

COVID-19 Action Newsletter

UT Southwestern Department of Internal Medicine
James Luby, M.D., and Robert Haley, M.D., editors

The Situation: U.S. Cases Approach 4.9 Million

In the world as of August 7, 2020, 19,127,091 cases of Covid-19 and 715,555 deaths have been confirmed. In the United States, there have been 4,884,406 cases, the most in the world followed in order by Brazil, India, Russia and South Africa. China is now 29th in the world with 88,549 cases. Deaths in the U.S. through August 7 have been estimated at 160,111.¹

From March 10 through August 6, there have been 52,869 confirmed cases of Covid-19 reported from Dallas County with 736 deaths, about 28% of these from long-term facilities.² Of hospitalized cases in Dallas County, more than two-thirds have been under 65 years of age. Diabetes mellitus has been seen in about one-third of all hospitalized patients. More men than women have died. Sixty percent of the cases have occurred in the Hispanic population. As of July 21, 530 deaths have been analyzed by race with 27% occurring in Whites (actual White population 29%), Hispanics 44% (population 41%), Blacks 24% (population 24%), Asians 4% (population 7%). Specimens submitted for diagnosis of respiratory viruses show continuing positivity for SARS-CoV-2 with the latest result on 8/7/20 being 19%.

References:

1. Covid-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) (Updated 8/7/20)
2. Dallas County Health and Human Services. Acute Communicable Disease Epidemiology Division 8/7/20

Feature Article

Mathematical Modeling for Infectious Diseases

Richard J. Medford, MD, Division of Infectious Diseases & Geographic Medicine, Clinical Informatics Ctr

Mathematical models for outbreaks of infectious diseases have become an integral component of the management of epidemics. They are simplified representations of complex systems that attempt to: a) understand the transmission dynamics (interactions between host and pathogen that allow for propagation/elimination) of an infection, b) forecast the future course of an outbreak, and c) evaluate mitigation/control strategies.¹

Model Framework: Understanding the objectives of modeling and type of data available, models can largely be classified into 4 main categories: a) compartmental, b) ecologic diffusion, c) occupancy or patch dynamic, and d) agent-based or individual-based. These model types can be used in isolation or in combination depending on the problem being addressed. Each has its unique advantages and disadvantages, and it is important to recognize the assumptions (implicit or explicit stated rules, choices or conventions) inherent to the model when choosing an appropriate method.²

Compartmental Models (SIR Model): Compartmental models assign individuals to a defined, mutually exclusive group, or compartment, based on disease status. An individual can only be in 1 compartment at any given time but can move, or transition, to another compartment based on the parameters of the model.

Likely due to its simplicity, the SIR model, named for its 3 compartments (susceptible, infected, recovered), has become a widely adopted framework that approximates disease behavior by estimating only 2 parameters (**Fig 1**).

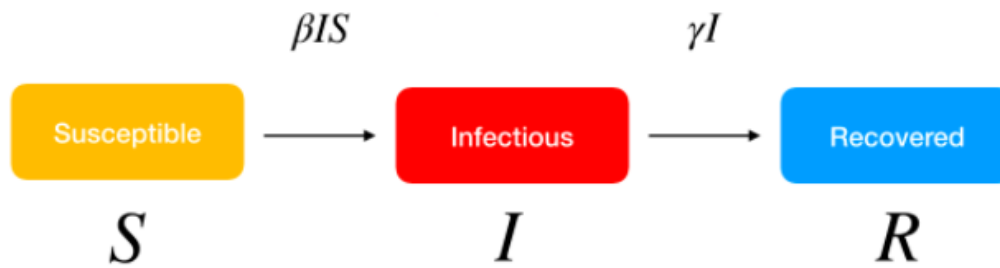


Figure 1. SIR Model

S: Susceptible - all individuals that may become infected if exposed to the pathogen

I: Infectious - all individuals who have the ability to infect those in the susceptible compartment (asymptomatic and symptomatic transmitters)

R: Recovered - all individuals who are no longer contagious (immunity or death)

β : Beta – a parameter that expresses the effective contact rate affecting transition from $S \rightarrow I$

γ : Gamma – a parameter that expresses the rate of recovery affecting transition from $I \rightarrow R$

The ratio of β to γ is termed R_0 (pronounced R naught) and is the *basic reproduction number*. It is unitless and refers to the mean number of expected cases from a single infected individual where all individuals are susceptible to the infection. In contrast, the *effective reproduction number*, R_t , is the average number of expected cases from a single infected individual at time t in a partially susceptible population. When trying to understand the direction of a pandemic, a R_t value >1 means the outbreak will continue to propagate while a value <1 means it will decline.³ At the time of this writing, the R_t values in Dallas and Tarrant County are ~ 0.9 .⁴

Applications of the SIR Model for COVID-19: Multiple institutions (Imperial College London, Columbia University, University of Pennsylvania)^{5, 6, 7} have adopted some form of the SIR model as their preferred method for modeling COVID-19, resulting in significant local, state and national policy impact. These models are used to forecast number of hospitalizations, ICU admissions, length of stay and trajectory of cases at local and national levels.^{5,6,7} Since the simplified SIR version does not take into account latency of a virus as an example, there are many derivatives of this basic form, including SEIR, where E represents an exposed but not yet infectious compartment (UT Southwestern uses the SEIR framework)⁵. Herd immunity and immunization have been proposed as cornerstones of addressing this pandemic, and similarly a modified SIR model can be used to model vaccination, known as SIRV, where the V compartment represents vaccinated individuals.⁸

Modeling in the DFW Area: As one looks at the epidemic curve of Dallas and Tarrant Counties, there have been clear fluctuations (**Fig 2**).⁴ It is important to understand this variation, not only in absolute number of cases but also in terms of age, gender, geographical region, occupation, race and type of dwelling.

The narrative of COVID-19 in Dallas County can be traced from its first entrance in March to the more affluent areas of

Dallas, to local outbreaks in assisted living facilities in April, to largely the working class in May, and to its transition from affecting the elderly to largely a younger population in June and July.

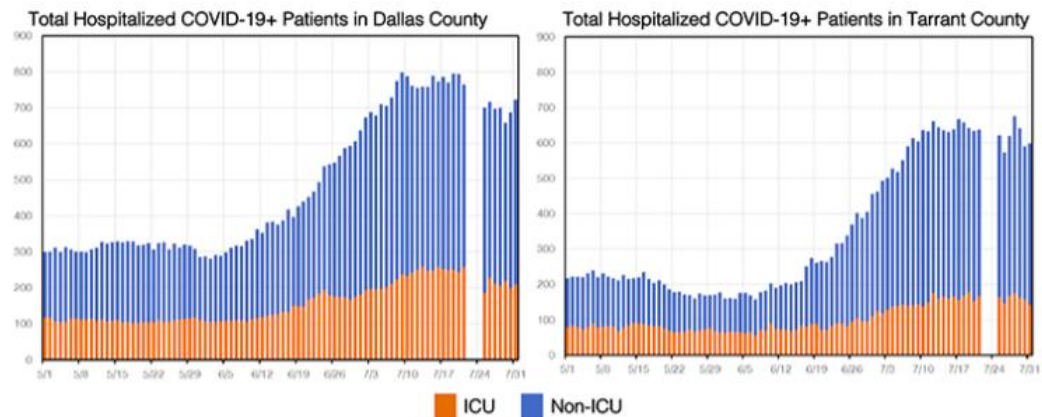


Figure 2. Epidemic curves of Dallas and Tarrant Counties (May 1 to July 31, 2020)

Our UTSW model also evaluates mitigation strategies to gain insight into the effectiveness of certain policy measures. Maximum likelihood estimates are established based on the R_t observed when the respective policy was put into place (**Fig 3a**). We then estimate total effectiveness through the assumption that policy effectiveness stacks by product of complements (**Fig 3b**).⁴

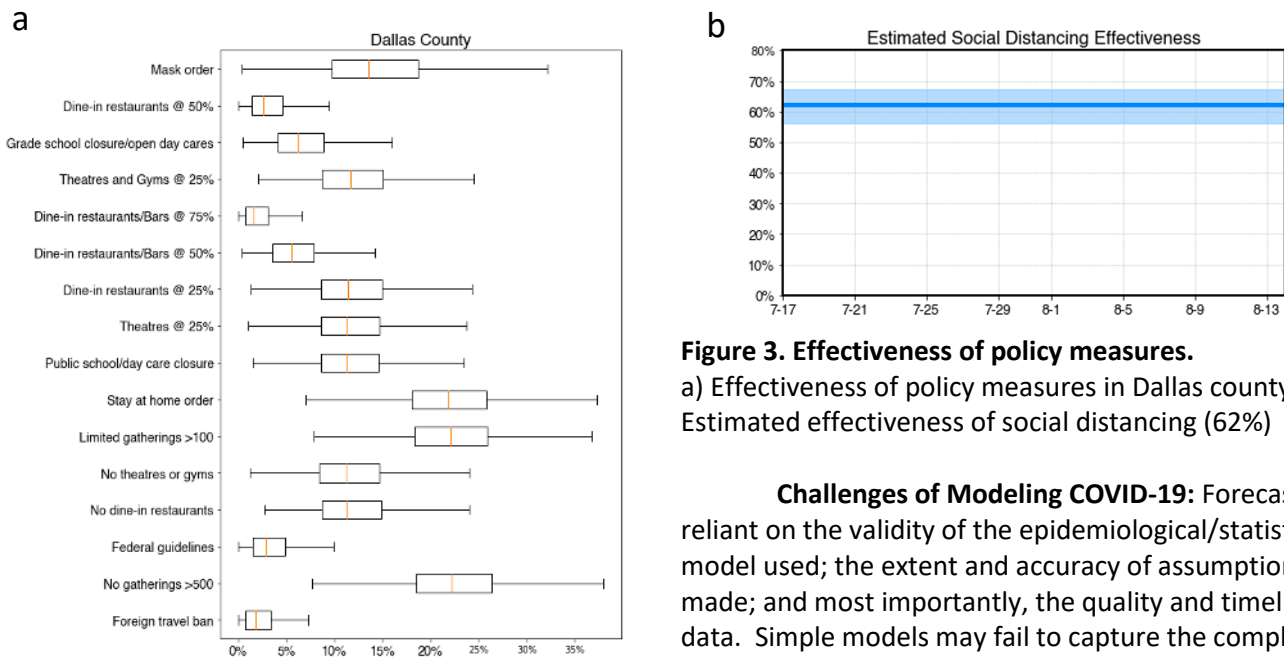


Figure 3. Effectiveness of policy measures.

a) Effectiveness of policy measures in Dallas county. b) Estimated effectiveness of social distancing (62%)

Challenges of Modeling COVID-19: Forecasting is reliant on the validity of the epidemiological/statistical model used; the extent and accuracy of assumptions made; and most importantly, the quality and timeliness of data. Simple models may fail to capture the complexity of human interaction and time varying characteristics of

infectious diseases spread. Assumptions are constantly changing, especially in volatile times when new non-pharmaceutical interventions are enacted. Difficulties related to testing, reporting and poor documentation result in data lags of 10-14 days, leading to under-detection or inaccurate forecasts.⁹

In summary, mathematical models are valuable tools, especially for the ongoing COVID-19 pandemic, that take complex systems and simplify them in a meaningful fashion to provide insight into an outbreak. Despite many challenges, they can inform public health decisions and ensure optimal use of resources.

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Clinical Update

Covid-19 and the Cardiovascular System

Since Dr. Mark Drazner's feature article on the cardiac manifestations of Covid-19 appeared on April 24, 2020 (C.A.N. Vol. 1, No. 2), there have been two major articles and one accompanying editorial that have appeared exploring the relationship between Covid-19 and the cardiovascular system.^{1,2,3}

The first study from Hamburg, Germany, studied myocardial tissue obtained at autopsy from 39 patients with SARS-CoV-2-positive pharyngeal PCR tests.¹ The patients were divided into 3 groups according to *myocardial* virus levels by PCR: the first having negative tests (15 patients), the second having positive tests with <1,000 copies (8 patients), and the third having copy numbers >1,000 (16 patients). Virus replication was measured in the 5 patients with the highest myocardial viral load (Figure 1; note the scales at the bottom of the figure). Virus load, relative cytokine gene expression, and CD lymphocyte number were expressed in a heat map (Fig 1).

Relative gene expression data showed an increased proinflammatory response in patients with the highest virus load. Immunohistochemistry staining revealed no group difference in leukocyte infiltrates. Virus presence was not associated with increased number of mononuclear cells. Lack of cellular infiltrate and cell necrosis indicated no myocarditis by Dallas criteria. By in situ hybridization, virus was present in interstitial cells and macrophages.

This was a large study primarily of elderly women where 16/39 patients showed virus at high copy number in the myocardium. Proinflammatory cytokines predominated in specimens with high viral loads. The Dallas criteria for myocarditis were not met. cardiac functional status was not studied.

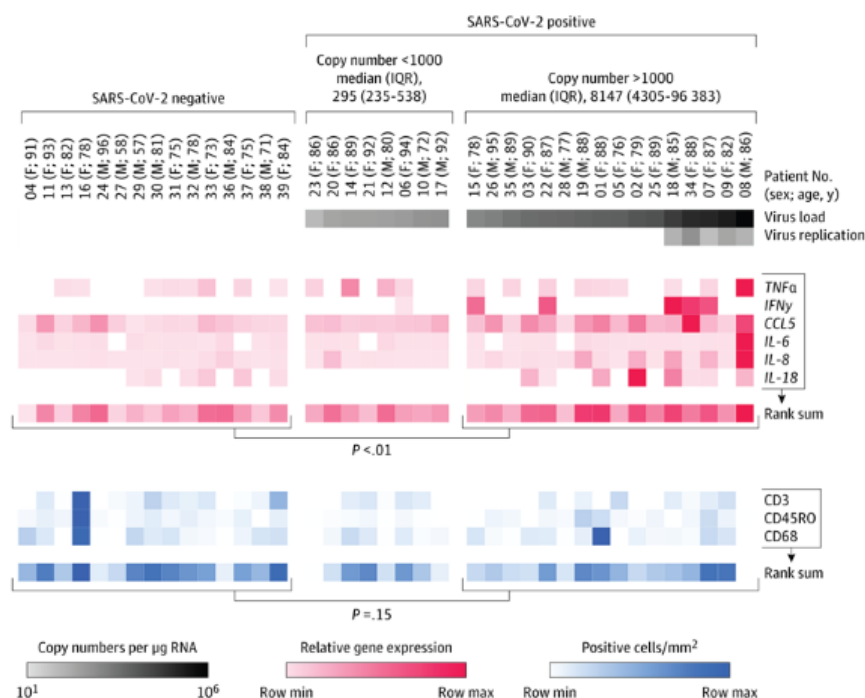
In the second study, from Frankfurt, Germany, 100 patients convalescing from virologically documented Covid-19 were studied by cardiac magnetic resonance (CMR) imaging and compared to 50 healthy controls and 57 risk-factor-matched controls at a median time of 71 days after diagnosis.² In 78% of the patients, CMR showed cardiac involvement and ongoing myocardial inflammation correlated with high sensitivity Troponin T elevation. Endomyocardial biopsy in severe cases showed active lymphocytic inflammation.

The editorial accompanying these two articles pointed out that in severe Covid-19 disease, myocardial involvement is frequent, persistent, associated with high cardiac viral loads, and occurring frequently in the setting of age and underlying cardiac disease.³ These findings suggest subsequent development of heart failure and other chronic cardiovascular complications.

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Figure 1. Virus Infection and Inflammatory Response in Cardiac Tissue From Coronavirus Disease 2019 Deaths



Dallas Epidemic Responding to Bar Closure and Mask Mandate

The massive statewide resurgence of the Covid-19 epidemic following the progressive relaxing of earlier control measures in early June escalated geometrically through the month, fueled by widespread socializing by young adults

Fig 1. Confirmed cases by day, Dallas Co.

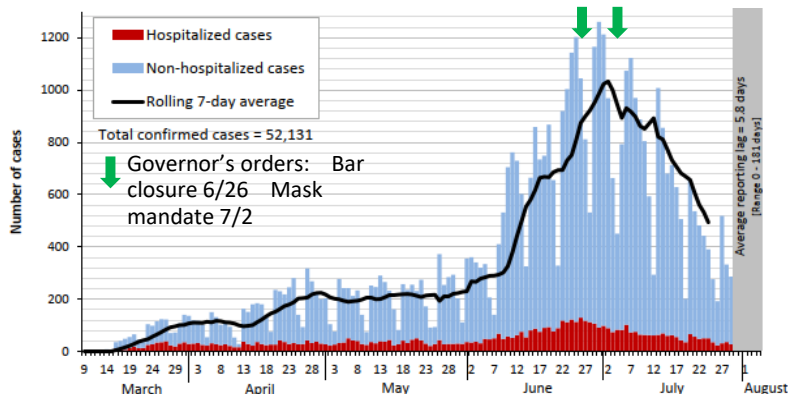


Fig 2. Confirmed hospital admissions by week, Dallas Co.

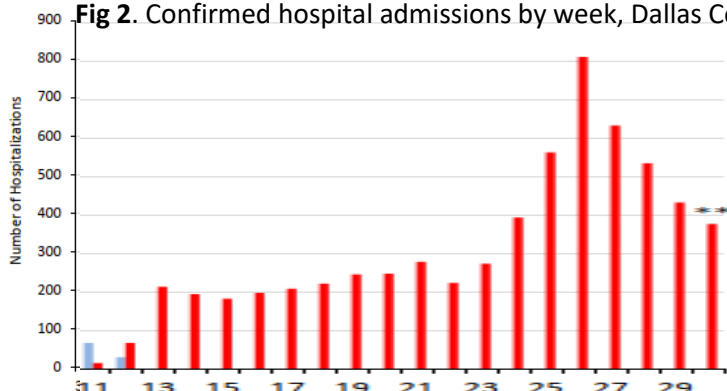


Fig 3. Confirmed ICU admissions by week, Dallas Co.

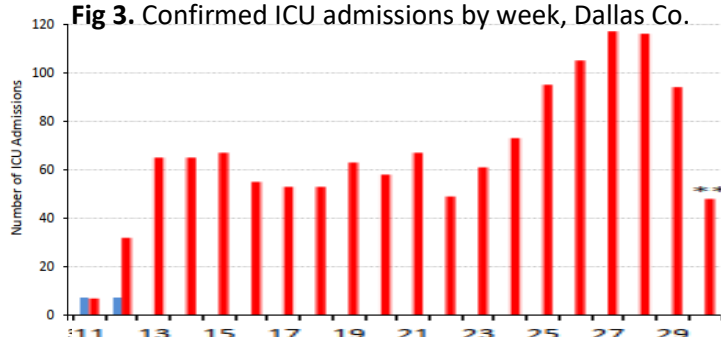
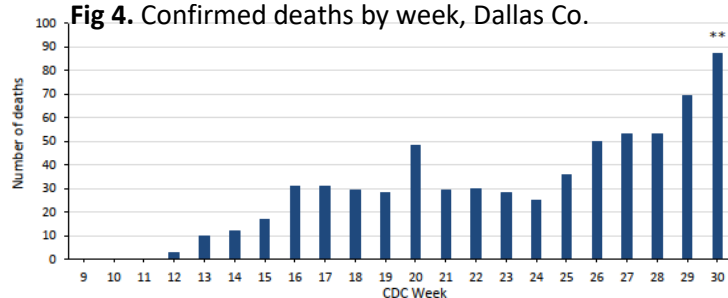


Fig 4. Confirmed deaths by week, Dallas Co.



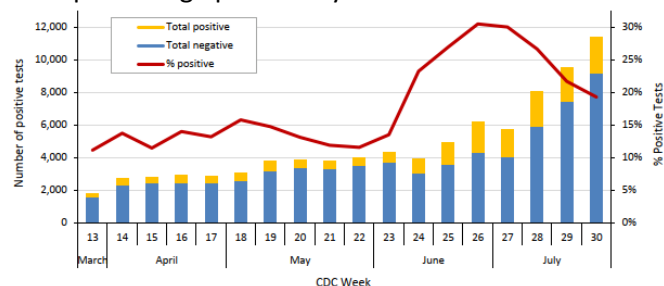
in bars, private gatherings and family get-togethers generally without masking or social distancing. With new cases exceeding 1,000 daily, the governor issued mitigation orders closing bars on June 26 and mandating masking on July 2. Within a week the daily case count began a progressive decline which continues (Fig 1).

Hospital admissions for Covid-19 rose and declined at the same time as cases (Fig 2), reflecting the fact that patients often first present for care when they become sick enough to require hospitalization. The curve for ICU admissions, however, is displaced to the right because patients often remain in the hospital for a week to 10 days before deteriorating enough to require ICU care (Fig 3). The curve for death is displaced even further to the right since the most severely ill often linger in the ICU for a month or more before succumbing (Fig 4). Consequently, deaths continue to climb after cases, hospital and ICU admissions begin declining.

These trends were not due to the amount of testing being done. The upward trend in cases in June occurred when the number of tests increased only slightly; whereas, the rapid decline in July occurred when testing was increasing (Fig 5).

These graphs are published bi-weekly by the county health department at: <https://www.dallascounty.org/departments/-dchhs/2019-novel-coronavirus.php>

Fig 5. Total Covid-19 tests done and the percentage positive by week



From the Editors

The editors thank Dr. Richard Medford for his feature article on mathematical modeling for infectious diseases.

The aim of this weekly newsletter is to serve as a source of information for the UT Southwestern community which can lead to better understanding and control of a new disease (COVID-19) caused by the pandemic spread of an emerging viral pathogen (SARS-CoV-2). We welcome questions, comments, and suggestions for topics and authors