LEADING MEDICINE:
A TOWN HALL CONVERSATION
WITH DR. MARC BOOM

Town Hall Conversation XXI

We will begin at 10 a.m.
COVID-19 Viral Load Detected in City of Houston Wastewater

Viral Load: 319% ( Compared to July 6, 2020)

Positivity Rate: 28%

https://covidwwtp.spatialstudieslab.org/
Comparison of Omicron Surge with Delta Surge
COVID-19 Key Statistics: Percent of Positive Patients Admitted to the Hospital

Percentage of Positive Patients Admitted to the Hospital

- **Percentage Admitted**
- **7 day % admitted**

6/3/21 to 1/25/22
Incidental COVID-19 Admissions

Houston Methodist internal data suggest that 32% to 40% of the COVID-19 hospitalizations in the Omicron Surge (Surge 5) are incidental (patient admitted for something else and discover diagnosis upon pre-admission testing).
Incidental Admissions from COVID-19 Higher with Omicron

• More Americans are now hospitalized with COVID-19 than at any previous point in the pandemic.
• Proportion of COVID-19 admissions that are “Incidental”:
  • 33% at UC San Francisco
  • 50% of Jackson Health System in Florida

“These ‘incidental’ infections are not so incidental for people with chronic conditions. Colds and other viral infections can also land people in the hospital by pushing their chronic diseases over the edge.”

Severity Assessment is Difficult

**Selection effects**
Covid-19 infections by severity and re-infection capacity, illustrative example

**Variant with little capacity for re-infection**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Susceptible population</th>
<th>Severe</th>
<th>Not Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection averted</th>
<th>Previously infected population</th>
</tr>
</thead>
</table>

**Variant with high capacity for re-infection**

- Symptoms
  - Severe
  - Moderate
  - Mild
  - Asymptomatic

- Fully susceptible population
- Previously infected population

“Omicron’s success at reinfecting people may give the impression a smaller fraction gets severely ill just by inflating the denominator. It could thus seem more benign even if, among those contracting covid for the first time, it were just as dangerous as Delta.”
Omicron very rapidly increased in only three weeks to cause 90% of all new Covid-19 cases.

Compared to patients infected with either Alpha or Delta variants at HM, Omicron patients were:

- Significantly younger;
- Significantly increased vaccine breakthrough rates;
- Significantly less likely to be hospitalized;
- Required less intense respiratory support; and
- Had a shorter length of hospital stay, consistent with decreased disease severity.
**Omicron Severity: Early Results**

<table>
<thead>
<tr>
<th></th>
<th>Omicron Variant</th>
<th>Delta Variant</th>
<th>Total</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) with data</td>
<td>4,468 (58.7%)</td>
<td>3,149 (41.3%)</td>
<td>7,617</td>
<td></td>
</tr>
<tr>
<td>Median Age</td>
<td>44.3</td>
<td>50.0</td>
<td>47.2</td>
<td>P&lt;0.0001 Mann-Whitney</td>
</tr>
<tr>
<td>Admitted</td>
<td>884 (19.8%)</td>
<td>1,719 (54.6%)</td>
<td>2,603 (34.2%)</td>
<td>P&lt;0.0001 Fisher’s exact test OR: 0.205 (95%CI: 0.185-0.227)</td>
</tr>
<tr>
<td>Median LOS (Days)</td>
<td>3.2</td>
<td>5.1</td>
<td>4.7</td>
<td>P&lt;0.0001 Mann-Whitney</td>
</tr>
</tbody>
</table>

### Max Respiratory Support

<table>
<thead>
<tr>
<th></th>
<th>Omicron Variant</th>
<th>Delta Variant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECMO</td>
<td>1 (0.1%)</td>
<td>7 (0.4%)</td>
<td>8 (0.3%)</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>49 (5.5%)</td>
<td>144 (8.4%)</td>
<td>193 (7.4%)</td>
</tr>
<tr>
<td>Non-Invasive Ventilation</td>
<td>63 (7.1%)</td>
<td>163 (9.5%)</td>
<td>226 (8.7%)</td>
</tr>
<tr>
<td>High Flow Oxygen</td>
<td>72 (8.1%)</td>
<td>364 (21.2%)</td>
<td>436 (16.7%)</td>
</tr>
<tr>
<td>Low Flow Oxygen</td>
<td>314 (35.5%)</td>
<td>722 (42.0%)</td>
<td>1,036 (39.8%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>38 (0.9%)</td>
<td>170 (5.4%)</td>
<td>208 (2.7%)</td>
</tr>
<tr>
<td>Vaccine Status – No Vaccine</td>
<td>1,971 (44.1%)</td>
<td>3,048 (96.8%)</td>
<td>5,019 (65.9%)</td>
</tr>
</tbody>
</table>
Clinical Outcomes Among Patients Infected with Omicron in S. California

https://www.medrxiv.org/content/10.1101/2022.01.11.22269045v1.full.pdf
FIGURE. Seven–day moving average number of COVID-19 cases, emergency department visits, hospital admissions, and deaths — United States, * December 1, 2020—January 15, 2022

https://www.cdc.gov/mmwr/volumes/71/wr/mm7104e4.htm
<table>
<thead>
<tr>
<th></th>
<th>Winter 2020-21 Peak 7 Day Average</th>
<th>Delta Period Peak 7 Day Average</th>
<th>Omicron Period Peak 7 Day Average</th>
<th>Omicron vs. Winter 2020-21 Period Peak 7 Day Average</th>
<th>Omicron vs. Winter Delta Period Peak 7 Day Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>250,335</td>
<td>164,249</td>
<td>798,976</td>
<td>+219.2%</td>
<td>+386.4%</td>
</tr>
<tr>
<td>Admissions</td>
<td>16,497</td>
<td>12,285</td>
<td>21,586</td>
<td>+30.8%</td>
<td>+75.7%</td>
</tr>
<tr>
<td>Deaths</td>
<td>3,422</td>
<td>1,924</td>
<td>1,854</td>
<td>-45.8%</td>
<td>-3.6%</td>
</tr>
<tr>
<td>Hospitalized as % of Total Hospitalizations</td>
<td>12.0%</td>
<td>9.4%</td>
<td>12.9%</td>
<td>+8.2%</td>
<td>+37.5%</td>
</tr>
<tr>
<td>ICU Admission</td>
<td>18.2%</td>
<td>17.5%</td>
<td>13.0%</td>
<td>-28.8%</td>
<td>-25.9%</td>
</tr>
<tr>
<td>In-Hospital Death Rate</td>
<td>12.9%</td>
<td>12.3%</td>
<td>7.1%</td>
<td>-44.9%</td>
<td>-42.3%</td>
</tr>
<tr>
<td>Mean LOS</td>
<td>8.0</td>
<td>7.6</td>
<td>5.5</td>
<td>-31%</td>
<td>-26.8%</td>
</tr>
</tbody>
</table>
Kaiser’s analysis found that for every 10,000 cases of Covid-19 detected outside of a hospital, 110 of those with the Delta variant had symptoms and ended up in the hospital. For those with the Omicron variant, only 16 were hospitalized.
Omicron May Be Milder, But It Is Still Straining Hospitals

Kaiser’s analysis found that for every 10,000 cases of Covid-19 detected outside of a hospital, 110 of those with the Delta variant had symptoms and ended up in the hospital. For those with the Omicron variant, only 16 were hospitalized.

But Omicron is estimated to be about three to five times more contagious than Delta. Consequently, the number of people infected is many times greater than during the Delta peak in late summer of 2021.

Omicron May Be Milder, But It Is Still Straining Hospitals

So even though Omicron is less likely to result in severe disease, the sheer scale of infections means the raw number of hospitalizations now exceeds the peak number when Delta was dominant.

You must never confuse faith that you will prevail in the end—which you can never afford to lose—with the discipline to confront the most brutal facts of your current reality, whatever they might be.

– Admiral Jim Stockdale, the highest-ranking U.S. officer held prisoner during the Vietnam War
COVID-19 Key Statistics: Deaths vs. Admissions Trend

7 Day Average Deaths (blue) versus 7 Day Average Admissions (orange)
Cumulative confirmed COVID-19 deaths per million people

For some countries the number of confirmed deaths is much lower than the true number of deaths. This is because of limited testing and challenges in the attribution of the cause of death.
Very Different Experience in the UK versus the US

https://ourworldindata.org/covid-cases
Why???????
A Partial List of Possible Explanations

1) Is there an age distribution difference between the UK and the US?

2) Are there underlying differences in the health status of the populations?

3) Is there a difference in the quality of the health systems, medical practice and/or sophistication?

4) Are there differences in social support and access to health care?

5) Is there an underlying difference in the virus itself, the mix of variants, etc.?

6) Is there a difference in social behaviors?

7) Have we used testing and/or contact tracing differently?

8) How have vaccines been used in each country?
Age Distribution of UK and US

United Kingdom: Age distribution from 2010 to 2020

Age distribution in the United States from 2010 to 2020

Health of Adults in UK and US

U.S. Adults Have the Highest Chronic Disease Burden

Notes: Chronic disease burden defined as adults age 18 years or older who have ever been told by a doctor that they have two or more of the following chronic conditions: joint pain or arthritis, asthma or chronic lung disease, diabetes, heart disease, including heart attack or hypertension/high blood pressure. Average reflects 11 countries shown in the exhibit that take part in the Commonwealth Fund’s International Health Policy Survey.

Data: Commonwealth Fund International Health Policy Survey, 2016.


The U.S. Has the Highest Rate of Avoidable Deaths


Health of Adults in UK and US

The U.S. Has the Highest Rate of Obesity

Percent (%)

<table>
<thead>
<tr>
<th>Country</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWZ</td>
<td>13.6</td>
</tr>
<tr>
<td>NOR</td>
<td>12.0</td>
</tr>
<tr>
<td>SWE</td>
<td>33.2</td>
</tr>
<tr>
<td>NETH</td>
<td>12.0</td>
</tr>
<tr>
<td>GER</td>
<td>23.6</td>
</tr>
<tr>
<td>CAN</td>
<td>28.7</td>
</tr>
<tr>
<td>UK</td>
<td>30.4</td>
</tr>
<tr>
<td>AUS</td>
<td>32.2</td>
</tr>
<tr>
<td>NZ</td>
<td>40.0</td>
</tr>
</tbody>
</table>

OECD average: 21%

Notes: Obese defined as body-mass index of 30 kg/m² or above. Obesity rates reflected are based on measurements of height and weight, except NETH, NOR, SWE, SWZ, for which data are self-reported. Self-reported rates tend to be lower than measured rates. 2017 data for all countries except 2016 for US; 2015 for FRA, NOR; 2014 for GER. OECD average reflects the average of 36 OECD member countries, including ones not shown here.


Reported In-Hospital COVID-19 Mortality After 1st Wave

11-12% 12.9%

https://www.thelancet.com/journals/lanep/issue/2666-7762(21)00081-8/fulltext#seccessectitle0021
https://www.cdc.gov/mmwr/volumes/71/rr/mm7104e4.htm
The poverty rate is the ratio of the number of people whose income falls below the poverty line; taken as half the median household income of the total population.

The poverty gap is the ratio by which the mean income of the poor falls below the poverty line. The poverty line is defined as half the median household income of the total population.
Variant Distribution Trend by Country

https://ourworldindata.org/covid-vaccinations
Testing and Contact Tracing in the UK and US

https://ourworldindata.org/grapher/daily-tests-per-thousand-people-smoothed-7-day?tab=chart&country=GBR
https://www.nature.com/articles/s41586-021-03606-z#:~:text=Our%20analyses%20suggest%20that%20a,19%20over%20the%20same%20period.~USA
Vaccination Rates by Country

Share of the population fully vaccinated against COVID-19
Total number of people who received all doses prescribed by the initial vaccination protocol, divided by the total population of the country.

United Kingdom
United States


0% 10% 20% 30% 40% 50% 60% 70%

Source: Official data collated by Our World in Data
Note: Alternative definitions of a full vaccination, e.g., having been infected with SARS-CoV-2 and having 1 dose of a 2-dose protocol, are ignored to maximize comparability between countries.

https://ourworldindata.org/covid-vaccinations
Vaccination Rates by Country

COVID-19 vaccine boosters administered per 100 people

Total number of vaccine booster doses administered, divided by the total population of the country. Booster doses are doses administered beyond those prescribed by the original vaccination protocol.

Source: Official data collated by Our World in Data

https://ourworldindata.org/covid-vaccinations
• VE was higher among persons who were fully vaccinated and had received a booster dose than among fully vaccinated persons who had not received a booster dose for cases and deaths during the period of Delta predominance and for cases during the period of Omicron emergence in December.

• Because of reporting lags, the influence of the Omicron variant on COVID-19–associated deaths by vaccination status in December could not be evaluated.

• The added benefits of booster doses were especially prominent among persons aged 50–64 and ≥65 years.
COVID-19 Weekly Death Rate by Vaccination Status in Switzerland

Switzerland: COVID-19 weekly death rate by vaccination status, All ages

Death rates are calculated as the number of deaths in each group, divided by the total number of people in this group. This is given per 100,000 people.

Source: Federal Office of Public Health
Note: Data coverage includes both Switzerland and Liechtenstein. Unvaccinated people have not received any dose. Partially-vaccinated people are excluded. Fully-vaccinated people have received all doses prescribed by the initial vaccination protocol. The mortality rate for the 'All ages' group is age-standardized to account for the different vaccination rates of older and younger people.

https://ourworldindata.org/covid-deaths-by-vaccination
Vaccinations in the UK and US

Vaccination Rates by Age

UK
US

>18 Years Old

>50 Years Old

>65 Years Old

1 Dose
2 Doses
3 Doses

Not Reported

https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total
PRO TIP: FOCUS ON THE ANTI-VAX CROWD.
A Partial List of Possible Explanations

1) Is there an age distribution difference between the UK and the US?  
2) Are there underlying differences in the health status of the populations?  
3) Is there a difference in the quality of the health systems, medical practice and/or sophistication?  
4) Are there differences in social support and access to health care?  
5) Is there an underlying difference in the virus itself, the mix of variants, etc.?  
6) Is there a difference in social behaviors?  
7) Have we used testing and/or contact tracing differently?  
8) How have vaccines been used in each country?

Conclusion: A complex interplay among the underlying health of the population, access to health care, testing, contact tracing, and especially vaccine uptake.
Consistent evidence-based decision making and communication

VACCINES – KEY QUESTIONS

1. Is the vaccine safe?
2. Does it cause a humoral (antibody) immune response?
3. Does it cause a cellular immune response?
4. Does the immune response neutralize the virus?
5. Does it prevent infection or disease?
6. How long does immunity last?
7. Can the vaccine be produced and distributed effectively?
8. Will people take it?
Booster Mandate Announcement

“All Houston Methodist employees are now required to get a booster dose – by January 31 for management and March 1 for all other employees.

It has been seven months since our deadline for the first two shots and most of us are boosted already, but we need to be sure all of us are. Like I said when we did this the first time, as health care workers we’ve taken a sacred oath to do everything possible to keep our patients safe and healthy – this includes getting a booster now.”

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COVID-19 booster mandate

Last spring, we required our employees and physicians to be fully vaccinated against COVID-19. We knew we needed to be leaders and take this move to protect our patients, ourselves and our families. You all stepped up and did the right thing for our patients and I am deeply grateful. Now with omicron surging and mounting evidence that a booster shot effectively protects individuals from severe illness, it is time for us to step up again. All Houston Methodist employees are now required to get a booster dose – by January 31 for management and March 1 for all other employees. After reviewing the mandate and the science behind it with the system medical staff leadership, we anticipate that each medical executive committee will also adopt the March 1 deadline.

It has been seven months since our deadline for the first two shots and most of us are boosted already, but we need to be sure all of us are. Like I said when we did this the first time, as health care workers we’ve taken a sacred oath to do everything possible to keep our patients safe and healthy – this includes getting a booster now.

We have battled courageously against COVID-19 for almost two years. And while we can’t foresee every variant like omicron, we need to remain nimble and do what we can to protect our patients. Vaccines are safe, and we know that boosters are the best available protection right now against this variant. We know without a doubt – based on science and the experience of our own employees – that vaccines work in preventing us from getting severely sick and hospitalized. Our scientific committee is recommending boosters for everyone four to six months after their second shot, and here’s
GET YOUR FREE COVID-19 BOOSTER TODAY

NOW ACCEPTING WALK-INS
Visit any of our 7 vaccination locations:
Monday – Thursday: 8 a.m. – 5 p.m.
Friday: 8 a.m. – Noon

PREFER AN APPOINTMENT?
Visit houstonmethodist.org/vaccine to schedule online.

HOUSTON Methodist
LEADING MEDICINE
COVID-19: Pandemic to Endemic

Town Hall, January 27, 2022

H. Dirk Sostman, MD FACR, Ernest Cockrell, Jr. Presidential Distinguished Chair, EVP & Chief Academic Officer
Summary of Vaccine Efficacy: Pre-Omicron

• Vaccines effective against COVID-19 infection for ~4-6 months
  – Lower viral load, reduced transmission – even with delta
• As time passes, vaccines offer less protection against infection
  – Related to lower levels of circulating antibodies
  – Antibody levels correlate with protection, but we do not know a “cut-off” value for an individual person
• Protection against hospitalization and death is longer lasting
  – Likely related to cellular immunity
  – How much longer lasting? Time will tell
• Boosters restore antibody levels and 85–90% protection from infection
  – About the same as two doses + prior infection
  – Will this last longer than first two doses? Time will tell
• Prior infection alone
  – About 80% effective (lower quality data than for vaccines)
  – Less effective in older people or if infection was mild
  – However, appears to be synergistic with vaccination
Boosters for Delta vs Omicron

UK HSA Technical Briefing December 31, 2021
### Omicron: Immunity Wanes, Restored by Booster

**MMWR January 21, 2022**

<table>
<thead>
<tr>
<th>Variant Predominance</th>
<th>Hazard Ratio for Infection</th>
<th>Hazard Ratio for Infection</th>
<th>Hazard Ratio for Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Two Doses vs Unvaccinated</td>
<td>Two Doses vs Two Doses + Booster</td>
<td>Two Doses vs Unvaccinated</td>
</tr>
<tr>
<td>Pre-delta</td>
<td>13.9</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td>Delta</td>
<td>5.1</td>
<td>16.3</td>
<td></td>
</tr>
<tr>
<td>Omicron</td>
<td>3.1</td>
<td>13.9</td>
<td>19.4</td>
</tr>
</tbody>
</table>

- Omicron has more mutations than delta
- These mutations interfere with antibodies (which protect from infection) more than with cellular immunity (which protects from severe disease and death)
- Booster helps overcome antibody resistance
Omicron: Booster Restores Neutralizing Abs for 4 Months

https://www.biorxiv.org/content/10.1101/2022.01.21.476344v1
Switzerland: COVID-19 weekly death rate by vaccination status, All ages, Jan 1, 2022

Death rates are calculated as the number of deaths in each group, divided by the total number of people in this group. This is given per 100,000 people.

- Unvaccinated: 13.06
- Fully vaccinated, no booster: 1.44
- Fully vaccinated + booster: 0.27

Source: Federal Office of Public Health
Note: Data coverage includes both Switzerland and Liechtenstein. Unvaccinated people have not received any dose, Partially-vaccinated people are excluded. Fully-vaccinated people have received all doses prescribed by the initial vaccination protocol. The mortality rate for the “All ages” group is age-standardized to account for the different vaccination rates of older and younger people.
### Hazard Ratio for UNVACCINATED and NO PRIOR INFECTION Versus Vaccinated No Prior Infection

<table>
<thead>
<tr>
<th>Date Range</th>
<th>Vaccinated No Prior Infection</th>
<th>Unvaccinated + Prior Infection</th>
<th>Vaccinated + Prior Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 30 – June 5</td>
<td>20.9 (18.9–22.9)</td>
<td>8.2 (6.6–9.9)</td>
<td>10.6 (8.1–13.2)</td>
</tr>
<tr>
<td>Nov 14 – Nov 20</td>
<td>7.3 (7.0–7.5)</td>
<td>25.4 (21.4–29.3)</td>
<td>32.5 (25.5–39.5)</td>
</tr>
</tbody>
</table>

- Antibody breadth against viral variants is less after infection than vaccination, but improves over several months
- Viral variant infection elicits variant-specific antibodies, while vaccination imprints serological responses toward Wuhan-Hu-1
Current Vaccine Strategies for COVID-19

- Immune-compromised people
  - Should have a three-shot primary vaccine series plus a booster shot six months later

- For people at “ordinary” risk – repeated doses of original vaccine all we have to offer
  - Third / booster shot at 4–6 months is supported by data
  - Fourth / booster shot has persuasive rationale but not much data
    - Israel recommends for all people over 18, five months after booster
      - Increases antibody levels
      - In over-60s, 2x protection against infection, 3x protection from severe disease

- No evidence for theoretical “immune exhaustion”

- With current vaccines, four shots (or three shots + infection) may have diminishing returns

- Some have used fourth shot (4–6 months after third shot) to cover a specific episode of increased risk – no data to support this
• Tailored boosters against SARS-CoV-2 variants
  – At some point this will be necessary – not clear when, but likely will be soon
  – Pfizer starting clinical trial of omicron-specific vaccine
  – Still amounts to playing catch-up

• Novel vaccines – at least a year away
  – Nasal vaccines
    • Theoretically ideal but not a simple task in practice
    • Alttimmune AdCOVID vaccine well tolerated but failed to generate immune response (June 2021 press release)
    • Intranasal AstraZeneca vaccine produced serum IgG and nasal IgA (van Doremalen et al Sci Trans Med August 2021)
    • Intranasal attenuated RSV bearing spike protein protected nonhuman primates, reduced viral load (Tioni et al, bioRxiv August 6, 2021)

  – Pan-coronavirus vaccines – multivalent antigens vs novel delivery systems
    • Ferritin nanoparticles (Joyce et al Sci Trans Med Dec 2021) protected nonhuman primates against major VOCs and SARS-CoV-1
    • Pan-sarbecovirus neutralizing antibodies in SARS survivors vaccinated with Pfizer vaccine (Tan et al, NEJM August 2021; Schmidt et al, Nature September 20, 2021)
Outpatient Treatments Authorized by FDA

Early treatment of high-risk outpatients is a critical part of the pandemic defense.
Monoclonal Antibodies

• Precise nature of mAbs makes them very sensitive to immune evasion by variants
  – Regen-Cov (Regeneron) and bamlanivimab + etesevimab (Lilly) – Not effective against omicron
  – Evushield (AstraZeneca) – for pre-exposure prophylaxis (not for treatment) – Neutralizes omicron

• Sotrovimab
  – Pan-sarbecovirus mAb (originally isolated from SARS patient)
  – Neutralizes alpha, beta, gamma and delta SARS-CoV-2 variants
  – Clinical trial (NEJM October 2021)
    • Treatment within 5 days of symptoms, high risk
    • 85% RR for hospitalization or death
  – Reduced effectiveness but neutralizes omicron (press release, 12/7/21)
“COVID Pills” – Effective Against Omicron

• Two FDA-authorized oral treatments that reduce hospitalization in high-risk people
  – Paxlovid – 89% reduction
  – Molnupiravir – 30% reduction

• One FDA-approved intravenous treatment (3x daily infusion)
  – Remdesivir – 87% reduction in hospitalization

• Possibilities of combined therapy
  – Protease inhibitor (paxlovid)
  – Polymerase inhibitor (molnupiravir, remdesivir)
  – mAb
At-home testing can rapidly identify those who have high viral loads.
Potentially major effect on transmission of infection & early treatment.
Why Are Lower Sensitivity Tests Still Useful?

The viral load below which a person is no longer infectious is still unclear. Low-sensitivity rapid antigen test and PCR test results are shown over time. The sensitivity of these tests is critical in determining the accuracy of results during the infectious period.
• Walk-up testing site
  – Among people with a positive PCR with no symptoms, the sensitivity of antigen tests was 89.8%
  – Among people with a positive PCR who were symptomatic, the sensitivity of antigen tests was 97.6%

• Higher the viral load → more accurate the antigen test

• Tests were equally accurate for all ages

• Tests performed similarly regardless of vaccination status

• Likelihood of a false positive was very small (0.4%)
• Hay et al, https://dash.harvard.edu/handle/1/37370587
  – 204 vaccinated people – who were tested daily
    • Omicron infection lasted, on average, 10 days
    • Delta infections lasted, on average, 11 days
  – Some cleared the virus faster and others cleared the virus more slowly
  – Roughly 50% still had high viral levels at Day 5 (they were likely infectious)

• UK Health Security Agency
  – After 7-day isolation (not using an antigen test), 1 in 6 chance to be still infectious
  – Negative antigen test on Day 7 of isolation, less than 1 in 10 chance to be still infectious
• Home Antigen Tests
  – BinaxNow – available online at pharmacies including Walgreens and Walmart but not Amazon
  – Access CareStart – online pharmacies and wholesalers, not Amazon
  – Quidel QuickVue – Amazon, others
  – iHealth – Amazon, others
  – Free antigen tests from US government ordered at https://www.covidtests.gov/. Unclear what test will be given but likely either iHealth or BinaxNow
  – US distribution of free antigen tests through pharmacies is unclear at this time. It is anticipated to begin soon in limited areas and in limited supply at the beginning.

• Home Virus nucleic acid tests
  – Lucira – Amazon
  – Cue Health – online at Cue Health
Transitioning from Pandemic to Endemic

What might be next?
What Do You Mean, Endemic???

Confirmed coronavirus cases in South Africa
Seven-day rolling average of daily confirmed cases

Source: Johns Hopkins University, NICD, data to 18 Jan
What Do You Mean, Endemic???
• All pandemics end, but diseases rarely disappear
• Likely entering a transition phase between pandemic (global outbreak) and endemic (local outbreaks)
  – Endemic doesn’t mean inconsequential (malaria, TB...)
• We can expect variants to continue to appear
  – Evolution in response to selective pressures
  – Chronic infection in immune-compromised hosts
  – Viral recombination
  – Human → animal → human transmission
• Influenza – infects ~10% of US population each year, with 20k–50k deaths
• How might endemic COVID compare?
Transitioning from Pandemic to Endemic: Theory
Trevor Bedford, Hutchinson Cancer Center, twitter @trvrb

• Key factors:
  1. \( R_0 \) (flu = 2, omicron = 12)
  2. Periodically waning immunity
  3. Antigenic drift in virus
  4. Infection to fatality rate (IFR) – (flu = 0.06%, original COVID = 0.6%)

• High \( R_0 \), waning immunity and antigenic drift together suggest substantial circulation with a guess of 20% or 30% of the population infected per year (“attack rate”, flu = 10%)

• Most infections likely to be relatively mild (like flu), but with enough infections, a small fraction of severe outcomes adds up
  - 40k deaths / year would be 20% attack rate with 0.06% IFR
  - 100k deaths / year would be 30% attack rate with 0.1% IFR
Transitioning from Pandemic to Endemic
Sostman commentary on Trevor Bedford Model

• Attack rate and IFR likely to be worse during the transition period than in the endemic phase
• As a respiratory virus, probably will be seasonal
• Like seasonal flu, should expect significant season-to-season variability
• Viral evolution unpredictable, but some guesses:
  – further immune evasion
  – little further change in $R_0$
  – could become more or less severe
• Better preventive measures and testing $\rightarrow$ reduce the attack rate
• Better therapeutics and vaccines $\rightarrow$ reduce the infection fatality rate
• Remember the difference between theory and practice!
Societal responses remain “wild cards.” Thus far, not encouraging.
- Dysfunctional social behavior
- Social media disinformation
- Self-serving politicians
- Government inefficiency
- Poor communication from leaders & scientists
- Poor international coordination
Tools to control the pandemic exist – and they will continue to improve. They are most effective if used correctly and consistently.
Alternatively, we can let nature take its course. Nature is ultimately very effective, but can be brutal. What if your family was collateral damage?
POST ACUTE COVID (LONG COVID) FOLLOW UP

• https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003871
  • 1 year follow up
  • 480% increase in all cause mortality

• jama_heesakkers_2022_oi_220002_1642801976.73468.pdf
  • 1 year follow up after ICU for COVID
  • 74.3% had physical symptoms, 26.2% mental symptoms, 16.2% cognitive symptoms

• https://www.nature.com/articles/s41586-021-03553-9
  • Mild COVID (not hospitalized) 30 days after infection
  • 159% increased risk of death

• https://www.medrxiv.org/content/10.1101/2022.01.05.22268800v2
  • Vaccinated people 54% - 68% less likely to have long COVID

• By the way........
  • https://www.cdc.gov/mmwr/volumes/70/wr/mm7043e2.htm#T1_down
  • Risk of all cause mortality after vaccination is 0.31 (Moderna), 0.34 (Pfizer) and 0.54 (J&J) compared with unvaccinated
THANK YOU FOR ATTENDING OUR TOWN HALL CONVERSATION

If you’d like more information about the topics discussed today, or would like to join The Society for Leading Medicine, please contact us at foundation@houstonmethodist.org

Take care and be well