LMU KLINIKUM

Abteilung für Infektions- und Tropenmedizin

HelmholtzZentrum münchen

Deutsches Forschungszentrum für Gesundheit und Umwelt

Prospective Covid-19 Cohort München *KoCo19*

- **Kooperation Klinikum der LMU und Helmholtz Zentrum München**

- InterTB 16.10.2020
- Prof. Dr. Michael Hoelscher

- Michael Pritsch, Inge Kroidl, Laura Olbrich, Jessica Guggenbühl, Andreas Wieser, Elmar Saathoff, Friedrich Rieß, Ahbishek Bakuli, Noemi Castelletti
- Katja Radon, Arbeitsmedizin (KUM)
- Jan Hasenauer, Universität Bonn
- Christiane Fuchs, Universität Bielefeld

Chronology of events

27. Jan 20 — Identification of the first SARS-CoV-2 infection in DE at the Tropical Institute in Munich (subsequently 15 cases)

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany

online: N ENGL J MED JAN 30, 2020

Science

Study claiming new coronavirus can be transmitted by people without symptoms was flawed

By Kai Kupferschmidt | Feb. 3, 2020 , 5:30 PM

THE 100 MOST INFLUENTIAL PEOPLE OF 2020

Camilla Rothe

Article

Virological assessment of hospitalized patients with COVID-2019

https://doi.org/10.1038/s41586-020-2196-x
Received: 1 March 2020
Accepted: 24 March 2020

Roman Wölfel[1,6], Victor M. Corman[1,6], Wolfgang Guggemos[1,6], Michael Seilmaier[1], Sabine Zange[1], Marcel A. Müller[2], Daniela Niemeyer[1], Terry C. Jones[1,3,4], Patrick Vollmar[1], Camilla Rothe[1], Michael Hoelscher[1], Tobias Bleicker[1], Sebastian Brünink[1], Julia Schneider[1], Rosina Ehmann[1], Katrin Zwirglmaier[1], Christian Drosten[2,7,8] & Clemens Wendtner[1,7,8]

"All the News That's Fit to Print"

The New York Times

Late Edition

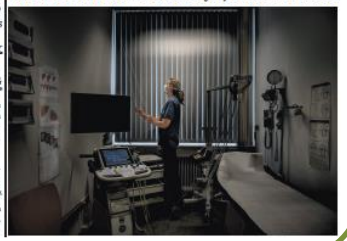
VOL. CLXIX ... No. 58,739 NEW YORK, SUNDAY, JUNE 28, 2020 $5.00

Voters' Moods: Tired, Anxious And Optimistic

Betting on the Election as a Turning Point

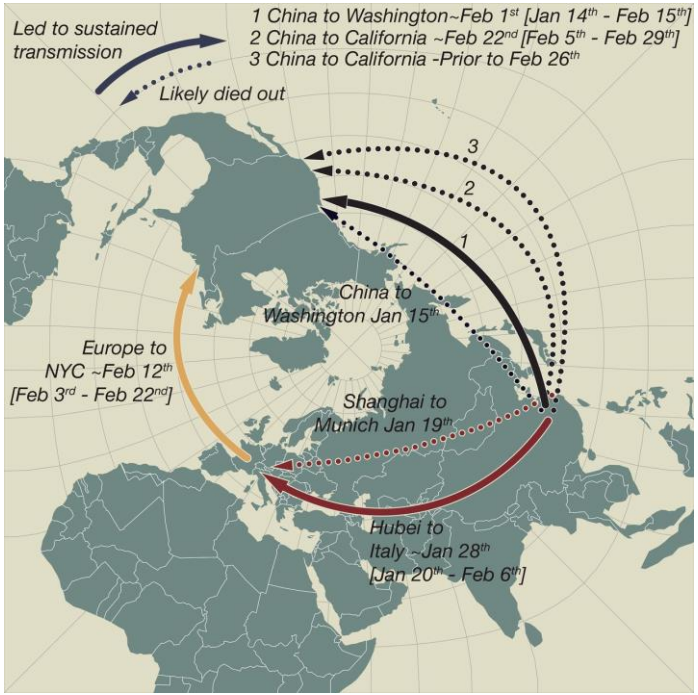
Cases Soaring As Leadership On Virus Fails

How the World Missed Covid's Symptom-Free Carriers



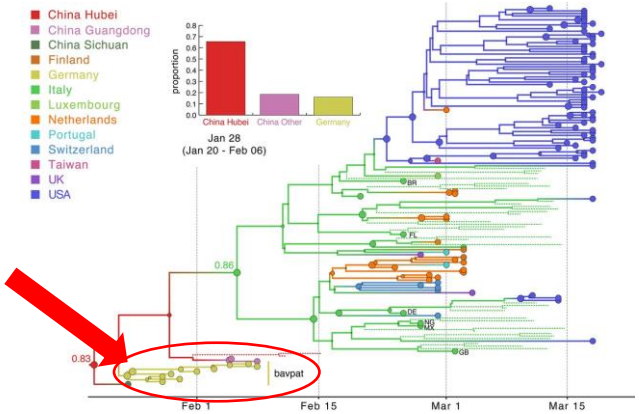
Initial spread of the virus

SARS-CoV-2 introductions to Europe and the US.



Michael Worobey et al. Science 2020

MCC tree of SARS-CoV-2 entry into Europe.

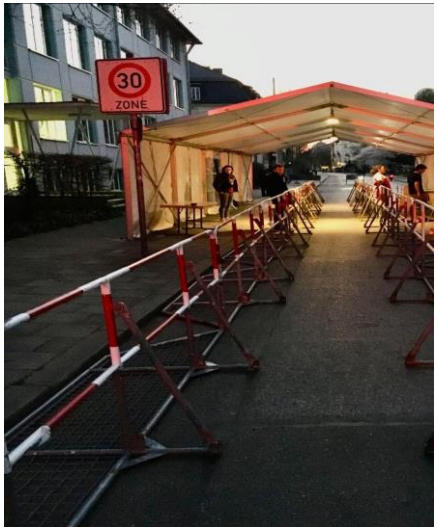


Michael Worobey et al. Science 2020

Science
AAAS

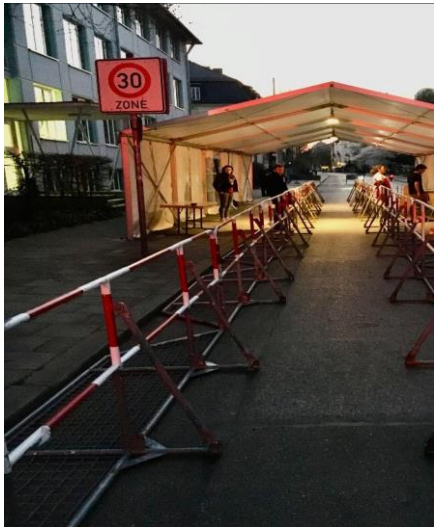
Chronology of events

27. Jan 20	Identification of the first SARS-CoV-2 infection in DE at the Tropical Institute in Munich (subsequently 15 cases)
02. Mar 20	Next SARS-CoV-2 cases in Munich after Ski-holidays
17. Mar 20	Establishment of a drive-through station at the institute

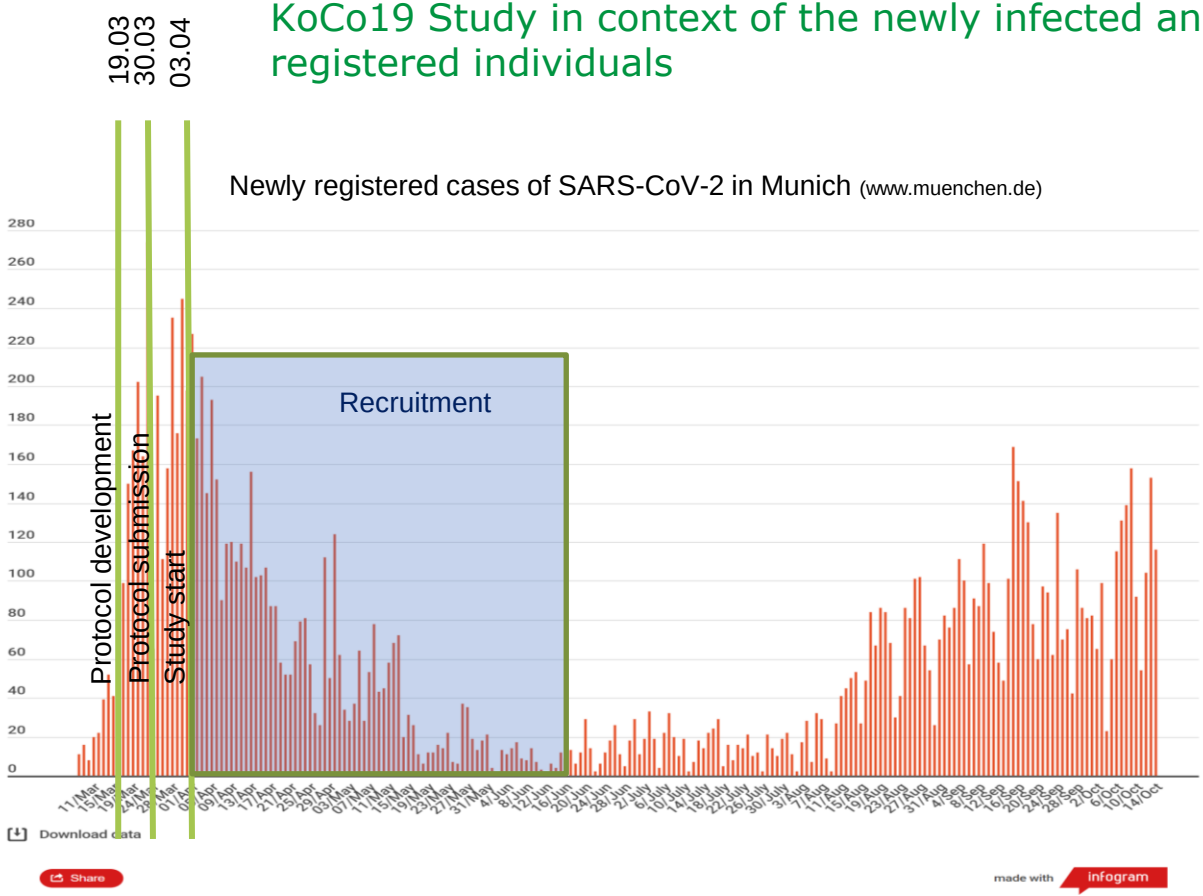


Chronology of events

27. Jan 20	Identification of the first SARS-CoV-2 infection in DE at the Tropical Institute in Munich (subsequently 15 cases)
02. Mar 20	Next SARS-CoV-2 cases in Munich after Ski-holidays
17. Mar 20	Establishment of a drive-through station at the institute
19. Mar 20	Concept idea for a population-based study to monitor the effect of social distancing measures
20. Mar 20	partial lock-down announced by the Bavarian Government
30. Mar 20	Submission of study protocol and temp. approval 2 days later
03. Apr 20	Official announcement of the study
05. Apr 20	Study start
12. Jun 20	Completion of the enrolment of 3.004 households and 5842 household members



KoCo19 Study in context of the newly infected and registered individuals



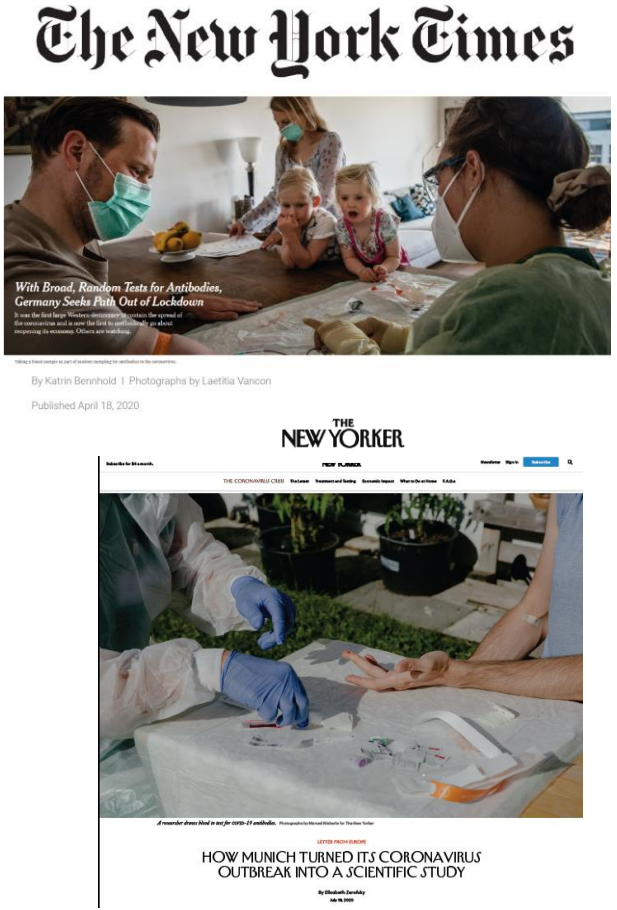
Start early or later?

- Expected low prevalence and uncertain sensitivity and specificity of serological assays –> positive predictive value very low.
- There was no clear forecast how the epidemic would evolve – so better start early than never.
- Assess data and samples that never can be retrieved anymore.
- Early data are important to refine strategy – an iterative process of learning and improving study concepts on the fly.

It is a long-term project

Challenges

- At the beginning of the pandemic (January - March) all "experts" were busy organizing local emergency aid and informing politicians and the public.
- A coordinated approach between different research groups was practically impossible.
- There were no established scientific networks. Infection epidemiology is a weakly developed field of research in Germany.
- We did not know of similar activities in Germany, Europe or world-wide.
- There were no immediate financial resources available.
- The lack of an established research toolkit (assays) requires until today a high degree of flexibility.
- The pace of scientific knowledge gain is still so high today that the concepts have to be constantly updated.
- **For the first time in the science of history, the project is in the middle of public interest and has become a live documentation.**

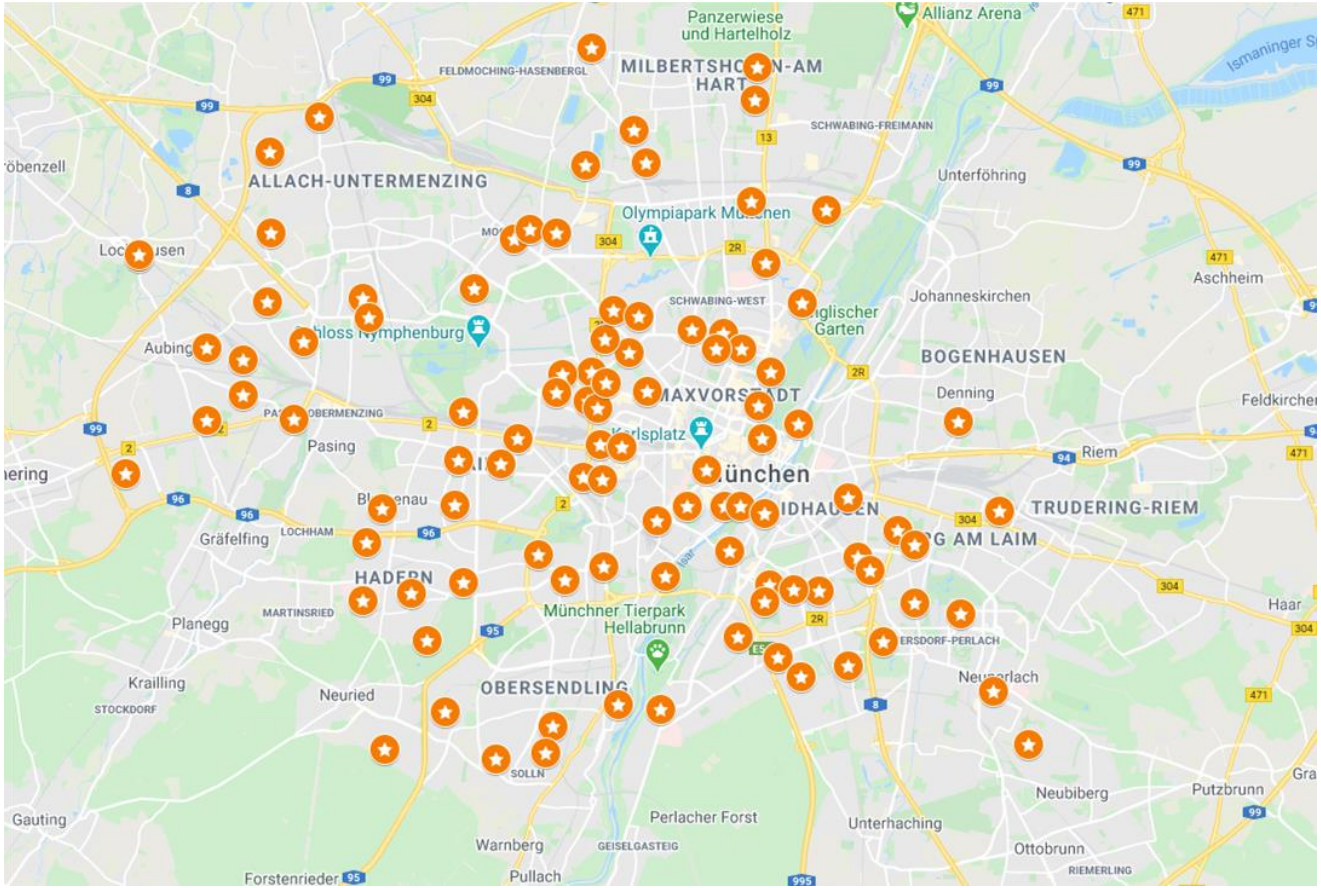


Study objectives:

- To describe the SARS-CoV-2 antibody prevalence in the a representative sample of the general population in Munich.
- To understand the proportion of identified versus unrecognized infections.
- In what regards are reognized and unrecognized individuals different (biologically and socioeconomical)
- What is the transmission rate in a household?
- Determine the durability of antibodies after infection.
- Describe the influence do social isolation measures on the incidence?
- To track changes of social behaviour change within the cohort, and what impact does individual behaviour have on the individual risk of infection?
- What is the socio-economic impact of the pandemic and the measures to combat it, in particular on the employment situation and psychological endpoints.

Study design

- Starting points of the random route in 100 of 755 constituencies
- 30 households are selected in each constituency
- Each HH includes all HH members
- For people over 14 years of age 2.7 ml of blood was taken. For children under 14 years of age 300ul was collected from the fingertip. (starting on 15.05)
- Everyone filled out a weekly electronic questionnaire on their state of health
- Repetitions every12 weeks or according to epidemiological situation



Practical implementation

- Complete look-down
- Had to train 80 medical students in outreach teams of two
- Have enough personal protective equipment
- Rented of fleet of 30 cars
- Support by police to avoid fraud by others
- Did built a complete new serology lab

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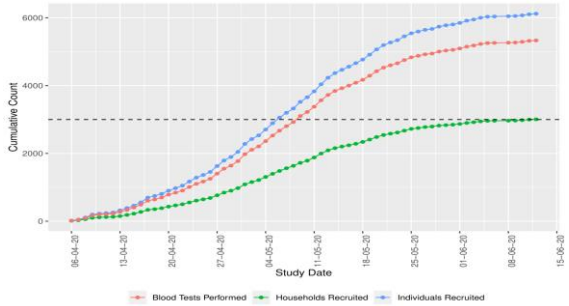
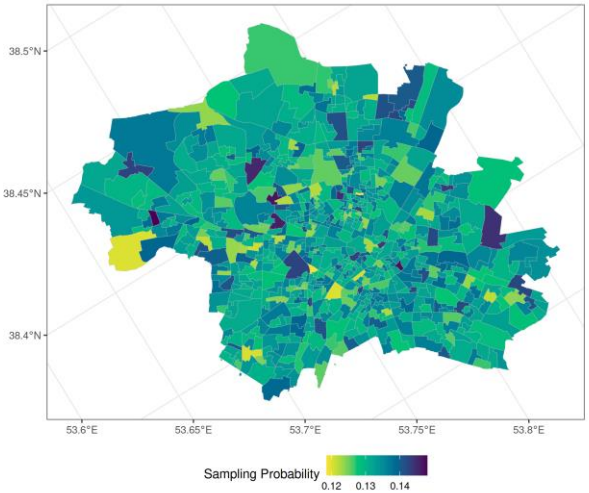
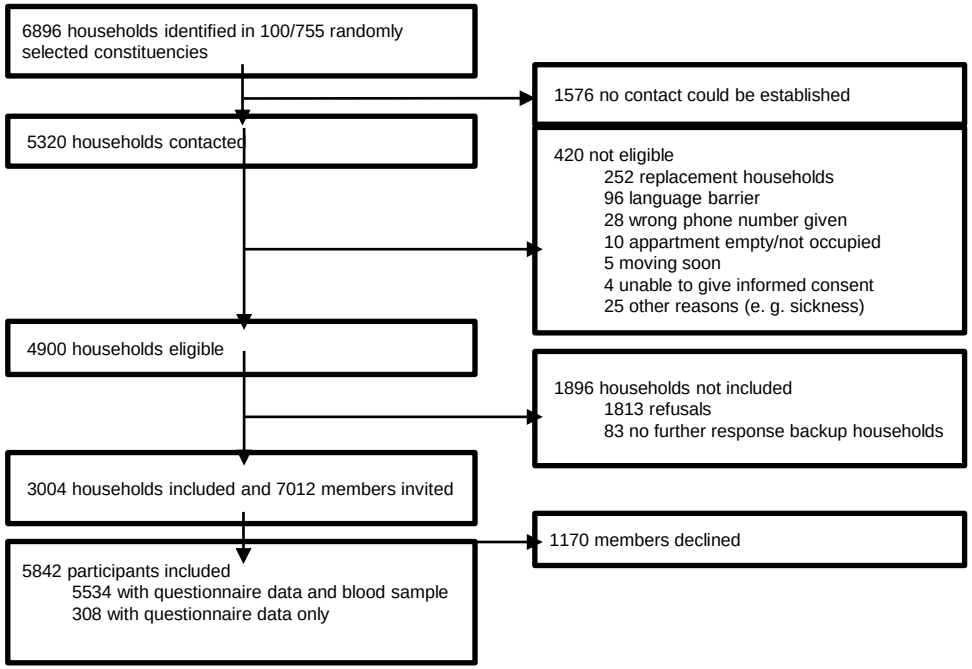
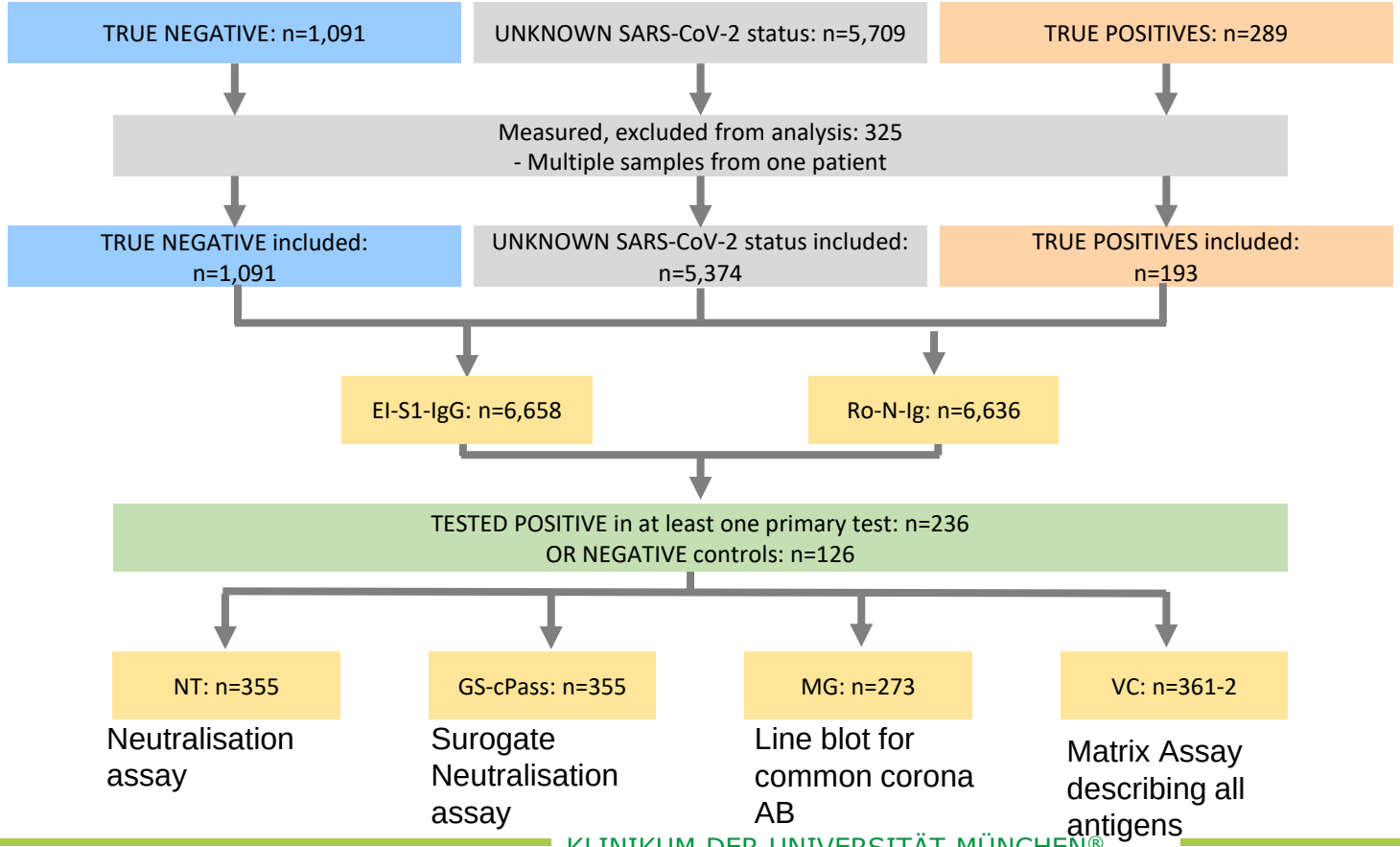
Recruitment:



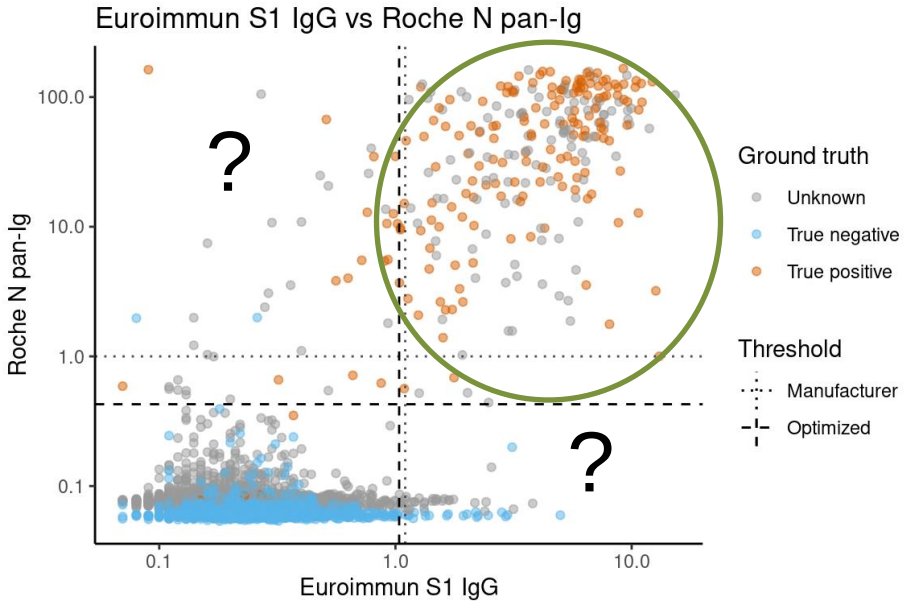




Validation of 7 assays

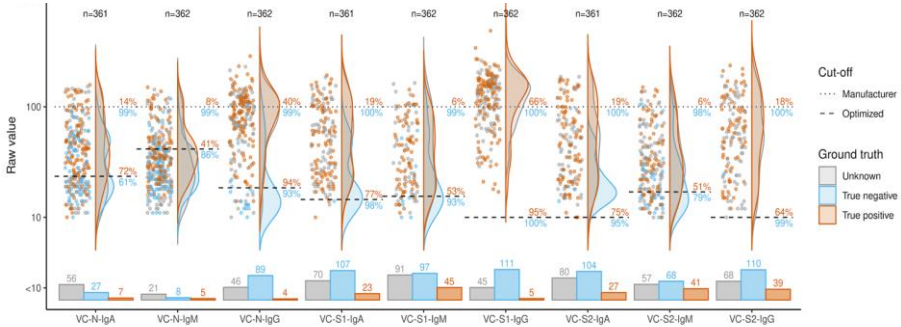


Performance of assays



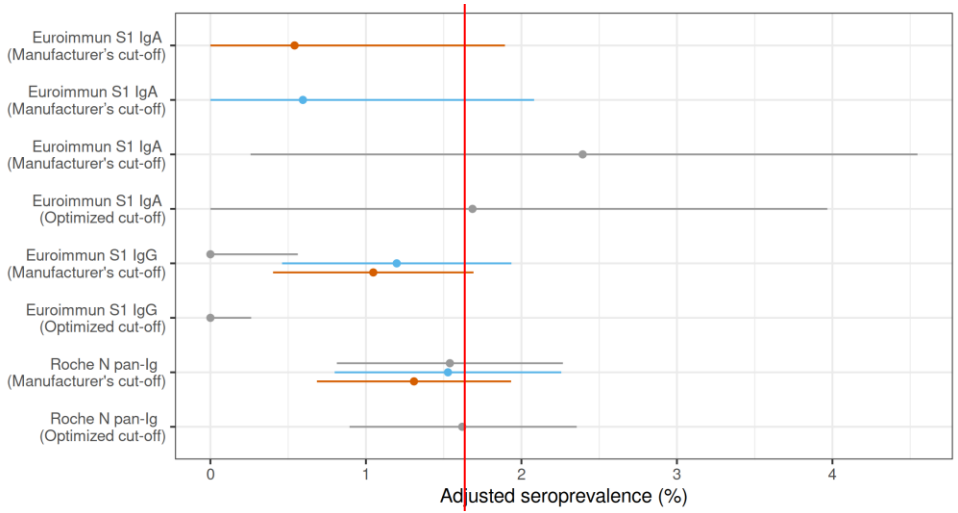
Classifier	Specificity Manufacturer	Specificity Optimized	Sensitivity Manufacturer (low)	Sensitivity Manufacturer (high)	Sensitivity Optimized
Euroimmun S1 IgA (Manufacturer's cut-off)	0.924	0.933	0.917	1.000	0.648
Euroimmun S1 IgA (Optimized cut-off)		0.926			0.648
Euroimmun S1 IgG (Manufacturer's cut-off)	0.993	0.980	0.875	1.000	0.772
Euroimmun S1 IgG (Optimized cut-off)		0.978			0.798
Roche N pan-Ig (Manufacturer's cut-off)	0.998	0.998	0.853	0.995	0.855
Roche N pan-Ig (Optimized cut-off)		0.997			0.886

Performance of confirmatory assays

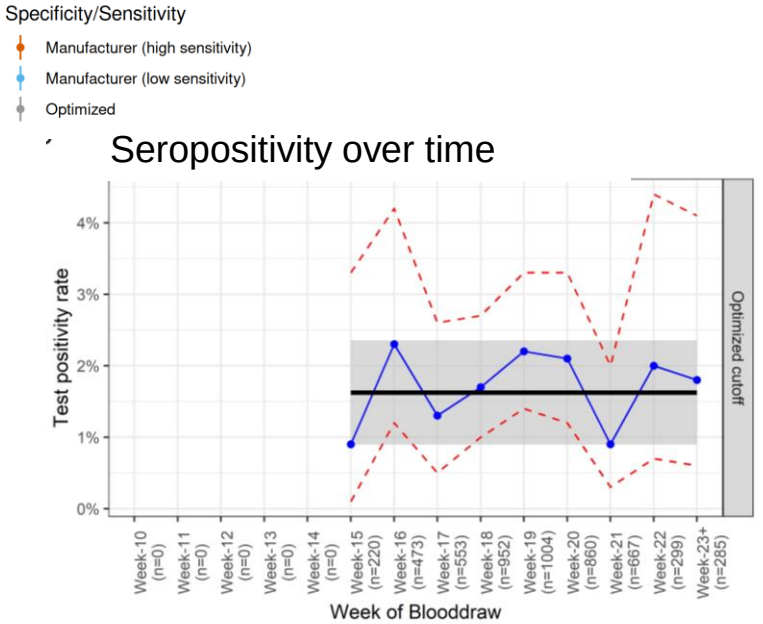


Prevalence

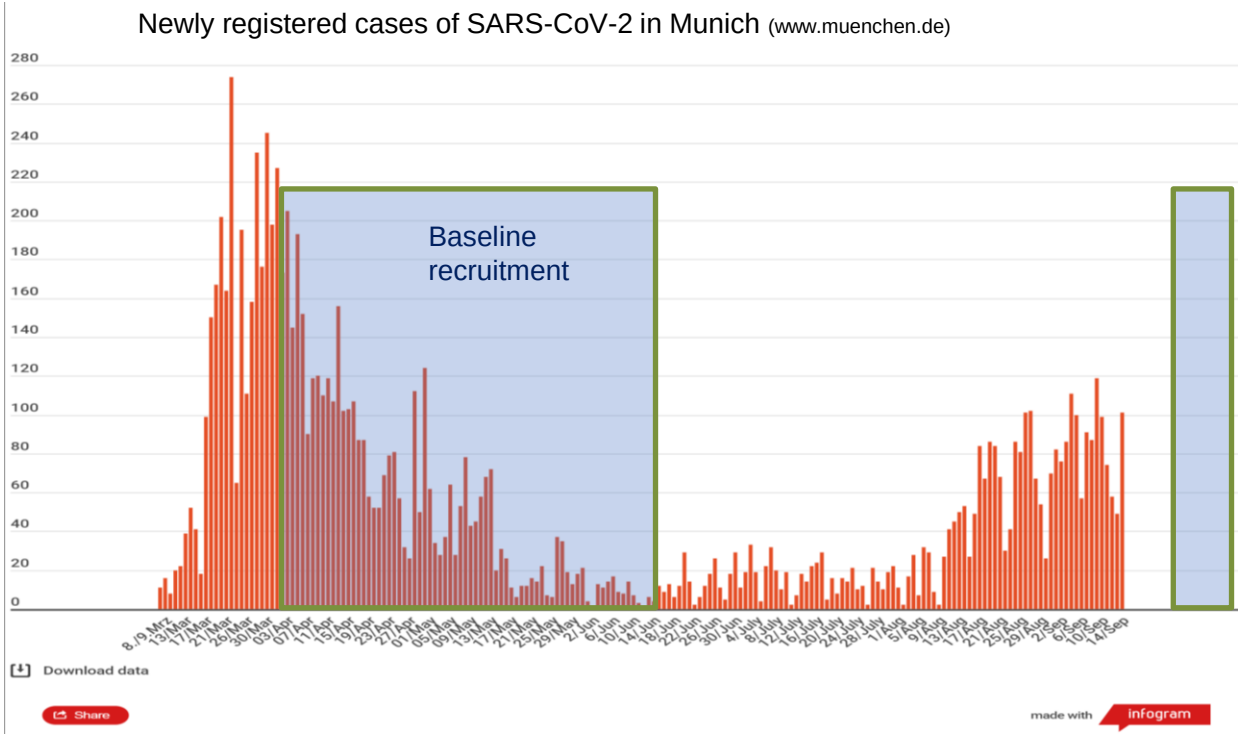
Prevalence adjusted for sensitivity and specificty



1,6% Seroprevalence
vs.
0,4% registered positive PCR cases



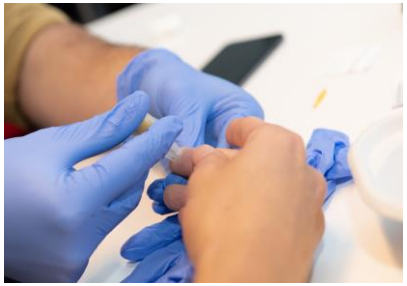
Next steps?



Follow-up

How much has the proportion of undetected cases has changed since we are testing 4-5 times more?

Fingerprick self-sampling

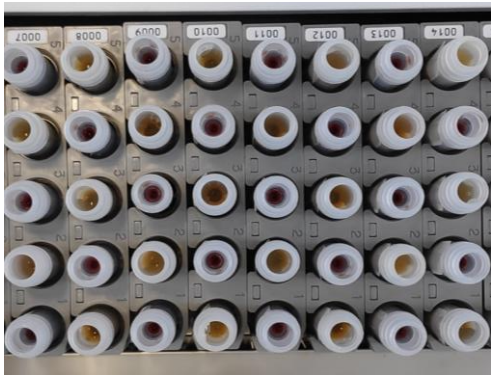


Automatisation of dried blood serology

Panthera puncher System

Elution of Antibodies

Robotic Cup-Transfer

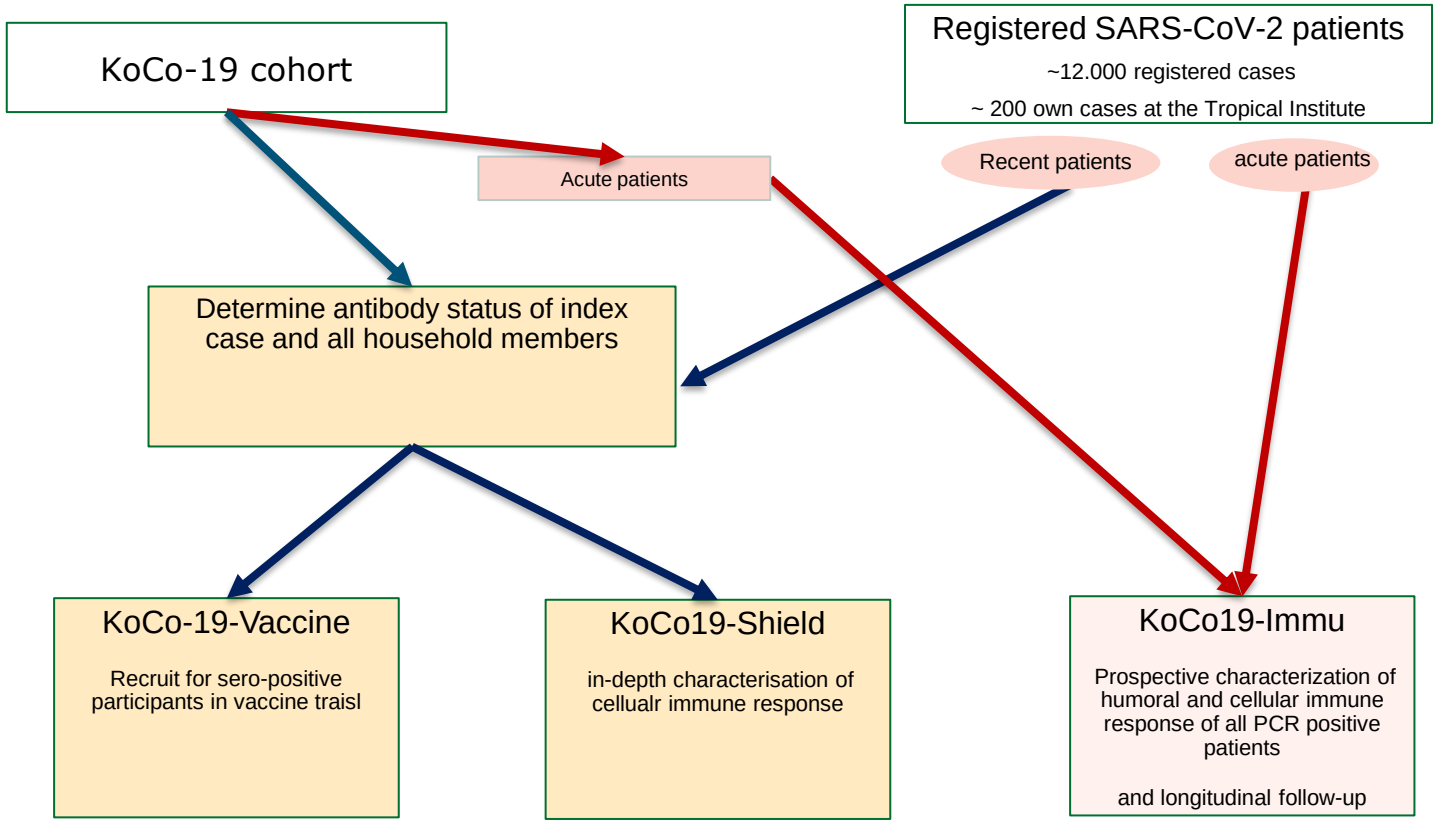


Measurement
(qualitative)

DBS are stable after drying:
Initial experiments compared: 4-7°C, 37°C, -20°C, -80°C
-> for at least 4 days no significant changes in eluted functional Antibodies
-> DBS are stable for extended periods; test now > 4 weeks

KoCo-19 study family

Acute infections
Retrospective analysis of transmission



KoCo19-Reinfection

To study the probability of reinfection and ist risk factors

Additional SARS-CoV-2 seroprevalence studies

German National Cohort: longitudinal serosurvey in an existing cohort of 180.000 individuals in 16 regions in Germany (starting in January 2021)

ORCHESTRA

CONNECTING EUROPEAN COHORTS TO INCREASE COMMON AND EFFECTIVE RESPONSE TO SARS-COV-2 PANDEMIC: **ORCHESTRA**

COVID-19 Serosurvey in Africa

Partner

- Jimma University Medical center (JUMC)
- Ludwig-Maximilians-University (LMU) Munich
- Helmholtz Center, Epidemiology

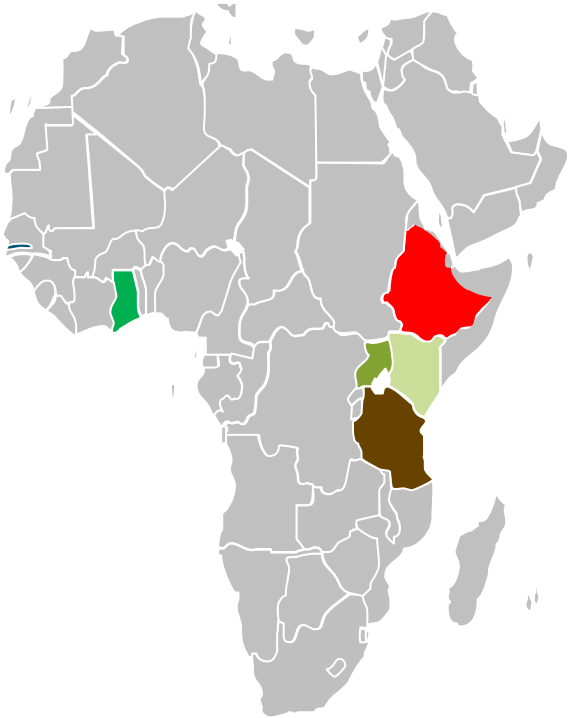
Populations

- Household based survey general population
- Target institutions (health facilities, schools, university, police)

Planned Activities:

- 1-3 monthly serosurveys (dry blood spots)
- eHealth data capture & dissemination (DHIS-2, SORMAS)
- Clinical, socio-economic, ecological, community assessments

Impact of Covid-19 infection on lung function in TB patients



Tanzania
- NIMR-Mbeya Medical Research Center, Mbeya
- Ludwig-Maximilians-University (LMU) Munich

Ethiopia
- Asella Teaching and Referral Hospital
- Heinrich-Heine-University Düsseldorf

Ghana
- Komfo Anokye Teaching Hospital (KATH) , Kumasi,
- University Hospital Hamburg Eppendorf

Rwanda
- Université National du Rwanda, Butare
- Charité – Universitätsmedizin Berlin

Kenya
- Kenyatta National Hospital, University of Nairobi
- Goethe University Frankfurt

Uganda
- Kiruddu National Referral Hospital, Kampala
- University Hospital Leipzig

Studyteam

- Study design: M. Hoelscher, E. Saathoff, K. Radon
- Modelling: J. Hasenauer, C. Fuchs, A. Bakuli, N. Castelletti, F. Theis
- Testing: A. Wieser, R. Wölfel, V. Fingerle, M. Münchhoff, E. Zeggini, C. Geldmacher
- Clinical team: M. Pritsch, I. Kroidl, L. Oblrich, G. Froeschl, V. Thiel, D. Metaxa, C. Rothe
- Data Collection & Management: F. Riess, M. Diefenbach
- Socio-economic analysis: R. Leidl, L. Schwettmann, M. Laxy, S. Prückner
- Project management: J. Guggenbühl, O. Geisenberger, L. Hoffmann, A. Mekota, A. Heiber
- Communication: J. Eckstein
- Field team in alphabetic order: Alexander, Alina, Alisa, Anna, Charlotte, Claire, Clemens, Dafni, Ekaterina, Elias, Elmar, Emma, Eva, Felix, Flora, Friedrich, Friedrich, Hannah, Inge, Isabel, Isabel, Jakob, Jan, Jan, Janna, Jared, Jasmin, Jeni, Jessica, Jonathan, Julia, Julian, Julius, Kerstin, Konstantin, Kristina, Lara, Laura, Laura, Lea, Leonard, Leonie, Magdalena, Marius, Matthias, Max, Maximilian, Michael, Michael, Niklas, Norah, Patrick, Paul, Paula, Philine, Rebecca, Rebecca, Sabine, Silvan, Simon, Sonja, Sophie, Stefan, Stefanie, Thomas, Tim, Tim, Tobias, Ursula, Valeria, Vera, Verena, Vitus

Thank you for your attention

More information

www.KoCo19.de