COMPLIMENTARY WEBINAR

Mitigating RSV and Influenza with Rapid Testing in Adults

RSV AWARENESS MONTH

Wednesday, October 18, 2023 | 1:00 – 2:00 PM ET

Stefan Riedel, MD, PhD, D(ABMM), FCAP

Associate Professor of Pathology

Associate Medical Director
Clinical Microbiology Laboratories

Beth Israel Deaconess Medical Center and
Harvard Medical School
Boston, MA

The speaker is presenting on behalf of Abbott.
The information presented is consistent with applicable FDA guidelines.
This program does not provide continuing medical education (CME) credits.
 COL-21772-01 10/23

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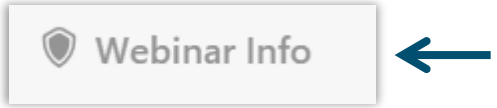

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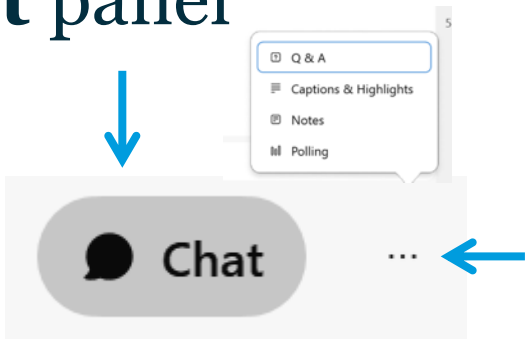


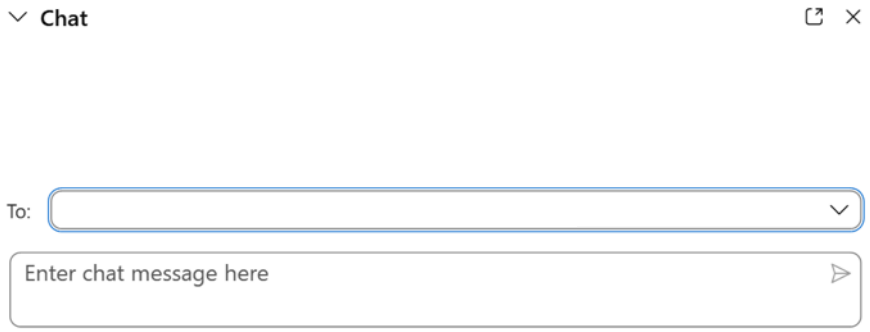
Other panels:

Q&A

Notes

Webinar communication tools

Chat



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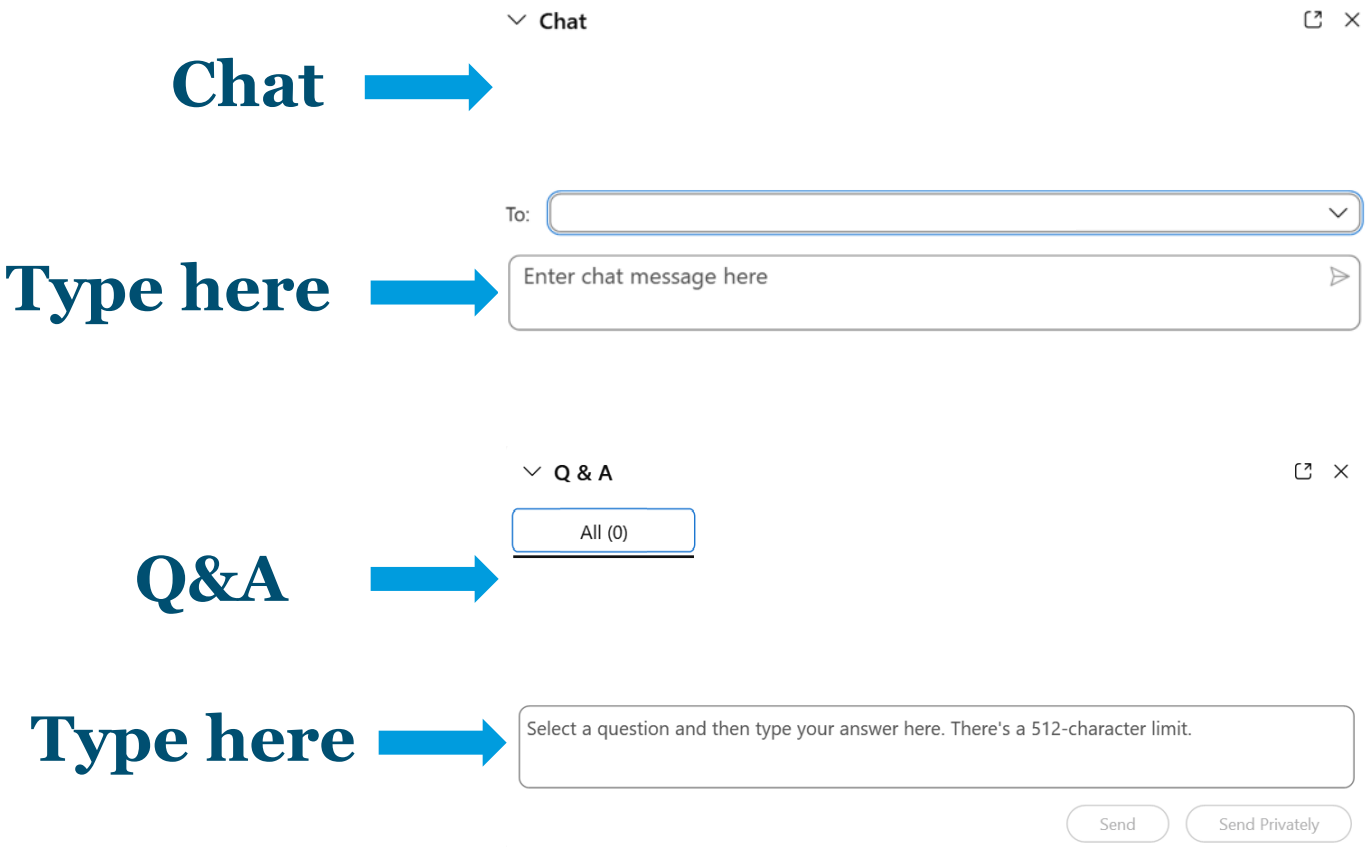
Webinar communication tools



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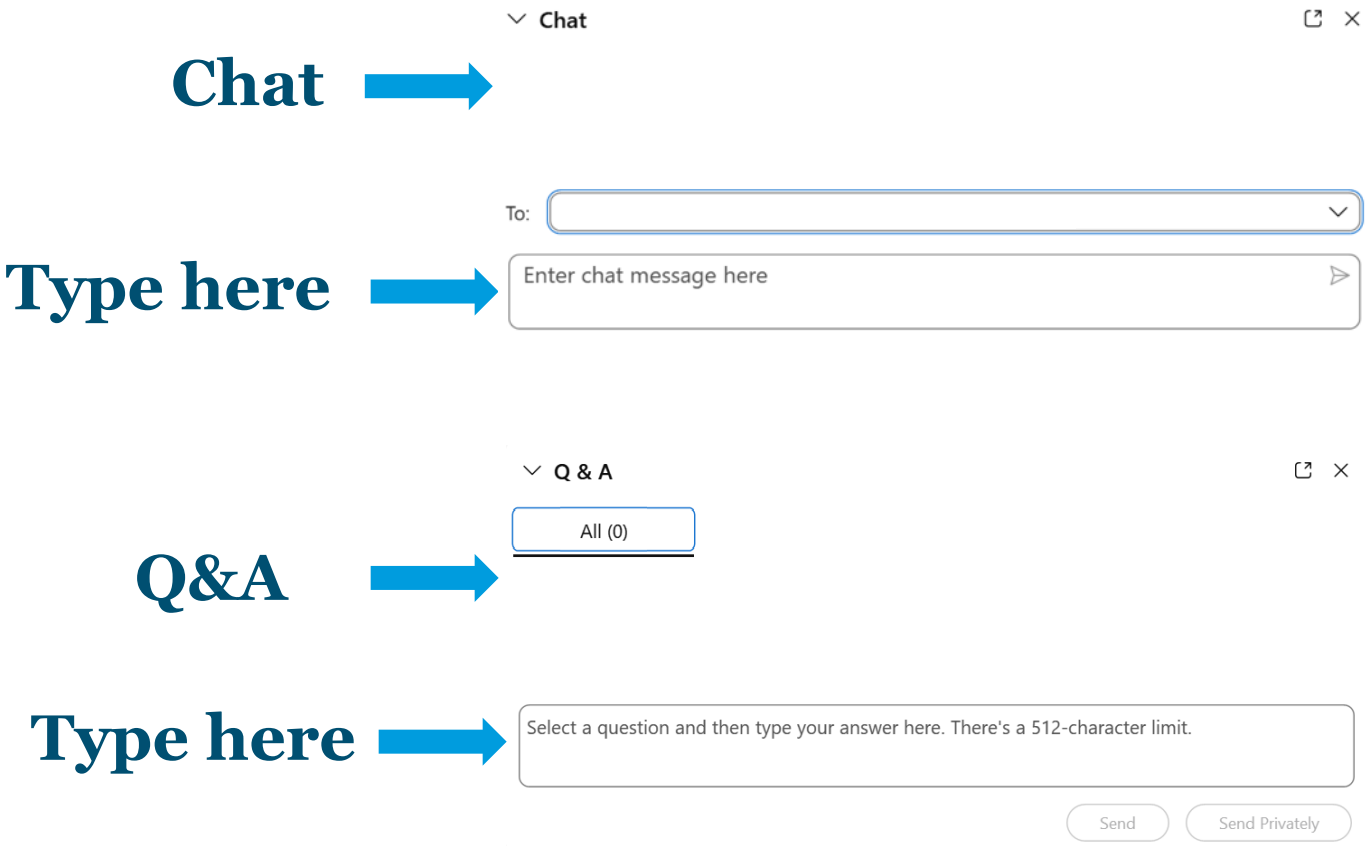

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- A certificate of attendance is available for all attendees
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- **For groups: Those logged in will receive Email from messenger@webex.com with link to evaluation. Forward email to colleagues who attended with you!!!**
- Double-check email address

Joined Using a Mobile Device?

- Evaluation won't appear automatically, but…
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Recording

Within a few days following today's event, visit

https://www.whitehatcom.com/abbott

Mitigating RSV and Influenza with Rapid Testing in Adults

Live Event: Wednesday, October 18, 2023 | 1:00 - 2:00 PM Eastern Time
P.A.C.E.® credit available until October 18, 2024
Florida Laboratory CE Credit available

RECORDING

SLIDES

Join this program for a timely update on respiratory infections and mitigation strategies in adult populations, particularly those at greater risk of severe illness and complications. A key element focuses on rapid testing with expert perspectives on test types, clinical utility, and improved testing efficiencies, including diagnostic stewardship.

The webinar will:

- Summarize epidemiological trends and risk factors for severe RSV and Influenza infections
- Review challenges and impact of RSV and Flu infections in acute and congregate care settings
- Describe rapid test technology types and differences
- Share perspectives on rapid test platform efficiency and diagnostic stewardship strategies within current healthcare constraints

Presenter:

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Conflict of Interest / Disclosures

Dr. Stefan Riedel

- Research Contracts/Grants: *
  - Beckman Coulter, Inc.; JMI Laboratories; Massachusetts Life Science Center (Grant funding support);
- Research Collaborators: *
  - JMI Laboratories; Abbott Diagnostics, Inc.
- Consulting/Clinical Advisory Board/Speakers Bureau:
  - OpGen, Inc.; Clear Labs Diagnostics, Inc.
  - Abbott Diagnostics, Inc.[a]
- USCAST advisor & voting member[a]

*Funding and materials used in the studies described in this presentation were provided by sponsors as indicated. The terms of these agreements are being managed by Beth Israel Deaconess Medical Center and HMS in accordance with its conflict of interest policies.

Images and discussion of any particular laboratory test does not constitute an endorsement of that particular test/assay/manufacturer by Dr. Riedel and/or BIDMC and/or HMS

[a]Dr. Riedel's participation in various biotech-industry sponsored speaking engagements and/or consulting engagements is managed by Beth Israel Deaconess Medical Center in accordance with its conflict of interest policies. All opinions expressed and/or implied in this presentation are solely those of Dr. Riedel. The content of this presentation does not represent or reflect the views of Beth Israel Deaconess Medical Center and/or the Beth Israel Deaconess Care Organization.

Objectives

1. Summarize epidemiological trends and risk factors for severe RSV and influenza infections
2. Review challenges and impact of RSV and influenza infections in acute and congregate care settings
3. Describe rapid test technologies for RSV & flu and differences
4. Share perspectives on rapid test platform efficiency and diagnostic stewardship strategies within current healthcare constraints

Epidemiology Review for Upper Respiratory Tract Infections

SARS-CoV-2

Influenza
(Flu-A / Flu-B)

RSV

Parainfluenza (1-4)

Adenoviruses

Rhinoviruses

Human Metapneumovirus

Coronaviruses

Differential Diagnosis

- Common cold
- Allergic rhinitis
- Sinusitis
- Tracheobronchitis
- Pneumonia
- “atypical” pneumonia
- Pertussis
- Epiglottitis
- Streptococcal pharyngitis/tonsillitis
- Infectious Mononucleosis

Epidemiology

- URTIs are one of the top three diagnosis in ambulatory setting
- account for an estimated 10 million outpatient visits a year
- Time off work and/or school is very common
- Patients spent $$$$$ on over-the-counter remedies
- While most URTIs have a benign course, complications can occur in specific and vulnerable patient populations
- Some URTIs are vaccine preventable

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What’s in Store for the Upcoming Respiratory Virus Season ?

Which of the following has the greatest risk for high transmission and severe disease this Fall? (select all that apply)

A. COVID-19

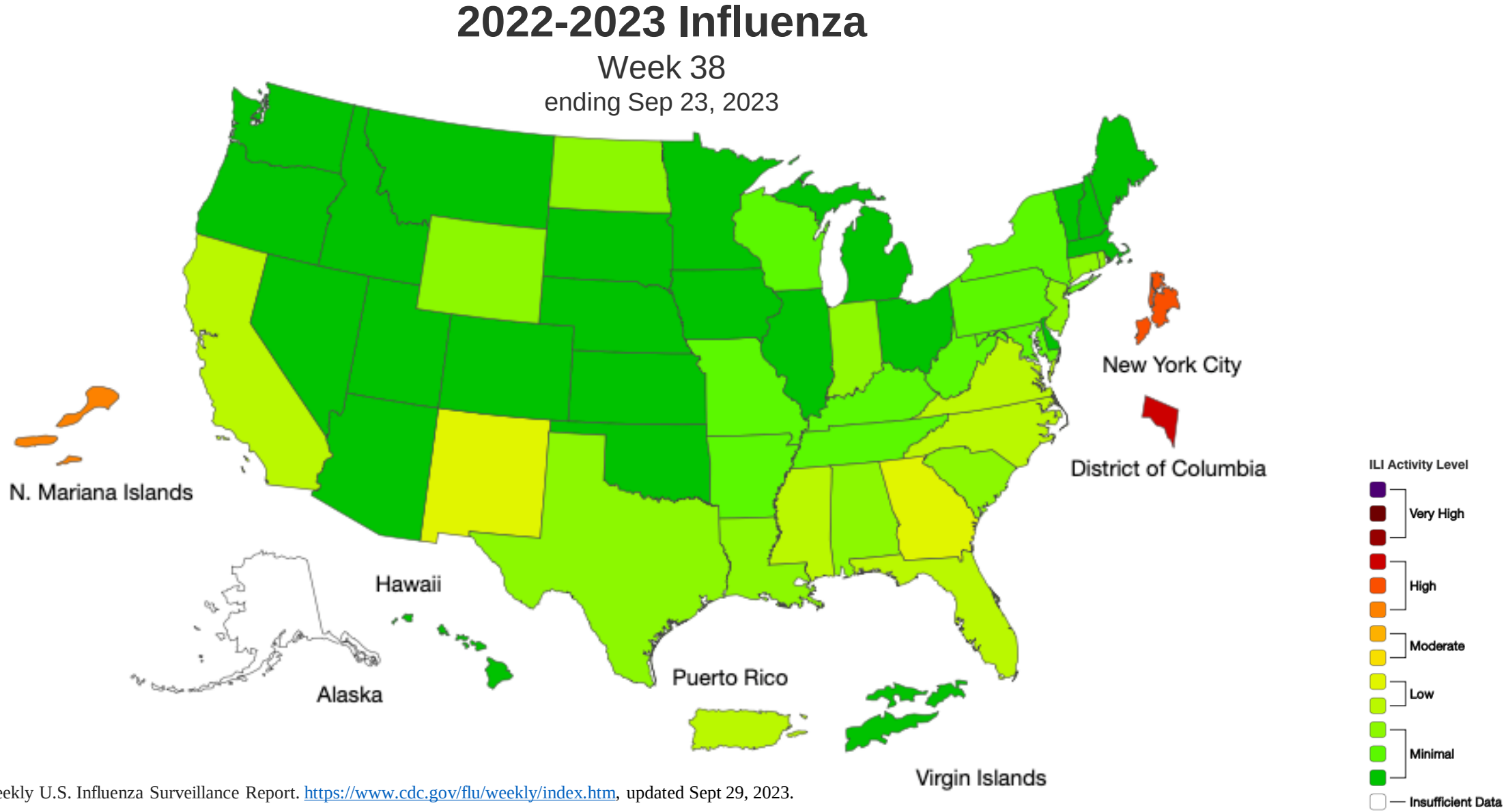
B. FLU

C. RSV

FOR HEALTHCARE SETTINGS

POLL QUESTION #1

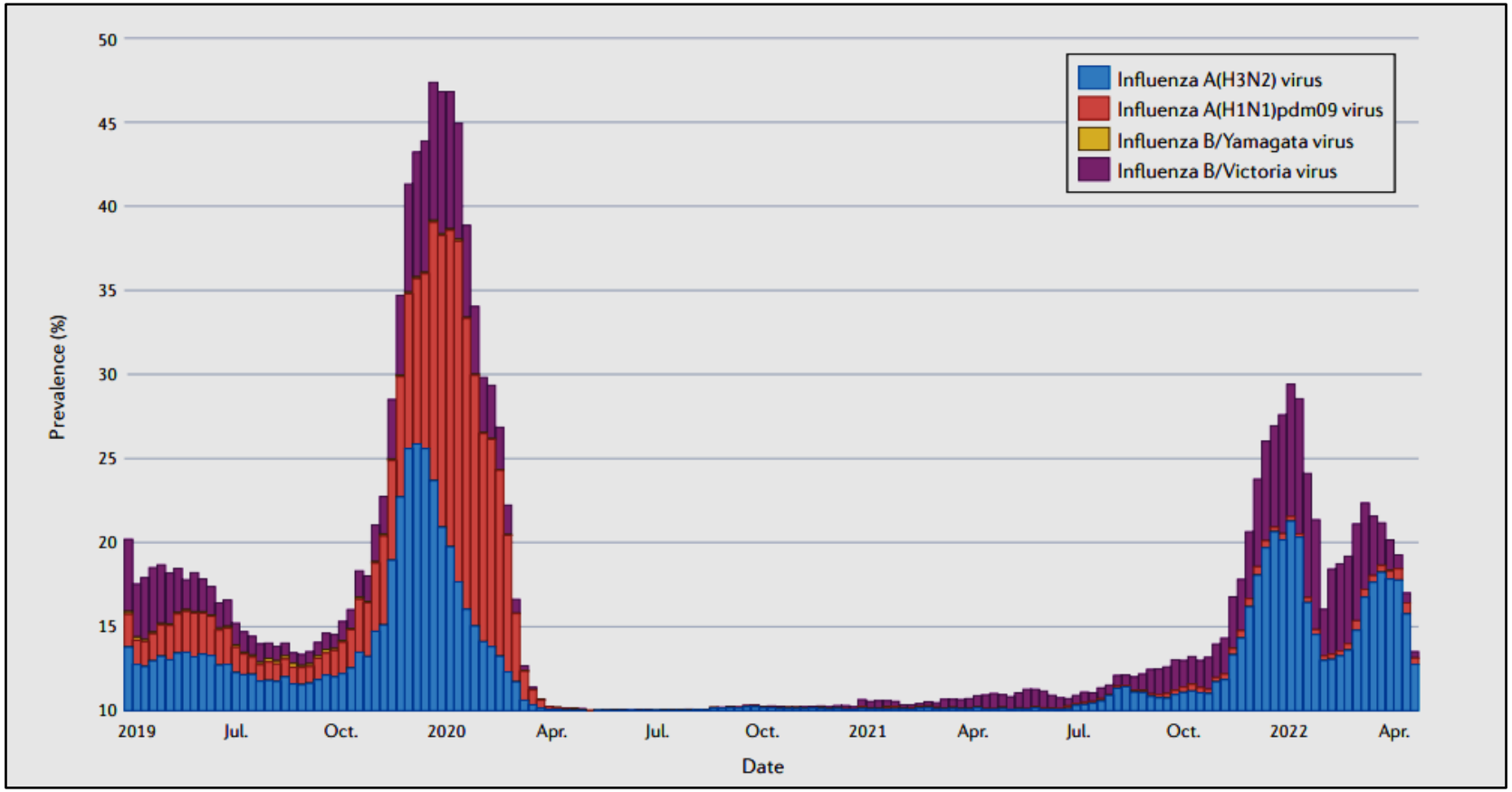
Summarize epidemiological trends and risk factors



CDC. Weekly U.S. Influenza Surveillance Report. https://www.cdc.gov/flu/weekly/index.htm, updated Sept 29, 2023.

Did Influenza disappear during the COVID Pandemic?

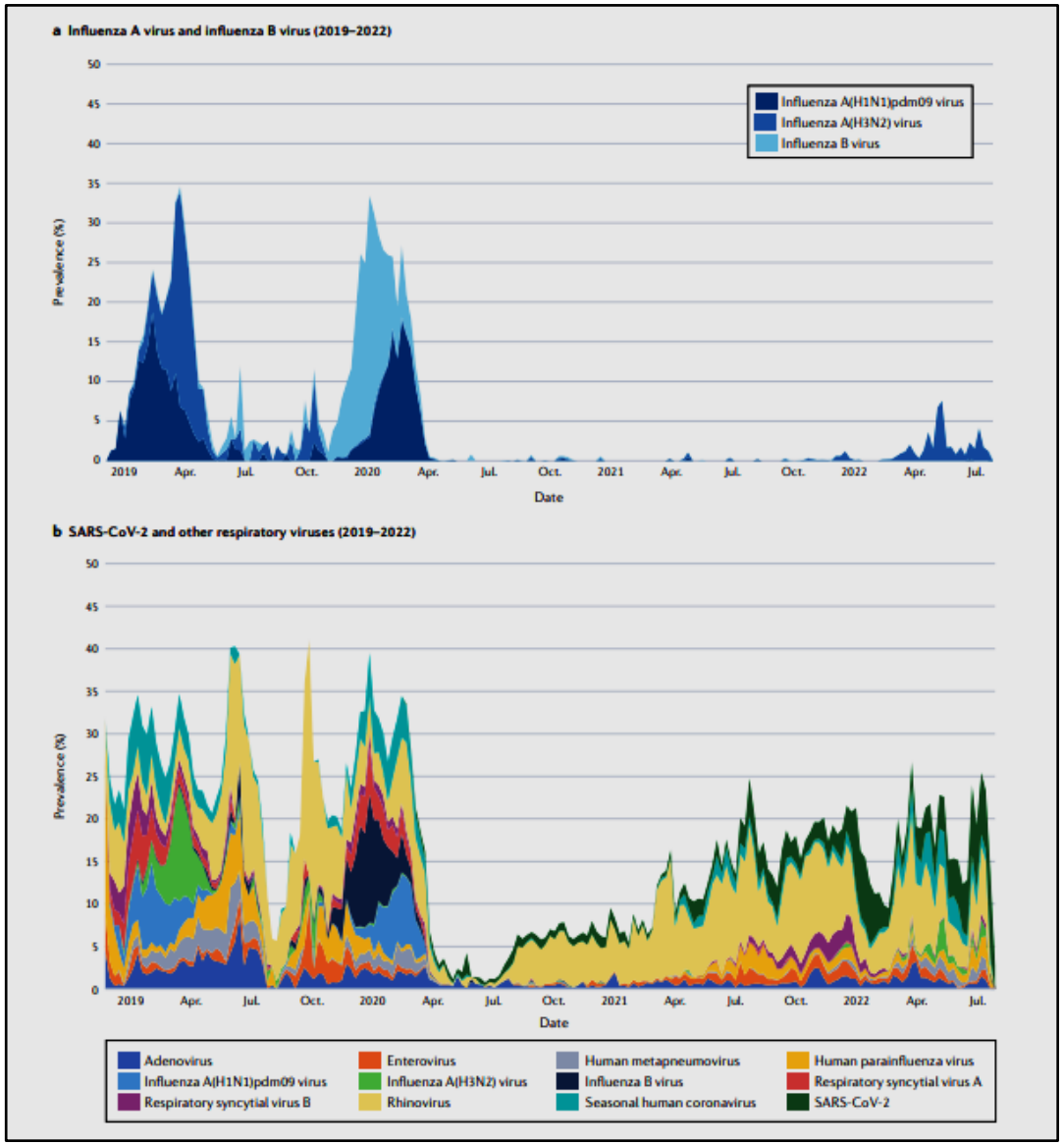
Nature Rev Microbiol 2023; 21: 195-210



- Initial “disappearance” of influenza only a reduction to extremely low levels of circulating virus
- Increase in vaccination rates in adolescences together with MCMs and NPIs contributed to decrease in influenza
- Cases of RSV significantly decreased due to NPIs and decreased social interactions

MCM: medical countermeasures NPI: non-pharmaceutical interventions (e.g., masks)

2022 "*Tripledemic*": when Influenza, COVID, and RSV collided



Nature Rev Microbiol 2023; 21: 195-210

www.yalemedicine.org/news/tripledemic-flu-rsv-and-covid-19, Jan 12, 2023

Many patients, incl. children were not exposed to usually circulating respiratory viruses during COVID pandemic

- Initial general lockdown, followed by staged reopening of certain businesses, schools, colleges, universities
- Required NPIs, e.g. masks, distancing, testing
- Use of HEPA filters to improve indoor air-quality
- General adherence to "stay home when sick" policies by people and employers

- Some viruses (e.g., **adenoviruses**) continued to co-circulate with SARS-CoV-2
- After general discontinuation of NPIs, some smaller outbreaks and resurgence of **influenza and RSV** in specific geographic locations
- Continued need to consider broader spectrum of causes of URIs

NPI: non-pharmaceutical interventions (e.g., masks)

Which of the following has the greatest risk for high transmission and severe disease this Fall? (select all that apply)

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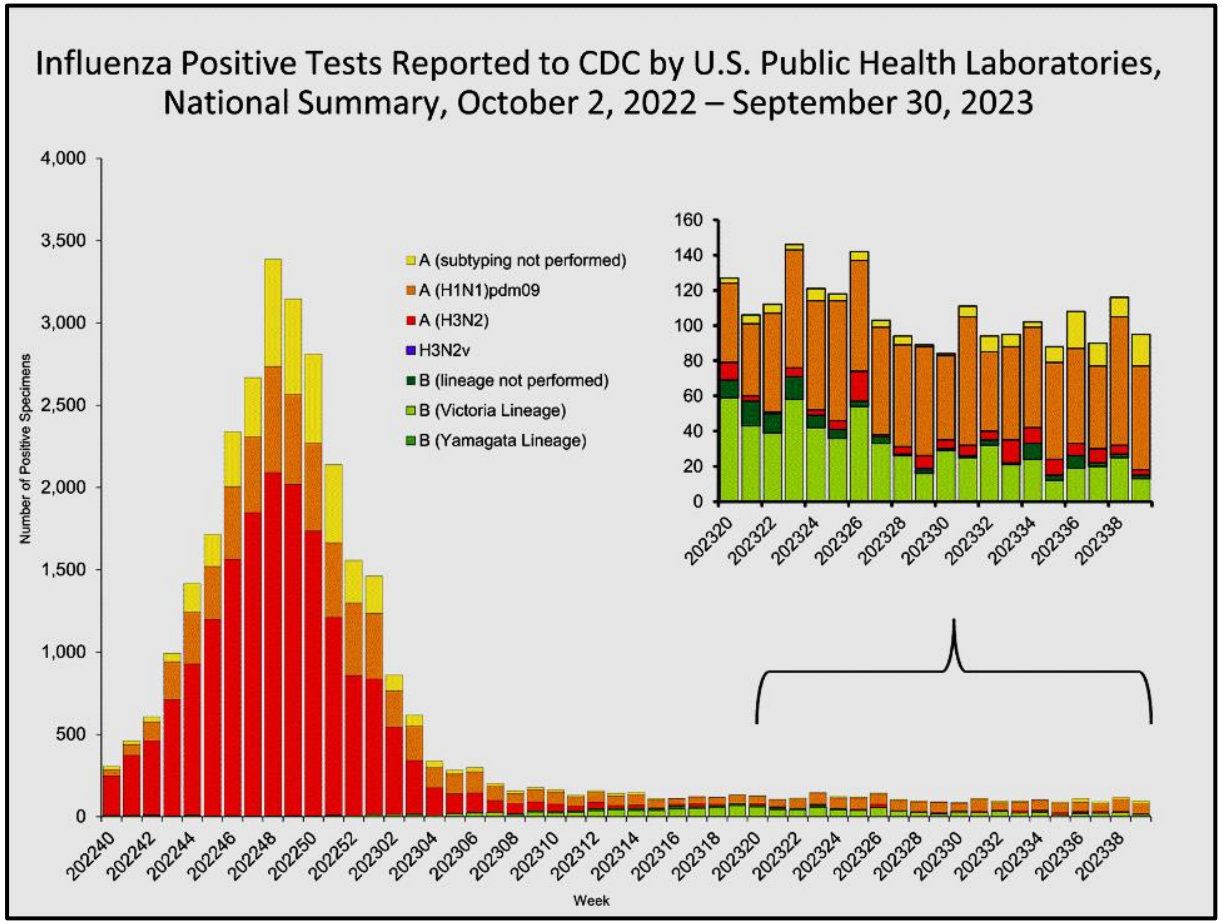
FOR HEALTHCARE SETTINGS

RESULTS

POLL QUESTION #1

2023 Surveillance for Influenza…



www.cdc.gov/flu/weekly/index.htm

- Influenza A & B virus
  - Seasonal epidemics & outbreaks
  - 5% to 20% of U.S. population infected annually
- Influenza A virus, subtyping
  - four pandemics in the past century (1918, 1957, 1968, 2009)
  - H1N1 [1918], H2N2 [1957], H3N2 [1968], H1N1 [2009]
  - **Currently circulating: A(H1N1)pdm09 and A(H3N2)**
  - Epidemics due to A(H3N2) have higher morbidity & mortality rates in older adults & children
- Incubation period (median):
  - 1.4 days (influenza A)
  - 0.6 days (influenza B)
- Viral shedding: peaks 1 – 3 days after symptom onset
  - young infants: more than 1 week
  - Immunocompromised adults: weeks to months
- Virus can be detected in upper respiratory tract 1-2 days before symptom onset (role in transmission, however, unclear)

BMC Infect Dis. 2014; 14: 480
Lancet 2022; 400: 693-706

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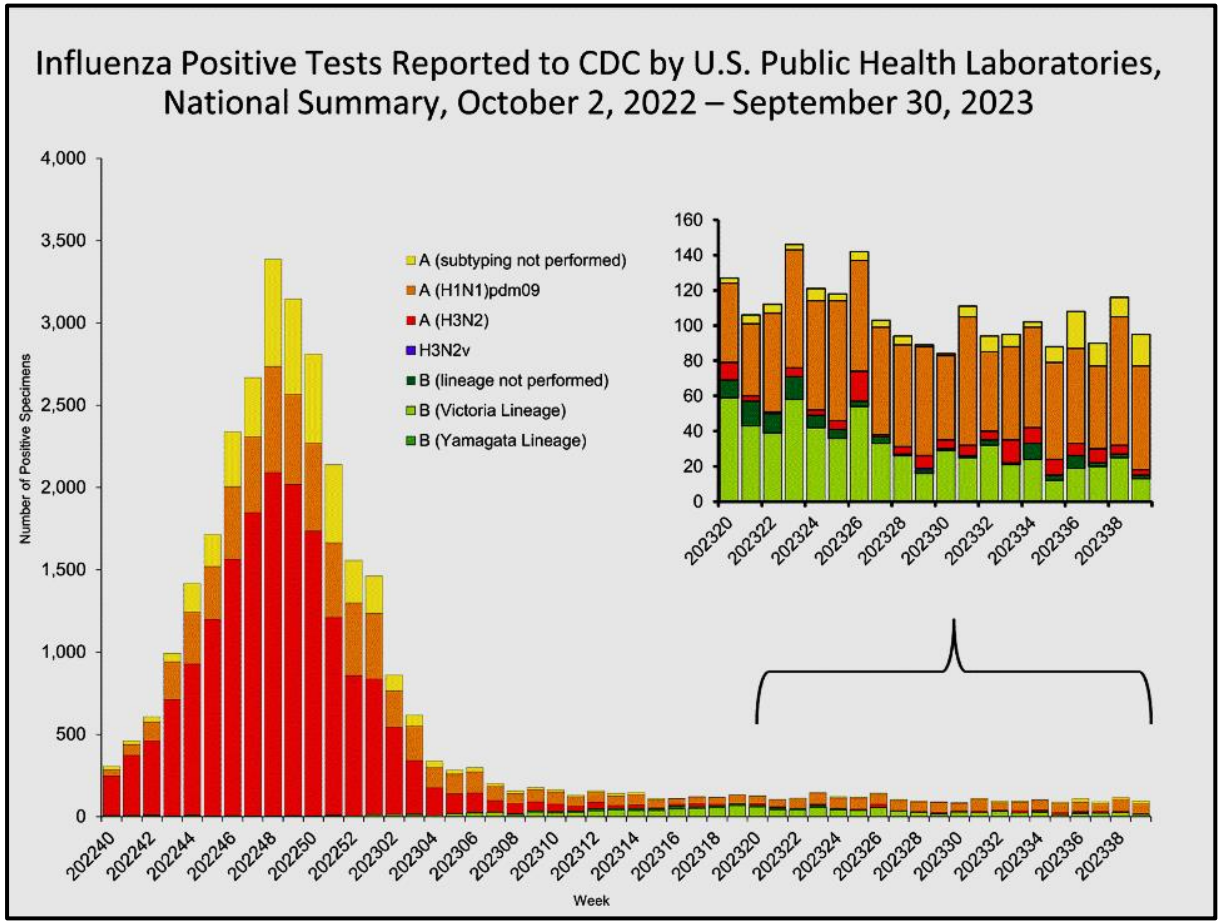

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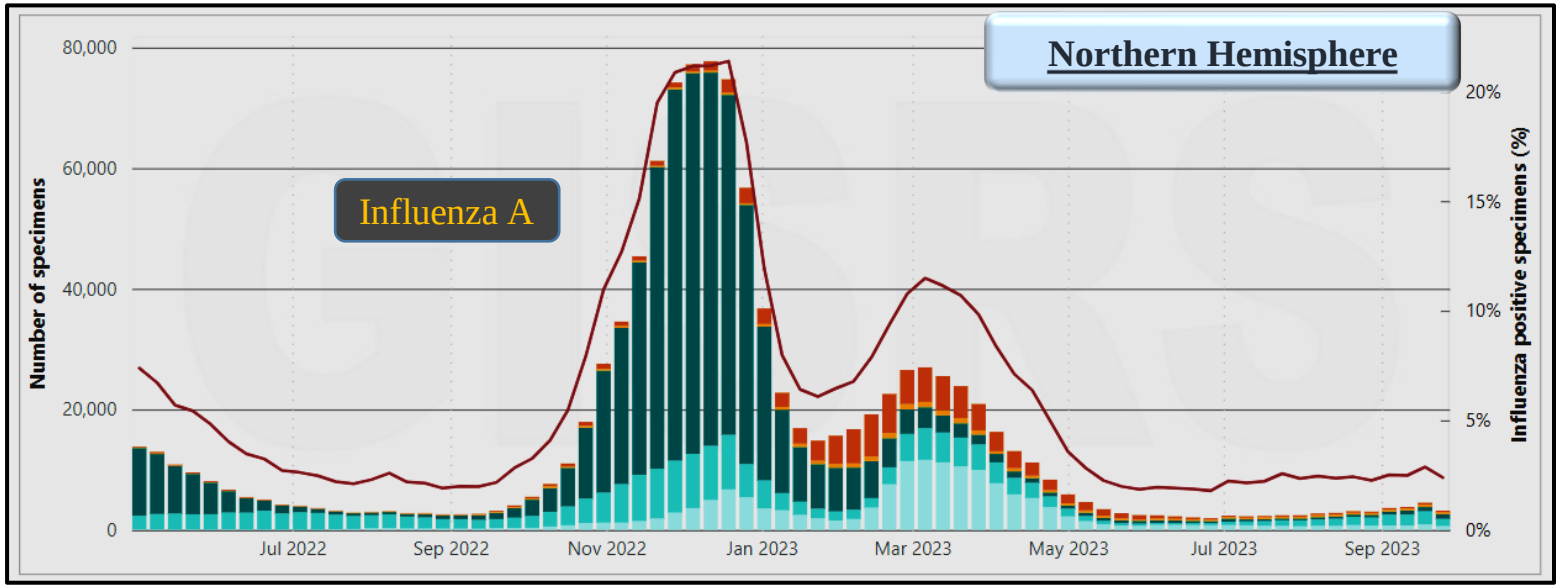
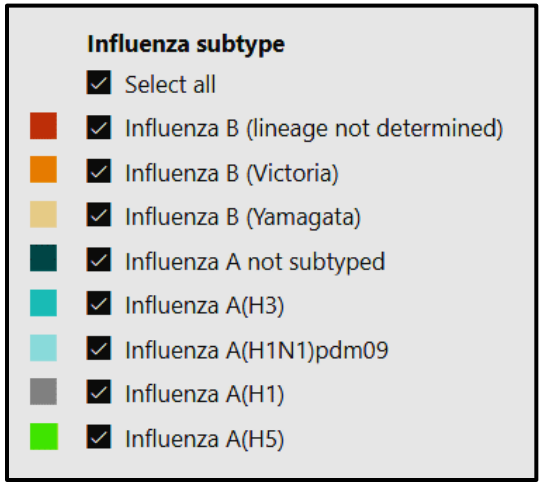
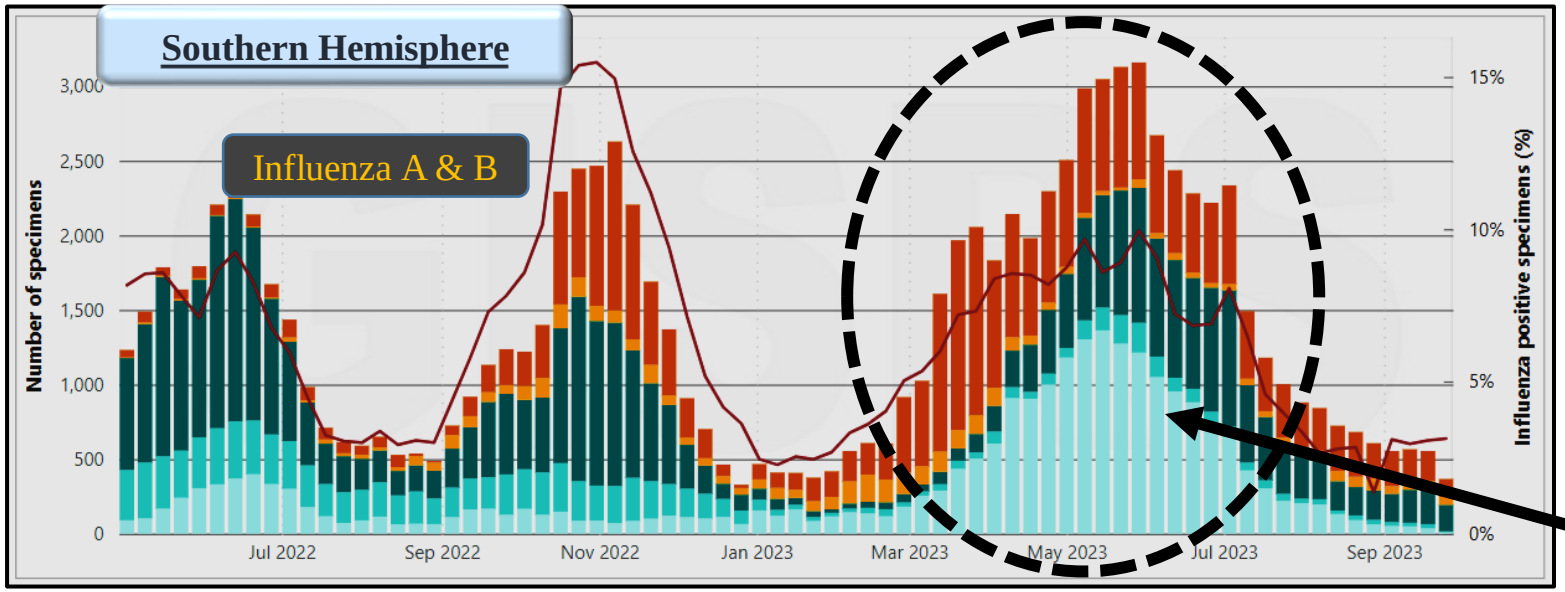
2022 / 2023 WHO Surveillance for Influenza

https://app.powerbi.com/view?r=eyJrIjoiZTkyODcyOTEtZjA5YS00ZmI0LWFkZGUtODIxNGI5OTE3YjM0IiwidCI6ImY2MTBjMGI3LWJkMjQtNGIzOS04MTBiLTNkYzI4MGFmYjU5MCIsImMiOjh9







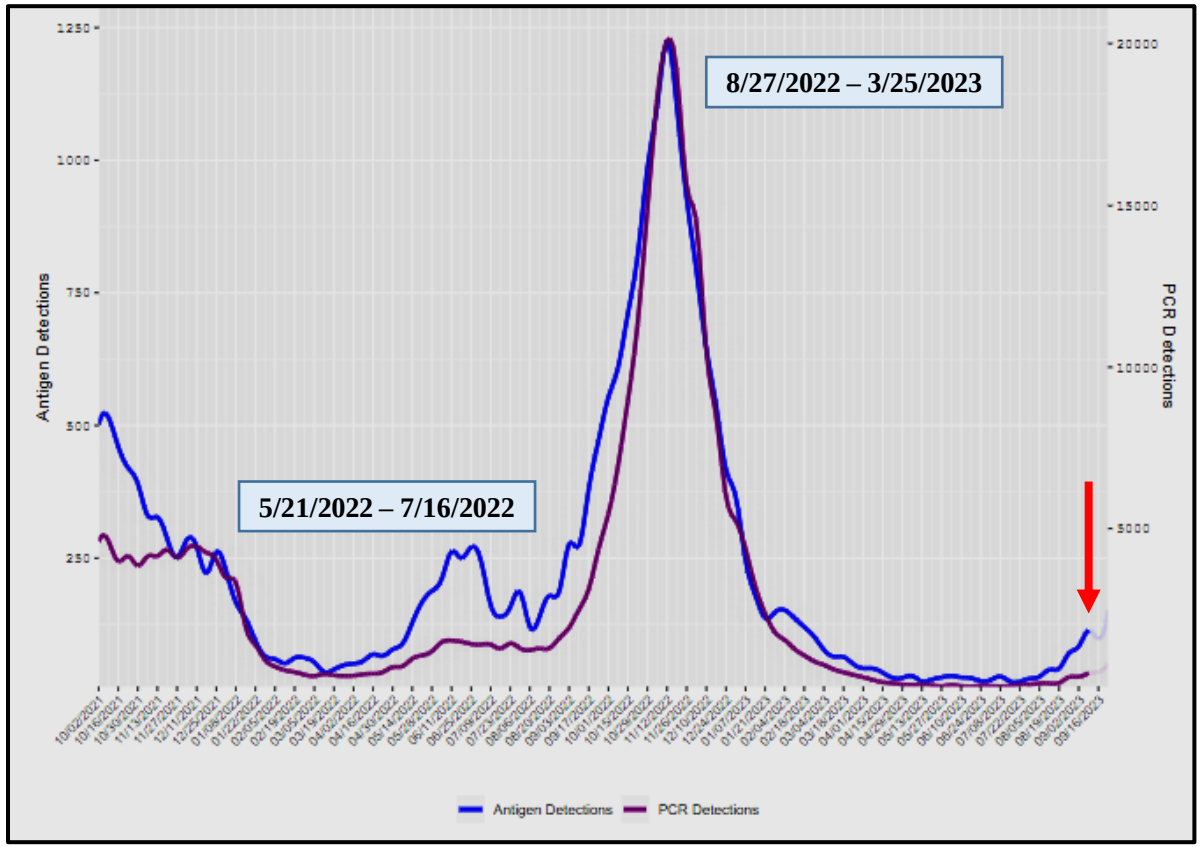
Southern Hemisphere

- In 2022, there were two spikes of influenza activity :
  May – July and then again October – November
- In 2023, pattern returned to the usual peak in May/June
- Influenza activity peaked in May 2023 : 9.95% positivity rate 38% - H1N1pdm09 ; 29% - Influenza A (not subtyped) ; 6% - influenza A(H3) ; 27% - influenza B
- South Africa reported predominantly Influenza A(H3N2) virus activity
  - experienced higher percentage of positive specimens, but moderate level of hospitalization compared to historic trends

Influenza A (H1N1)pdm09

Surveillance for RSV 2023…

RSV Cases in the U.S. 10/02/2021 to 09/16/2023



www.cdc.gov/surveillance/nrevss/rsv/natl-trend.html

What to expect for 2023 / 2024 ?

Some States & Territories in Australia have seen almost 10x the number of RSV cases compared to 2022

Increased Respiratory Syncytial Virus (RSV) Activity in Parts of the Southeastern United States: New Prevention Tools Available to Protect Patients

Print

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

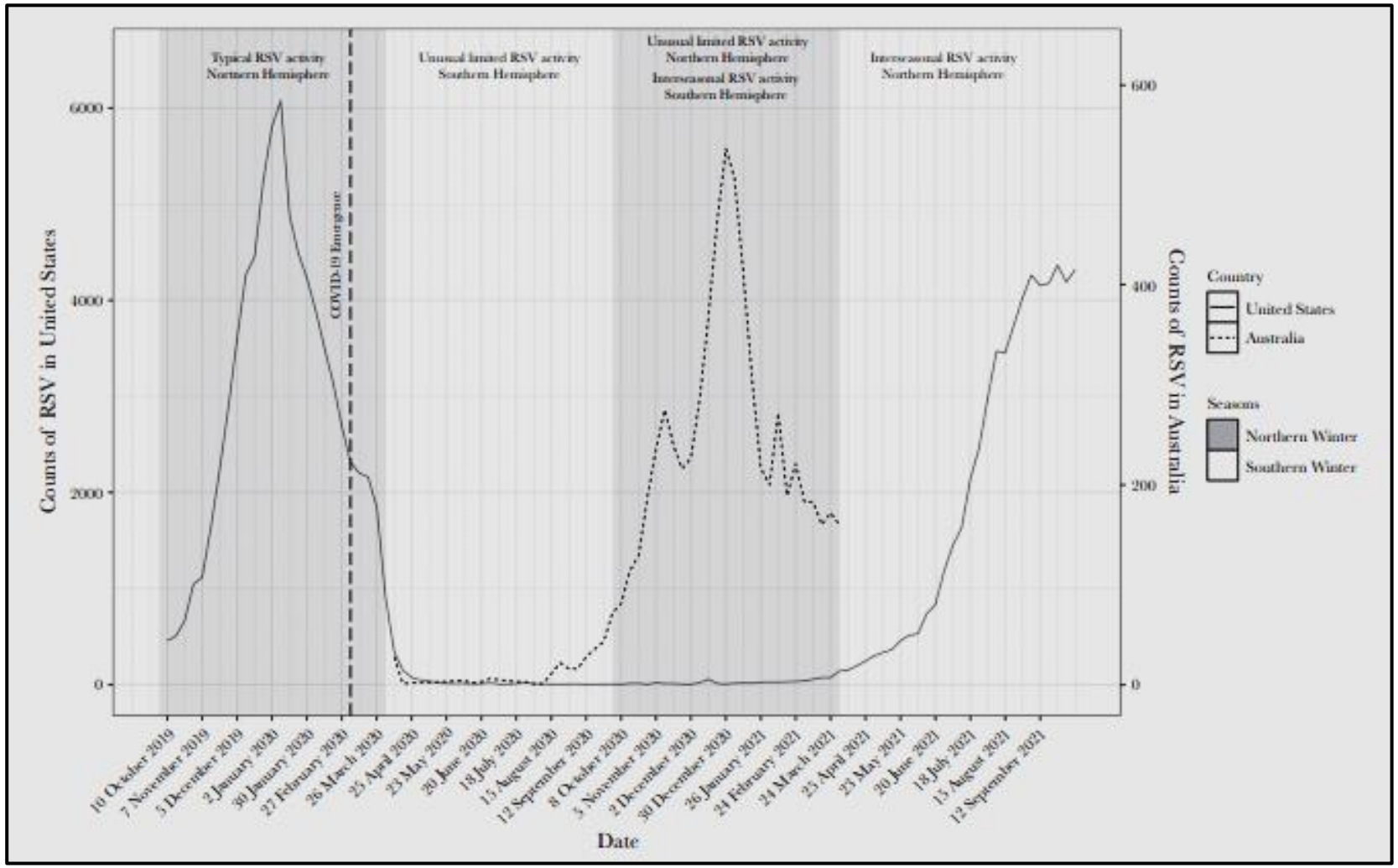
Distributed via the CDC Health Alert Network
September 05, 2023, 2:00 PM ET
CDCHAN-00498

https://emergency.cdc.gov/han/2023/han00498.asp

- **Unusual Inter-Seasonal RSV Activity in Southern and Northern Hemispheres in 2022/2023**
- **Why has the epidemiology changed ?**
  - waning of immunity due to decreased exposure during COVID-pandemic
  - immune dysregulation following SARS-CoV-2 infection
  - increased RSV virulence

Abu-Raya B, et al. *Lancet* 2023; 61: https://doi.org/10.1016/j.eclinm.2023.102089

2023 Surveillance for RSV (Australia and U.S.)



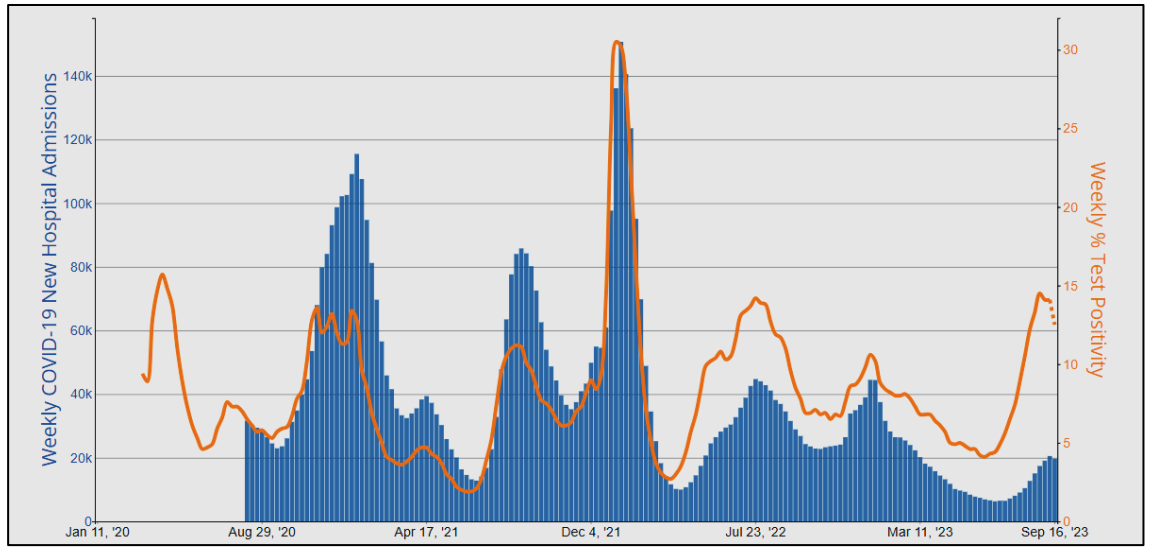
J Infect Dis 2022; 225: 1680-1682

- Unusual Inter-Seasonal RSV Activity in Southern and Northern Hemispheres in 2020 to 2023
- Rates for RSV infections remained high during 2023/2024 season, and are similar to rates in 2022/2023
  - 113,502 laboratory confirmed cases as of October 3, 2023
  - Rates varied by territory; highest in New South Wales and Queensland
- Distribution across age-groups unchanged compared to prior year

https://www.immunisationcoalition.org.au/news-data/respiratory-syncytial-virus-rsv-statistics/

Surveillance for COVID-19, Influenza, and RSV 2023……

COVID-19 New Hospital Admissions and Nucleic Acid Amplification Test (NAAT) Percent Positivity, by Week

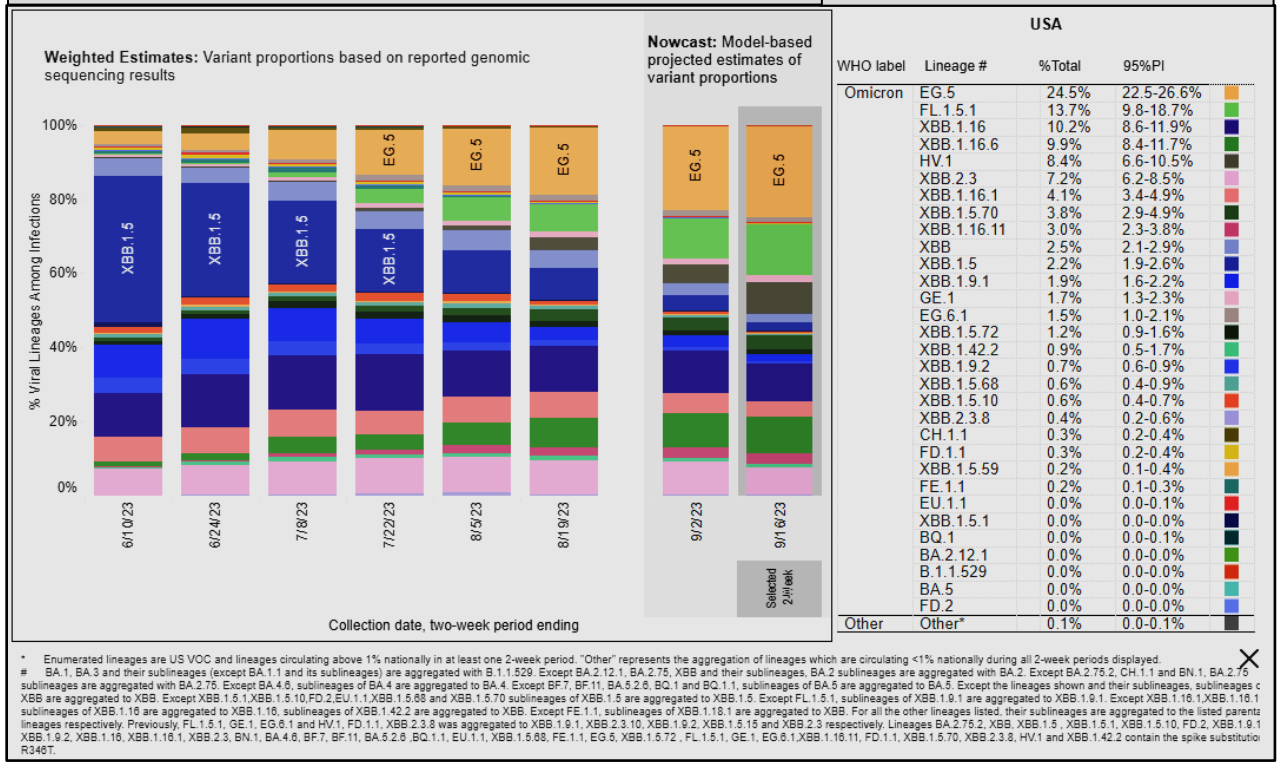


https://covid.cdc.gov/covid-data-tracker/#trends_weeklyhospitaladmissions_testpositivity_00

- EG.5 (a sub-lineage of XBB.1.9.2) continues to increase in proportion
- BA.2.86 – new variant of SARS-CoV-2
  - first detected in samples from people in Denmark
  - contains > 35 spike mutations with respect to XBB.1.5
  - greater concern for escape from existing immunity

Weighted and Nowcast Estimates in United States for 2-week Periods in 5/28/2023 – 9/16/2023

Nowcast Estimates in United States for 9/3/2023 – 9/16/2023



https://covid.cdc.gov/covid-data-tracker/#variant-proportions

www.cdc.gov/respiratory-viruses/whats-new/covid-19-variant.html

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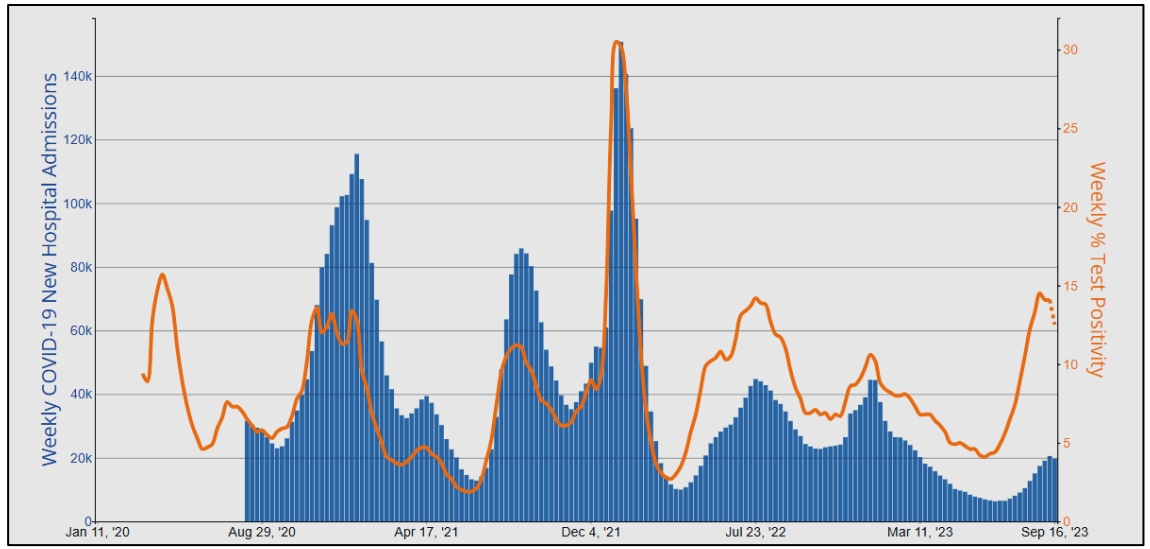

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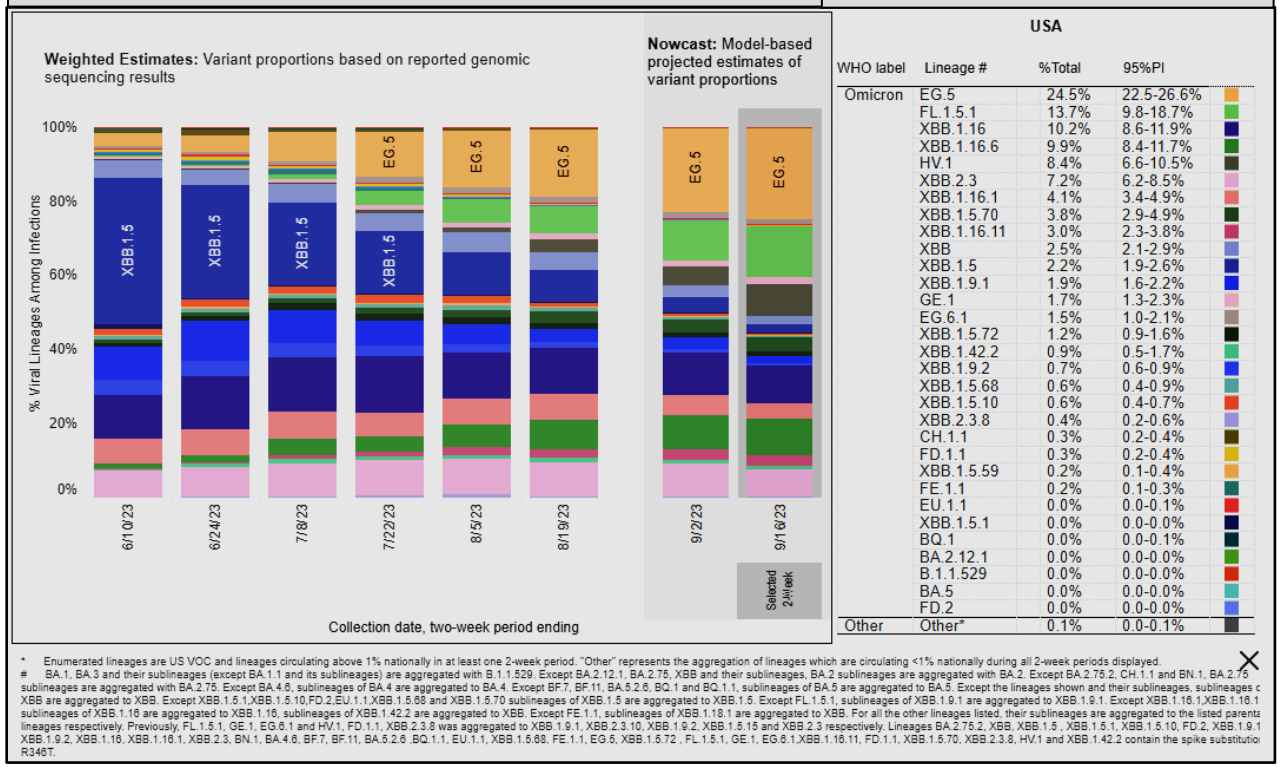


USA

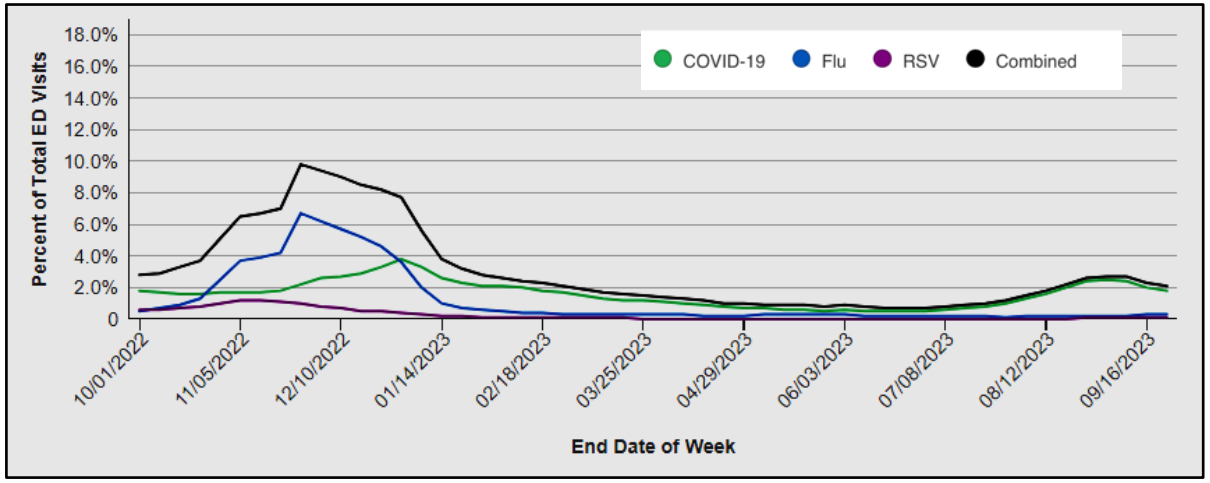
WHO label	Lineage #	%Total	95%PI
Omicron	EG.5	24.5%	22.5-26.6%
	FL.1.5.1	13.7%	9.8-18.7%
	XBB.1.16	10.2%	8.6-11.9%
	XBB.1.16.6	9.9%	8.4-11.7%
	HV.1	8.4%	6.6-10.5%
	XBB.2.3	7.2%	6.2-8.5%
	XBB.1.16.1	4.1%	3.4-4.9%
	XBB.1.5.70	3.8%	2.9-4.9%
	XBB.1.16.11	3.0%	2.3-3.8%
	XBB	2.5%	2.1-2.9%
	XBB.1.5	2.2%	1.9-2.6%
	XBB.1.9.1	1.9%	1.6-2.2%
	GE.1	1.7%	1.3-2.3%
	EG.6.1	1.5%	1.0-2.1%
	XBB.1.5.72	1.2%	0.9-1.6%
	XBB.1.42.2	0.9%	0.5-1.7%
	XBB.1.9.2	0.7%	0.6-0.9%
	XBB.1.5.68	0.6%	0.4-0.9%
	XBB.1.5.10	0.6%	0.4-0.7%
	XBB.2.3.8	0.4%	0.2-0.6%
	CH.1.1	0.3%	0.2-0.4%
	FD.1.1	0.3%	0.2-0.4%
	XBB.1.5.59	0.2%	0.1-0.4%
	FE.1.1	0.2%	0.1-0.3%
	EU.1.1	0.0%	0.0-0.1%
	XBB.1.5.1	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.1%
	BA.2.12.1	0.0%	0.0-0.0%
	B.1.1.529	0.0%	0.0-0.0%
	BA.5	0.0%	0.0-0.0%
	FD.2	0.0%	0.0-0.0%
Other	Other*	0.1%	0.0-0.1%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all 2-weeks periods displayed.
# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.2.75.2, CH.1.1 and BN.1, BA.2.75 sublineages are aggregated with BA.2.75. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except the lineages shown and their sublineages, sublineages of XBB are aggregated to XBB. Except XBB.1.5.1,XBB.1.5.10,FD.2,EU.1.1,XBB.1.5.68 and XBB.1.5.70 sublineages of XBB.1.5 are aggregated to XBB.1.5. Except FL.1.5.1, sublineages of XBB.1.9.1 are aggregated to XBB.1.9.1. Except XBB.1.16.1,XBB.1.16.1 sublineages of XBB.1.16 are aggregated to XBB.1.16, sublineages of XBB.1.42.2 are aggregated to XBB. Except FE.1.1, sublineages of XBB.1.18.1 are aggregated to XBB. For all the other lineages listed, their sublineages are aggregated to the listed parental lineages respectively. Previously, FL.1.5.1, GE.1, EG.6.1 and HV.1, FD.1.1, XBB.2.3.8 was aggregated to XBB.1.9.1, XBB.2.3.10, XBB.1.9.2, XBB.1.5.15 and XBB.2.3 respectively. Lineages BA.2.75.2, XBB, XBB.1.5 , XBB.1.5.1, XBB.1.5.10, FD.2, XBB.1.9.1 XBB.1.9.2, XBB.1.16, XBB.1.16.1, XBB.2.3, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 ,BQ.1.1, EU.1.1, XBB.1.5.68, FE.1.1, EG.6, XBB.1.5.72 , FL.1.5.1, GE.1, EG.6.1,XBB.1.16.11, FD.1.1, XBB.1.5.70, XBB.2.3.8, HV.1 and XBB.1.42.2 contain the spike substitution R346T.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

- Currently available treatments (Paxlovid, Veklury, Lagevrio) likely effective against BA.2.86
- Based on BA.2.86 mutation profile, anticipated impact on molecular diagnostic tests is low

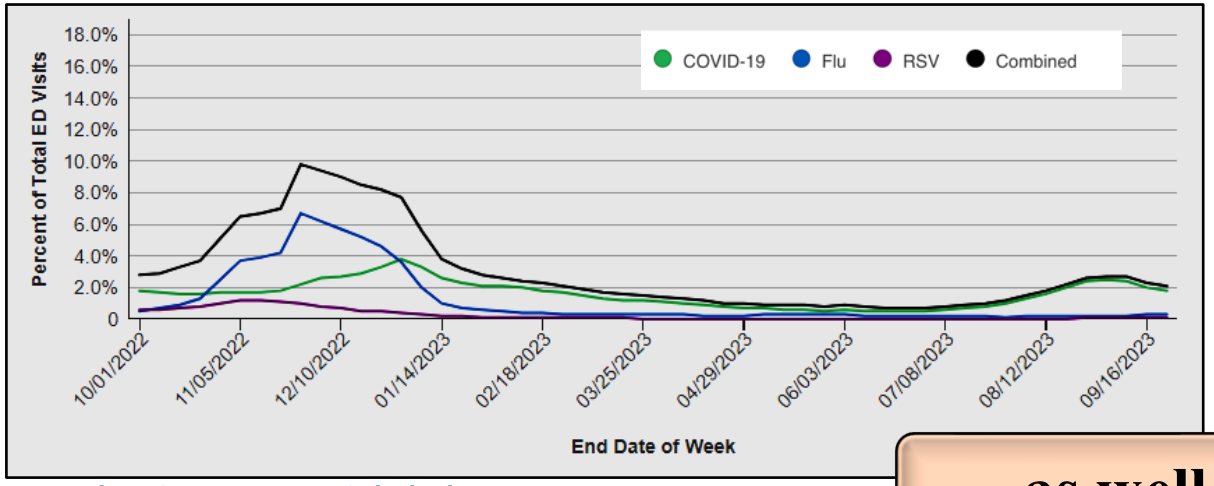
Respiratory Virus Activity – what to expect ?



www.cdc.gov/respiratory-viruses/index.html

Expect the unexpected……

Respiratory Virus Activity – what to expect ?



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Expect the unexpected……

…. as well as the usually expected seasonal Flu & RSV !

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- RSV and COVID-19 will be significantly contributing to the burden of respiratory tract infections

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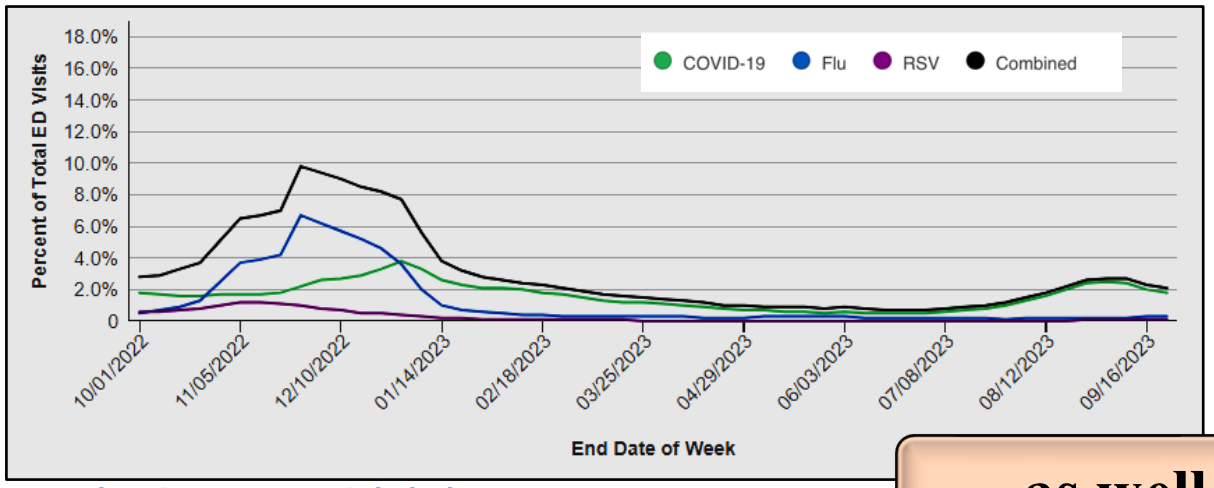

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CDC : Center for Forecasting and Outbreak Analytics

- **Upcoming Fall and Winter respiratory season will likely have a similar number of total hospitalizations compared to last year**
- possibility remains that hospitalizations may be higher than last year, with more widespread illness and healthcare system strain
- increase could result from the emergence of a new COVID-19 variant or a more severe influenza season
- vaccination remains the best way to protect against respiratory illness
- at this time not enough data on BA.2.86 SARS-CoV-2 variant to assess the potential impact on the upcoming respiratory disease season
- Uncertainties: immunization uptake ; timing & overlap of peaks for influenza, RSV, and COVID

www.cdc.gov/forecast-outbreak-analytics/about/season-outlook.html

Challenges & Impact of RSV and Influenza Infections in Acute & Congregate Care Settings

Estimated Influenza Disease Burden, United States

2010/20211 through 2019/2020 Seasons

Annual Burden

Illnesses : 9,000,000 to 41,000,000

Hospitalizations : 140,000 to 710,000

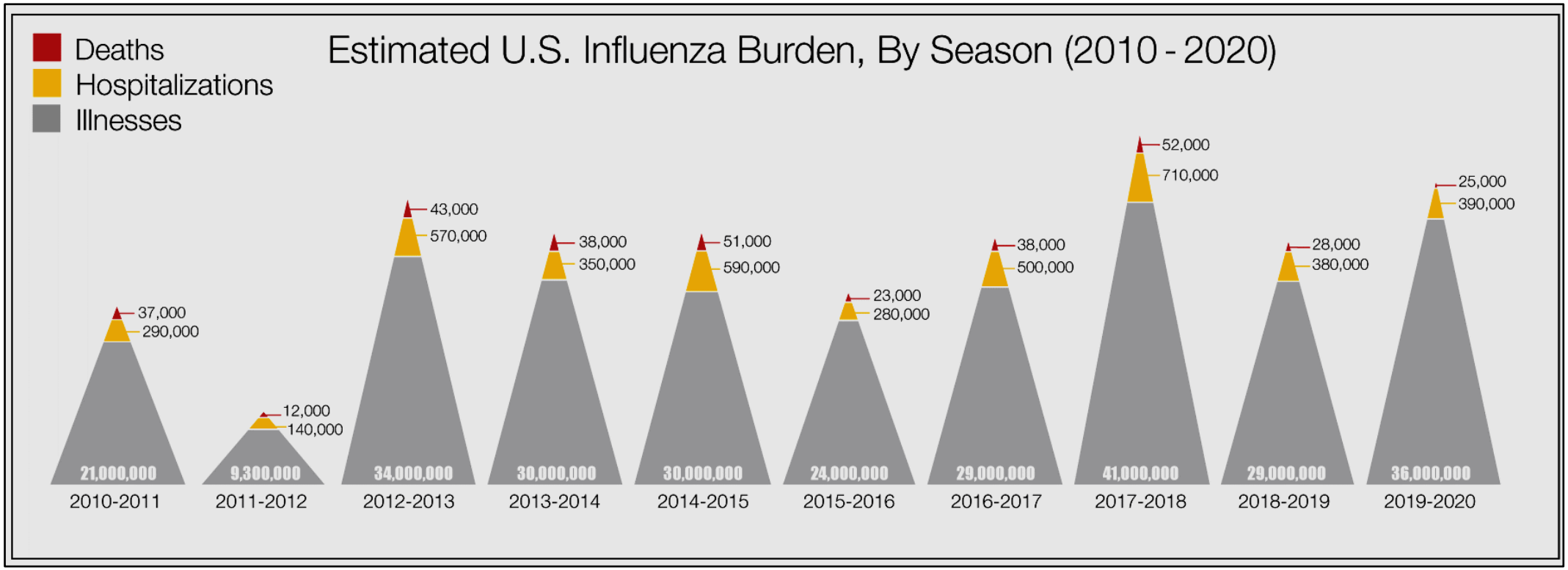
Deaths: 12,000 to 52,000

Factors affecting Burden

Characteristics of the circulating Influenza strain

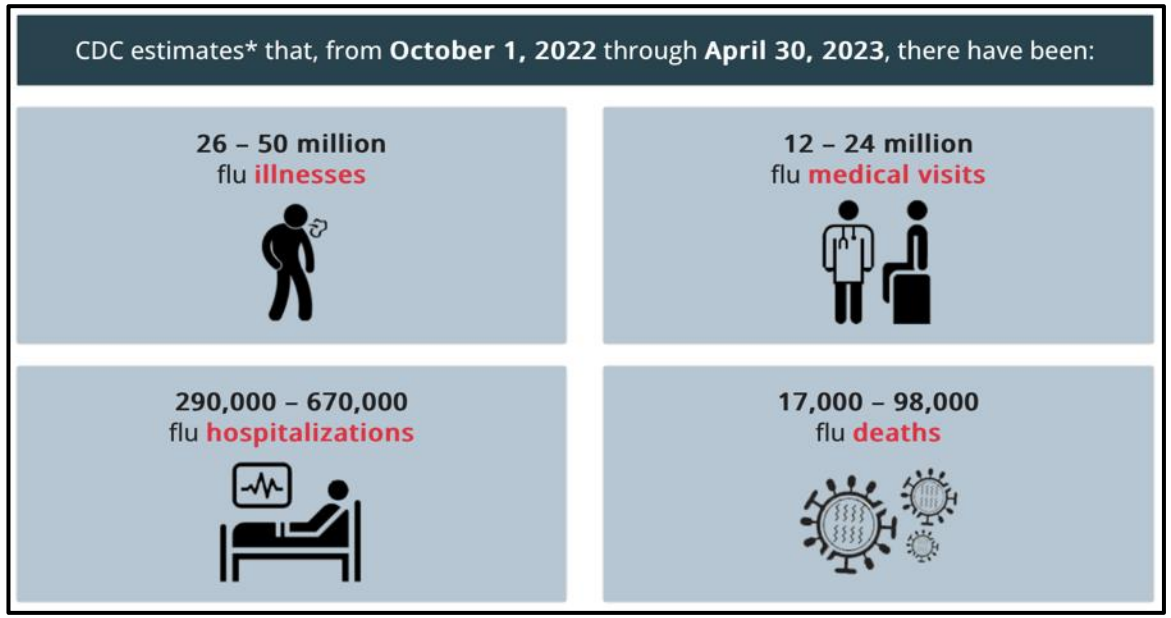
Timing of the "Flu Season"

Extent of use & Effectiveness of Influenza Vaccine



www.cdc.gov/flu/about/burden/index.html

Influenza – Disease Burden and Risk Factors



www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm

Other people at higher risk from flu:

- Pregnant people and people up to 2 weeks after the end of pregnancy
- People who live in nursing homes and other long-term care facilities
- People from certain racial and ethnic minority groups are at increased risk for hospitalization with flu, including non-Hispanic Black persons, Hispanic or Latino persons, and American Indian or Alaska Native persons

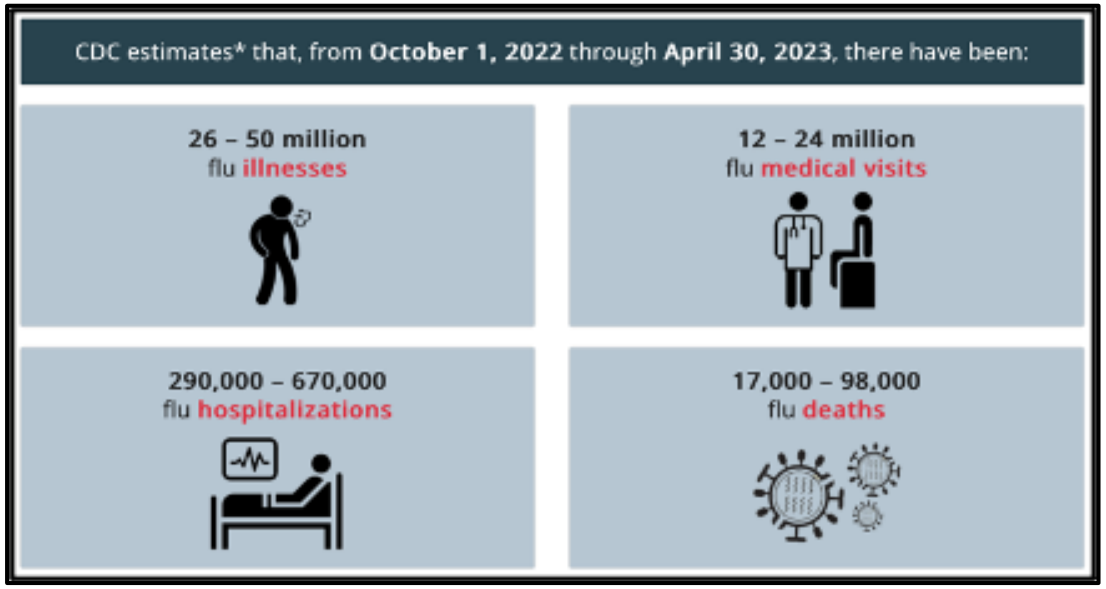
Health and age factors known to increase risk of serious flu complications:

- Adults 65 years and older
- Children younger than 2 years old*
- Asthma
- Neurologic and neurodevelopment conditions
- Blood disorders (such as sickle cell disease)
- Chronic lung disease (such as chronic obstructive pulmonary disease [COPD] and cystic fibrosis)
- Endocrine disorders (such as diabetes mellitus)
- Heart disease (such as congenital heart disease, congestive heart failure and coronary artery disease)
- Kidney diseases
- Liver disorders
- Metabolic disorders (such as inherited metabolic disorders and mitochondrial disorders)
- People who are obese with a body mass index [BMI] of 40 or higher
- People younger than 19 years old on long-term aspirin- or salicylate-containing medications.
- People with a weakened immune system due to disease (such as people with HIV or AIDS, or some cancers such as leukemia) or medications (such as those receiving chemotherapy or radiation treatment for cancer, or persons with chronic conditions requiring chronic corticosteroids or other drugs that suppress the immune system)
- People who have had a stroke

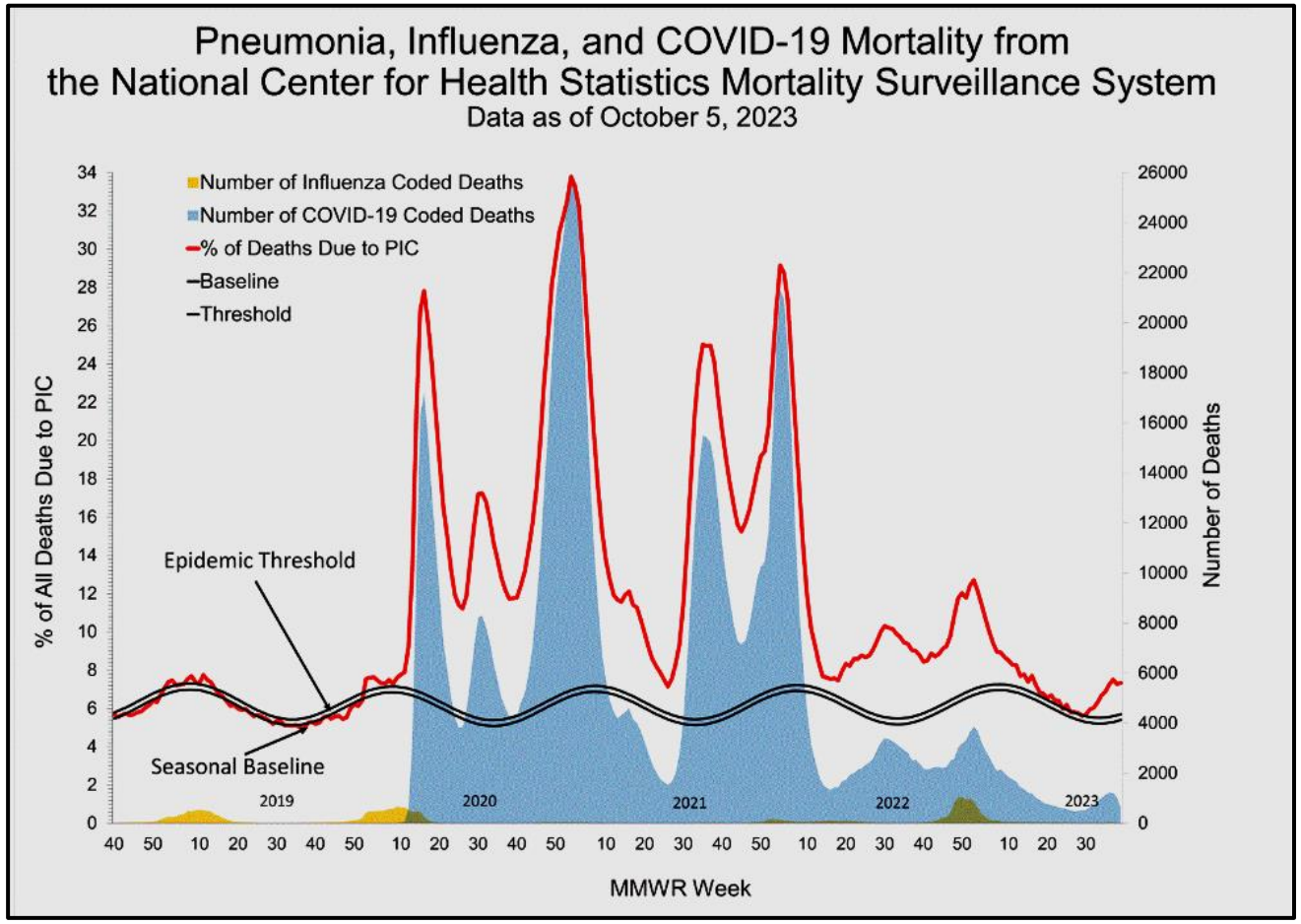
*Although all children younger than 5 years old are considered at higher risk of serious flu complications, the highest risk is for those younger than 2 years old, with the highest hospitalization and death rates among infants younger than 6 months old.

CDC. People at Higher Risk of Flu Complications. https://www.cdc.gov/flu/highrisk/index.htm, updated Aug 25, 2023.

Influenza – Disease Burden and Risk Factors



www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm



https://www.cdc.gov/flu/weekly/index.htm

NCHS Mortality Surveillance

(10/05/2023 for week ending 09/30/2023, preliminary data)

- 7.3% of deaths due to PIC
- percentage is above the Epidemic Threshold (5.7%) for this week
- 37% had COVID-19 listed as underlying CoD
- 1% had Influenza listed as CoD

NCHS: National Center for Health Statistics ; PIC: pneumonia, influenza, and/or COVID ; CoD: cause of death

RSV – Burden and Risks in Pediatrics

- RSV first described / discovered in 1956 (recovered from a chimpanzee with respiratory symptoms)
- Found to be the cause of serious respiratory infections in infants and young children
- Reported in adults with pneumonia since the 1960s
- Recognized in 1990s as a (potential) cause of serious URTIs in adults

Clin Microbiol Rev. 2000 Jul;13(3):371-84.

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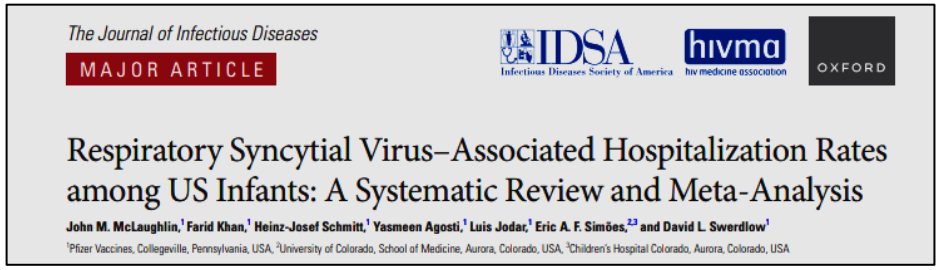
RSV & Children (< 5 years)

58,000 – 80,000 hospitalizations

100 – 500 deaths

> $ 500 Million annual cost of bronchiolitis hospital admissions for children < 2 years


The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Respiratory Syncytial Virus–Associated Hospitalization Rates among US Infants: A Systematic Review and Meta-Analysis

John M. McLaughlin,[1] Farid Khan,[1] Heinz-Josef Schmitt,[1] Yasmeen Agosti,[1] Luis Jodar,[1] Eric A. F. Simões,[2,3] and David L. Swerdlow[1]

[1]Pfizer Vaccines, Collegeville, Pennsylvania, USA, [2]University of Colorado, School of Medicine, Aurora, Colorado, USA, [3]Children's Hospital Colorado, Aurora, Colorado, USA

Children at high risk for severe RSV infection

- premature infants
- infants 12 months and younger
- children younger than 2 years with chronic lung disease
- immunocompromised children
- children with neuromuscular diseases

www.cdc.gov/rsv/high-risk/infants-young-children.html#severe-rsv-infection

J Infect Dis. 2022; 225(6): 1100-11
JAMA Network Open. 2022 Feb; 5(2): e220527
New Engl J Med. 2009; 360(6): 588–98
Clin Microbiol Rev. 2000 Jul;13(3):371-84.

RSV – Burden and Risks in Adults

- RSV was sporadically reported in adults with pneumonia since the 1960s
- Only recognized during the past 10 years as a (potential) cause of serious RTIs in adults
- Estimating true incidence has historically been difficult due to incorrect diagnosis of RTIs in adults, technical issues with diagnostic testing, lack of specific diagnostic testing for RSV, low public awareness of RSV in adults as cause of illness
- Incidence & impact of RSV infection in older people who live independently in the community have not been well understood

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RSV & Adults

900,000 – 1,400,000 medical encounters

60,000 – 160,000 hospitalizations

6,000 – 10,000 deaths

Adults at high risk for severe RSV infection

- Older adults (age ranges vary by study: >50 years to >65 years)
- Adults living in nursing homes or LTCFs
- Adults with certain co-morbidities:
  - Asthma
  - Coronary artery disease
  - Congestive heart failure
  - COPD
  - Chronic oral corticosteroid use
  - Diabetes mellitus
  - Immunosuppression (e.g., HSCT, SOT, cancer)

J Infect Dis. 2004; 189(2): 233-238
J Clin Virol 2023; 161: 105399
Clin Microbiol Rev. 2000 Jul;13(3):371-84.

www.cdc.gov/rsv/high-risk/older-adults.html
www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

Vaccine Recommendations for the Upcoming Winter

https://publichealth.jhu.edu/2023/looking-ahead-at-covid-flu-and-rsv-vaccines-for-fall-2023

Influenza

all 2023 vaccines will be quadrivalent

www.cdc.gov/flu/season/faq-flu-season-2023-2024.htm

Egg-based vaccines

- an A/Victoria/4897/2022 (H1N1)pdm09-like virus; (Updated)
- an A/Darwin/9/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
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Cell- or recombinant-based vaccines

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Routine annual influenza vaccination recommended for all persons aged ≥6 months who do not have contraindications

SARS-CoV-2

New XBB Monovalent Vaccine (Single Dose)

www.idsociety.org/globalassets/idsa/multimedia/clinician-call-slides--qa/9-14-23-clinician-call-final.pdf

Key changes from bivalent mRNA recommendations

2022 – 2023 bivalent recommendations	2023 – 2024 vaccine recommendations	Rationale
Everyone ages **6 years** and older recommended for a single bivalent dose	Everyone ages **5 years** and older recommended for a single 2023 – 2024 dose	Eliminates complex recommendations for 5-year-olds
Two Moderna dosages authorized for 6 months – 5 years, depending on vaccination history and immune status	All Moderna doses in ages 6 months – 11 years are now 25 µcg	Reduces the number of COVID-19 vaccine products in use
Optional 2nd bivalent dose for those ages 65 years and older	No additional dose recommendation **at this time**	Will monitor epidemiology and vaccine effectiveness to determine if additional doses are needed

Everyone aged 5 years and older should get 1 dose of the updated Pfizer-BioNTech or Moderna COVID-19 vaccine

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RSV

June 2023 CDC's ACIP Recommended the First Two RSV Vaccines for Older Adults

www.fda.gov/news-events/press-announcements/fda-approves-first-respiratory-syncytial-virus-rsv-vaccine
www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

- May 3, 2023 : FDA approved first RSV Vaccine
- RSVPreF3 (Arexvy, GSK) is a 1-dose adjuvant (AS01E) recombinant prefusion F protein)preF) vaccine - reduced LRTi by 74.5% (season 1&2)
- ASVpreF (Abrysvo, Pfizer) is a 1-dose recombinant preF vaccine - reduced LRTi by 84.4% (season 1&2)

Adults ≥60 years receive a single dose of RSV vaccine

Pregnancy: 1 dose of maternal RSV vaccine during weeks 32 to 36 of pregnancy

SARS-CoV-2

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www.idsociety.org/globalassets/idsa/multimedia/clinician-call-slides--qa/9-14-23-clinician-call-final.pdf

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Transmissibility of RSV, Influenza, and SARS-CoV-2

Basic Reproduction Number : R_0

- R_0 : average number of secondary infections caused by a single infected patient
- R_0 is NOT a measure of the severity of an infectious disease or the rapidity of its spread
- It is an estimate of contagiousness as a function of
  - human behavior
  - biological characteristics of the pathogen

SARS-CoV-2	Influenza	RSV
R_0 : 2.7 – 3.3	R_0 : 1.27	R_0 : 3.0

Secondary Attack Rate : SAR

- Proportion of infected among those susceptible in contact with the primary (index) case
- Most often used to estimate the transmission risk in households or congregate care settings
- Influenza : SAR of 1% to 38%
- For other viruses (incl. RSV, SARS-CoV-2) the estimated SAR is much lower than the SAR for influenza

BMC Infect Dis 2014; 14: 480 *Emerg Infect Dis* 2022; 28 (7): 1345-1354 *PLOS Comput Biol* 2016; 12 (10): e1005133

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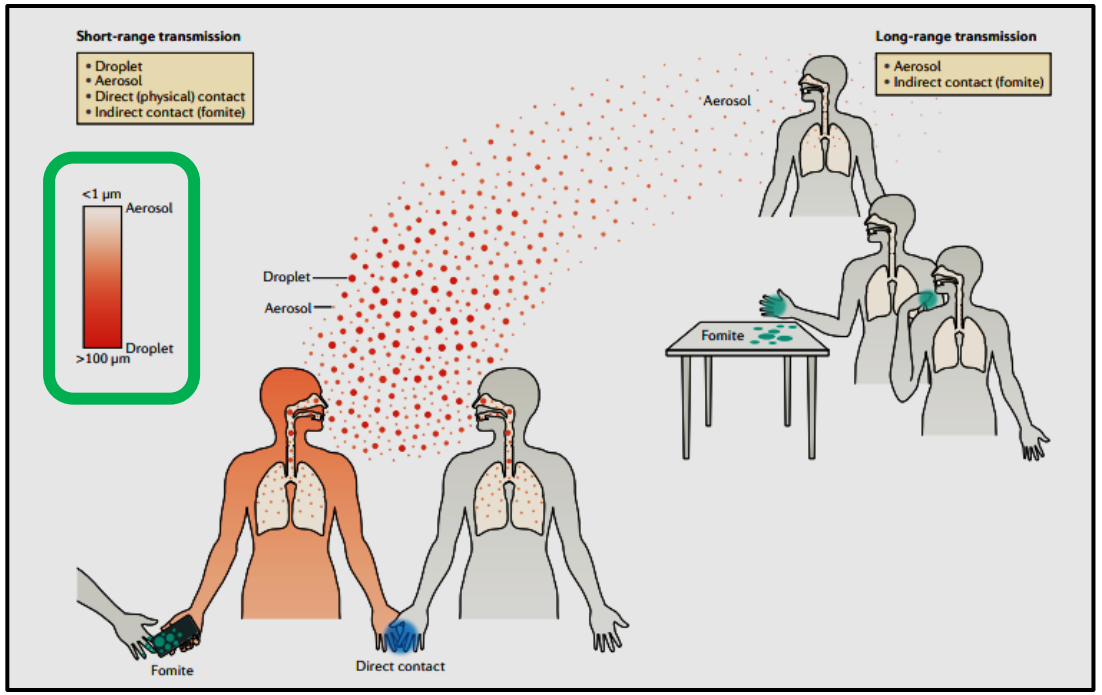
Determinants of Transmission



Direct Contact	Indirect Contact
Droplet	Aerosol

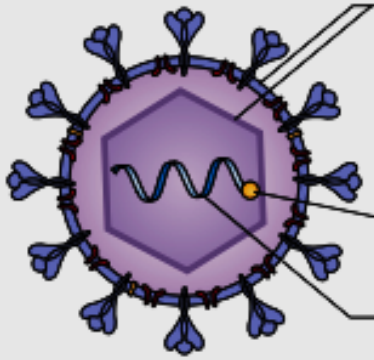
- Transmission may occur via multiple routes independently or simultaneously
- Lack of standardization of terminology, e.g., “droplet” *vs.* “aerosol”
- Increased concern for aerosol transmission for many respiratory viruses

J Virol 2010; 84 (8): 3974-3983 *Clin Infect Dis* 2020; 71 (5): 1186-1194 *Nat Rev* 2021; 19: 528-545

Determinants of Virus Transmission

VIRUS - HOST - ENVIRONMENT

Viral determinants of virus survival and transmission



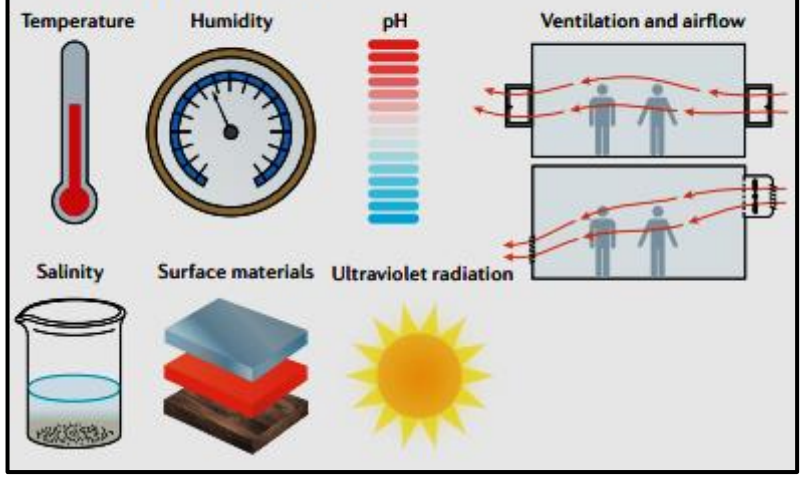
Viral envelope (if present) and capsid
- **Surface protein expression and modification**
  → site of infection
  → host receptor binding specificity and affinity
  → formation of viral aggregates
- **Capsid structure** → virus stability

Internal proteins and viral genomes
- **Densely packaged** → virus stability
- **Polymerase** → host-adapted virus replication

Viral genomes
- **Mutations** → host adaptation

Environmental determinants of virus survival and transmission

The following environmental factors could influence virus survival, host susceptibility and human behaviour:

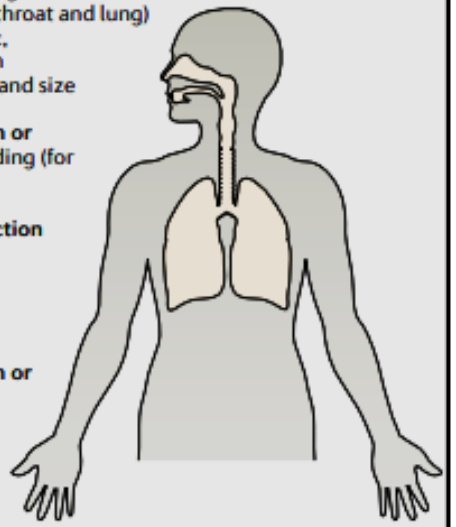


Host determinants of contagiousness, susceptibility and transmission

Factors affecting host contagiousness at the individual level
- **Tissue and cellular tropism** → viral shedding at different sites of the respiratory tract (for example, nose, throat and lung)
- **Symptom presentation** → presymptomatic, asymptomatic or symptomatic transmission
- **Lung function** → exhaled particle number and size distribution
- **Pre-existing immunity from prior infection or vaccination** → heterogeneity in viral shedding (for example, supershedder)

Factors affecting host susceptibility to infection at the individual level
- **Tissue-specific receptor expression, glycosylation and glycan expression**
  → site of infection
  → risk of infection
- **Pre-existing immunity from prior infection or vaccination** → risk of infection
- **Lung anatomy** → site of virus-laden particle deposition

Factors affecting transmission at the population level
- **Social contact patterns** → mode of transmission
- **Age-related mixing patterns** → age-specific risk of transmission



Determining transmissibility of a respiratory illness is more complex than simply using the R_0 or the SAR.

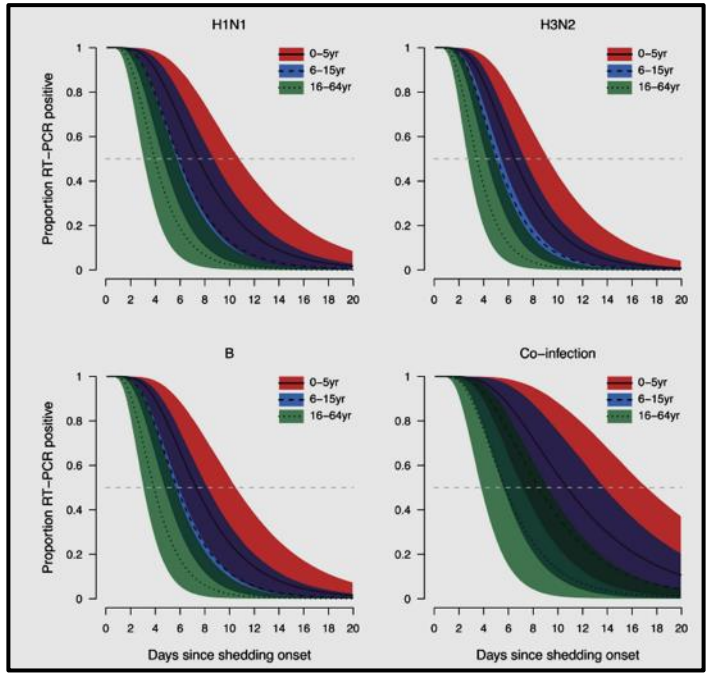
Understanding the various factors is critical for selecting the best non-pharmaceutical intervention to control spread of the virus

Intervening against multiple modes of transmission is likely to be more effective than acting on a single mode.

Nat Rev 2021; 19: 528-545

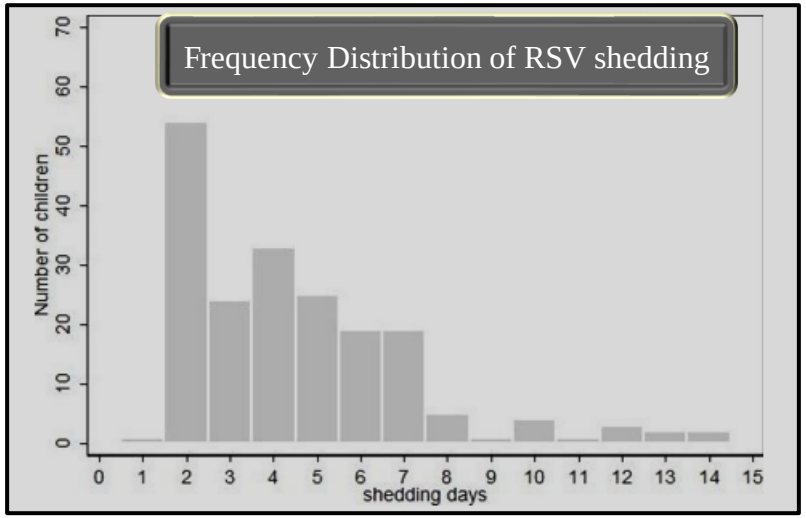
Viral Shedding before, during, and after Infection

Influenza

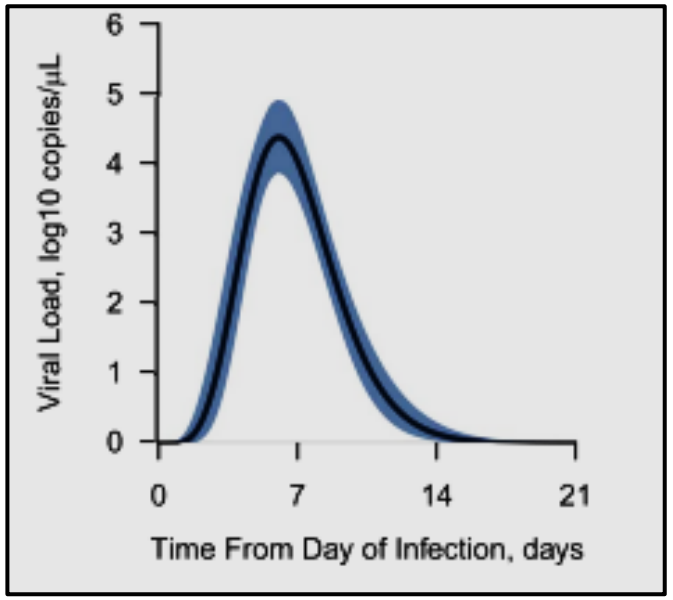


Pediatr Infect Dis 2016; 35 (5): 583-586

RSV



BMC Infect Dis 2010, 10: 15



Am J Epidemiol 2021; 190 (12): 2536-2543

- Children shed influenza virus earlier than adults; pre-symptomatic shedding frequently occurs in children
- **Shedding of influenza virus ("contagious period") : 4 – 8 days**
- RSV shedding of RSV in children has a mean duration of 4.5 days
- Younger children (< 5 years old) have higher viral loads
- **Shedding of RSV ("contagious period") : 3 – 8 days**

Clin Infect Dis 2023; 76 (3): e1012–e1020
J Infect Dis 2015; 212 (9): 1420-1428

How can one differentiate between these URTIs ?

Signs & Symptoms	INFLUENZA	RSV	COVID-19
Symptoms onset	Sudden	Gradual	Sudden
Fever (°F)	≥100 ; 3-4 days	≥100 ; 3-7 days	≥100 ; 2-7 days
Chills	Common	Uncommon	Common
Headache	Prominent	Common	Common
Cough	Dry ; sometimes severe	Dry ; sometimes severe	Dry ; often more severe
Sore throat	Sometimes	Common	Very Common
Runny nose	Sometimes	Common	Common
Dyspnea	Sometimes	Common, may be prominent	Common, often prominent
Wheezing	Rare	Common	Sometimes
Fatigue	Early & Prominent	Common	Common
Myalgia	Usual & often severe	Sometimes	Common
Diarrhea	Sometimes	Uncommon	Sometimes
Cyanosis	Rare	Sometimes	Sometimes
Sudden loss of taste/smell	Very uncommon	Rare	Common

Impossible to differentiate between FLU, RSV, and COVID based on clinical symptoms, alone!

www.cdc.gov/flu/symptoms/flu-vs-covid19.htm

Impact of Influenza in Congregate Care Settings

Influenza in long-term care facilities

Louise E. Lansbury[1] | Caroline S. Brown[2] | Jonathan S. Nguyen-Van-Tam[1]

[1]Health Protection and Influenza Research Group, Division of Epidemiology and Public Health, City Hospital, University of Nottingham, Nottingham, UK

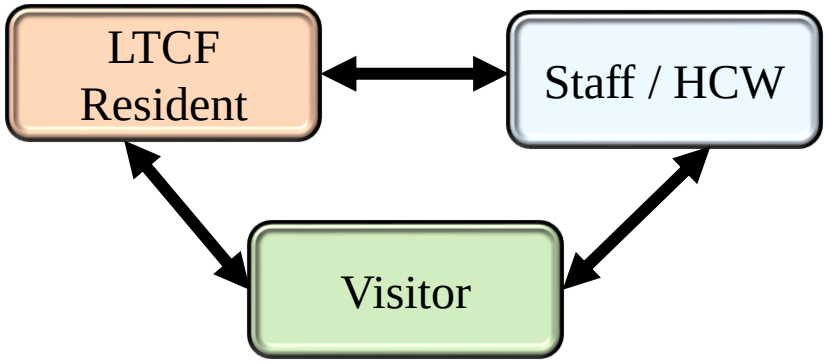
[2]Influenza & Other Respiratory Pathogens Programme, Division of Communicable Diseases and Health Security, WHO Regional Office for Europe, UN City, Copenhagen, Denmark

Correspondence
Louise E. Lansbury, Health Protection and Influenza Research Group, Division of Epidemiology and Public Health, City Hospital, University of Nottingham, Nottingham, UK.
Email: louise.lansbury@nottingham.ac.uk

Funding information
World Health Organization

Long-term care facility environments and the vulnerability of their residents provide a setting conducive to the rapid spread of influenza virus and other respiratory pathogens. Infections may be introduced by staff, visitors or new or transferred residents, and outbreaks of influenza in such settings can have devastating consequences for individuals, as well as placing extra strain on health services. As the population ages over the coming decades, increased provision of such facilities seems likely. The need for robust infection prevention and control practices will therefore remain of paramount importance if the impact of outbreaks is to be minimised. In this review, we discuss the nature of the problem of influenza in long-term care facilities, and approaches to preventive and control measures, including vaccination of residents and staff, and the use of antiviral drugs for treatment and prophylaxis, based on currently available evidence.

KEYWORDS
antivirals, infection control, influenza, long-term care, vaccines



Clin Infect Dis 2019; 68: e1
Influenza Other Respir Viruses 2017; 11: 356-366

www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm

People residing in LTCFs are very susceptible to the acquisition and spread of diseases !

- Gastro-intestinal illness (e.g., Norovirus outbreaks)
- Respiratory illness (e.g., Influenza, RSV)

- LTCF residents are a greater risk due to
  - overall fragility
  - close quarter living arrangements
  - shared caregivers
  - resident transfers and movements of staff and visitors in and out of the home
- Greater risk for hospitalization due to influenza
  - RR: 1.43 (95% CI 0.99 – 2.08)
- Greater risk of death due to respiratory illness
  - RR: 2.77 (95% CI 1.55 – 4.91)
- Overall greater risk for complications
  - bronchitis & pneumonia
  - secondary bacterial pneumonia (*S. pneumoniae*, *S. aureus*, *H. influenza*)
  - cardiac complications (myocarditis, pericarditis, exacerbation of underlying, preexisting cardiac illness)
  - neurologic complications (aseptic meningitis, encephalitis, GBS)
  - renal failure
  - difficulties ambulating (fall risk); may last for up to 6 weeks

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Influenza Other Respir Viruses 2017; 11: 356-366

- **LTCFs are susceptible to seasonal influenza outbreaks, which may be explosive and with high attack rates**
- written Infection Prevention & Control (IPC) Practices and policies, vaccination policies for residents and HCWs/staff must be in place
- provision of ongoing staff IPC training and requirement of facilities to promote compliance with IPC guidelines
- Influenza vaccination for LTCFF residents
- Influenza vaccination for staff and HCWs (strong recommendation *vs.* mandate)

Healthcare Personnel

Influenza vaccination prevents
- transmission of influenza
- staff illness & absenteeism
- influenza-related illness & death among LTCF residents

Surveillance

- **Active daily surveillance among all new & current residents**
- **Active surveillance when laboratory-confirmed index case is identified**

Influenza Testing

- **Testing should be performed when any resident has signs/symptoms of ILI**

www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm

Impact of Influenza in Congregate Care Settings

Influenza in long-term care facilities

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KEYWORDS
antivirals, infection control, influenza, long-term care, vaccines

Influenza Other Respir Viruses 2017; 11: 356-366

- **Clinical diagnosis is difficult**
- **Diagnosis requires laboratory testing**
- **Testing should be done as early as possible**
- **Administer antiviral treatment and chemoprophylaxis according to current recommendations**

- **LTCFs are susceptible to seasonal influenza outbreaks, which may be explosive and with high attack rates**
- written Infection Prevention & Control (IPC) Practices and policies, vaccination policies for residents and HCWs/staff must be in place
- provision of ongoing staff IPC training and requirement of facilities to promote compliance with IPC guidelines
- Influenza vaccination for LTCFF residents
- Influenza vaccination for staff and HCWs (strong recommendation *vs.* mandate)

What is the Role of Rapid Testing *vs*. Central Core Lab Testing?

What is the Role of Near-Patient Laboratory Testing ?

www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm

Impact of RSV in Acute & Congregate Care Settings

LTCF : nursing homes ; skilled nursing facilities

- Pathogenesis of RSV LRTIs in elderly patient not well understood
  - Giant-cell pneumonia with viral inclusions
  - Declining immune system, cardiac and other pulmonary comorbidities
  - Unchecked viral replication (?)
- Potential for nosocomial spread
  - Infected patients shed virus for 3 – 6 – 12 days
- Complication rates are variable: 0% to 55%
- Role of bacterial superinfections has not been well studied
  - *Streptococcus pneumoniae; Haemophilus influenza; Staphylococcus aureus*

TABLE 2. Reports of RSV infections in LTCF

Study[a] (reference)	Yr	Study method	No. of RSV cases	Attack rate (%)	Method of diagnosis[b]	Pneumonia (% of cases)	Death (% of cases)	Comment
Hornsleth et al. (100)	1975	Prospective	10	7	CF*	0	0	Most asymptomatic
CDC (18)	1977	Outbreak	15	19	CF	47	40	Several employees ill
Garvie and Gray (60)	1980	Outbreak	40	43	CF		3	
Mathur et al. (123)	1980	Prospective	8	1.4	Culture, CF	25	0	Concurrent influenza A outbreak
BCDSC[c] (155)	1983	Outbreak	15	NA[d]	Culture, CF		53	
		Outbreak	24	89	Culture, CF		10	
		Outbreak	16	40	CF		0	
Morales et al. (133)	1983	Prospective	12	10	Culture, CF	16	5	All RSV cases had lower respiratory tract disease
Hart (90)	1984	Outbreak	20	40	Culture, CF		20	Steady trickle of cases
Sorvillo et al. (165)	1984	Outbreak	40	40	Culture, CF	55	20	High rate of radiographic pneumonia
Mandal et al. (120)	1985	Outbreak	8	30	CF	13	13	
Arroyo et al. (8)	1988	Prospective	5	9	CF*	0	0	
Gross et al. (73)	1988	Prospective	8	3.4	CF*		0	Concurrent influenza outbreak
Agius et al. (1)	1990	Outbreak	52	12	CF, IFA, WB	42	12	Pharyngitis, gastrointestinal complaints uncommon
Nicholson et al. (140)	1990	Prospective	9	2	Culture, CF		0	
Falsey et al.[c] (39)	1990	Prospective	2	2.3	EIA*			Marked difference in attack rates at two local nursing homes
		Prospective	11	18	EIA*			
Osterweil and Norman (148)	1990	Prospective	34	15	CF	3	2	
Falsey et al. (44)	1992	Prospective	40	7	Culture, EIA*	10	5	Clear clustering on floors
Wald et al. (179)	1995	Prospective	9	3.5	Culture	22	0	Gastrointestinal symptoms uncommon
Orr et al. (147)	1996	Prospective	3	2	CF	33		Only evaluated febrile illnesses

Influenza Other Respir Viruses 2016; 10 (4): 268-290
Clin Microbiol Rev 2000; 13 (3): 371-384

DOI:10.1111/irv.12379
www.influenzajournal.com
Review Article

Risk of nosocomial respiratory syncytial virus infection and effectiveness of control measures to prevent transmission events: a systematic review

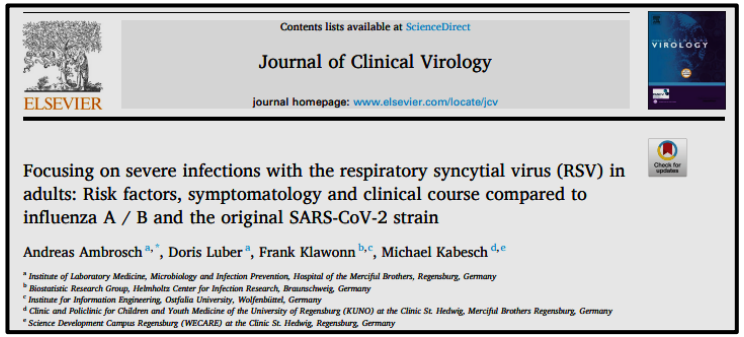
Clare E. French,[1,2] Bruce C. McKenzie,[3] Caroline Coope,[1,2,4] Subhadra Rajanaidu,[3] Karthik Paranthaman,[4] Richard Pebody,[4] Jonathan S. Nguyen-Van-Tam,[3] Noso-RSV Study Group, Julian P. T. Higgins,[1,2] Charles R. Beck[1,2,4]

[1]School of Social and Community Medicine, University of Bristol, Bristol, UK. [2]NIHR Health Protection Research Unit in Evaluation of Interventions at University of Bristol, Bristol,UK. [3]University of Nottingham, Nottingham, UK. [4]Public Health England, London, UK.
Correspondence: Clare E. French, School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol BS8 2PS, UK.E-mail: clare.french@bristol.ac.uk

Accepted 10 February 2016. Published Online 24 March 2016.

- Risk of nosocomial infections is known & best described in acute care settings
  - Neonatal / pediatric units, incl. NICUs
  - Adults with hematologic malignancies, and/or bone marrow stem cell transplant patients
- Transmission risk varied by hospital setting
  - Neonatal/pediatric patients: 6% - 56%
  - Adult patients: 30% - 32%
- Multicomponent infection prevention strategies appear broadly successful

Impact of RSV in Adult Patients



Contents lists available at ScienceDirect

Journal of Clinical Virology

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

Focusing on severe infections with the respiratory syncytial virus (RSV) in adults: Risk factors, symptomatology and clinical course compared to influenza A / B and the original SARS-CoV-2 strain

Andreas Ambrosch [a,*], Doris Luber [a], Frank Klawonn [b,c], Michael Kabesch [d,e]

[a] Institute of Laboratory Medicine, Microbiology and Infection Prevention, Hospital of the Merciful Brothers, Regensburg, Germany
[b] Biostatistic Research Group, Helmholtz Center for Infection Research, Braunschweig, Germany
[c] Institute for Information Engineering, Ostfalia University, Wolfenbüttel, Germany
[d] Clinic and Policlinic for Children and Youth Medicine of the University of Regensburg (KUNO) at the Clinic St. Hedwig, Merciful Brothers Regensburg, Germany
[e] Science Development Campus Regensburg (WECARE) at the Clinic St. Hedwig, Regensburg, Germany

J Clin Virol 2023; 161: 105399

Table 1
Demographic, clinical and laboratory parameters of RSV compared to Influenza A, Influenza B and SARS-CoV-2.

Parameter / virus (n)	RSV (318)	Influenza A (591)	Influenza B (289)	SARS-Cov-2 (342)	p
Demographic data					
Age years	75.1 (14.3)[&]	72.9 (15.3)[&&]	75.7 (13.7)[&&]	70.8 (15.9)[&&&]	< 0.001
Gender f/m	135/183	261/330	135 / 154	168 / 174	0.301
Clinical symptoms					
Cough%	71[&]	68	66	51[&&]	< 0.001
Headache%	7[*,**]	13	18	14	< 0.001
Weakness%	67[#,##]	67[###,####]	83	78	< 0.001
Enteritis	10[$]	21	20	17	< 0.001
Laboratory parameters					
Body temperture °C	37.31 (0.97)[&]	37.54 (1.03)[&&,&&&]	37.27 (0.86)	37.31 (0.93)	< 0.001
Leukcocytes n/ul	10.1 (7.6)[*,***]	8.4 (5.8)	7.4 (6.7)	8.5 (11.7)	< 0.001
C-reactive protein mg/dL	62.6 (77.1)[#]	65.9 (81.0)	48.8 (68.8)[##]	83.4 (83.1)[###]	< 0.001
Lactate dehyrogenase IU/mL	265 (114)[%]	309 (474)	273 (176)	409 (632)[%%]	< 0.001
Glucose mg/dL	145 (64)[$]	137 (57)	135 (69)	129 (53)	0.03

- **Patients' mean ages** > 70 years for Influenza A/B, RSV, and SARS-CoV-2, but **highest in the RSV group**
- Data differ regarding Influenza, when compared to other studies in other countries (e.g., U.S.), and likely due to differences in Flu-vaccination rates
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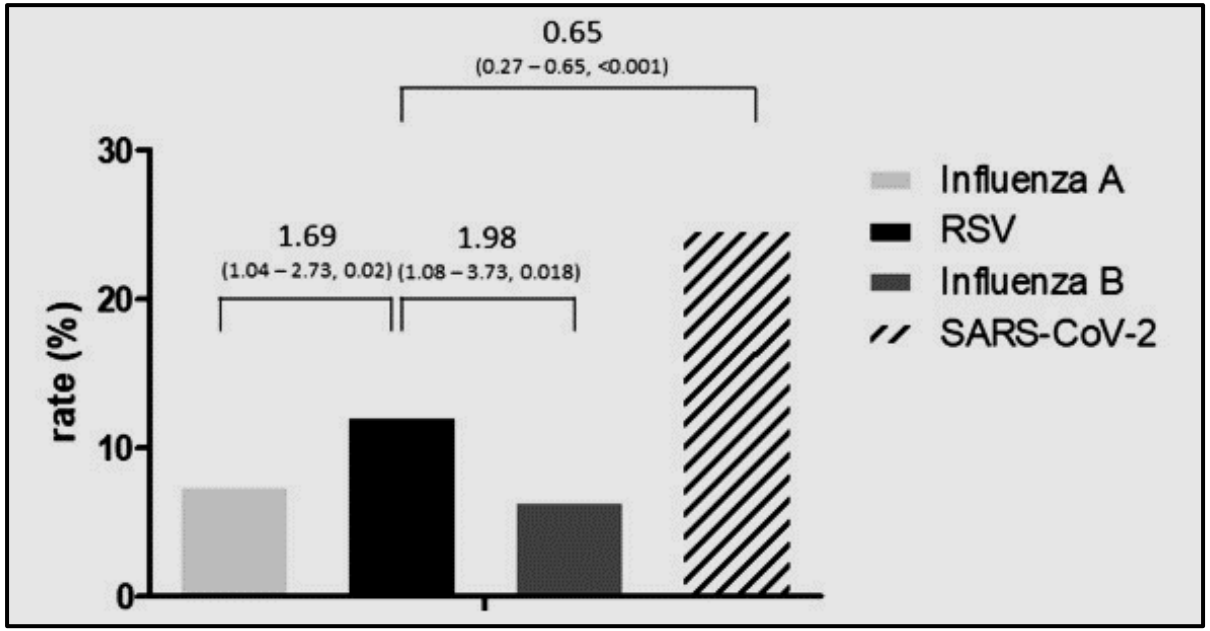
- Clinical course was worst in patients with SARS-CoV-2, followed by RSV, and then influenza infections



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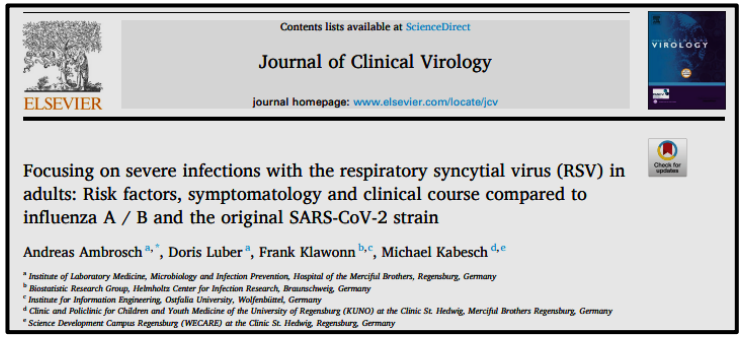
Impact of RSV in Adult Patients



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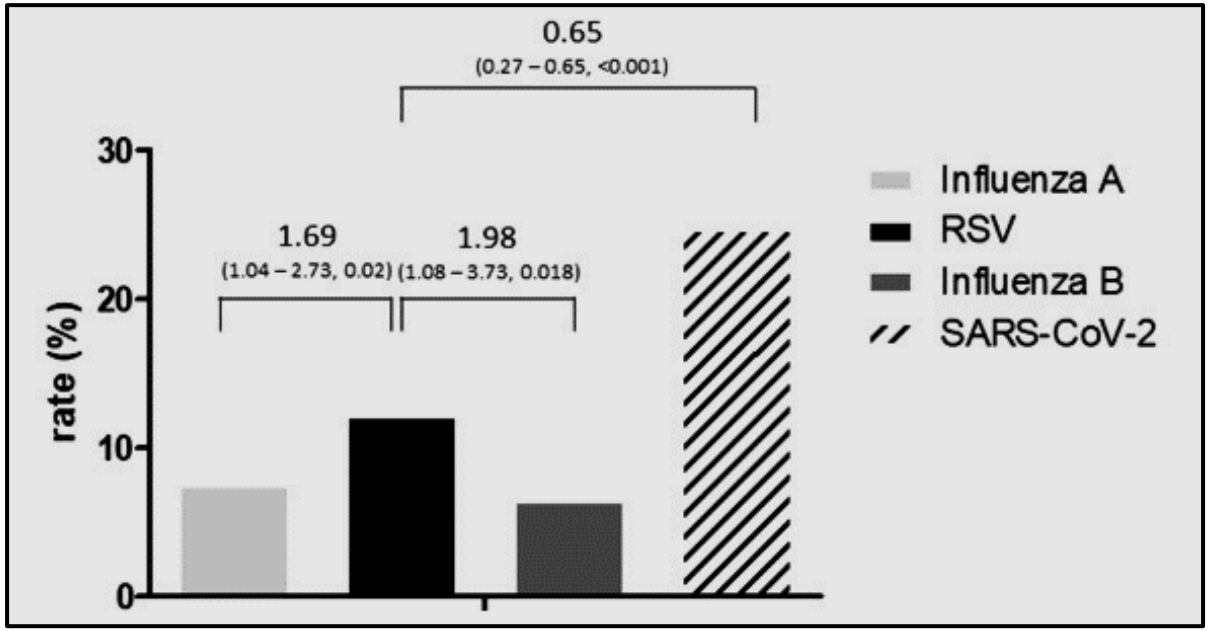
RSV is in the spotlight for severe URTIs & LRTIs in elderly patients !



Influenza Other Respir Viruses 2016; 10 (4): 268-290
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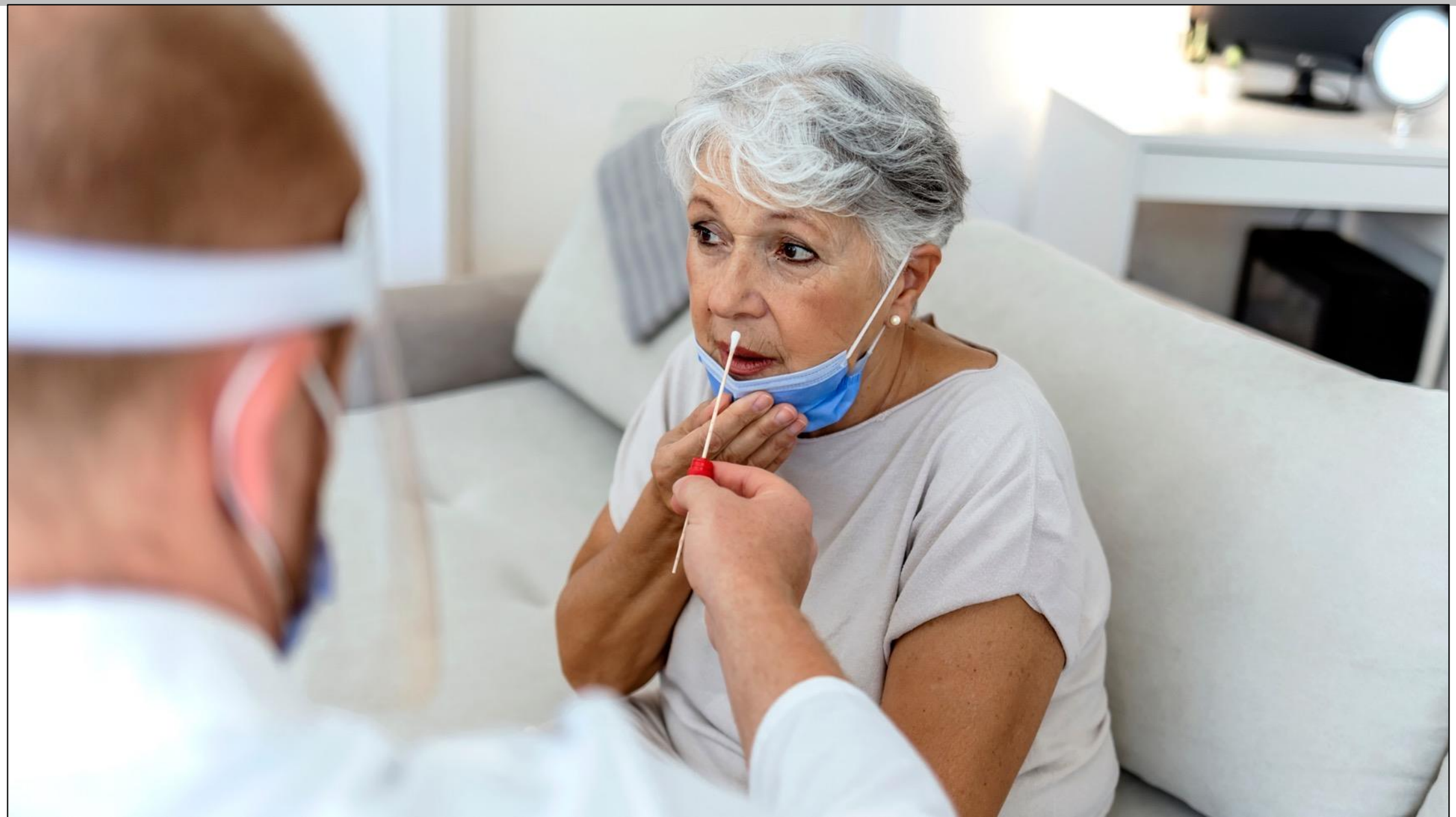
Describe rapid test technologies for RSV & Flu and differences between them



The Effects of the COVID-19 Pandemic on Laboratory Testing Practices

White House, COVID-19 Protections After Public Health Emergency, May 9, 2023.

The Federal Public Health Emergency (PHE) for COVID-19, declared under Section 319 of the Public Health Service (PHS) Act, expired on May 11, 2023.

Reminder: The PHE has ended – COVID-19 has not

We did things that we never considered doing before

- initial increase in LDTs and/or submission of EUAs ; manufacturing of swabs and VTM for specimen collection
- using multiple diagnostic tests, including testing for screening and surveillance
- providing PCR Cycle Thresholds in patient reports

Diagnostic

Screening

Surveillance

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- providing PCR Cycle Thresholds in patient reports

Diagnostic | **Screening** | **Surveillance**

How do we now return to established protocols & procedures for laboratory testing ?

Consider Influenza & RSV ! | **Anticipated Test Volumes ?** | **Clinical Settings for Testing ?**

Subsequent to the COVID-19 public health emergency, how has ***respiratory testing*** changed in your institution?

(select all that apply)

A. Reduced the diversity of platform (fewer test manufacturers)

B. Platform reduction/consolidation (fewer testing platforms)

C. Reduced the complexity (ease of use/CLIA waived)

D. Decentralizing/Broader access (POCT)

E. We have not changed our respiratory testing

FOR HEALTHCARE SETTINGS

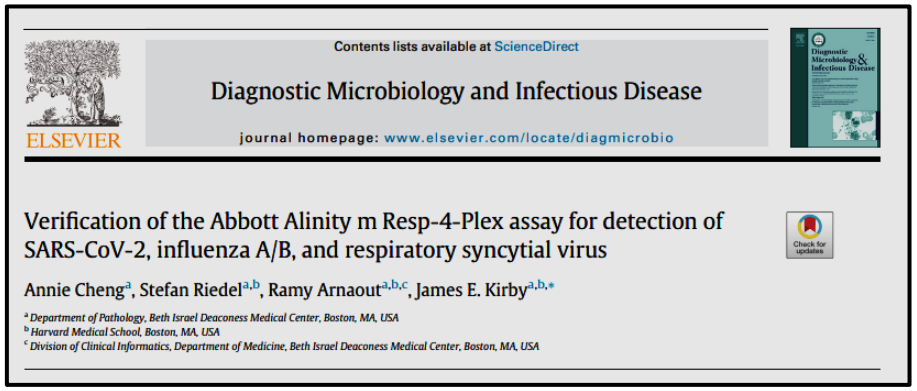
POLL QUESTION #2

2022 : Changing from COVID-19-Focused Testing to Multiplex Respiratory Virus Detection

~~Surveillance~~

~~Pre-procedure Screening~~

Diagnostic



Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

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

Verification of the Abbott Alinity m Resp-4-Plex assay for detection of SARS-CoV-2, influenza A/B, and respiratory syncytial virus

Annie Cheng[a], Stefan Riedel[a,b], Ramy Arnaout[a,b,c], James E. Kirby[a,b,*]

[a] Department of Pathology, Beth Israel Deaconess Medical Center, Boston, MA, USA
[b] Harvard Medical School, Boston, MA, USA
[c] Division of Clinical Informatics, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA

Abbott Alinity m analyzer at BIDMC

Use of Test Methods (rapid *vs*. lab-based) specific to Patientcare Setting

- Emergency department
- ICUs
- Regular patient rooms
- Ambulatory care clinics
- Urgent Care Centers

- Results of sample testing (in comparison with other previously established lab methods) were highly accurate, sensitive, and precise
- The Alinity-m Resp-4-Plex assay* provides
  - high-throughput testing
  - sample-to-answer testing
  - random access and semi-batch functionality
  - sample-to-answer TAT : 115 minutes
  - ability to load and perform multiple different tests (on board reagents for various tests)

*This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the Clinical Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform moderate or high complexity tests. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID 19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or the authorization is revoked sooner.

Reference Document: Alinity m Resp-4-Plex AMP Kit Package Insert 53-608211/R6. For In Vitro Diagnostic Use. Rx Only.

Why do physicians order a laboratory test ?

- Diagnosis (e.g., to rule in or rule out a disease/diagnosis)
- Monitoring (e.g., the effect of therapeutic interventions)
- Screening (e.g., PSA, neonatal thyroxine testing)
- Research (e.g., to understand pathophysiology of a disease)

Lab Medicine 2009; 40 (2): 105-113

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Approaches to Establishing a Diagnosis based on Laboratory Test Results

Hypothesis Deduction

Pattern Recognition

Medical Algorithms

"Rifle *vs*. Shotgun" Approach

Lab Medicine 2009; 40 (2): 105-113

What Questions to Ask Before Ordering a Lab Test?

Laboratory Test Results May Influence up to 70% of Medical Decision Making !

Are the test results being interpreted correctly ?

How will incorrect / inappropriate interpretation of laboratory test results affect the accuracy of the diagnostic decision making ?

How will incorrect / inappropriate interpretation of laboratory test results affect the subsequent treatment decisions?

What Questions to Ask Before Ordering a Lab Test?

Clinical / Healthcare Provider

- **Why is the test being ordered?**
  - clinical signs & symptoms
  - prevalence of illness
  - pre-test probability
  - PPV & NPV
  - patient population (e.g., immunosuppressed, LTCF)

- **What are the consequences of not ordering the test?**
  - communicable disease ; disease spread
  - complications due to delayed diagnosis

- **If test is ordered, how will results influence patient care management?**
  - availability of treatment
  - need & frequency of re-ordering test

Diagnostic Laboratory

- **Why is the test being ordered?**
  - diagnosis *vs*. screen *vs*. monitoring of illness
  - pre-test probability
  - post-test probability
  - PPV & NPV
  - specimen requirements & specimen transport

- **What are the Test Method Performance Characteristics?**
  - analytical sensitivity & specificity
  - accuracy & precision
  - Quality Control & Quality Assurance

- **If test is ordered, how will results influence patient care management?**
  - importance of TAT of results reporting
  - frequency of testing / re-testing

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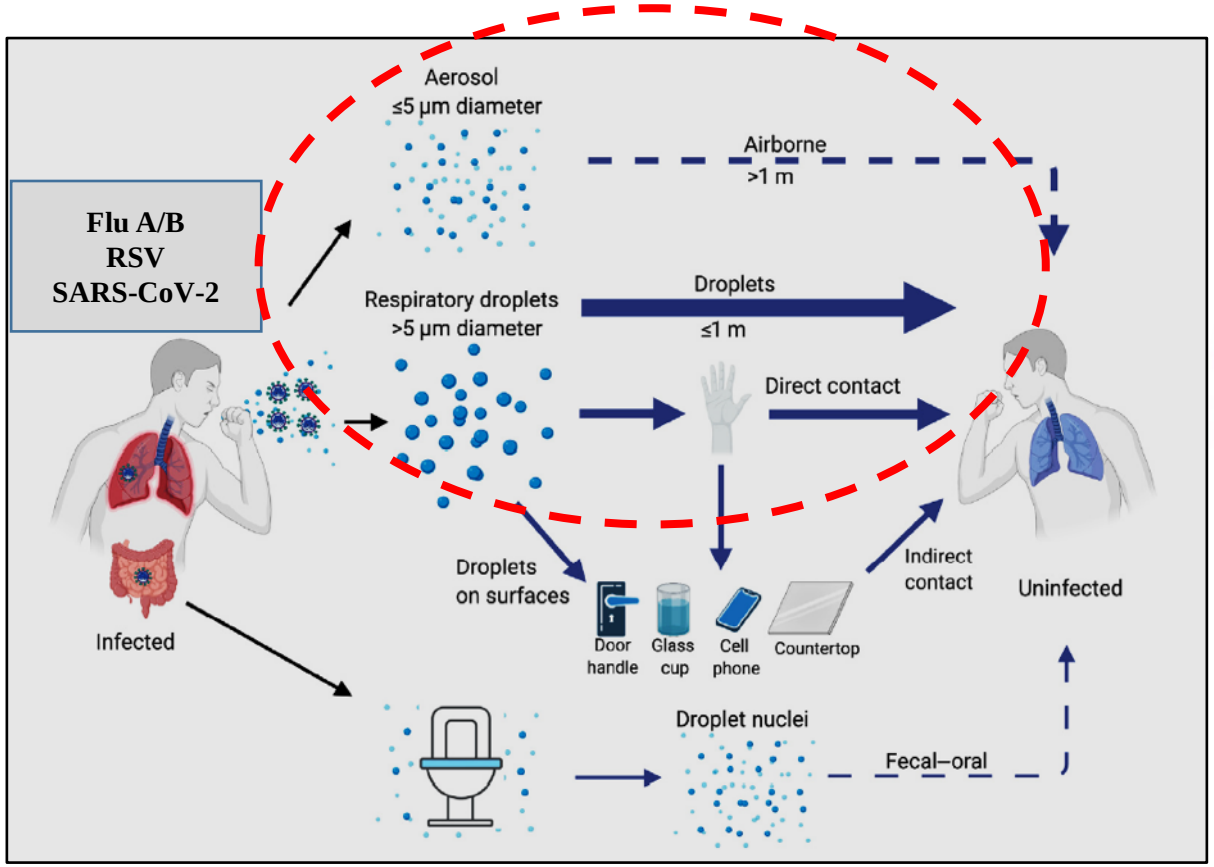
FOR HEALTHCARE SETTINGS

RESULTS

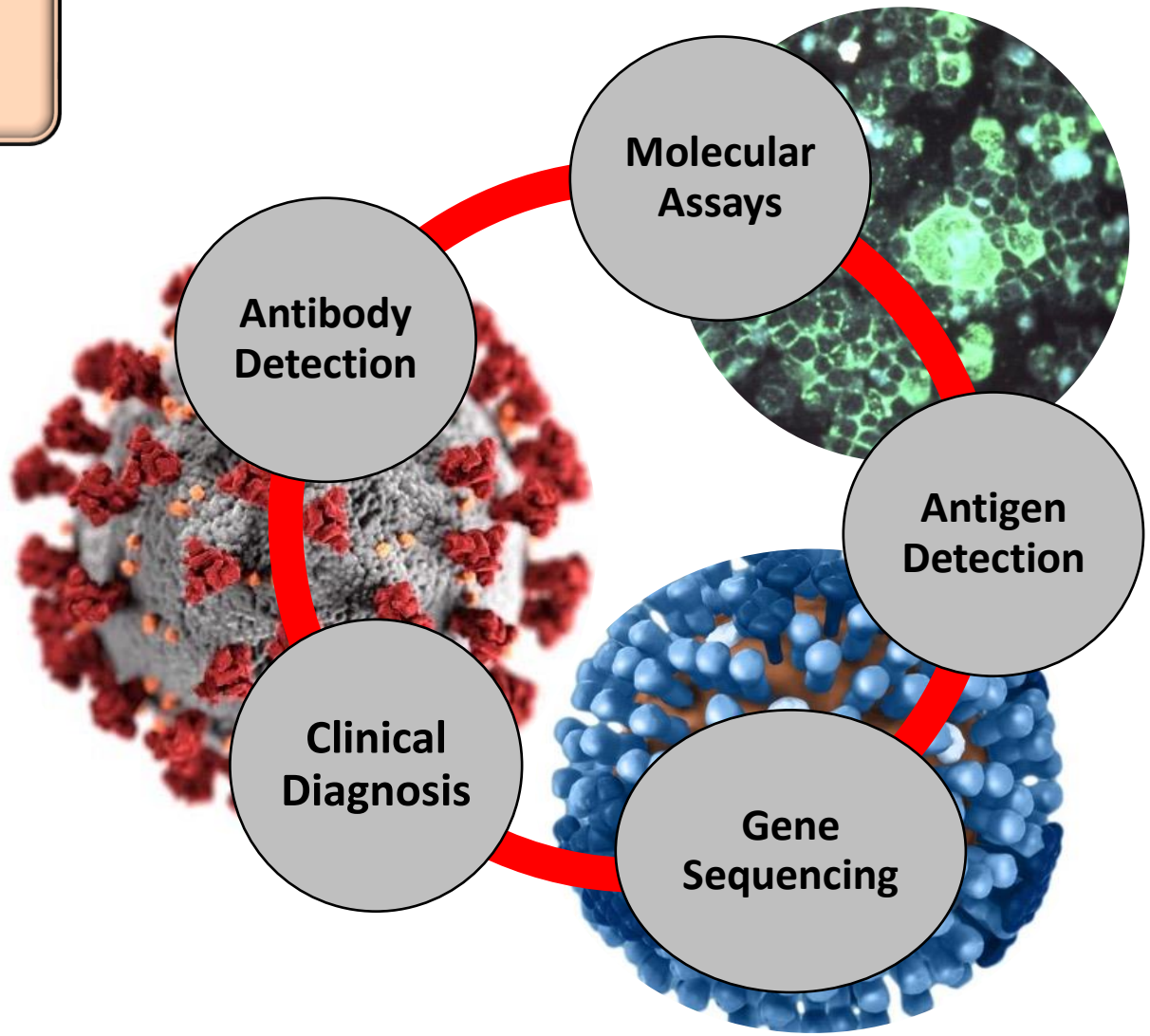
POLL QUESTION #2

Laboratory Testing: pre-pandemic, during pandemic, post pandemic

First, requires understanding of the disease, its pathophysiology, and clinical management & treatment !

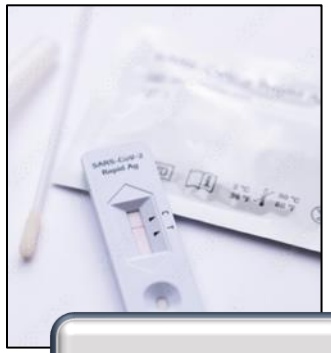


Modified from: Harrison AG, et al. *Trends in Immunology* 2020; 41 (12): 1100-1115.



Images: CDC, Public Health Image Library, COVID-19, Influenza, RSV

Antigen *vs.* Molecular Test Methods



Multitude of different laboratory tests are available – how does one chose the most appropriate test ?

Clinical Factors

- Pathophysiology of the disease
- Viral shedding in upper respiratory tract may decline after 4 days of illness
- When is testing performed in relation to time of symptom onset / clinical care setting
- How urgent will test results be needed to make a decision for patient care management/treatment

Laboratory Factors

- Sensitivity & Specificity of test
- Accuracy & Precision of test
- Test Complexity : lab personnel staffing needs
- Anticipated test volume, frequency of testing, cost of test
- Specimen requirements for testing
- QC / QA requirements

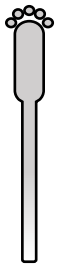
Antigen *vs.* Molecular Test Methods

Why using Molecular Tests for RTI Diagnostics?

Gold Standard : RT-PCT and RT-qPCR

Patient with Flu, RSV, or COVID-19
("positive patient")

Sample Containing Antigen/RNA



ANTIGEN TESTS

"Rapids" "RADTs" "Lateral Flow"

NO AMPLIFICATION

Detects the presence of pathogens/antigens (virus or bacteria) present in the sample

Lower levels of Target (Antigen) may not be detected

MOLECULAR TESTS

"NAATs" ("PCR" and "IAT - isothermal")

AMPLIFICATION

Amplifies any target NA of virus / bacteria present in the sample until necessary amplification reached

Lower levels of Target (NA) can still be detected / amplified

RTI: Respiratory tract infection; **RADTs**: rapid antigen detection tests; **NAAT**: nucleic acid amplification test; **PCR**: polymerase chain reaction; **IAT**: Isothermal amplification test; **NA**: nucleic acid; **RT-PCR**: reverse transcriptase PCR; **RT-qPCR**: RT quantitative PCR; **qPCR** = real-time PCR.

www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm

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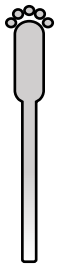

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Lower levels of Target (NA) can still be detected / amplified

Sensitivity / Specificity of Test Method

Time of sample collection in relation to symptom onset

Singleplex vs. Multiplex Assay
(Influenza – RSV – SARS-CoV-2)

Variation/mutation of target
(e.g., COVID variant; novel influenza strain)

Sample quality
(technique, nasal *vs.* NP swab)
(i.e., does the sample contain sufficient target material)

Assay/test TAT
(sample collection to results reporting)

RTI: Respiratory tract infection; **RADTs**: rapid antigen detection tests; **NAAT**: nucleic acid amplification test; **PCR**: polymerase chain reaction; **IAT**: Isothermal amplification test; **NA**: nucleic acid; **RT-PCR**: reverse transcriptase PCR; **RT-qPCR**: RT quantitative PCR; **qPCR** = real-time PCR; **NP**: nasopharyngeal; **TAT**: turn around time.

www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm

Why using Molecular Tests for RTI Diagnostics?

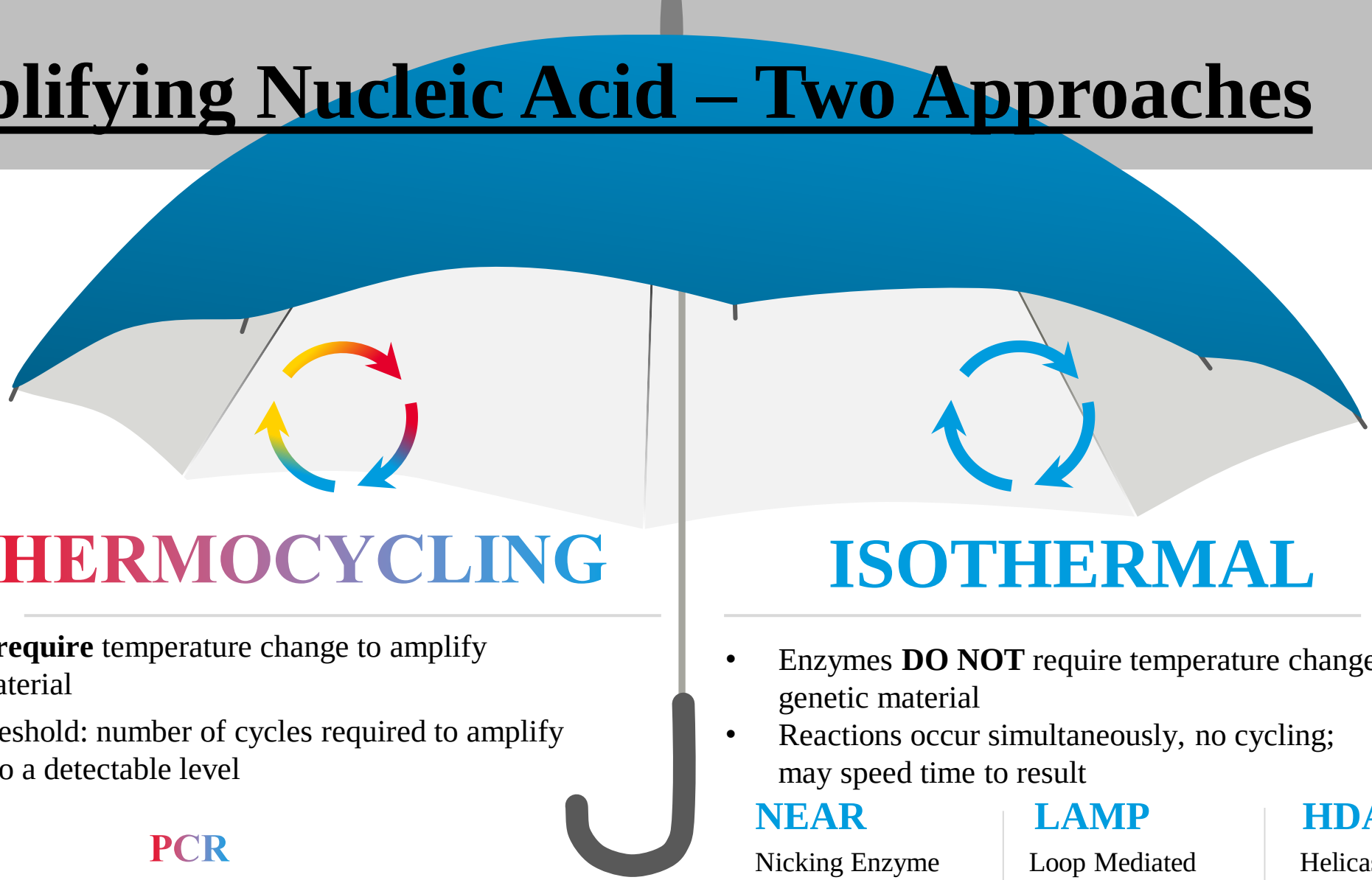
Advantages

- More sensitive pathogen detection compared to RADTs (e.g., influenza, RSV, SARS-CoV-2)
- Likelihood of false-negative or false-positive results is relatively low
- Test result is less impacted by prevalence of the disease in the greater community
- May be able to distinguish between specific virus subtypes (e.g., influenza H3)
- Isothermal amplification assays have usually shorter TATs compared to PCR and may be more suitable for near-patient testing

Disadvantages

- TAT for results may be longer for RT-PCR than RADTs, and these assays may not be as suitable for certain clinical settings
- Most molecular assays are not FDA-cleared to test lower respiratory tract specimens
- Some molecular assays may not specifically identify all circulating subtypes of viruses
- Some molecular assays are more expensive than RADTs
- Limited number of rapid CLIA waived platforms, CLIA high complexity assays are laboratory based

Amplifying Nucleic Acid – Two Approaches



THERMOCYCLING

- Enzymes **require** temperature change to amplify genetic material
- Cycle Threshold: number of cycles required to amplify viral NA to a detectable level

PCR

Polymerase Chain Reaction

- Roche LIAT™
- Cepheid GeneXpert®
- Biofire®
- Thermo Fisher Accula™
- Visby Medical™

ISOTHERMAL

- Enzymes **DO NOT** require temperature change to amplify genetic material
- Reactions occur simultaneously, no cycling; may speed time to result

NEAR

Nicking Enzyme Amplification Reaction

- Abbott ID NOW™

LAMP

Loop Mediated Isothermal Amplification

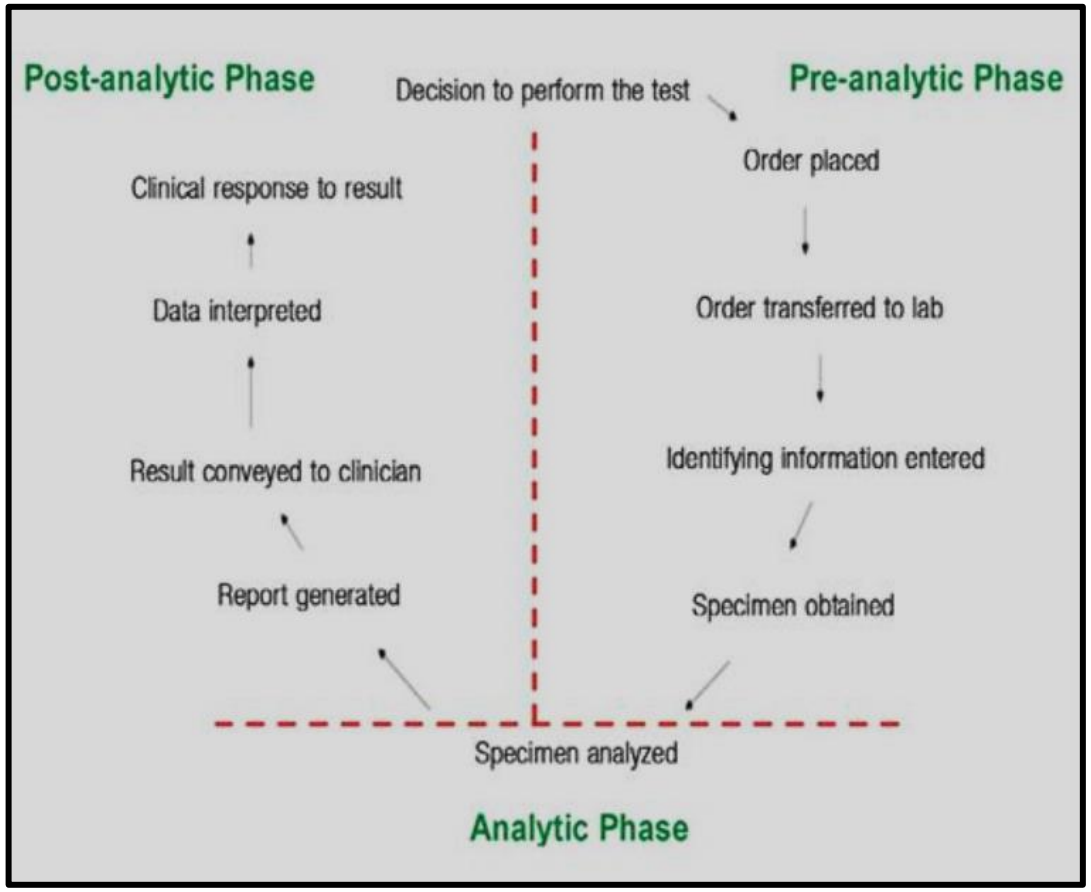
- Meridian Alethia®

HDA

Helicase Dependent Amplification

- Quidel Solana™

Impact of Laboratory Test Phases on Accuracy of Test Results



Lab Medicine 2009; 40 (2): 105-113

Pre-analytical Phase

- Specimen collection
- Specimen transport
- Errors: e.g., patient ID error; improper collection; incorrect test request

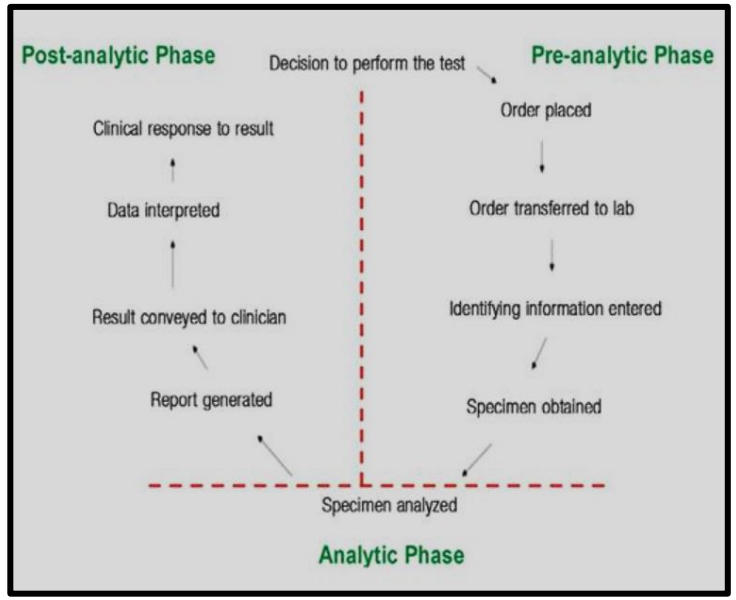
Analytical Phase

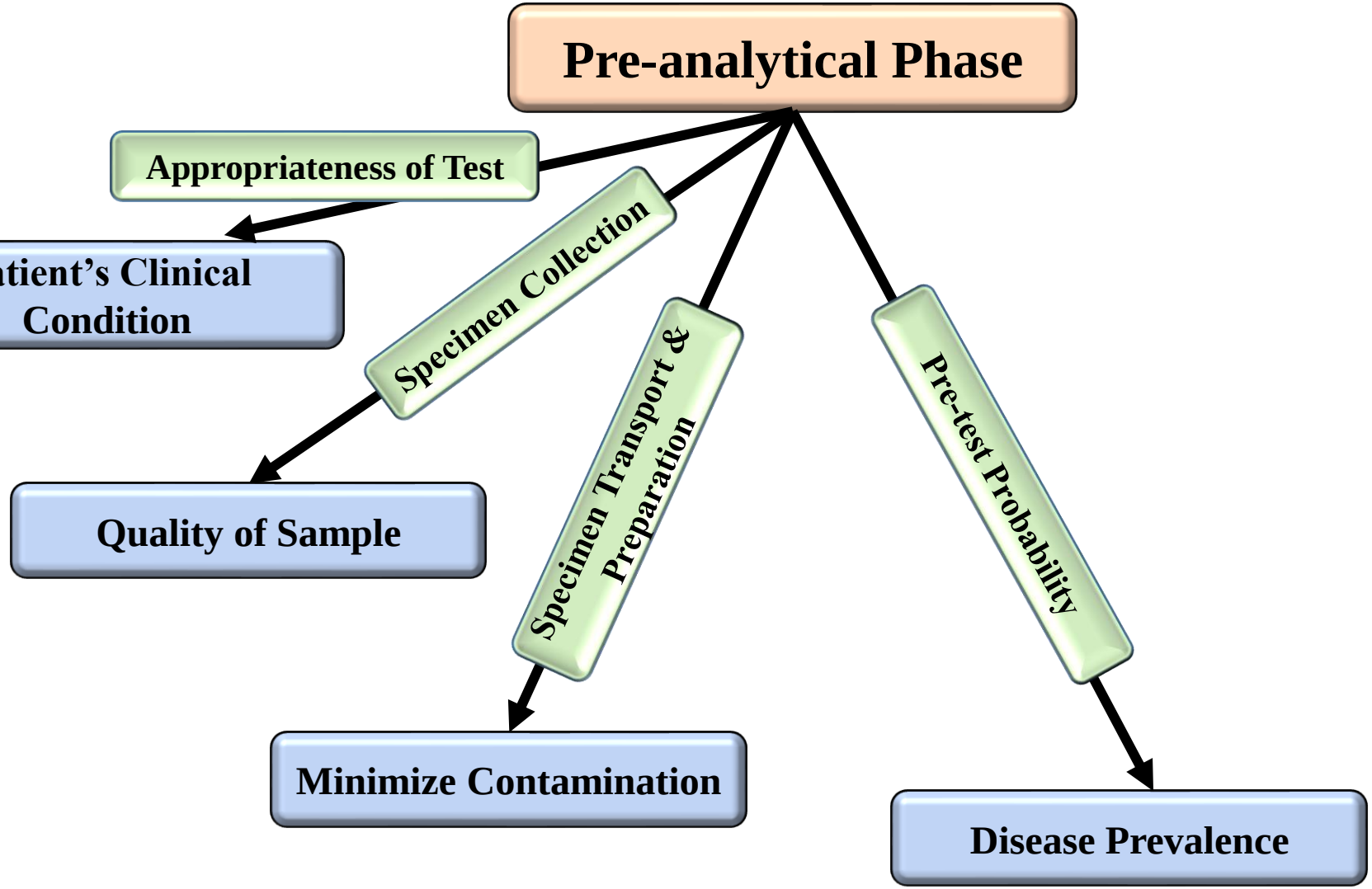
- Errors: random errors and/or systematic errors

Post-analytical Phase

- Testing ; Reflex testing ; Selective testing
- Results reporting & LIS/HIS
- Data interpretation & clinical response / treatment plan
- Errors: transcription / reporting (e.g., wring value, wrong patient)

Impact of Laboratory Test Phases on Accuracy of Test Results





Lab Medicine 2009; 40 (2): 105-113

Impact of Disease Prevalence on Accuracy of Test Results

Even molecular tests and not 100% accurate !

Consider the **disease prevalence** and the **pre-test probability** when assessing the sensitivity, specificity, PPV, and NPV for a laboratory test to detect the disease

When are tests less accurate ?

- asymptomatic people
- low-risk population
- person who sheds little virus
- person who is at a later stage of the illness

Shuren J, Stenzel T. *NEJM* 2021; 383 (17): e97
Woloshin S, et al. *NEJM* 2020; 383 (6): e38(1)

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Test Case Example: sensitivity 98% ; specificity 99%

- 2 / 100 results are false negative

Now, we test 5 million patients daily, and prevalence is 1%

(50,000 people have disease ; 4.95 M do not have disease)

- 1,000 positive cases will be missed
- 49,500 people will receive a FP result

Shuren J, Stenzel T. *NEJM* 2021; 383 (17): e97
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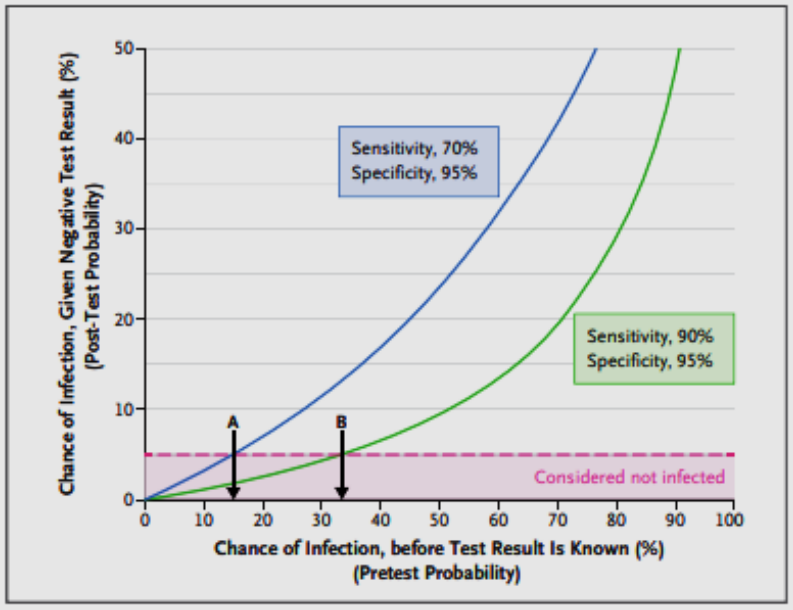


When are tests less accurate ?

- asymptomatic people
- low-risk population
- person who sheds little virus
- person who is at a later stage of the illness

Example: PCR test has 100% specificity ; 95% sensitivity

Testing of a person after close contact with confirmed sick person

- Assume pre-test probability : 20%
- Post test probability of infection with a **negative test** would be 1%
- Even with 50% pre-test probability, post-test probability is <5%

Now use a test with 70% sensitivity :

- With pre-test probability 50%
- Post-test probability of infection with negative test is 23% - way too high !

Shuren J, Stenzel T. *NEJM* 2021; 383 (17): e97
Woloshin S, et al. *NEJM* 2020; 383 (6): e38(1)

Selecting the Best Laboratory Testing Strategy

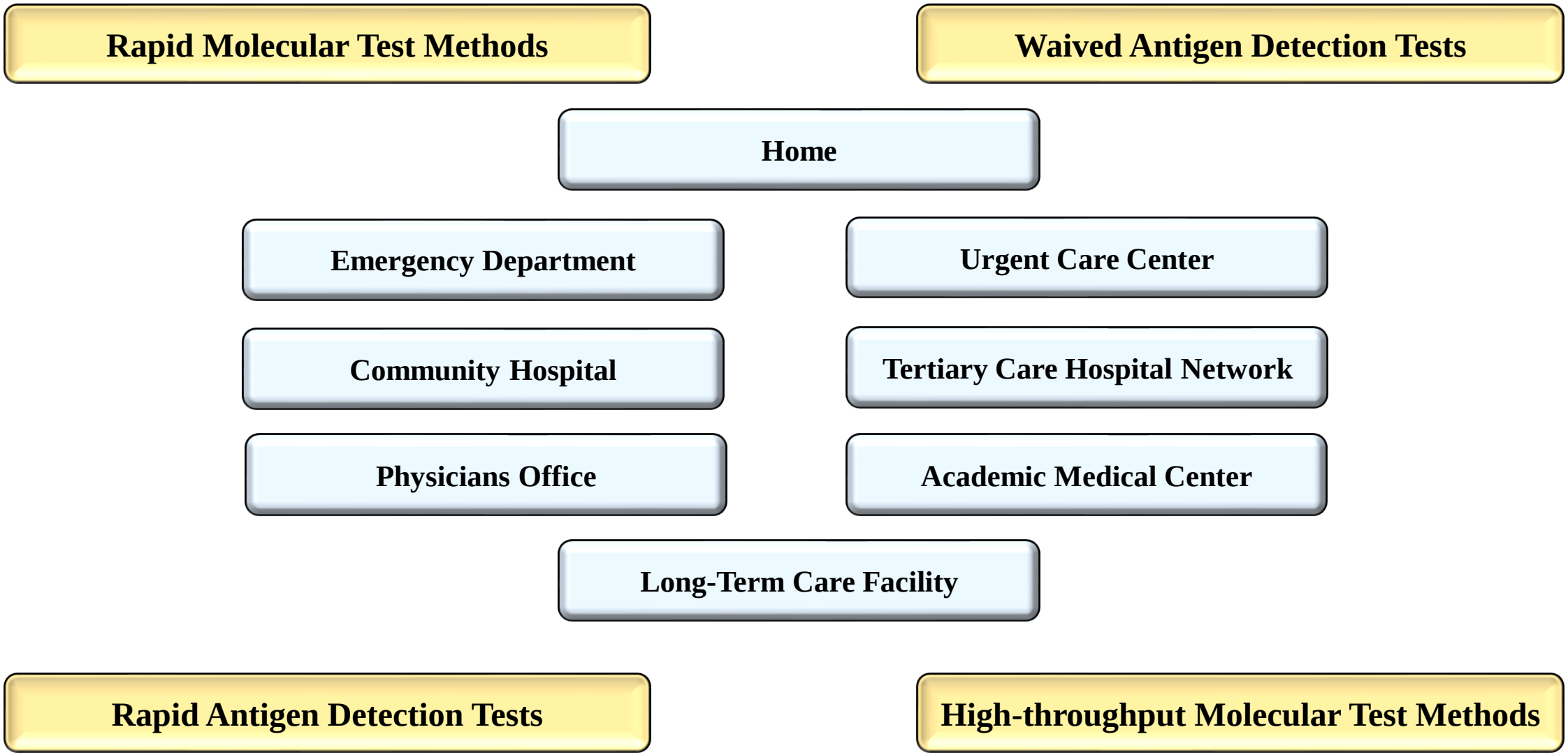
Rapid Molecular Test Methods

Waived Antigen Detection Tests

Rapid Antigen Detection Tests

High-throughput Molecular Test Methods

Selecting the Best Laboratory Testing Strategy



Selecting the Best Laboratory Testing Strategy

Rapid Molecular Test Methods

Waived Antigen Detection Tests

Patient Age

Home

Available Treatments

Emergency Department

Urgent Care Center

Community Hospital

Tertiary Care Hospital Network

Physicians Office

Academic Medical Center

Co-Morbidities

Long-Term Care Facility

Non-pharmaceutical Interventions

Rapid Antigen Detection Tests

High-throughput Molecular Test Methods

Respiratory Testing Availability Across Clinical Settings

	Outpatient / Ambulatory Care (Physicians' Offices)	Urgent Care Centers	Emergency Department	Hospital Inpatient Care
Rapid antigen detection assays	YES	YES	NO	NO
Rapid molecular assays (singleplex)	YES	YES	YES	YES
Rapid molecular assays (multiplex)	YES	YES	YES	YES
High-throughput molecular assays (singleplex or multiplex)	NO	NO	YES	YES

- **Historically, RADTs for respiratory viruses were associated with suboptimal test performance**
- **Rapid molecular tests have improved detection of respiratory virus in ambulatory care settings**
- **Traditionally, multiplex molecular testing increasingly plays a role in hospital settings to detect a range of viruses & bacteria, and can support antimicrobial stewardship programs and provide insight to local transmission of respiratory pathogens**

www.cdc.gov/flu/professionals/diagnosis/overview-testing-methods.htm

Post Pandemic: Laboratory Testing still Depends on Clinical Needs

Outpatient / Ambulatory Care
(Physicians' Office)

Urgent Care Centers

- Rapid antigen detection assays (RADTs)
- Rapid molecular assays (singleplex)
- Rapid molecular assays (multiplex)

Emergency Department

- Rapid molecular assays (singleplex)
- Rapid molecular assays (multiplex)

Hospital Inpatient Care

- High-throughput (singleplex or multiplex) molecular assays
- Rapid molecular assays (singleplex)
- Rapid molecular assays (multiplex)

Questions to consider when testing for respiratory viruses

- **Will the test result change the approach to treatment & patient care management ?**
- **Is there a risk for co-infections or bacterial superinfections ?**
- **Is there a risk for spread of a virus among other patients ? – specifically of concern in LTCFs and among immunosuppressed / hospitalized vulnerable patient populations**

Key features for test selection: Accuracy / sensitivity / specificity & TAT

Clin Infect Dis 2020; 71: 2744-2751

Laboratory Diagnostic Testing for URTIs / RTIs

qPCR tests
("gold standard")


Rapid Molecular tests


Antigen-detection tests


Targets[a]	Approved Specimen Types	Time[b]	Cost[c]
CLIA-waived assays			
Influenza A/B only	NS direct, NPS direct, NP, NPS	15–30 minutes	$$–$$$
RSV only	NPS direct, NS, NPS	15 minutes	$$$
Flu A/B plus RSV	NS, NPS	20–30 minutes	$$–$$$
Multiple viruses plus atypical bacteria	NPS	60 minutes	$$$$
Moderate- to high-complexity assays			
Influenza A/B only	NS, NPS	0.5–2 hours	$$
PIV only	NPS	3.5 hours	$$
Flu A/B plus RSV	NS, NPS, NPA, NW	0.5–3.5 hours	$$–$$$$
RSV plus hMPV	NS, NPS	0.75 hours	$S
AdV, hMPV plus RV	NPS	3.5 hours	$$
Multiple viruses plus atypical bacteria	NPS	0.75–5 hours	$$$$
Multiple bacteria with resistance	ETA	4–5 hours	$$$$$
Multiple viruses and bacteria with resistance	S, ETA, BAL	60 hours	$$$$$

Clin Infect Dis 2020; 71 (10): 2744-2751

To test or not to test?

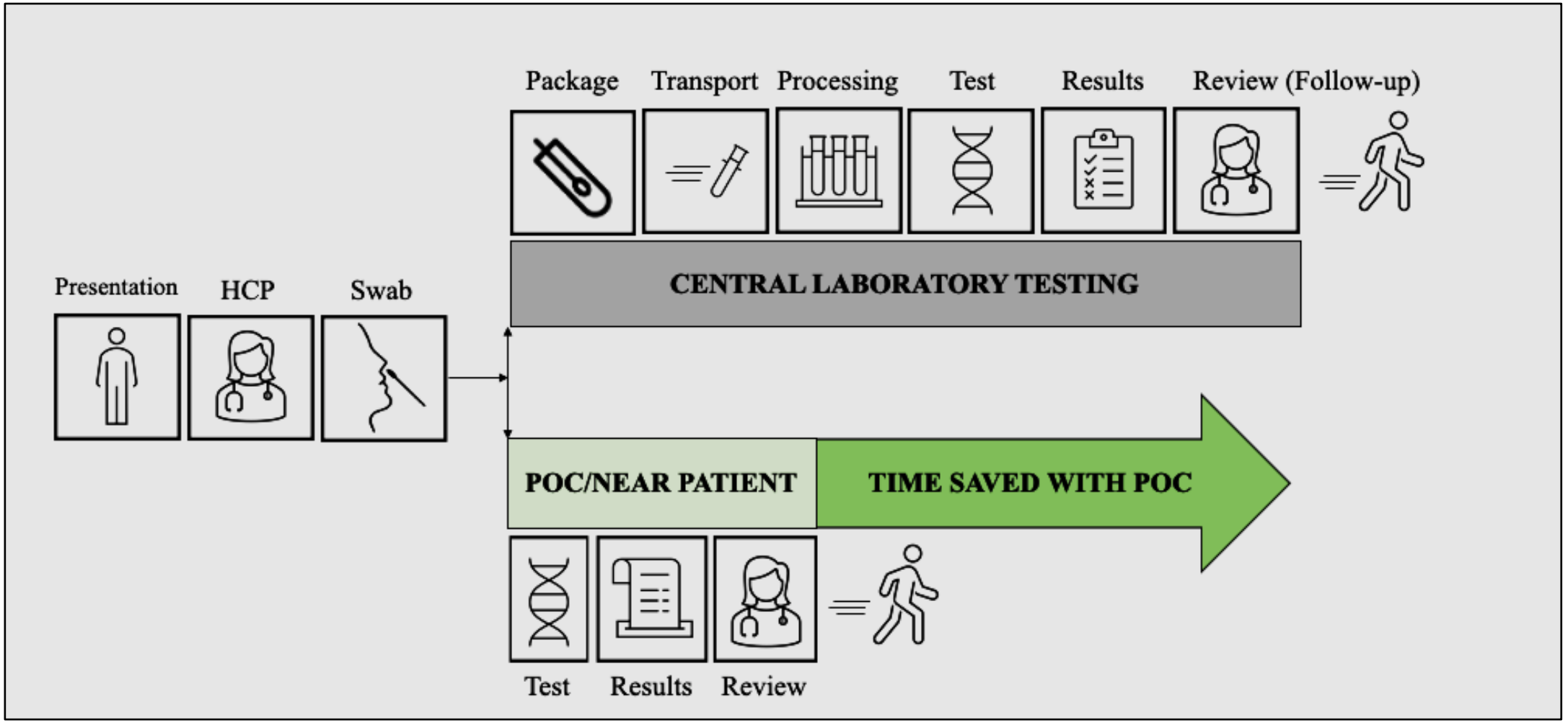
Workflow Considerations?

If testing, what is the best approach?

Is there a partnership with Antimicrobial Stewardship?

Workflow for the Diagnostic Testing for URTIs / RTIs

FASTER – ACCURATE – RELIABLE – PRECISE – COST



Rapid laboratory tests to detect URIs ?

Clinical Infectious Diseases

REVIEW ARTICLE

Rapid Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review and Meta-analysis

Andrea H. L. Bruning,[1] Mariska M. G. Leeflang,[2] Johanna M. B. W. Vos,[1] Rene Spijker,[3] Menno D. de Jong,[4] Katja C. Wolthers,[4] and Dasja Pajkrt[1]

[1]Department of Pediatric Infectious Diseases, Emma Children's Hospital, [2]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, [3]Medical Library, and [4]Department of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands

- Older study, meta-analysis of various rapid antigen detection tests for Influenza and RSV
- Sensitivity (Influenza)
  - 4.4% to 100% ; summary estimate: 61.1%
  - Specificity: 98%
- Sensitivity (RSV)
  - 41.2% to 88.6% ; summary estimate: 75.3%
  - Specificity: 98.7%

FDA : Reclassification of RIDTs from Class I to Class II
(January 12, 2017)

	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)
Influenza		
Virus type		
Influenza A	68.1 (58.9–76.0)	99.2 (98.5–99.6)
H1N1	54.0 (47.6–60.3)	99.1 (98.5–99.5)
Influenza B	71.0 (56.8–82.1)	99.6 (99.2–99.8)
Influenza A+B	61.1 (53.3–68.3)	98.9 (98.4–99.3)
Population		
Children	66.1 (52.9–79.3)	98.3 (97.2–99.5)
Adults	34.1 (14.0–54.1)	99.2 (98.2–100.0)
Point-of-care testing	62.1 (47.6–74.7)	98.4 (96.7–99.2)
Rapid test		
QuickVue Influenza A+B	44.6 (29.1–60.0)	99.3 (98.8–99.9)
Sofia Influenza A+B	75.3 (59.2–91.5)	95.3 (91.5–99.2)
BinaxNow Influenza A&B	44.1 (23.3–64.9)	99.4 (98.6–100.0)
Directigen Flu A+B	35.8 (11.8–59.7)	99.2 (98.0–99.4)
mariPOC	76.1 (53.5–98.7)	99.4 (98.3–100.0)
RSV		
Population		
Children	75.9 (73.1–78.5)	98.5 (968–99.4)
Mixed	70.9 (63.0–77.8)	99.1 (95.9–99.8)
Point-of-care testing	76.0 (69.8–81.2)	99.1 (95.5–99.8)
Rapid test		
BD Veritor RSV	76.9 (71.0–82.8)	98.9 (97.1–100.0)
BinaxNOW RSV	72.2 (65.2–79.1)	98.6 (96.5–100.0)
Sofia RSV	80.0 (73.0–86.9)	97.8 (93.8–100.0)

Abbreviations: CI, confidence interval; RSV, respiratory syncytial virus.

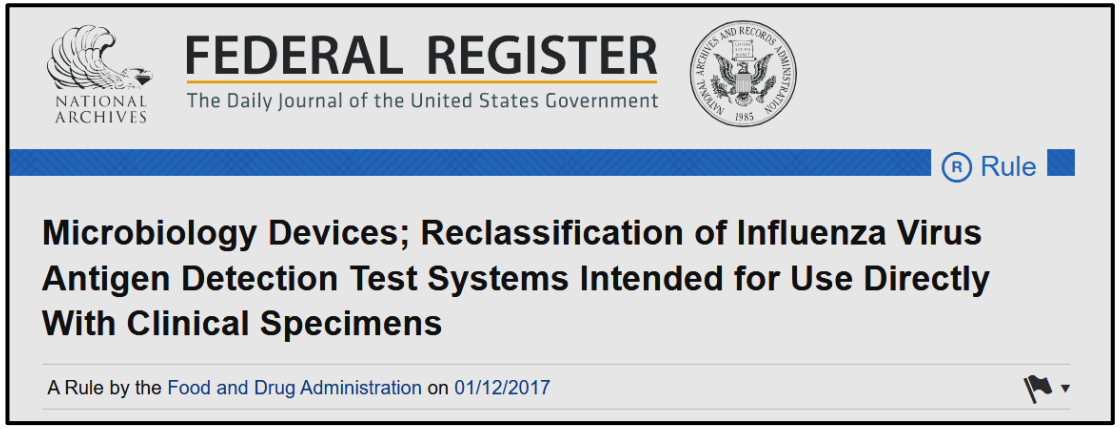
Clin Infect Dis 2017; 65 (6): 1026-1032
J Clin Microbiol 2018; 56 (10): e00711-18

Rapid Antigen Tests for Influenza – FDA Device Reclassification

RIDTs have been widely used since the 1990s due to their ease of use, rapid results, and suitability for point of care (POC) testing.

RIDTs are known for lower diagnostics sensitivity (depending on prevalence) !

RIDTs demonstrated poor performance during 2009 H1N1 Influenza Pandemic.



RIDTs reclassified from Class I to Class II Devices

SENSITIVITY

- Compared to RT-PCR, FDA-cleared RIDTs must achieve 80% sensitivity for detection of influenza A and influenza B viruses.
- Compared to viral culture, FDA-cleared RIDTs must achieve 90% sensitivity for detection of influenza A and 80% sensitivity to detect influenza B viruses.

SPECIFICITY

- Compared to RT-PCR, FDA-cleared RIDTs must achieve 95% specificity for detection of influenza A and influenza B viruses.
- Compared to viral culture, FDA-cleared RIDTs must achieve 95% specificity for detection of influenza A and influenza B viruses.

J Clin Microbiol 2018; 56 (10): e00711-18
www.federalregister.gov/documents/2017/01/12/2017-00199/microbiology-devices-reclassification-of-influenza-virus-antigen-detection-test-systems-intended-for

Rapid Diagnostic Tests for Influenza: Predictive Value depends upon Prevalence

if Influenza Prevalence is	and Test Specificity is	then PPV is	False Positive Rate is
Very low (2.5%)	Moderate (80%)	Very Low (6-12%)	Very High (88-94%)
Very low (2.5%)	High (98%)	Low (39-56%)	High (44-61%)
Moderate (20%)	Moderate (80%)	Low (39-56%)	High (44-61%)
Moderate (20%)	High (98%)	HIGH (86-93%)	LOW (7-14%)

- **RIDTs are not recommended for use in hospitalized patients with suspected influenza**
- Molecular assays, including RT-PCR, are recommended for testing respiratory tract specimens from hospitalized patients because of their high sensitivity and high specificity
- interpretation of positive results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested
- if an important clinical decision is affected by the test result, the RIDT result should be confirmed by a molecular assay, such as reverse transcription polymerase chain reaction (RT-PCR).

www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm

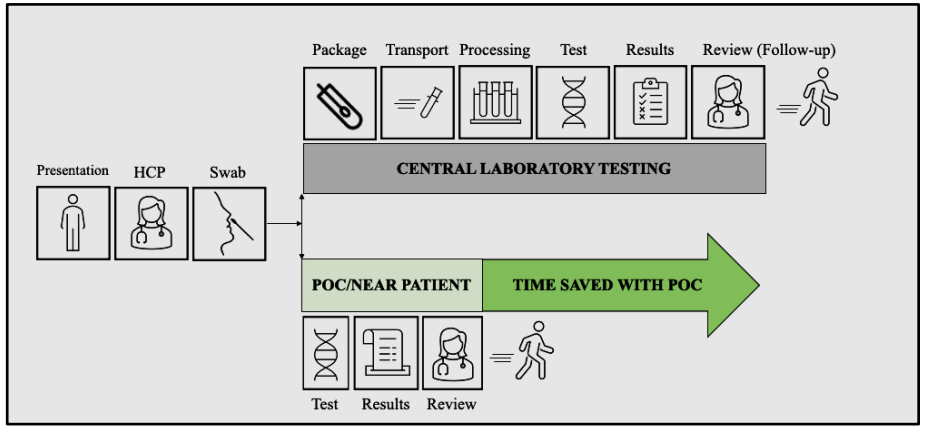
Rapid Diagnostic Tests for Influenza: Predictive Value depends upon Prevalence

if Influenza Prevalence is	and Test Specificity is	then PPV is	False Positive Rate is
Moderate (20%)	Low (50%)	Moderate (86-89%)	Moderate (11-14%)
Moderate (20%)	**High (90%)**	**HIGH (97-99%)**	**LOW (2-3%)**
High (40%)	Low (50%)	Moderate (70-75%)	Moderate (25-35%)
High (40%)	**High (90%)**	**HIGH (93-94%)**	**LOW (6-7%)**

- **RIDTs are not recommended for use in hospitalized patients with suspected influenza**
- Molecular assays, including RT-PCR, are recommended for testing respiratory tract specimens from hospitalized patients because of their high sensitivity and high specificity.
- interpretation of negative results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested
- if an important clinical decision is affected by the test result and influenza is still suspected, then the RIDT result should be confirmed by a molecular assay, such as RT-PCR

www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm

When is the use of a Rapid Influenza Diagnostic Test useful ?



Useful when Results TAT matters !

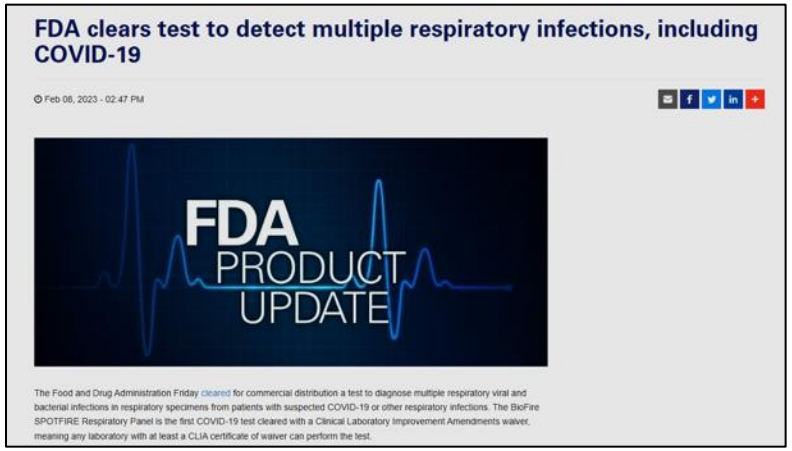
Useful when Resources are Limited !

- Testing to identify or monitor an outbreak (e.g., in LTCF, nursing homes, cruise ships, summer camps, schools, etc.)
- Testing during "regular" Influenza season
  - testing of selected patients presenting with acute respiratory illnesses compatible with influenza
  - can help establish whether influenza is present in a specific outpatient population
  - Can help health-care providers determine how to use their clinical judgment for diagnosing and treating respiratory illness
  - Testing does not need to be done for every patient
- For outpatients with suspected influenza:
  - rapid molecular assays are recommended over RIDTs
- For hospitalized patients with suspected influenza:
  - molecular assays are recommended

www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm

Home Respiratory Testing - Beyond Traditional Clinical Settings

Rapid Antigen Detection Assays



www.fda.gov/news-events/press-announcements/fda-authorizes-first-over-counter-home-test-detect-both-influenza-and-covid-19-viruses

Benefits

- Easy to use at the point of care
- May provide assurance to patients
- May provide immediately actionable test results

Challenges/Limitations

- May be difficult to interpret when "borderline" results are present
- Currently no clear guidance on follow-up and/or interventions on positive tests
- No ability to capture data for surveillance and/or Flu / SARS-CoV-2 sequencing testing
- If negative:
  - Repeat antigen test at 48-hours[1]
  - Confirm negatives with NAAT, if suspicion remains high[1]

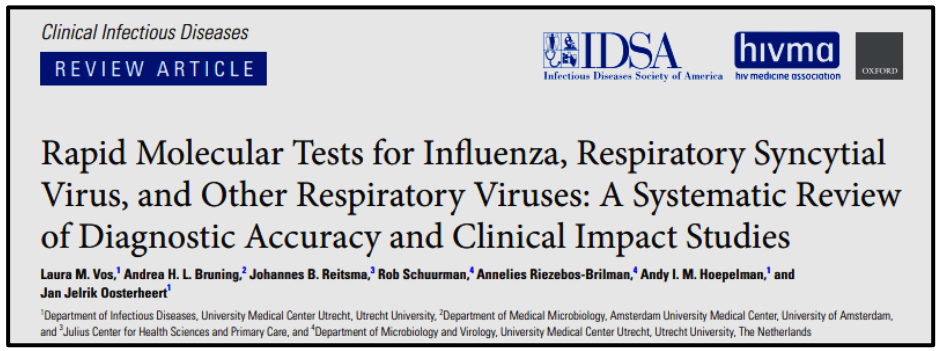
Future Trends/Needs?

- Integration of testing approaches across various healthcare settings, incl. home testing
- Use of AI technology to connect results of At-Home-Testing to continued clinical care and further laboratory testing

- At-Home Testing became a useful measure during the COVID-19 pandemic to reduce the further spread of illness in the community (e.g., schools, workplaces, universities)
- At-Home testing coupled with NPIs could be beneficial to prevent extended spread of respiratory illness (Flu, COVID), but depends on peoples ability to isolate at home when test-positive
- Need to understand that false-positive as well as false-negative test results can occur

1. CDC. COVID-19 Testing: What You Need to Know., updated Sept 25, 2023.

Rapid Molecular Tests for Influenza, RSV, and COVID



Clinical Infectious Diseases

REVIEW ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Rapid Molecular Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review of Diagnostic Accuracy and Clinical Impact Studies

Laura M. Vos,[1] Andrea H. L. Bruning,[2] Johannes B. Reitsma,[3] Rob Schuurman,[4] Annelies Riezebos-Brilman,[4] Andy I. M. Hoepelman,[1] and Jan Jelrik Oosterheert[1]

[1]Department of Infectious Diseases, University Medical Center Utrecht, Utrecht University, [2]Department of Medical Microbiology, Amsterdam University Medical Center, University of Amsterdam, and [3]Julius Center for Health Sciences and Primary Care, and [4]Department of Microbiology and Virology, University Medical Center Utrecht, Utrecht University, The Netherlands

Systematic Meta-Analysis of various rapid molecular assays

- Pooled sensitivity: 90.9%*
- Pooled specificity: 96.1%*

- Higher sensitivity in children than adults

- Difference between singleplex *vs*. multiplex assays
- Multiplex assays had lower specificity

- Two studies implemented guidelines for treatment decisions & antibiotic stewardship

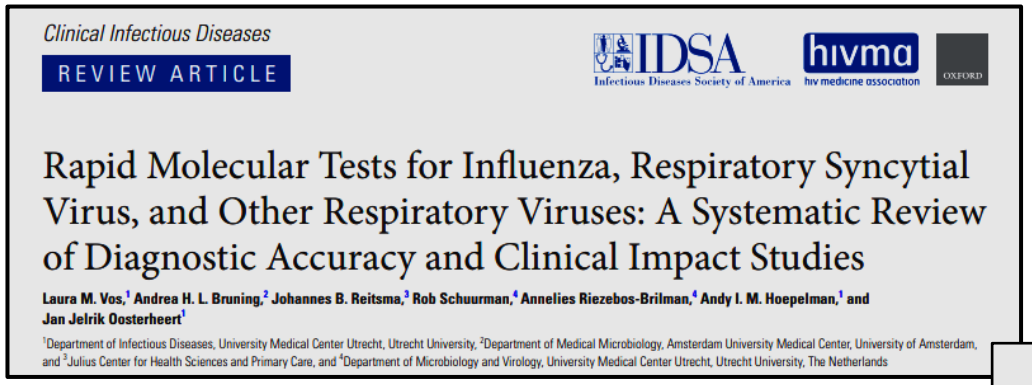
Characteristic	No. of Studies	Pooled Sensitivity, % (95% CI)	*P* Value[a]	Pooled Specificity, % (95% CI)	*P* Value[a]
Population age group					
Children	8	93.0 (91.5–94.5)	.010	80.8 (73.1–88.4)	.001
Adults	7	79.8 (70.7–88.9)		98.6 (95.5–100)	
Population symptoms					
Respiratory/ILI	34	90.4 (87.2–93.7)	.655	96.2 (93.6–98.7)	.478
Unclear	29	91.4 (88.6–94.2)		94.8 (91.9–97.7)	
Viruses					
Influenza	29	87.9 (83.7–92.1)	.078[b]	97.4 (94.2–100)	.009[b]
Influenza + RSV	19	94.1 (90.9–97.4)		96.4 (93.6–99.2)	
Panel of viruses	14	91.8 (88.7–95.0)		88.8 (82.7–95.0)	
Index test					
Alere i Influenza A&B	14	81.6 (75.4–87.9)	.000[c]	94.0 (86.0–100)	.623
Cobas Liat Influenza A/B	5	98.1 (90.8–100)		99.7 (88.5–100)	
FilmArray	10	89.2 (86.4–92.0)		96.1 (90.5–100)	
Simplexa Flu A/B & RSV	9	99.0 (98.3–99.6)		98.2 (93.3–100)	
Verigene RV Plus test	5	96.2 (88.0–100)		97.1 (87.6–100)	
Cepheid Xpert Flu	9	94.9 (91.1–98.6)		100 (97.8–100)	
Study design					
Cohort	28	94.7 (92.5–96.8)	.009	96.5 (94.3–98.8)	.147
Case-control	28	88.8 (85.2–92.5)		91.2 (84.5–97.9)	
Prospective or retrospective study					
Prospective	25	91.4 (89.2–93.6)	.461	95.9 (93.4–98.5)	.200
Retrospective	29	89.7 (86.0–93.4)		91.9 (85.7–98.1)	

- **Results of Clinical Impact Studies were heterogenous**
- **Rapid molecular tests:**
  - **Significantly faster than traditional PCR (reference test method)**
  - **Reduced length of hospital stay in some studies**
  - **Increased appropriate use of oseltamivir in influenza–positive patients**
  - **Potentially reduced costs and additional radiographs**
  - **Overall did not decrease number of antibiotic prescriptions**

*Reported test performance analysis may not represent the current sensitivity and specificity of newer generation rapid assays.

Clin Infect Dis 2019; 69 (7): 1243-1253

Rapid Molecular Tests for Influenza, RSV, and COVID



Clinical Infectious Diseases

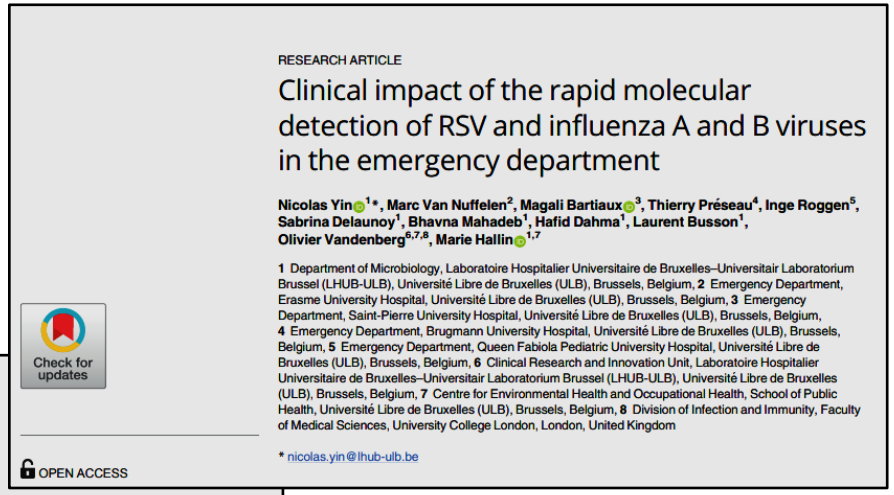
REVIEW ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Rapid Molecular Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review of Diagnostic Accuracy and Clinical Impact Studies

Laura M. Vos,[1] Andrea H. L. Bruning,[2] Johannes B. Reitsma,[3] Rob Schuurman,[4] Annelies Riezebos-Brilman,[4] Andy I. M. Hoepelman,[1] and Jan Jelrik Oosterheert[1]

[1]Department of Infectious Diseases, University Medical Center Utrecht, Utrecht University, [2]Department of Medical Microbiology, Amsterdam University Medical Center, University of Amsterdam, and [3]Julius Center for Health Sciences and Primary Care, and [4]Department of Microbiology and Virology, University Medical Center Utrecht, Utrecht University, The Netherlands



RESEARCH ARTICLE

Clinical impact of the rapid molecular detection of RSV and influenza A and B viruses in the emergency department

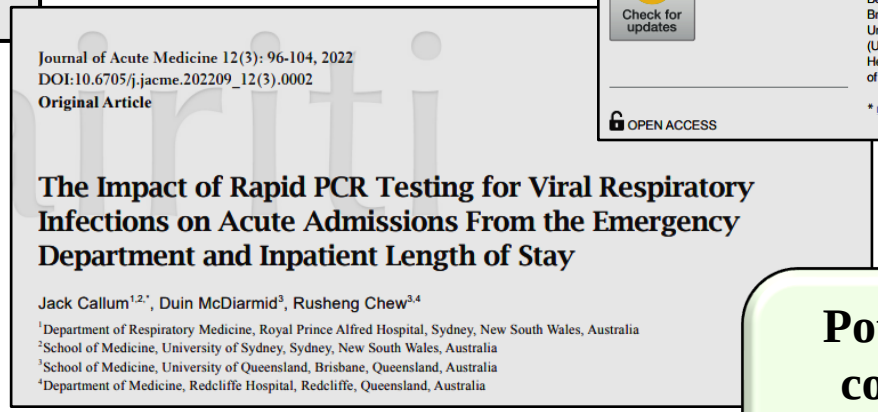
Nicolas Yin[1]*, Marc Van Nuffelen[2], Magali Bartiaux[3], Thierry Préseau[4], Inge Roggen[5], Sabrina Delaunoy[1], Bhavna Mahadeb[1], Hafid Dahma[1], Laurent Busson[1], Olivier Vandenberg[6,7,8], Marie Hallin[1,7]

1 Department of Microbiology, Laboratoire Hospitalier Universitaire de Bruxelles–Universitair Laboratorium Brussel (LHUB-ULB), Université Libre de Bruxelles (ULB), Brussels, Belgium, 2 Emergency Department, Erasme University Hospital, Université Libre de Bruxelles (ULB), Brussels, Belgium, 3 Emergency Department, Saint-Pierre University Hospital, Université Libre de Bruxelles (ULB), Brussels, Belgium, 4 Emergency Department, Brugmann University Hospital, Université Libre de Bruxelles (ULB), Brussels, Belgium, 5 Emergency Department, Queen Fabiola Pediatric University Hospital, Université Libre de Bruxelles (ULB), Brussels, Belgium, 6 Clinical Research and Innovation Unit, Laboratoire Hospitalier Universitaire de Bruxelles–Universitair Laboratorium Brussel (LHUB-ULB), Université Libre de Bruxelles (ULB), Brussels, Belgium, 7 Centre for Environmental Health and Occupational Health, School of Public Health, Université Libre de Bruxelles (ULB), Brussels, Belgium, 8 Division of Infection and Immunity, Faculty of Medical Sciences, University College London, London, United Kingdom

* nicolas.yin@lhub-ulb.be

Check for updates

OPEN ACCESS



Journal of Acute Medicine 12(3): 96-104, 2022
DOI:10.6705/j.jacme.202209_12(3).0002

Original Article

The Impact of Rapid PCR Testing for Viral Respiratory Infections on Acute Admissions From the Emergency Department and Inpatient Length of Stay

Jack Callum[1,2,*], Duin McDiarmid[3], Rusheng Chew[3,4]

[1]Department of Respiratory Medicine, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia
[2]School of Medicine, University of Sydney, Sydney, New South Wales, Australia
[3]School of Medicine, University of Queensland, Brisbane, Queensland, Australia
[4]Department of Medicine, Redcliffe Hospital, Redcliffe, Queensland, Australia

Rapid Molecular Assays for Influenza, RSV, and COVID-19 are accurate with reasonably high sensitivity & Specificity

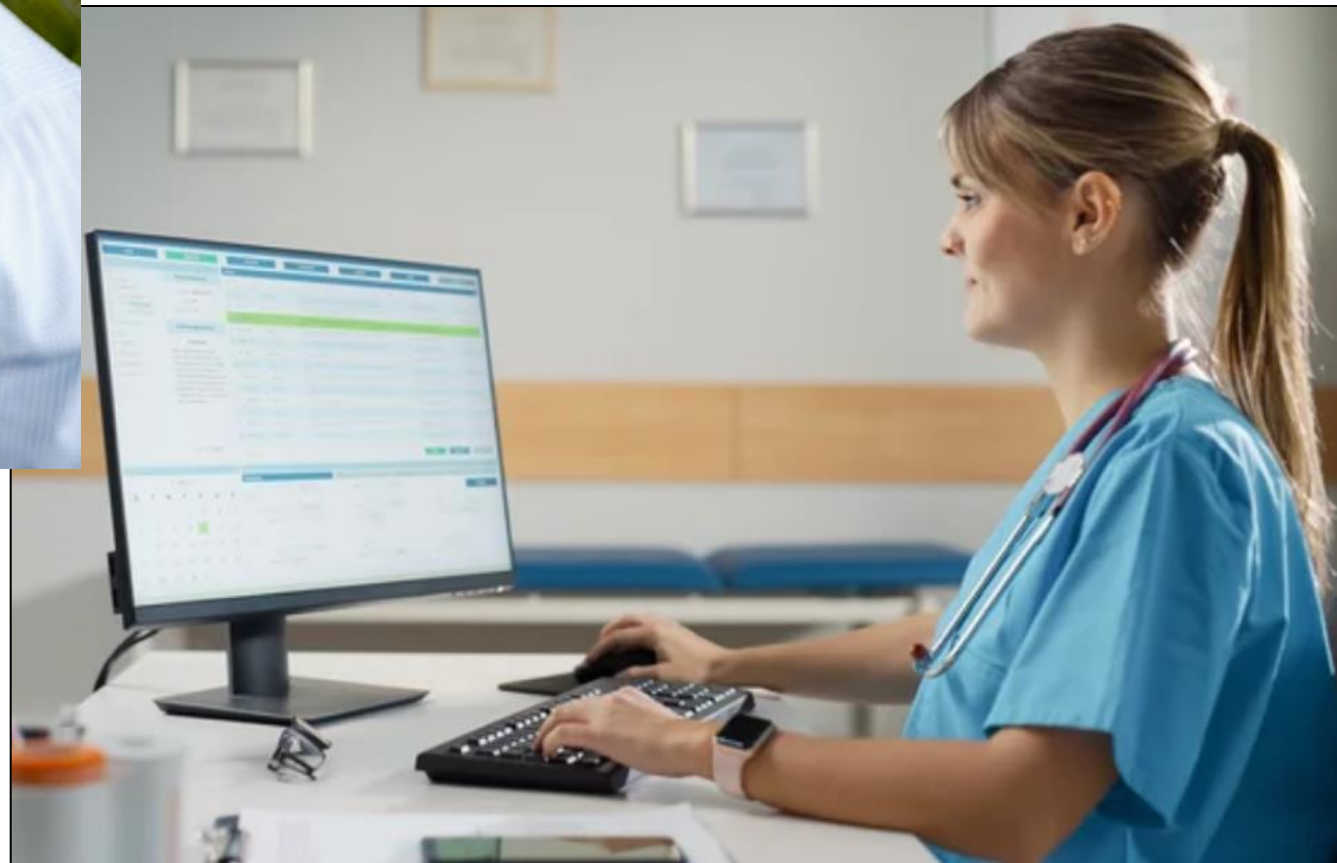
Rapid Molecular Assays for Influenza, RSV, and COVID-19 improve clinical management in patient admitted to the Emergency Room

To assess the impact on Antibiotic Stewardship, use of antiviral medications, and hospital LoS, further studies will be necessary

Potential concerns regarding cost and TAT (compared to RADTs) have largely been overcome by recent technological innovations

Clin Infect Dis 2019; 69 (7): 1243-1253
PLOS ONE 2022; 17 (9): e027422
J Acute Med 2022; 12 (3): 96-104

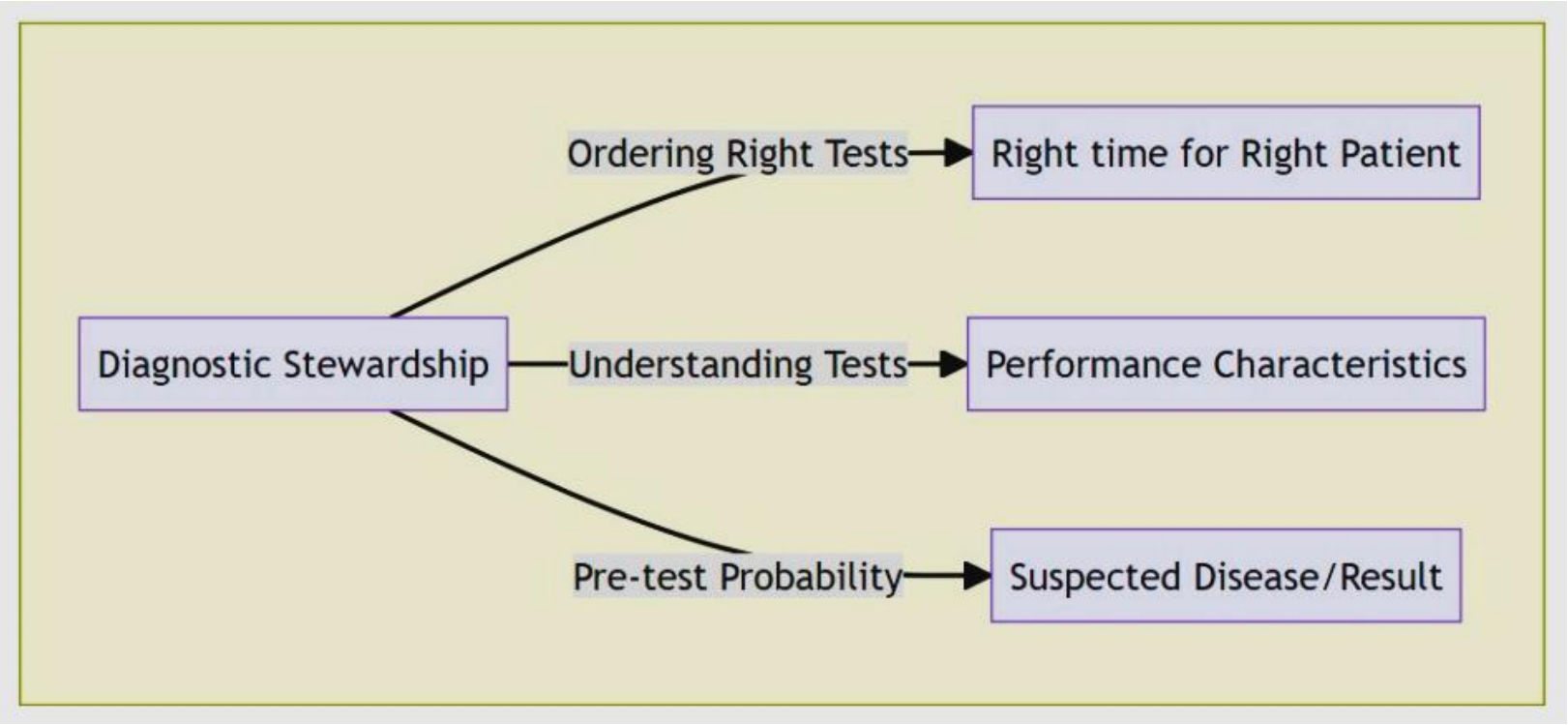
Perspectives on rapid test platform efficiency and diagnostic stewardship strategies within current healthcare constraints



Laboratory Diagnostic Stewardship

Antimicrobial Stewardship Programs

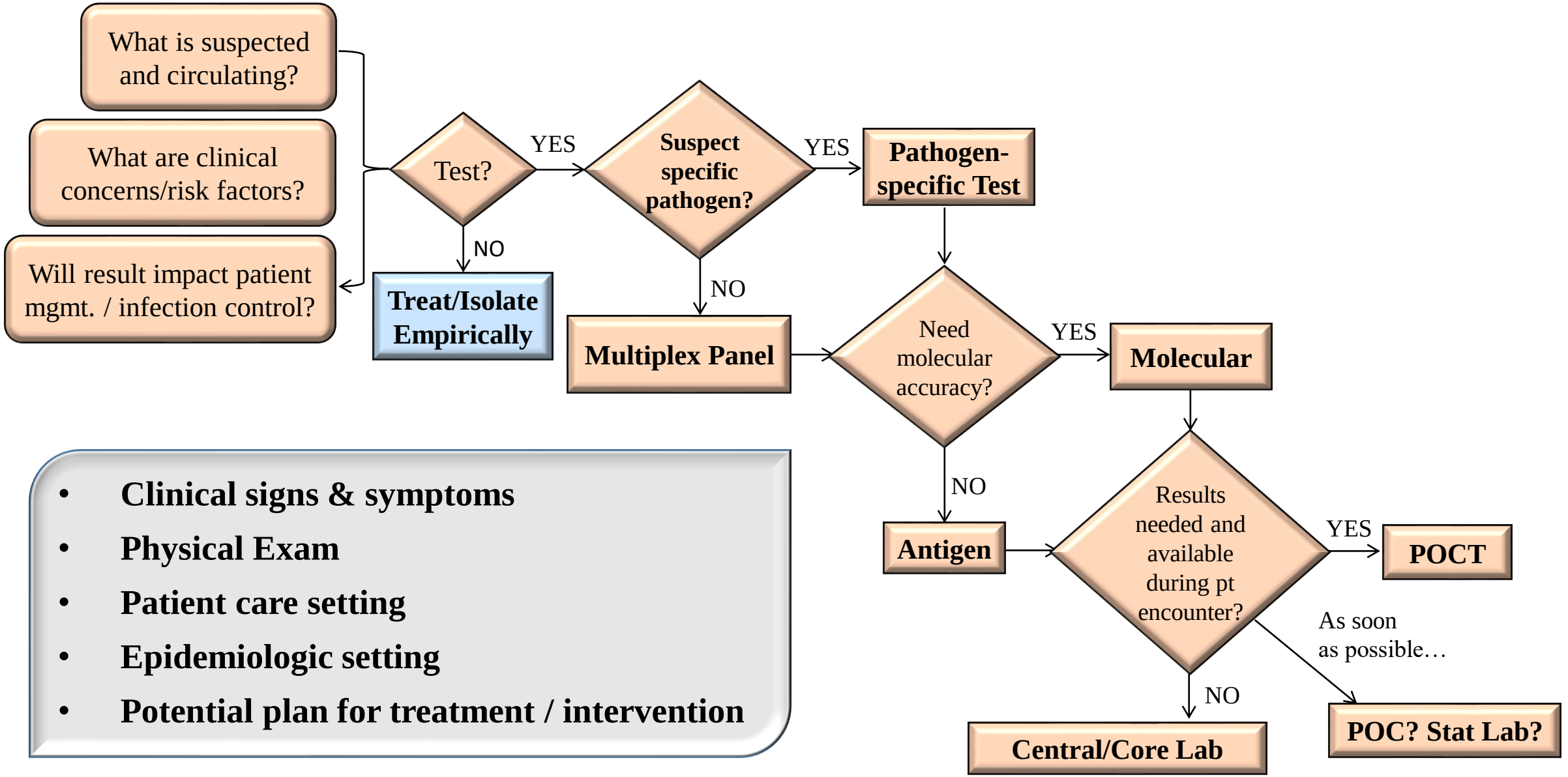
- to ensure that patients receive timely & appropriate antimicrobial therapy
- to reduce the overuse of unnecessary and/or inappropriate antimicrobial therapy
- to reduce (unnecessary and excessive) cost of therapy
- to reduce occurrence of medication-related adverse events



- **Diagnostic stewardship across the entire diagnostic pathway**
- **Diagnostic stewardship touches on all 3 phases of laboratory testing**
- **Important considerations for pre-test probability must be taken into account when ordering laboratory tests**
- **Diagnostic stewardship is not just applicable to Acute Care settings, but also in ambulatory care and other settings, e.g., LTCFs**
- **Diagnostic stewardship might be useful for infection control & prevention**

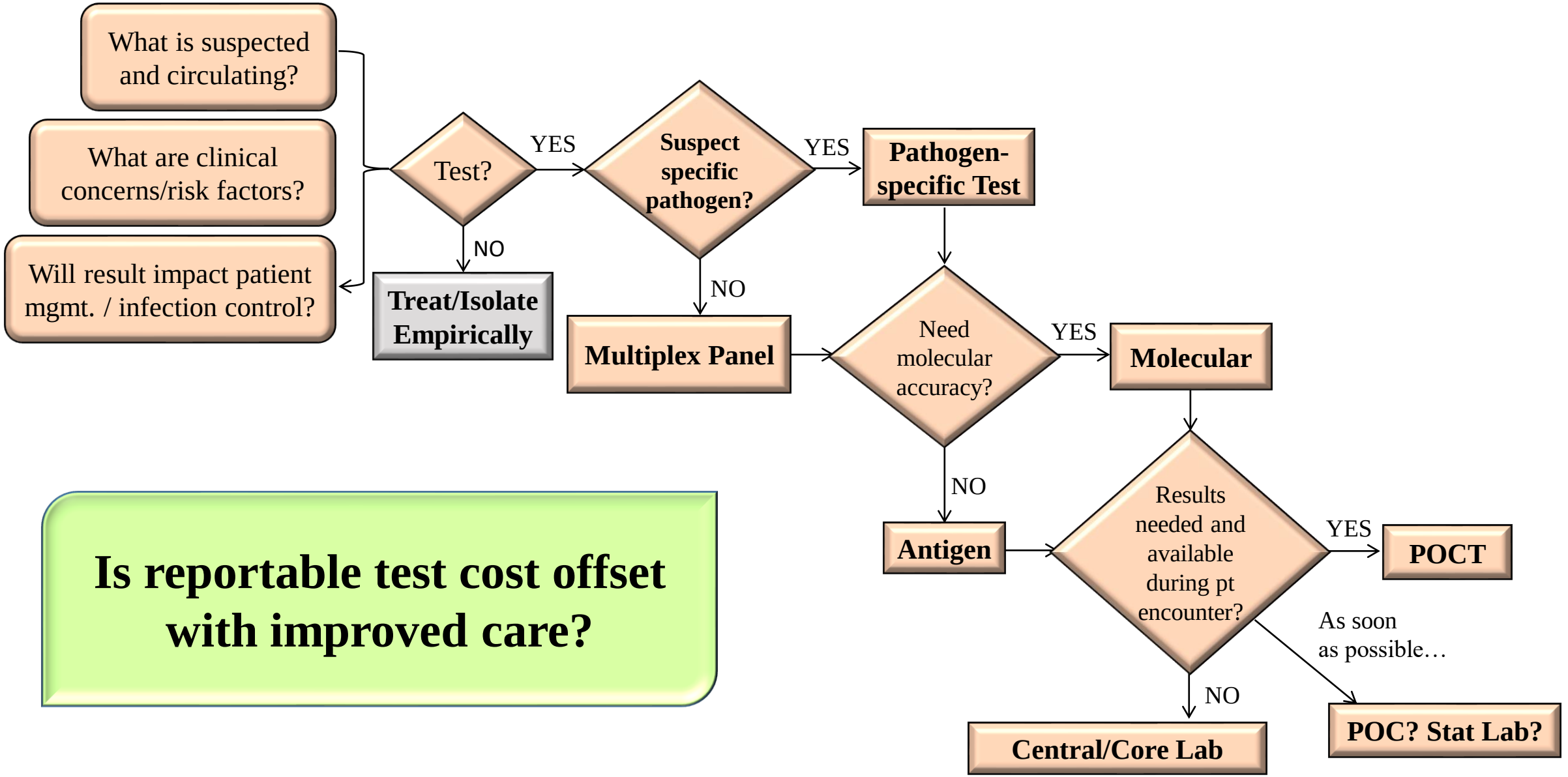
Microorganisms 2023, 11, 2214. https://doi.org/10.3390/microorganisms11092214
Int J Antimicrob Agents 2023; 62 (1): 106816

Diagnostic Testing Based On Clinical Needs and Utility



- **Clinical signs & symptoms**
- **Physical Exam**
- **Patient care setting**
- **Epidemiologic setting**
- **Potential plan for treatment / intervention**

Diagnostic Testing Based On Clinical Needs and Utility



Is reportable test cost offset with improved care?

Molecular POC Testing for Influenza A/B and RSV

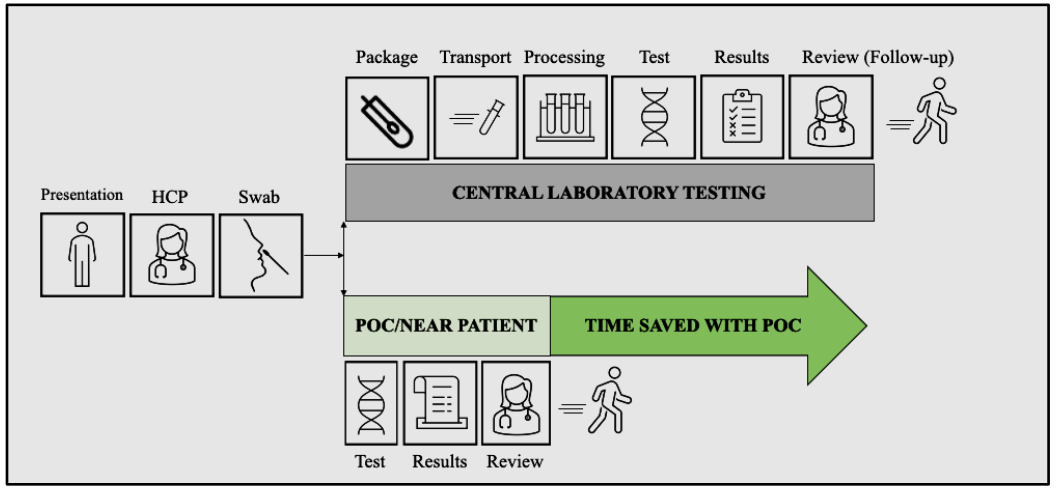
Original research

OPEN ACCESS

Molecular point-of-care testing for influenza A/B and respiratory syncytial virus: comparison of workflow parameters for the ID Now and cobas Liat systems

Stephen Young [1,2] Jamie Phillips,[3] Christen Griego-Fullbright,[2] Aaron Wagner,[2] Patricia Jim,[2] Sheena Chaudhuri,[4] Shaowu Tang,[4] Joanna Sickler[4]

- Comparison of workflow with Abbott ID NOW (Abbott Diagnostics) and the Liat PCR system (Roche Diagnostics)
- Both systems are rapid molecular, potentially POC testing systems
- Both systems offer different workflow options



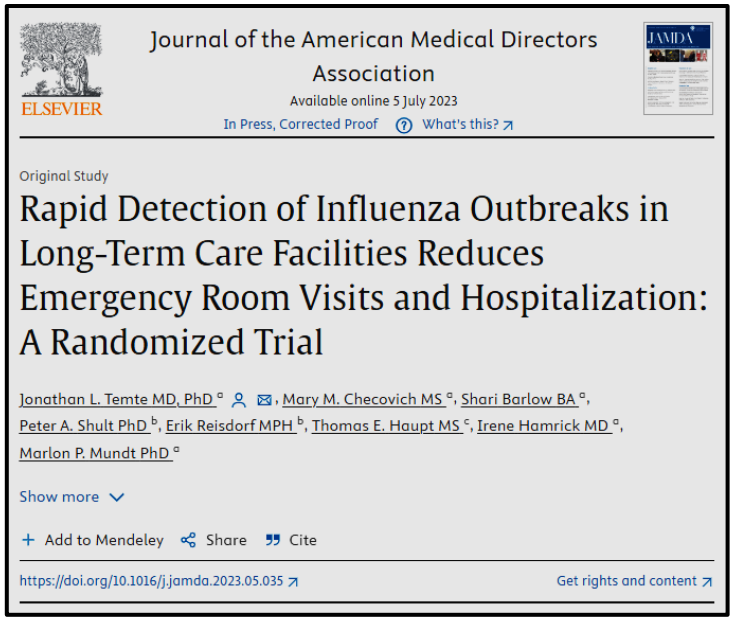
- **Liat PCR had a TAT of 21.6 min.**
- **ID NOW sequential testing had longest TAT for influenza & RSV (up to 30 min.)**
- **ID NOW parallel testing had shortest TAT (15 min.)**

Both analyzers have comparable analytical performance characteristics

With comparable analytical performance characteristics, approach to selection of rapid molecular tests system depends on TAT and workflow considerations, incl. use of multiple analyzers

J Osteopath Med 2023; 123 (1): 39-47
Clin Lab Med 2022; 42: 223-236
J Clin Pathol 2020; 73: 328-334

Impact of Rapid Diagnostics tests in LTCFs



Journal of the American Medical Directors Association

Available online 5 July 2023

In Press, Corrected Proof What's this?

Original Study

Rapid Detection of Influenza Outbreaks in Long-Term Care Facilities Reduces Emergency Room Visits and Hospitalization: A Randomized Trial

Jonathan L. Temte MD, PhD [a], Mary M. Checovich MS [a], Shari Barlow BA [a], Peter A. Shult PhD [b], Erik Reisdorf MPH [b], Thomas E. Haupt MS [c], Irene Hamrick MD [a], Marlon P. Mundt PhD [a]

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https://doi.org/10.1016/j.jamda.2023.05.035 Get rights and content

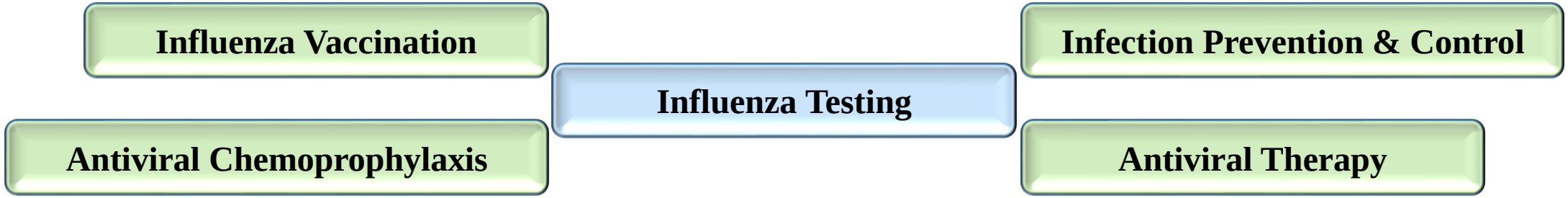
- Cost associated with influenza for LTCF residents is enormous
- Methods for Influenza detection in LTCFS are
  - difficult to implement
  - reactive & often delayed, or nonexistent
- When influenza activity is present in the local community, daily active surveillance for influenza among all new and current residents should be conducted
- Even if it's not influenza season, influenza testing should occur when any resident has signs and symptoms of acute respiratory illness or influenza-like illness.

Nurse-initiated nasal specimen collection and testing for influenza with an on-site RIDT during influenza season resulted in :

- **Significantly increased use of oseltamivir for prophylaxis**
- **Decreased ED visits (22%), hospitalizations (21%), and hospital length-of-stay (36%)**

www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm

Preventing Influenza Transmission in LTCFs



- **Perform testing for symptomatic residents, even if influenza is not circulating in community**
- **Perform testing with molecular assays, including rapid molecular assays, other molecular tests, or reverse transcription polymerase chain reaction (RT-PCR)**
- **If molecular tests are not available, and antigen detection tests are used such as rapid influenza diagnostic tests (RIDTs) or immunofluorescence assays, false negative results can occur**
- **If influenza is suspected and RIDTs or immunofluorescence results are negative, perform confirmatory testing using molecular influenza assays**
- **If Influenza and COVID-19 are co-circulating test for both viruses, using NAAT**
  - if NAAT is not available, may use RADT
  - if RADT is negative for COVID or Flu confirm with NAAT or 2nd RADT 48 hrs. after 1st test for COVID
  - if repeat test negative, consider testing for other viral and/or bacterial pathogens

1. CDC. Interim Guidance for Influenza Outbreak Management in Long-Term Care and Post-Acute Care Facilities. Updated Nov 21, 2022.
2. CDC. Testing and Management Considerations for Nursing Home Residents with Acute Respiratory Illness Symptoms when SARS-CoV-2 and Influenza Viruses are Co-circulating, updated Nov 22, 2022.

Choosing the best diagnostic test – an ongoing challenge

Rapid Molecular Test Methods

- Disease Prevalence
- Patient Age
- Co-Morbidities
- Available Treatments
- Non-pharmaceutical Interventions

Rapid Antigen Detection Tests

Waived Antigen Detection Tests

- Home
- Physicians Office
- Urgent Care Center
- Emergency Department
- Community Hospital
- Tertiary Care Hospital Network
- Academic Medical Center
- Long-Term Care Facility

High-throughput Molecular Test Methods

Choosing the best diagnostic test – an ongoing challenge

Rapid Molecular Test Methods

Waived Antigen Detection Tests

- Disease Prevalence
- Patient Age
- Co-Morbidities
- Available Treatments
- Non-pharmaceutical Interventions

- Pathogen-specific *vs.* Pathogen Panel
- What is the desired / most appropriate TAT ?
- What is the utility for prevention of further spread?
- What is the impact on clinical patient care?
- What is the acceptable cost per reportable?

- Home
- Physicians Office
- Urgent Care Center
- Emergency Department
- Community Hospital
- Tertiary Care Hospital Network
- Academic Medical Center
- Long-Term Care Facility

Rapid Antigen Detection Tests

High-throughput Molecular Test Methods

Lessons Learned from Pandemics…… (?)

https://www.cdc.gov/h1n1flu/cdcresponse.htm#:~:text=CDC%20released%20its%20first%20official,time%20on%20May%2014%2C%202010.

2009 : H1N1 – Influenza Pandemic

2019 : SARS-CoV-2 / COVID-19 Pandemic

www.reuters.com/world/americas/brazils-covid-19-response-cost-thousands-lives-says-humanitarian-group-2021-04-15/

2011: ASM Working Group
Current Best Practices for Respiratory Virus Testing

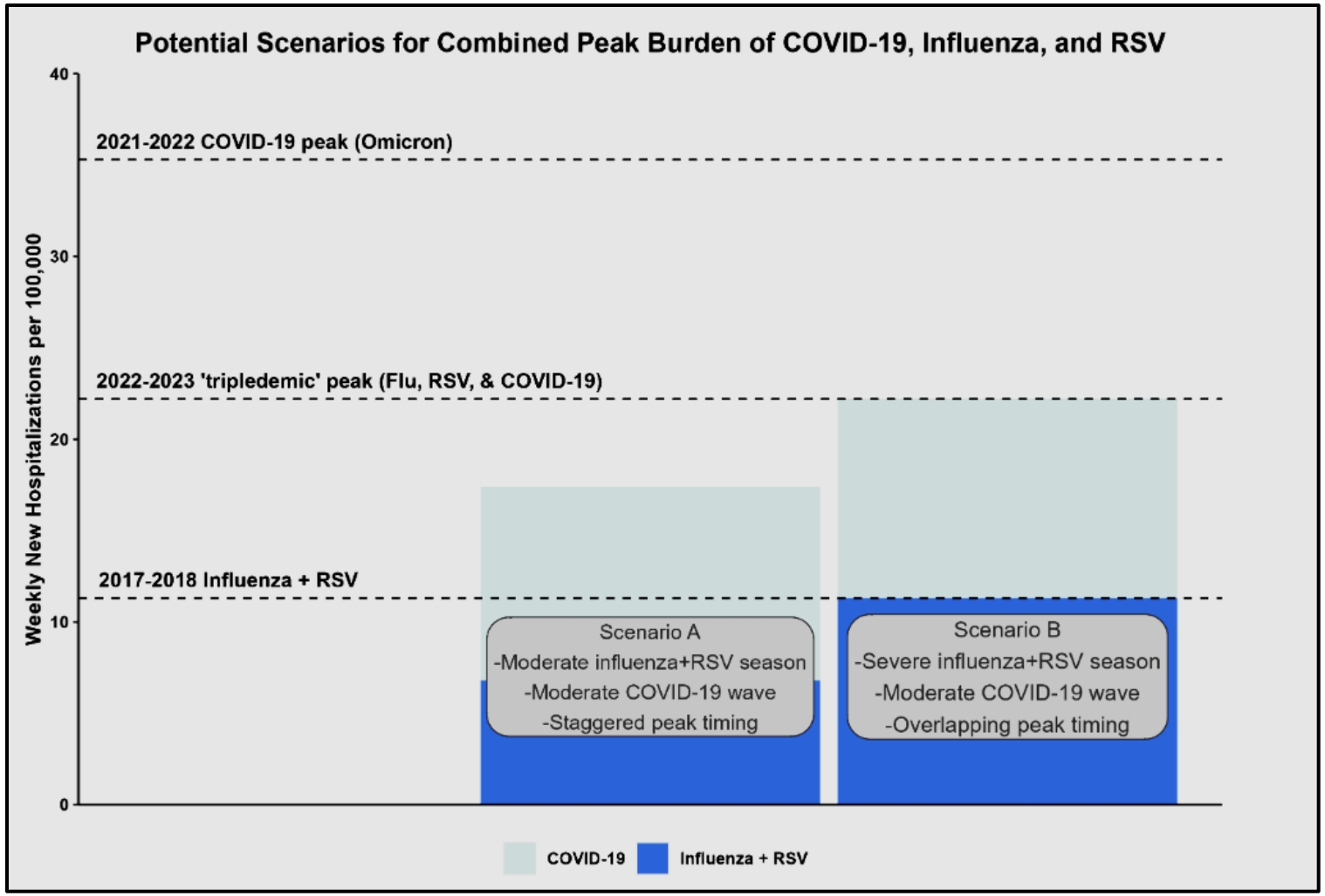
- Traditional virus detection (prior to 2011) : RADTs ; DFA testing ; viral culture
- Easy-to-use and/or POC NAAT were not yet widely available in 2011 (some in consideration & in development)
- Use of NAATs has dramatically changed the approach to diagnosis of viral respiratory tract infections
- Questions regarding scope of testing, multiplex-testing remained unanswered (considering experiences from the 2009 H1N1 pandemic (e.g., testing the "worried well", specimen selection criteria, test performance characteristics)

Ginocchio CC, McAdam AJ. *J Clin Microbiol* 2011; 49 (9): S44-S48

- **Laboratory Testing for respiratory viruses continued to evolve in the years following the H1N1 pandemic**
- **sample-to-answer Molecular Tests for Influenza & RSV, and then COVID-19 were developed**
- **RADT (e.g., RIDT) less useful in hospitalized and ER patients**

Similar Lessons Learned after 2009 H1N1 and recent COVID-19 Pandemic

Respiratory Virus Activity 2023 – what to expect ?



www.cdc.gov/forecast-outbreak-analytics/about/season-outlook.html

Scenario A

- Moderate past season peak for influenza equal to 2019/2020
- Moderate COVID-19 wave equal to Winter 2022/2023
- COVID-19 peaks ~3 weeks prior to Influenza & RSV
- Peak hospitalization rate is ~20% lower than 2022/2023
- Influenza/RSV peak is higher than level of severity or influenza & RSV combined

Scenario B

- **Severe** past season peak for influenza equal to 2017/2018
- Moderate COVID-19 wave equal to Winter 2022/2023
- COVID-19 peak is shifted so that peak occurs in the same week as Influenza & RSV hospitalizations
- Peak hospitalization rate is similar to that of the 2022/2023 season
- Peak hospitalization slightly higher than hospitalization rate for COVID-19 alone (2020/2021)

Future trends for laboratory testing during “Flu Season”

Return of Influenza & RSV transmission during the Winter months (as prior to pandemic)

SARS-CoV-2 may cause Mini-Waves and/or regional outbreaks rather than seasonal surges

Co-infections among SARS-CoV-2, Influenza and/or RSV may occur

Improved treatment options for all 3 illnesses and vaccines are available

Future trends for laboratory testing during “Flu Season”

Return of Influenza & RSV transmission during the Winter months (as prior to pandemic)

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Co-infections among SARS-CoV-2, Influenza and/or RSV may occur

Improved treatment options for all 3 illnesses and vaccines are available

Laboratory testing should include assays for SARS-CoV-2, Influenza A/B, and RSV for hospitalized patients, LTCF patients, and immunosuppressed patients in accordance with their clinical presentation, signs & symptoms, and the respective disease prevalence

Selection of testing method (rapid molecular, cartridge-based tests *vs*. high-throughput testing) should be based on clinical needs in a specific patient care setting & location (ED *vs*. Hospital Inpatient *vs*. Urgent Care *vs*. Near-Patient-Testing/LTCF)

Conclusions

RSV & Influenza are predictable causes of URTIs in LTCF Patients

The landscape for URTI testing methods is constantly evolving

Continued need to implement integrated approaches to testing for specific healthcare settings (molecular tests *vs*. RADTs)

In hospitalized patients, molecular multiplex assays for Influenza, RSV, and SARS-CoV-2 may reduce time and increase efficiency to detect multiple pathogens

Rapid molecular testing in conjunction with diagnostic stewardship efforts in LTCFs and ambulatory care settings will likely improve patient care management

Thank You!

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Within a few days following today's event, visit

https://www.whitehatcom.com/abbott

Mitigating RSV and Influenza with Rapid Testing in Adults

Live Event: Wednesday, October 18, 2023 | 1:00 - 2:00 PM Eastern Time
P.A.C.E.® credit available until October 18, 2024
Florida Laboratory CE Credit available

RECORDING

SLIDES

Join this program for a timely update on respiratory infections and mitigation strategies in adult populations, particularly those at greater risk of severe illness and complications. A key element focuses on rapid testing with expert perspectives on test types, clinical utility, and improved testing efficiencies, including diagnostic stewardship.

The webinar will:

- Summarize epidemiological trends and risk factors for severe RSV and Influenza infections
- Review challenges and impact of RSV and Flu infections in acute and congregate care settings
- Describe rapid test technology types and differences
- Share perspectives on rapid test platform efficiency and diagnostic stewardship strategies within current healthcare constraints

Presenter:

Stefan Riedel, MD, PhD, D(ABMM), FCAP

Associate Medical Director
Clinical Microbiology Laboratories
Beth Israel Deaconess Medical Center
Boston, MA

Please direct additional questions to:

ardxmedicaleducation@abbott.com

Mitigating RSV and Influenza with Rapid Testing in Adults

NOTE: If you have just viewed the archived recording of this webinar, you can access the evaluation using the link in the email you received after submitting the recording request form. Alternatively, you can access the evaluation for **12 months** after the live event at:

https://www.whitehatcom.com/Abbott_Evals/RSV_101823/Flu_101823_eval.html

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