

## A Tale of Many New York Cities

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The United States continues to lead the world in total reported COVID-19 cases and deaths, with 32,923,303 confirmed cases and 585,708 deaths reported as of May 15<sup>th</sup>, 2021 [1]. The New York City (NYC) metropolitan area was the initial epicenter of the US COVID-19 pandemic and, because of this, bears a disproportionate share of COVID-19 fatalities. Four out of NYC's five counties rank in the top 20 across the US for total COVID-19 deaths: Kings (2<sup>nd</sup>), Queens (5<sup>th</sup>), Bronx (6<sup>th</sup>), and Manhattan (13<sup>th</sup>). The 943,246 confirmed COVID-19 cases in NYC account for just 45.3% of all New York State (NYS) cases, but its 39,301 confirmed deaths represent three-fourths (74.3%) of all COVID-19 deaths in NYS [1].

Of course, diagnosed cases and deaths represent only portions of the COVID-19 epidemiologic iceberg [2]. Measurement of the total population experience with infection, including those undiagnosed, allows one to understand the full extent of the pandemic, the subgroups and factors most associated with infection, and provides denominators for the calculation of other timely public health measures such as the percent diagnosed and infection fatality ratio [3]. Three overarching study designs have been deployed to measure infection history, each with their own strengths and weakness: 1) Serological studies that measure the presence of anti-SARS-CoV-2 antibodies, a marker of previous infection [4-7], 2) Multiplier methods to adjust surveillance data for underdiagnosis [2], and 3) Dynamic simulation models based upon a variety of surveillance and other epidemiologic inputs [8].

Serological studies can be further differentiated by the use of passively-available residual serum from clinical procedures or blood donation, which offer large scale in exchange for a lack of in-depth information on covariates and a well-defined sampling frame, versus active studies conducted in the field to collect specimens and additional survey questions that contextualize the lab results. Since early in the epidemic, both serological study approaches have been applied towards assessing the extent of infection in the NYC area [4-7, 9, 10]. These exist on a continuum, with the studies from Spring 2020 providing rapid estimates of cumulative incidence, illumination of

critical disparities by demographic features, and calculation of secondary epidemiological measures [4, 5, 7]. More recent studies, including the report by Parrott et al. in this issue of *the Journal of Infectious Diseases*, dive deeper into social determinants and causes underlying the disparities revealed in the earlier work [10].

In the first of the general-population residual serum studies, Stadlbauer et al tested for antibodies in weekly cross-sections (N≈250) taken from different clinical settings at Mount Sinai Hospital, finding approximately 19% prevalence during the April-May period [4]. The Centers for Disease Control and Prevention (CDC) conducted monthly waves antibody testing from NYC-area commercial laboratories, finding 20.9% prevalence in April and 23.2% in May (N≈2,500), with additional stratifications by sex and age [5, 6]. While limited by lack of additional covariates, these projects documented some of the first longitudinal trajectories of population-level antibodies, showing slight declines by the end of the first wave in NYC, consistent with waning antibody detection.

A third study, in which we were involved, actively sampled patrons in grocery stores across NYC in April 2020 (N=5,946), via a convenience sampling design adjusted via post-stratification weighing. This project combined phlebotomy with a brief questionnaire that collected demographic information and county of residence [7]. This project found 22.7% prevalence, of which 7.1% were estimated as diagnosed. Substantial racial and ethnic disparities were documented, providing the first US population-based estimates of disparities in infection (as opposed to cases or deaths), which were later incorporated in a more complete analysis of disparities in COVID-19 outcomes [11].

Taken together, these studies provided key epidemiological measures and initial documentation of disparities by the second month of the epidemic in New York, which informed policies regarding testing, the potential for herd immunity, and focused further study and efforts aimed at health equity in the state, and these were available to guide efforts in other jurisdictions not yet affected [12, 13]. However, these studies provided limited explanations for disparities in

terms of contributing occupational, environmental, neighborhood exposures, or factors related to medical susceptibility.

The new study by Parrott et al joins another recent publication in *the Journal of Infectious Diseases* from NYC (Pathela et al), which sampled a few months later, but still the end of the 'first' wave, and together add this next layer of nuance to earlier estimates by having more extensive collection and analysis of questionnaires [9, 10]. Pathela et al conducted a larger convenience sample than the grocery store study (N=45,367), at walk-in sites around NYC, and found 23.6% prevalence during May-July. Parrott et al used a probability sampling design (N=1,074), finding 24.3% prevalence during June-October. This project combined online and at-home visits (n=497 specimens at-home), procedures that naturally yielded a smaller study, but one based on a more rigorous statistical design.

The study design of Parrott et al features two innovations that potentially address limitations of the earlier work [10]. First, the inclusion of home visits afforded access to those unavailable for sampling in the other studies, who may have been more medically vulnerable or have had a different level of exposure (e.g. high degree of self-isolating). As not all persons participated in this at-home portion, the study used a combined outcome of antibody detection from at-home collection and self-reported history of a positive antibody test. The self-report measure was found to have high agreement, when a specimen was available, although the large portion of participants not providing an at-home specimen (54%) may ultimately move the study design more towards a convenience sample and the combined measure was necessarily mixing one signal known to decay (antibody detection) with one less likely to (self-report). Second, the study leveraged the existing platform of the NYC Community Health Survey, a probability survey from a defined sampling frame. This facilitates claims of representativeness, although with a 7.4% response rate this feels elusive and one, at best, may be positioned to better characterize sampling bias than the other studies.

Both recent NYC studies found essentially the same prevalence as the earlier ones, despite being a few months later into the tail end of the first wave, when some new infections were being added. This triangulation suggests either truly minimal new infections or that antibody was waning in some persons, which was counterbalanced by ongoing infections. Given how much time has elapsed since the sampling period, during which New York experienced an extended second wave, and given that the present epidemiologic situation is transformed by widespread vaccine availability, these estimates of prevalence, or any associated epidemic measures, are no longer actionable for public health. Nonetheless, we can still learn from the *associations* found by Parrott et al, if not the absolute estimates. Their results help to unpack the higher prevalence among Hispanic and Black persons, by illustrating the increased prevalence associated with living in the Bronx, non-English interview language, high neighborhood poverty, and degree of leaving the home. Causality remains murky, but in context with other studies from the COVID-19 pandemic and other infectious diseases like HIV and tuberculosis, it is clear that structural and social factors shape the exposure environment that places persons of color at higher risk [14-18].

The COVID-19 pandemic has recreated, in record time, the same well-known racial and ethnic disparities in outcomes seen in other infectious diseases. And while this reality cannot be undone, it can at least be attended to during this next recovery phase of the pandemic. Public health and other government officials must ensure that that communities of color have equal access to the COVID-19 vaccines, including the necessary resources and tools for accessing them. We must ensure that vaccine uptake and disease burden rates are tracked by community characteristics in real time, and that adjustments to vaccine programming are made as necessary to ensure that the social determinants of health are lessor factors in overcoming the COVID-19 pandemic than they were in its manifestation.

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