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

Source: WHO
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
- Rotavirus: 1,233
- Seasonal Flu: 1,027
- Swine Flu H1N1 2009: 743
- Norovirus: 548
- Whooping Cough: 440
- Typhoid: 396
- Cholera: 392
- Meningitis: 329
- Measles: 247
- Rabies: 162
- Yellow Fever: 82
- Leishmaniasis: 55
- Echinococcosis: 53
- Dengue Fever: 50
- Hepatitis A: 20
- Chicken Pox: 12
- Sleeping Sickness: 10
- Ebola: 5.3
- SARS: 3.2
- MERS: 2.3

**Updated 24th Apr 2020**

- **causes severe diarrhea, kills young children**
- **“vomiting bug” kills mostly children in poorer countries**
- **parasitic diseases infecting millions in poorer countries**
- **during peak outbreaks**

**Sources:** US Centres for Disease Control, WHO, The Lancet

**Pandemic** (global outbreak)  **Endemic** (always around)
Coronavirus Infection Trajectories

Growth of Outbreaks

Avg Daily Deaths • Toggle China

7-day growth rate: <0% • 0% • >10%

US

Italy

Spain

Turkey

Sweden

Iran

sources: Johns Hopkins University, Financial Times, Leading infected nations
Flattening the Curve

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

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**Outbreak without protective measures**

- High fatality rate
- Patients cannot all be treated effectively

**Outbreak with protective measures**

- Health system capacity

**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

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Source: Drew Harris - New York Times
Impact of epidemic suppression of current and future SARS-CoV2 spread

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
The case fatality rate (CFR) only shows the % of confirmed cases who have died. CFR is unreliable during a pandemic.
Contact tracing finds cases quickly so they can be isolated to reduce 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 had physical contact with a COVID-19 case
- who had unprotected direct contact with infectious secretions of a COVID-19 case (for example by being coughed on)
- 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 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 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.
Table 1. Classification of contact based on level of exposure

<table>
<thead>
<tr>
<th>High-risk exposure (close contact)</th>
<th>Low-risk exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>A person:</td>
<td>A person:</td>
</tr>
<tr>
<td>• having had face-to-face contact with a COVID-19 case within two metres for more than 15 minutes;</td>
<td>• having had face-to-face contact with a COVID-19 case within two metres for less than 15 minutes;</td>
</tr>
<tr>
<td>• having had physical contact with a COVID-19 case;</td>
<td>• who was in a closed environment with a COVID-19 case for less than 15 minutes;</td>
</tr>
<tr>
<td>• having unprotected direct contact with infectious secretions of a COVID-19 case (e.g. being coughed on);</td>
<td>• travelling together with a COVID-19 case in any mode of transport*;</td>
</tr>
<tr>
<td>• 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;</td>
<td>• 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].</td>
</tr>
<tr>
<td>• 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);</td>
<td></td>
</tr>
<tr>
<td>Actions</td>
<td>High-risk exposure (close contact)</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **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.

<table>
<thead>
<tr>
<th>Fever Detection</th>
<th>Screening &amp; Diagnosis</th>
<th>Patient Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Remote or no-touch thermometers for basic fever screening</td>
<td>A. In house Nucleic Acid tests (NAT) • Primer Kits • Manual rt-PCR • Automated rt-PCR</td>
<td>A. Imaging (e.g. X-ray or CT scan for disease progression)</td>
</tr>
<tr>
<td></td>
<td>B. Rapid Diagnostic Tests A. Antigen based B. IgM/IgG</td>
<td>B. Pulse Oximetry (e.g. fingertip devices for oxygen saturation and other severity triage tests)</td>
</tr>
<tr>
<td></td>
<td>C. Intensive Care testing (e.g. chemistry tests - blood gas. Electrolytes, ECG monitoring, etc)</td>
<td>C. Surveillance</td>
</tr>
</tbody>
</table>

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.”
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

GOOD:
- Back of the throat
- Tonsils

UNSUITABLE:
- Sides of the mouth
- Tongue

Nasal (anterior nares) - self collection?
ACTIONS

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.

<table>
<thead>
<tr>
<th>SARS-CoV-2 Nucleic acid test platforms - examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott</td>
</tr>
<tr>
<td>Roche</td>
</tr>
<tr>
<td>Cepheid</td>
</tr>
<tr>
<td>ThermoFisher</td>
</tr>
<tr>
<td>Da An</td>
</tr>
<tr>
<td>BGI</td>
</tr>
<tr>
<td>bioMerieux</td>
</tr>
<tr>
<td>Becton Dickinson</td>
</tr>
<tr>
<td>SD Biosensor</td>
</tr>
</tbody>
</table>

>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

- Referral sites sending sample to reference lab for conventional testing
- Laboratory testing was available on-site
- POC testing available onsite
Where do delays occur?

Test turn around time

- Result return to patient: 42%
- Sample transport: 14%
- Lab testing: 14%
- Test to result dispatch: 7%
- Result return to clinic: 23%
- Result return to patient: 42%
A new Standard for Test Turn-around-Time is needed

Reductions in Test Turn Around Time Needed to Control COVID-19

- Sample transport
- Lab testing
- Result return to clinic
- Test to result dispatch
- Result return to patient
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.

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%

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

1Estimated based off hands-on time requirements for spin-column extraction, sample prep, rt-PCR run time, and manual results interpretation
2Supplier 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
3Estimated 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

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
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**
  - Sample and results transport to and from PCR lab

- **Paper results dispatched**
  - Results automatically sent to EID/VL LIMS server and National dashboard

- **Cloud server**
  - 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 and results transport to and from PCR lab**
  - Sample and results transport to and from PCR lab
Results return to clinics by SMS Printers

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

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

Sample transport to PCR lab

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

Health facility

District hospital

Central testing lab

Cloud server

Auto SMS sent to hospital/ facility with result

Lab tech transfers results to facility mobile phone through modem at lab

Lab tech transfer the compact disc to a computer to load results, print hard copy results, transfer soft copy results to national dashboard

Results receipt on SMS printer and mobile phone

Paper results dispatched

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

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

Results receipt on SMS printer and mobile phone

Auto SMS sent to hospital/ facility

Sample flow

Results flow

Sample transport to PCR lab

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

- Results receipt on email/as SMS
- Auto Email/SMS sent to clinic with result
- Results automatically sent to EID/VL LIMS server and National dashboard
- Auto Email/SMS sent to hospital with result
- Lab tech transfer the compact disc to a computer to load results, print hard copy results, transfer soft copy results to cloud server
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**Central testing lab**
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- Auto Email/SMS sent to hospital with result
- Results automatically sent to EID/VL LIMS server and National dashboard
- Paper results dispatched

**Sample transport to PCR lab**
- Sample transport to PCR lab

**Sample flow**

**Results flow**
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.

- **Norovirus** ("vomiting bug")
- Pneumonia
- **Rotavirus** ("stomach bug")
- Seasonal Flu
- Cholera
- Bacterial Meningitis
- Swine Flu H1N1
- **Typical Time**
- **Average**
- COVID-19 Coronavirus
- SARS
- MERS
- Measles
- Ebola
- Chickenpox

Contact tracing works by alerting everyone in close contact. It may also be possible to send alerts to indirect contacts.

Infected with Covid-19 ➔ Alerts sent to direct contacts ➔ Alerts may be relayed to more distant contacts
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