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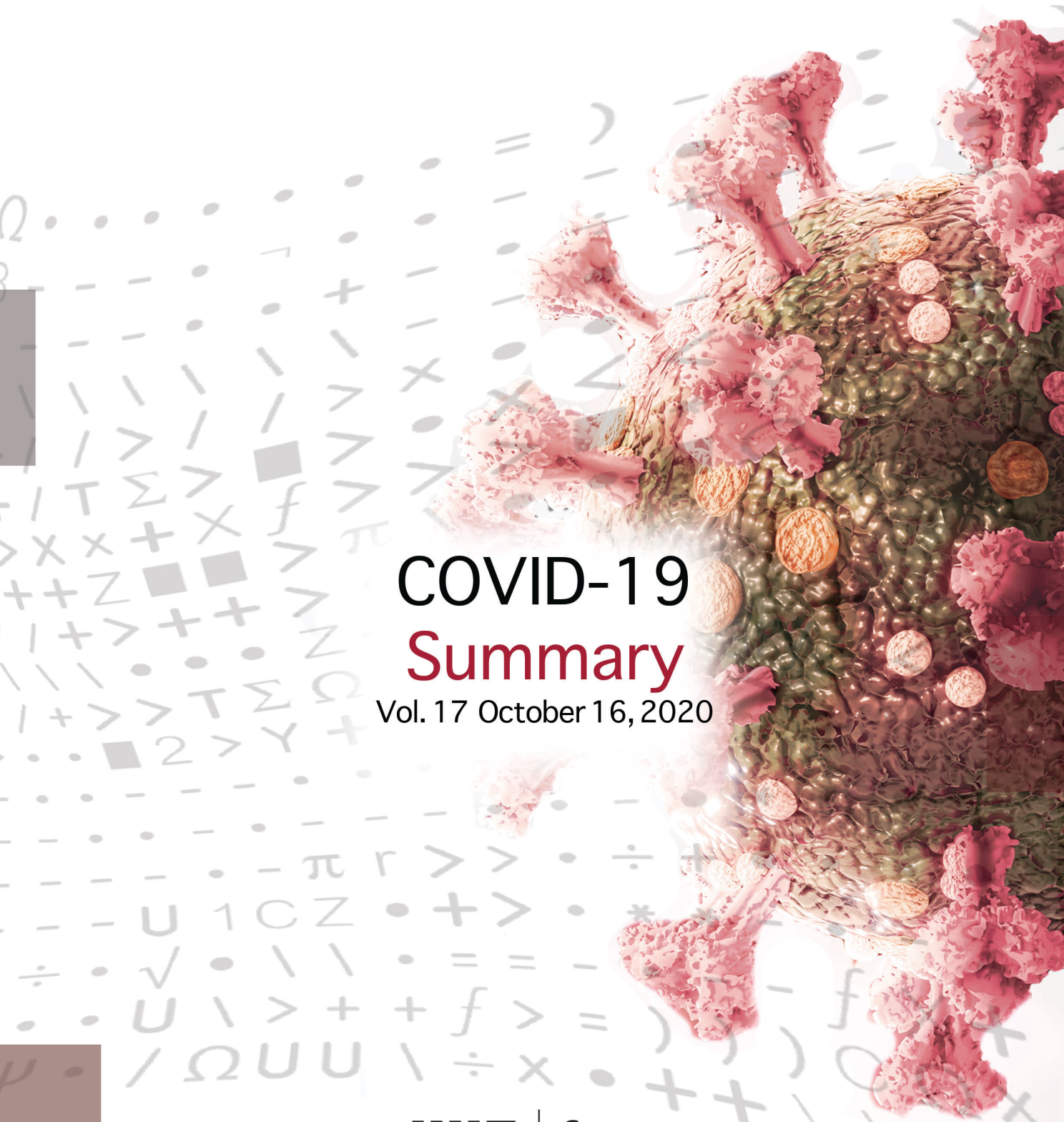

COVID-19 Summary

Vol. 17 October 16, 2020

MIT Corporate Relations

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MIT ILP UPDATES // COVID-19 RELATED

This is a very brief collection of current resources and information from MIT's Industrial Liaison Program covering a range of issues related to COVID-19 and is offered to help us all navigate during this ongoing unprecedented and disruptive time.

UPCOMING EVENTS

MIT ILP WEBINARS

See: https://ilp.mit.edu/search/event?f%5B0%5D=event_type_term%3A24

19 OCTOBER, 10:00 AM: FINTECH AT THE CROSSROADS: DIGITAL TRANSFORMATION GETS REAL

MIT Corporate Relations / ILP
Agenda: https://ilp.mit.edu/attend/fintech-crossroads-digital-transformation-gets-real

27 OCTOBER, 10:00 AM: DIGITIZATION OF RETAIL AND THE URBAN EXPERIENCE

MIT Corporate Relations / ILP
Agenda: https://ilp.mit.edu/attend/digitization-retail-and-urban-experience

FRIDAYS (2:00-3:00 PM) – DECEMBER 4: 21H.000: THE HISTORY OF NOW—PLAGUES & PANDEMICS EDITION

MIT History, https://history.mit.edu/news/21h000-history-now

We will look transnationally and across discipline at how plagues and pandemics have made an impact on human and non-human history. The course will have a roundtable format, meeting for one-hour sessions each week with brief presentations by the invited speakers followed by Q&A with enrolled students. The course will also be broadcast live as a webinar each week for the benefit of interested members of the larger MIT community and the public.

PROJECTS, INITIATIVES, RESEARCH

INFECTION / VACCINES: CONTROLLING THE SPREAD OF FLU

PIs: Richard Larson, Professor (Post Tenure), Data, Systems, and Society,
Stan Finkelstein, Senior Research Scientist, Engineering Systems, IDSS
IDSS https://idss.mit.edu/vignette/controlling-the-spread-of-flu/

Researchers examined the best ways to reduce the likelihood that individuals and groups will become infected with the flu, both by diligent use of non-pharmaceutical interventions and by effective deployments of vaccine. The research suggests that up to 5 million Americans who became ill with H1N1 flu in 2009 might not have become infected if an alternative, more adaptive vaccine allocation plan had been in effect—and provides the essentials for such a plan.

This research used a service-systems framing and mathematical modeling approach, incorporating theories and data on the spread and control of influenza. Researchers found that behavioral actions and governmental policies can minimize influenza's societal impact.

Researchers argued its the value of R0, characterized as the numerical constant of a given virus, is actually largely determined by local conditions and actions, many under our individual and collective control. This control is, in the absence of vaccine, intelligent use of non-pharmaceutical interventions—highly effective in reducing the spread of influenza. This vaccine analysis relied on government data depicting flu-like cases and vaccines administered during the 2009 H1N1 outbreak. During that outbreak, barely half of all states received allotments of vaccine in time to protect any citizens. This method of vaccine deployment—in proportion to census population—ignored the temporally uneven flu wave progression across the United States.

MIT AGELAB: VIRTUAL RESEARCH METHODS

Samantha Brady and Julie Miller Talk Virtual Research Methods at NVivo Conference September 2020
https://agelab.mit.edu/index.php/news/samantha-brady-and-julie-miller-talk-virtual-research-methods-nvivo-conference

The COVID-19 pandemic has demanded that many professionals reimagine how they do their work – and scientists are no exception. To highlight how ways that qualitative research might be done successfully in a time of social distancing, **AgeLab researchers Samantha Brady** and **Dr. Julie Miller** presented on their experience in transitioning a focus group study to an online environment at the 2020 NVivo Virtual Conference.

The aim of the study was to understand and compare how members of two generations, Gen Z and Gen X, view work and careers, and how economic and world events, such as the Great Recession or the COVID-19 pandemic, influence how generations view and make decisions regarding their career paths. The study was initially conceived of as in-person focus groups but transitioned to the virtual realm using the Zoom platform in March 2020. The virtual focus groups also included a photo-elicitation exercise, in which participants were showed emotionally resonant photographs to more deeply explore the emotions participants attach to work and careers.

The results of the study highlight differing attitudes about work and careers among members of Gen X and Gen Z, but the study's methodology is also a foray into virtual qualitative research methods that highlights some of the format's advantages, including the ability to reach participants across geographic areas, greater financial feasibility, and increased convenience for participants. In its use of photos to elicit reactions from participants, the study also offers insight into how to engage virtual participants effectively using interactive tools and into facilitation techniques better suited for the virtual group environment.

RAGON INSTITUTE OF MGH, MIT & HARVARD

https://www.ragoninstitute.org/
Members are primarily located at the Ragon, while our Associate Members and Steering Committee Members conduct research both at the Ragon and their primary research institute, indicated in parenthesis.

In addition to the following two outlined below, research is also conducted on HIV/AIDS, Global Infectious Diseases, Basic and Applied Immunology, and Clinical Studies… see: https://www.ragoninstitute.org/research-2/

Emerging Infectious Diseases

Our deep immunological and infectious disease expertise, coupled with our flexible funding structure, has allowed us to respond quickly to emerging infectious diseases, including the current COVID-19 pandemic. Ragon scientists were able to start working on the SARS-CoV-2 virus from the moment its genome was sequenced, and we helped establish and lead an unprecedented, cross-institutional, multidisciplinary research effort, the Massachusetts Consortium on Pathogen Readiness (MassCPR).

Member labs: Yu, Schmidt, Pillai, Alter, Kwon, Lingwood, Balazs
Associate Member labs: **Shalek (MIT)**
Steering Committee Member labs: Burton (Scripps)

Vaccine Development

The ultimate goal of our basic and applied immunology studies is to prevent infections that have global impact through development of effective vaccines and immunotherapies. We use a detailed understanding of the immune response to various pathogens, and how these pathogens evade that response, to drive rational vaccine development. An HIV vaccine is currently in clinical trials, and a COVID-19 vaccine will be entering clinical trials soon, with efforts to develop a more effective influenza vaccine, among others, underway.

Member labs: Lingwood, Alter, **Walker**, Balazs
Associate Member labs: **Shalek (MIT)**
Steering Committee Member lab: Barouch (BIDMC)

Alex Shalek

Pfizer-Laubach Career Development Associate Professor, Core Member of the Institute for Medical Engineering and Science (IMES), an Associate Professor of Chemistry, and an Extramural Member of The Koch Institute for Integrative Cancer Research
https://www.ragoninstitute.org/portfolio-item/shalek/
Lab: http://shaleklab.com/

Research in the Shalek group is directed towards the development and application of new technologies that will facilitate a better understanding of how cells collectively perform systems-level functions in healthy and diseased states.”. With respect to technology development, the group is leveraging recent advances in nanotechnology and chemical biology to establish a host of core, cross-disciplinary platforms that will collectively enable them to extensively profile and precisely control cells and their interactions within the context of complex systems.

With respect to biological applications, the group is focusing on how cellular heterogeneity and cell-to-cell communication drive ensemble-level decision-making in the immune system, with an emphasis on “two-body” interaction (e.g., host cell-virus interactions, innate immune control of adaptive immunity, tumor infiltration by immune cells). The goal is to not only provide broadly applicable experimental tools but also help transform the way in which we think about single cells, cell-cell interactions, diseased cellular states and therapeutics so as to create a new paradigm for understanding and designing systems-level cellular behaviors in multicellular organisms.

Bruce Walker
Founding Director of the Ragon Institute of MGH, MIT and Harvard
Professor of the Practice, Department of Biology, https://www.ragoninstitute.org/portfolio-item/walker-lab/? ; https://biology.mit.edu/profile/bruce-walker/

Areas of Research:
Define the relative antiviral efficacy of epitope-specific CTL responses in infected persons
Define the predictable pathways to immune escape in infected persons
Define the mechanisms that underlie effective cell killing
Define the mechanisms of spontaneous control of HIV infection using a genome wide association scan.

Viral epitope profiling of COVID-19 patients reveals cross-reactivity and correlates of severity
Shrock, E, Fujimura, E, Kula, T, Timms, RT, Lee, IH, Leng, Y, Robinson, ML, Sie, BM, Li, MZ, Chen, Y et al.. Bruce D. Walker… 2020. Science 29 Sep 2020: eabd4250, DOI: 10.1126/science.abd4250, https://pubmed.ncbi.nlm.nih.gov/32994364/ , https://science.sciencemag.org/content/early/2020/09/28/science.abd4250

Understanding humoral responses to SARS-CoV-2 is critical for improving diagnostics, therapeutics, and vaccines. Deep serological profiling of 232 COVID-19 patients and 190 pre-COVID-19 era controls using VirScan revealed over 800 epitopes in the SARS-CoV-2 proteome, including 10 epitopes likely recognized by neutralizing antibodies. Pre-existing antibodies in controls recognized SARS-CoV-2 ORF1, while only COVID-19 patients primarily recognized spike and nucleoprotein. A machine learning model trained on VirScan data predicted SARS-CoV-2 exposure history with 99% sensitivity and 98% specificity; a rapid Luminex-based diagnostic was developed from the most discriminatory SARS-CoV-2 peptides. Individuals with more severe COVID-19 exhibited stronger and broader SARS-CoV-2 responses, weaker antibody responses to prior infections, and higher incidence of CMV and HSV-1, possibly influenced by demographic covariates. Among hospitalized patients, males make greater SARS-CoV-2 antibody responses than females.

Loss of Bcl-6-Expressing T Follicular Helper Cells and Germinal Centers in COVID-19
Kaneko, N, Kuo, HH, Boucau, J, Farmer, JR, Allard-Chamard, H, Mahajan, VS, Piechocka-Trocha, A, Lefteri, K, Osborn, M, Bals, J et al.. 2020. Cell 183, 143-157.e13. doi: 10.1016/j.cell.2020.08.025, https://pubmed.ncbi.nlm.nih.gov/32877699/

Humoral responses in coronavirus disease 2019 (COVID-19) are often of limited durability, as seen with other human coronavirus epidemics. To address the underlying etiology, we examined post mortem thoracic lymph nodes and spleens in acute SARS-CoV-2 infection and observed the absence of germinal centers and a striking reduction in Bcl-6+ germinal center B cells but preservation of AID+ B cells. Absence of germinal centers correlated with an early specific block in Bcl-6+ TFH cell differentiation together with an increase in T-bet+ TH1 cells and aberrant extra-follicular TNF-α accumulation. Parallel peripheral blood studies revealed loss of transitional and follicular B cells in severe disease and accumulation of SARS-CoV-2-specific “disease-related” B cell populations.

These data identify defective Bcl-6+ TFH cell generation and dysregulated humoral immune induction early in COVID-19 disease, providing a mechanistic explanation for the limited durability of antibody responses in coronavirus infections, and suggest that achieving herd immunity through natural infection may be difficult.

Focusing In: Modeling Immunodominance in the Flu Antibody Response
https://www.ragoninstitute.org/focusing-in-modeling-immunodominance-in-the-flu-antibody-response/
Related paper: https://www.cell.com/cell-systems/fulltext/S2405-4712(20)30335-5 or https://doi.org/10.1016/j.cels.2020.09.005

Arup K. Chakraborty, Robert T. Haslam Professor of Chemical Engineering, Physics, Chemistry, and Biological Engineering; founding Director of MIT's Institute for Medical Engineering and Science… https://www.ragoninstitute.org/portfolio-item/chakraborty/

Ragon and MIT researchers develop computational model to understand drivers of immunodominance; create vaccine strategy in mice that focuses antibody response to universal flu vaccine target.

When the body responds to an infection like the flu virus, it makes different antibodies to recognize different pieces, or antigens, of the virus. But many times, one or several antibodies are made in much larger quantities that the rest. These antibodies known as the immunodominant response.

In the flu, this immunodominant response is usually to antigens that rapidly mutate. Once the antigen mutates, the antibodies formed can no longer recognize it, and the immune system cannot protect against re-infection. This is why each flu season requires a different flu vaccine to train the immune system against each year's new strains. However, a small number of antibodies, called broadly neutralizing antibodies, are developed to recognize antigens that rarely mutate and look the same in different flu strains, which could provide long-lasting protection against the rapidly mutating flu virus.

Ragon Group Leader Daniel Lingwood, PhD, and **MIT Professor and Ragon Associate Member Arup Chakraborty, PhD**, recently published a study in Cell Systems in which they created a model that allowed them to identify ways in which they could re-focus the common immunodominant response to a more favorable response, which would allow for long-term immunological memory of the flu.

"If we can engineer a response where these broadly neutralizing antibodies were the immune-dominant response, instead of being rare subsets of the response," says Lingwood, "then we could create a flu vaccine that would provide protection for years, instead of needing a new one each flu season."

Towards this, Arup and Daniel's groups created a computational model that mapped out immunodominant responses as they formed, allowing them to identify key features that drove the response, such as the geometry of the viral proteins and pre-existing antibodies. They used this information to test out flu vaccine strategies in a mouse with a humanized immune system and found that, with the right conditions, they could drive the immunodominant response away from antibodies against rapidly mutating antigens and towards broadly neutralizing antigens.

This finding could help researchers develop a long-lasting influenza vaccine by allowing them to develop a vaccine that promotes an immunodominant response with broadly neutralizing antibodies.

The model isn't limited to influenza, however.

"Even though we developed this model with influenza," says Lingwood, "we can use it to look at any other pathogen where the immunodominant response is against the 'wrong' antigens, and works towards a vaccine strategy to create the immunodominant response that provides the best protection."

PAPERS, ARTICLES, PRESENTATIONS, TALKS'

TRANSMISSION / RISK: BOOSTING BUSINESS VALUE BY REDUCING COVID-19 TRANSMISSION RISK

Initiative on the Digital Economy (IDE), September 2020
Avinash Collis, Digital Fellow
Seth Benzell, Digital Fellow
Christos Nicolaides, Research Affiliate
http://ide.mit.edu/publications
In Sloan Management Review,
https://sloanreview.mit.edu/article/boosting-business-value-by-reducing-covid-19-transmission-risk/
http://ide.mit.edu/publications/boosting-business-value-reducing-covid-19-transmission-risk
More publications: http://ide.mit.edu/publications

New research measuring the value-risk proposition of different business openings offers insights and strategies for how to minimize pandemic transmission risk.

MOBILITY / IMPACTS: THE INTERDEPENDENT IMPACTS OF REGIONAL COVID-19 REOPENINGS IN THE UNITED STATES

Initiative on the Digital Economy (IDE), September 2020
Michael Zhao, PhD Candidate
Sinan Aral, Director, IDE, David Austin Professor of Management, Professor of IT & Marketing, and Professor in the Institute for Data, Systems and Society
http://ide.mit.edu/publications/interdependent-impacts-regional-covid-19-reopenings-united-states
More publications: http://ide.mit.edu/publications

After limits on human mobility effectively reduced the spread of COVID-19 around the world 1,2, many countries began to reopen. When these reopenings began in the U.S., several COVID-19 hotspots emerged, causing some local governments to reimpose local shutdowns. However, we know little about the impacts of regional reopenings or subsequent shutdowns 3,4, and have no quantitative evidence on the direct impact of a

region's reopening policies on its own population's mobility; the spillover effects of peer regions' policies on a focal region's mobility; the mediation of these effects by endogenous peer behavior across regions; or the impacts of origin and destination policies on cross-region travel.
Here we show that individual states' ad hoc local reopening policies significantly influenced mobility across the entire U.S. due to inter-state travel and social influence. When all peer states locked down, focal county mobility dropped by 15-20% but increased by 19-32% once peer states reopened. When an origin county was subject to a statewide shelter-in-place order, travel to counties yet to impose lockdowns increased by 52-65%. If the origin reopened, but the destination remained closed, travel to destination counties was suppressed by 9-17% for nearby counties and 21-27% for distant counties. But, when a destination reopened while an origin remained closed, people from the closed origins flooded into the destination by 11-12% from nearby counties and 24% from distant counties. Our findings demonstrate how reopenings contribute to the emergence of new hotspots and, counterintuitively, how the reimposition of shutdown orders can increase mobility as citizens flee to open peer regions. The research highlights the risks of ad hoc local reopenings and the urgent need to coordinate COVID-19 reopenings across regions.

PUBLIC HEALTH / MODELING: WHAT DOES AND DOES NOT CORRELATE WITH COVID-19 DEATH RATES

Christopher R. Knittel (Professor of Applied Economics at MIT Sloan), Bora Ozaltun (graduate research assistant, MIT Center for Energy and Environmental Policy Research, IDSS) NBER Working Paper No. 27391, Issued in June 2020, https://www.nber.org/papers/w27391
https://www.medrxiv.org/content/10.1101/2020.06.09.20126805v1
https://doi.org/10.1101/2020.06.09.20126805

We correlate county-level COVID-19 death rates with key variables using both linear regression and negative binomial mixed models, although we focus on linear regression models. We include four sets of variables: socio-economic variables, county-level health variables, modes of commuting, and climate and pollution patterns. Our analysis studies daily death rates from April 4, 2020 to May 27, 2020. We estimate correlation patterns both across states, as well as within states. For both models, we find higher shares of African American residents in the county are correlated with higher death rates. However, when we restrict ourselves to correlation patterns within a given state, the statistical significance of the correlation of death rates with the share of African Americans, while remaining positive, wanes. We find similar results for the share of elderly in the county. We find that higher amounts of commuting via public transportation, relative to telecommuting, is correlated with higher death rates. The correlation between driving into work, relative to telecommuting, and death rates is also positive across both models, but statistically significant only when we look across states and counties. We also find that a higher share of people not working, and thus not commuting either because they are elderly, children or unemployed, is correlated with higher death rates. Counties with higher home values, higher summer temperatures, and lower winter temperatures have higher death rates. Contrary to past work, we do not find a correlation between pollution and death rates. Also importantly, we do not find that death rates are correlated with obesity rates, ICU beds per capita, or poverty rates. Finally, our model that looks within states yields estimates of how a given state's death rate compares to other states after controlling for the variables included in our model; this may be interpreted as a measure of how states are doing relative

to others. We find that death rates in the Northeast are substantially higher compared to other states, even when we control for the four sets of variables above. Death rates are also statistically significantly higher in Michigan, Louisiana, Iowa, Indiana, and Colorado. California's death rate is the lowest across all states.

ECONOMICS / WORK: WORKING REMOTELY AND THE SUPPLY-SIDE IMPACT OF COVID-19

Dimitris Papanikolaou (Northwestern University - Kellogg School of Management; National Bureau of Economic Research (NBER))
Lawrence Schmidt (Victor J. Menezes (1972) Career Development Professor of Finance, MIT Sloan School of Management)
SSRN, Posted: 2 Jun 2020 Last revised: 27 Jul 2020,
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3615334

We analyze the supply-side disruptions associated with COVID-19 across firms and workers. To do so, we exploit differences in the ability of workers across industries to work remotely using data from the American Time Use Survey (ATUS). We find that sectors in which a higher fraction of the workforce is not able to work remotely experienced significantly greater declines in employment, significantly more reductions in expected revenue growth, worse stock market performance, and higher expected likelihood of default. Further, we find evidence that the Paycheck Protection Program provided smaller relief on a per-employee basis to the most exposed sectors. In terms of individual employment outcomes, lower-paid workers, especially female workers with young chidren, were significantly more affected by these disruptions. Last, we combine these ex-ante heterogeneous industry exposures with daily financial market data to create a stock return portfolio that most closely replicates the supply-side disruptions resulting from the pandemic.

GENOME / NEW DRUG TARGET: SILVI ROUSKIN ON SOLVING THE STRUCTURE OF THE CORONAVIRUS GENOME (PODCAST; 17:25 MINUTES)

AudioHelicase Podcast, Whitehead Institute, October 2020, http://wi.mit.edu/multimedia/audiohelicase-podcast-silvi-rouskin-solving-structure-coronavirus-genome

Silvia Rouskin, Andria and Paul Heafy Whitehead Fellow, http://wi.mit.edu/people/fellows/rouskin ; https://www.rouskinlab.com/;
https://pubmed.ncbi.nlm.nih.gov/?term=Rouskin+S%5Bauth%5D&sort=date&size=50

In this episode of AudioHelicase Podcast, Whitehead Fellow Silvi Rouskin discusses her research on solving the structure of the novel coronavirus's RNA genome, with the goal of revealing weak points in the virus's gene regulation that new drugs could potentially target.

INFECTIOUS DISEASE / TRANSMISSION: THE FLUID DYNAMICS OF DISEASE TRANSMISSION

Lydia Bourouiba, Annual Review of Fluid Mechanics, Vol. 53:473-508 (Volume publication date January 2021)

Review in Advance first posted online on October 6, 2020. (Changes may still occur before final publication.) https://doi.org/10.1146/annurev-fluid-060220-113712
https://www.annualreviews.org/doi/abs/10.1146/annurev-fluid-060220-113712
Expected final online publication date for the Annual Review of Fluid Mechanics, Volume 53 is January 6, 2021. Please see http://www.annualreviews.org/page/journal/pubdates for revised estimates.

Lydia Bourouiba, Associate Professor, Civil and Environmental Engineering and Mechanical Engineering; Affiliate Faculty of the Institute for Medical Engineering and Science; Harvard-MIT Health Sciences and Technology (HST) Faculty
https://lbourouiba.mit.edu/home
https://lbourouiba.mit.edu/publications

For an infectious disease such as the coronavirus disease 2019 (COVID-19) to spread, contact needs to be established between an infected host and a susceptible one. In a range of populations and infectious diseases, peer-to-peer contact modes involve complex interactions of a pathogen with a fluid phase, such as isolated complex fluid droplets or a multiphase cloud of droplets. This is true for exhalations including coughs or sneezes in humans and animals, bursting bubbles leading to micron-sized droplets in a range of indoor and outdoor settings, or impacting raindrops and airborne pathogens in foliar diseases transferring pathogens from water to air via splashes. Our mechanistic understanding of how pathogens actually transfer from one host or reservoir to the next remains woefully limited, with the global consequences that we are all experiencing with the ongoing COVID-19 pandemic. This review discusses the emergent area of the fluid dynamics of disease transmission. It highlights a new frontier and the rich multiscale fluid physics, from interfacial to multiphase and complex flows, that govern contact between an infected source and a susceptible target in a range of diseases.