"Breathe Easy": The Power of Timely Testing in Respiratory Care

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Speaker Disclosure

> **The speaker reports a relevant financial relationship, research grant, or scientific advisory board position with the following commercial entities:**
>> – Abbott Diagnostics
>> – Giner
>> – InBios International
>> – QuidelOrtho (Ortho-Clinical Diagnostics Inc.)
>> – Revvity
>> – Roche

> **The content and views expressed in this presentation are those of the speaker and may not reflect those of the funding agencies and/or sponsors.**

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About me - Paul K. Drain, MD, MPH

> **Medical Doctor – Internal Medicine (Stanford), Infectious Diseases Fellowship (Harvard)**

> **Infectious Diseases physician at the University of Washington (Seattle)**

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– *Research Group: https://depts.washington.edu/drainglobalresearch/*

> **Published seminal articles in Diagnostics for Respiratory Diseases:**

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Contents lists available at ScienceDirect

Journal of Clinical Virology

ELSEVIER

journal homepage: www.elsevier.com/locate/jcv

Duration of viral infectiousness and correlation with symptoms and
diagnostic testing in non-hospitalized adults during acute SARS-CoV-2
infection: A longitudinal cohort study

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The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Rapid Diagnostic Testing for SARS-CoV-2

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Tenth Edition | Volume One

Mandell, Douglas, and Bennett's
Principles and Practice of Infectious Diseases

Martin J. Blaser
Jeffrey I. Cohen
Steven M. Holland
Yohei Doi
Ann R. Falsey
Wendy S. Garrett
Steven A. Marr
Edward Mitre
Eleanor Wilson

2-Volume Set

134 | Immunology and Diagnosis of SARS-CoV-2 and COVID-19
Paul K. Drain and Michael Gale, Jr.
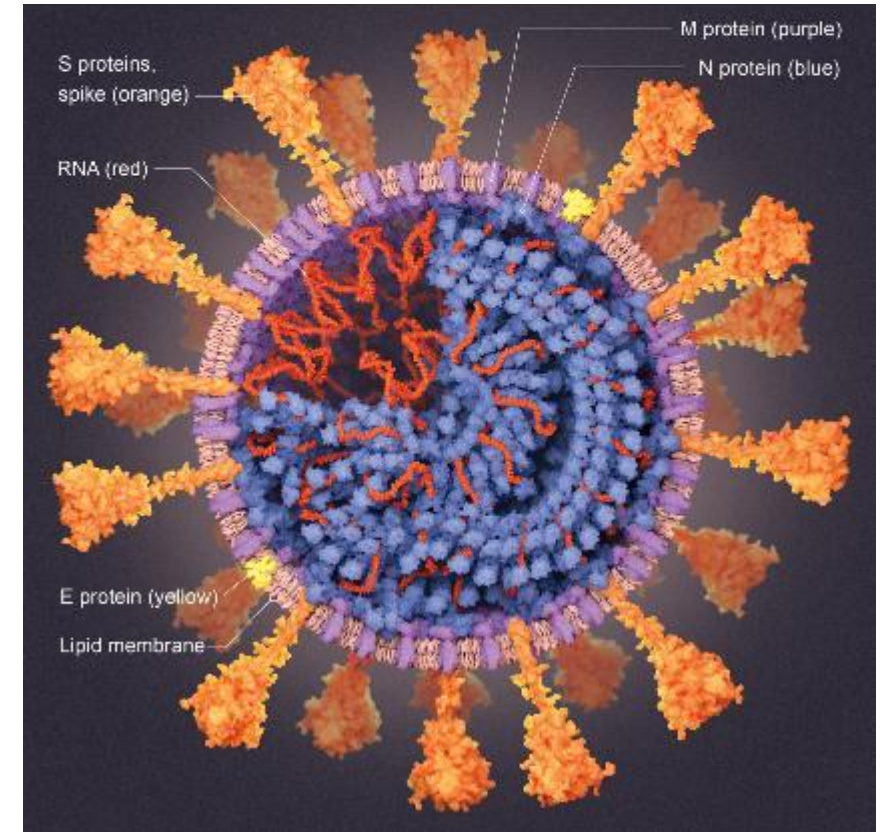
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Objective

1. **To describe the clinical importance of detecting respiratory illnesses like Flu and COVID-19 early in the course of illness.**
   - **(within 48 hours for Influenza; within 5 days for COVID-19)**

2. **To emphasize how antigen testing, particularly with the Advanced immunoassay platform, can play a critical role in supporting timely treatment decisions by delivering fast, actionable results.**

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Outline

> **Epidemiology of SARS-CoV-2 and Influenza**

> **Clinical Guidelines and Symptoms (by US CDC)**

> **Diagnostic Kinetics for Antigen vs Nucleic acid amplification (NAAT)**

> **Experience with Advanced Immunoassay Platform**

> **Diagnostic Implementation in Real-world Settings**

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SARS-CoV-2 and Covid-19 Disease

> **Virus is SARS-CoV-2; Covid-19 is disease**

> **Long genome (30k base pairs) with several mutagenic variants**

> ***Genes - N, S,* and *E* genes, and open reading frame 1ab (*ORF1ab*)**

> **Antigens - nucleocapsid, spike, and receptor binding domains**

M protein (purple)
N protein (blue)
S proteins, spike (orange)
RNA (red)
E protein (yellow)
Lipid membrane

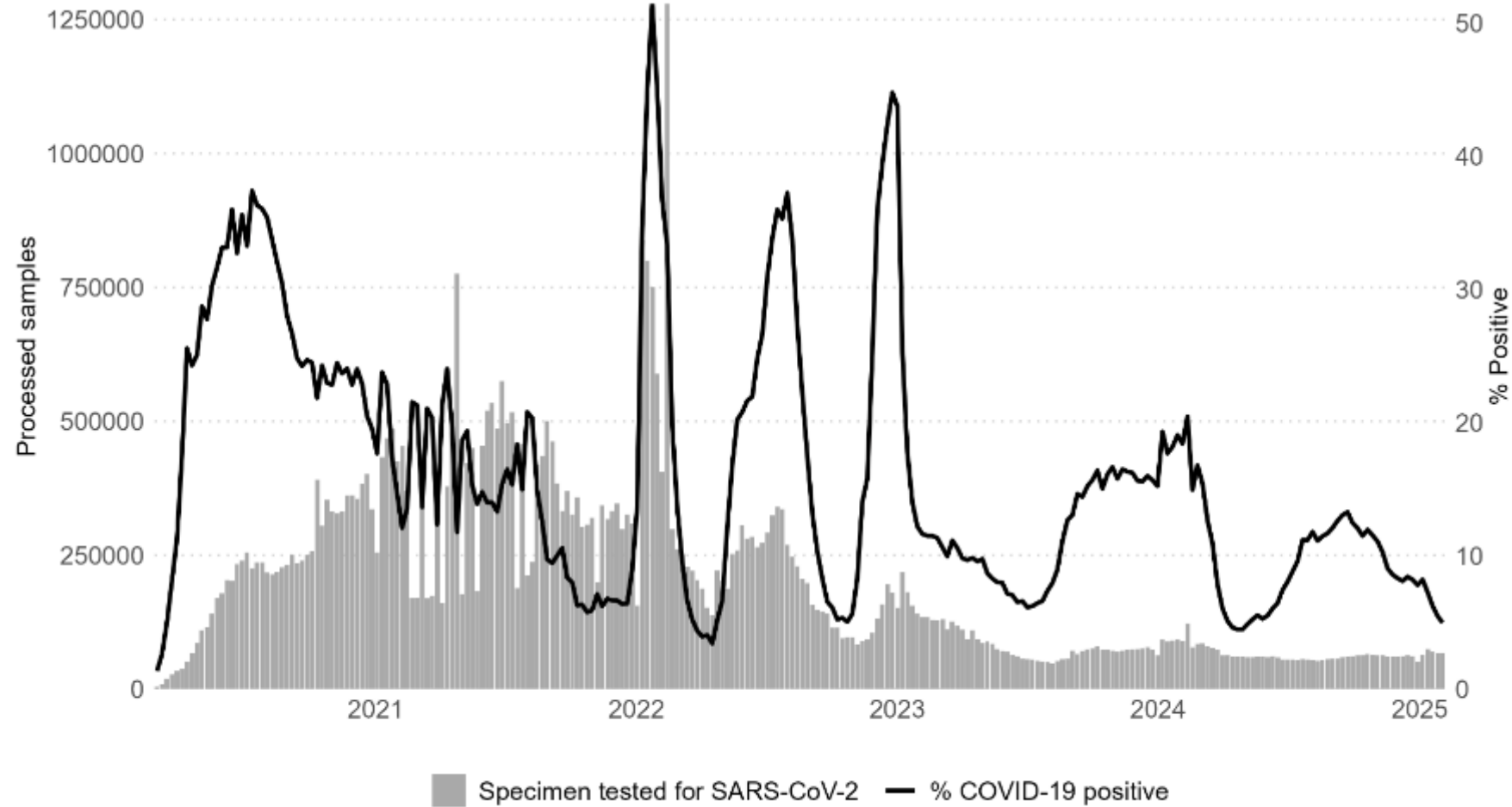# Global Epidemiology of SARS-CoV-2 (as of March 2025)

> **Cumulative reporting to/by World Health Organization (WHO)***
> – **Approximately 777 million cases (may be vastly under-reported)**
> – **More than 7 million deaths**

> **WHO is monitoring eight SARS-CoV-2 variants**
> – **One Variant of Interest – (JN.1)**
> – **Seven Variants under Monitoring – including NB.1.8.1**

> **Wastewater surveillance monitoring ongoing in many/most countries**

> **WHO urges member states to maintain their established Covid-19 infrastructure**

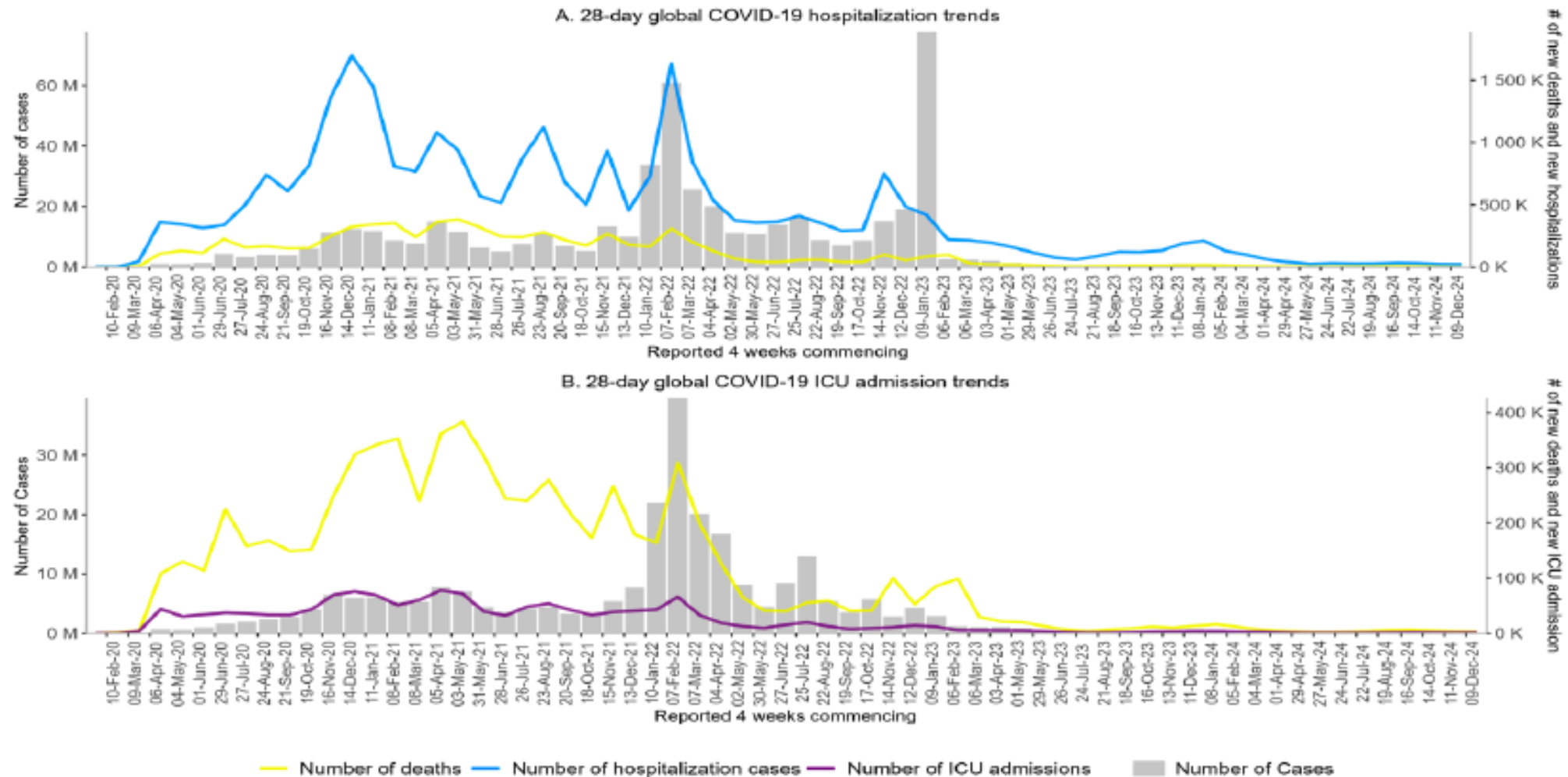* By end of 2024, many countries had stopped reporting cases/deaths to WHO

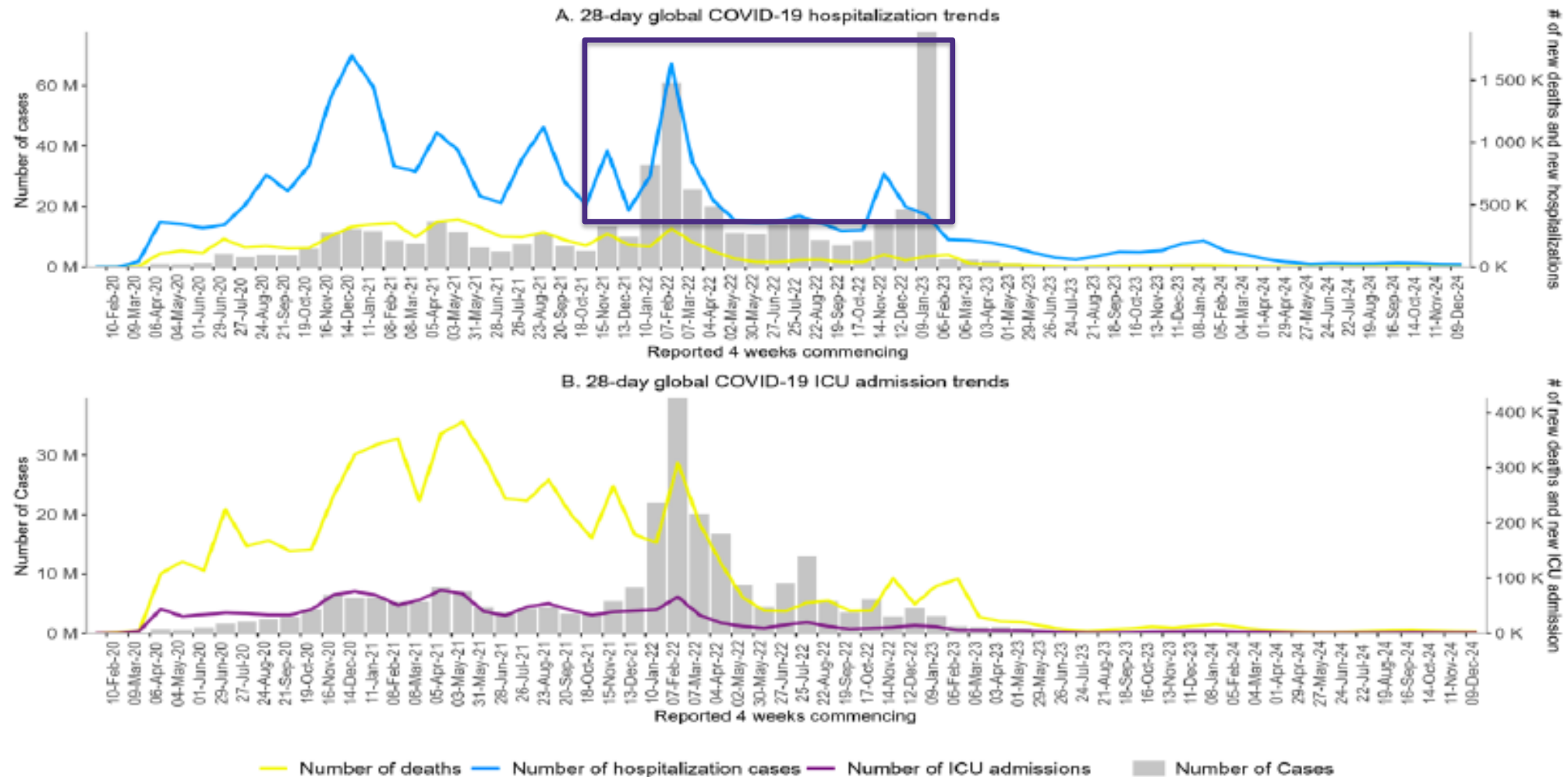* USA is no longer a member of the WHO

WHO, Covid-19 Epidemiological Update, March 2025

Weekly SARS-Cov-2 percent test positivity (March 2020 - Jan 2025)

Legend: Specimen tested for SARS-CoV-2 — % COVID-19 positive

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WHO, Covid-19 Epidemiological Update, March 2025

Weekly Covid-19 Hospitalizations (Feb 2020 - Dec 2024)

A. 28-day global COVID-19 hospitalization trends

B. 28-day global COVID-19 ICU admission trends

Number of deaths — Number of hospitalization cases — Number of ICU admissions — Number of Cases

Weekly Covid-19 Hospitalizations (Feb 2020 - Dec 2024)

A. 28-day global COVID-19 hospitalization trends

B. 28-day global COVID-19 ICU admission trends

— Number of deaths   — Number of hospitalization cases   — Number of ICU admissions   ▨ Number of Cases

WHO, Covid-19 Epidemiological Update, March 2025

SARS-CoV-2 in the United States (as of July 2025)

> **Infections and Covid-19 Cases**
  - **>100k Cases - difficult to measure due to home RDTs**
  - **Typically see a 'summer wave'**

> **Cumulative Deaths from Covid-19***
  - **Over 1.2 million Deaths (~17% of global total)**
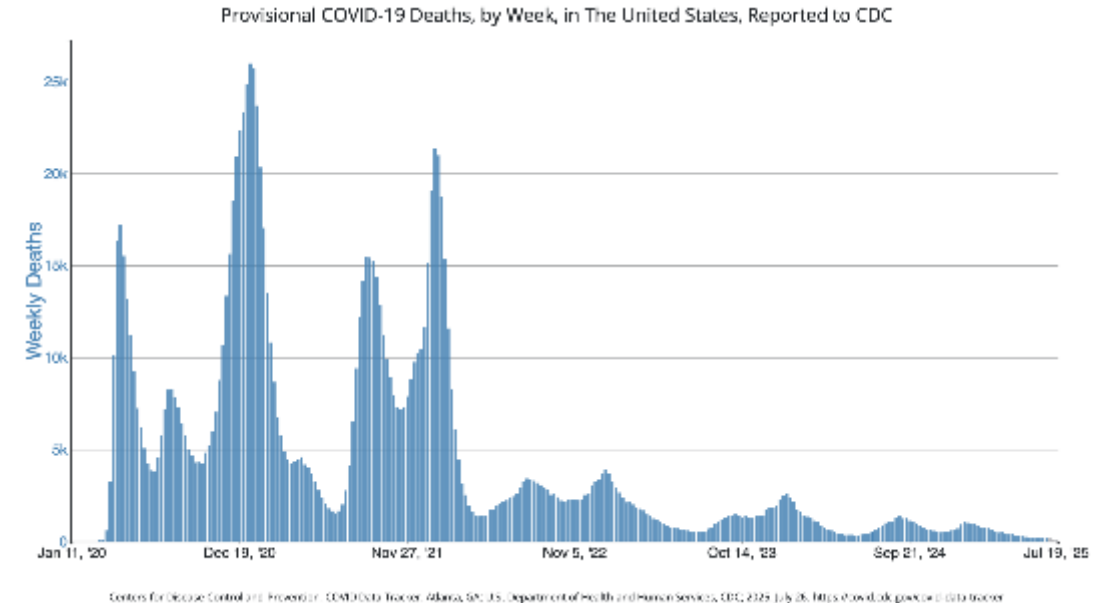 - **Reduced mortality rate among vaccinated**

> **Circulating Variants**
  - **Omicron NB.1.8.1 – "Nimbus" variant is ~45%**
    > **"razor blade throat"**
  - **Omicron LP.8.1 (40%); XFG - "Stratus" variant (10%)**

> **Trends in July 2025**
  - **Test positivity is ~5%; Cases rate increasing in ~26 states**

> **Wastewater surveillance – "low" overall; "high" in Florida, Louisiana, Hawaii**

> **Need to maintain Covid-19 infrastructure**

Covid-19 Mortality by week in USA; Jan 2020-July2025

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* Data from US CDC, July 26, 2025

Influenza Virus

> **Two viruses with multiple subtypes**

- **Influenza A (~90%) - H1N1, H3N2, H5N1**
- **Influenza B (~10%) – Victoria, Yamagata lineage**

> **Shorter genome (~13k base pairs) with *M (matrix), HA (hemagglutinin), and NS (non-structural) genes***

> **Immunoassays detect nucleoprotein antigens**

- **Can distinguish A and B viruses, but not subtypes**
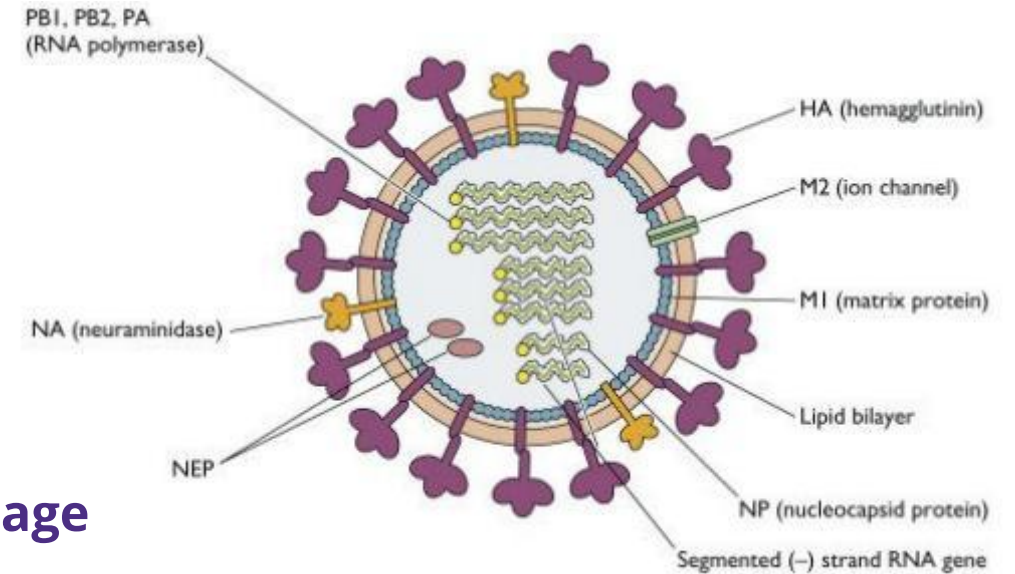
Global Epidemiology of Influenza (July 2025)

> **Cumulative reporting to/by World Health Organization (WHO)**
>   – **Data completeness and quality will vary by country**

> **Estimated 290,000 – 650,000 deaths annually**

Virus detections by subtype reported to FluNet, 15 July 2024 to 07 July 2025
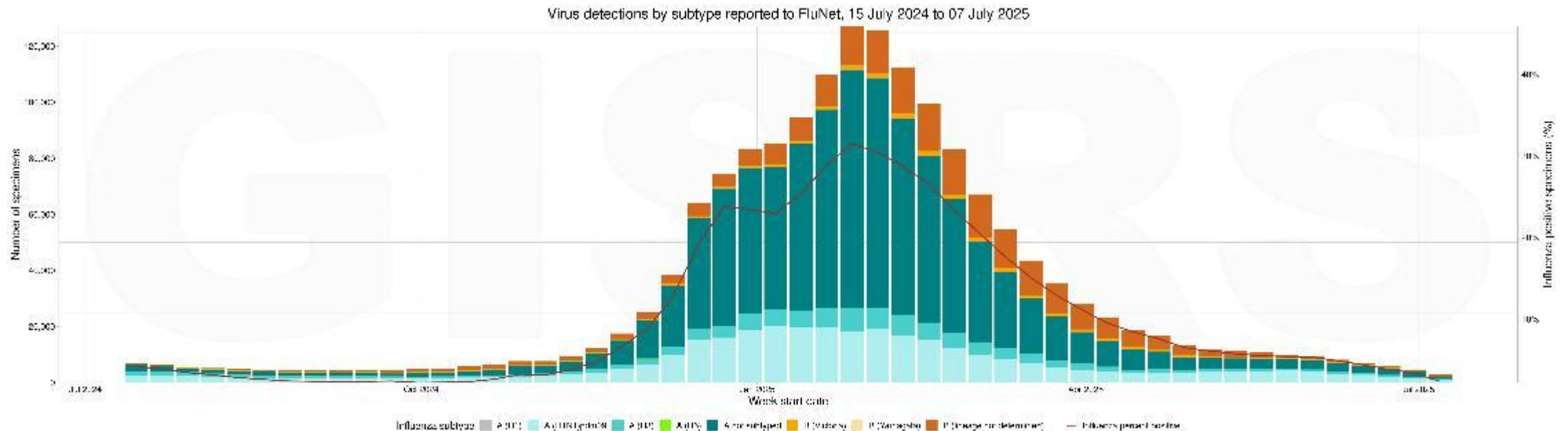
WHO, FluID, July 2025

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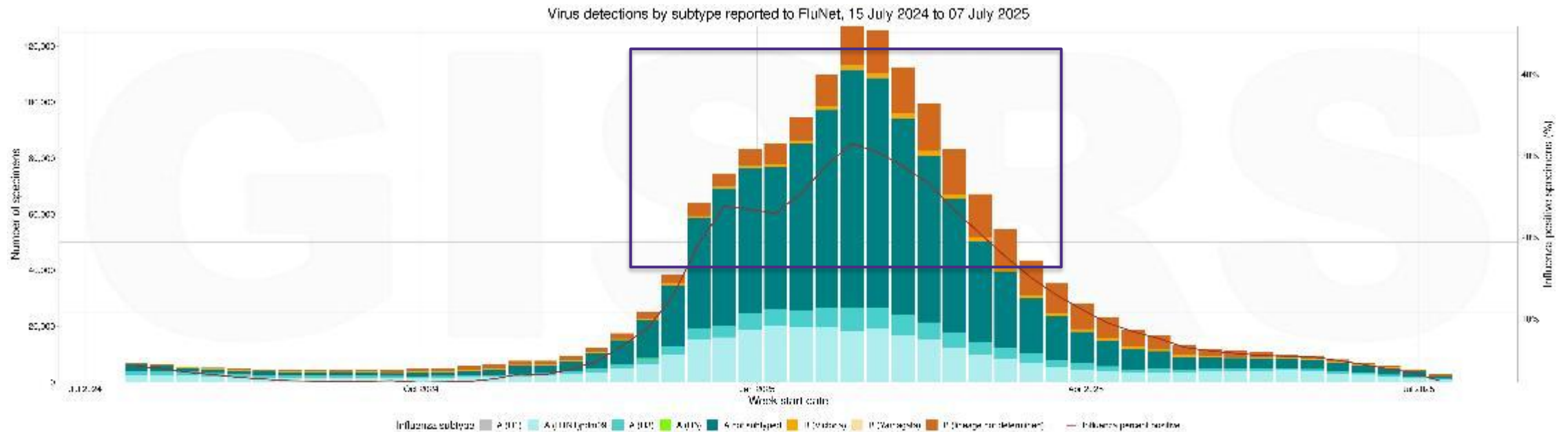
WHO, FluID, July 2025

Influenza in the USA (as of July 2025)

> **99,000 reported cases during Winter 2024/25***

- **Influenza A (94%) - mostly H1N1, H3N2**

- **Influenza B (6%) - Victoria and Yamagata lineage**

> **~23,000 Influenza-related deaths**

- **High rate of pediatric deaths (~140 children)**

> **2024/25 Season considered one of the most severe, compared to recent years**

> **Vaccination rate was ~50% and <u>decreasing trend</u> in prior years**

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* Data from US CDC, July 26, 2025
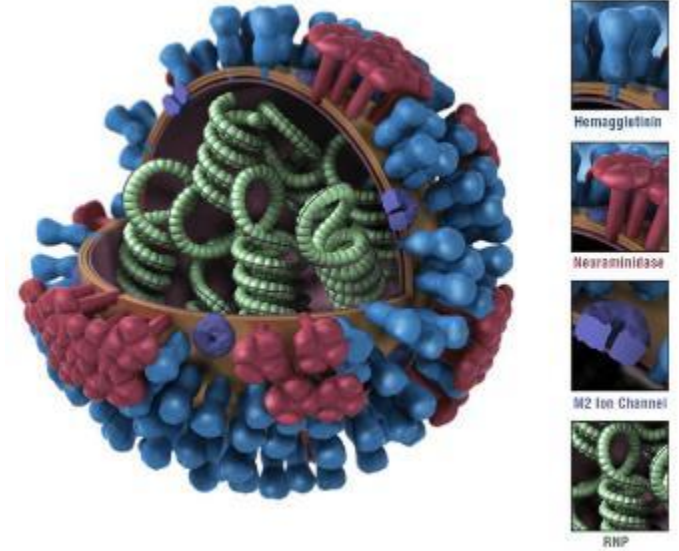
Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2024-25 Season, week ending Jul 12, 2025
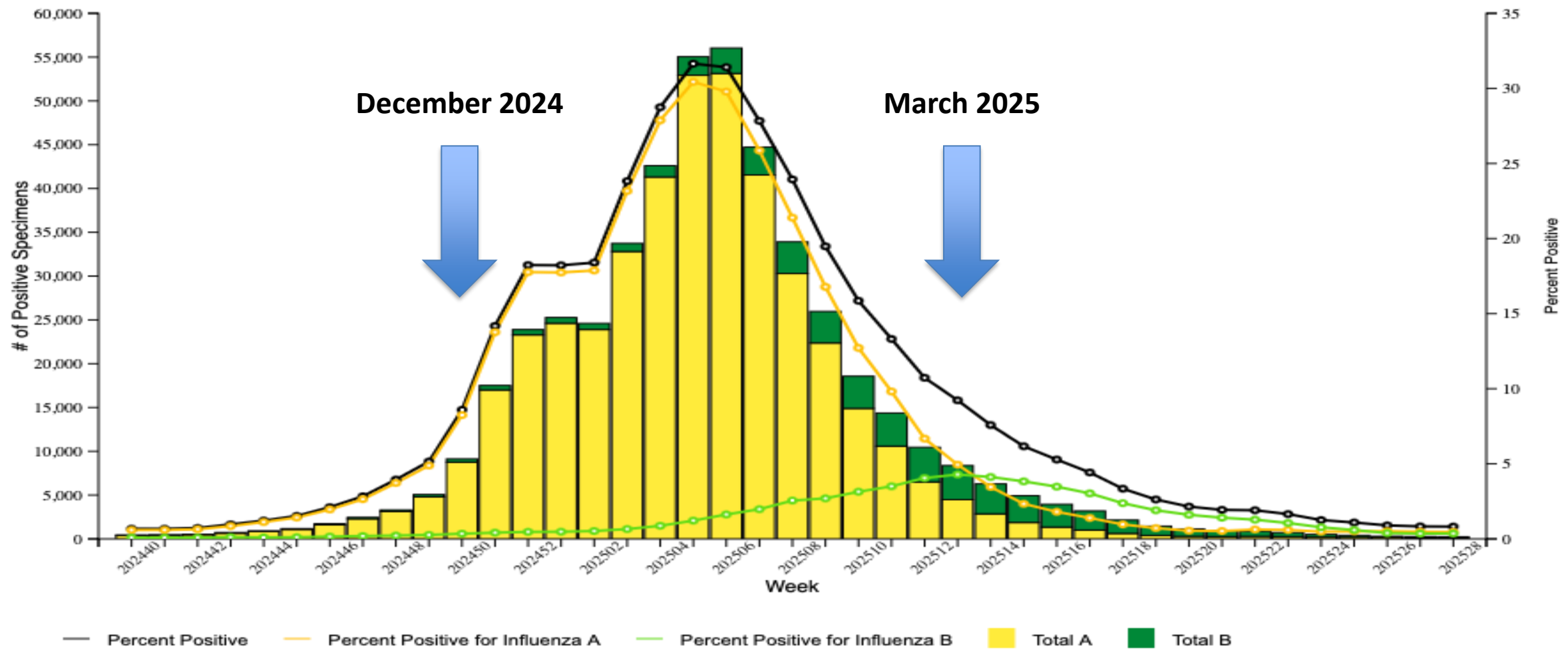
Outline

> Epidemiology of SARS-CoV-2 and Influenza

> **Clinical Guidelines and Symptoms (by US CDC)**

> Diagnostic Kinetics for Antigen vs Nucleic acid amplification (NAAT)

> Experience with Advanced Immunoassay Platform

> Diagnostic Implementation in Real-world Settings

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SARS-CoV-2 and Covid-19 (US CDC)

> **Federal Public Health Emergency (PHE) ended May 2023**

1. **Stay up to date with Covid-19 vaccines**

2. **Test for possible treatment and/or prevention***

    – **Antigen testing may be faster (more convenient)**

    – **Rt-PCR testing may have higher sensitivity (fewer false negative)**

* CDC has different guidelines for testing in various health care settings

Clinical Guidelines for Covid-19 (US CDC)

> Signs/symptoms generally appear 2-4 days after exposure

> May start as mild, can can progress to severe in some people

> Vaccine helps to protect against severe illness and death

> Typical Signs/Symptoms of Covid-19 (depend on immunization status):
  - Fever or chills
  - Cough
  - Shortness of breath or difficulty breathing
  - Sore throat
  - Congestion or runny nose
  - New loss of taste or smell
  - Fatigue
  - Muscle or body aches
  - Headache
  - Nausea or vomiting
  - Diarrhea

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Clinical Guidelines for **Influenza** (US CDC)

> **Signs/symptoms generally appear** ~~2-4~~ **1-3 days after exposure**

> **May start as mild, can can progress to severe in some people**

> **Vaccine helps to protect against severe illness and death**

> **Typical Signs/Symptoms of** ~~Covid-19~~ **Influenza (depend on immunization status):**
>   - **Fever or chills**
>   - **Cough**
>   - **Shortness of breath or difficulty breathing**
>   - **Sore throat**
>   - **Congestion or runny nose**
>   - **New loss of taste or smell** **(more common for SARS-CoV-2)**
>   - **Fatigue**
>   - **Muscle or body aches**
>   - **Headache**
>   - **Nausea or vomiting**
>   - **Diarrhea**

Clinical Differences between Influenza and Covid-19

> **Covid-19 is <u>spread/transmitted more easily</u> than flu**
> **Covid-19 may cause <u>more severe illness</u> than flu**
>   – **Depends on vaccine status and efficacy**
> **Covid-19 takes <u>longer to show symptoms</u> than flu**
>   – **Flu - symptoms appear 1-4 days after infection**
>   – **SARS-CoV-2 – symptoms appear 2-5 days (and up to 14 days) after infection**
> **Covid-19 is <u>contagious longer</u> than flu**
>   – **Flu – most contagious for first 3 days of symptoms**
>   – **SARS-CoV-2 – may be contagious before symptom onset; contagious for ~8 days of symptoms**
> **Additional Complications of Covid-19:**
>   – **Blood clots in veins/arteries (lungs, heart, legs, brain)**
>   – **Multisystem Inflammatory Syndrome in children (MIS-C) and adults (MIS-A)**
>   – **Long COVID – chronic conditional lasting >3 months**

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Diagnostic Difference between Influenza and Covid-19

> **Clinical Perspective**
  - **Can <u>not</u> tell the difference using signs/symptoms alone**
  - **Testing is needed to differentiate and confirm the diagnosis**

> **Laboratory**
  - **Differentiated by Antigen Test or Nucleic Acid Testing (PCR)**

> **CDC recommends a test that detects <u>both</u> Covid-19 and Influenza**

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Treatment Recommendations for Covid-19 (US CDC)

> **Acute Covid-19**
  – **Treat if mild/moderate illness and with 1+ risk factor for severe Covid-19**
  – **Treatment to be started <u>within 5 days of symptom onset</u>**

> **Risk factors**
  – **Age (>50 years) is most important risk factor for severe disease**
  – **Being unvaccinated or not up to date**
  – **Specific medical conditions***
  – **Immunocompromised conditions***

> **Treatment Options**
  1. **Nirmatrelvir-Ritonavir (Paxlovid®) – Adults and children >12 years old**
     > **Oral, start within 5 days of symptom onset**
  2. **Remdesivir (Veklury®) – Adults and children >28 days old**
     > **Intravenous, start within 7 days of symptom onset**
  3. **Molnuparavir (Lagrevio®) – Adults**
     > **May be used if other options are not available; Oral, within 5 days of symptom onset**

* refer to US CDC website

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Treatment Recommendations for Influenza (US CDC)

> **Acute Influenza**
> - Treat if illness, which can lessen symptoms and shorten duration of illness
> - Treatment to be started <u>within 2 days (48 hours) of symptom onset</u>

> **Risk factors**
> - Pregnant women
> - People with asthma or chronic lung disease
> - Heart disease
> - Immunocompromised conditions*

> **Treatment Options**
> 1. Oseltamivir phosphate (Tamiflu®) – Adults and children >14 days old
>   > Oral (pill or liquid), start within 48 hours of symptom onset
> 2. Zanamivir (Relenza®) – Adults and children >7 years old
>   > Inhaled (powder), start within 48 hours of symptom onset
> 3. Peramivir (Rapivab®) – Adults and children >6 months old
>   > Intravenous administration
> 4. Baloxavir marboxil (Xofluza®) – adults and children >5 years old
>   > Single oral pill, start within 48 hours of symptom onset (<u>not</u> for hospitalized patients)

* refer to US CDC website

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> Epidemiology of SARS-CoV-2 and Influenza

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> **Diagnostic Kinetics for Antigen vs Nucleic acid amplification (NAAT)**

> Experience with Advanced Immunoassay Platform Diagnostic Implementation in Real-world Settings

# Viral Testing – NAAT, Antigen, Antibody, Viral Culture

> **NAAT (nucleic acid amplification test), such as rt-PCR**
  – **RNA genes (*N, S, E, ORF 1ab*) for SARS-CoV-2**
  – ***M (matrix), HA (hemagglutinin), and NS (non-structural) genes* for Influenza A & B**

> **Antigens**
  – **Nucleocapsid (N), spike (S), receptor binding domains (RBDs) for SARS-CoV-2**
  – **Hemagglutinin (HA) for Influenza A & B**

> **Antibodies**
  – **Anti-nucleocapsid Ab, anti-spike Ab, neutralizing Ab for SARS-CoV-2**

> **Viral culture**
  – **Growth of *in vitro* SARS-CoV-2 in VeroE6AT cells for viability**
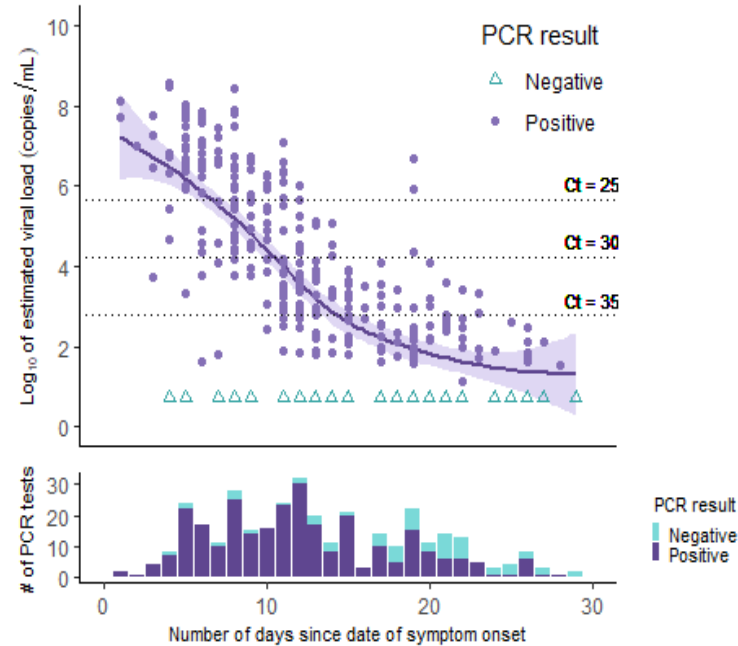
Longitudinal Covid-19 Diagnostic Study

> **To measure diagnostic kinetics of SARS-CoV-2 infection**
> **To determine risk factors for transmission (i.e. viable virus in culture)**

Funded by Bill and Melinda Gates Foundation
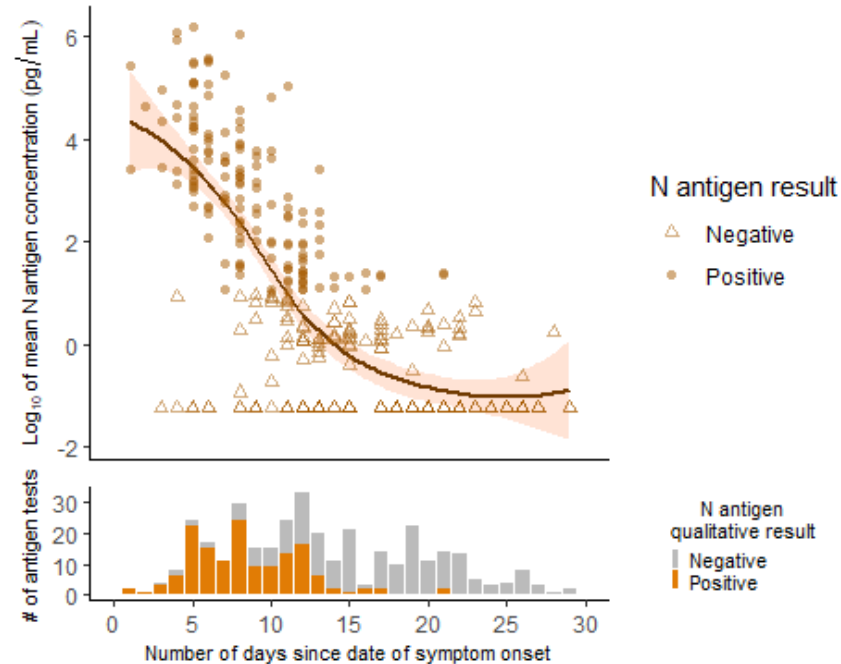
Longitudinal Covid-19 Diagnostic Study

> **To measure diagnostic kinetics of SARS-CoV-2 infection**

> **To determine risk factors for transmission (i.e. viable virus in culture)**

> **Enrolled 100 ambulatory people with acute Covid-19**

> **7 serial visits over 6 months**

> **Assessments:**
  - **Clinical Symptoms**
  - **RNA genes (*N, S, E, ORF 1ab*)**
  - **Nucleocapsid (N), spike (S)**
  - **Anti-nucleocapsid Ab, anti-spike Ab**
  - **Viral Growth in VeroE6AT cells**
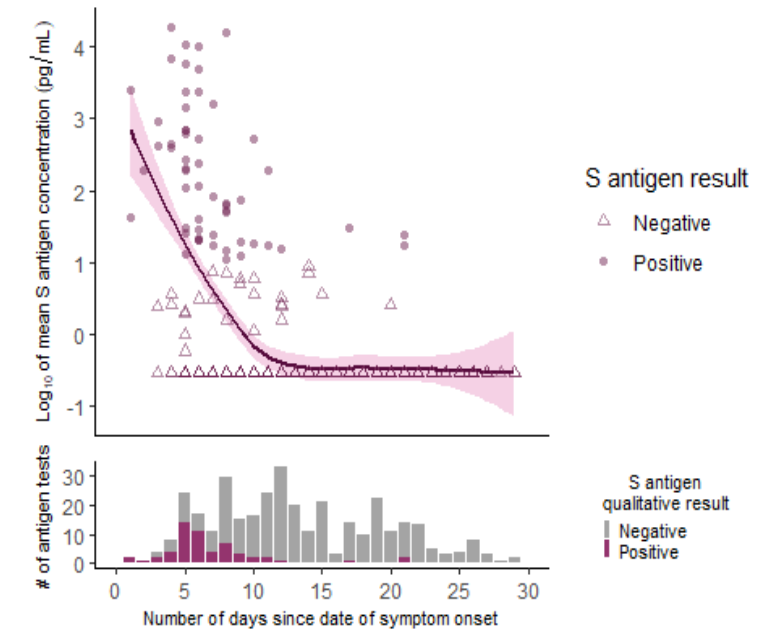
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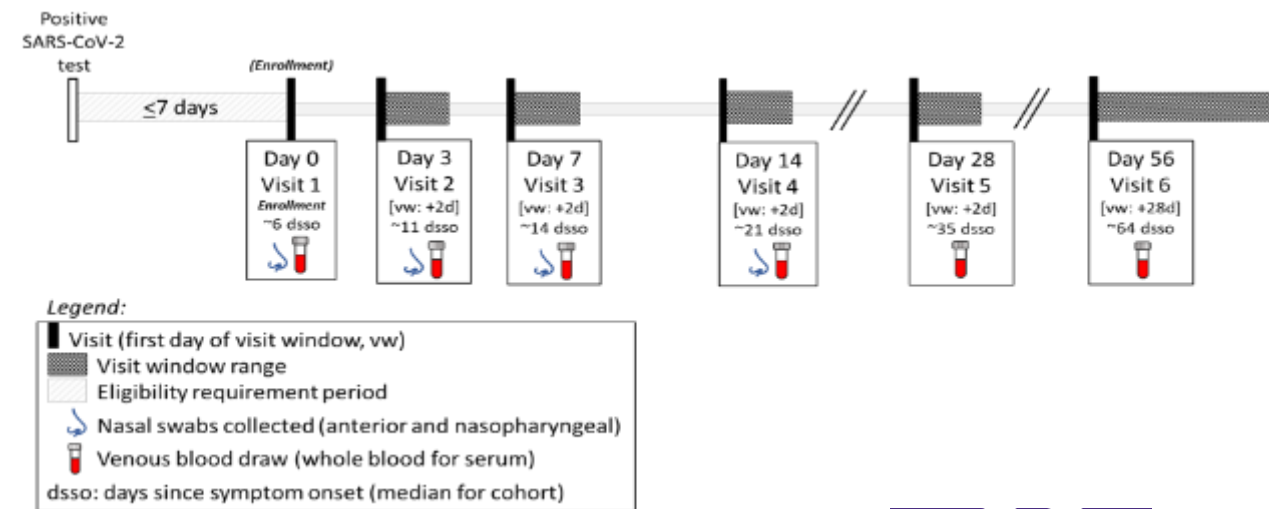
Longitudinal Covid-19 Diagnostic Study

PCR cycle threshold (Ct)

Nucleocapsid Antigen

Spike Antigen
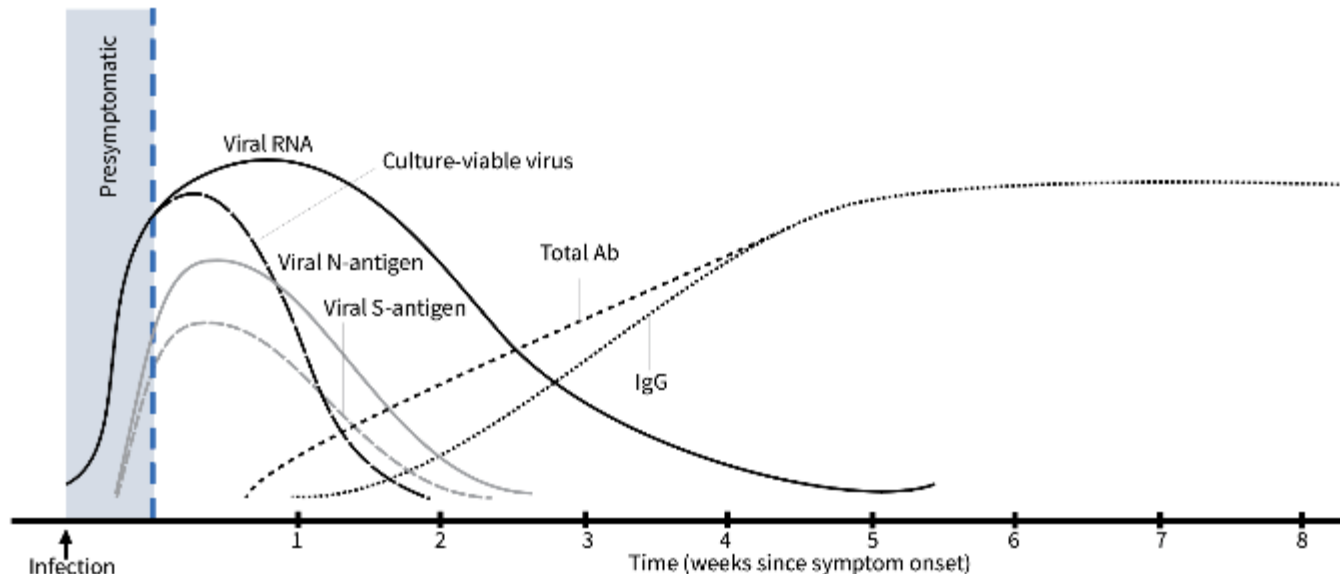
Longitudinal Covid-19 Diagnostic Study

Antigen-based Testing was more predictive of viral culture (infectivity) than PCR testing

Positive test coefficient	Antigen test	PCR test
All tests 0-14d	7.61 (4.33-13.35)	7.14 (2.09-24.43)
0 - 5d	8.6 (3.5-21.14)	>1,000*
6 - 10d	7.61 (3.01-19.22)	3.35 (0.65-17.3)
11 - 14d	0 (0-0)	0.83 (0.08-8.55)

Covid-19 Diagnostic Study – Conclusions

- Ambulatory people have viable SARS-CoV-2 for 10-14 days after symptom onset
- PCR tests can remain positive for weeks/months after infection
- N antigen testing was the best predictor of viral infectiousness
- Within 14 days from symptom onset, N antigen testing, rather than the absence of symptoms or viral RNA, may be used to safely discontinue SARS-CoV-2 isolation
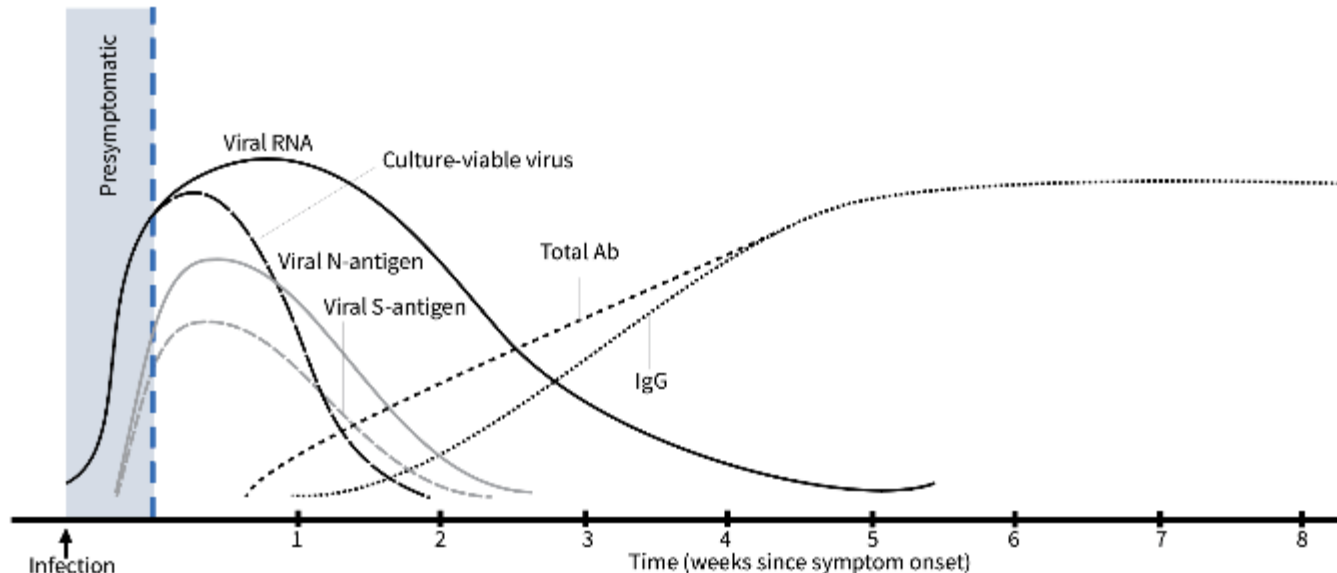
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Role of Global Diagnostic Testing (March 2020 – May 2020)

Cases Keep Climbing

Coronavirus cases are growing in New York, New Orleans, Detroit and dozens of other metropolitan areas.

New Orleans – metro

4 per week

3 per week

New York City metro area

2 per week

Detroit metro

New confirmed cases
Per 1,000 residents

1 per week

Seattle metro

└ Lombardy region of Italy

Other U.S. metros

March 15   March 22   March 29

Role of Global Diagnostic Testing (March 2020 – May 2020)

Total confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

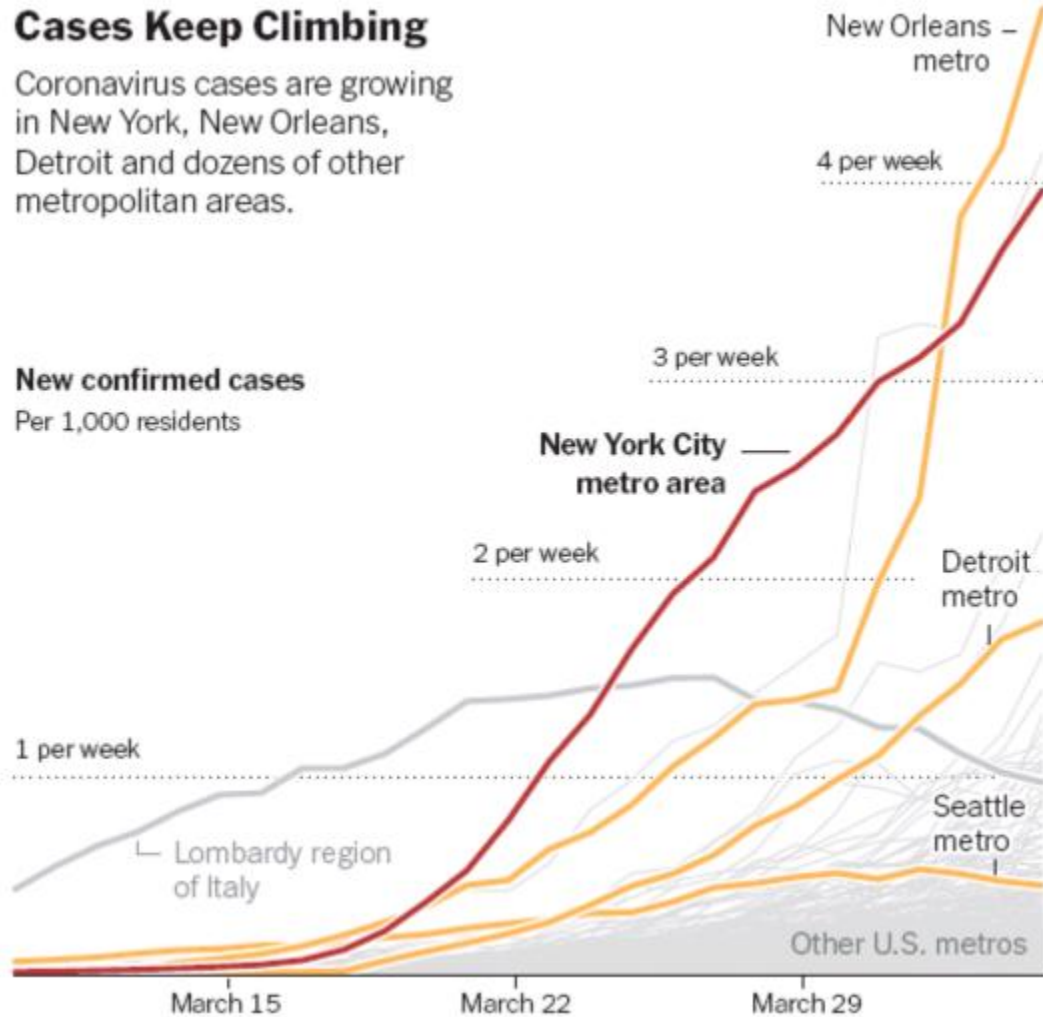Source: European CDC – Situation Update Worldwide – Last updated 9th May, 11:15 (London time)   OurWorldInData.org/coronavirus • CC BY
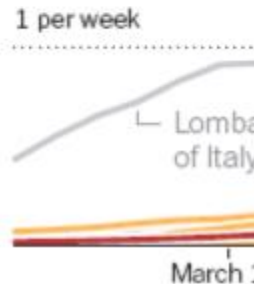
Role of Global Diagnostic Testing (March 2020 – May 2020)

Cases Keep

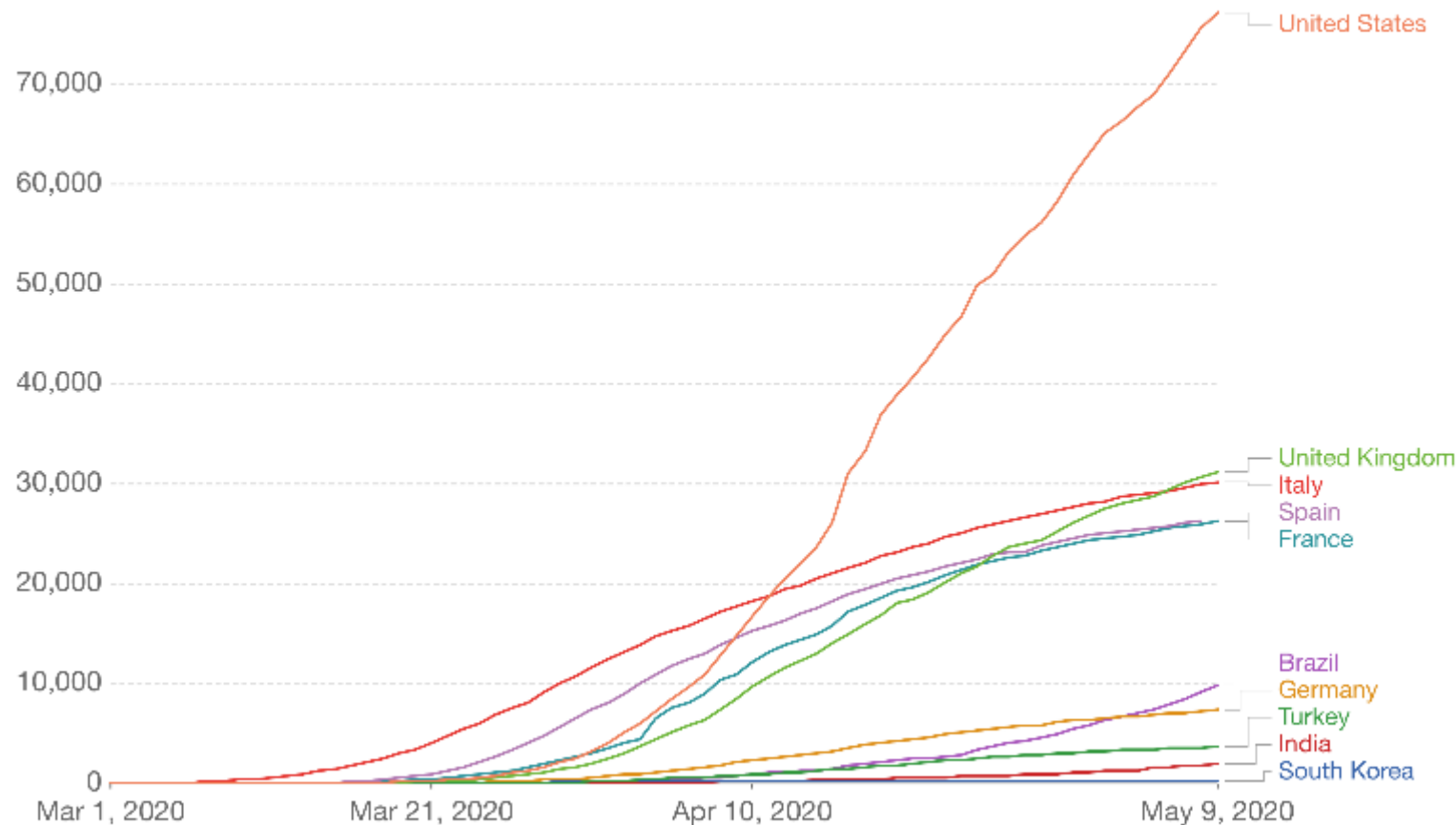Coronavirus case
in New York, New
Detroit and doze
metropolitan are

New confirmed ca

Per 1,000 residents

1 per week

Lomba
of Italy

March

Total confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths
may not be an accurate count of the true number of deaths from COVID-19.

— United States

70,000

60,000

50,000

40,000

30,000 — United Kingdom
— Italy
Spain
France

20,000

Brazil
10,000 Germany
Turkey
India
0 South Korea

Mar 1, 2020   Mar 21, 2020   Apr 10, 2020   May 9, 2020

Source: European CDC – Situation Update Worldwide – Last updated 9th May, 11:15 (London time)   OurWorldInData.org/coronavirus • CC BY
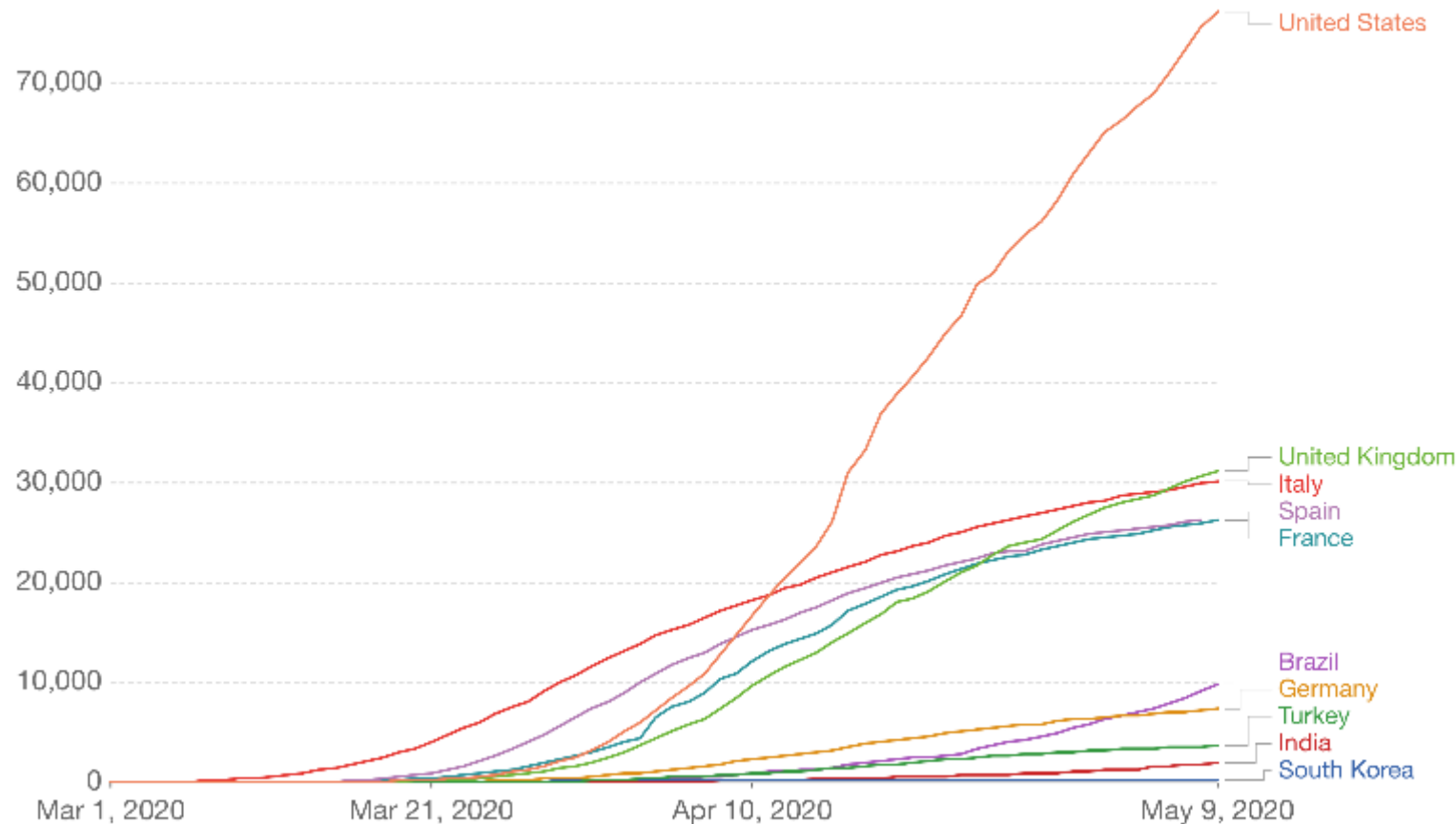
Our World
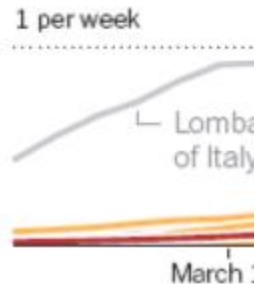in Data

**High early mortality
in USA**

**What lessons should
be learned?**

Role of Global Diagnostic Testing (March 2020)

U.S. Lags Behind Other Countries In Coronavirus Testing

Number of COVID-19 tests performed per million of the population (Mar 17, 2020)*

Country	Tests per million
United Arab Emirates	12,738
South Korea	5,567
Italy	2,514
Sweden	1,413
United Kingdom	749
Japan	130
United States	125
Vietnam	99

* U.S. and UAE data from March 16.
Source: Respective governments via Our World in Data

Forbes   statista

Role of Global Diagnostic Testing (March 2020)

U.S. Lags Behind Other Countries In Coronavirus Testing

Number of COVID-19 tests performed per million of the population (Mar 17, 2020)*

Country	Tests
United Arab Emirates	12,738
South Korea	5,567
Italy	2,514
Sweden	1,413
United Kingdom	749
Japan	130
United States	125
Vietnam	99

* U.S. and UAE data from March 16.
Source: Respective governments via Our World in Data
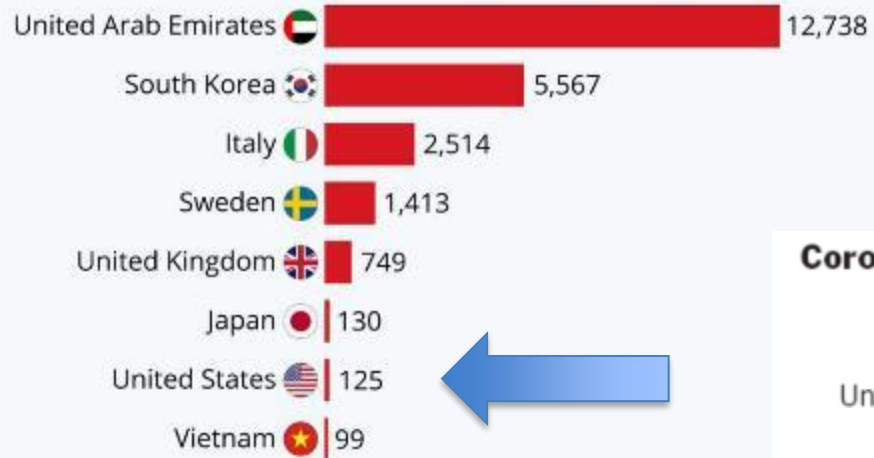
Forbes statis

DEPARTMENT OF GLOBAL HEALTH

Coronavirus Tests Per One Million People

Country	
United States	
Greece	
Czech Republic	
United Kingdom	
Austria	
Australia	
Italy	
South Korea	

Role of Global Diagnostic Testing (M

South Korea

Daily tests
■ Positive results ■ Negative results
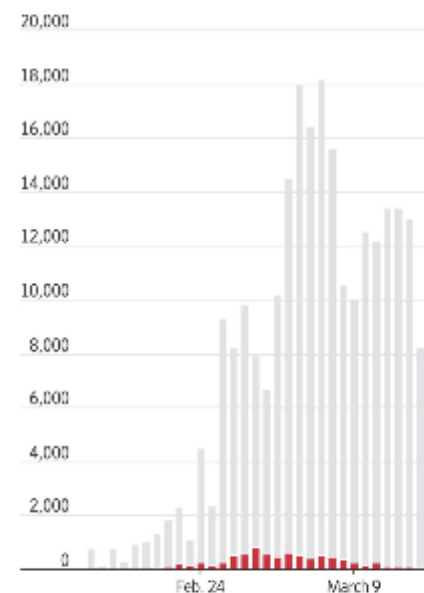
Source: South Korea Centers for Disease Control and Prevention

United States

Daily tests

The BIG miss

U.S. Lags Behind Other Countries In Coronavirus Testing

Number of COVID-19 tests performed per million of the population (Mar 17, 2020)*

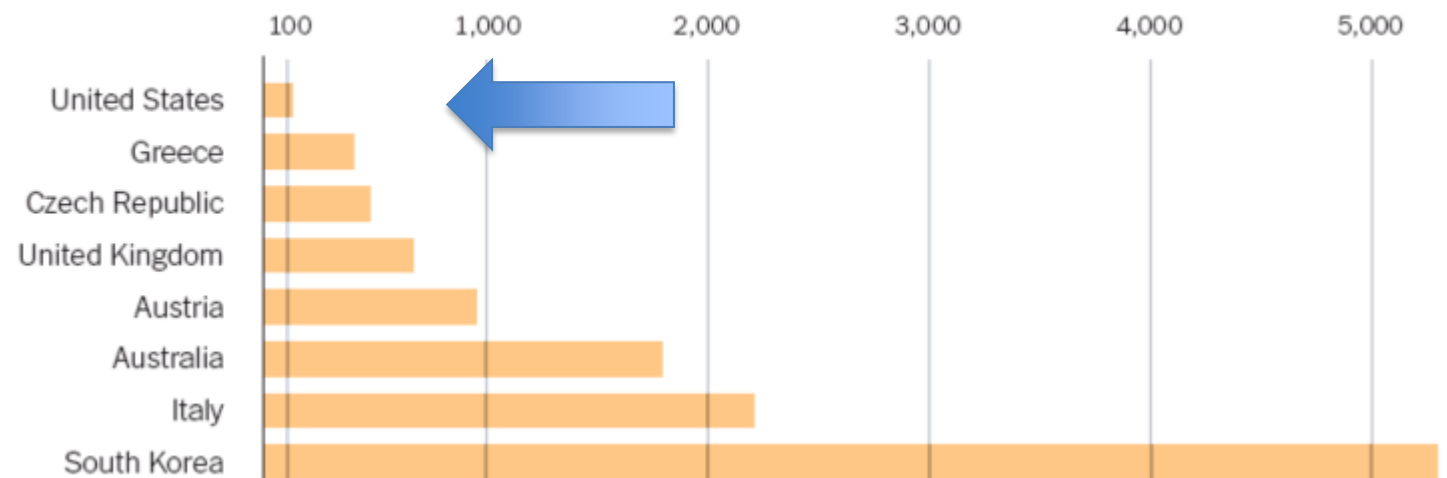| Country	Tests
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Source: Respective governments via Our World in Data

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Coronavirus Tests Per One Million

100   1,000

United States
Greece
Czech Republic
United Kingdom
Austria
Australia
Italy
South Korea

DEPARTMENT OF GLOBAL HEALTH

Role of Global Diagnostic Testing (March 2020 – June 2022)

Cumulative COVID-19 tests
Comparisons across countries are affected by differences in testing policies and reporting methods

800 million

600 million

400 million

200 million

0

- United States
  tests performed
- India
  samples tested

- United Kingdom
  tests performed

- France
  people tested
- Germany
  tests performed
- South Korea
  people tested
- Australia
  tests performed
- Brazil
  tests performed
- Canada
  tests performed

Mar 1, 2020   Nov 16, 2020   Jun 4, 2021   Jun 22, 2022

Source: Official data collated by Our World in Data
Note: Our data on COVID-19 tests and positive rate is no longer updated since 23 June 2022.

CC BY

Over 4 Billion diagnostic tests had been reported!

In April 2022, China reporting having conducted 9 Billion diagnostic tests

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Role of Global Diagnostic Testing (Jan 2020 – June 2022)

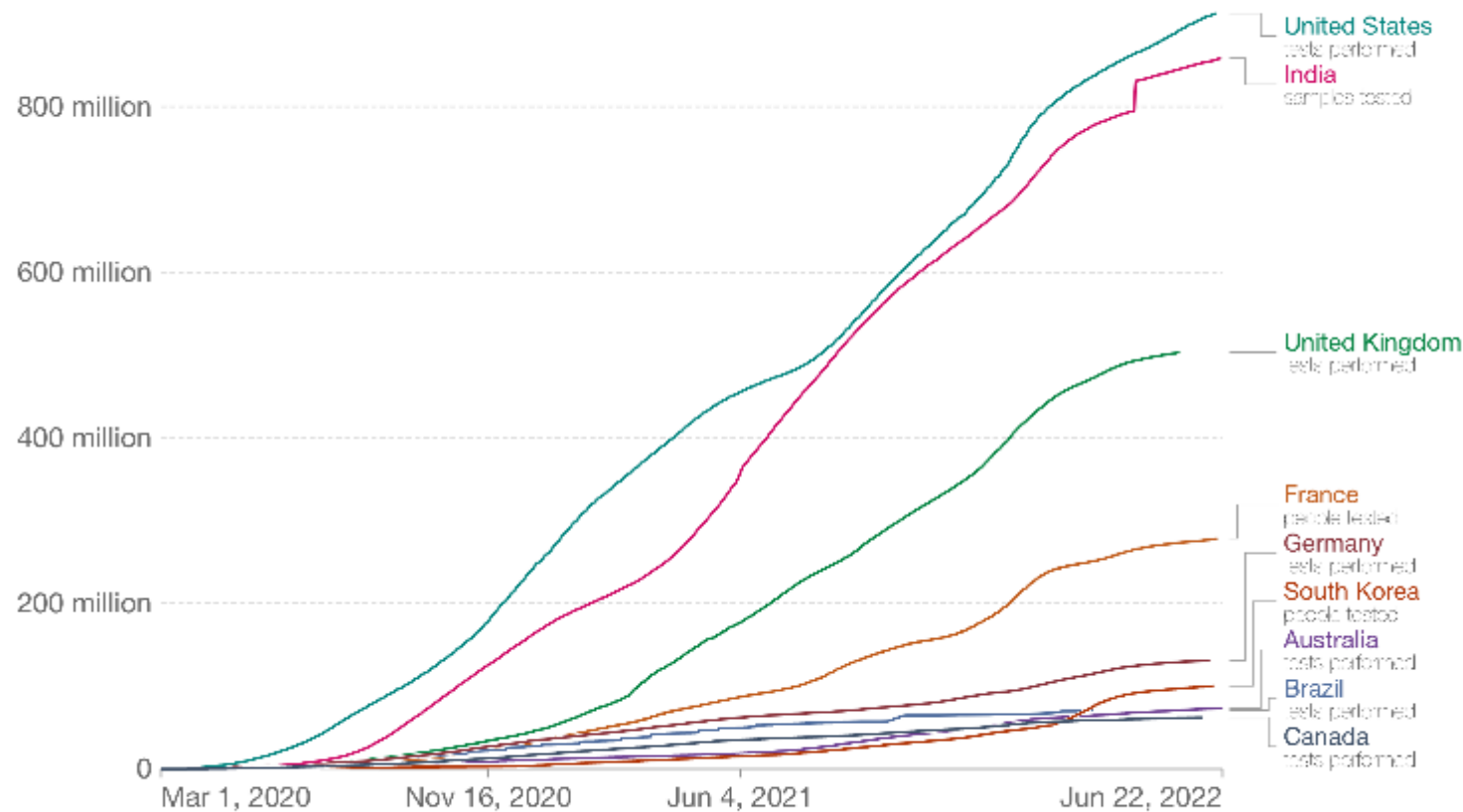Cumulative COVID-19 tests per 1,000 people

Comparisons across countries are affected by differences in testing policies and reporting methods

Our World in Data

Denmark
tests performed

10,000

8,000

United Kingdom
tests performed

6,000

Portugal
tests performed

France
people tested

Australia
tests performed

4,000

United States
tests performed

South Korea
people tested

Canada
tests performed

2,000

Germany
tests performed

India
samples tested

Brazil
tests performed

0

Jan 31, 2020   Feb 24, 2021   Sep 12, 2021   Jun 22, 2022

Source: Official data collated by Our World in Data
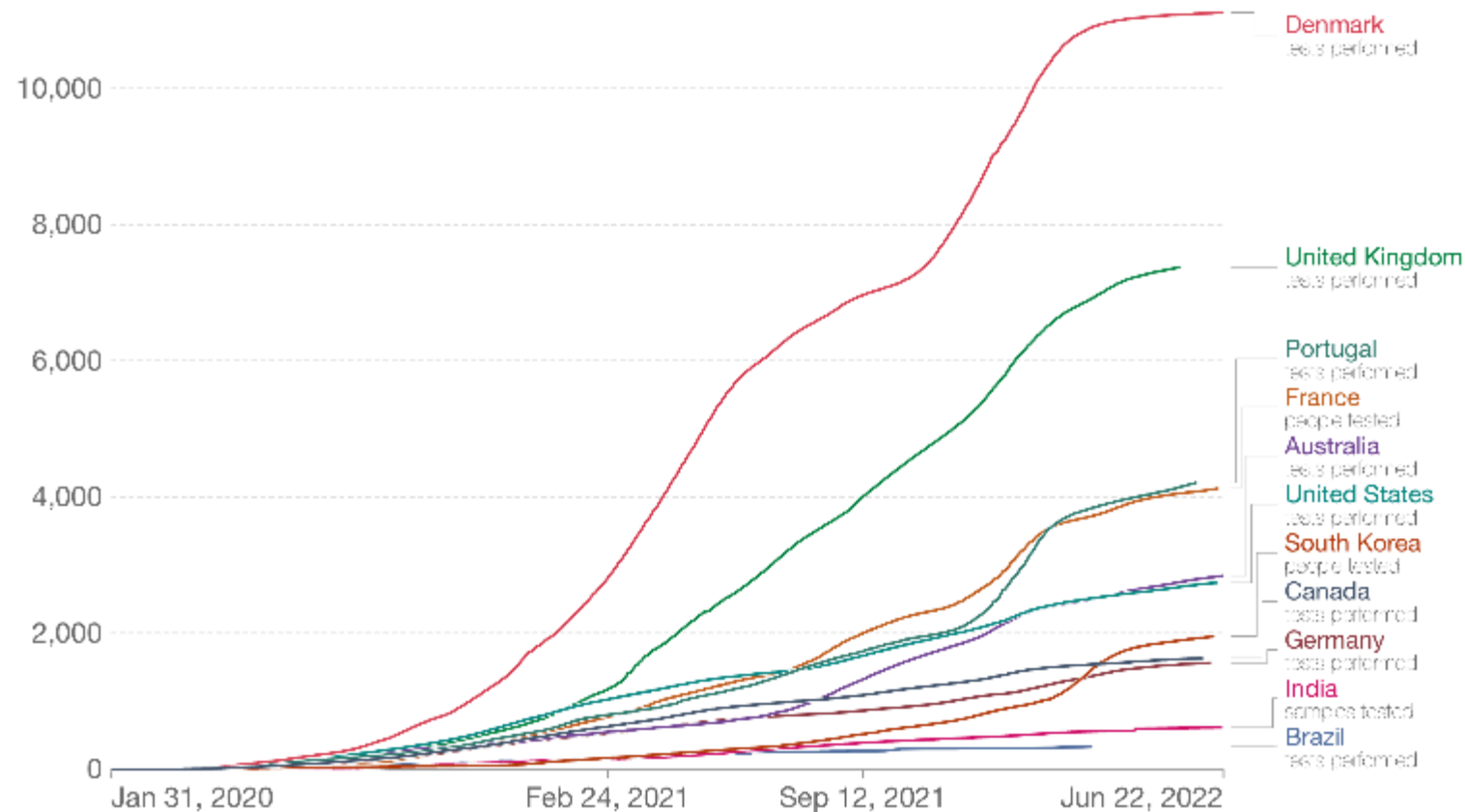Note: Our data on COVID-19 tests and positive rate is no longer updated since 23 June 2022.

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Testing rates per capita may be more informative than total testing

Role of Global Diagnostic Testing (June 2022)

The share of COVID-19 tests that are positive, Jun 23, 2022

7-day rolling average. Comparisons across countries are affected by differences in testing policies and reporting methods.
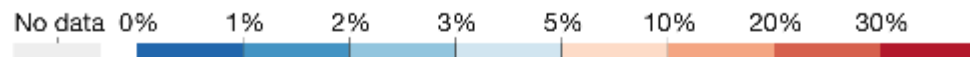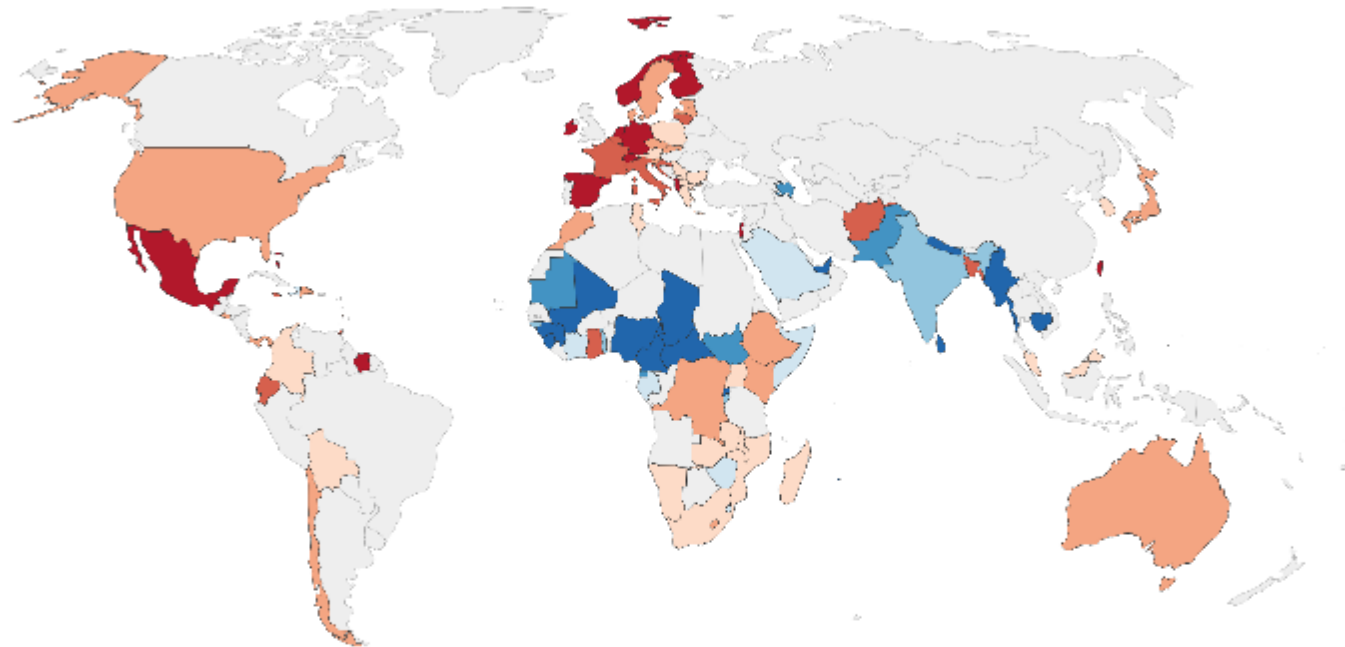
Our World in Data

Diagnostic testing is an

essential global tool:

(1) monitor infection rates

(2) variant surveillance

No data   0%   1%   2%   3%   5%   10%   20%   30%

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510(k) Approval of Home-testing for SARS-CoV-2, June 2023

FDA Permits Marketing of First COVID-19 At-Home Test Using Traditional Premarket Review Process

"Today's authorization is the first at-home COVID-19 test granted marketing authorization outside of emergency use authorities, representing a new era of consumer access to diagnostic tests that can be performed entirely at home," said Jeff Shuren, M.D., J.D., director of the FDA's Center for Devices and Radiological Health. "The FDA continues to proactively work with test developers that desire to market their products beyond emergency use authorities. This is part of the FDA's broader effort to advance the development and availability of at-home tests for a variety of medical conditions to expand patient access to testing."

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Outline

> Epidemiology of SARS-CoV-2 and Influenza

> Clinical Guidelines and Symptoms (by US CDC)

> Diagnostic Kinetics for Antigen vs Nucleic acid amplification (NAAT)

> **Experience with Advanced Immunoassay Platform**

> Diagnostic Implementation in Real-world Settings

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Advanced Immunoassay Platform

> Advanced immunoassay benchtop analyzer built around a proprietary fluorescence technology detection with an ultraviolet LED energy source

> An optical sensor inside the analyzer quickly scans and reliably collects hundreds of data points to generate test result

> Sample Type for SARS2 and Influenza

– Nasal swab, nasopharyngeal swab

> CLIA-waived, and ideal for

– primary care, urgent care, and community health settings

> Delivers automated results in 3-15 minutes

Advanced Immunoassay Platform

> SARS-CoV-2 – Nucleocapsid protein

– Approved by FDA in February 2023

– Symptomatic participants:

> Positive percent agreement (PPA) = 89%

> Negative percent agreement (NPA) = 99%

> Influenza A and B – Nucleocapsid protein

– Approved by FDA in May, 2017

– When presenting 1-2 days after symptom onset:

> Positive percent agreement (PPA) = 95%

> Negative percent agreement (NPA) = 100%

> Assay available as a combined SARS-CoV-2, Influenza A, and Influenza B

– Currently has Emergency Use Authorization (EUA) status by US FDA

Studies of Advanced Immunoassay Testing – SARS-CoV-2 and Influenza A/B

> **SARS-CoV-2 - Analytical Validation study[1]**
>   – **Small retrospective study in Finland (158 positive; 40 negative)**
>   – **Sensitivity ~85% overall, and 94% when Ct value <30.**

> **SARS-CoV-2 - Clinical Validation[2]**
>   – **Symptomatic (N=227) – Sens. 80%; Spec. 98.9%; PPV 94%**
>   – **Asymptomatic (N=871) – Sens. 41%; Spec 98.4%; PPC 33%**

> **SARS-CoV-2 - Implementation Study at U. of Washington[3]**
>   – **23K paired PCR/Ag samples**
>   – **Ag testing identified infection prior to PCR on 89 occasions (with 234 days of isolation gained)**
>   – **Specificity was high (>99%) throughout the study**

> **Influenza – Performs better for lower Cycle Threshold (Ct) values (more disease)[4]**
>   – **98% sensitivity for Ct <34**
>   – **100% sensitivity for Ct <29**
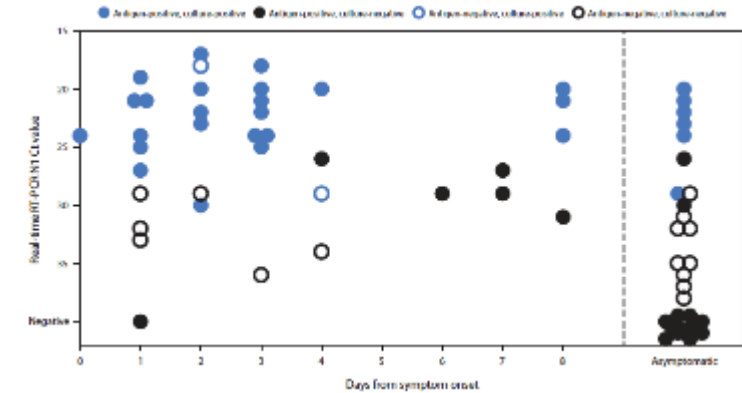
1. Jaackelainen AE, et al. J Clin Virology, 2021.
2. Pray IW, et al, MMWR, 2021.
3. Harmon KG, et al. pre-print, 2021.
4. Schweiger B, Lehmann H. Presented a CVS 2012, Cologne, Germany.

Outline

> Epidemiology of SARS-CoV-2 and Influenza

> Clinical Guidelines and Symptoms (by US CDC)

> Diagnostic Kinetics for Antigen vs Nucleic acid amplification (NAAT)

> Experience with Advanced Immunoassay Platform

> **Diagnostic Implementation in Real-world Settings**

Diagnostic Implementation in Real-world Settings
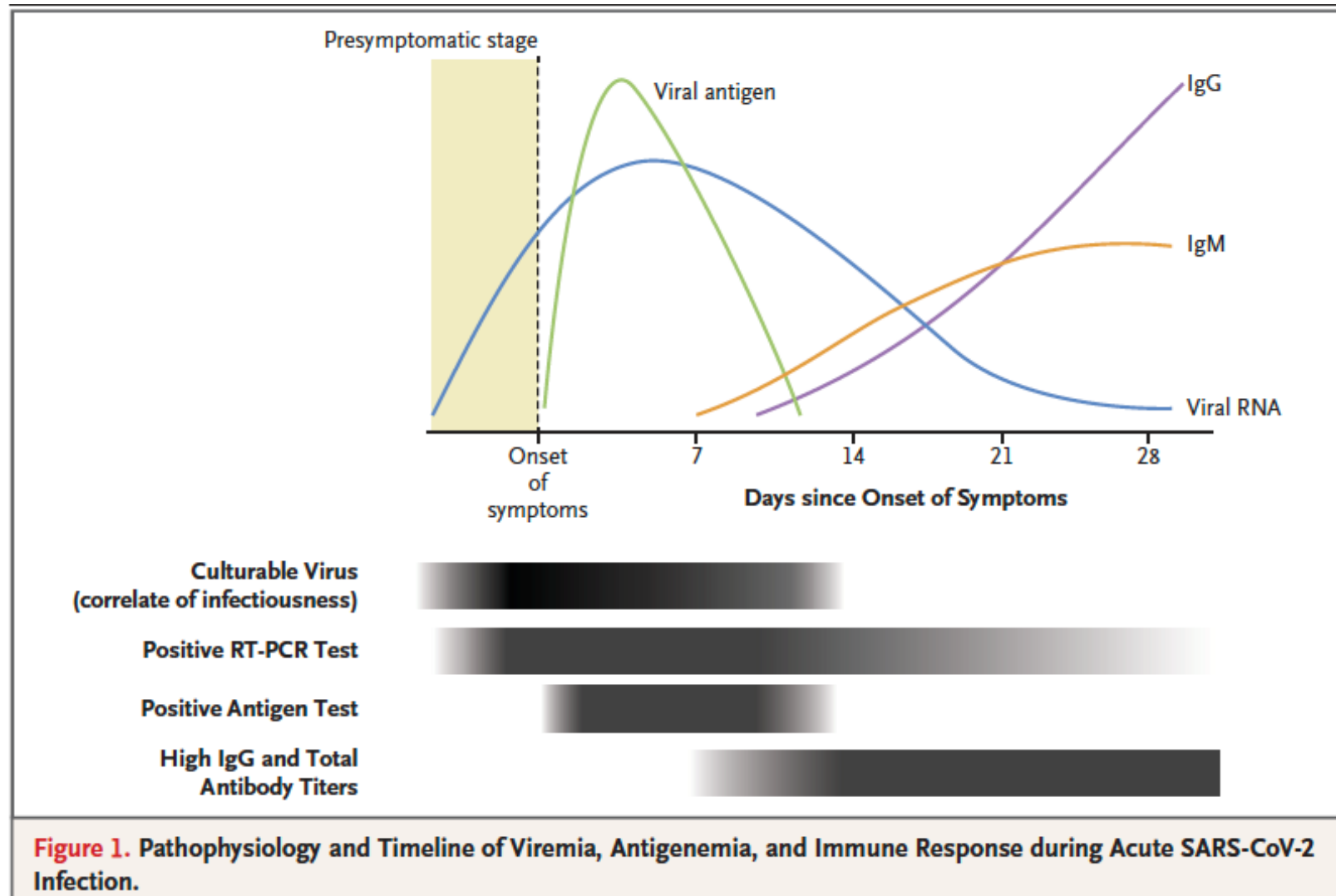
Figure 1. Pathophysiology and Timeline of Viremia, Antigenemia, and Immune Response during Acute SARS-CoV-2 Infection.

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., Editor

Rapid Diagnostic Testing for SARS-CoV-2

Paul K. Drain, M.D., M.P.H.

Published Jan 22, 2022

Diagnostic Implementation in Real-world Settings

> Rapid Antigen Tests are easier, faster, more convenient

– Moderate Sensitivity – may have ~5-20% false negative results

– High Specificity – if positive, almost certainly a true positive

> May do Antigen testing first in primary/urgent care settings

– If positive, consider/initiate Treatment
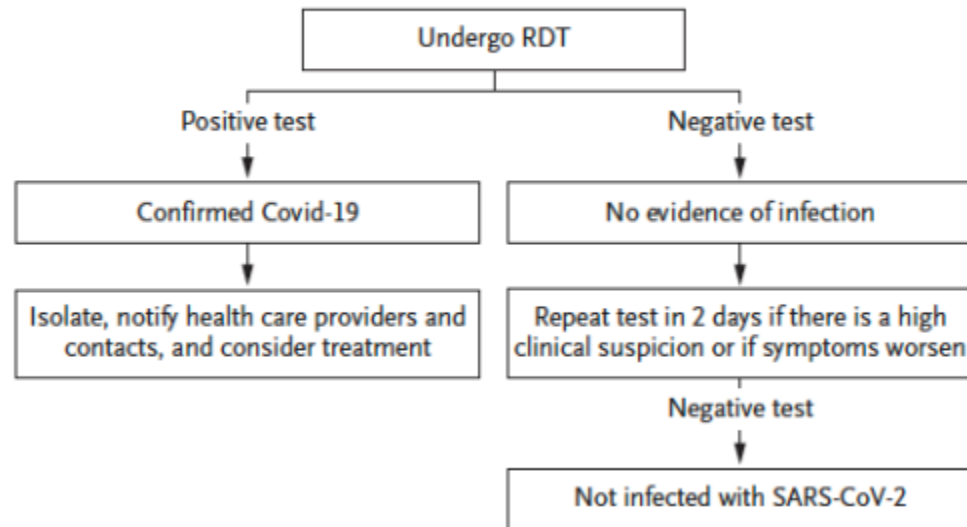
– If negative, consider rt-PCR testing

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*
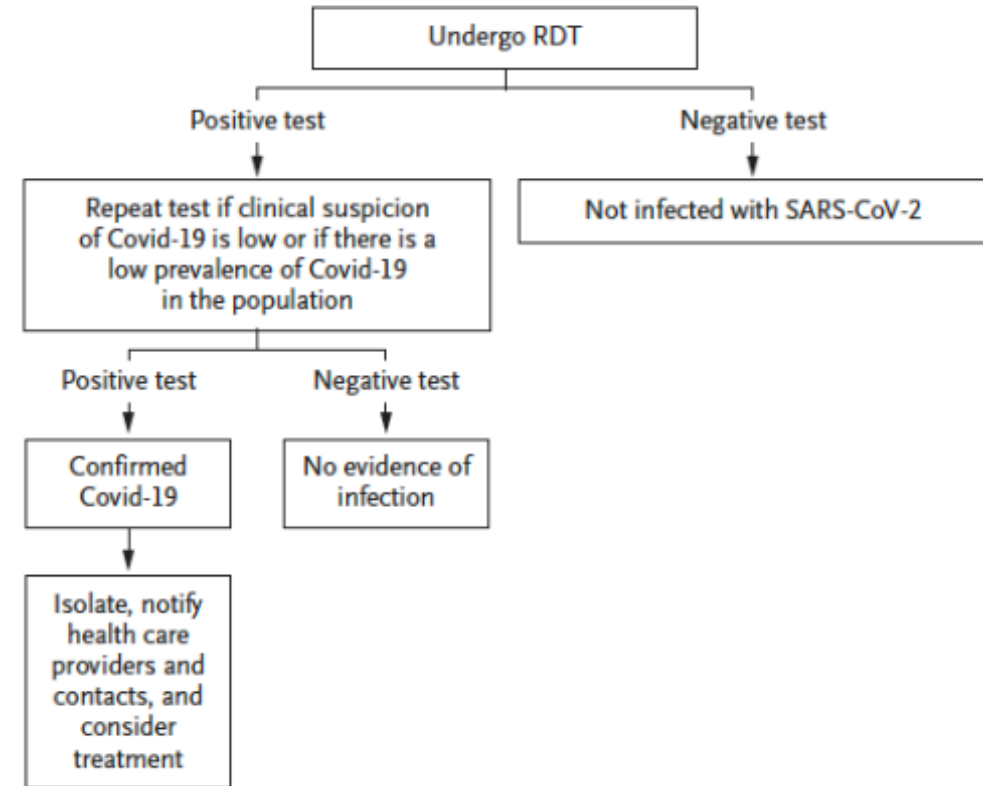
Rapid Diagnostic Testing for SARS-CoV-2

Paul K. Drain, M.D., M.P.H.

A   High Pretest Probability of Infection — Any Person with Symptoms of Covid-19, Regardless of Vaccination Status

```
                    ┌─────────────────┐
                    │   Undergo RDT   │
                    └─────────────────┘
              Positive test        Negative test
                    │                   │
         ┌──────────────────┐   ┌──────────────────┐
         │ Confirmed Covid-19 │   │ No evidence of infection │
         └──────────────────┘   └──────────────────┘
                    │                   │
┌─────────────────────────────┐  ┌──────────────────────────────────┐
│ Isolate, notify health care │  │ Repeat test in 2 days if there is a high │
│ providers and contacts, and │  │ clinical suspicion or if symptoms worsen │
│ consider treatment          │  └──────────────────────────────────┘
└─────────────────────────────┘              │
                                       Negative test
                                             │
                              ┌──────────────────────────────┐
                              │ Not infected with SARS-CoV-2 │
                              └──────────────────────────────┘
```

C   Low Pretest Probability of Infection — Asymptomatic Person in a Potential High-Risk Transmission Setting

```
                    ┌─────────────────┐
                    │   Undergo RDT   │
                    └─────────────────┘
              Positive test        Negative test
                    │                   │
    ┌──────────────────────────────┐  ┌──────────────────────────────┐
    │ Repeat test if clinical      │  │ Not infected with SARS-CoV-2 │
    │ suspicion of Covid-19 is low │  └──────────────────────────────┘
    │ or if there is a low         │
    │ prevalence of Covid-19       │
    │ in the population            │
    └──────────────────────────────┘
         Positive test    Negative test
              │               │
      ┌──────────────┐  ┌──────────────┐
      │ Confirmed    │  │ No evidence of │
      │ Covid-19     │  │ infection     │
      └──────────────┘  └──────────────┘
              │
      ┌──────────────┐
      │ Isolate,     │
      │ notify       │
      │ health care  │
      │ providers and│
      │ contacts, and│
      │ consider     │
      │ treatment    │
      └──────────────┘
```

If HIGH pre-test probability – Positive RDT is Real

If LOW pre-test probability – Negative RDT is Real

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Diagnostic Implementation in Real-world Settings

Table 2. Summary of Major Guidelines and Recommendations for RDTs to Detect SARS-CoV-2.*

Guideline or Recommendation	WHO	CDC	ECDC	IDSA
Endorsement of RDTs				
Antigen-based RDT	Yes	Yes	Yes	No
Molecular RDT	Yes	Yes	Yes	Yes
Testing indication				
Person with symptoms of Covid-19	Yes	Yes	Yes	Yes, molecular test only
Asymptomatic person with high pretest probability of infection	Yes	Yes	Yes	Yes, molecular test only
Screening in asymptomatic person with low pretest probability of infection	Yes†	Yes	Yes, if population prevalence ≥10%	Yes, molecular test only
Specific situation				
Repeat serial RDTs after negative test, if high clinical suspicion	Yes†	Yes	Yes	No
Confirmatory testing recommended	No	No	Yes‡	Yes§
Timing for testing an asymptomatic person after an exposure	NC	5–7 days	2–7 days	NC
Provide support for patient performing swab specimen collection	No	Yes	No	Yes
Endorse home-based RDT	No	Yes	NC	NC
Case registration, isolation, and contact tracing	Yes	Yes	Yes	NC

Published Jan 22, 2022

International Guidelines are NOT well aligned

Use your Local/National Guidelines for Testing & Treatment

Case Example #1

> **62-year-old Female presents to the urgent care center with ~4 days of fever, rhinorrhea, cough, and loss of taste/smell. She received the Flu vaccine before the flu season, but can't remember when she last received a Covid-19 vaccine.**

> ***What would you do next?***

W

Case Example #1

> **62-year-old Female presents to the urgent care center with ~4 days of fever, rhinorrhea, cough, and loss of taste/smell. She received the Flu vaccine before the flu season, but can't remember when she last received a Covid-19 vaccine.**

> ***What would you do next?***

Recommended Approach:
- Patient is at high risk for Covid-19; advanced age is a risk for complications
- Rapid antigen testing, if available, in urgent care clinic
- Consider rt-PCR lab-testing for SARS-CoV-2 and Influenza A/B
- Initiate Paxlovid based in high-probability, age, and symptoms <5 days
- Isolation based on test results/symptoms

Case Example #2

> **In February, a 37-year-old pregnant women presents to the primary care clinic with ~28 hours of onset of cough, body/muscle aches, and mild fever. She has a toddler son in daycare, who also has a fever and rhinorrhea.**

> ***What would you do next?***

Case Example #2

> **In February, a 37-year-old pregnant women presents to the primary care clinic with ~28 hours of onset of cough, body/muscle aches, and mild fever. She has a toddler son in daycare, who also has a fever and rhinorrhea.**

> *What would you do next?*

Recommended Approach:
- **Women is high risk for Influenza, and pregnancy increases risk of complications**
- **Rapid antigen testing, if available, in primary care clinic**
- **Consider rt-PCR lab-testing for SARS-CoV-2 and Influenza A/B**
- **Initiate Tamiflu based in high-probability, age, and symptoms <48 hours**
- **Isolation based on test results/symptoms**

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Case Example #3

> **A 52-year-old male tested positive for SARS-CoV-2 and completed a full 5-day course of Paxlovid. About 5 days after completing treatment, patient began experiencing cough, fatigue, and body aches. He does not have any dyspnea or shortness of breath. He asks for another prescription of Paxlovid and the risk of transmission.**

> *What would you advise?*

W

Case Example #3

> **A 52-year-old male tested positive for SARS-CoV-2 and completed a full 5-day course of Paxlovid. About 5 days after completing treatment, patient began experiencing cough, fatigue, and body aches. He does not have any dyspnea or shortness of breath. He asks for another prescription of Paxlovid and the risk of transmission.**

> *What would you advise?*

Recommended Approach:

- Covid rebound is a return of symptoms 3-7 days after starting to improve
- Antigen test results can become positive (rt-PCR is not recommended)
- Nearly all cases are mild, and resolve with supportive care
- Patient may be contagious, so should re-isolate from family members
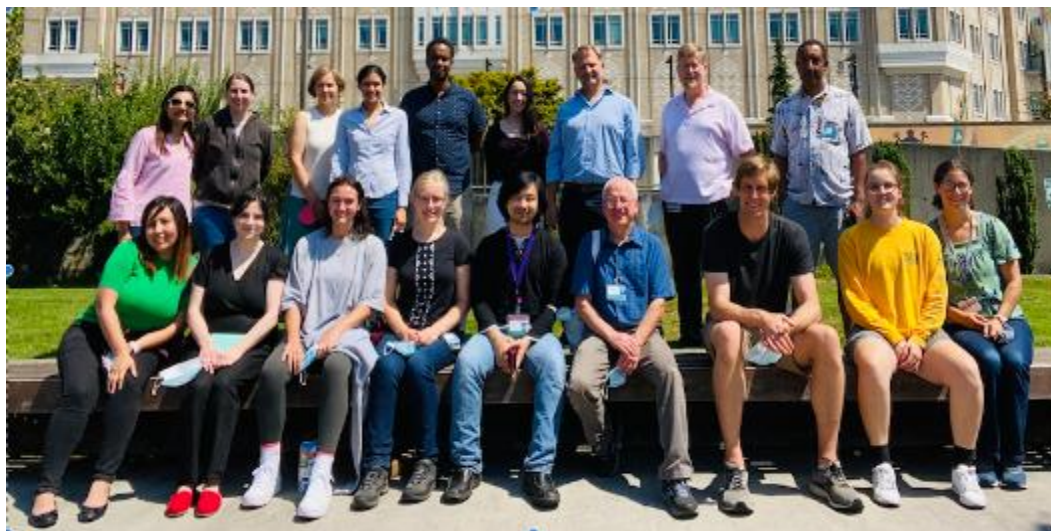- most cases of Covid rebound last ~3 days

Summary and Conclusions

> **Diagnostic testing has been an essential tool for <u>both</u> personal and population health measures**

> **Individual Testing – both Antigen and PCR testing have merits**
>   – **NAAT is most sensitive, but may detect remnant viral RNA long after infection**
>   – **Antigen is sensitive during acute infection <u>and</u> correlates better with viral viability**

> **Rapid Antigen-based Tests are excellent at detecting the circulating variant**

> **Proposed Algorithms for Antigen-based Testing should be used sensibly**

> **Need coordinated efforts to inform health leaders, clinicians, and patients**

Acknowledgments for Covid-19 Study

U. of Washington's Study Team

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