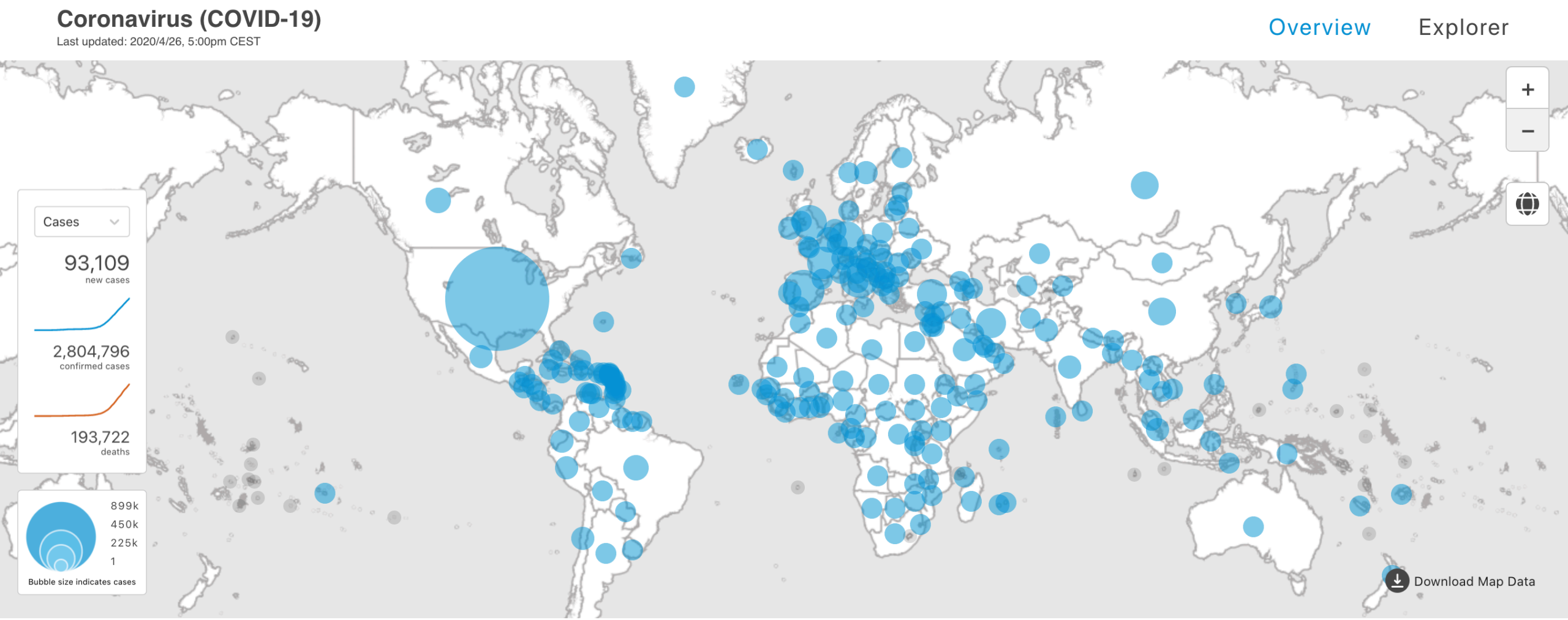
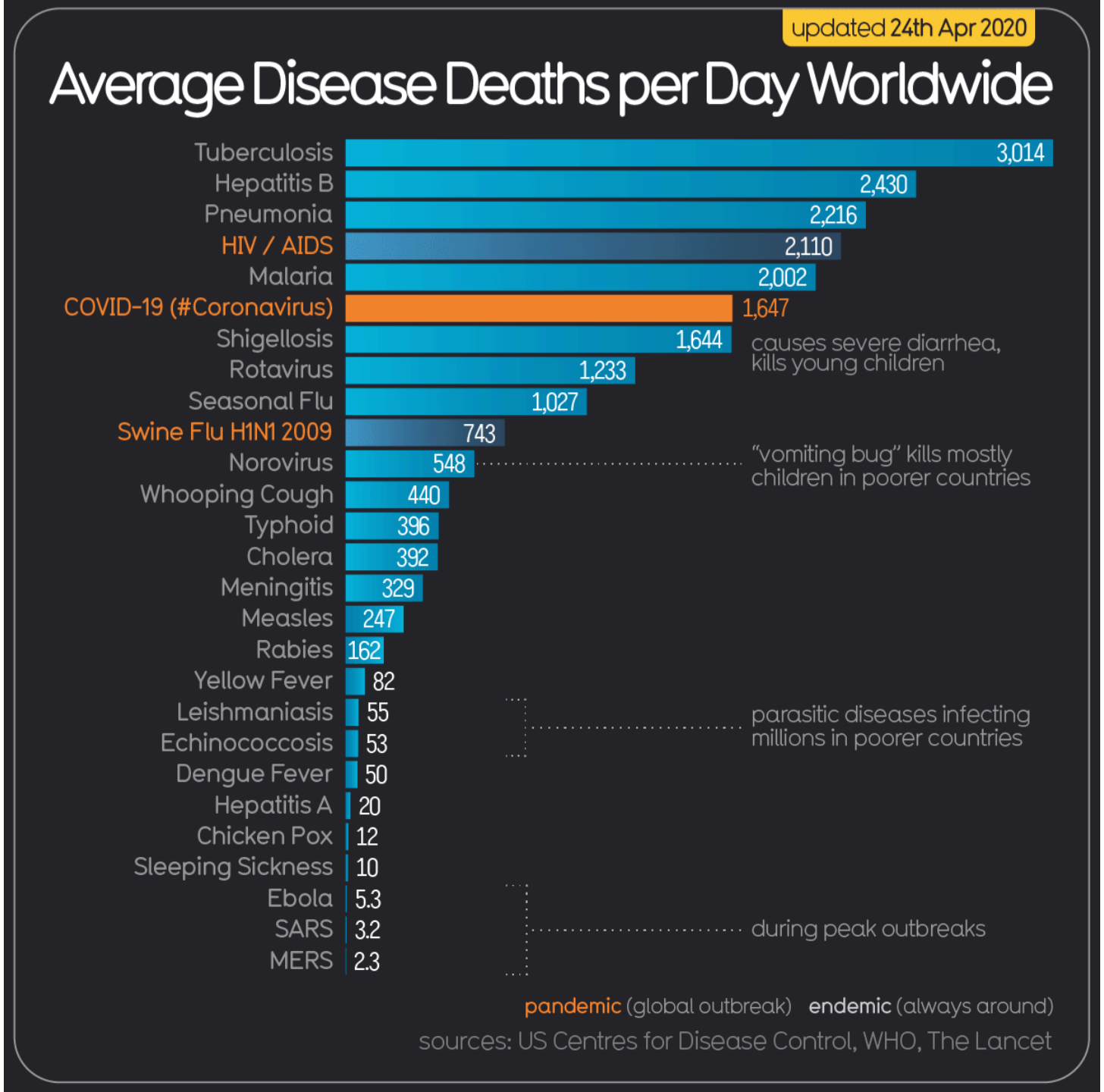
Strategies to Implement Fast Turn-Around Laboratory Testing for Control of COVID-19

April 29, 2020

Status of the COVID-19 Pandemic



Source: WHO


updated 24th Apr 2020
Average Disease Deaths per Day Worldwide
Tuberculosis 3,014
Hepatitis B 2,430
Pneumonia 2,216
HIV / AIDS 2,110
Malaria 2,002
COVID-19 (#Coronavirus) 1,647
Shigellosis 1,644
causes severe diarrhea, kills young children
Rotavirus 1,233
Seasonal Flu 1,027
Swine Flu H1N1 2009 743
Norovirus 548
"vomiting bug" kills mostly children in poorer countries
Whooping Cough 440
Typhoid 396
Cholera 392
Meningitis 329
Measles 247
Rabies 162
Yellow Fever 82
Leishmaniasis 55
Echinococcosis 53
Dengue Fever 50
parasitic diseases infecting millions in poorer countries
Hepatitis A 20
Chicken Pox 12
Sleeping Sickness 10
Ebola 5.3
SARS 3.2
MERS 2.3
during peak outbreaks
pandemic (global outbreak) endemic (always around)
sources: US Centres for Disease Control, WHO, The Lancet

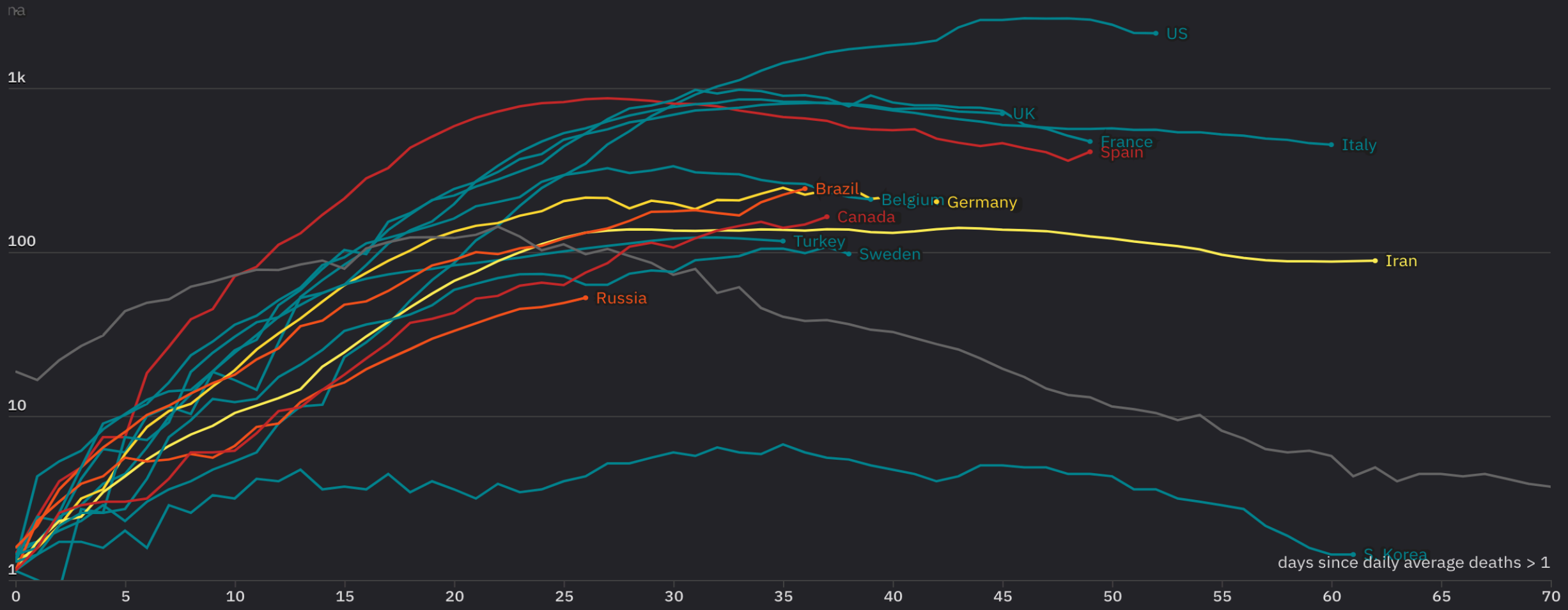
Coronavirus Infection Trajectories

Growth of Outbreaks

updated 26 Apr 2020

Avg Daily Deaths | Toggle China

7-day growth rate: <0% >10%

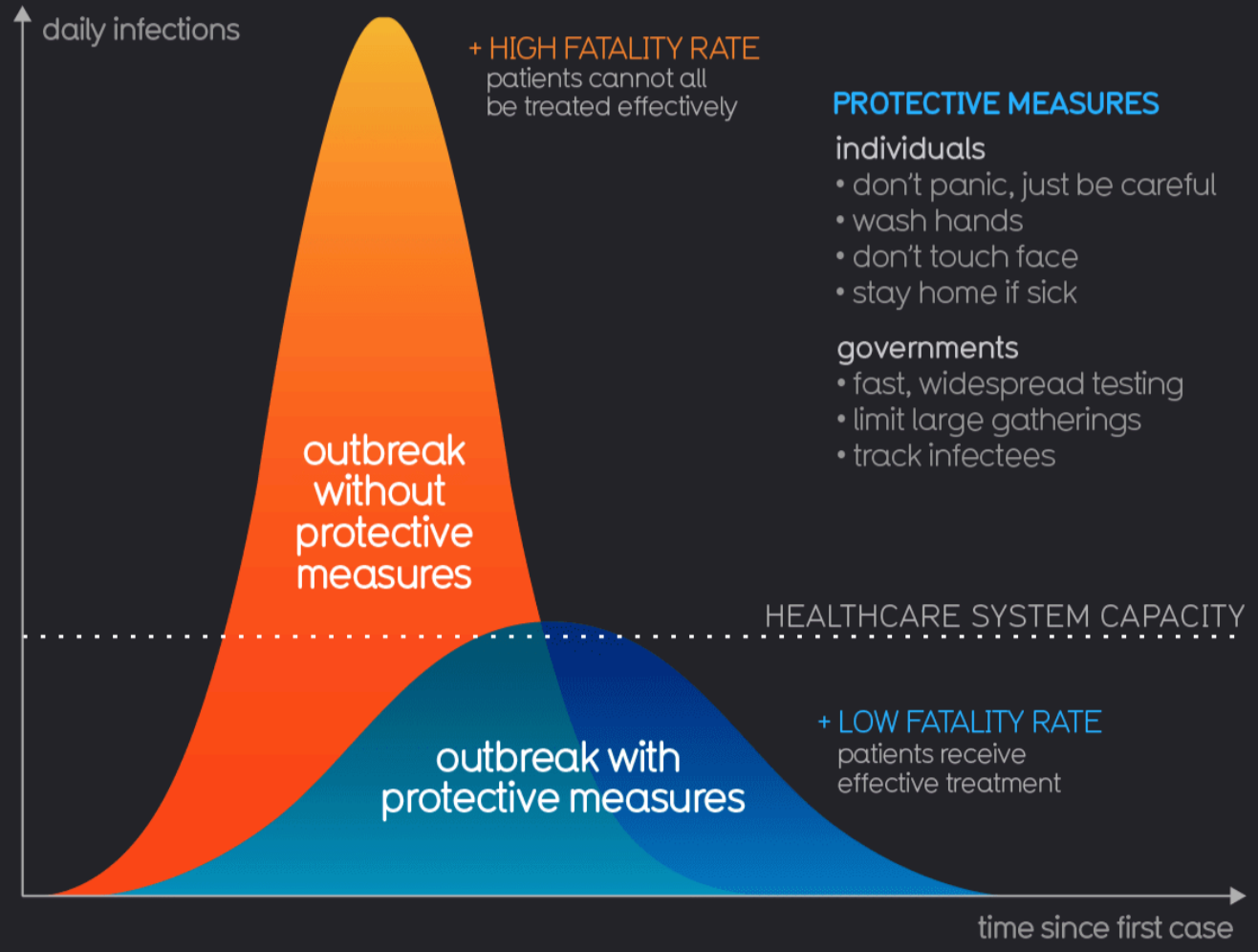


informationisbeautiful

sources: Johns Hopkins University, Financial Times. Leading infected nations

Flattening the Curve

Fast, intelligent action slows pandemic effects, stops the overwhelm of healthcare systems



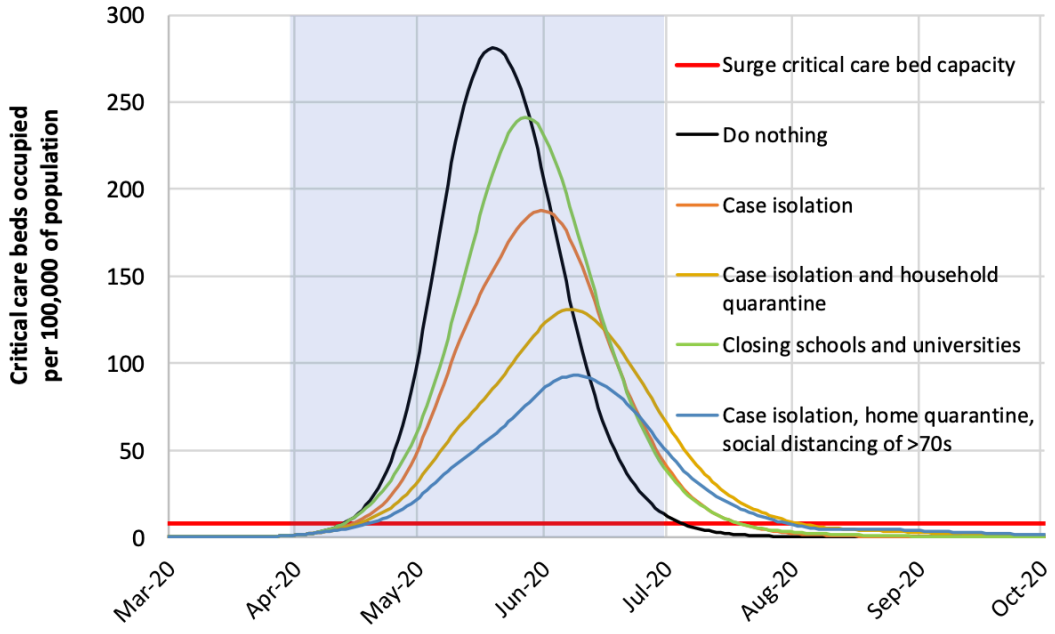
PROTECTIVE MEASURES

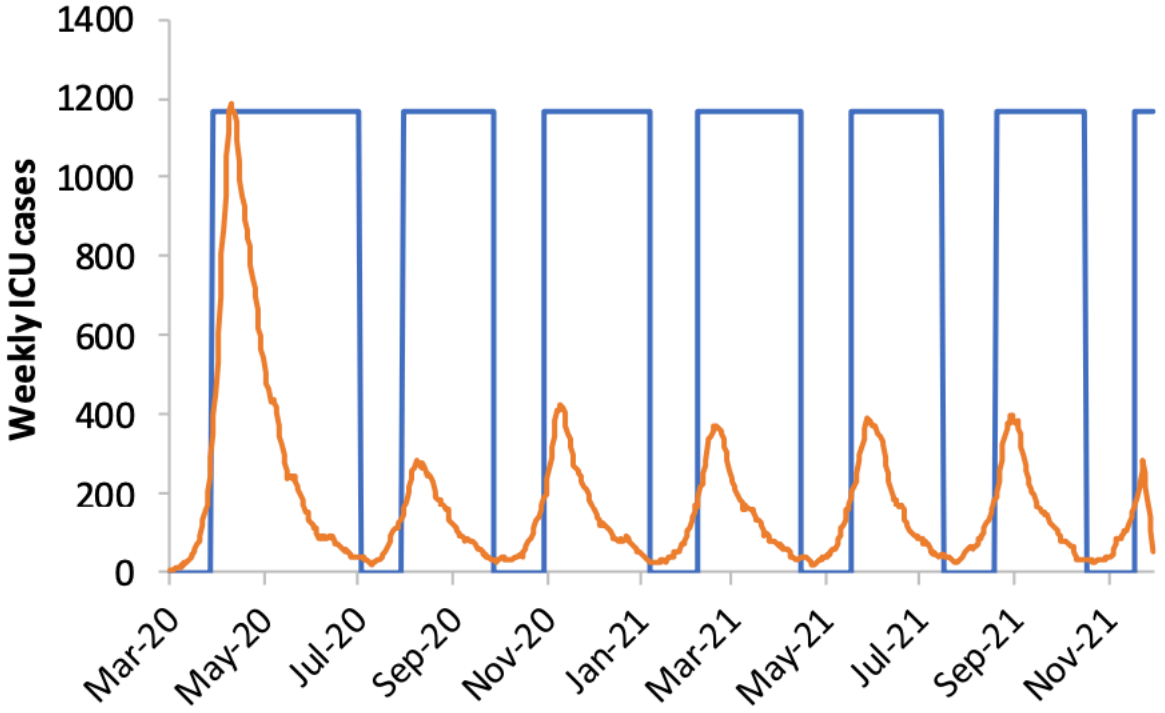
individuals
- don't panic, just be careful
- wash hands
- don't touch face
- stay home if sick

governments
- fast, widespread testing
- limit large gatherings
- track infectees

source: Drew Harris - New York Times

Impact of epidemic suppression of current and future SARS-CoV2 spread



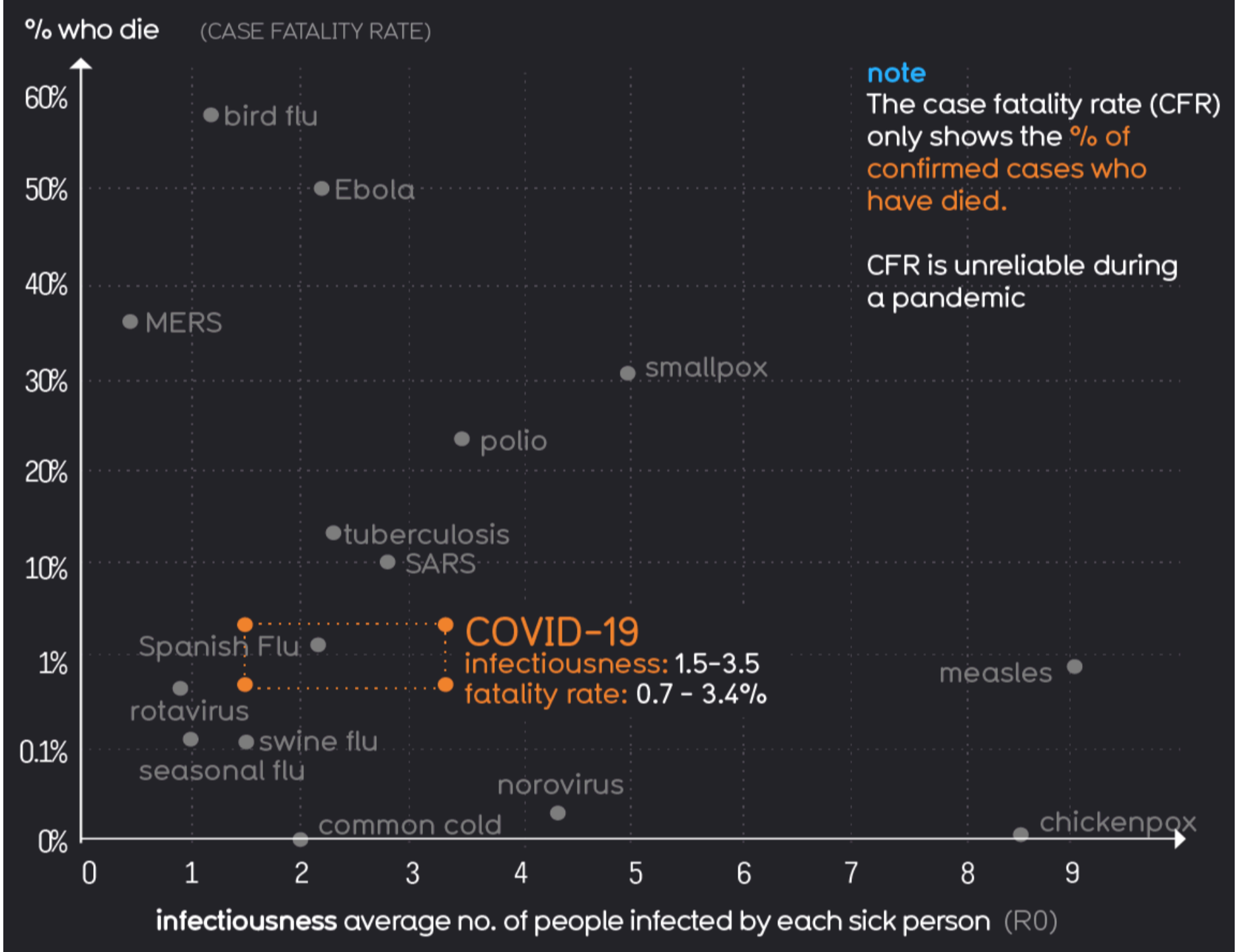


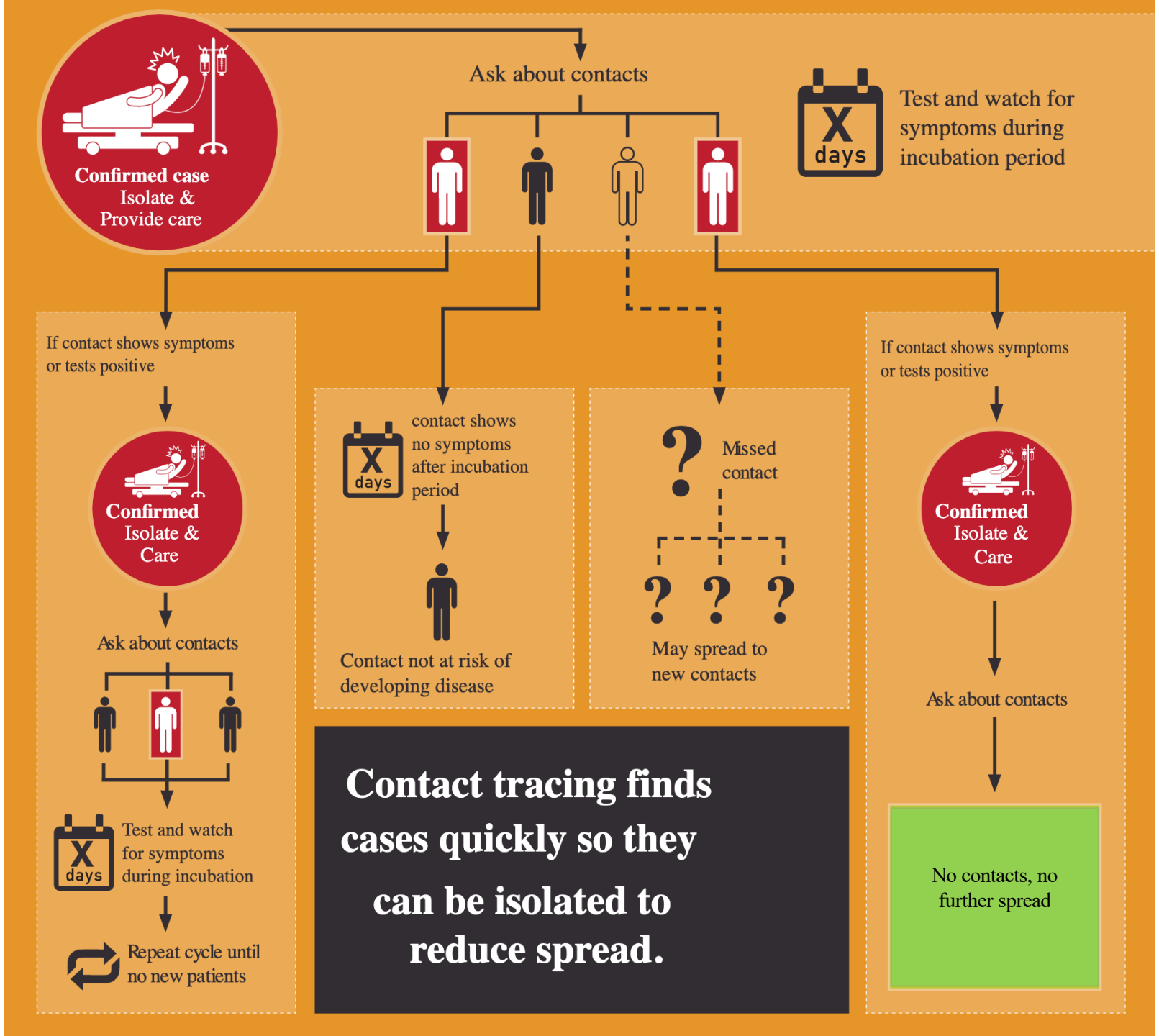
Fergusen N. et al., (2020). DOI: https://doi.org/10.25561/77482

Why do we test?

- Patient care
- Surveillance
- Epidemic control using classic public health methods to identify and isolate those infected to break the chain of transmission

- After lock-downs end, active surveillance will be needed to track and identify new cases and their contacts. Testing is essential to identify cases and new infections amongst contacts, and to isolate and break the chain of transmission
- If this is done effectively, further lockdowns may not be needed


% who die
(CASE FATALITY RATE)
60%
50%
40%
30%
20%
10%
1%
0.1%
0%
bird flu
Ebola
MERS
smallpox
polio
tuberculosis
SARS
COVID-19
infectiousness: 1.5-3.5
fatality rate: 0.7 - 3.4%
Spanish Flu
rotavirus
swine flu
seasonal flu
measles
norovirus
common cold
chickenpox
0
1
2
3
4
5
6
7
8
9
infectiousness average no. of people infected by each sick person (R0)
note
The case fatality rate (CFR) only shows the % of confirmed cases who have died.
CFR is unreliable during a pandemic


Confirmed case
Isolate &
Provide care
Ask about contacts
X days
Test and watch for symptoms during incubation period
If contact shows symptoms or tests positive
Confirmed
Isolate &
Care
Ask about contacts
X days
Test and watch for symptoms during incubation
Repeat cycle until no new patients
X days
contact shows no symptoms after incubation period
Contact not at risk of developing disease
?
Missed contact
? ? ?
May spread to new contacts
Contact tracing finds cases quickly so they can be isolated to reduce spread.
If contact shows symptoms or tests positive
Confirmed
Isolate &
Care
Ask about contacts
No contacts, no further spread

A **close contact** of a COVID-19 case is any person:

who had face-to-face contact with a COVID-19 case within two metres for more than 15 minutes

who was in a closed environment (household, classroom, meeting room, hospital waiting room, etc.) with a COVID-19 case for more than 15 minutes

who had physical contact with a COVID-19 case

who was in an airplane within two seats of a COVID-19 case or people who were in close contact with the case during the flight; if the case showed strong symptoms or moved around the airplane, all passengers may be ‘close contacts’

who had unprotected direct contact with infectious secretions of a COVID-19 case (for example by being coughed on)

who was providing care to a COVID-19 case, or laboratory workers who were handling specimens from a COVID-19 case without proper personal protective equipment or with a possible breach of such equipment.

ecdc.europa.eu

#COVID19

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Table 1. Classification of contact based on level of exposure

High-risk exposure (close contact)	Low-risk exposure
A person: • having had face-to-face contact with a COVID-19 case within two metres for more than 15 minutes; • having had physical contact with a COVID-19 case; • having unprotected direct contact with infectious secretions of a COVID-19 case (e.g. being coughed on); • who was in a closed environment (e.g. household, classroom, meeting room, hospital waiting room, etc.) with a COVID-19 case for more than 15 minutes; • in an aircraft, sitting within two seats (in any direction) of the COVID-19 case, travel companions or persons providing care, and crew members serving in the section of the aircraft where the index case was seated [23] (if severity of symptoms or movement of the case indicate more extensive exposure, passengers seated in the entire section or all passengers on the aircraft may be considered close contacts); • A healthcare worker or other person providing care to a COVID-19 case, or laboratory workers handling specimens from a COVID-19 case, without recommended PPE or with a possible breach of PPE [24].	A person: • having had face-to-face contact with a COVID-19 case within two metres for less than 15 minutes; • who was in a closed environment with a COVID-19 case for less than 15 minutes; • travelling together with a COVID-19 case in any mode of transport*; • A healthcare worker or other person providing care to a COVID-19 case, or laboratory workers handling specimens from a COVID-19 case, wearing the recommended PPE [24].

Table 2. Key actions for management of contacts

Actions	High-risk exposure (close contact)	Low-risk exposure
Individual	For a period of 14 days after the last exposure to a COVID-19 case, high-risk contacts should be advised to: • quarantine at home if possible*. If not possible, respect physical distancing measures and avoid travel; • daily self-monitoring for COVID-19-compatible symptoms, including fever of any grade, cough, fatigue or difficulty breathing; • take and record temperature daily (contacts should avoid the use of fever-reducing medication a few hours before they take their temperature); • remain contactable by public health authorities; • implement rigorous hand hygiene and respiratory etiquette; • self-isolate immediately should symptoms develop and seek medical advice, preferably by phone first, following recommendations of the national/local authorities.	For a period of 14 days after the last exposure, low-risk contacts should be advised to: • daily self-monitoring for COVID-19-compatible symptoms, including fever of any grade, cough, fatigue or difficulty breathing; • respect physical distancing measures and avoid travel; • implement rigorous hand hygiene and respiratory etiquette measures; • self-isolate immediately should symptoms develop and seek medical advice, preferably by phone first, following recommendations of the national/local authorities.

Public health authorities	For a period of 14 days after the last exposure to a COVID-19 case:
	• Active follow-up of the contacts (e.g. daily phone calls, e-mails, text messages). Contacts can be encouraged to also proactively contact public health authorities as soon as they develop any compatible symptoms, outside of the scheduled follow-up;
	• testing of contacts that develop COVID-19-compatible symptoms if possible**
	  • if test is negative, continue individual actions for a period of 14 days after the last exposure;
	  • if the test is positive, notify the case and initiate contact tracing.
		For a period of 14 days after the last low-risk exposure to a COVID-19 case:
		• Encourage low-risk contacts to proactively contact public health authorities if they develop any compatible symptoms;
		• If the contact develops COVID-19-compatible symptoms, follow steps as for high-risk contacts.
		Based on individual risk assessments, public health authorities may consider excluding low-risk exposure contacts from work if they work with vulnerable populations (e.g. those who provide care to elderly).

Three categories of technologies are critical for COVID-19 screening, diagnosis, patient management, and contact tracing

SARS-CoV2 Testing

Fever Detection

A. **Remote or no-touch thermometers** for basic fever screening

Screening & Diagnosis

A. **In house Nucleic Acid tests (NAT)**
   - **Primer Kits**
   - **Manual rt-PCR**
   - **Automated rt-PCR**

B. **Rapid Diagnostic Tests**
   A. **Antigen based**
   B. **IgM/IgG**

Patient Management

A. **Imaging**
   (e.g. X-ray or CT scan for disease progression)

B. **Pulse Oximetry**
   (e.g. fingertip devices for oxygen saturation and other severity triage tests)

C. **Intensive Care testing**
   (e.g. chemistry tests - blood gas. Electrolytes, ECG monitoring, etc)

Surveillance

A. **Serological tests – rapid tests (RDTs) and laboratory-based assays for population-based screening**.

WHO guidance recommends the use of nucleic acid testing

Interim Guidance

"WHO recommends that all suspect cases be tested for COVID-19"

"Any persons meeting the criteria for testing should be tested…

using **available molecular tests.**

However, depending on the intensity of the transmission, the number of cases and the laboratory capacity, only a subset of the suspect cases may ***prioritized for testing****."*

World Health Organization

WHO Interim Guidance: Laboratory testing for coronavirus disease (COVID-19) in suspected human cases, *2020*

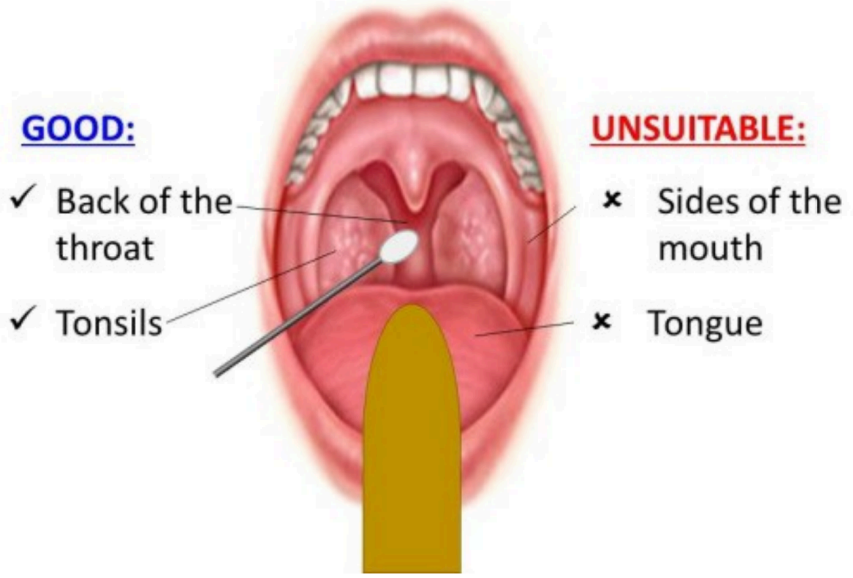
Rules for “wartime” COVID testing

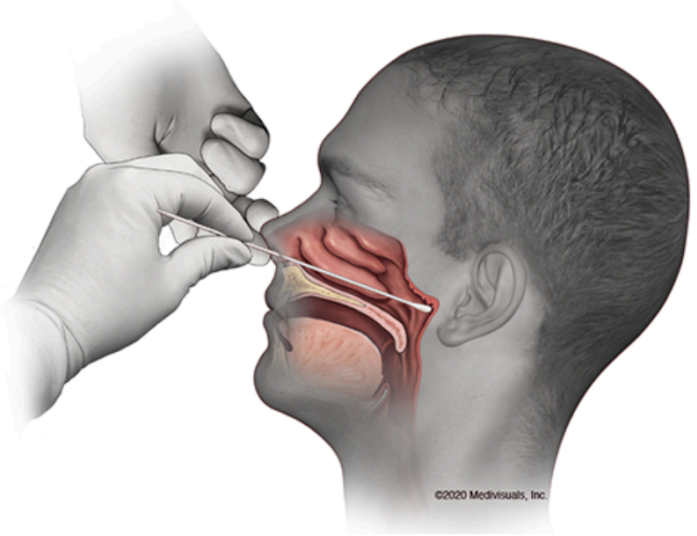
1. Rapidly expand sample collection and test capacity
2. Transport samples to the lab daily
3. Test samples the same day
4. Return results the same day

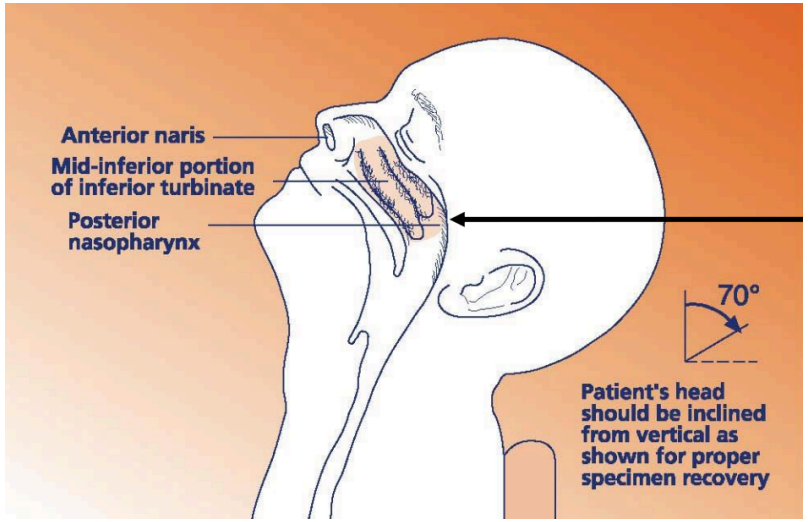
Sample Collection

Nasopharyngeal

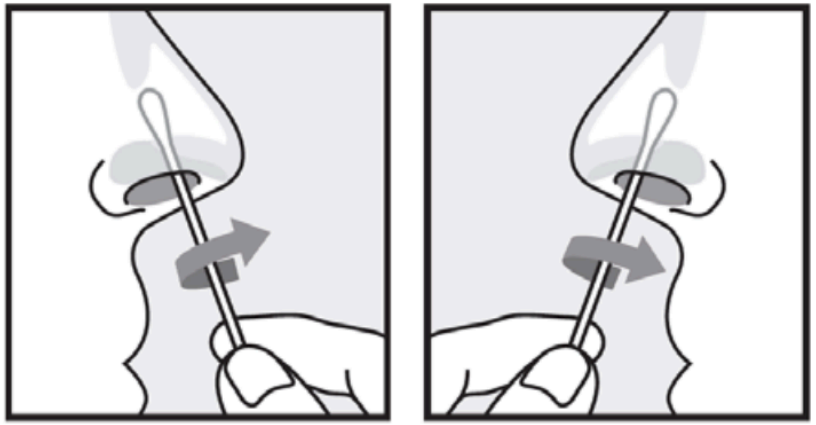
Oropharyngeal







Nasal (anterior nares)
- self collection?

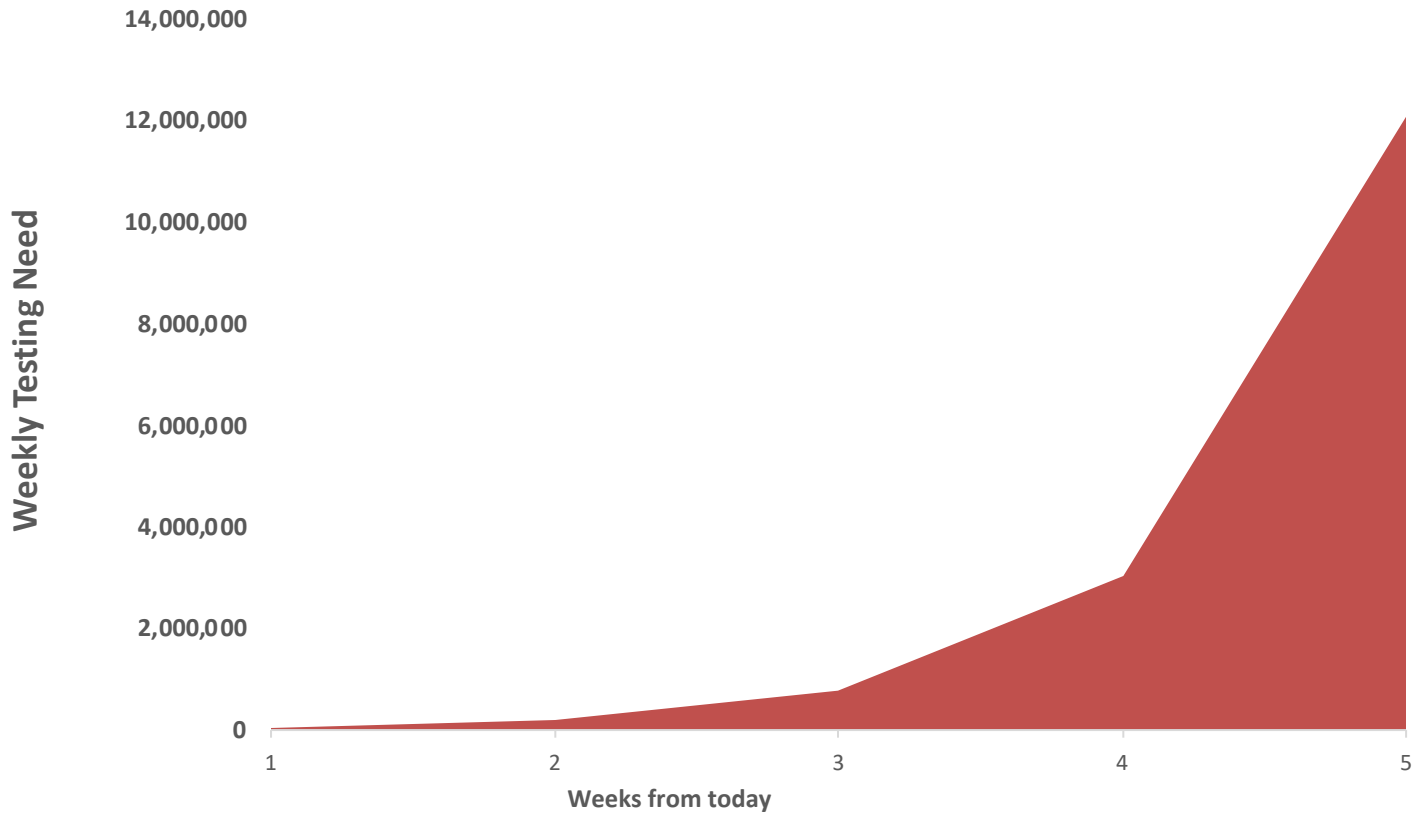



UTM-RT transport medium for:
Viruses, Chlamydia, Mycoplasma
& Ureaplasma
330 C
LOT
FLOQSwabs
COPAN FLOCKED SWABS
COPAN
MDD
CE 0123
503CS01
519CS01

ACTION

Laboratories should help lead the training of healthcare workers on how to collect the right types of samples to ensure reliable results and wide access to testing

In Africa, testing needs may exceed 12M tests per week without effective control measures



Tests are needed in the next five weeks across SSA as we are seeing exponential growth of the epidemic assuming a low clinical attack rate (10%), doubling rate of 5 days.

The scenario modeled here assumes: a prioritized testing approach modeled based on a global population; all critical/severe cases and 10% of mild/suspected cases are tested; all critical/severe patients are tested 3 times (1 to diagnose and 2 to discharge); mild/suspected cases are tested once; and that there are 3 suspected cases for every confirmed case.

Many **approved SARS-CoV-2 nucleic acid tests** can be run on a global network of automated and manual extraction PCR platforms – a few examples below

SARS-CoV-2 Nucleic acid test platforms - examples

Abbott	**Roche**	**Cepheid**
ThermoFisher	**Da An**	**BGI**
bioMerieux	**Becton Dickinson**	**SD Biosensor**

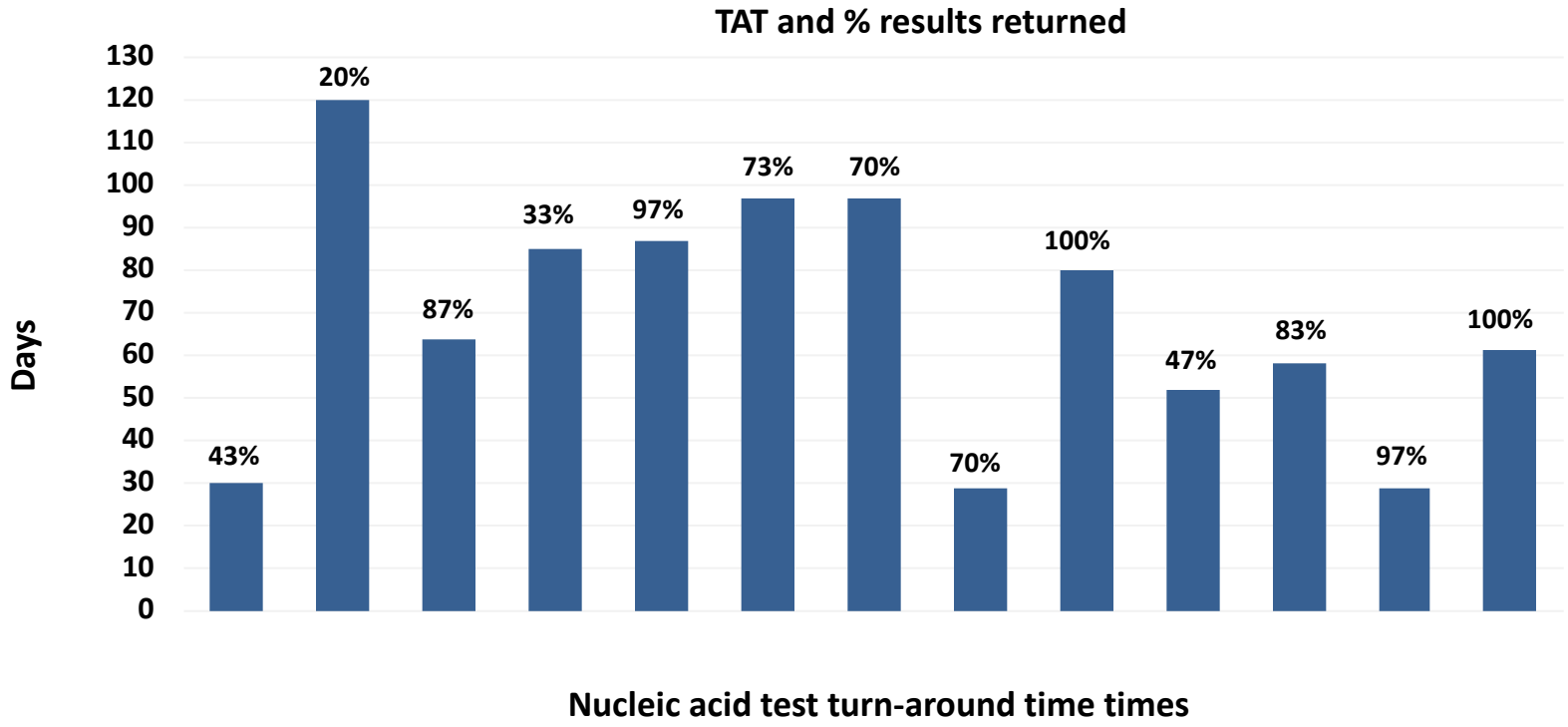
>15,000
instruments
placed

capable of
>20M
tests per week

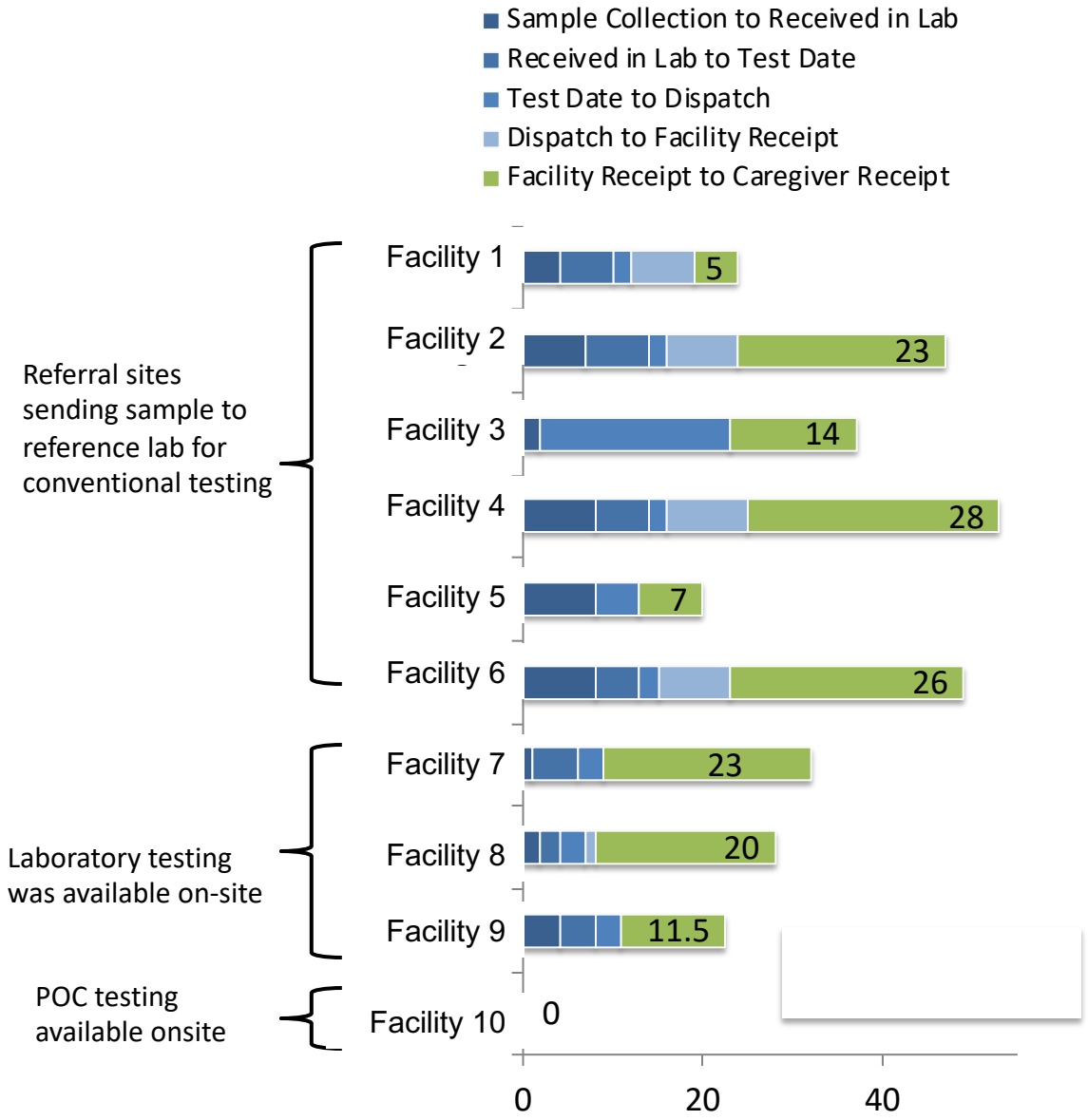
*Not FDA approved

Current laboratory results return is slow and will no impact on COVID-19 control and patient care

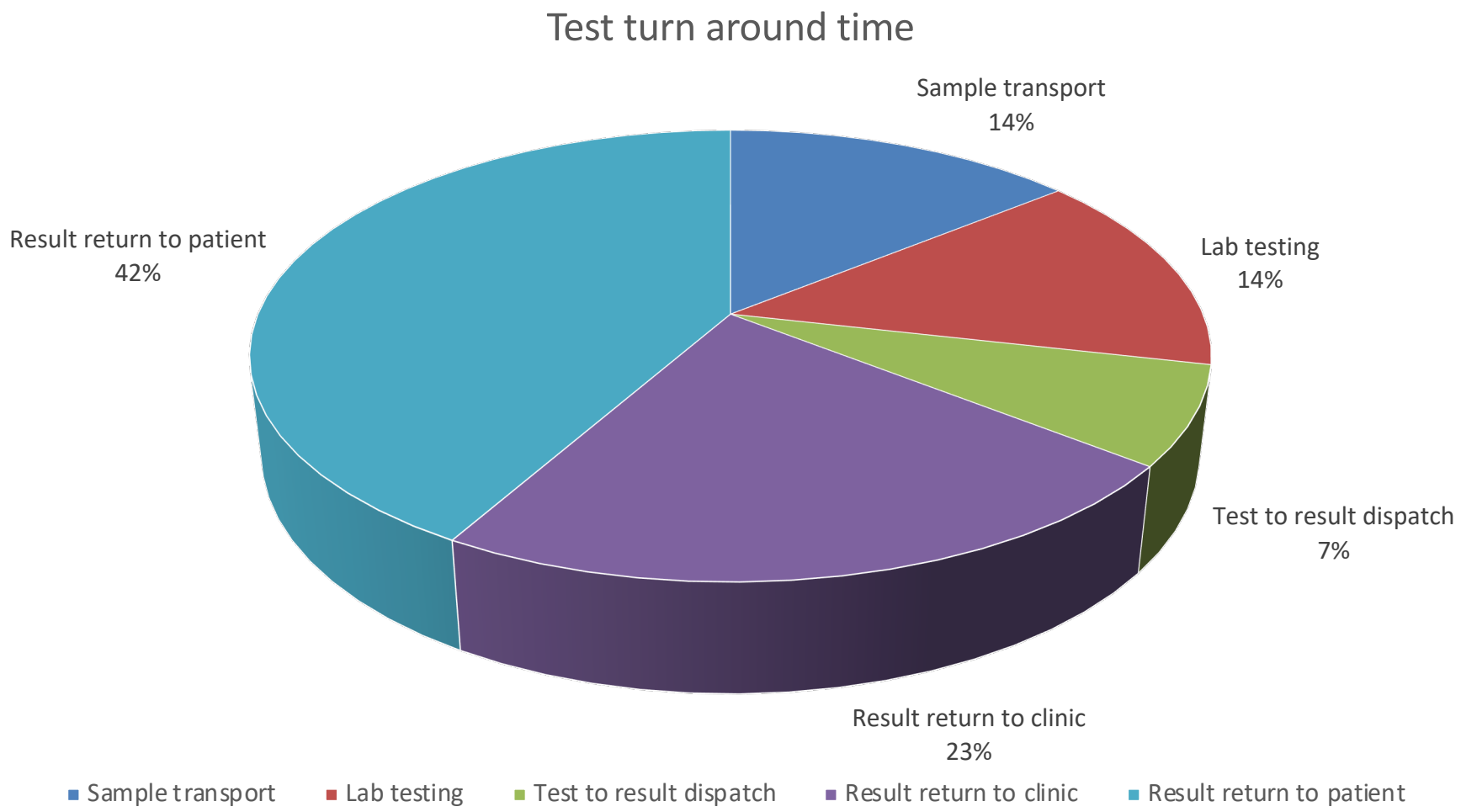
Median turnaround time from sample collection to results return of 64 days and ~70% results delivery rate



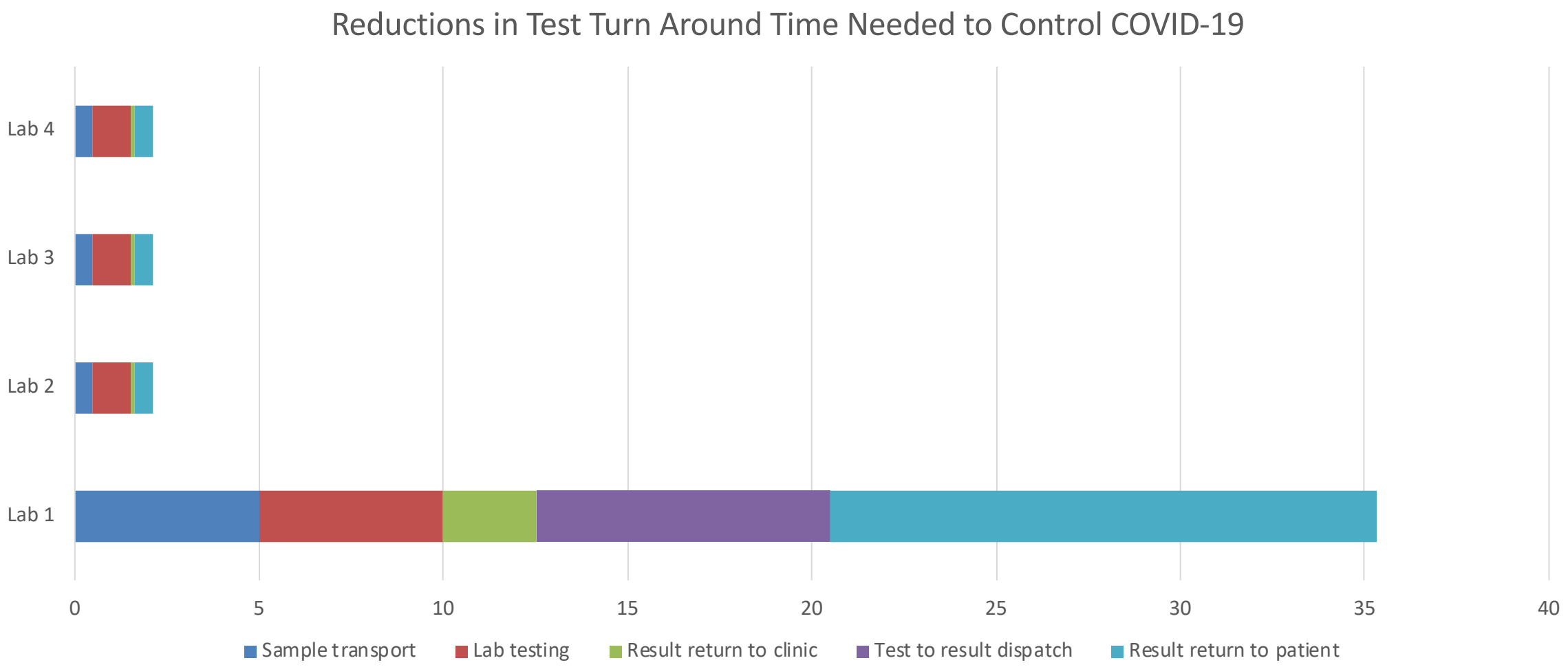
However, lengthy test turnaround times are common and have different causes



Where do delays occur?



A new Standard for Test Turn-around-Time is needed

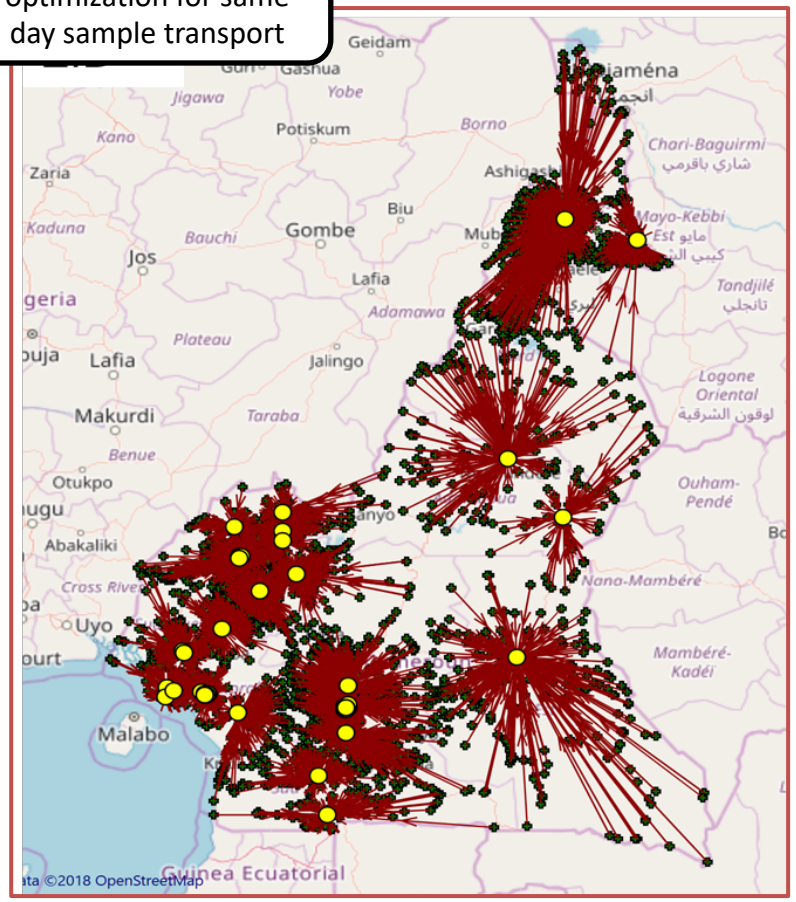


The new Standards for COVID-19 testing

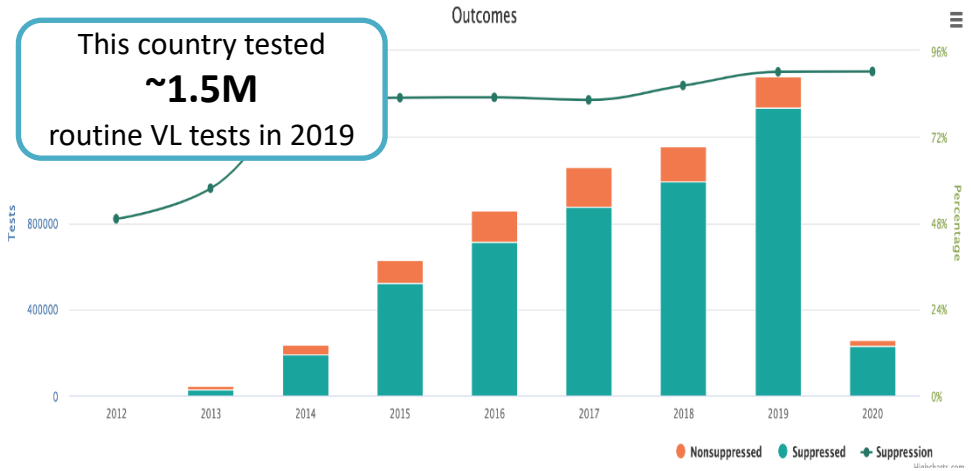
1. Rapidly expand sample collection and test capacity
2. Transport samples to the lab daily
3. Test samples the same day
4. Return results the same day

COVID-19 Testing can be integrated into established HIV VL/EID and TB NAT testing networks that include sample collection and transport, data management, supply chains, and training capacity

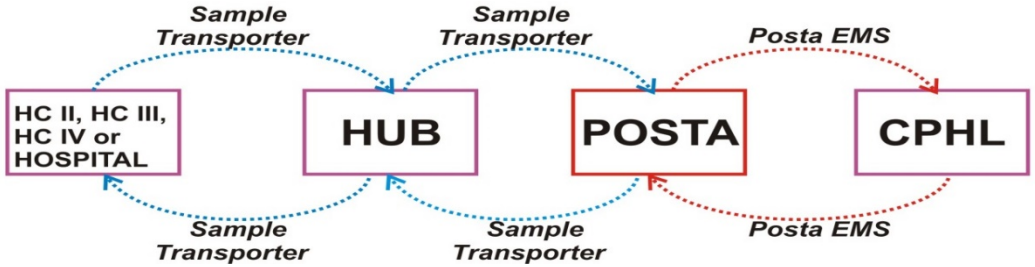
Diagnostic network optimization for same day sample transport



This country tested **~1.5M** routine VL tests in 2019



Structure of a specimen and referral network



The new Standards for COVID-19 testing

1. Testing Need and Testing Strategy
2. Transport samples to the lab daily
3. Test samples the same day
4. Return results the same day

To enable same day laboratory testing additional shifts can increase throughput

An extra 4-6 hours per day can increase throughput by at least 50%

Manufacturer	Abbott Laboratories	Roche	Da An	Cepheid	BGI	Thermo Fisher
Platform	m2000 sp/rt	6/8800	nCoV RNA COVID test	GeneXpert	AB7500 /	m2000 sp/rt
Manual or automated extraction	Automated	Automated	Manual	Automated	Manual	Automated
Throughput 8 hours	94	**6800 –** 384 **8800 –** 960	188	**GX4** – 40 **GX16** – 160	282	376
Throughput 12 hours	188	**6800 –** 490 **8800 –** 1,490	376	**GX4** – 64 **GX16** – 256	376	564
Throughput 16 hours	282	**6800 –** 628 **8800 –** 1920	470	**GX4** – 84 **GX16** – 336	564	752
Throughput 24 hours	470	**6800 –** 1344 **8800 –** 3072	752	**GX4** - 120 **GX16** – 512	846	1128

[1]Estimated based off hands-on time requirements for spin-column extraction, sample prep, rt-PCR run time, and manual results interpretation
[2]Supplier supplied estimates based off hands-on time requirements for manual 96-well magnetic bead extraction, sample prep, rt-PCR run time, and automated results interpretation
[3]Estimated based off hands-on time requirements for manual single tube magnetic bead extraction, sample prep, rt-PCR run time, and manual results interpretation

Rules for “wartime” COVID testing

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2. Transport samples to the lab daily
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Paper-based results return through courier

Health facility

Sample collection, transport to district hospital hub/directly to PCR testing lab

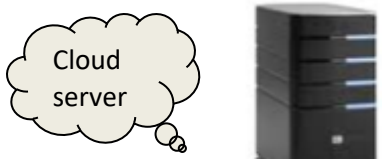
Hard copy results receipt from hub, communicated to caregiver and then to patient

District hospital

Samples collection and preparation, transport to PCR testing lab by courier/sample transporter

Hard copy results receipt from PCR testing lab, sent to HC/caregivers for further communication

Sample and results transport to and from PCR lab



Results automatically sent to EID/VL LIMS server and National dashboard

Paper results dispatched

- Lab tech transfer the compact disc to a computer to load results and print hard copy results

- Results review and approval by Lab tech on testing platform screen
- Results download by Lab tech on a compact disc

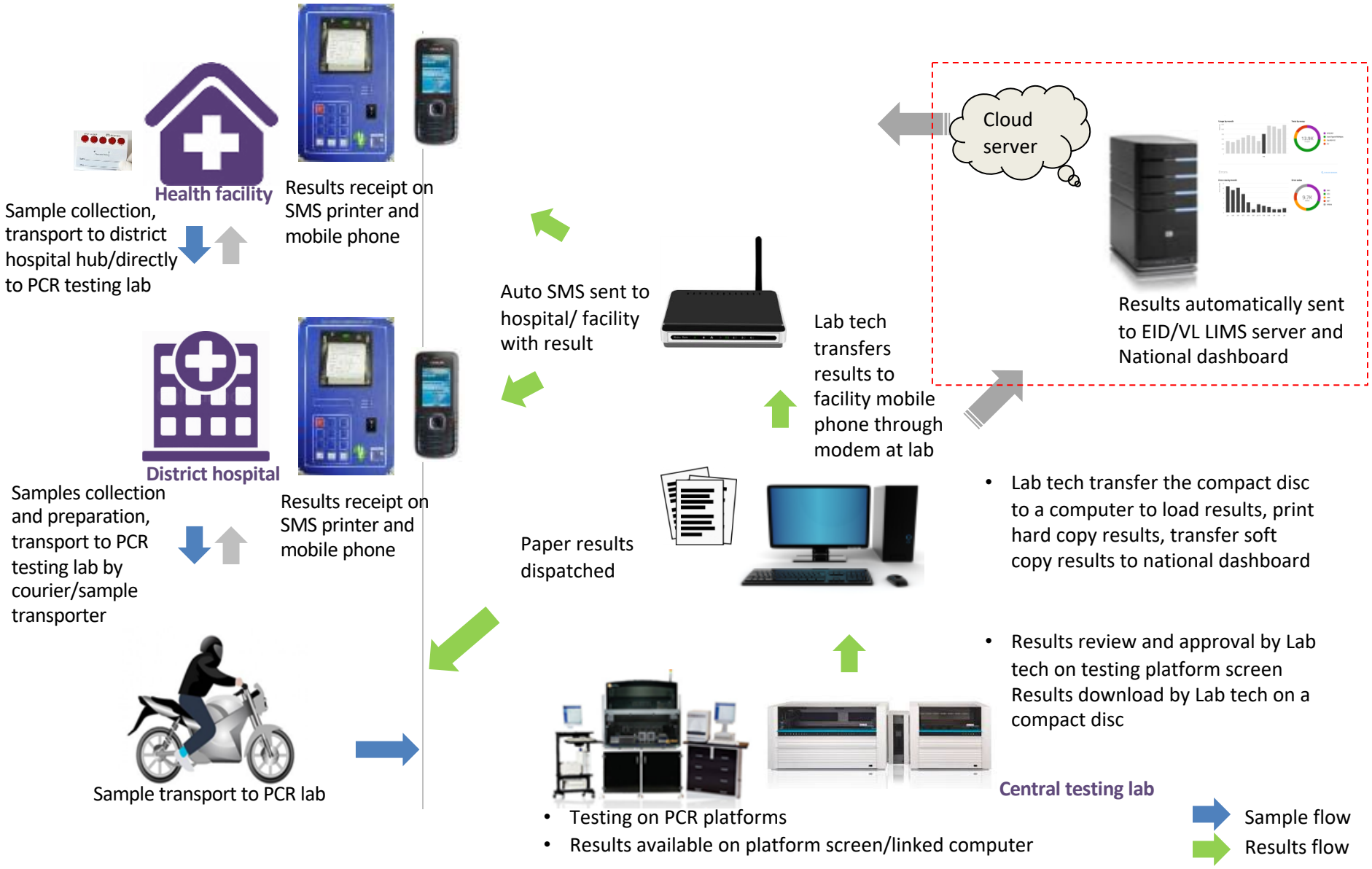
Central testing lab

- Testing on PCR platforms
- Results available on platform screen/linked computer

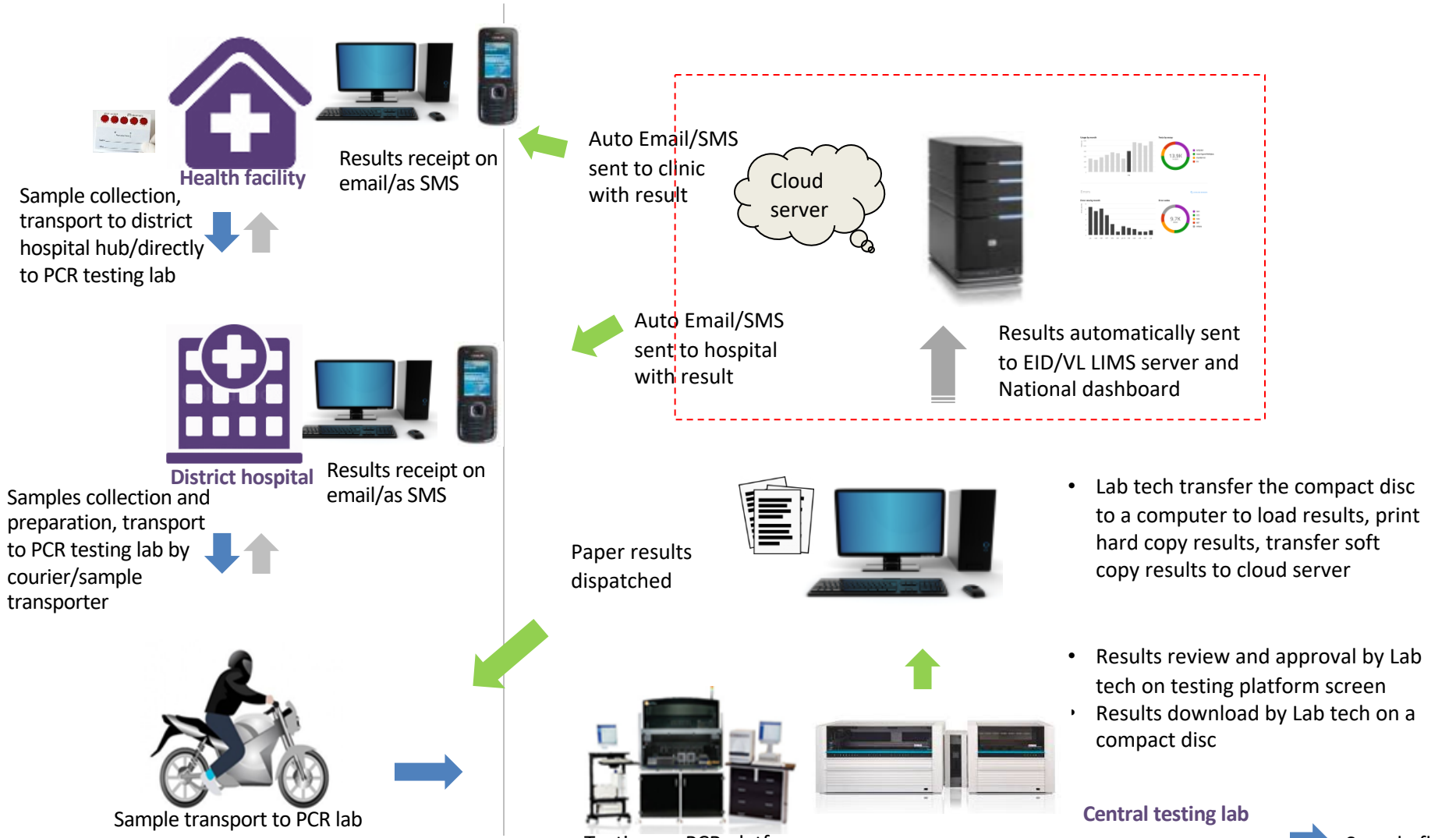
Sample flow

Results flow

Results return to clinics by SMS Printers

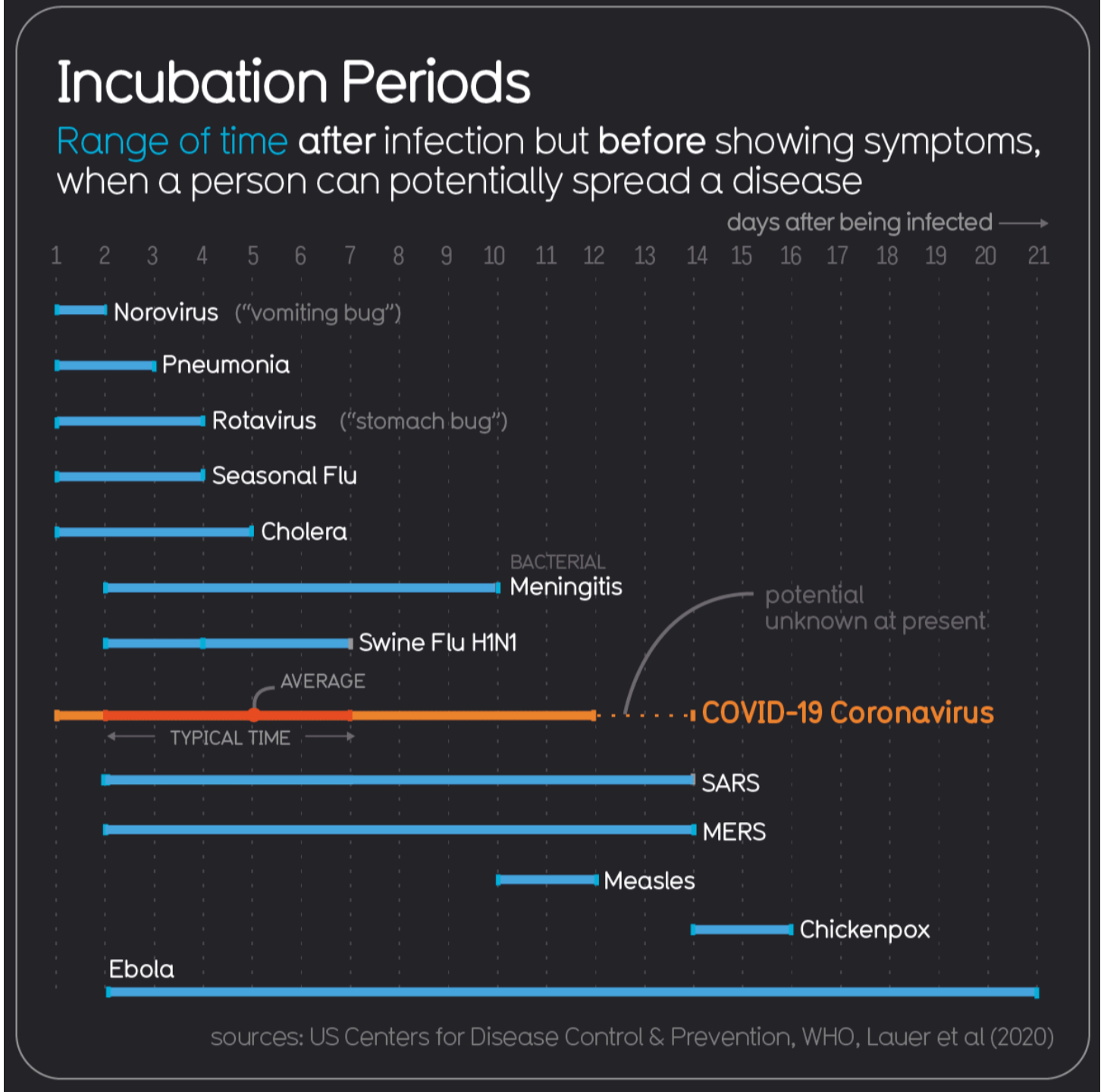


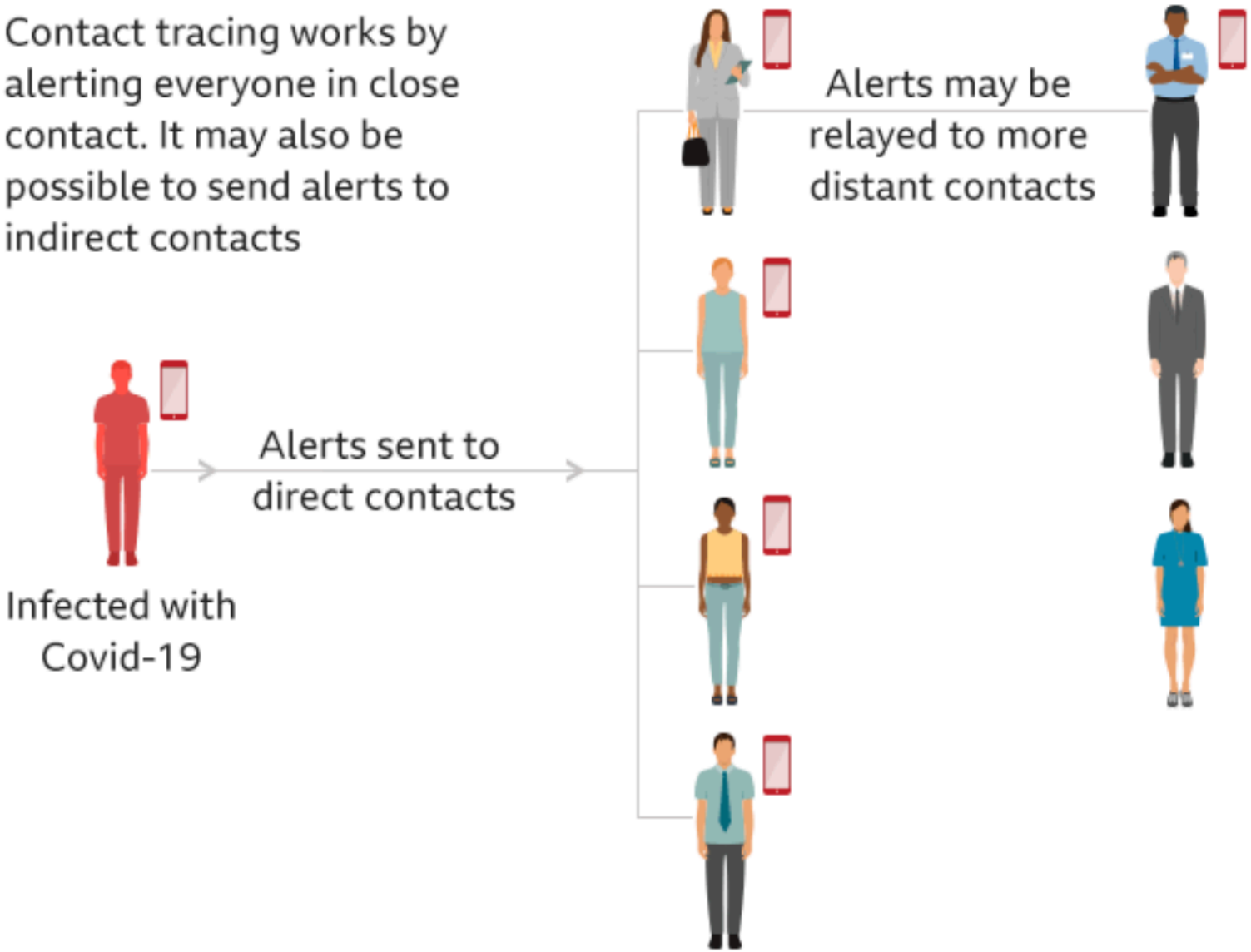
SMS and E-mail results return and SMS reminders to patients



The importance of electronic result delivery

- SARS-CoV2 infectiousness appears to start 1-2 days before clinical symptoms and so fast diagnosis of cases and quick identification and isolation of contacts is important for epidemic control
- Some countries are using or exploring the use of mobile apps to notify contacts of possible risk and suggest isolation


Incubation Periods
Range of time after infection but before showing symptoms, when a person can potentially spread a disease
days after being infected
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Norovirus ("vomiting bug")
Pneumonia
Rotavirus ("stomach bug")
Seasonal Flu
Cholera
BACTERIAL
Meningitis
Swine Flu H1N1
potential
unknown at present
AVERAGE
TYPICAL TIME
COVID-19 Coronavirus
SARS
MERS
Measles
Chickenpox
Ebola
sources: US Centers for Disease Control & Prevention, WHO, Lauer et al (2020)


Contact tracing works by alerting everyone in close contact. It may also be possible to send alerts to indirect contacts
Alerts may be relayed to more distant contacts
Alerts sent to direct contacts
Infected with Covid-19
BBC

The new rules for COVID-19 testing

- Rapidly expand access to sampling and testing
- Transport samples to lab the same day
- Test samples the same day
- Return results the same day

1-2 day test turn around - a key metric for measuring the national COVID-19 response