SARS-CoV-2 transmission metrics webinar (27/07/20)

• Transmission-related criteria to adapt public health and social measures (Stéphane Hugonnet/WHO)
• Real-time reproductive number (Pragati Prasad, Velma Lopez/CDC Domestic Modelling Task Force)
• Incidence (Matt Lozier/CDC Domestic Case Surveillance Task Force)
• Q&A
Background

• Annex to “Considerations in adjusting public health and social measures in the context of COVID-19”
• Published 12 May (epi situation at this time in figure)
• NOTE
  • Is about public health criteria
  • Need be useful for all countries
  • Not prescriptive
  • Need be adapted
  • Thresholds and quantities are indicative
  • Combination of criteria
  • Help conduct systematically a risk assessment to inform pragmatic decision process

Three domains

**Epidemiology** - Is the epidemic controlled?

**Health system** - Is the health system able to cope with a resurgence of COVID-19 cases that may arise after adapting some measures?

**Public Health Surveillance** - Is the public health surveillance system able to detect and manage the cases and their contacts, and identify a resurgence of cases?
Epidemiology

• Effective reproductive number below 1
• Decline of at least 50% over a 3-week period since the latest peak and continuous decline in the observed incidence of confirmed and probable cases
• Less than 5% of samples positive for COVID-19 at least for the last 2 weeks, assuming that surveillance for suspected cases is comprehensive
• Less than 5% of samples positive for COVID-19 at least for the last 2 weeks among influenza-like-illness samples tested at sentinel surveillance sites
• Less than 5% of samples positive for COVID-19 at least for the last 2 weeks among severe-acute-respiratory-illness samples tested at sentinel surveillance sites
Epidemiology

• At least 80% of cases are from contact lists and can be linked to known clusters
• Decline in the number of deaths among confirmed and probable cases at least for the last 2 weeks
• Continuous decline in the number of hospitalization and ICU admissions of confirmed and probable cases at least for the last 2 weeks
• Decline in the age-stratified excess mortality due to pneumonia
Conclusions

• Keeping in mind that decision to adapt PHSM influenced by other non-PH criteria
• No single indicator is sufficient *per se*
• Cannot be a purely quantitative assessment
• Epi indicators very dependent on quality of surveillance
• Next step
  – Evaluate utility and feasibility
  – Provide more user guidance
  – Identify important missing indicators (and less useful indicators)
Real-time reproductive number: Practical considerations for use in the COVID-19 response

Velma K Lopez, PhD, MPH
Epidemiologist for the Modeling Unit

Pragati Prasad, MPH
Analyst for the Modeling Unit

ITF Webinar
July 27, 2020
Real-time reproductive number, $R_t$, is a metric that quantifies an outbreak’s transmission rate at a given point in time.

- U.S. daily national estimate of time-varying reproduction number, with daily state estimates (grey dots).
- The horizontal dashed line represents the threshold value.
- The grey shaded area on the right represents the lag time in reporting at the national level.

Source: MTF MMWR (under review)

Real-time reproductive number, $R_t$, is a metric that quantifies an outbreak’s transmission rate at a given point in time.

Real-time reproductive number, $R_t$, is a metric that quantifies an outbreak’s transmission rate at a given point in time.

- U.S. daily national estimate of time-varying reproduction number, with daily state estimates (grey dots).
- The horizontal dashed line represents the threshold value.
- The grey shaded area on the right represents the lag time in reporting at the national level.


*Must also be < 1.0 in all subpopulations.*
$R_t$ can be a useful metric for assessing epidemic control

The CDC ITF uses $R_t$ within an internal dashboard as a monitoring indicator.

WHO recommends using $R_t$ over a 14-day period as the primary metric of outbreak control.
$R_t$ can be a useful metric for assessing epidemic control. Several factors affect the accuracy of $R_t$ and bias is common.
Calculating $R_t$ requires estimating the time of infection.
Calculating $R_t$ requires estimating the time of infection.
Calculating $R_t$ requires estimating the time of infection.
Calculating $R_t$ requires estimating the time of infection...which is usually done by using available information in the surveillance system.
Calculating $R_t$ requires estimating the time of infection...which is usually done by using available information in the surveillance system.
The R-software package called ‘EpiEstim’ is one tool for quantifying transmissibility throughout an epidemic as first described in Cori et al. (2013).

The following inputs are required:

• Daily COVID-19 incidence by country or subnational level

• Date of symptom onset

• Serial interval distributions:
  • Time duration between symptom onsets of a primary case (infector) and symptom onset of a secondary case (infectee)

• The exact serial interval is unknown, so estimates are used

Many factors influence the accuracy of $R_t$ estimation, including but not limited to:

- Model misspecification
- Reporting lags and their adjustment
- Missing data and their adjustments
- Changes in data collection and reporting
- Changes in testing criteria or capacity
- Approach taken for smoothing and serial interval time
- Change in the serial interval
- Differences in sub-national outbreak response & pooling data
For example: Figures A and B show common methods (blue and purple lines) of estimating the true number of infections (yellow line) from available case counts (green line). Figure A applies a 7 day lag to cases and Figure B a 20 day lag to deaths.

Figure adapted from Gostic et al. https://www.medrxiv.org/content/10.1101/2020.06.18.20134858v2.full.pdf
For example: Figures A and B show common methods (blue and purple lines) of estimating the true number of infections (yellow line) from available case counts (green line). Figure A applies a 7 day lag to cases and Figure B a 20 day lag to deaths. Both approaches result in poor proxies of true infections.
For example: Figure C shows the true $R_t$ estimate (black line) compared to estimates using different lag times from case reporting (pink line) and death reporting (turquoise line).

Both approaches result in biased estimation at different time points.

Gostic et al. https://www.medrxiv.org/content/10.1101/2020.06.18.20134858v2.full.pdf
Before estimating $R_t$ for COVID-19 response, we recommend working with your surveillance colleagues to answer the following questions:

- Does the surveillance system capture cases and deaths well?
  - Are they missing at the same frequency? Is the lag in reporting known? What is the timeliness in reporting? Does the lag differ between cases and deaths?

- Which date information is collected?

- Is there subnational/regional surveillance? And what is the overall quality of those surveillance systems?

- Does the system systematically exclude certain populations that may have a greater risk of infection?
It is important not to make decisions based on biased estimates

If you do not have the data needed to calculate and adjust $R_t$ accordingly, use the WHO indicators for epidemic control: “Public health criteria to adjust public health and social measures in the context of COVID-19” from May 12, 2020.

$R_t$ should be used as one of many indicators to inform response strategies. It’s important to interpret $R_t$ alongside recent case count data.
Acknowledgements:
Rachel Slayton & Michael Johansson
Roma Bhatkoi, Sara Kada, Rebecca Kahn, Prabasaj Paul,
and other modeling team members

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Introduction to CDC COVID-19 Trajectory Analysis

A Session For CDC Country Offices and Global Partners

Today’s Session

OBJECTIVE:
To describe how trajectory analysis of COVID-19 incidence rates are applied to surveillance data

AUDIENCE:
CDC staff overseas, Ministries of Health, global partners

PRESENTING:
CDR Matt Lozier, PhD, MPH
US Public Health Service; CDC Case Surveillance Section
Why Indicators
Incidence

- Definition: The occurrence of new cases of disease (COVID-19) in a population over a specific period of time.
- Period of time can vary:
  - Day, week, month, etc.

\[
\text{Number of new cases of disease during specified period.} \times 100,000 = \text{Cases per 100,000 population}
\]
Why use incidence?

- Standardizes disease burden across populations.
- Allows for comparisons across districts, regions, countries.
- Informs public health actions and resource allocation.

Considerations

- Timeliness of reporting determined by surveillance system.
## How to calculate incidence

<table>
<thead>
<tr>
<th>Country</th>
<th>COVID-19 Cases</th>
<th>Population</th>
<th>Rate</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>178,000</td>
<td>67M</td>
<td>X 100,000</td>
<td>= 265</td>
</tr>
<tr>
<td>Denmark</td>
<td>13,500</td>
<td>5.8M</td>
<td>X 100,000</td>
<td>= 232</td>
</tr>
</tbody>
</table>

Created by Denis Sazhin from Noun Project
Country Analyses
Overview of country analyses

- Purpose: To provide national and sub-national timely, integrated data from a variety of sources, along with derived indicators of trends in the data. The objective is to provide a resource that can inform policies and mitigation efforts when used in the context of additional relevant data at the national and local level.

- National maps can be updated daily, or as often as new data is available.
- Cases map.
- Trajectory status map.
- Tables and graphs.
Cases reported in the past 2 weeks per 100,000

- **Purpose:** To look at recent incidence to capture the potential burden of currently ill people who may be infectious and/or accessing healthcare.

- **Specification:**
  - Sum the total number of new cases reported during the past 14-day period [count].
  - Divide by country/regional population estimate from most recent census.
  - Multiply by 100,000 to calculate incidence rate per 100,000.
Coronavirus Disease 2019 (COVID-19)
Number of New Cases per 100,000 in the past 2 weeks,
U.S. States and Territories, 22 June 2020 - 06 July 2020

Note: Defined using the number of new cases per 100,000 in the past 2 weeks. Low is >0 to 10, moderate is >10 to 50, moderately high is >50 to 100, and high is >100. Jurisdictions denoted as 0 cases in the past 2 weeks have had at least 1 case previously.
Changes in the 3-day average number of new daily cases per 100,000

- **Purpose:** To define whether illnesses have been increasing, stable, or decreasing.

- **Specification:**
  - Calculate daily incidence of new cases per 100,000.
  - Calculate the 3-day average of daily incidence per 100,000 (current day + 2 preceding days divided by 3).
  - Using the R procedure `smooth.spline` with smoothing parameter `spar` set to 0.5, fit a spline model to the curve.
  - For each day, calculate the first derivative of the splines as the slope (daily change per 100,000).
3-day average incidence example

- For June 27 (retrospectively), the 3-day average incidence would be:
  
  \[\text{June 27 incidence + June 26 incidence + June 25 incidence}\]

- On July 27 (real-time), the 3-day average incidence would be:
  
  \[\text{July 26 incidence + July 25 incidence + July 24 incidence}\]
Trends in sub-national indicators
Epidemic curve status

- **Overview:** Categorizes jurisdictions into various epidemic curve status categories based on two-week incidence:
  - Elevated incidence (above 10 per 100,000)
  - Low incidence (below 10 per 100,000)
  - Slope: increasing (above 0.1); plateau (0 to 0.1); decreasing (below 0)

- **Purpose:** To provide a composite metric that includes both the burden of illness and the trajectory of new illnesses (i.e., growth, plateau, decline) These statuses give an instantaneous and historic picture of the shape of an epidemic curve.
Methodology for trajectory classification

Slope cutoff: 0.10

Rate cutoff: 10 per 100,000

Notes: Jurisdictions are allowed a 5-day grace period of departure from downward trajectory before the downward trajectory is considered over.
Example of 3-day average:

Epidemic Curve Status
- 1-5 cases in the past two weeks
- Elevated incidence growth
- Elevated incidence plateau
- Low incidence growth
- Low incidence plateau
- No reported cases
- Rebound
- Sustained decline
- Spike

Brazil

The United Kingdom

Australia
Coronavirus Disease 2019 (COVID-19)
Current consecutive days of downward trajectory in case reports,
U.S. States and Territories, 06 July 2020

Days in downward trajectory*
- 1-6 days
- 7-13 days
- 14-20 days
- 21-41 days
- ≥42 days
- Not in downward trajectory
- 1-5 cases in the past 2 weeks
- 0 cases in the past 2 weeks
- No reported cases

*The number of days in a downward trajectory represents the number of consecutive days for which the jurisdiction experienced either a negative slope or a low incidence plateau (two-week incidence ≤10 cases per 100,000 and slope ≤-0.1 and ≤0.1).

Jurisdictions are allowed a 5 day grace period of departure from downward trajectory before the downward trajectory is considered over.
Sources: State reported aggregate counts, US Census
Epidemic trajectory status: CDC COVID-19 International Task Force Dashboard

https://app.powerbi.gov.us/groups/me/apps/8498de59-7f3f-4db4-87fd-49ec8a7565f5/reports/2f3f1d58-2d05-4ca7-a7e0-c3ac9a39b47d/ReportSection
Other examples of data visualization

**WHO-EURO dashboard**

Epidemiological key measure: Effective reproduction number (Rt) < 1 for at least 2 weeks

An Rt value below 1 indicates that the epidemic is controlled or declining.

Epidemiological criteria #5: Decline in the number of deaths among confirmed and probable cases for at least the last 3 weeks

A decline in the number of deaths, with an approximate 3-week lag-time, indicates that the total number of cases within a population is also decreasing.

[https://who.maps.arcgis.com/apps/opsdashboard/index.html#/ead3c6475654481ca51c248d52ab9c61](https://who.maps.arcgis.com/apps/opsdashboard/index.html#/ead3c6475654481ca51c248d52ab9c61)

**Proposed view for External CDC Tracker Global Dashboard**

- **slope cut: 0.10**
- **rate cut: 10.00**
Conclusion

- We reviewed several indicators that are used at CDC to track the COVID-19 pandemic:
  - Cases reported in the past 2 weeks per 100,000
  - Changes in the 3-day average number of new daily cases per 100,000

- These indicators are being tracked to determine the status of epidemic curves in the US, and can be implemented in other countries.

- The trajectory classification method is currently implemented in R for domestic data by the CDC Case Surveillance Task Force and for international data by the International Task Force.

- CDC ITF is working towards clearance of the R code for external sharing via GitHub.
Questions/comments: eocevent223@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.