun
JUL
aug

Vaccinatiestrategie*

Afbeelding 1

*Let op! De gegevens waarop deze afbeelding is gebaseerd veranderen continue. Start en snelheid van vaccineren zijn voortdurend aan veranderingen onderhevig. De planning is afhankelijk van o.a. goedkeuring, werking, levering en distributie van de vaccins. Op basis van ontwikkelingen en adviezen kan ook veranderen welke groep welk vaccin krijgt.



Vaccinerende zorgmedewerkers mogen zichzelf inenten met het vaccin dat ze toedienen.

**De totale omvang van de groep mobiele en niet mobiele thuiswonenden vanaf 60 jaar bedraagt circa 4.300.000 personen.

Data collection

- Baseline questionnaire including sociodem, health status, behavior regarding COVID-19 measures
- Baseline self-administered fingerprick blood sample for SARS-CoV-2 antibodies
- Vaccination data through self-report and/or check/linkage with vaccination register CIMS
- Follow-up for endpoints through questionnaires, app, GP dossier, hospital
  - Self reported positive SARS-CoV-2 test?
- Covariate information can change of time → questionnaire at time of vaccination?

Study population

- Community dwelling adults 18-80 years who become eligible for COVID-19 vaccination
- Exclusion:
  - Contraindication for COVID-19 vaccination?

Sample size calculation

Parameter	Estimate (range)
Infection rate	27 per 100,000 per day (5-40)
Follow up period	12 months (6 months?)
Vaccination coverage	90% (60-90%)
Vaccine effectiveness	80% (70-90%); H0: 0%
Relative effectiveness	2.5 fold difference? (80% vs 50%)
Subgroups	4-6 vaccines, 3 age groups, 2 medical risk groups → 24-36 (equal?) strata
Power	80%
Alpha	5%
Sample size	~50,000

Statistical analysis

- Cox regression to compare incidence of infection in unvaccinated and vaccinated person time
- By vaccine product, age group, medical risk group
- Adjustment/stratification for calendar time
- Adjustment/stratification for region, sociodem, health status, behavior regarding measures (at time of vaccination?), e.g. using propensity score matching
- Exclude participants with SARS-CoV-2 antibodies at baseline in sensitivity analysis