Highlights from Corona Immunitas

A Switzerland-wide research program on SARS-CoV-2

SSPH+ online Faculty Meeting, June 17 2020

The Corona Immunitas Team
Why viral detection (PCR) alone is not enough to determine the spread

Infection

- Incubation period 5-6 days
- Latency period 2-3 days
  - Infected but not infectious

Symptoms

- Infectious for approx. 10 days
  - No symptoms yet but infectious
  - Possibly symptoms and infectious

→ Symptoms only in around 50% and often mild
→ Virus testing (PCR) usually only with symptoms (in CH)
→ Number of persons with positive virus testing ≈ 10-20% of all
Immune response as proof of infection
Surveillance using serological (antibody) studies – main questions

- How many of a population has been infected by SARS-CoV-2?
- How many persons with SARS-CoV-2 infection illness have or little symptoms?
- Is an infection associated with immunity? Factors associated with (partial) immunity?
- How is the spread changing over time?
- How do protective measures impact on the spread of SARS-CoV-2 infections?

Rapid review of serological studies worldwide (so far)

Bobrovitz et al May 14 2020; https://www.medrxiv.org/content/10.1101/2020.05.10.20097451v1
Estimates and limitations of serological studies worldwide (so far)

- Mostly cross-sectional surveys
- No estimates at low risk of bias
- Inadequate sampling methods (mostly convenience samples)
- Unclear antibody test performance
- Lack of coordinated efforts → test fatigue and patchwork
- Lack of additional information (symptoms, risk factors, behavior, etc)

### Table: Serological Studies Worldwide

<table>
<thead>
<tr>
<th>Region</th>
<th>Test Characteristics</th>
<th>Sampling frame and method</th>
<th>N</th>
<th>Seropositive Prevalence</th>
<th>Total Cases/1M Pop.</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing Study</strong></td>
<td></td>
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</tr>
<tr>
<td>Chelsea, US</td>
<td>LFIA (88.7%, 96.6%)</td>
<td>General pop.: convenience</td>
<td>200</td>
<td>31.5%</td>
<td>6,287</td>
<td>High</td>
</tr>
<tr>
<td>Brevard County, US</td>
<td>LFIA (100%, 100%)</td>
<td>RT-PCR-tested: self-referral</td>
<td>1,000</td>
<td>1%</td>
<td>11,33</td>
<td>High</td>
</tr>
<tr>
<td>New York State, US</td>
<td>NR</td>
<td>Supermarket shoppers: convenience</td>
<td>7,500</td>
<td>14.9%</td>
<td>14,985</td>
<td>Unclear</td>
</tr>
<tr>
<td>New York City, US</td>
<td>NR</td>
<td>Supermarket shoppers: convenience</td>
<td>24.7%</td>
<td>14,985</td>
<td>Unclear</td>
<td></td>
</tr>
<tr>
<td>Westchester/Rockland, US</td>
<td>NR</td>
<td>Supermarket shoppers: convenience</td>
<td>NR</td>
<td>15.1%</td>
<td>14,985</td>
<td>Unclear</td>
</tr>
<tr>
<td>Long Island, US</td>
<td>NR</td>
<td>Supermarket shoppers: convenience</td>
<td>14.4%</td>
<td>14,985</td>
<td>Unclear</td>
<td></td>
</tr>
<tr>
<td>New York upstate, US</td>
<td>NR</td>
<td>Supermarket shoppers: convenience</td>
<td>NR</td>
<td>3.2%</td>
<td>14,985</td>
<td>Unclear</td>
</tr>
<tr>
<td>Idaho, US</td>
<td>NR</td>
<td>Patients: self-referral</td>
<td>1,946</td>
<td>1.8%</td>
<td>1,046</td>
<td>Moderate</td>
</tr>
<tr>
<td>Miami, US</td>
<td>Immunochromatography (88.7%, 90.6%)</td>
<td>General pop.: random</td>
<td>NR</td>
<td>6% (4.4-7.9%)</td>
<td>1,439</td>
<td>Unclear</td>
</tr>
<tr>
<td>San Miguel County, US</td>
<td>NR</td>
<td>General pop.: entire population</td>
<td>986</td>
<td>9.8%</td>
<td>1,121</td>
<td>High</td>
</tr>
<tr>
<td>Lebanon/Claremont, US</td>
<td>NR</td>
<td>Healthcare workers: self-referral</td>
<td>47</td>
<td>2%</td>
<td>1,442</td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Completed Study</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Denmark</td>
<td>LFIA (85%, 100%)</td>
<td>Blood donors: sequential</td>
<td>9,496</td>
<td>1.7% (0.9-2.3%)</td>
<td>754</td>
<td>Moderate</td>
</tr>
<tr>
<td>Oise, France</td>
<td>ELISA, S-FLOW, LIPS (~59%)</td>
<td>Teachers: cluster-based</td>
<td>53</td>
<td>43.4%</td>
<td>615</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parents: cluster-based</td>
<td>211</td>
<td>11.4%</td>
<td>615</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Students’ siblings: cluster-based</td>
<td>127</td>
<td>10.2%</td>
<td>615</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Students: cluster-based</td>
<td>240</td>
<td>38.3%</td>
<td>615</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-teacher staff: cluster-based</td>
<td>27</td>
<td>59.3%</td>
<td>615</td>
<td>High</td>
</tr>
<tr>
<td>Paris/Oise, France</td>
<td>ELISA, S-FLOW, LIPS</td>
<td>Blood donors: unclear</td>
<td>200</td>
<td>3%</td>
<td>168</td>
<td>High</td>
</tr>
<tr>
<td>Gauget, Germany</td>
<td>NR</td>
<td>General pop.: unclear</td>
<td>500</td>
<td>14%</td>
<td>1,552</td>
<td>High</td>
</tr>
</tbody>
</table>

Bobrovitz et al May 14 2020; [https://www.medrxiv.org/content/10.1101/2020.05.10.20097451v1](https://www.medrxiv.org/content/10.1101/2020.05.10.20097451v1)
Corona Immunitas – a compass for Switzerland

• Provides a consistent picture of the spread of SARS-CoV-2 across Switzerland

• Thanks to a standardized protocol

• And carefully developed antibody testing strategy

• Longitudinal!

• Aims at strengthening public health research in Switzerland
Study flow

Same protocol for most studies

Standardized questionnaires and testing
Corona Immunitas - phases

Neue Fälle von Corona-Infektionen pro Tag

PHASE I
PHASE II
PHASE III

Bevölkerungsanteil mit SARS-CoV-2 Antikörper (kumulativ)

0%
5%
10%
15%

Projizierte Annahme der Entwicklung

Erster Fall der Schweiz
Erste Lockerung
Zweite Lockerung
Lockdown

Februar
März
April
Mai
Juni
Juli
August
September
Oktober
November
Corona Immunitas studies
BUS SANTE STUDY
(30’000 participants since 1993)

annual health examination survey of representative sample of the population of the Canton 20 to 75 y

10’000 with emails

Postal letters to update emails + phone calls if no emails

1000-1500/week recontacted to take part in serosurvey with family members (children >5)

- REDCap questionnaire
- Blood collection for serological testing
SEROCOV-POP – Results
SerocoViD study

Part 1
- COVID-19 confirmed cases
  - Vaud Registry
  - 200 index cases
  - Qualitative study
  - N=30
  - Household contacts
  - N = 800

Part 2
- Federal Office Statistics population registry
  - N=100
  - Seropositives
  - 100
  - Seronegatives
  - Visit 2 (Month 2)
  - Visit 3 (Month 4)
  - Visit 4 (Month 6)

Part 3
- Poste T-I
- Blanchisseries Migros
- Asylum seekers centers
- N specific populations: 5 x 200
Total N recruited (15.06) = 1590

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Participation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index cases</td>
<td>181</td>
<td>39.4%</td>
</tr>
<tr>
<td>close contacts - households</td>
<td>244</td>
<td>38.3%</td>
</tr>
<tr>
<td>close contacts - outside</td>
<td>56</td>
<td>39.7%</td>
</tr>
<tr>
<td>FSO</td>
<td>653</td>
<td>30.3%</td>
</tr>
<tr>
<td>Migros</td>
<td>92</td>
<td>30.8%</td>
</tr>
<tr>
<td>Public transport</td>
<td>83</td>
<td>25.7%</td>
</tr>
<tr>
<td>La Poste</td>
<td>94</td>
<td>30.3%</td>
</tr>
<tr>
<td>Asylum seekers</td>
<td>124</td>
<td>38.3%</td>
</tr>
<tr>
<td>Blanchisseries Generales SA</td>
<td>63</td>
<td>25.7%</td>
</tr>
</tbody>
</table>
Séroprévalence des anticorps anti-SARS-CoV-2 dans la population suisse - Enquête multicentrique CH
Objectives of our study

1) Analyse the COVID epidemic from a socio-demographic perspective

2) Between 15.02.2020 and 01.05.2020 and depending on the measures taken by the authorities, assess:
   • among those listed as "probable cases" (2500)
     • The positivity rate (10% in the beginning? 30% – 70% At epidemic peak?)
   • among the positive people (700 + X of 2500)
     • The proportion of transmission of Covid-19 in different areas (travel, work, family, leisure...)
     • Acceptance of sanitary measures (isolation, social distancing, hygiene measures...)
     • The degree of risk awareness

3) Assess the risk of transmission within the professional area
   a. depending on the field of activity
   b. based on physical interactions

4) Create a cantonal serotheque of Sars-Cov-2 positive cases
Corona Immunitas - Fribourg: Team

Population Health Laboratory - #PopHealthLab

- Dr Arnaud Chiolero, MD PhD, prof of public health
- Dr Stephane Cullati, PhD, senior lecturer epidemiology & public health
- Dr Adina Epure, MD, and Daniela Anker, MSc, PhD students
- Catherine Girard, Daniel Marc Aebi, Lucille Fragnière, administrative staff

Institute of Family Medicine

- Dr Pierre-Yves Rodondi, MD, prof of primary health care

Websites:
- #PopHealthLab: https://www3.unifr.ch/med/de/research/groups/pophealthlab/
- Corona Immunitas - Fribourg: https://www3.unifr.ch/med/imf/fr/news/covid19/corona-immunitas/
Study design
- Cross-sectional seroprevalence study with 2 recruitment phases
- Optional: digital cohort

Population
- Population-based samples of 600 individuals per phase
  - 300 aged 20-64 yrs
  - 300 aged 65+ yrs (no kids)
- Volunteers welcome (max 200 in each phase)

Data collection
- Baseline questionnaire: online or paper form
- Blood sample collection: at 5 sites of cantonal hospital or at home

Serological analyses
- Laboratory: cantonal hospital Fribourg

Calendar
- Recruitment start: Jun 15th and Sep 15th
- Results expected: Aug and Nov (governmental report)
Institute of Public Health (IPH), Università della Svizzera italiana (USI)
• Prof. Dr. Emiliano Albanese – Project leader
• Prof. Suzanne Suggs
• Dr. Rebecca Amati – Project manager
• Dr. Anne Linda Camerini – Responsible for population <20

Department of Business Economics, Health and Social Care (DEASS), University of Applied Sciences and Arts of Southern Switzerland (SUPSI)
• Prof. Luca Crivelli – Project leader
• Prof. Laurie Corna – Responsible for population 65+

Laboratorio microbiologia applicata (SUPSI)
Prof. Mauro Tonolla

Clinical Trial Unit, Ente Ospedaliero Cantonale (EOC)
• Prof. Dr. Alessandro Ceschi
• Prof. Dr. Paolo Ferrari

Institute for Research in Biomedicine (IRB), Università della Svizzera italiana (USI)
• Prof. Dr. Federica Sallusto
Research program in Ticino: General population, health workers, nursing homes

Corona Immunitas population-based study designs

DIGITAL COHORT

July

CROSS-SECTIONAL 1
N=400-1000

Blood sampling in 6 hospitals EOC

REPEATED CROSS-SECTIONAL

Sept/Oct

CROSS-SECTIONAL 2
(BLOOD 1)
N=1000

N=1000

<20

<20 and 65+

N=50 (+)

N=50 (-)

N=50 (-)

N=50 (-)

Blood sampling MULTI-SITE + HOME VISITS

<20

<20 and 65+

N=50 (+)

N=50 (-)

N=50 (-)

N=50 (-)

N=50 (-)

N=50 (-)

N=50 (-)

BLOOD 2
N=1000

65+

BLOOD 3
N=1000

Grandparents

BLOOD 4
N=1000

Grandchildren

Focus Ticino
- <20 and 65+
- Households

N=2000

20 – 64

Digital f-up (W + M)

N=1000

<20

Digital f-up (W + M)

N=1000

65+

Digital f-up (W + M)

N=1000

+ GRANDPARENTS

+ GRANDCHILDREN

N=1000

+ GRANDCHILDREN

Jun/July

Mar/Apr

Dec/Jan

Blood sampling in 6 hospitals EOC
CoV-Co Basel

### Seroprevalence Cohort
- **June 2020 - August 2020**
  - 18-49
    - N=200
  - 50-64
    - N=200
  - 65+
    - N=200
- **September 2020 - November 2020**
  - 18-49
    - N=200
  - 50-64
    - N=200
  - 65+
    - N=200
- Repeat Testing
  - N≈400 (Families)

### Digital Cohort
- **June 2020 - May 2021**
  - 18-49
    - N=2'600
  - 50-64
    - N=2'600
  - 65+
    - N=2'600

### Serological Assessment
- N= 2'500 venous blood
- N= 2'500 dried blood spots
- N= 400 saliva

### Digital Assessment
- Baseline
- Weekly
- Monthly

### Long-term follow-up
- N≈10'000
Corona Immunitas Objectives

equally sized population-based samples BS and BL – adults 18-65+ - children and adolescents recruited from within households of adult index participants with a additional focus on family/household environment

CoV-Co-Basel Objectives

long-term impact of epidemic and its containment measures on various domains of behavior, life circumstances, health and well-being of individuals and families/households

Reference for comparative studies in low- and middle-income countries (i.e. Ethiopia; Kosovo; Palestine)
Populations and visits

Comparison of special groups with general pop

Quite some focus on how antibodies develop over time

<table>
<thead>
<tr>
<th>Random sample 1 (n=800)</th>
<th>Subgroup samples (n=800)</th>
<th>Proactive sample (n=500)</th>
<th>Nested cohort sample (n=200)</th>
<th>Random sample 2 (n=400)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 age groups (20-44 / 44-64 / 65+)</td>
<td>Spitex &amp; nursing home employees • Patients with opioid substitution • SwissPrEPared study participants</td>
<td>Persons who had symptoms but could not be tested</td>
<td>100 seropositive persons • 100 seronegative persons</td>
<td>2 age groups (20-64 / 65+)</td>
</tr>
</tbody>
</table>
30 randomly selected schools
Canton ZH (out of 600)

1st school visit (~ 2500 children)
Blood sample, sputum, questionnaire

2nd school visit (~ 2500 children)
Blood sample, sputum, questionnaire

3rd school visit (~ 2500 children)
Blood sample, sputum, questionnaire

Questionnaires:
children, parents, head of school

Jun / Jul
(3 weeks)

Jul Aug Sep
Oct/Nov
(3 weeks)

Nov Dec Jan
Feb/Mar
(3 weeks)
Supporters – public und private
Political advisory board

Bettina Balmer  Michel Matter  Marina Carobbio  Angelo Barrile  Frank Rühli

https://www.corona-immunitas.ch/politics
Testimonials

Doris Leuthard  Ruth Dreifuss  Ursula Zybach  Felix Gutzwiler

https://www.corona-immunitas.ch/testimonialsenn