Surveillance to “Restore Illinois”

15 May 2020

Sarah Cobey, PhD, and lab members, University of Chicago, cobey@uchicago.edu
Jaline Gerardin, PhD, Northwestern University, jgerardin@northwestern.edu

Contents

Motivation

As Illinois reopens, it is important to prevent new outbreaks of COVID-19. **All regions remain vulnerable**, since all populations are far from the herd immunity threshold. We estimate approximately 5-8% of the population of Illinois has gained immunity through infection, but 60-80% need immunity to avoid future outbreaks. We need to know as quickly and accurately as possible if it looks like current interventions are working in different areas, and how much adjustment they might need. This insight can be obtained by tracking transmission rates. Therefore we need **well-designed surveillance** to get us **fast and actionable information** on **COVID-19 spread across Illinois.** This surveillance system **provides clear criteria for shifting between phases** and will enable a more nimble long-term response.

Summary of prerequisites for a safe reopening

- A **sentinel surveillance system** should be in place to monitor changes in transmission. **This system will indicate whether we can move to the next phase**. Upstream

(sentinel) indicators, such as new infections, are superior to downstream indicators, such as hospitalizations and ICU census, because changes in trends are observable days to weeks earlier in upstream indicators.
- A **data sharing pipeline** should be established so the data can be analyzed quickly.
- Multiple interventions, including a **contact tracing system** that we have reason to believe is effective, must be in place. A corollary is **easily accessible testing** throughout the state. Appropriate interventions will be discussed in another document.

A gold standard for how to advance through phased re-opening

Logic dictates **we should advance to the next phase of reopening when**:

1. Our control measures are working: transmission is decreasing
   AND
2. There is relatively little infection in the population, healthcare capacity is not exceeded, and the death rate is not overwhelming.

We should **backtrack or delay moving to the next phase** when:

1. Our control measures are insufficient: transmission is not decreasing
   OR
2. There is substantial infection in the population, healthcare is strained, or the death rate is too high.

How can we tell where we are on these metrics? The most reliable way to assess changes in the transmission rate (Indicator 1) is through a sentinel surveillance system. A structured surveillance system can help us assess quickly if the prevalence of infection might soon or is already exceeding acceptable demands on healthcare (Indicator 2). The system we propose is effectively a **slight, but critically important, modification of infrastructure and reporting** already extant or in development.

We will describe how to calculate and use these two indicators more precisely in a later section, but it is worth highlighting important policy considerations here. First, policymakers must decide **what level of infection, hospitalization, or death is acceptable** in each area. If deaths fall below this level, is it acceptable to promote policies that increase transmission? We currently assume not. Second, as we will explain, the minimum amount by which transmission must decline before moving on to the next phase depends partly on **how much future policies increase transmission again**. Over time and with good surveillance, the effects of interventions on disease dynamics can be inferred, and the effects of potential policies forecasted more precisely. Current uncertainty in these effects underscores the need for a **sensitive surveillance system to detect changes in transmission rapidly** and **scientifically grounded criteria for evaluating preparedness** for the next phase (Figure 1). This will promote the kind of rapid adaptation necessary to minimize suffering from COVID-19 and the interventions themselves.

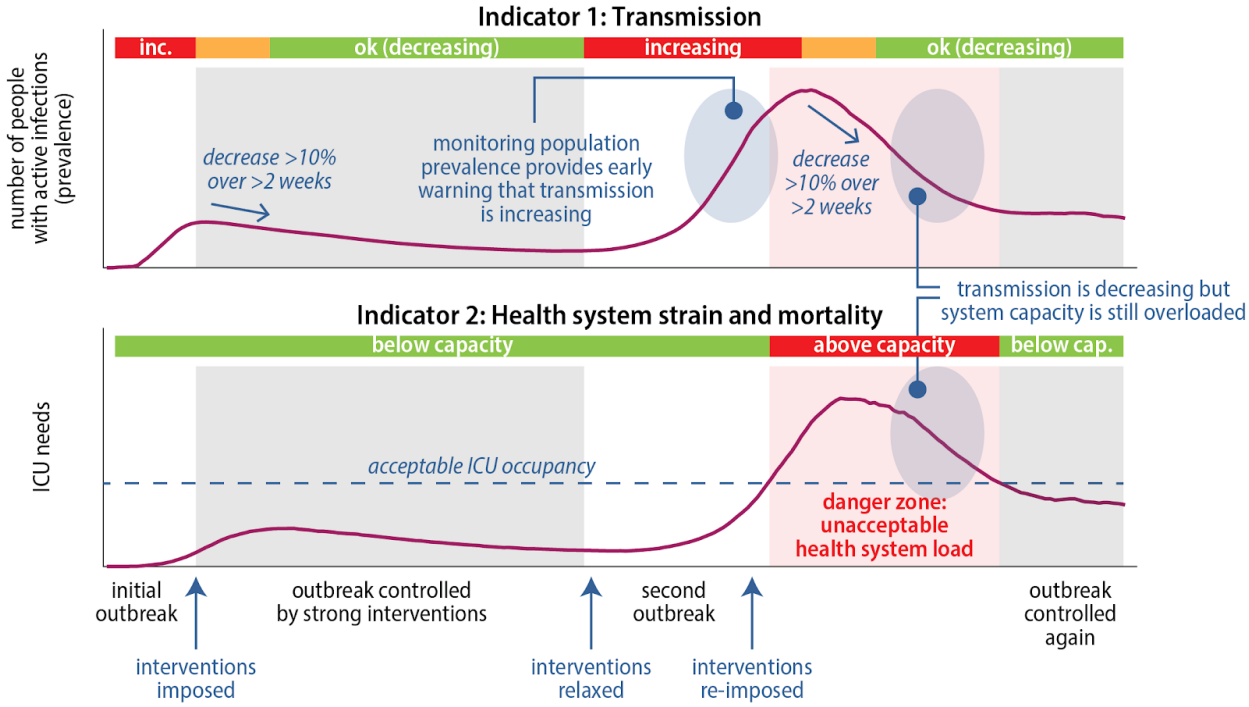

Figure 1. Two proposed indicators for evaluating when to move into the next phase of reopening. Top: indicator of transmission, such as prevalence, reports on whether the outbreak is growing or shrinking. Bottom: indicator of burden, such as hospitalization rates, ICU occupancy, or deaths reports on the outbreak's current impact on the health system and population health.

Surveillance can accurately track rates of disease spread

Surges in hospitalizations and deaths are preceded by increases in prevalence. Ideally, we would **assess changes in prevalence**--which reveal current transmission rates--through random testing of the general population over time. This is impractical due to costs. In the best of all worlds, we would be able to anticipate increases in prevalence through other indicators, such as changes in perception of disease risk and mobility, but this research is only beginning.

Surrogate populations can instead be used to track recent infections and transmission rates in the general population. Surrogate populations are a key feature of surveillance systems, including systems for monitoring seasonal and pandemic influenza (Lipsitch et al. 2009, 2011). A defining feature of surveillance is that the **testing criteria and sampling "effort"** (e.g., number of tests given) are **predefined and do not change over time**. This is critical: changes in the total number of test-positive cases in a region or the fraction of all tests that are positive are an unreliable measure of shifts in transmission because testing capacity and demand for testing can fluctuate for reasons unrelated to disease prevalence. Thus, case counts obtained from ad hoc samples should not be the basis for policy.

Proposed surveillance

We propose tracking infections in two sentinel populations: (1) symptomatic individuals appearing at outpatient testing sites, and (2) pregnant women presenting for delivery.

Hospitalizations, ICU occupancy, and deaths are all later events in the course of disease, so measuring more recent infections is closer to a "real-time" estimate of the rate of transmission in the community. After a 5-day incubation period, symptom onset precedes hospitalization by approximately 4.2 days, ICU admission by 6.7 days, and death by 11.7 days. Thus, changes in hospitalization rates follow changes in transmission by at least 9 days. **Tracking newly symptomatic infections provides sooner notice** that trends are moving in the right or wrong direction, allowing faster responses--potentially a quicker shift to the next phase, or suppression of a new outbreak (Figure 2).

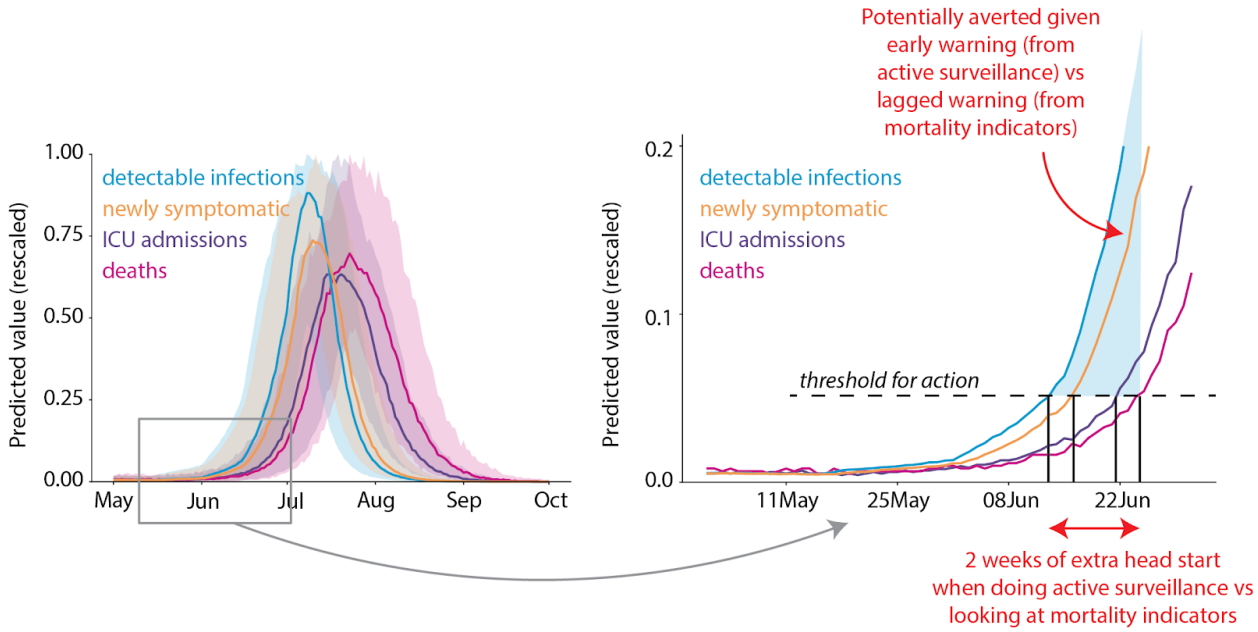

Figure 2. Surveillance of upstream indicators such as newly symptomatic cases or all detectable infections, including asymptomatic and presymptomatic infections, would give decision-makers extra lead time to decide a proper course of action if metrics are increasing. Model: predicted daily incident infections, symptomatics, ICU admissions, and deaths over all of Illinois following gradual reopening of all but the northeast region, beginning in mid-May, with no contact tracing (Northwestern model).

Another useful surrogate but non-sentinel population are **patients admitted to medical ICUs**. As long as ICU capacity is not exceeded, this is an excellent, though lagged, indicator of epidemic activity. Testing all ICU patients was recommended to track influenza activity in 2009 (Lipsitch et al. 2009, 2011), and is among the strategies used in Hong Kong for COVID-19. ICU patients are considered a slightly more reliable surrogate than all hospitalized patients because criteria for hospitalization can change, and testing all of them is harder to sustain over time. An advantage of having this additional population is that it can be used to confirm the reliability of

the outpatient sentinel indicators: generally, increases in the ICU population should follow increases in the outpatient population by nearly a week.

General approach

Again, the defining feature of surveillance is that testing criteria do not change in time. For the purposes described here, the surrogate populations do not have to be perfectly representative of the general population, and they furthermore do not have to be non-representative in exactly the same ways. For instance, testing may be easier at one site than another, leading to different participation rates. However, the sampling strategies should be stable in their identity in time.

Symptomatic individuals at outpatient testing sites. Estimates of transmission rates can be obtained from systematic sampling of symptomatic people who appear for outpatient COVID-19 testing. To increase the reliability of sampling, a **fixed number of test results** should be reported each day from symptomatic individuals presenting to a network of sites. Symptoms determining eligibility, patient surveys, and **sampling protocols should be standardized across sites**. The design becomes much more complicated if some individuals are prioritized for testing.

Women in delivery. Approximately 390 women give birth per day in Illinois. Even two-thirds of this population is a large enough sample to show meaningful changes in prevalence from week to week, although it will be less able to pick up on regional differences. An advantage of this population is that it is **relatively invariant to fluctuating levels of interest in COVID-19 testing**. Additionally, this population is used throughout the U.S. to track COVID-19 dynamics in different locations, and is the basis for several new CDC surveillance studies. As many women should be enrolled as possible.

Hospitalizations in the MICU. In select hospitals and clinics, all patients admitted to the medical ICU should be tested for COVID-19 on admission. This helps **validate the outpatient indicators** of epidemic activity and improves their ability to predict demands on healthcare.

Vulnerable populations. In addition to tracking infection in the general populations, vulnerable populations and their close contacts should receive close monitoring because they suffer an inordinate burden of disease. They might also serve as sentinel populations for the community. These populations include residents and staff of long-term care facilities, prisons, meat processing plants, homeless shelters, and other congregate settings. All symptomatic individuals in these populations should be sampled quickly.

Individual-level data needed. From each individual sampled, healthcare workers should obtain the age; sex; patient ZIP code; test type; symptoms; date of symptom onset; travel in past week outside the state; whether the individual has had any known contact with a confirmed case, including a case associated with contact tracing; and whether the individual lives in a

congregate facility. Once contact tracing becomes widespread, **data from contact tracing should be combined with the surveillance described here**.

Regional coverage. Given the operational units of decision (EMS regions or super-regions), we can calculate how many sites (clinics, hospitals, etc.) and how many daily samples are needed to identify transmission changes and estimate prevalence with confidence and speed in the region. We estimate that at minimum, **initially, test results from 3500 symptomatic people should be reported each day for each region, although 1000 could still work**. This number will change as prevalence drops, and it becomes harder to track infections. A larger sample size will increase capacity to detect changes in transmission rates quickly. The sampling scheme can also be adapted to monitor key subpopulations (such as racial/ethnic groups, urban/rural populations, etc.) if that is of interest. Not all hospitals, clinics, and testing sites need to participate. What is most important is to ensure that the **sites involved maintain a stable sampling strategy and communicate reliably** over time, and that enough sites are included to establish a good statistical signal. This will require ongoing communication with site leadership.

The importance of fast, easy testing. To maximize the ability of surveillance to inform policy, **infections must be identified early**. It must be **easy for individuals to get tested**, so they are swabbed when they have a suspicious cough, not when they are wondering if they are sick enough to go to urgent care. Additionally, **test results must be obtained quickly**, at least within 24 hours. (These are also requirements for effective contact tracing.)

How this surveillance can inform decision-making

This surveillance provides clear **public health indicators** for when it is safe to shift to a more relaxed phase of reopening, or when to increase precautions. Good surveillance also underpins an adaptive strategy that **minimizes economic costs and disease burden** in the long run.

Public health indicators

Indicator 1. Decreasing transmission (R_t). The number of individuals positive in the sentinel populations (women in delivery and symptomatic individuals presenting to testing sites) will track transmission rates. We estimate that transmission rates have dropped 75-90% under shelter-in-place in Chicago. Advancing to a more relaxed phase could easily involve a 10% increase in contact rates, which would cause a commensurate increase in transmission in the absence of opposing forces, such as warmer weather. Thus, **we propose that before proceeding to a new phase, transmission declines enough to produce at least a 10% drop in daily new cases in the surveilled populations over at least a two-week period (initially), ensuring R(t) < 0.9.** With more experience, this interval could be shortened; the 10% threshold could also be adjusted as more research is completed on the effects of different interventions on transmission. Structured surveillance with regular reporting should reduce variation present in current case counts, making it easier to detect trends quickly and

confidently. Weekend effects and minor reporting delays can also be adjusted for statistically (e.g., McGough et al. 2020).

Indicator 2. Health system usage and deaths are not "too high". For each region, a "maximum acceptable capacity" -- the maximum acceptable hospitalization occupancy or number of deaths -- needs to be established. We suspect the maximum fraction of med/surg hospital beds that should be occupied by COVID-19 patients is approximately 15-20%, given usual occupancy and 14% surge capacity requested under "Restore Illinois", but **it is important to assess variability in local capacity and acceptability of transfers between hospitals.** The Chicago plan allows advancing to the next phase of reopening when med/surg bed usage by COVID-19 patients falls below 24%, all hospital bed usage below 20%, ICU usage below 42%, and ventilator usage below 23% (corresponding to 1800 hospitalized, 600 in the ICU, and 450 on ventilators). As long as occupancy is below this capacity and Indicator 1 is met, reopening can proceed.

The **criteria for moving "backward", or increasing interventions, need not be symmetric**: The thresholds for responding to any statistically significant increase in transmission or excess hospitalization or death should be lower than for advancing phases.

Improvements to policy and forecasting

These indicators are also an **early warning system for healthcare demands**. By studying the association between cases in the sentinel populations and later changes in hospitalizations, especially in the MICU surveillance population, we can better forecast when hospital populations will exceed defined thresholds, and by how much.

This surveillance can also be used to **measure precise changes in transmission rates to fine-tune interventions**. We can apply statistical methods to these data to measure the local effective reproductive number (R_t) with minimal delay (Wallinga & Teunis 2004, Cori et al. 2013, Thompson et al. 2019, Bettencourt & Ribeiro 2008). This will tell us directly if the epidemic is being suppressed (R_t < 1; Indicator 1) or if transmission has simply been reduced (with R_t declining but > 1), and provides a quantitative framework for **anticipating how much interventions can be relaxed** (i.e., transmission can increase by up to 40%) while avoiding an unacceptable surge in severe cases and deaths. Thus, this system can augment existing modeling and forecasting efforts, and studying trends in R_t can reveal which interventions have been particularly successful in Illinois. However, we emphasize that a drop in the reproductive number (effectively Indicator 1) alone is insufficient reason to advance phases because it does not consider current disease burden, or the absolute rate of hospitalization or death.

After careful examination of different methods to calculate R_t (paper in prep.), we are preparing a dashboard to track recent transmission rates (Figure 3). Without **reliable surveillance of new infections**, including information on date of symptom onset, these estimates of R_t will be more historical (lagged), biased, imprecise, and overall less useful for decision-making.

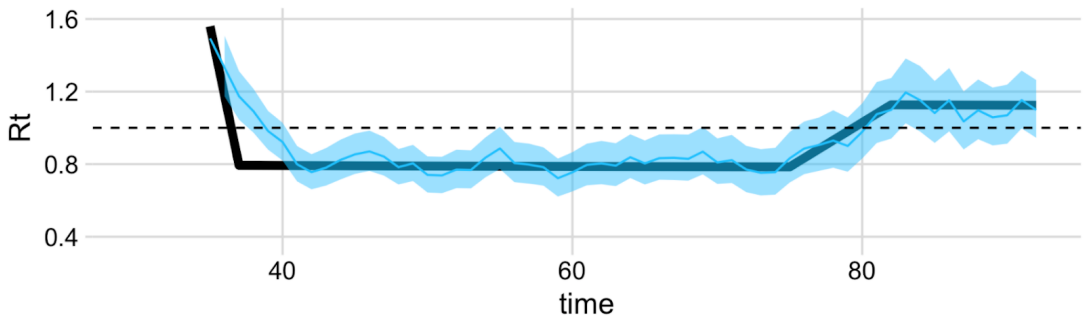

Figure 3. Example estimation of the effective reproductive number (R_t) in a simulation study. The true number over time is in black. The estimated reproductive number, assuming incomplete sampling, is in blue. This curve can indicate how well interventions are working: the outbreak is growing when R_t is above 1 (dashed line) and shrinking when R_t is below 1, which corresponds to Indicator 1.

Summary of suggested enhancements to “Restore Illinois”

1. Rather than relying on arbitrary cutoffs based on the percentage of all tests that are positive, establish a **structured surveillance program focused on identifying infections soon after they start** and **link this surveillance to hospital capacity**. Trends in hospitalizations and deaths will track changes in the sentinel surrogate populations.
2. Critically, **trends in percent positivity do not determine whether it is appropriate to transition between phases**. What matters is the number positive in defined surrogate populations, which track prevalence in the general population and presage hospital demand.
3. With reliable measures of recent changes in transmission, it could be possible to transition safely between phases faster than every 28 days.
4. Additionally, by using surveillance to estimate R_t, it should be possible to **quantify exactly how effective the interventions need to be** to maintain suppression or avoid hospital surges.
5. **Vulnerable populations** that suffer the highest morbidity and mortality need to be monitored especially closely. These are also possibly sentinel populations that can further inform forecasts.

We caution that **we have not described the requirements for different types of interventions**, such as contact tracing, to mitigate or suppress transmission. It would be foolish to proceed from one phase to the next just because prevalence is low and transmission is declining if the next phase in fact involves a 50% increase in transmission, potentially sending $R_t > 1$. A discussion of these requirements will come in a separate document.

Appendix 1. Structure and protocols for the surveillance network

Symptomatic individuals at outpatient testing sites

Testing of symptomatic individuals at outpatient sites should be the backbone of sentinel surveillance and rolled out first in regions closest to reopening and in regions where contact tracing may be particularly challenging.

Surveillance sites

To **enable the most adaptive policy**, enough sites would be included so that several thousand symptomatic people would be tested each day in each region (e.g., EMS super region, region, city) for which an R_t is desired. However, useful estimates of R_t can be derived from **as few as 1000 symptomatic, recently infected people**.

Testing sites that deserve priority for inclusion in the surveillance network are those that

- see high numbers of mildly symptomatic (ambulatory) people, as the aim is to maximize surveillance of recently infected individuals,
- remain open seven days per week,
- plan to remain open for at least 12 months (though this is not required),
- do not prioritize sampling of more symptomatic over less symptomatic individuals or use any other triage system (aside from symptomatic/asymptomatic),
- use only one type of specimen collection and virological test on all samples at a time, and ideally the same one over time (though this is not required),
- consistently return test results within 24 hours, and ideally in less than 12 hours, and
- have a track record of reliable, fast communication.

Each site should identify the minimum daily number of symptomatic individuals it has tested over a recent week. Assuming the capacity will not be permanently increased in the near future, this will be **the daily number of test results (*n*) reported by that site for surveillance**, *regardless of the number actually tested on any day*. (If there is high variability in typical test numbers due to sites' being closed certain days of the week, this can be adjusted for statistically, but this variation in "sampling effort" must be communicated. It is not ideal. In such cases, sites should commit to reporting on their open days a number of tests that corresponds to the minimum daily number they have reported in their open days in the past few weeks.)

A testing site **should only be included if it can commit to a fixed testing strategy** in all the areas above. If it must make a change (e.g., to the virological test used), **these deviations must be communicated rapidly.**

If many testing sites fit these criteria and it is easier not to work with all of them, the modelers can help identify which sites to include to increase representativeness for regional R_t estimation.

Eligible individuals

All individuals who report symptom onset in the past four days should be enrolled up to the site's predefined daily limit, *n*. No restrictions should be made to age, ethnicity, etc., although it is understood that presenting individuals may not be a random sample of the population, and some sites might exclude children. (Additional eligibility restrictions should be communicated in each site's protocol.) We are currently identifying the appropriate list of symptoms to facilitate comparison with other studies.

Data to collect and report

1. Self-reported date of symptom onset (up to and including 4 days ago)
2. Age in years
3. Gender
4. Current symptoms (from set, TBD)
5. ZIP code of residence
6. Race and ethnicity
7. Known contact with a confirmed case in week before symptom onset?
8. Contacted as part of contact tracing program?
9. Live in congregate facility? (Dormitory, long-term care facility, etc.)
10. Travel out of state in week before symptom onset? (Origin at state/country level)
11. Specimen collection type (nasal, NP, OP, etc.)
12. Test date and time
13. Test type (method)
14. Test result
15. Date and time of test result

The results of the first *n* tests each day should be reported as soon as possible. If fewer than *n* subjects enroll that day, their results should still be reported.

Women in labor and delivery

Surveillance sites

Due to the relatively small number of women who give birth each day in Illinois (<400), all medical centers that assist with labor and delivery and that have the capacity for regular testing and reporting should be included. As for the ambulatory testing sites, these sites should commit to a fixed protocol (with consistent criteria for eligibility, consistent virological testing methods, and consistent turnaround times). Any deviations from the protocol must be communicated. If testing all women in labor and delivery is impractical, a site should commit to a smaller, fixed daily number to report.

Eligible individuals

All women presenting for labor and delivery would ideally be included. If only a subset can be included, they should be selected “randomly” (e.g., the first 5 giving birth each day), not on the basis of suspected COVID-19 status or potential correlates of COVID-19 status.

Data to collect and report

The same data fields would be reported as for the ambulatory symptomatic population, with “self-reported date of symptom onset” replaced with “self-reported date of symptom onset (if any)”, and without the four-day restriction.

Admissions to MICUs

Surveillance sites

Any site with an ICU and consistent criteria for admission to the ICU should be included, prioritizing larger sites that have a history of consistent reporting. If a separate COVID-19 ICU has been established, it should be included with statistics on the MICU. It is acceptable that hospitals group ICU patients differently, as long as the criteria for entering each ICU or MICU (including COVID-19 ICU) are consistent over time.

Critically, the surveillance program here entails **testing all admissions to the ICU/MICU who have not already tested positive for COVID-19 in the past two weeks.** Sites must commit to this testing protocol, ideally for at least 12 mos. Many hospitals are already doing this.

Eligible individuals

All admissions to the MICU or general ICU, if no MICU exists. If an admission has not tested positive for COVID-19 in the past two weeks, he or she should be tested again on the day of admission.

Data to collect and report

1. Self-reported date of symptom onset (if any)
2. Age in years
3. Gender
4. ZIP code of residence
5. Specimen collection type (nasal, NP, OP, etc.)
6. Test date and time
7. Test type (method)
8. Test result
9. Date and time of test result
10. Date of hospital admission
11. Date of ICU admission