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## Background

- Post-COVID condition (PCC): Substantial global burden of disease
- The combined effect of preceding SARS-CoV-2 infections and vaccinations on PCC is unclear
- Aim: Evaluate the influence of hybrid immunity on development of PCC

## Methods

### Study Design

- German National Cohort (NAKO)
- Prospective cohort study
- Recruitment: 2014 – 2019
- Over 200,000 participants
- 18 study centers (Figure 1)
- 2022: Online Survey

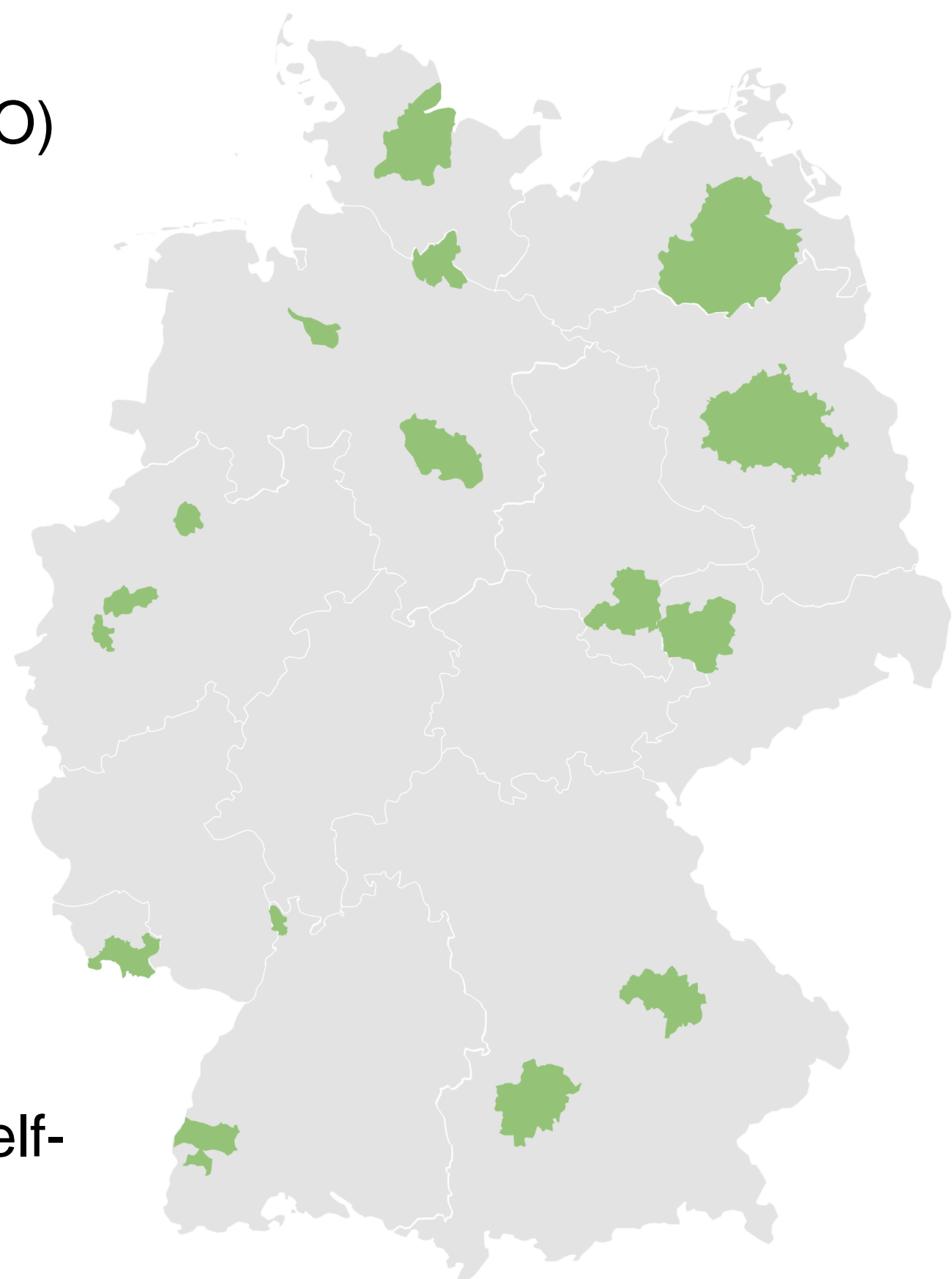


Figure 1. Study regions

### Measures

- Retrospective information:
  - SARS-CoV-2 infection(s)
  - Vaccinations
  - Symptoms
- Any PCC:
  - at least one out of 21 self-reported symptoms
  - 4-12 months post-infection
- High symptom burden PCC:
  - nine or more symptoms

### Statistical Analysis

- Multivariable logistic regression (for vaccinated individuals)
  - Sex
  - Age
  - Study Center
  - Time since last vaccination
  - Time since last infection
  - Virus variant (based on time in which infection occurred)
  - Symptoms at acute infection
- Each individual is included only once
- Two infections:
  - only analyzed the second infection, in case they did not develop PCC at their first infection
- Time components of protection: generalized additive models

## Conclusion

- Risk of developing PCC was strongly reduced for the second SARS-CoV-2 infection, if the first infection did not result in PCC
- The two components of risk reduction after a preceding infection suggest different immunological mechanisms
- More recent virus variants: associated with a lower risk
- Protective effect linked to the fourth vaccination
- Increased vulnerability towards PCC when a breakthrough SARS-CoV-2 infection occurred within 0 to 3 months of vaccination
- Hybrid immunity is likely to considerably decrease the long-term incidence of PCC

## Results

### Characteristics

- 109,707 NAKO participants analyzed
- 65,773 (60%) reported at least one SARS-CoV-2 infection (Figure 2)
- 5,621 (5%) reported more than one SARS-CoV-2 infection
- 92,021 (84%) had received three or more COVID-19 vaccinations

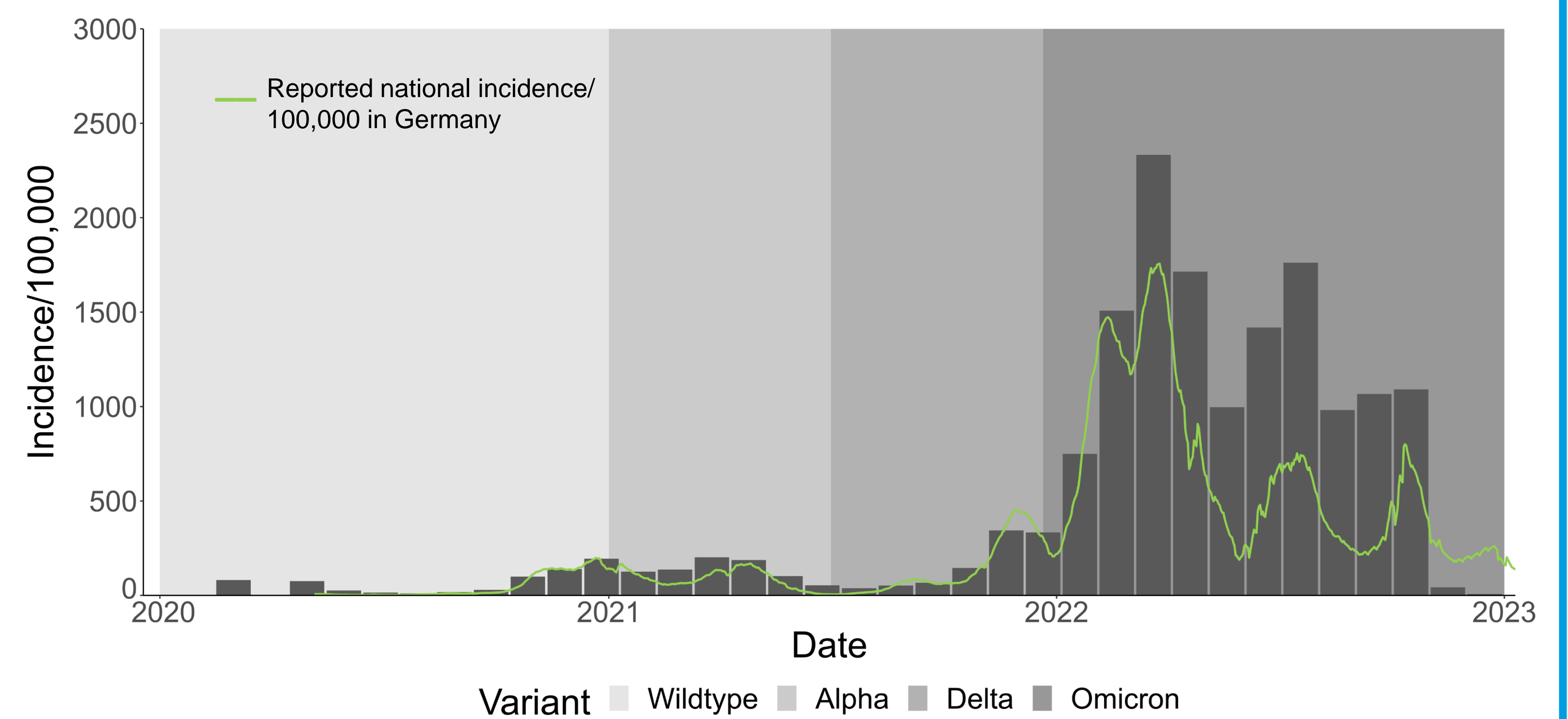


Figure 2. Monthly SARS-CoV-2 incidence in the NAKO study

### PCC

- 19,476 individuals
- 35% of respondents who were infected and observed for at least 4 months
- 4,525 (23%) were classified as a high symptom burden PCC

### Influence of virus variant, previous infections and vaccinations

- Individuals with previous infection:
  - Lower risk of developing PCC after the second infection
- Four vaccinations during Omicron:
  - Better protection against any PCC
- Multivariable analysis:
  - Previous infection: Long-term risk reduction of around 50%
  - Additional temporary risk reduction (Figure 3)
  - Risk of developing PCC: higher within the first 3 months after receiving a SARS-CoV-2 vaccination
  - Results similar for the endpoints of any PCC and high symptom burden PCC

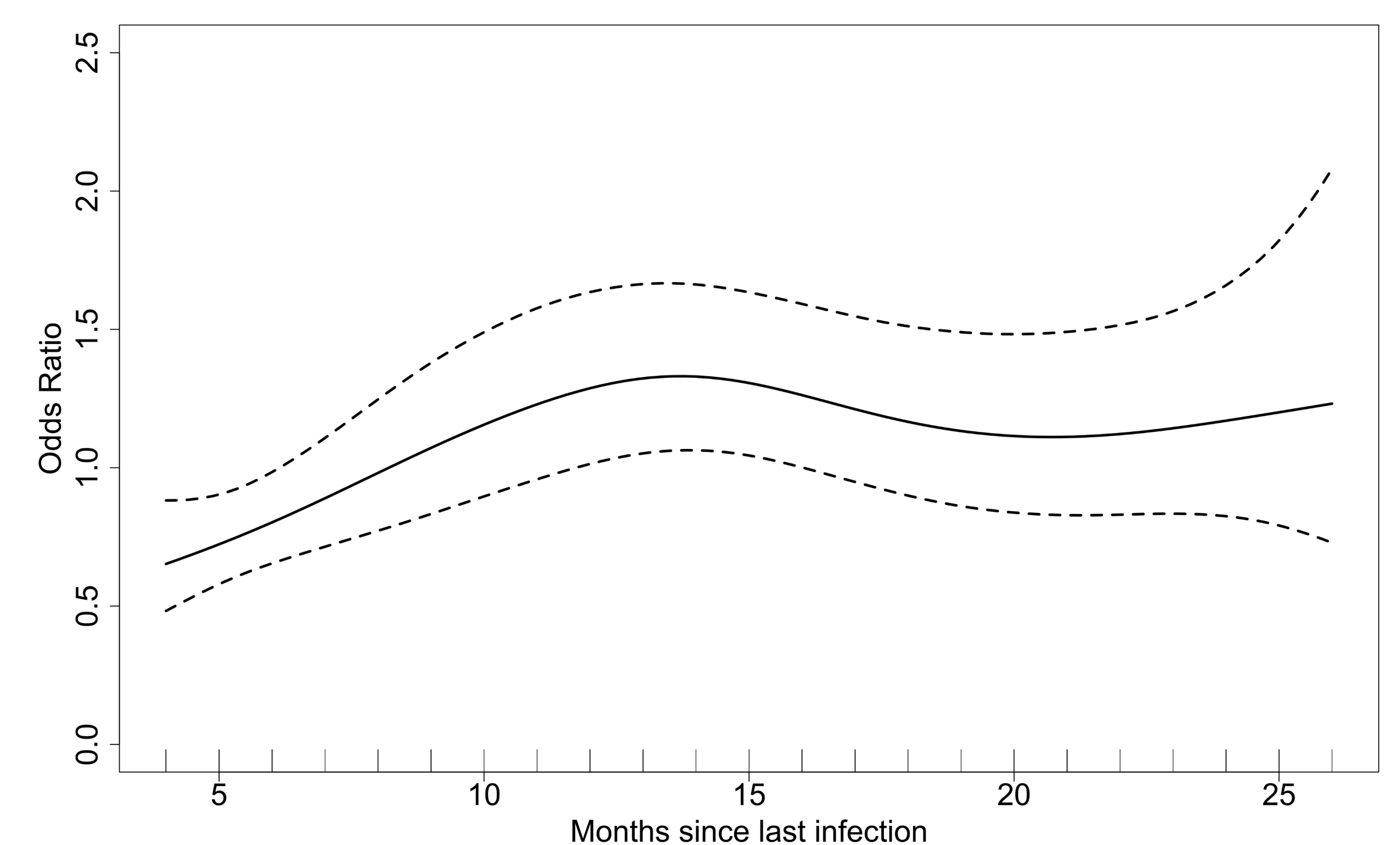


Figure 3. Association between time since preceding infection and the expected risk of experiencing any PCC after a reinfection

