

# Volunteer recruitment for controlled human infection models

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# Definition & purpose

# Definition



- Controlled
- Human
- Infection
- Model

CHIM

Clinical trials that expose volunteers to an infectious pathogen “**challenge agent**” to evoke an infection under well controlled conditions.

*“human challenge studies” (HCT), “human infection studies” (HIS), “human infection challenge studies” (HICS)*



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Clinical trials that expose volunteers to an infectious pathogen “**challenge agent**” to evoke an infection under **well controlled conditions**.

## All volunteers

- the same virus (strain)
- at the same dose
- exposure under the same conditions

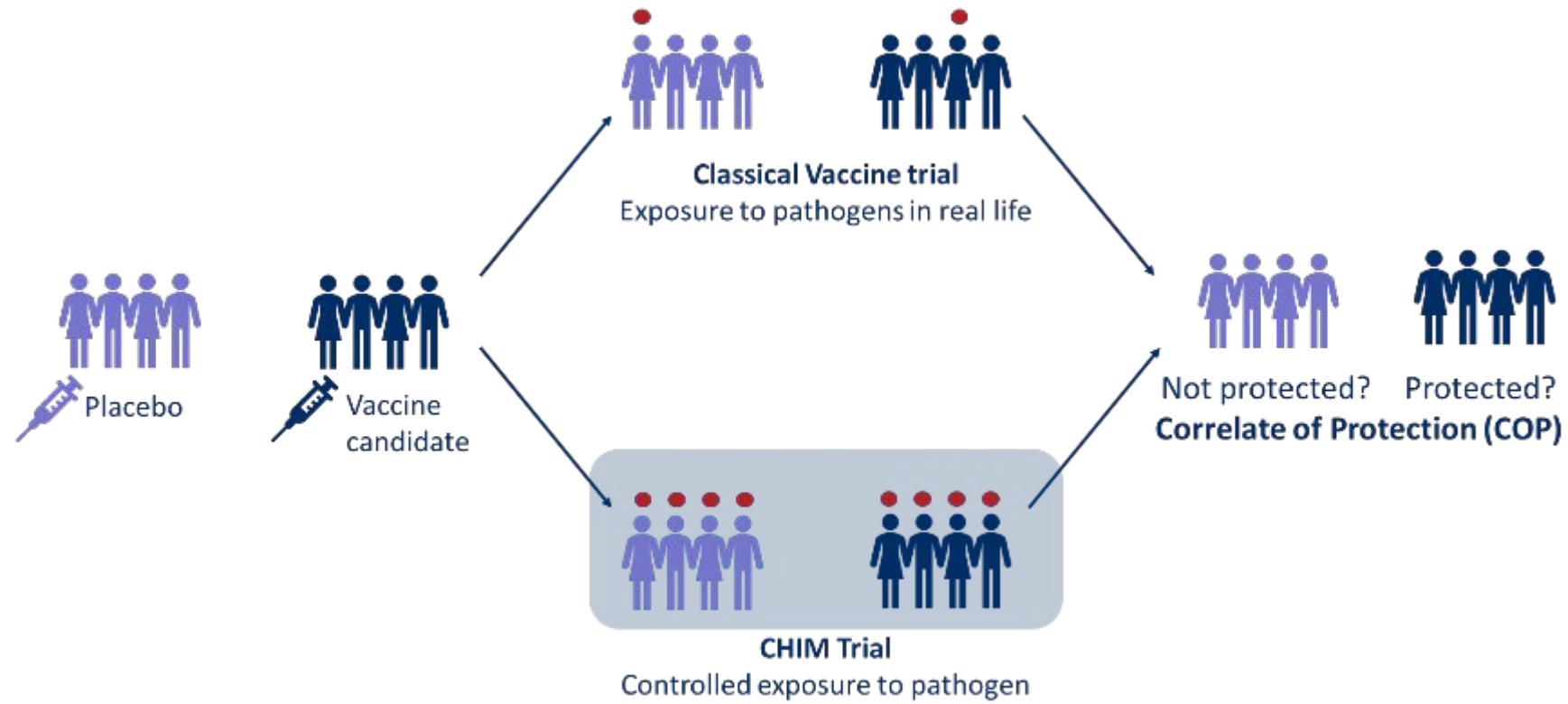


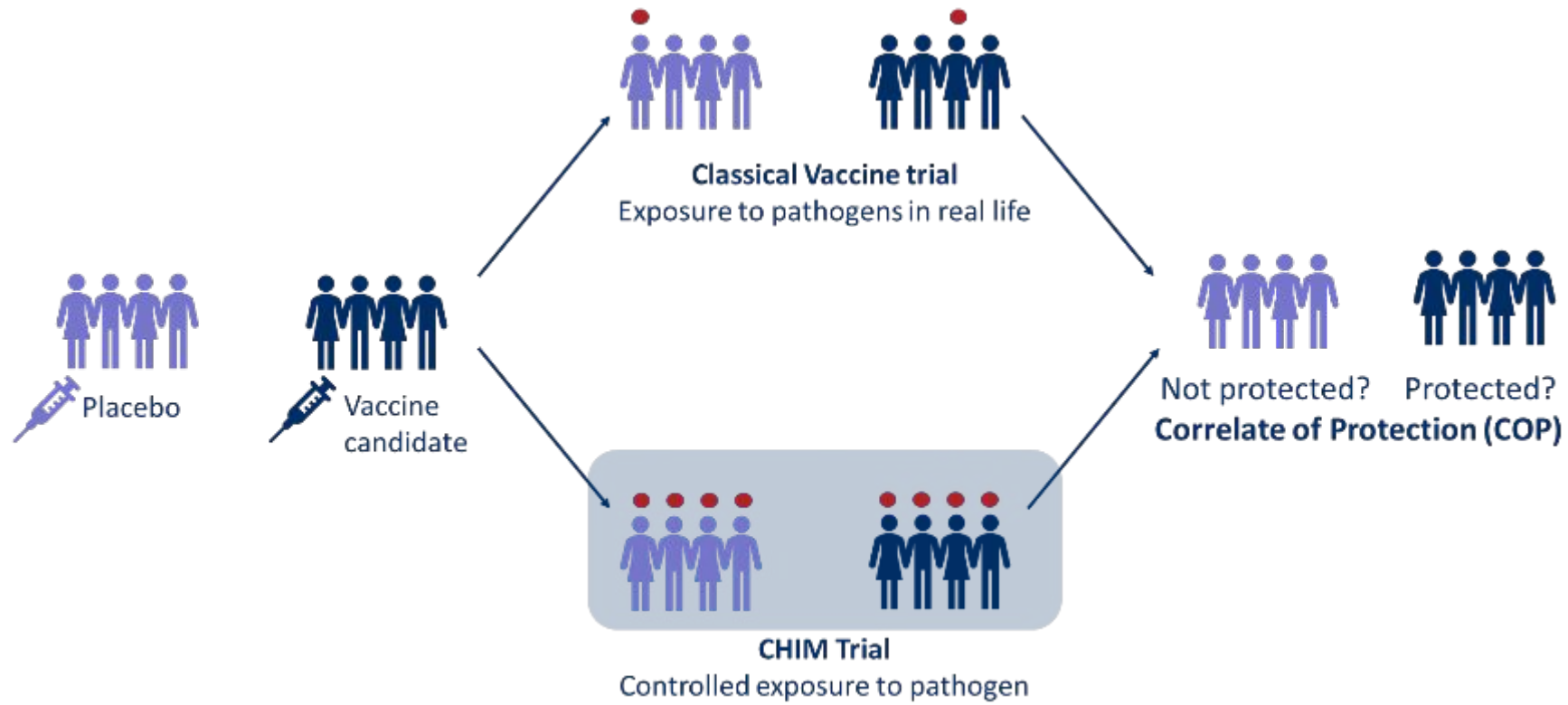
# Purpose?

- Develop models of infection (+ disease)
- Study
  - Processes of infection and immunity from inception
  - Correlates of immune protection
  - Transmission (potential)
- Test (novel) diagnostics, vaccines and therapeutics



Can accelerate the development of pharmaceutical interventions





	Classical Vaccine “field” Trial	CHIM Vaccine Trial
# Volunteers	1000 - 40 000	20 - 200
Trial duration	Long (years)	Shorter (months)
Cost	Very high	Less expensive
Low incidence of disease	Not feasible	Feasible
Generalisability	High	Low

# Safety & ethical considerations



# Safety

## Health risk?

Adverse events related to challenge

- **Systematic AE review of trials 1900–2017<sup>1</sup>**
  - 4 SAE and 0 deaths/permanent damage among 23 307 participants (0,2%)
- **Systematic AE review of trials 1980–2021<sup>2</sup>**
  - 24 SAE and 0 deaths/permanent damage among 15 046 participants (0,2%)

*Meta Roestenberg et al., Experimental infection of human volunteers. Lancet Infect Dis. 2018*

*Jupiter Adams-Phipps et al., A Systematic Review of Human Challenge Trials, Designs, and Safety., Clin Inf Dis 2023*

Statbel (Algemene Directie Statistiek - Statistics Belgium)

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## Comparators?

‘socially accepted risks’

- **Road traffic accidents Belgium 2023<sup>3</sup>**
  - 3.040 severe injuries and 475 deaths among 11.7M inhabitants (0.3%)
- **SAE in published phase I trials in healthy volunteers (2008–2012)<sup>4</sup>**
  - 15 possibly related SAE among 27,185 participants (0.1%)
- **Major surgical complication from living kidney donation (ICU/organ failure/death)**
  - 2.5% in US registry (2008–2012,  $n=14,964$ )

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  - **Experimental product**
    - Not different from classical trial
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## Benefits

- **Public health**
  - Develop better products faster
  - Reduce N volunteers exposed to product
  - Improve scientific understanding
- **Volunteers**
  - Health check/advise
  - Lower infection-related risk vs community
  - Natural immunity
  - Vaccine immunity (if received)

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**Ethical oversight ensures scientific soundness without unnecessary risk**

# Risk mitigation/minimization

## Volunteers

- Careful selection of low-risk volunteers (e.g. healthy young adults)
- Self-limiting or treatable diseases
- Challenge Agent
  - Attenuated strains instead of wild-type
  - Careful titration of pathogen dose
- Optimal medical care

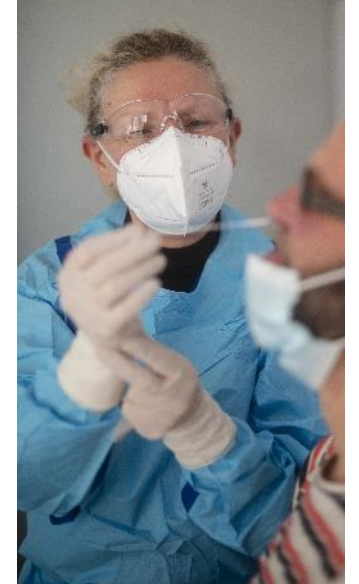
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## Staff & community

- Infection prevention and control
  - Protective equipment
  - Isolation of contagious volunteers
  - Desinfection
- Specialized facilities

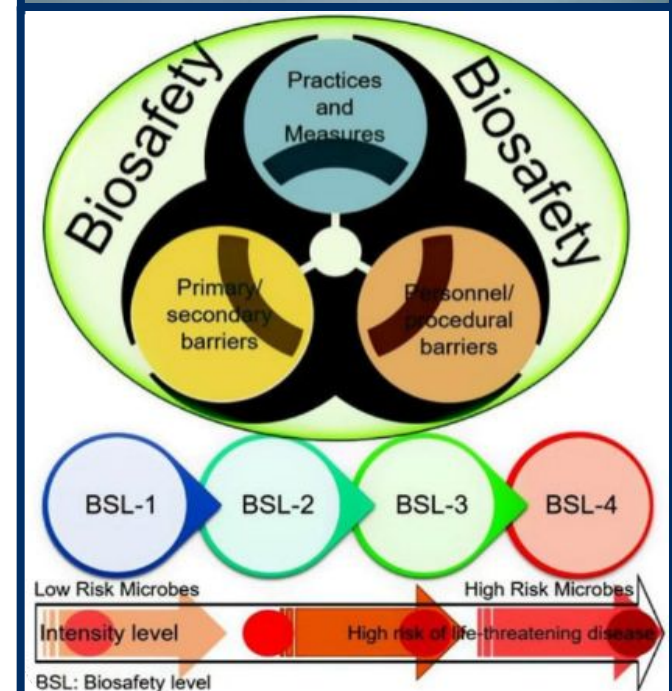




# Risk mitigation/minimization – quarantine

- **Specialised facilities**

- 30 individual negative-pressure rooms
- Individual sanitation & anteroom



# Ethical payment

- **Practical example:** Omicron BA.5 dose finding study pays £4935 ( $\approx$ £10.5/h). Minimum wage UK: £8,6/h
- **Traditional reimbursement frameworks** and controversies apply

Reimbursement

+ compensation

+ incentive & risk

- See also “Guidance on Compensation of Clinical Research Participants” from the Belgian Association of Research Ethics Committees (BAREC)

# Emerging pathogens: altered calculus

- Need for speed!
- More uncertainty about immediate and long-term health risks
- Higher (personal) risk in trial, but also in community
- Higher (societal) benefit (?)

# Recruitment

Specifics to CHIMS

# Who usually participates in a CHIM?

- **Survey of 201 subjects of enteric pathogen CHIMs in Oxford 2011–2017**
  - Demographics
    - Age: median 27
    - Education level: 57% bachelor or higher
    - Employment: 62% had employment 30% were students, 5% unemployed
  - Motivations
    - Contribute to the progress of medicine: 85% (strongly) agree
    - Financial reimbursement: 83% (strongly) agree
    - Opportunity to participate in a clinical trial: 69% (strongly) agree
    - To learn more about own health: 54% (strongly) agree

# Who usually participates in a CHIM?

- **Survey of 201 subjects of enteric pathogen CHIMs in Oxford 2011–2017**
  - 69% asked someone else's opinion before enrolling in the trial, of which 33% had some positive and some negative advice, versus 33% mostly negative advice
  - 79% would 'probably' advise friends & family to join a CHIM

# Who usually participates in a CHIM?

- **Survey of 1911 willing to join CHIMs through 1DaySooner, and 999 controls between**
  - Demographics: the 'CHIM willing' were skewed towards young, white, male, highly educated, employed, high income, health insured persons



# Who usually participates in a CHIM?

Motivation	Number (%) rating motivation in the top three reasons for volunteering <sup>1</sup>
I wanted to help others and potentially save lives	1832 (95.9)
I wanted to contribute to the progress of medicine	1513 (79.2)
I feel helpless and this is a way to do something positive	890 (46.6)
Another factor not mentioned	380 (19.9)
I wanted to be part of a clinical trial	348 (18.2)
I am likely to be infected by COVID-19 anyway	282 (14.8)
I was curious about COVID-19	170 (8.9)
I wanted to be guaranteed access to critical care should I be infected with COVID-19	156 (8.2)
I wanted to find out more about my own health	83 (4.3)
I wanted to receive the financial reimbursement for participating	79 (4.1)

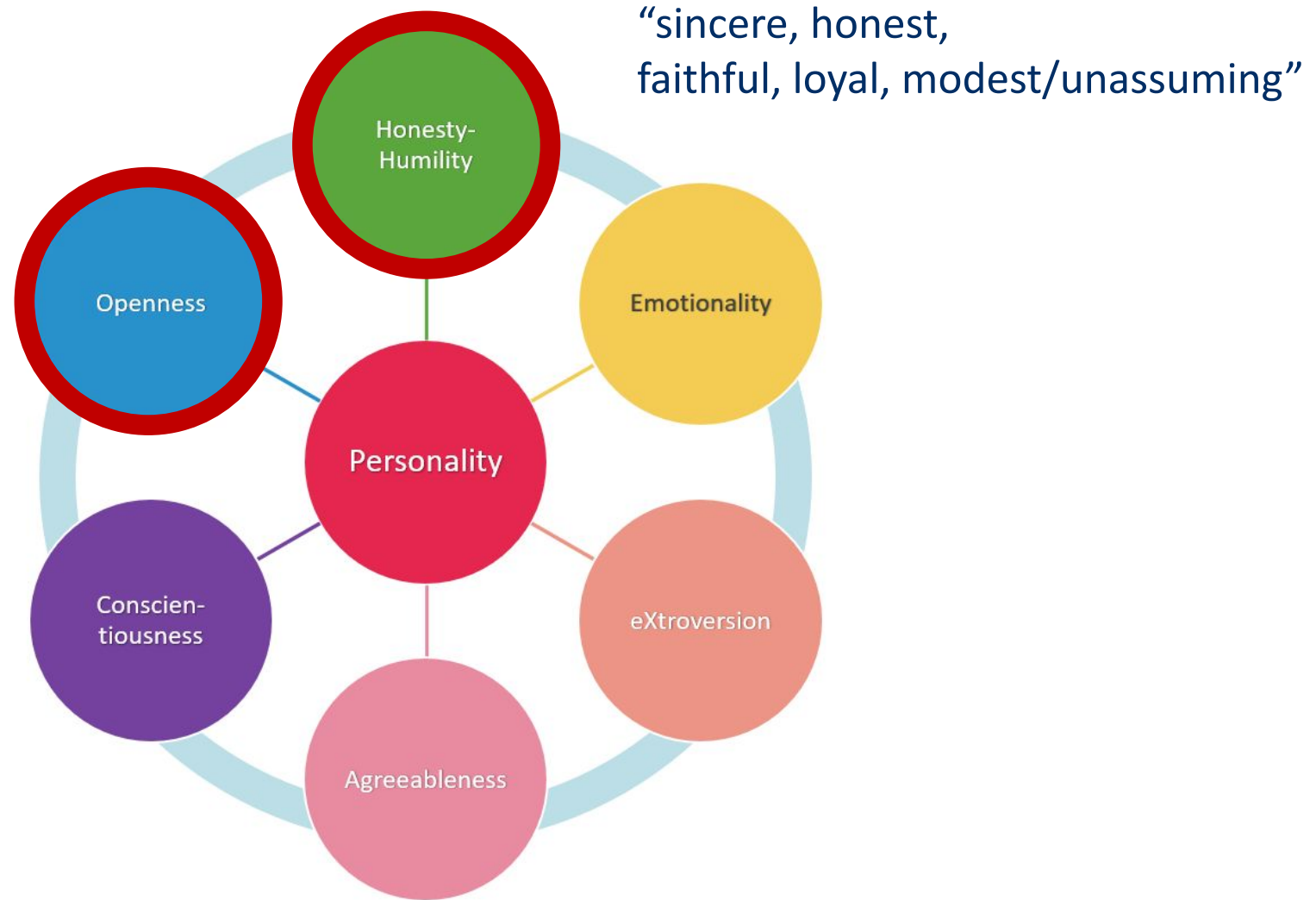
<sup>1</sup> Since volunteers were asked to rate whether the choices above were in their top three reasons, percentages total 300% instead of 100% (with exceptions due to rounding).

<https://doi.org/10.1371/journal.pone.0275823.t002>



# Who usually participates in a CHIM?

“intellectual, creative,  
unconventional, innovative,  
ironic”



# How are participants best reached?

- **Survey of 299 participants screened for a ‘first in the country’ CHIM in Blantyre, Malawi (2021–2022)**
  - Recruitment methods
    - Sensitisation events at 8 colleges
    - ‘Snowball’ or ‘word-of-mouth’ recruitment
    - Traditional media outreach: 4 radio shows and 2 television broadcasts
    - Digital media outreach: Youtube video on Wellcome Trust Malawi (100s of views)
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  - How were you motivated to join the study?
    - Word of mouth: 72%
    - Sensitisation event: 27%

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- **Survey of 136 healthy subjects of phase 1 trials Portugal 2007**
  - How were you motivated to join the study?
    - Word of mouth: 95%
    - Posters in public area's: 13%
  - Personal contact factors
    - 88% asked someone else's opinion before enrolling in the trial, of which 80% had at least some negative advise
    - 89% would advise friends & family to join a study, while 10% 'may'

# Important considerations in CHIM recruitment

# 1. Quarantaine

## For participants

- What is available and provided?
- What activities are allowed/restricted?
- Hygiene measures?
- How to stay in touch with outside world?

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## For trial site

- Assess possible psychological impact of quarantine at screening?

Questionnaires (PHQ-9, GAD-7)

Clinical psychological evaluation

- Assess/manage group dynamics?

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“Speci  
al”  
proto

Distinction between study withdrawal and  
lifting isolation





## 2. Informed Consent

- Often more complex
  - Multiple screening visits
  - Comprehension test
  - Updates to scientific knowledge

# Recruitment at Vaccinopolis CHIM unit

# Recruitment at Vaccinopolis

## Completed efforts

- Focus on existing participant pool, which means focus on the Antwerp area
- Understand knowledge, perceptions and willingness to join CHIMs (research project at FAGG)

# Participate in a human infection study

## What to expect?

[Study, registration & screening](#) | [Your stay at Vaccinopolis](#)



## Human infection study?

Also known as human challenge study or controlled human infection model "CHIM" study where you are deliberately exposed to an infectious pathogen (like a virus, bacteria or parasite) under well controlled and safe conditions to evoke an infection.

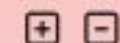


# Universiteit Antwerpen

Centrum voor de Evaluatie van Vaccinaties  
Vaccin en Infectieziekten Instituut

Returning?

AAA



## CHIM volunteer database

Als u gezond bent en tussen 18 en 65 jaar oud bent, kan u zich inschrijven in onze vrijwilligersdatabank om op de hoogte te blijven van gecontroleerde besmettingsstudies bij mensen in Vaccinopolis. Uw gegevens worden vertrouwelijk behandeld en enkel gebruikt om u te informeren over de studies waarvoor we deelnemers zoeken en waarvoor u misschien in aanmerking komt. De eerste studies zullen in 2025 plaatsvinden. Gelieve alle velden in te vullen.

*If you are healthy and between 18 and 65 years old, you can register in our volunteer database to stay informed about controlled human infection studies conducted at Vaccinopolis. Your data will be treated confidentially and only used to inform you about the studies for which we are looking for participants and for which you might be eligible. The first studies will take place in 2025. Please complete all fields.*

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# Recruitment at Vaccinopolis

## Completed efforts

- Focus on existing participant pool, which means focus on the Antwerp area
- Understand knowledge, perceptions and willingness to join CHIMs (research project at FAGG)

## In the works

- Wider geographical area (in-patient studies)
- Social media
- Active community engagement as part of an “inbound marketing strategy”

# Conclusions

- **CHIMs can generate early efficacy data on a limited number of subjects**
- **Stringent recruitment to balance benefits & harms**
- **Ethical compensation follows traditional frameworks**
- **Participants join because of both altruistic and financial reasons**
- **Recruitment requires additional emphasis on**
  - Informed consent
  - The burden of quarantine
- **Expanding recruitment from an existing ‘community’ and focussing on those scoring high on ‘honesty/humility’ and ‘openness’**

Questions / comments?