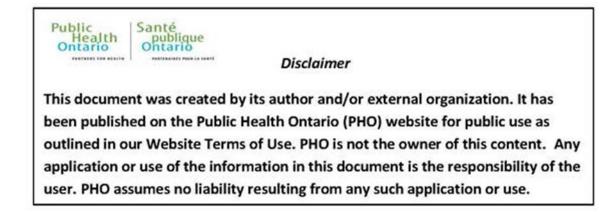


To view an archived recording of this presentation please click the following link: https://youtu.be/Vemd9IWFiBk

Please scroll down this file to view a copy of the slides from the session.





### COVID-19 Diagnostics to Save Lives and Livelihoods: Promises and Challenges

Rosanna W Peeling Professor and Chair, Diagnostic Research Director, International Diagnostics Centre



www.idx-dx.net

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## **Plan of Presentation**



- The role that diagnostic tests play in the COVID-19 pandemic response
- Diagnostic innovations to save lives and livelihoods
- Lessons learnt from the COVID-19 pandemic: promises and challenges going forward

**Disclaimer: Mention of company products does not imply endorsement** 

## COVID-19 Pandemic: Test, Test, Test



#### The Director-General of the World Health Organization urged countries to "test, test, test."

He said **testing**, **isolation**, **and contact tracing** should be the backbone of the global pandemic response.

World Health Organization. Director general's opening remarks at the March 16 2020 media briefing. <u>https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---16-march-2020</u>

## The Value of Diagnostics for Infectious Diseases of Epidemic Potential

#### For patient management:

- Confirm clinical diagnosis in symptomatic patients
- Enable patients to get the right treatment and appropriate care
- Inform patients of measures to stop spread of infection

#### For disease control & prevention

- Enable contact tracing and screening of those at enhanced risk of acquiring and transmitting infection to interrupt the chain of transmission
- Map location of cases to track pattern of transmission and identify hotspots
- Guide the implementation of disease control strategies such as wearing masks, quarantines, lockdowns, border measures

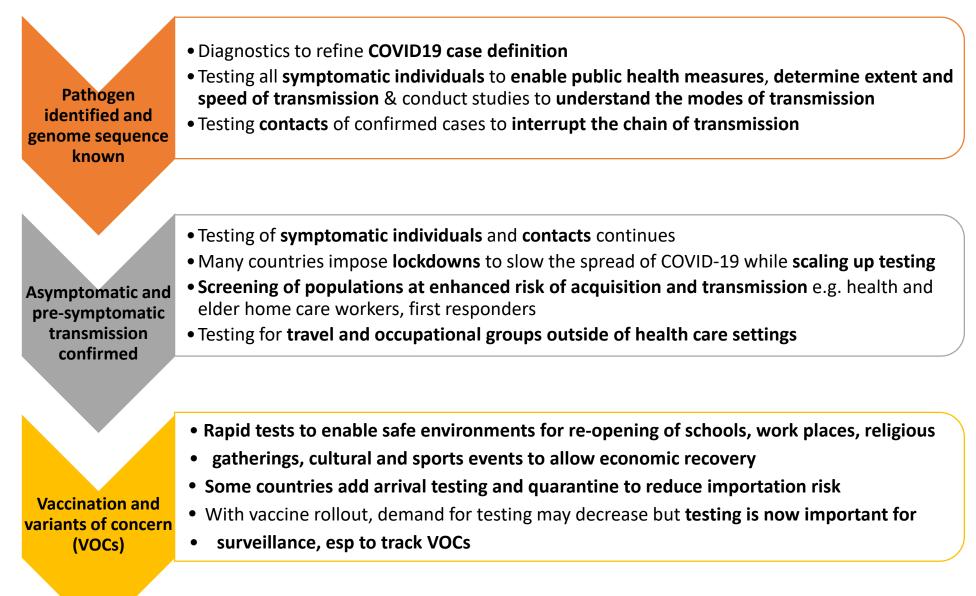
### The <u>Right Test</u> for the <u>Right Patient</u> at the <u>Right Time</u> in the <u>Right Setting</u>

COVID-19	Target	Optimal	Optimal Use Case Accuracy		racy	Access-	Affordability
Diagnostic tests commercialised		time for use post onset symptoms		Sens	Spec	ibility	
Molecular: Lab N=388 POC	Viral RNA	day 0-7	confirm infection	***	***	<mark>∨</mark> √√	\$\$\$
Antigen: Lab N=165 POC	Viral Proteins	day 0-7	confirm infection	**	***	√√ √√√	\$\$
Serology: Lab N=412 POC	Host Antibodies	day 7-40	exposure, surveillance	***	* * *	√√ √√√	\$

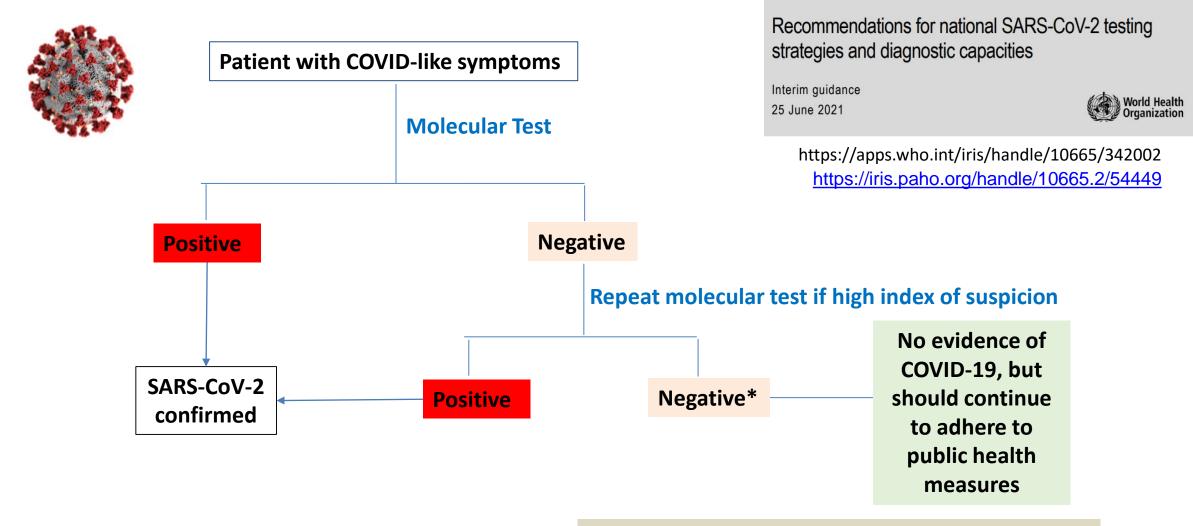
COVID-19 Test pipeline:

https://www.finddx.org/covid-19/pipeline/?avance=all&type=all&test\_target=all&status=all&section=show-all&action=default#diag\_tab WHO Emergency use authorization listing: 16 molecular tests and 3 antigen rapid tests

## Evolving Role of Diagnostics: from Pandemic Response to Control

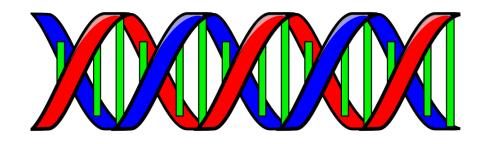


## **Covid-19 Diagnostic Algorithm**



\*Still high index of suspicion: Do Antibody test – not part of WHO recommendation

## Challenges with Scaling up Molecular Testing Worldwide



High per test cost



• Requires laboratory and expensive equipment



- Requires skilled personnel
  - Results take hours or even days, depending on volume



• POC tests - supply limited by speed of manufacturing



Global competition led to inequities of access

## **Testing Truck Drivers in Kenya**



- May 2020: Much of Africa's multibillion-dollar cross-border trade has been halted because of the COVID-19 pandemic
- Trucks at the port carry cargo destined for Uganda, Rwanda, Burundi, South Sudan and the Democratic Republic of the Congo are stuck at the port of Mombasa, Kenya
- Truck drivers identified as a high-risk group for spreading the virus have to be tested for coronavirus before they leave the port but <u>results can take up to 2 weeks</u>

The International Organization for Migration (IOM) provided rapid COVID-19 PCR tests to truck drivers across Kenya as part of an effort to reinvigorate regional economies in Eastern and Central Africa.

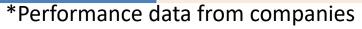
Test results were available within 24-36 hours. IOM staff tested >17,000 drivers from July to Oct 2020 with ~2% positive rate. Where once there was a 90-kilometer traffic jam at a border, there is a relatively freer flow of goods out of the port of Mombasa to countries in the region.

https://www.voanews.com/covid-19-pandemic/rapid-covid-19-tests-kenyan-truckers-revive-african-economies https://reliefweb.int/report/kenya/timely-covid-19-testing-mombasa-port-truckers-helps-reinvigorate-economie

## FDA EUA approved COVID-19 Antigen Instrument-based Assays

WHO has recommended Ag Test sensitivity of 80% and Specificity of 97% vs Molecular test e.g. PCR

Company/test	Assay Technology	Ag	Sym/ Asym	Nasal/ NP swab	Time to result	Sensitivity (95% CI)*	Specificity (95% CI)*	
Becton- Dickinson/ Veritor	Chromatographic Digital Immunoassay + flu A and B	NuP	A+Sym	N	15 min	84% (67-93)	100% (98-100)	
Luminostic /ClipCOVID	Lateral flow immunoluminescent assay	NuP	Sym d.1-5	N	30 min	97% (84-99.9)	100% (97-100)	
Lumira	Microfluidic Immunofluorescence assay	NuP	Sym d.1-12	N, NP	12 min	97.5% (87-99.6)	97.7% (94.7-99)	
Quidel Sofia	Lateral Flow, Fluorescence + flu	NuP	A+Sym d.1-5	N,NP	15 min	96.7% (83-99)	100% (98-100)	



NuP = nucleocapsid protein; sym= symptomatic; A=asymptomatic; N=nasal; NP= nasopharyngeal









## Examples of Single-use Disposable COVID-19 Antigen Rapid Tests

Company/test	Home test	Asym/ Sym	Nasal/ NPswab	Sensitivity	Specificity	Limit of detection	
DA EUA: (performance data from companies)							
Abbott BinaxNOW	-	A+S	Ν	93.3%	99.9%	-	
Abbott BinaxNOW home test (app)	V	A+S	Ν	91.7%	100%	-	
Abbott BinaxNOW self-test (app)	V	A+S	Ν	84.6%	98.5%	-	
Access Bio/CareStart	V	A+S	N, NP	88.4%	100%	-	
Ellume/Ellume home test (app)	V	A+S	Ν	96.0%	100%	-	
Princeton BioMedtech/Status	-	Sym	NP	93.9%	100%	-	
Quidel/Quikvue home test	V	A+S	Ν	84%	99%	-	
WHO EUAL: (performance data from	n FIND)					_	
Abbott PanBio	-	A+S	NP	90.9%;	99.2%	6.88 x 10 <sup>5</sup>	
			Ν	86.4% <b>CT&lt;25: 96.8%</b>	99.2%	Viral copy/mL	
SD Biosensor/Standard Q	-	sym	NP	89%; CT <u>&lt;</u> 25: 97%	99.7%	1.15x 10 <sup>6</sup> Viral copy/mL	
Premier Sure Status	-	Sym	NP	74-91%	99.6%	5.97x 10⁵ Viral copy/mL	

WHO has recommended: Sensitivity of 80% and Specificity of 97% Compared to molecular test

Most Ag-RDTs use the SARS-CoV-2 Nucleocapsid Protein of as target – performance <u>unlikely to be</u> <u>affected by variants of</u> <u>concern</u>

Home tests available over the counter for 2.5- 5 USD

sym= symptomatic; A=asymptomatic; N=nasal; NP= nasopharyngeal; CT=cycle threshold  https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medicaldevices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2
 https://www.finddx.org/sarscov2-eval-antigen

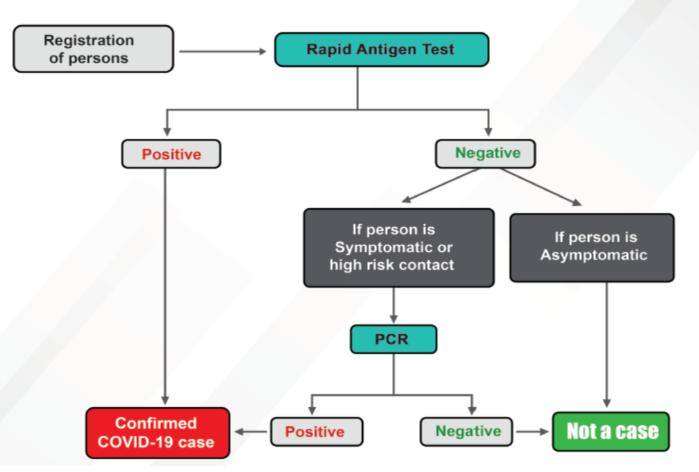
### **Evolution of COVID-19 Detection among Symptomatic patients**



#### PHEOC

#### NATIONAL ALGORITHM FOR COVID-19 TESTING

REPUBLIC DU CAMEROON MINISTRY OF PUBLIC HEALTH



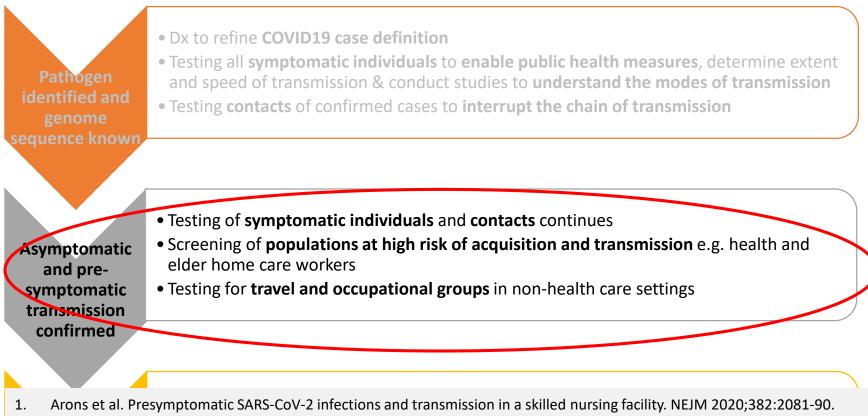
### **Use of Antigen RDTs**

- 80,000 Reported cases (pop 26 million)
- 60% Detected with Antigen RDTs



Boum Y, et al. Lancet Infect Dis. March 25, 2021

### Evolving Role of Diagnostics: from Pandemic Response to Control



- 2. Almadhi et al.. The high prevalence of asymptomatic SARS-CoV-2 infection reveals the silent spread of COVID-19. Int J Infect Dis. 2021 Feb 26:S1201-9712(21)00186-7.
- 3. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. NEJM 2020;382(10): 970-1.
- 4. Furukawa et al. Evidence supporting transmission of severe acute respiratory syndrome coronavirus 2 while presymptomatic or asymptomatic. Emerg Infect Dis. Jul 2020.
- 5. Gandhi et al. Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19. NEJM Apr 24 2020

## Testing strategy for the COVID-19 pandemic: Need for a broader framework for policy consultations

## Scaling up testing – policy decision-making needs to be:

- Science-based
- Inclusive not limited to:
  - Public health, health professionals
  - Education
  - Civil societies e.g. indigenous groups, disabled persons
  - Finance
  - Trade
  - Tourism
  - Border security
- Context specific: political, cultural, social, and economic
- Agile evolve with pandemic trends and new issues:
  - Variants of concern
  - Vaccination
- Conveyed in clear and compelling messages to the public

#### Testing in healthcare settings to save lives

- Hospitals
- Care homes for the elderly
- Clinics/doctor's offices
- Nursing stations in remote settings

## Testing in non-healthcare settings to save livelihoods:

- Pharmacies
- Schools
- Workplaces
- Mass gatherings
- Border crossings

## COVID-19 Rapid Antigen Tests to Save Lives and Livelihoods\*

### As a diagnostic tool:

- Confirm clinical diagnosis in symptomatic patients:
  - hospitals
  - clinics, doctors' offices
  - testing centres
- Contact tracing
- Case finding in individuals at risk of acquiring and transmitting infection:
  - health care workers
  - first responders
  - essential workers

#### As a public health tool:

Test to protect: vulnerable populations



- Time to release: quarantine
- Test to enable: re-opening of schools, return to work; mass gatherings; travel

#### Home or self-testing:

- Tests available over-the-counter
- Can download an app for instructions and use phone app to read results

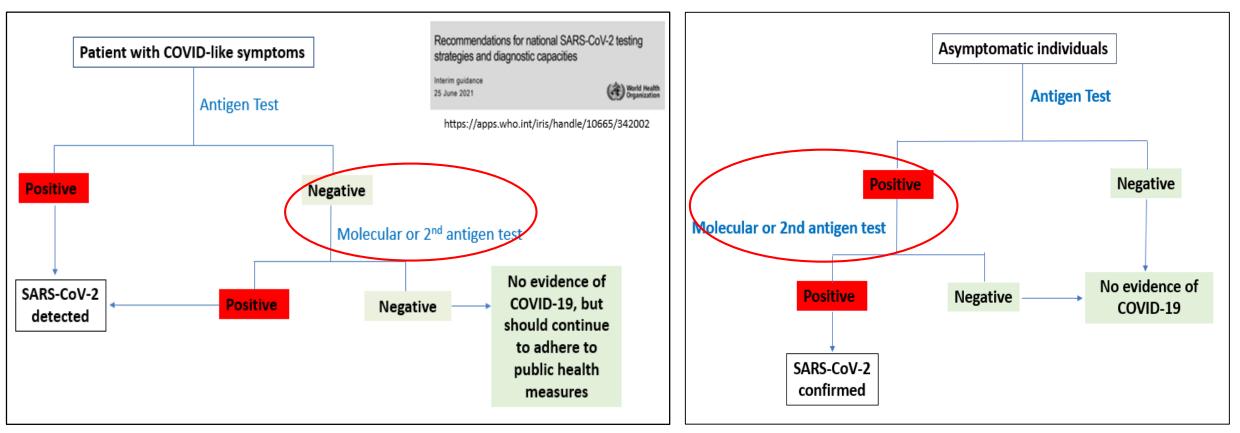
\*World Health Organization. Speech of the Director-General.

https://www.who.int/news/item/28-09-2020-global-partnership-to-make-available-120-million-affordable-qualitycovid-19-rapid-tests-for-low--and-middle-income-countries

 Significant logistics and capacity constraints – ranging from the availability of trained personnel to take specimen and perform the tests correctly to the procurement and distribution of test kits and data available in real-time to inform control measures



## **COVID-19 Diagnostic Algorithms**



Peeling et al. Scaling up COVD-19 rapid antigen tests: promises and challenges. Lancet Infect Dis. 2021 Feb 23 2021. Watson et al. Interpreting a COVID-19 test result. BMJ May 2020;369:m1808 Schwartz et al. Rapid antigen screening of asymptomatic people as a public health tool to combat COVID-19. *CMAJ* 2021 March 29;193:E449-52 Test to Protect the Vulnerable and Save Lives

Who to screen? What Test? Frequency?

## Tests to Protect:

WHO to screen: at increased risk of acquisition and transmission of COVID-19.

- Healthcare and elder care home workers
- essential frontline workers (including first responders)
- public and aviation transport operators

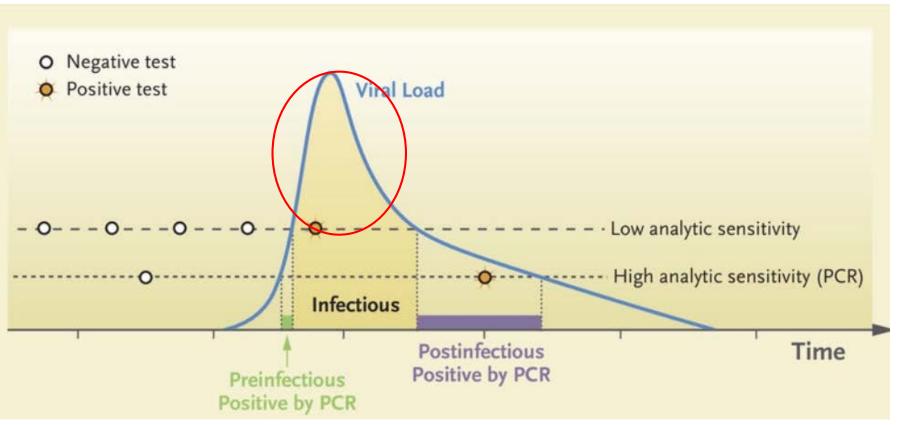
#### Testing sensitivity and time to result:

With R <sub>0</sub> =1.5, daily testing:	Effectiveness			
Test sensitivity 20%	85%> 81%			
Test result delay of 3 days	85%> 57%			
Test result delay of 5 days	85%> 26%			

What test to use: Rapid antigen tests should therefore be considered if time to result of molecular tests is suboptimal.

Ref: Chin et al. Frequency of Routine Testing for COVID-19 in High-risk Healthcare Environments to Reduce Outbreaks. Clin Infect Dis. Oct 2020. Black et al. COVID-19: the case for health-care worker screening to prevent hospital transmission. Lancet. 2020;395:1418–20.

### For COVID-19 Screening, Test Sensitivity is Secondary to Frequency and Turnaround time



Larremore et a. Test Sensitivity is Secondary to Frequency and Turnaround time for COVID-19 Screening. Sci Adv 2020

Mina MJ et al. Rethinking strategy for containment. N Engl J Med 2020; 383:e120

RNA tests can be positive for weeks after onset of symptoms

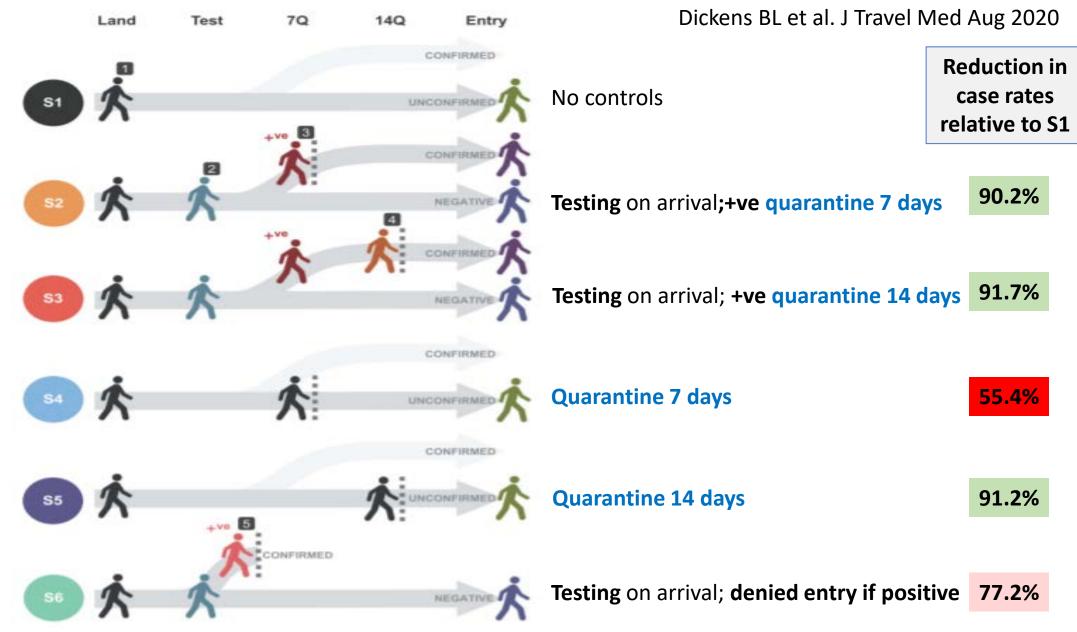
Period of infectiousness ~8 days post onset of symptoms

Although less sensitive most antigen Test should be able to detect individuals who are at risk of transmission (viral loads equivalent to PCR Cycle Thresholds (CT) of <25)

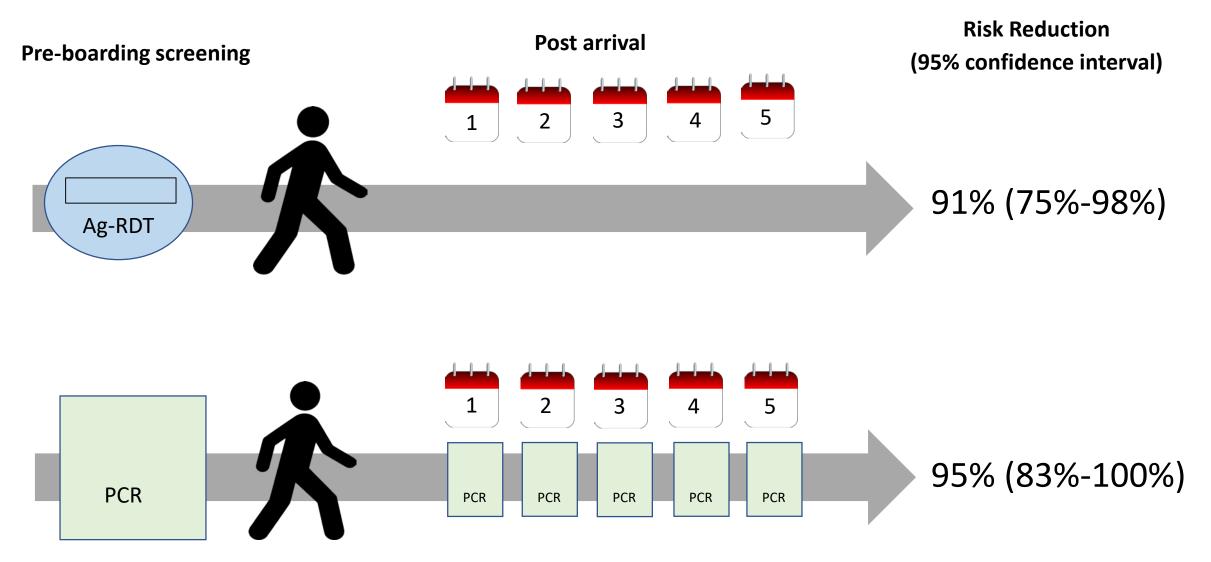
## Test to Release

from Quarantine to Save Livelihoods

### Modelling Strategies for Reducing Importation Risk of COVID-19 Cases



## Testing on Arrival + No Quarantine



Quilty BJ, et al. Quarantine and testing strategies to reduce transmission risk from imported SARS-CoV-2 infections: a global modelling study. medRxiv preprint doi: https://doi.org/10.1101/2021.06.11.21258735; posted June 14, 2021.

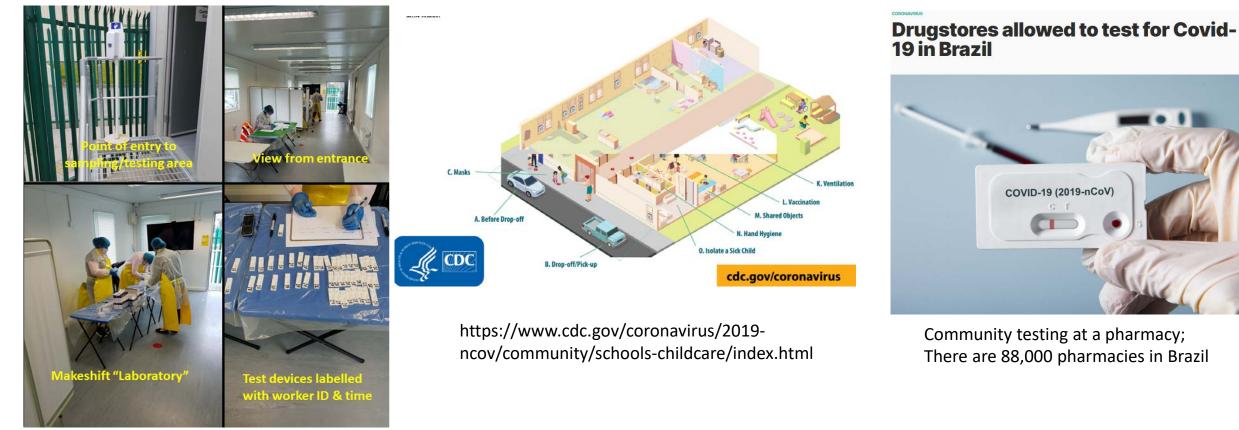
## Test to Enable and Save livelihoods

Return to schools, workplaces mass gatherings

## Test to enable: re-opening of schools and workplaces

#### Who to test? Frequency? What test? Where?

Strategies often based on modelling projections vs evidence of effectiveness

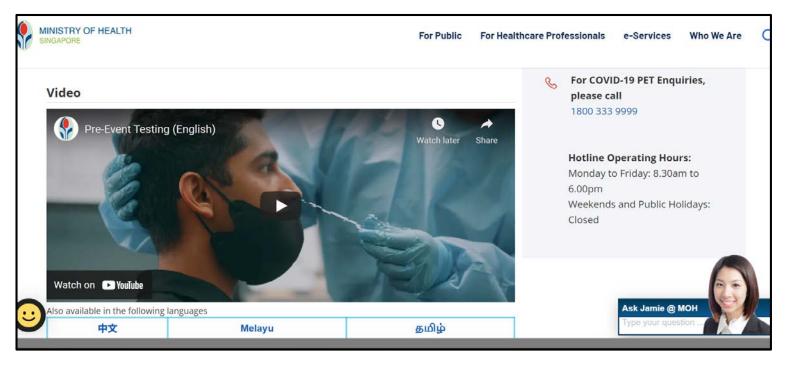


Testing: meat processing plant, Ireland

https://www.hiqa.ie/reports-and-publications/healthtechnology-assessment/radts-meat-processing-plants An Evidence Co-op for Sharing Antigen Testing Strategies and Shaping Best Practices <u>https://courses.globalhealthcpd.com/courses/evidence-</u> <u>coop-for-antigen-testing-strategies</u>

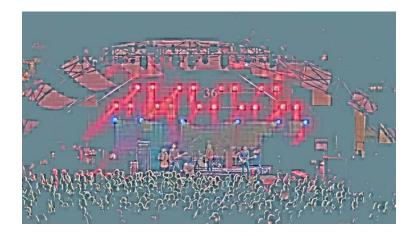
## Tests to enable: mass gatherings

Singapore: Pre-event testing e.g. trade shows, conferences, weddings



https://www.moh.gov.sg/covid-19/statistics/pet





The COVID-19 Evidence Co-op #2: Travel & Mass Gathering Events <u>https://courses.globalhealthcpd.com/courses/covid-19-evidence-coop-2-travel-mass-gatherings</u>

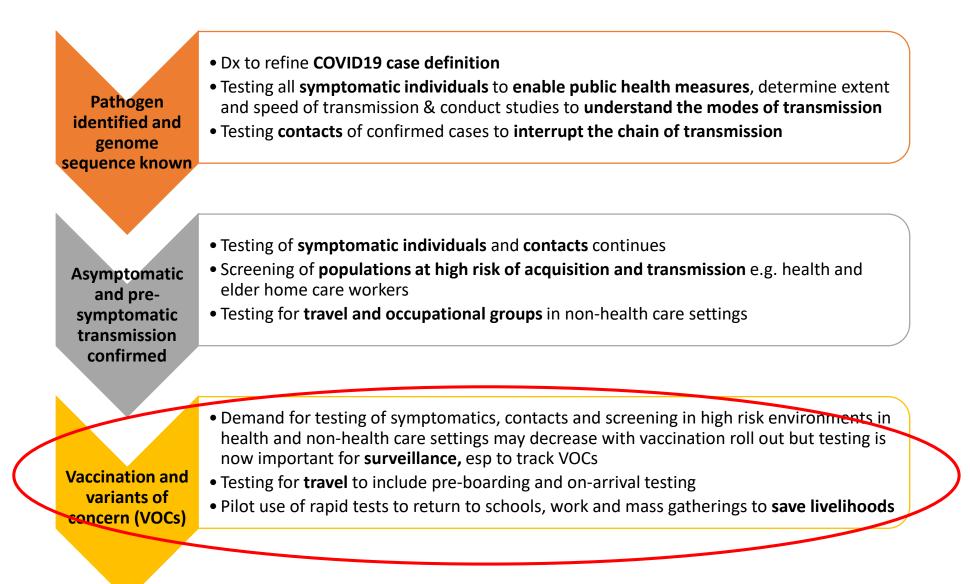
## Mass Gathering: Music Event, Barcelona

Venue: indoor centre # Participants: 465 (RCT, control group of 495 did not enter the venue)

Entry	Concert	Post-event	
Checks: • temperature	<b>Contact time</b> : mean 2.5 hours, max. 5 hours	Monitoring of safe environment:	
• Preventive measures: • Wearing masks	Ventilation: standard + windows and doors open Preventive measures:	All participants, including control group, tested 8 days post event.	
• <b>Testing</b> : • Who: all • What test: antigen tests	Wearing masks <b>Physical distance</b> : None – all can sing/dance	None tested positive among case group vs 2 in control group	
When: 9 hours before entry	On site medical and security personnel		

Ref: Revello et al. Lancet Inf Dis May 2021; Peeling RW, Heymann D. Innovations in COVID-19 testing: the road from pandemic response to control. Lancet Infect Dis. May 2021.

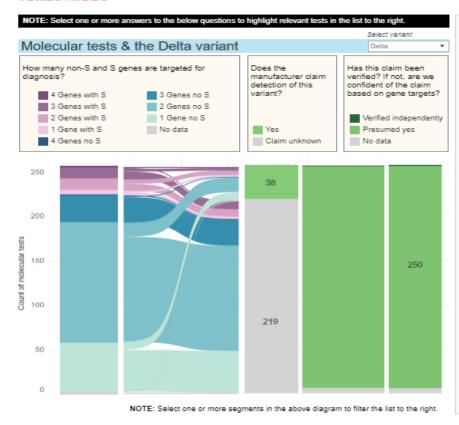
### Evolving Role of Diagnostics: from Pandemic Response to Control



## SARS-CoV-2 Variants of Concern

Variant of Concern	First identified	Mutations of concern	#countries Reporting	Increased Transmission*	Impact on vaccine efficacy
Alpha B.1.1.7	UK Sept 2020	<b>N501Y</b> ; 570D; P681H	118	59-74%	Minimal reduction in neutralization
Beta B.1.351	South Africa May 2020	N501Y K417N; E484K;	64	~50%	Reduced neutralization
Gamma P.1	Brazil Nov 2020	N501Y; K417N; E484K;	38	not clear	Significant reduction in neutralization
Delta B.1.672.2	India Oct 2020	L452R, 478K, D614G, P681R	>100	>50% compared to Alpha variant	Reduction in neutralization

#### PATH

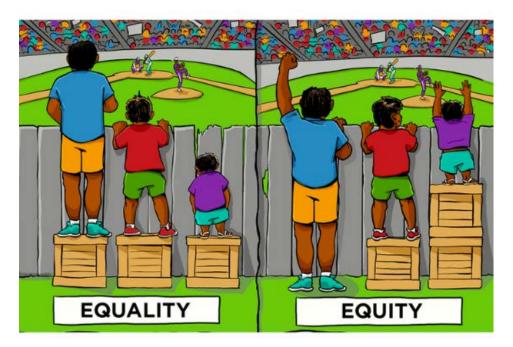


US Food and Drug Administration. <u>https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests</u>

Program for Appropriate Technology for Health. Do COVID-19 tests still work against Delta and other variants? https://www.path.org/articles/new-variants-will-covid-19-tests-still-work/

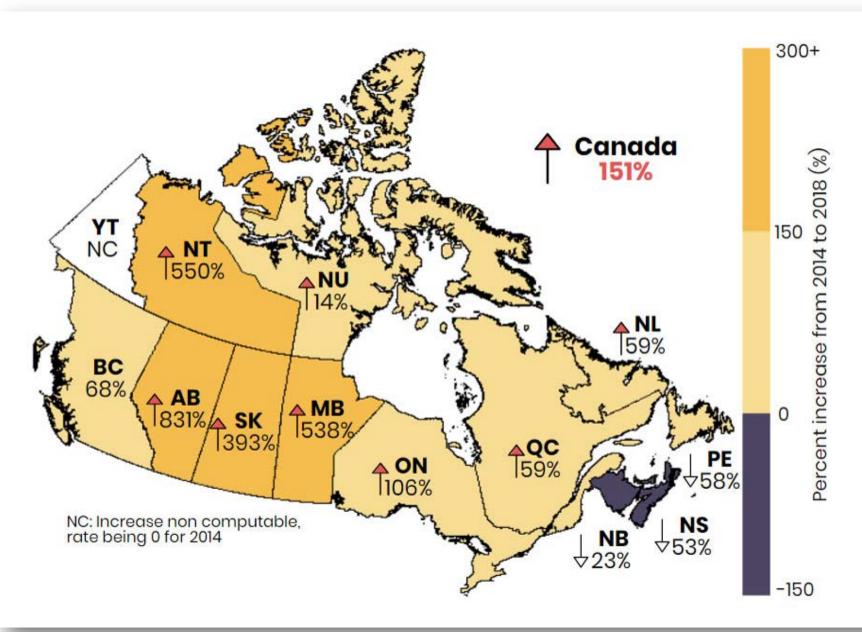


- COVID exposed fault-lines and inequities in health care systems, esp. access to quality-assured diagnostics and care in remote and marginalised communities
- Rethink public health approaches and how to gain trust and confidence in public health measures
- Build back better: resilient health systems with better community engagement and people-centred services



Courtesy of Dr. Yap Boum, Cameroon

#### Increase in Syphilis rates across Canada: Urgent Need for More Accessible Diagnostics



**Ontario:** 2019 outbreak in London; 2020-21: syphilis cases continue to rise with sharp spikes reported in Hastings and Prince Edward counties.

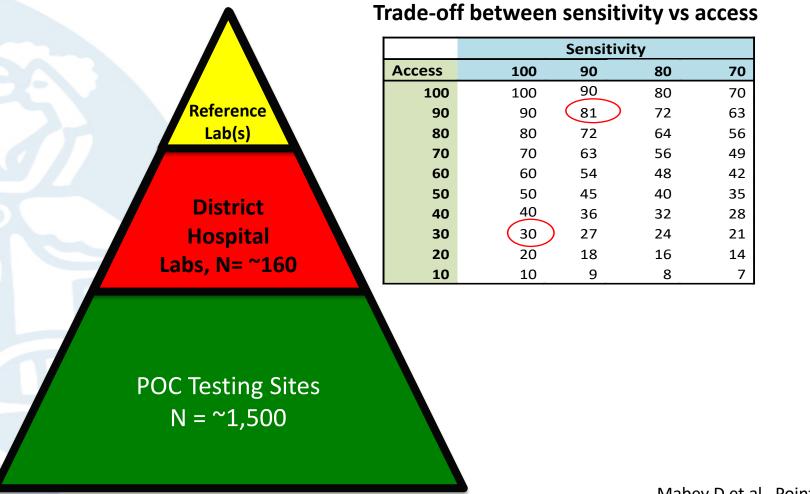
Cases of syphilis among Indigenous people in **Saskatchewan** have skyrocketed, according to Indigenous Services Canada medical health officer Dr. Ibrahim Khan. (CTV News)

If **Manitoba** continues at its current pace, it could see as many cases of congenital syphilis this year as all of Canada recorded in 2019. In fact, Manitoba is on track to have as many newborns infected with syphilis this year as the entire country did in 2019. The province had recorded 30 cases of congenital syphilis in babies as of Aug. 17, 2020. (CBC News)

An outbreak was declared last year(July 2019) by **Alberta** Health Services after 12 stillborn births and 1,753 newly diagnosed cases of syphilis. Case counts have continued to rise.(Associated Press)

## Rapid Syphilis Tests have been deployed around the world to save newborn lives





Garcia et al. Rapid Syphilis Tests as catalysts for health system strengthening: the case of Peru. PLoS One 2013; **8:**e66905

Mabey D et al. Point-of-care Tests to Strengthen Health Systems and Save Newborn Lives: the Case of Syphilis. *PLoS Med.* 2012 Jun;9(6):e1001

## WHO has Pre-qualified 3 Dual HIV-Syphilis Rapid Tests









Dual Rapid Tests	H	V	T. pallidum		
	Sensitivity*	Specificity*	Sensitivity*	Specificity*	
Abbott Bioline	<b>100</b> (98-100)	<b>99</b> (97-100)	<b>87</b> (82-91)	<b>99.5</b> (97-100)	
Premier First Response	<b>100</b> (98-100)	<b>99</b> (96-100)	<b>99</b> (96-100)	<b>100</b> (98-100)	
SD Biosensor Standard Q	<b>100</b> (98-100)	<b>99</b> (97-100)	<b>95</b> (91-98)	<b>99.5</b> (97-100)	
ChemBio DPP	<b>100</b> (98-100)	<b>97.5</b> (94-99)	<b>87</b> (81-91)	<b>100</b> (98-100)	
Medmira Multiplo	<b>99.5</b> (97-100)	<b>99.5</b> (97-100)	<b>74</b> (67-80)	<b>99.5</b> (97-100)	
Biolytical Insti	<b>99.5</b> (97-100)	<b>94</b> (89-97)	<b>81</b> (75-86)	<b>99</b> (96-100)	
*					

\*values in % (95% Confidence Intervals); 3 tests in red box received WHO Pre-qualification

Source: Van Den Heuvel, A., Smet, H., Prat, I. et al. Laboratory evaluation of four HIV/syphilis rapid diagnostic tests. BMC Infect Dis 19, 1 (2019). <u>https://doi.org/10.1186/s12879-018-3567-x</u> and from WHO PQ reports

### **Covid-19 Tests approved by Health Canada**

#### Number of authorized testing devices

Device type	Number authorized
Authorized testing devices intended for point-of-care use (often referred to as rapid tests)	19
Self-testing devices	3
Antigen Testing Devices	13
Nucleic Acid Testing Devices (often referred to as PCR)	45
Serological Testing Devices	22
Total number of authorized COVID-19 testing devices	80

https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19industry/medical-devices/authorized/list.html

### Building Back Better: making diagnostics more accessible



Invest in a connected diagnostic system that forms the backbone of the health care system

- More accessible services at community level, esp for remote locations
- Data digitisation and sharing for more timely and effective health communication early alerts of outbreaks and to inform disease control strategies
- The diagnostic system serves as the eyes and ears of the health care system in peace time and can respond efficiently to outbreaks

Ref Lab Prov Labs POC Testing

https://www.cna-aiic.ca/-

/media/cna/files/en/integration\_new\_direction\_canadian\_healthcare\_brief\_e.pdf?la
=en&hash=1459F2A10EA1ED9ED39C64A9F5EE96D446057F6C

## The Laboratory as a Command Centre



With the introduction of more community-based testing services, the laboratories need to take on the role of a Command Centre that provides:

- evaluation of new tests
- training, quality assurance and supervision of POC testing sites
- Collate surveillance data and turn data into intelligence for outbreak alerts and control interventions
- Conduct research into implementation of new technologies

Ref: Boeras DI, Nkengasong JN, Peeling RW. Implementation science: the laboratory as a command centre. Curr Opin HIV AIDS 2017: 12:171–174.

# After the pandemic: perspectives on the future trajectory of COVID-19

https://doi.org/10.1038/s41586-021-03792-w

Received: 12 May 2021

Accepted: 1 July 2021

Amalio Telenti<sup>1,2</sup>, Ann Arvin<sup>1</sup>, Lawrence Corey<sup>3</sup>, Davide Corti<sup>4</sup>, Michael S. Diamond<sup>5,6,7</sup>, Adolfo García-Sastre<sup>8,9,10,11</sup>, Robert F. Garry<sup>12</sup>, Edward C. Holmes<sup>13</sup>, Phil Pang<sup>1</sup>, Herbert W. Virgin<sup>1,14,15</sup>

Globally accessible diagnostics and deep-sequencing tools to establish continuous and sustained global surveillance of disease and variants.

Telenti A, et al. Nature (2021). https://doi.org/10.1038/s41586-021-03792-w

What are the current key gaps in developing an effective global response?

#### **Research questions**

#### Epidemiology

- What are the effects of geographical and socioeconomic variations in vaccine coverage and disease on the ability to convert the pandemic to an endemic or epidemic disease?
- What is the contribution of immunosuppressed populations to the rapid evolution of SARS-CoV-2?
- Virology
- What are the mechanisms by which viruses adapt to different hosts, thereby crossing species barriers?
- Is viral sequence evolution effectively reduced by vaccination? Immunology
- What are the correlates of protection for vaccines and natural immunity? The assessment of protection will require the coherent application of reproducible immunologic assays in populations to follow disease incidence and severity.
- What is the impact of antigenic drift?
- What are the criteria for the renewal or boosting of vaccines?
- What is the role of mucosal immunity in limiting viral shedding and preventing severe disease?

#### Tools and technologies

#### Surveillance

• Globally accessible diagnostics and deep-sequencing tools to establish continuous and sustained global surveillance of disease and variants.

Vaccines

- Pan-sarbecovirus vaccines and monoclonal antibodies that will address both SARS-CoV-2 variants and the future introduction of pandemic coronaviruses into the human population. Therapeutics
- Next-generation therapeutics in the form of cheap oral antiviral agents.
- Long-acting monoclonal antibody prophylaxis for persons not likely to achieve effective vaccination.
- Addressing inequalities in pandemic healthcare and access worldwide to the most effective vaccines and therapeutics.





- COVID-19 tests are critical not only for clinical medicine but also as public health tools to protect public safety, to release from quarantine and to enable economic recovery, reopening of schools and workplaces, in combination with other preventive measures such as mask wearing, quarantine, hand hygiene and distancing
- Testing for surveillance and genomic sequencing are important means of monitoring COVID-19 case rates and the emergence and spread of variants of concern
- The use of tests for saving lives and livelihoods during the COVID-19 pandemic has taught us the importance of equitable access to diagnostics with real time data connectivity for early alerts of outbreaks and more timely and effective health communication so that policy makers, politicians and the public can all play their part
- The challenge is to build a connected diagnostic system that forms the backbone of the health care system, extending from top level laboratories to point-of-care testing in communities, alerting public health authorities to unusual patterns of disease and to guide disease control strategies