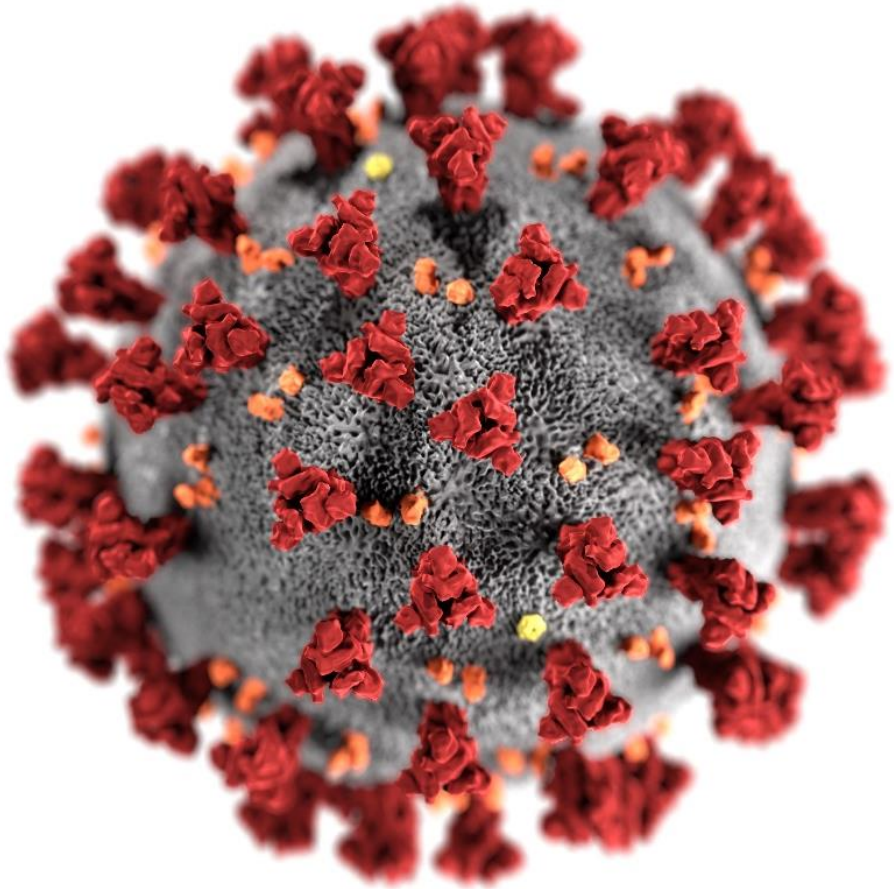
COVID-19 Surveillance Webinar

COVID-19 Seroprevalence surveys

Laboratory considerations for SARS-CoV-2 testing

WHO UNITY Studies: Seroepidemiological investigations for COVID-19

Seroprevalence surveys and other serological studies in the CDC COVID-19 response



Myrna Charles, Influenza Division
Hetal Patel, Division of Global HIV & TB
Isabel Bergeri, WHO Global Influenza Program
Aron Hall, Division of Viral Diseases

Monday, June 29, 2020

For more information: **www.cdc.gov/COVID19**

Overview of Seroprevalence Surveys for COVID-19

Myrna Charles
International Task Force, Epidemiology Team
Influenza Division

COVID-19 Seroprevalence Survey

- What percent of a population has been infected by and generated an antibody response to the SARS-CoV-2 virus?

Seroprevalence Study Goals

- **Primary objectives:**
  - To measure the prevalence of antibodies to SARS-CoV-2 in the general population by sex and age group
  - To estimate the fraction of asymptomatic, pre-symptomatic or subclinical infections in the population overall
- **Secondary objectives:**
  - To determine risk factors for infection by comparing the exposures of infected and non-infected individuals
  - To understand the true case fatality ratio, and
  - To examine antibody kinetics following COVID-19 infection

Seroprevalence Study Designs

Cross-sectional study	Repeated cross-sectional study	Longitudinal cohort study
One point in time	Several points in time	Several points in time
One sample population	Different sample populations	Same sample population
Analyze numerous variables at once	Analyze numerous sub-groups at once, flexible, allows changing of data collection tools	Follow changes in participants over time
Collect demographic information once	Collect demographic data each time	Collect demographic data at initial visit only
Cannot calculate incidence, only prevalence	Cannot calculate true incidence, allows for approximation of denominator	Can calculate incidence over time, measure changes in antibodies over time

Sampling Strategy

- **Convenience sampling**

  Examples

  - Individuals attending medical services
  - Use residual sera taken from patients for other investigations

- **Random sampling**
  - Simple random sampling
  - Stratified random sampling: population divided into strata (e.g. geographic, age, sex)
  - Random cluster sampling: individuals assigned to a cluster
  - Multistage random sampling: combination of different sampling methods

Use of Findings

- Determine what proportion of a community or population is infected
  - Understand scale of the current pandemic
- Identify people with antibody response to serve as convalescent plasma donors
- Determine if a person had an immune response to SARS-CoV-2, regardless of clinical symptoms
  - Assess extent of age-specific infections;
  - Determine infection attack rates, fraction of asymptomatic infections, and case fatality ratios
- Share information globally for timely public health response and policy decisions

International Task Force (ITF) Support

- International Task Force (ITF) Support
  - Modification of protocol to country context and resources
  - Technical support for epidemiologic and virologic study design planning
  - Data collection form modifications

CGH Process for Technical Review for Global COVID-19 Activities

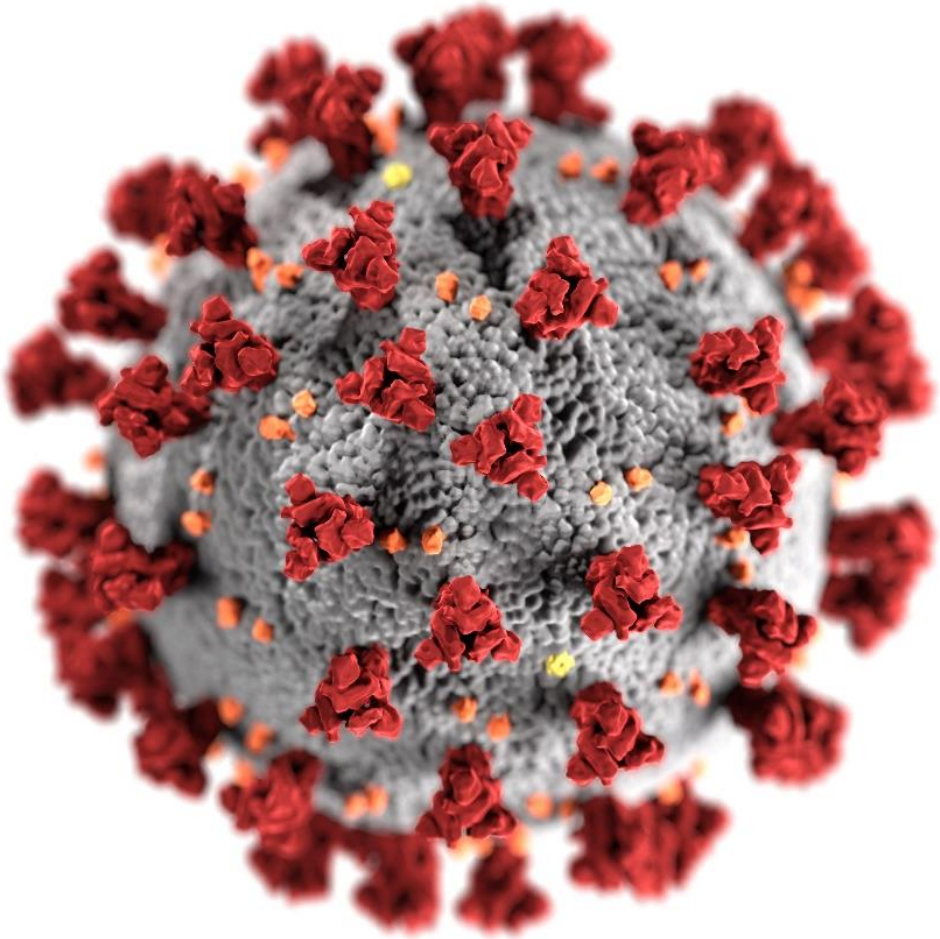
ITF Serosurveillance Team

- Chung-Won Lee, Associate Director for Science
- Steven Yoon, Epi Team Lead
- Amitabh Suthar, Surveillance Lead
- Myrna Charles, Serosurveillance Point of Contact
- Todd Davis, International Laboratory Team Lead
- Keisha Jackson, International Lab Advisor

- Toni Whistler, Health Advisor, CGH, STARS UNITY Study Point of Contact

Questions/protocol submissions for ITF

eocevent223@cdc.gov



For protocol review: place in subject line “For ITF ADS”

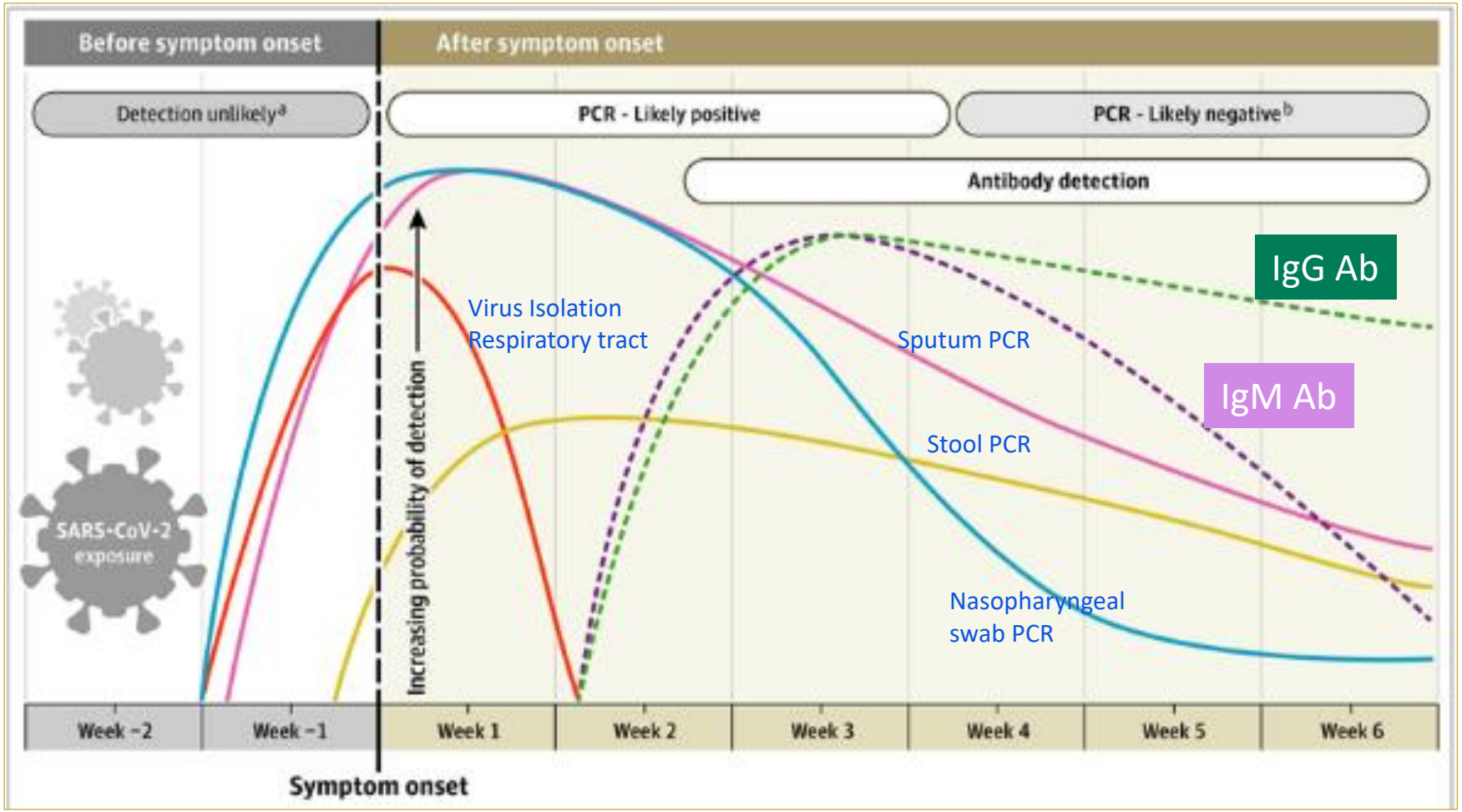
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Seroprevalence Surveys for COVID-19 Laboratory Considerations

Hetal Patel
International Task Force – Laboratory Team
Division of Global HIV & TB
Team Lead, Survey Support Team

Types of SARS-CoV-2 Antibody Assay



- Detection of total antibody (IgM; IgG)
- Detection of IgG
- Detection of IgM

Sethuraman N, Jeremiah SS, Ryo A. JAMA. Published online May 06, 2020.

Summary of SARS-CoV-2 Serology Tests

FDA Emergency Use Authorization (EUA)	COVID-19 Testing Project (UCSF Berkeley)	Foundation for Innovative New Diagnostics (FIND)
• 5 rapid tests • 5 ELISA (3 commercial) • 11 Others (CLIA or others)	• 10 rapid tests • 2 ELISAs	• 26 rapid tests • 8 ELISAs Results Pending

Results available via links shared below

ELISA - Enzyme-linked immunosorbent assay

CLIA – Chemiluminescence immunoassay

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-serological
https://www.finddx.org/covid-19/sarscov2-eval-immuno/
https://covidtestingproject.org/

Improving Overall Positive Predictive Value

Estimates of the positive predictive value using a one test versus two test (i.e., orthogonal) strategy based on the prevalence of SARS-CoV-2 antibodies in the population tested.

Prevalence	PPV for one test (SE=90%, SP=95%)	PPV for two tests (SE=90%, SP=95%)
2%	26.9%	86.9%
5%	48.6%	94.5%
10%	66.7%	97.3%
30%	88.5%	99.3%

PPV = positive predictive value
SE = sensitivity
SP = specificity

https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html#table1

Serosurvey Planning

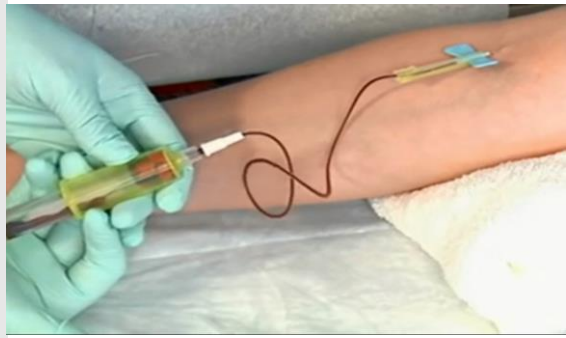
- Types of serosurveys needed to address key scientific questions
- Participant selection and sampling methods
- Selection of appropriate test methodology – additional verification/evaluation maybe required
- Review of appropriate algorithms – including two-test approaches
- Staff training, proficiency test panels, positive/negative controls, logistics and planning

Serosurveys Considerations

- **Survey group (population to be surveyed)**
- **Specimen type and testing** (Finger-prick; venous draw; plasma; DBS – under review)
- **Safety and Personal Protective Equipment** (guidelines for data collectors and lab testers)
- **Testing – Test selection and location** (e.g., central lab, interim-mid level labs; health facility, etc…)
- **Data interpretation** (positive; negative and return of results; clinical relevance)

Venous Draw vs. Finger Prick Specimen Collection

Collection Type	Advantages	Disadvantages
Venous Draw (> 4 mL)	• Sufficient volume for all testing (repeat, QA, etc.) • Closed system – ensures no contamination • Time efficient	• Requires additional equipment • Perception its more painful and large volume
Finger prick (500 µL to 1 mL)	• Limited supplies required • Reduced waste management • More acceptable within communities	• Increased risk of blood contamination • Limited sample volume • Potential for clotting • Requires specific training • Misconception that it can be added directly to a test device (not recommended)

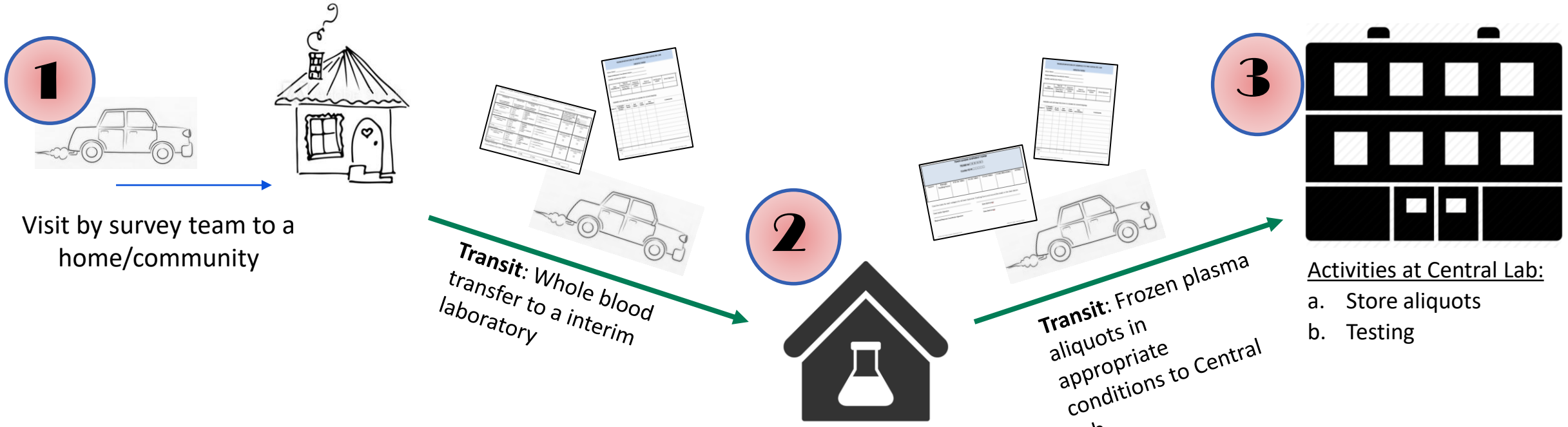


Example Specimen Flow: serosurveys

Whole blood collection
Venous draws
Finger prick

Processing
Plasma/Serum
Interim storage

Testing
QA/QC Review
Results reporting



Planned Serosurveys – Sub Saharan Africa

Country	Status	Population & Setting	Test Name/Platform	Proposed Duration
Zambia	Protocol Approved	General Population (3 urban & peri urban), Outpatients (30 sites) and Healthcare Workers (n=8,166)	Euroimmun ELISA Panbio IgM/IgG (RDT) (*parallel algorithm)	July/August (peak of influenza season)
Cameroon	Protocol Development	Urban setting in 10 regional capitals Adults and children (n=10,000)	Abbott Architect IgG Biorad Platelia ELISA (**serial algorithm)	~2 months
Nigeria	Protocol Development	Pending (TBD) Urban; Two states	Under review: Euroimmun ELISA Abbott Architect Biorad Platelia ELISA (two-test algorithm pending)	TBD

*Parallel – Performing both tests concurrently

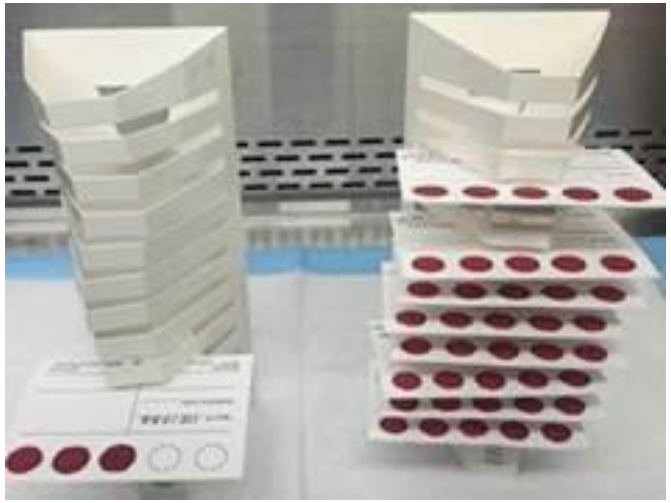
**Serial – Performing one test at a time, results from first test will indicate if second test is needed

Planned Serosurveys – Other Countries

Country	Status	Population & Setting	Test Name/Platform	Proposed Duration
Indonesia	Protocol Development	Urban and rural population in Bali (eligible participant age > 1 year)	Multiplex to detect antibodies to the spike protein sub unit; Other ELISA based assay	TBD
Peru	Protocol Development	Healthcare workers (asymptomatic & pre-symptomatic infections) (n=2,100)	CDC Headquarters; SARS-CoV-2 ELISA	TBD
Vietnam	Protocol Development	Hospital transmission among healthcare workers and surrounding communities	TBD	TBD

Summary

- Antibodies most commonly become detectable 1-3 weeks after symptom onset.
- Currently, there is no identified advantage of assays whether they test for IgG, IgM and IgG, or total antibody.
- Minimize false positive test results by choosing an assay with high specificity.
- Two ELISA test algorithm at a central location is ideal with proposal to perform additional testing as new high quality assays become available.
- On-going technical questions under investigation is utilization of dried blood spot (DBS) as a sample type for testing.



“UNITY” STUDIES: WHO early sero-epidemiological investigations for COVID-19

Transmission dynamics, severity and immunity/sero-prevalence

Dr. Isabel Bergeri
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HQ Focal point for Unity sero -epideniological investigations
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"UNITY" STUDIES:
WHO early sero-epidemiological investigations for COVID-19

Transmission dynamics, severity and immunity/sero-prevalence

Contact points at WHO/HQ:

Isabel Bergeri (bergerii@who.int)

Web: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

Generic email address: EarlyInvestigations-2019-nCoV@who.int

WHO "chapeau" for COVID-19 sero-epidemiological investigations/ studies

- In collaboration with technical partners, WHO developed standardized **early sero-epidemiological investigations protocols** for COVID-19 (Unity studies) to better understand these characteristics and how they may be used to inform public health measures (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations) and **support countries** to develop country specific protocols and implement them timely

- Within WHO's Solidarity II global collaboration, WHO is working with partners to facilitate the global sharing of well **characterized panels of sera** to enable standardization of serologic assays worldwide, and to develop **standardized serologic assays** for collaborators to use
- WHO is working with global network of laboratories and FIND on **the development, evaluation and validation of serologic assays for SARS-CoV-2**

UNITY STUDIES: Early sero-epidemiological Investigations for COVID-19

Transmission dynamics & severity, infection/sero-prevalence

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

- Work started 10 years ago, after last 2009 influenza pandemic
- WHO has adapted influenza and MERS-CoV standardized protocols for 2019-nCoV
- These protocols will allow to gather robust data on **transmission dynamics & severity, infection/sero-prevalence, etc.**
- **Standardized** protocols and questionnaires/forms are designed, so that data can be rapidly and systematically collected and shared in a format that facilitates aggregation, tabulation and analysis across different settings globally
- The **ownership** of the primary data **remains firmly with the individual countries/sites**

World Health Organization

Email: EarlyInvestigations-2019-nCoV@who.int.
Web: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

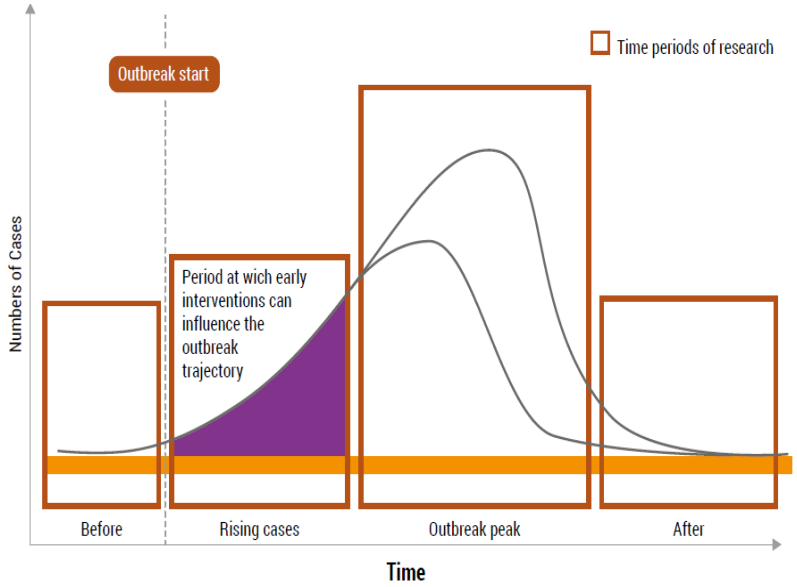
HEALTH EMERGENCIES programme

"Why" and "How"

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

Why ?

- As of today, **most of the population is still susceptible to COVID-19** as of today.
- Surveillance of immunity level trend in the population is of utmost importance to **inform flexible intervention/mitigation strategies**
- Understanding of transmission patterns, severity, clinical features and risk factors for infection remains limited
- Provides **robust** information on key epidemiological, clinical, and virological characteristics, including to improve modelling and forecasting (assumptions, etc.)



Opportunities for operational investigations and research in the COVID-19 epidemic cycle

How ?

→ in a few, but representative sites,
with already existing capacities (epi and lab)

MANTRA:
"key questions, key generic protocols, key sites"

World Health Organization

HEALTH EMERGENCIES programme

Expected outputs

COVID-19 "UNITY" STUDIES: early sero-epi investigations

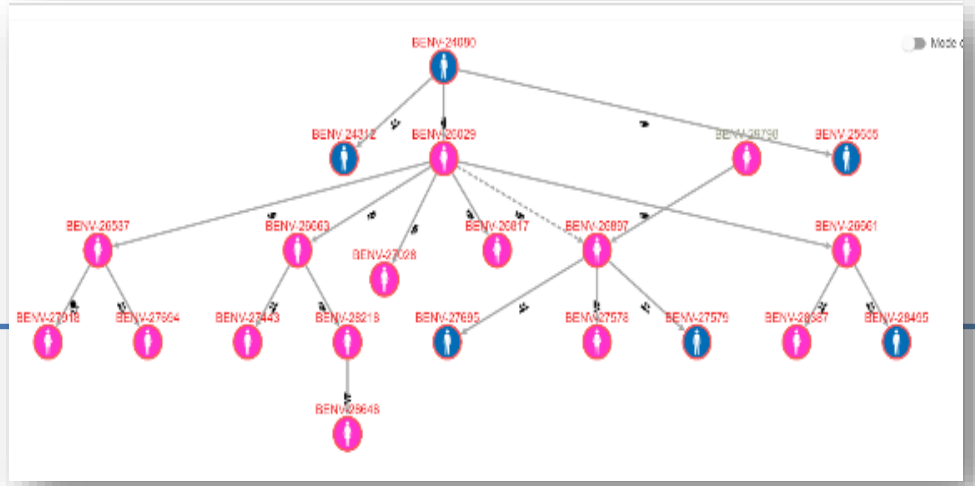
Analytics (epi parameters) (to be further used to improve forecasting through modelling) such as:

- Susceptibility to SARS-CoV-2 (Sero prevalence and incidence) in the population and in specific target groups, e.g. HCWs
- Secondary infection rate and clinical attack rate among close contacts (serology)
- Asymptomatic fraction (through serology)
- Symptomatic proportion
- The basic reproductive number (R_0)
- Serial interval
- Incubation period
- Viral load and virus shedding profiles
- Preliminary infection and diseases-severity ratios (e.g. case-hospitalization and case-fatality ratios)

"Most wanted" in orange color

Descriptive epi

- Chain of transmission/ transmissibility
- Severity
- Clinical presentation and course of associated disease
- Clinical risk factors, especially for severe outcome
- High-risk population subgroups
- Geographical mapping of outbreaks
- Health-care seeking patterns
- Possible routes of transmission
- Extent of, and risk factors for transmission



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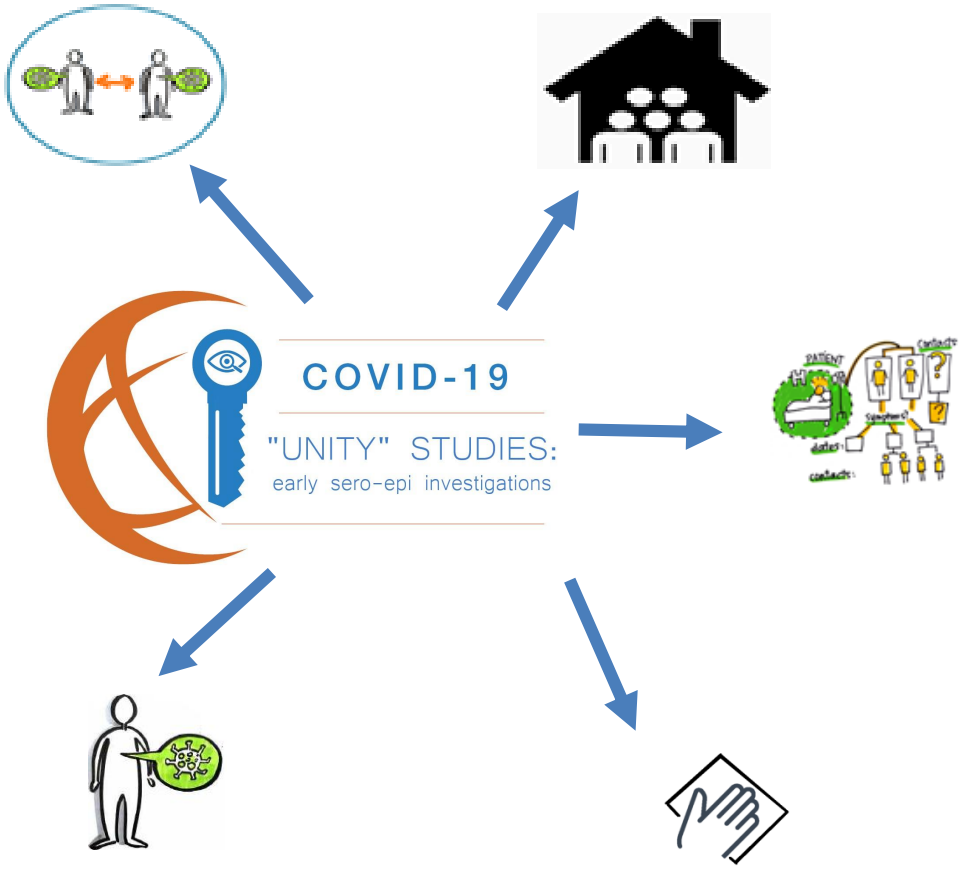
UNITY STUDIES: Early sero-epidemiological Investigations for COVID-19

Transmission dynamics & severity, infection/sero-prevalence

- **Standardized** protocols and questionnaires/forms are designed, so that data can be rapidly and systematically collected and shared in a format that facilitates aggregation, tabulation and analysis across different settings globally.

- The **ownership** of the primary data **remains firmly with the individual countries/sites.**



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UNITY STUDIES: Early sero-epidemiological Investigations for COVID-19

Transmission dynamics & severity, infection/sero-prevalence

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

Core protocols and template questionnaires for COVID-19 available for

Early sero-epidemiologic investigations for public health response

Web: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations. Generic email address: EarlyInvestigations-2019-nCoV@who.int

	Why ?	For whom ?	Which early investigations protocol ?
with sero-epi component 	Community transmission mainly (or closed settings)	Cases and close contacts **in the general population**	The First Few COVID-19 X cases and contacts transmission investigation protocol (FFX)
	Community infection	Virus infection **in the general population**	Population-based age-stratified seroepidemiological investigation protocol for COVID-19
	School transmission (*pending*)	Cases and close contacts **in school (and other educational institutions) setting**	School and other educational institutions transmission of COVID-19 investigation protocol (S)
	Health facilities transmission	**For health workers** in a health-care setting	Assessment of risk factors for COVID-19 in health workers (HW): protocol for a prospective study of a cohort of HW
			Assessment of risk factors for COVID-19 in health workers (HW): protocol for a case-control study (NEW)
	Households transmission	Cases and close contacts **in households setting**	Households transmission of COVID-19 investigation protocol (HH)
	Surface	**For environmental**	Surface sampling of COVID-19: A practical "how to" protocol for health care

UNITY STUDIES: Objectives of each study

Why Unity Studies?	Study focus	Objectives
The First Few COVID-19 X cases and contacts transmission investigation protocol (FFX)	Cases and close contacts in the general population or can be restricted to close settings (like households, health care settings, schools).	The primary objectives are to provide descriptions or estimates of : • clinical presentation of COVID-19 infection and course of associated disease; • secondary infection rate (SIR) and secondary clinical attack rate of COVID-19 infection among close contacts (overall, and by key factors such as setting, age and sex, for various end-points); • serial interval of COVID-19 infection; • symptomatic proportion of COVID-19 cases (through contact tracing and laboratory testing); and identification of possible routes of transmission. The secondary objectives are to support the estimation of: • the basic reproduction number (R0) of COVID-19 virus; • the incubation period of COVID-19; and • the preliminary COVID-19 infection and disease-severity ratios (for example, case-hospitalization ratio [CHR] and case-fatality ratio [CFR]).
Household transmission of COVID-19 investigation protocol (HH)	Cases and close contacts in household setting	Primary objectives • To better understand the extent of transmission within a household by estimating the secondary infection rate for household contacts at an individual level, and factors associated with any variation in the secondary infection risk. • To characterize secondary cases including the range of clinical presentation, risk factors for infection, and the extent and fraction of asymptomatic infections • To characterize serologic response following confirmed COVID-19 infection
Population-based age-stratified seroepidemiological investigation protocol for COVID-19 infection	Virus infection in the general population	Primary objectives: • To measure the seroprevalence of antibodies to COVID-19 in the general population by sex and age group, in order to ascertain the cumulative population immunity; and • To estimate the fraction of asymptomatic, pre-symptomatic or subclinical infections in the population and by sex and age group. Secondary objectives, such as, but not limited to: • To determine risk factors for infection by comparing the exposures of infected and non-infected individuals; • To contribute to determine the case fatality ratio; and • To contribute to an improved understanding of antibody kinetics following COVID-19 infection.

Serial Investigations for COVID-19

Web: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

UNITY STUDIES: Objectives of each study

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

Why Unity Studies?	Study focus	Objectives
Assessment of risk factors for COVID-19 in health workers: protocol for a prospective study of a cohort of Health workers	Health workers in a health care setting in which patient(s) with a laboratory-confirmed COVID-19 infection are receiving care	Primary objectives • To better understand the extent of human-to-human transmission among health workers by estimating the secondary infection rate for health worker contacts at the individual level. • To characterize the range of clinical presentations of infection and the risk factors for infection among health workers. • To evaluate the effectiveness of infection prevention and control measures among health workers. • To evaluate the effectiveness of infection prevention and control programmes at health facility and national level. Secondary objectives such as, but not limited to: • To determine the serological response of health workers with symptomatic and possibly asymptomatic COVID-19 infection; To characterize the duration and severity of COVID-19-associated disease among health workers.
Assessment of risk factors for COVID-19 in health workers: protocol for a case-control study	Health workers at occupational risk for COVID-19	Nested case-control study of health workers exposed to confirmed COVID-19 patients. Similar objectives to the cohort study but case-control studies may be cheaper and provide more robust evidence to characterize and assess the risk factors for SARS-CoV-2 infection in health workers exposed to COVID-19 patients. Health workers with confirmed COVID-19 will be recruited as cases and other health workers in the same health care setting without infection will be recruited as controls (incidence density sampling). Secondary objectives are similar to the cohort study. WHO is coordinating an international multi-centre study that will undoubtedly lead to a more robust analysis of potential factors affecting the secondary infection risk, and to a more detailed characterization of serological responses following infection. A Go.Data data collection template is available upon request.
Surface sampling of COVID-19 virus: A practical "how to" protocol for health care and public health professionals	For environmental surfaces	Primary objectives: • To assess the extent and persistence of surface contamination of COVID-19; and • To identify environmental surfaces and fomites that may play a role in onward transmission of COVID-19. Secondary objectives such as, but not limited to: • To characterize of the sequence diversity of COVID-19 in environmental samples, as capacity and resources permit.

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UNITY STUDIES: Objectives of each study

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

Why Unity Studies?	Study focus	Objectives
Investigation protocol for severe respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in schools and other educational institutions	**Students and staff of schools and other educational institutions with a laboratory confirmed case of COVID-19**	Understand the dynamics of SARS-CoV-2 infection in the school and other educational institutions by **primarily:** • estimating overall infection and secondary attack rates • estimating clinical secondary attack rate • estimating fraction of asymptomatic infections • describing the epidemiological and clinical characteristics of primary and secondary cases • identify potential risk/ protective factors associated with infection risk This protocol does not address the further transmission from school to household. Study teams willing to include this component should adapt the investigation using the household transmission protocol

UNITY STUDIES: Early sero- epi investigations COVID-19:
Transmission dynamics & severity, and immunity/sero prevalence

INCREASING THE EVIDENCE-BASED KNOWLEDGE FOR ACTION: country uptake of WHO investigation protocols

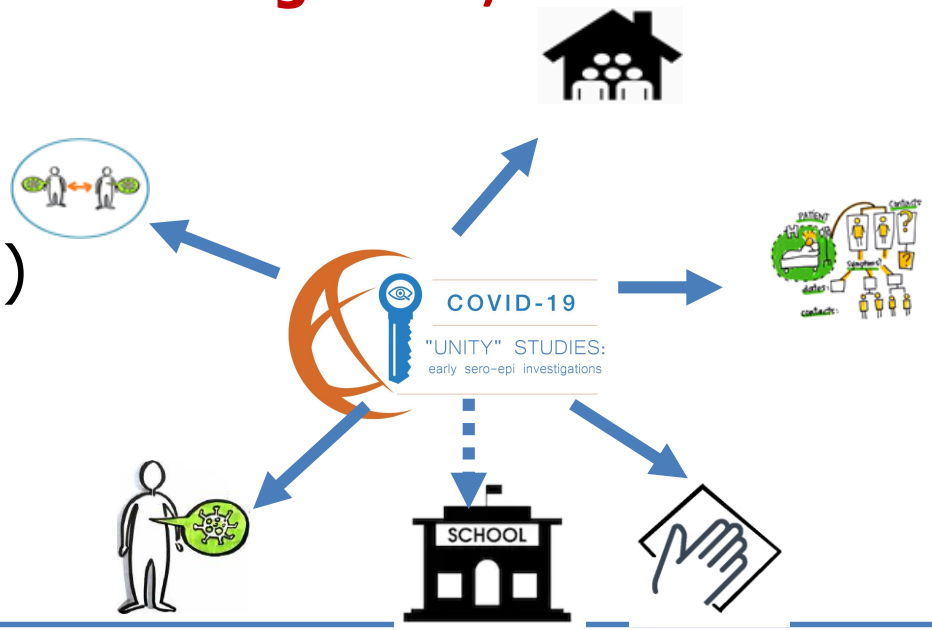
91 COUNTRIES INTEND to implement one or several of WHO sero-epi investigations (66 % being LMIC)

45 COUNTRIES STARTED implementation (57 % being LMIC)

By WHO region

Intention confirmed: 79 countries
(AFR 19, PAHO 8, EMR 8, EUR 26, SEAR 7, WPR 11)

Implementation started: 45 countries
(AFR 11, PAHO 4, EMR 3, EUR 17, SEAR 1, WPR 9)



World Health Organization

Data as of 25 June 2020.

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UNITY STUDIES: Early sero- epi investigations COVID-19:
Transmission dynamics & severity, and immunity/sero prevalence

COVID-19
"UNITY" STUDIES:
early sero-epi investigations

INCREASING THE EVIDENCE-BASED KNOWLEDGE FOR ACTION: country uptake of WHO investigation protocols

By protocol

✓ **FFX (First Few X cases and their close contacts) transmission protocol**

33 intention - **22 implemented** (Albania, Australia, CAR, Colombia, Cote d 'Ivoire, Ethiopia, Finland, France, Georgia, Jordan, Kenya, Lebanon, Liberia, Madagascar, Mongolia, Republic of Korea, Senegal, South Sudan, Togo, UK, US, Vietnam)

✓ **Population-based age-stratified sero-epi investigation protocol**

50 intention - **23 implemented** (Belgium, Canada, Finland, France, Germany, Italy, Israel, Japan, Kyrgyzstan, Madagascar, Malaysia, Netherlands, New Zealand, Norway, Pakistan, PNG, Portugal, Russian Federation, South Africa, Spain, Switzerland, US)

✓ **Households (HH) transmission protocol**

24 intention - **13 implemented** (Australia, Canada, Cote d 'Ivoire, Finland, French Guyana, Kenya, Lebanon, Madagascar, New Zealand, Senegal, Singapore, UK, US)

✓ **Risk factors assessment for Health Workers (HW) protocol (cohort one, new case control data pending)**

16 intention - **11 implemented** (Armenia, Belgium, Lebanon, Liberia, Madagascar, Malaysia, Niger, Singapore, UK, US, Vietnam)

✓ **School transmission investigation protocol (forthcoming)**

World Health Organization

Data as of 25 June 2020.

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HEALTH EMERGENCIES programme

Engagement process & WHO support: simple and operational

- To be recognized as a WHO UNITY collaborator : 3 principles
  1. Methodological alignment of national protocol with WHO master protocols
  2. Documentation of local ethical clearance or exemption needs to be shared with WHO
  3. Willingness to share early findings for aggregated analysis at regional/global level
- No formal process or application
  - **Pro-active engagement with WHO** :countries and partners through direct correspondence with WHO focal points at CO and RO& HQ
  - **Pro-active engagement through generic email address** earlyinvestigations-2019-nCoV@who.int: : MOH, national institutes and other governmental researcher partners, PH partners had been informing HQ since January of intent and implementation status
  - **Active reach out by WHO** : Since Jan, in coordination with WHO CO, countries contacted to encourage use of UNITY protocols and sharing of data upon hearing about their investigation plans
- Support available for countries intending to apply UNITY protocols
  - **Epidemiological, laboratory and data analysis** technical support
  - **Financial** requests made directly to CO and RO, then collated and prioritized together by RO/ HQ
  - **Serology test kits** could be provided to countries in need for free. First procurement by HQ started in June are received
  - Free **serology research panels** available for validating in-house assays

Laboratory investigations

Contact points at WHO/HQ:

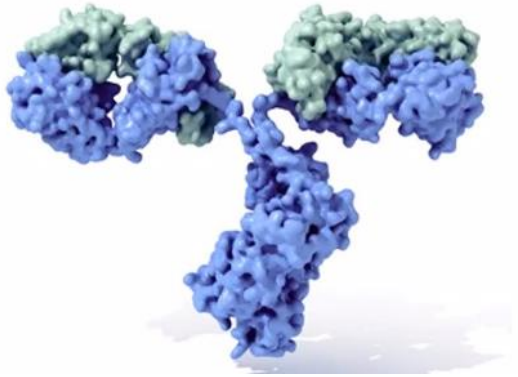
- Lorenzo Subissi (subissil@who.int)

Serological assays status

- **Many** serologic assays currently under development / in the process of being validated
  - **No WHO recommendation yet for immuno-assays** especially for individuals diagnostic purposes
  - WHO Collaborating Centre : Foundation for Innovative New Diagnostics (FIND) https://www.finddx.org/covid-19/sarscov2-eval-immuno/ : generate **independent data on assay performance** of molecular tests and immunoassays to support accurate, affordable, accessible testing in LMIC
- Tests available (for **IgM, IgA and IgG** available)
  1. RDT (Rapid diagnostic test (not advised to be used, Se and Sp issues)
  2. Enzyme linked immunosorbent assay (ELISA) or indirect immunofluorescence (IIFA): facility with at least BSL-2 required
  3. Confirmation through neutralization assay: facility with at least biosafety level 3 (BSL-3) required
- Current advice : if case serum not processed immediately or no serology testing capacity (yet), **store sample in aliquots** at **-20°C**
- Standardization / comparability of results (free procurement by WHO to countries) :
  - Use of common **serum panels** between studies/assays for comparability purposes. Research reagents and panels start to be available to countries (ex: NIBSC Solidarity II).
  - No WHO recommendation yet for a **serological-assay, but for Unity (research or enhanced surv purpose) a preferred choice**

NIBSC serology research reagents and panels (Solidarity II)

- The following products are made available by WHO **for free** to countries :



1. **A research reagent**, high titer convalescent human plasma: https://www.nibsc.org/products/brm_product_catalogue/detail_page.aspx
2. **Antibody panel**: 5 ampoules of
   - High titre plasma (individual donor)
   - Medium titre (pool of 2 donors)
   - Low titre (high titre against N antigen) (individual donor)
   - Low titre (individual donor)
   - Negative (individual donor)

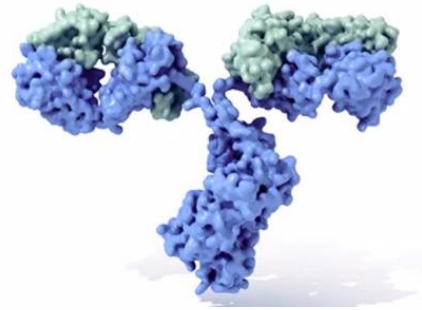
By default we will send 3 panels per requestor, unless the requestors ask for more.

- You can place your order by following this simple procedure:
  - Complete the attached request form to collect basic information: name of the requestor, email, phone, institution, country, status of sample collection, nature of the assay, shipping address and any other information that requestor would like to share.
  - Send an email to the solidarity2@who.int requesting the panel attaching the completed form.
  - CC Subissi Lorenzo subissil@who.int, Massinissa Si Mehand simehandm@who.int, and, if relevant, your WHO Regional/Country office focal points.

Ensure comparability between countries (on the lab side)

- **WHO plans to procure specific ELISA kit(s) for free** for countries that have not yet tested their serum, and exclusively for use within the UNITY studies (research or enhanced surveillance purpose)

- Ongoing discussions to design a strategy that will allow comparability between countries which will not have data using the specific WH[illegible] serological kit(s) :
  - NIBSC research Ab panel (5 samples),and research reagent
  - Large validation panel of negative and positive samples (eg: 200 + , 400 -)
  - Set up EQA for serology
  - Head-to-head comparison of kits/other in-house tests



- Analysis: WHO plan to **adjust for sensitivity and specificity of each assay ("correction factor")** provided they are assessed using a good and large panel of negative and positive samples.

RESULTS

Available evidence: Early published/pre-print studies

- More than 150 seroepidemiologic studies are underway (not all are necessarily aligned with WHO UNITY studies).
- 42 countries started implementation (57 % being LMIC) using Unity studies approaches and methodology
- "Attrition" to WHO effort easy when WHO supported them technically and /or financially (so mainly for LMIC), more difficult for the other ones
  - Available studies include peer-reviewed publications (n=16), pre-print publications (n=35), and publications released by government institutions (see previous today's presentation) Attrition to WHO studies in process
  - Systematic bibliography on weekly basis for RO/ CO consumption

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Date of notification/ publication (DD/MM/YY)	WHO Region or Global	Country	Location (name of cities, localities if	Title	Reference /citation (DOI)	Link to document	Source of information	Journal or source, if available	Principal Investigator (or first author if article) Name and Institution	RESULTS: seroprevalence and 95% CI (Overall and by subgroups)	RESULTS: If PCR used, proportion of positive by PCR and 95% CI (Overall and by subgroups)	RESULTS: others of importance (in the abstract)	Protocol used *(own protocol, WHO_SEROPOP, WHO_HCW cohort, WHO_HH, WHO_FFX,*	Study design (One time cross-sectional,	Study perio *(if defined with dates, include dat*
22/06/2020	WPRO	China	Wuhan	Seroprevalence and epidemiologica	10.1101/2020.06.1	https://www.mec	pre-print		Ling, R., et al	IgG: 3·37% (3·11–3·64%); Standa		Standardized seroprevalence of Ig	own protocol	Cross-sectional,	26/03/2020-2
22/06/2020	EURO	Spain	Barcelona	Seroprevalence against COVID-19	https://doi.org/10.1	https://www.mec	pre-print		Brotons, C., et al	Study population 1: 5,47% (3.44-8		Study pop 1: Women had a higher		Cross-sectional	21/04-05/05/
22/06/2020	EURO	Spain	Barcelona	SEROPREVALENCE AND CLINIC	https://doi.org/10.1	https://www.mec	pre-print		Crovetto, F., et al	14.3% (1st semester; 14.5%; 3rd s		The rates of symptomatic infection I		Cross-sectional	14/04-05/05/

Success story from the field: Pasteur Institutes/ WHO collaboration in 5 African countries for implement COVID-19 sero -epi study among Health Workers





- Partners collaboration (Pasteur Institutes + WHO) **worked hands in hands** since Feb to implement **COVID-19 sero -epi study** among **Health Workers**
- **5 francophone African countries** (Niger, Madagascar, Cameroon, RCA, Burkina Faso)
- same protocol, adapted from WHO Unity studies master protocol,
- jointly, and in a synchronized manner
- 200 HWs from each countries (so **1000 individuals** when data will be pooled)
- followed up prospectively **for 6 months to 1 year**
- implementation started May

World Health Organization

INSTITUT PASTEUR

Success story from the field: Pak

- **Despite facing various humanitarian crises,** (priority country in WHO Global Humanitarian Response Plan)
- Yet these difficulties have not detracted national agencies in Pakistan to understand the spread of COVID-19 in the population and to inform the public health response:
- Implementing a national COVID sero-epidemiological study, adapted from a WHO UNITY studies master protocol, with WHO technical and financial support
  - From the 22 June
  - representative sample of 6,000 individuals
  - from 5 standardized age groups
  - in all four provinces of Pakistan and 2 regional entities
  - using a specific ELISA serological assay procured by WHO (same as other countries supported by WHO for comparability purpose)

- Initial results are expected to be made available in the coming months.

CONCLUSION, KEY CAVEATS

Conclusion

- Early serological studies show that **most of the population is still susceptible to COVID-19** (Most study results* suggest **<10%** prevalence less than 10 %)
- Natural exposure during the pandemic might not soon deliver the required level of population immunity to prevent further epidemics peaks
- **Surveillance of immunity level** trend in the pop is of utmost importance to inform flexible intervention/mitigation strategies
- **Immunoassays test results are only as good as the assay** (sensitivity, specificity, reproducibility) underscoring the critical need for independent evaluation/validation and access to pos and neg controls.
- Additional studies needed to understand the immune responses that lead to **protection** (including the relationship between serological test results and risk of reinfection) and **duration of protection** Ethical implications of using serological testing as a return-to-work "passport" with our current state of knowledge.
- For the time being and until there is a vaccine, the comprehensive package of **public health and social measures (PHSM)** is our most effective set of tools to tackle the virus.

*from early publications, pre-prints, subject to change

Thank you, any questions ?

Contact points at WHO/HQ:

Isabel Bergeri (bergerii@who.int)

Web: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

Generic email address: EarlyInvestigations-2019-nCoV@who.int

Seroprevalence Surveys and Other Serological Studies in the CDC COVID-19 Response

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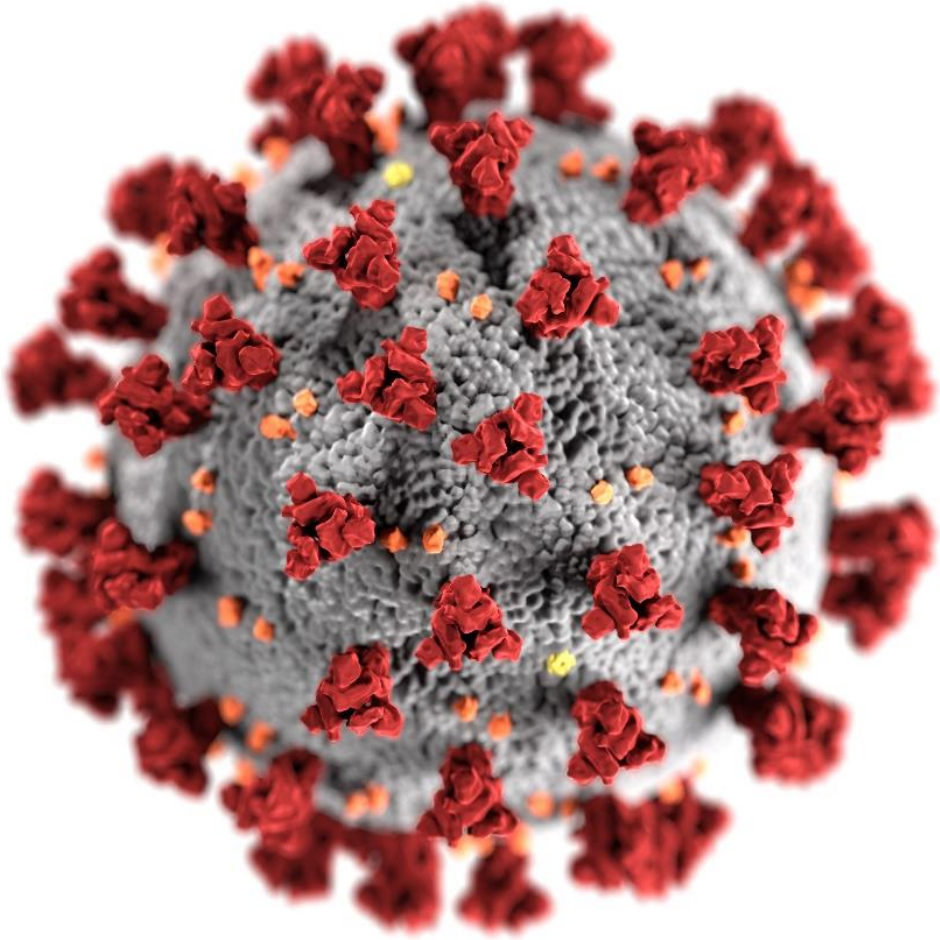
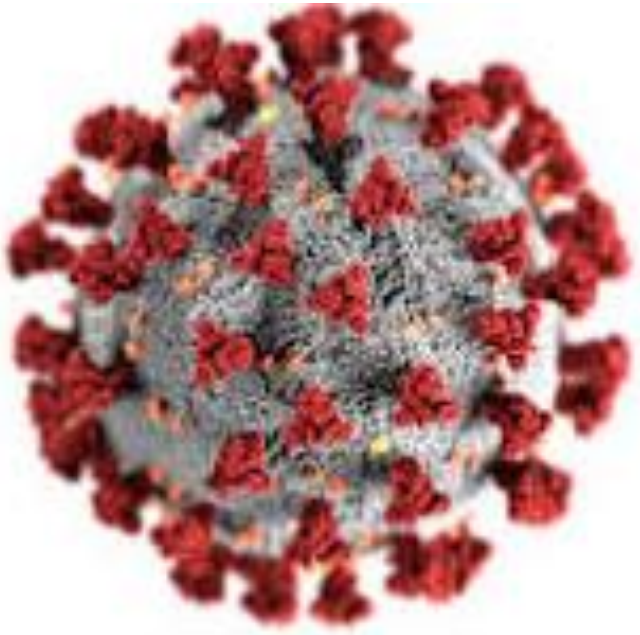
June 29, 2020



cdc.gov/coronavirus

Goals of serologic studies in CDC COVID-19 public health response

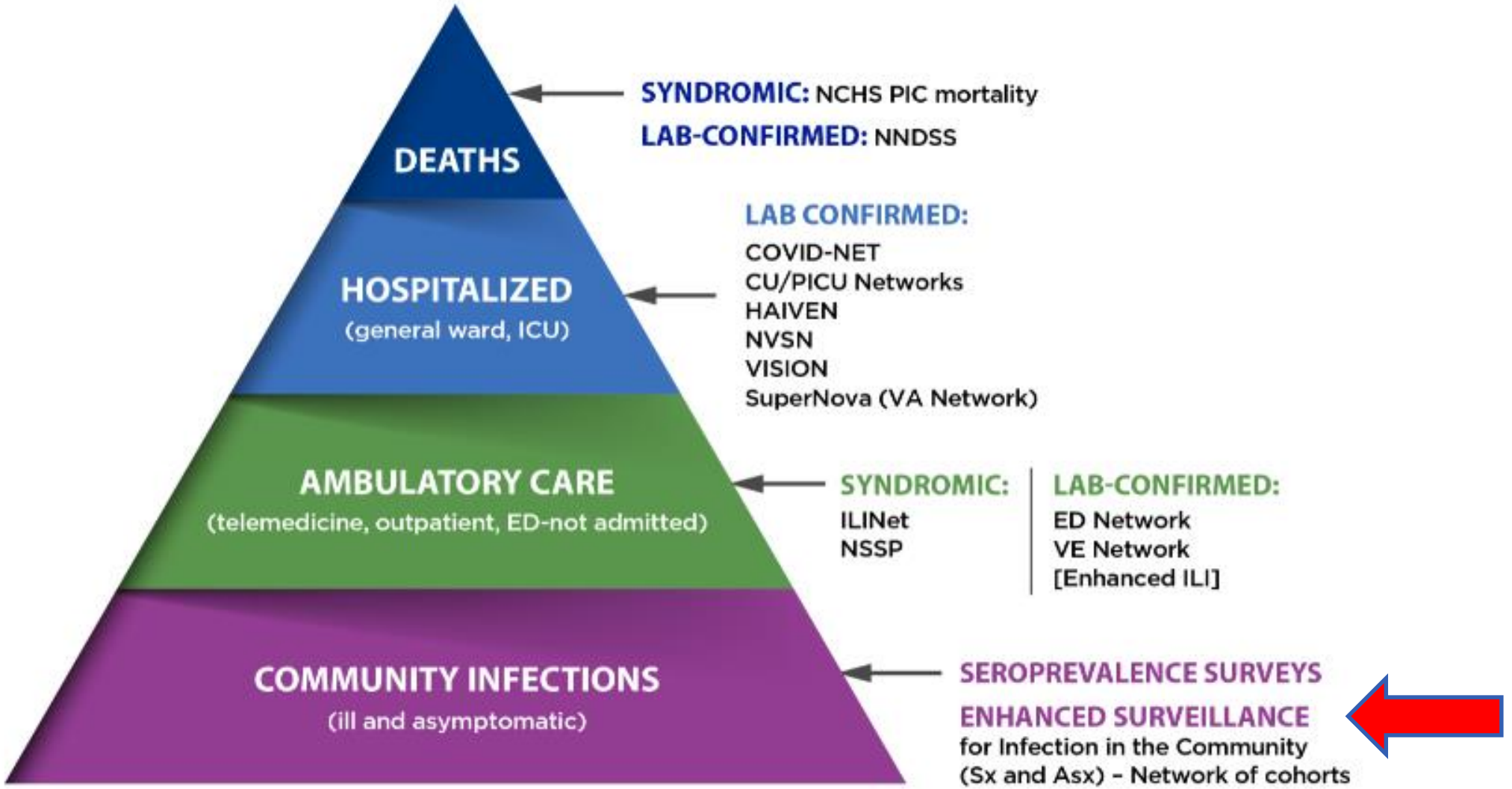
- Determine proportion of population exposed to SARS-CoV-2 and how this changes over time
- Determine risk factors associated with SARS-CoV-2 infection, including household transmission, and transmission in health care settings
- Determine spectrum of illness associated with SARS-CoV-2 infection
- Determine immunologic profile following infection
- Determine whether presence of antibodies indicates decreased transmissibility following infection or immunity/protection from future infection



Multiple study designs used to address different issues

	Monitor prevalence of infection, many locations over time	Monitor incidence of symptomatic and asymptomatic infection, many locations over time	Natural history of infection, severity, immunology, sequelae	Reinfection, Correlates of protection	Transmission dynamics
Large Geographic Serosurveys	X				
Longitudinal Cohorts	X	X	X	X	X
Household studies		X	X		X
Natural history studies			X	X	X

Surveillance to assess disease burden



Antibody detection as indicator for past infection

Large-scale Geographic Seroprevalence Surveys

The largest surveys that CDC is conducting are called "large-scale geographic seroprevalence surveys." These surveys are being conducted in locations across the United States and are first focusing on areas highly impacted by COVID-19, such as Washington State and New York State, including New York City. Large-scale surveys may perform serology testing on additional blood samples that were originally used for other purposes (e.g., routine cholesterol test). No names are linked to the blood samples used in these surveys. This means the identity and privacy of people whose blood is tested is protected. One limitation of these surveys is that people tested are not necessarily representative of the population for that area.

Special Populations Seroprevalence Surveys

These seroprevalence surveys answer questions about specific populations, such as healthcare workers or pregnant women. Because they examine samples from a specific population, their findings cannot necessarily be applied to other populations. However, such surveys can help answer important questions about the risk of infection within specific populations.

Community-level Seroprevalence Surveys

These surveys cover smaller areas than a "large-scale geographic survey." They sample from select counties, and within this area, the selection of participants is completed in a systematic way. This allows for a more representative population to be tested where results might apply to other similar populations. CDC is working with state and county health departments to learn more about how COVID-19 is spreading in communities by performing serology tests in households in various communities.

Questions CDC **wants to answer** through Serology Surveillance

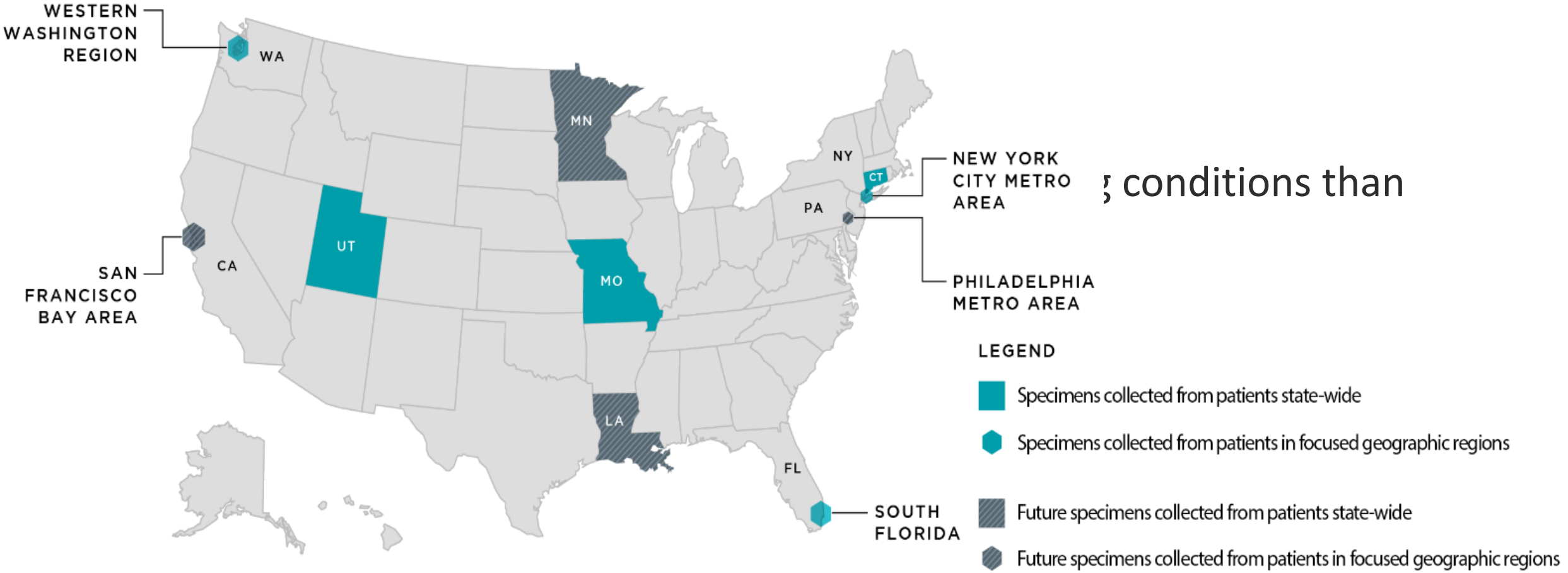
- How much of the U.S. population has been infected with the virus causing COVID-19 (SARS-CoV-2)?
- How is this changing over time?
- Are there different characteristics, or risk factors, that are associated with SARS-CoV-2 infection, such as age, location, or underlying health conditions?
- How many U.S. residents experienced mild or asymptomatic COVID-19 illness?
- How long can antibodies be found after a COVID-19 infection?

Questions CDC **cannot answer** through Serology Surveillance

- How much of the U.S. population is immune to COVID-19 and not able to get infected again?
- How many antibodies are needed to protect someone from COVID-19?
- How long will someone with antibodies be protected from COVID-19?
- Can you be re-infected with COVID-19?
- Can people with antibodies return to work?

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/serology-surveillance/index.html

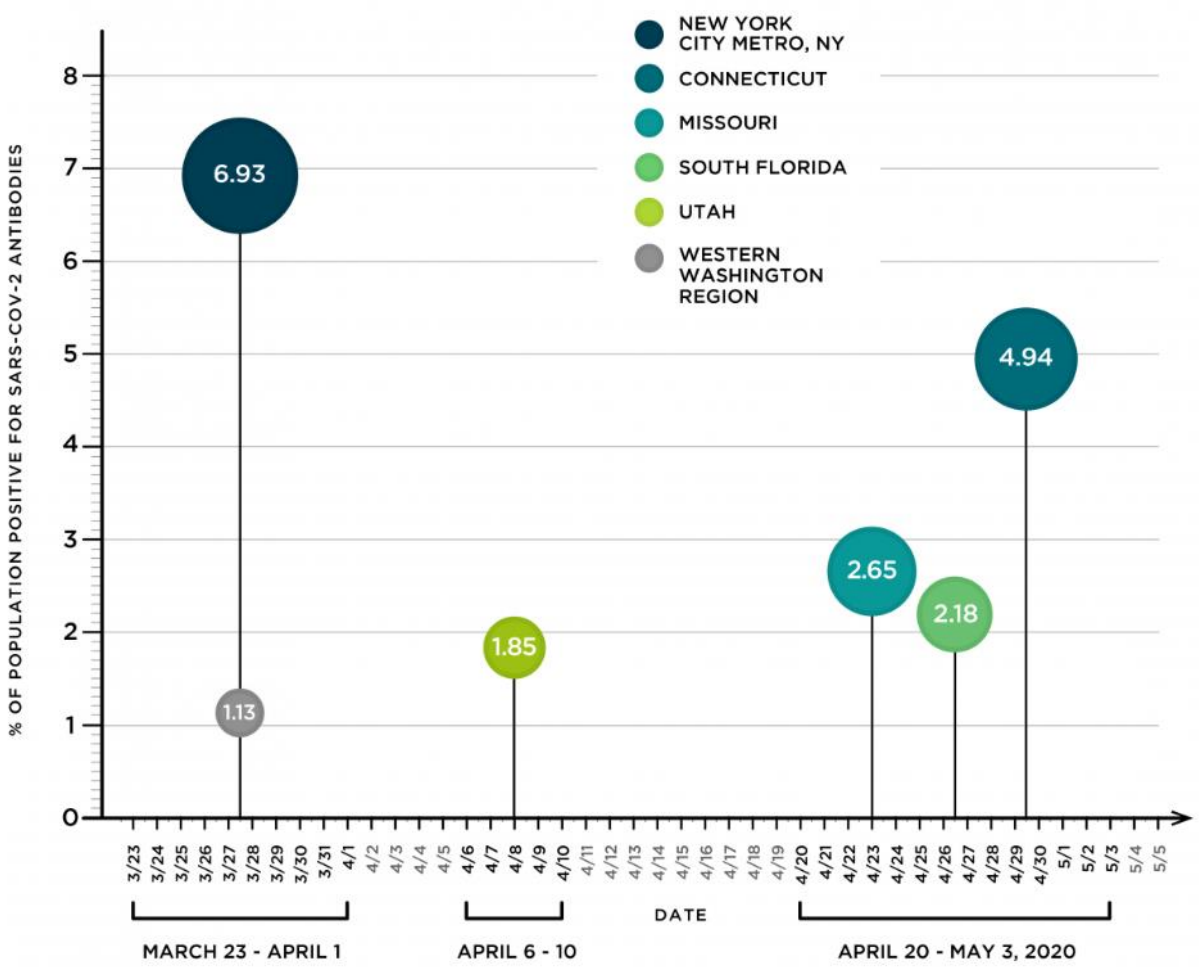
Large-scale geographic seroprevalence surveys using residual clinical specimens from commercial labs



; conditions than

https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/commercial-lab-surveys.html

Initial seroprevalence, estimated infections and ratio to reported cases, 6 commercial lab sites



Site	Sero-prevalence	Estimated Infections[1]	Reported Cases	Ratio
WA	1.13%	48.300	4,300	11.2
NYC	6.93%	641,800	53,800	11.9
S.FL	1.85%	117,400	10,500	11.2
MO	2.65%	161,900	6,800	23.8
UT	2.18%	47,400	4,500	10.5
CT	4.94%	176,700	29,300	6.0

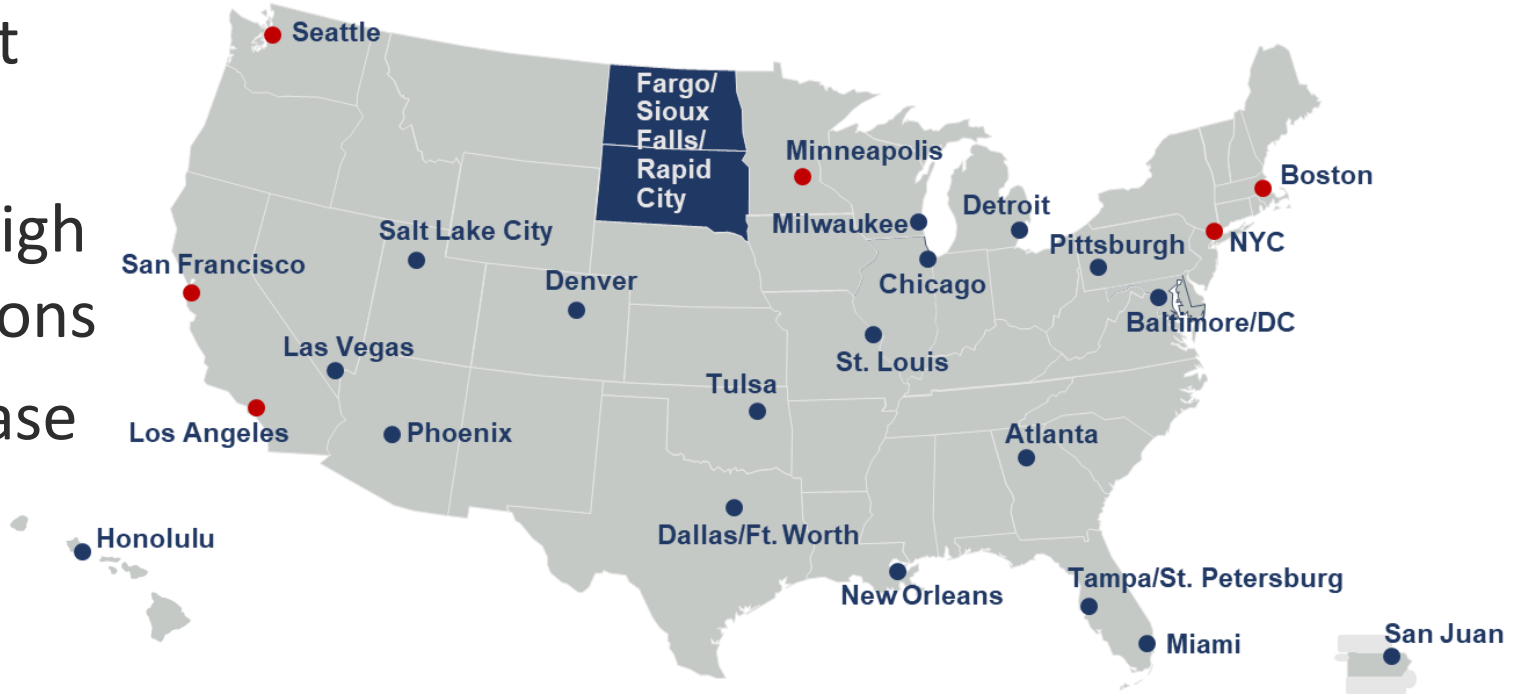
[1]As of the last day of specimen collection

https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/commercial-lab-surveys.html

Large-scale geographic seroprevalence surveys using blood bank donor sera

- 25 metropolitan areas
- 1000 specimens
- Monthly x 12 months and at 18 months
  - Broad distribution of high and low incidence regions
  - Oversampling to increase younger donors and racial/ethnic diversity

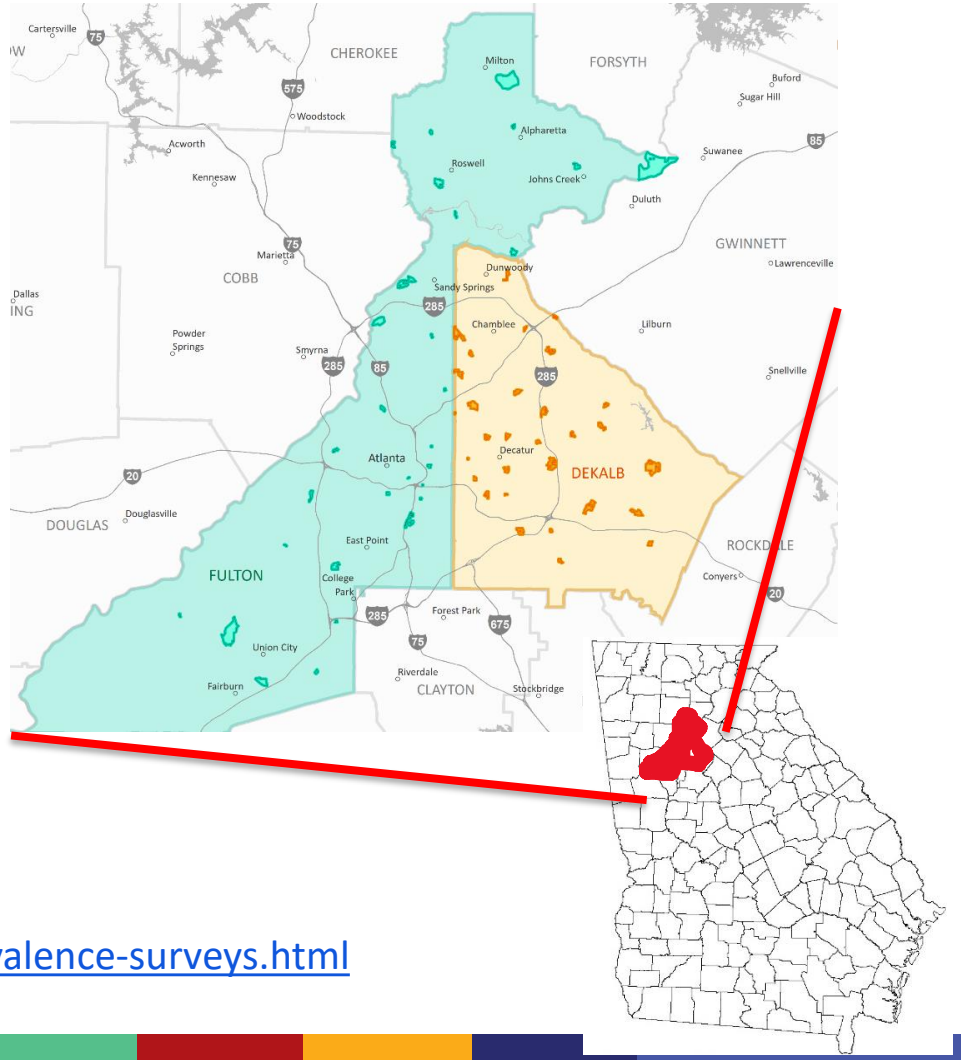
Preliminary sites for longitudinal serosurvey among blood bank donors



https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/geographic-seroprevalence-surveys.html#BloodDonorSurvey

Community level seroprevalence pilot survey: DeKalb and Fulton Counties, GA, April 28-May 3

- Multistage cluster sampling design based on modified CDC Community Assessment for Public Health Emergency Response (CASPER) framework
- Provides representative sampling for extrapolation to catchment population
- Within each county, 30 census blocks randomly selected with probability proportional to the number of occupied households (2010 U.S. Census)
- Within each of 60 selected census blocks, households systematically sampled with goal of 7 households/census block (total 420 households)

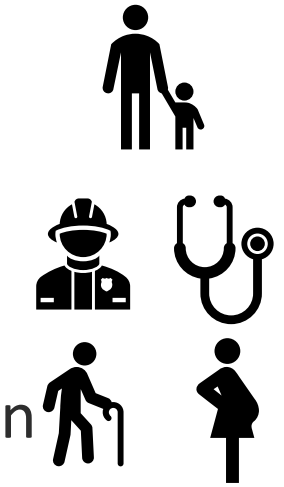


https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/community-level-seroprevalence-surveys.html

Longitudinal cohorts and natural history studies

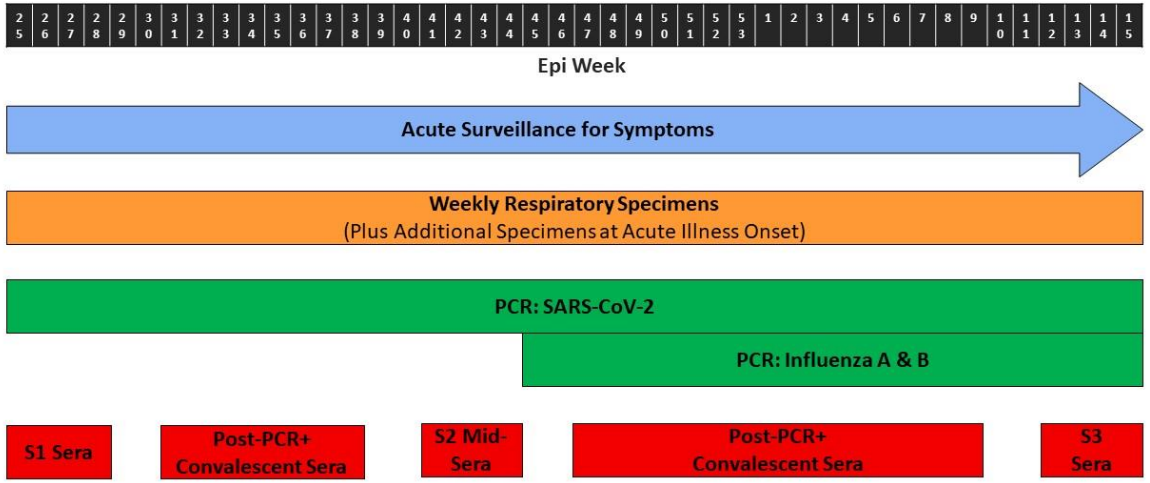
- Assess
  - Antibody kinetics
  - Function
  - Correlates of immunity
  - Risk factors for infection
- Determine if antibodies
  - Prevent/attenuate reinfection
  - Persist
  - Cross-protect

- Planned cohorts and studies in special populations
  - Households with children
  - Community cohorts
  - Cohorts of HCP, 1st responders
  - Cohorts of older adults
  - Cohorts of pregnant woman
  - Cohorts of previously infected

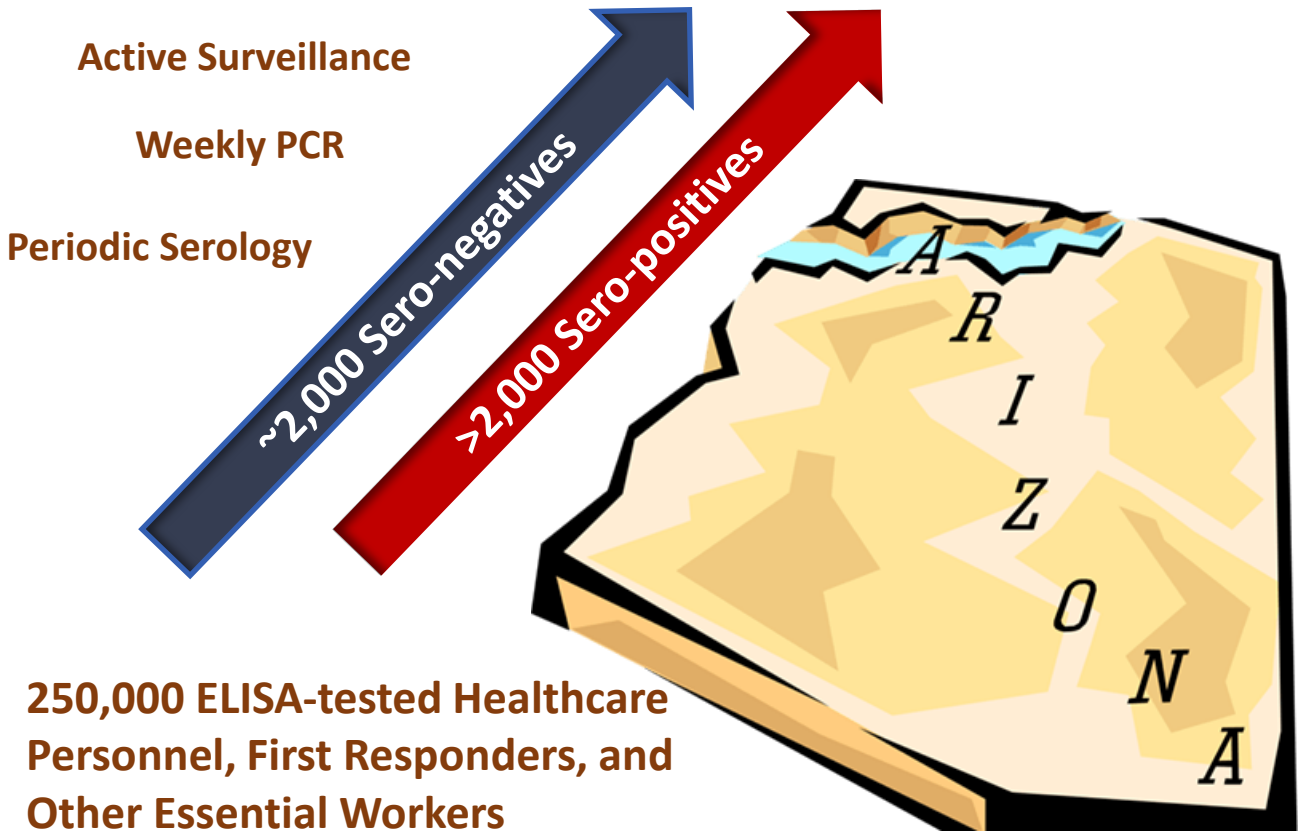


Harmonized approach across cohort studies

- Enroll cohort representative of source population
- Prospective follow-up over 8-12 months (including Fall/Winter)
- Weekly respiratory specimen collection regardless of participant symptoms *plus* additional specimen with acute illnesses
- Weekly symptom surveillance
- Periodic serum collection
- Medical record surveillance



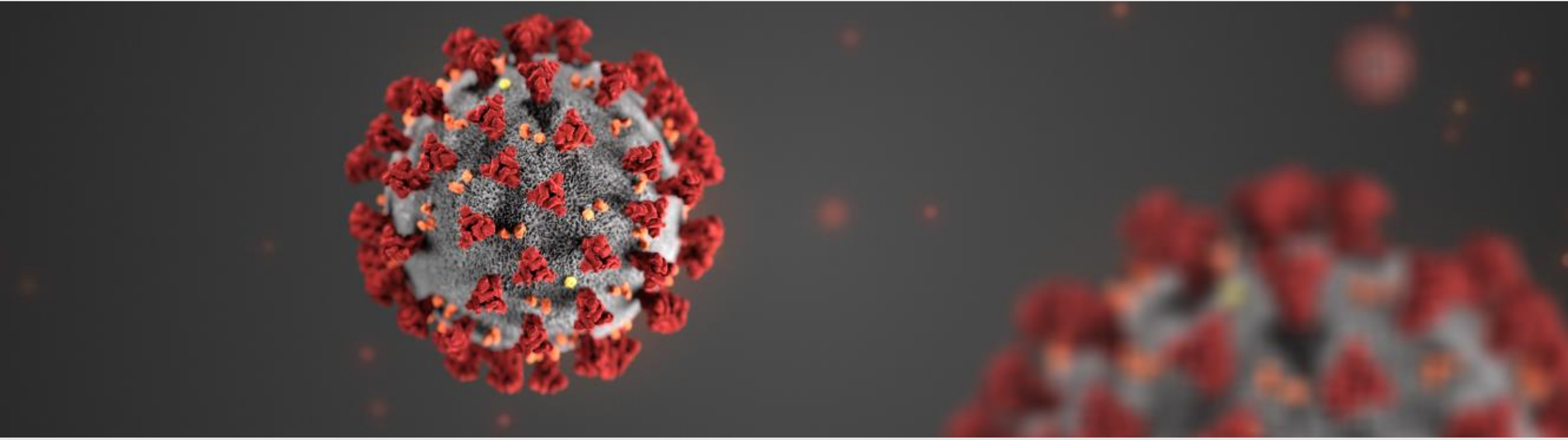
Arizona healthcare, emergency response and other essential workers surveillance (HEROES)



- Incidence of symptomatic COVID-19 and asymptomatic SARS-CoV-2
  - By PCR and Serology
  - Statistically powered to detect re-infection of 1-2%
  - Critical to burden and population susceptibility forecasting
  - Examine correlates of protection
- Healthcare personnel, first responders, and essential workers
  - Hispanic, Native American, and both urban and rural populations
- Partnership between University of AZ, State Health Department, NIH, and CDC

Conclusions

- Seroprevalence surveys implemented across a wide range of levels
  - Large longitudinal serosurveys assess temporal and geographic trends
  - Community serosurveys assess representative infection rates
  - Compare with reported cases to assess under-ascertainment and estimate disease burden
- Longitudinal cohort studies
  - Characterize natural history of SARS-CoV-2 infection
  - Define antibody kinetics and immune response
  - Assess variability across different populations
- Inform development and potential impacts of preventive measures, including future vaccines



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Thank you!

Seroprevalence Surveys for COVID-19

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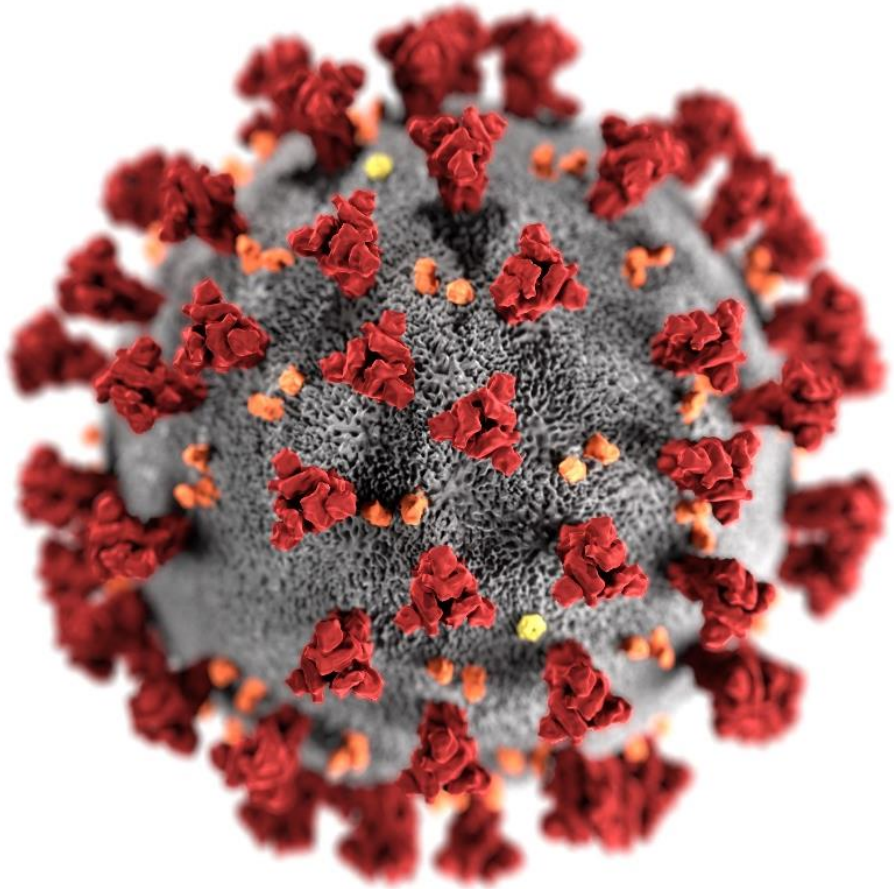

For more information: **www.cdc.gov/COVID19**