

Infectious Diseases Epidemiology and Applied Studies Initiative



IDEAS Seminar Series Spring 2024

Jeffrey D. Klausner, MD, MPH

Professor of Population and Public Health Sciences Professor of Medicine and Infectious Diseases

Jennifer Unger, PhD

Professor of Population and Public Health Sciences

With Support from Frank Gilliland, MD, PhD Professor of Population and Public Health Sciences



Through discovery, training and action, we are solving public health and health equity challenges, from local to global, for today and tomorrow.

Keck School of Medicine of USC

Department of Population and Public Health Sciences



JSC Institute on Inequalities in Global He

The Infectious Disease Epidemiology and Applied Studies (I.D.E.A.S.) Initiative and USC IIGH present:

Refugee Health and Infectious Disease With an emphasis on STI Research in Refugees and Internally Displaced Populations

SC



challenges, from local to global, for today and tomorrow.

Our Previous Seminars

2022-2023

Through discovery, training and action, we are solving public health and health equity

Keck School of Medicine of USC

Department of Population and Public Health Sciences itute on Inequalities in Global H

The Infectious Disease Epidemiology and Applied Studies (I.D.E.A.S.)

Initiative and USC IIGH present:

Pediatric Vaccine Hesitancy in the US &

Around the World

Department of Population and Public Health Sciences



Our Upcoming Seminars

Keck School of Medicine of USC Department of Population and **Public Health Sciences**

USC Institute on Inequalities in Global Health

The Infectious Disease Epidemiology and Applied Studies (I.D.E.A.S.) Initiative and USC IIGH present:

Highly Effective Infectious Disease Prevention Strategy: Changing the Community Narrative



Lourdes Baezconde-Garbanati PhD, MPH

Professor of Population and **Public Health Sciences** Keck School of Medicine University of Southern California



Sheila Teresa Murphy PhD

Professor of Communication Annenberg School of Communication and Journalism University of Southern California

February 20, 2024 11:30 - 12:30PM PST **SSB 103E & ZOOM Register for Zoom link**



Keck School of Medicine of USC Department of Population and **Public Health Sciences**

USC Institute on Inequalities in Global Health

PhD

The Infectious Disease Epidemiology and Applied Studies (I.D.E.A.S.) Initiative and USC IIGH present:

Vector Borne Infections in the US and Around the World with an Emphasis on Chikungunya & Dengue Viruses



Chair, Department of Microbiology & Immunology Director, Institute for Human Infections & Immunity Professor, Microbiology & Immunology and Pathology The University of Texas (UTMB)

March 19, 2024 12:00 - 1:00PM PST **SSB 114 & ZOOM Register for Zoom link**



Keck School of Medicine of USC

Department of Population and Public Health Sciences



Through discovery, training and action, we are solving public health and health equity challenges, from local to global, for today and tomorrow.



Happy New Year!

Welcome to SPRING 2024

Happening Today!!!

Keck School of Medicine of USC Department of Population and Public Health Sciences

USC Institute on Inequalities in Global Health

The Infectious Disease Epidemiology and Applied Studies (I.D.E.A.S.) Initiative and USC IIGH present:

SARS-CoV-2 Infection and Excess Mortality in Canada, China, India and Sierra Leone 2020-2023





Professor of Global Health and Epidemiology Dalla Lana School of Public Health Professor, Faculty of Medicine University of Toronto

January 29, 2024 10:00 - 11:00PM PST SSB 114 & ZOOM Register for Zoom link





Through discovery, training and action, we are solving public health and health equity challenges, from local to global, for today and tomorrow.

Keck School of Medicine of USC

Department of Population and Public Health Sciences

SARS-CoV-2 infection and mortality: lessons learned from various countries

Prabhat Jha for many others

Prabhat.Jha@utoronto.ca Twitter: @counthedead

University of Toronto

Supported by the Bill and Melinda Gates Foundation, Queen Elizabeth Scholarships and Mastercard Foundation, CIHR, CITF and University of Toronto, Canada







Worldwide excess and reported COVID deaths, 2020-2022

Excess death rate per 100,000

Cumulative reported COVID-19 deaths Cumulative excess deaths b Death rate per 100,000 population 20 10 0 January 2020 July 2020 January 2021 July 2021 January 2022 Month Year

Reported COVID-19 death rate per 100,000

Cumulative ~15M excess deaths vs 6M reported Likely ~20M by 2023, including ~1M in China

Of ~9 million "Missing" deaths by 2022, ~ 3-4M were in India

Ab-C Investigators

Unity Health Toronto

Prabhat Jha, Director CGHR, Scientist (PI) Arthur Slutsky, Scientist (Chair, Advisory Committee) Patrick Brown, Scientist Nico Nagelkerke, CGHR Senior Fellow Aiyush Bansal, Post Doctoral Fellow (PDF) Peter Rodriguez, CGHR Database Coordinator Maria Pasic, Lead Scientist Chaim Birnboim, Senior Technical Advisor Jeff Companion, Lab Scientist Abha Sharma, PDF Xuyang Tang, PDF Eo Rin Cho, PDF Richard Wen, PDF Bapujee Biswabandan, PDF Hellen Gelband, Senior Fellow Justin Slater, Research Fellow Sze Hang (Hana) Fu, GIS Technician Daphne C Wu, Research Fellow Catherine Meh, Research Fellow Wilson Suraweera, Research Fellow Leslie Newcombe, Research Fellow Divya Santhanam, Research Intern Shreya Jha, Research Intern Zoe Greenwald, PhD Student Vedika Jha, Research Intern Varsha Malhotra, Economist

Sinai Health Toronto

Anne-Claude Gingras, Senior Investigator Karen Colwill, Staff Scientist Geneviève Mailhot, Technician Melanie Delgado-Brand, Technician Adrian Pasculescu, Senior Bioinformatician Miriam Barrios-Rodiles, Scientific Associate Jenny Wang, Lab Automation Specialist Kento T Abe, Graduate Student Bhavisha Rathod, Research Assistant Mahya Fazel-Zarandi, Student Research Assistant Samir Sinha, Director of Geriatrics

<u>University Health Network</u> Isaac Bogoch, Scientist Rupert Kaul, Clinician Scientist

<u>Children's Hospital of Eastern Ottawa and University of Ottawa</u> Pranesh Chakraborty, Associate Professor Marc-André Langlois, Professor

Angus Reid Institute and Angus Reid Forum Angus Reid Ed Morawski Demetre Eliopoulos Teresa Lam Andy Hollander Ben Aloi

Conclusions: Canada (population 37 million)

- 1. Low cumulative adult COVID infection (~13%) prior to Omicron waves
- 2. Omicron BA.1/1.1 period incidence of ~23%
- 3. Omicron BA.2/5 period incidence of ~42%
- Cumulatively, at least 25M Canadian adults infected, along with 30M+ double vaccinated, so "hybrid immunity" is high
- Low COVID death rates, except for Alpha wave infections among nursing homes (incidence ~12-16%) accounting for 80% of all COVID deaths till that time period
- 6. Simple home-based dried blood spots are a practicable strategy in highincome settings.

Ongoing epidemiological studies (serosurveys, mortality studies) essential for response and to guide vaccine programs

Seven-day rolling averages of PCR-confirmed COVID cases in CANADA (black solid and dotted line), and SARS-CoV-2 vaccinations (any dose; red line) in relation to Ab-C data collection phases



* Dotted line indicates period after restrictions to PCR testing eligibility

[†] Major variants include AE.8, B.1.36.36, B.1.2, B.1.160, B.1.438.1

Action to Beat Coronavirus in Canada (Ab-C) Study

- 12 min poll of symptoms, risk factors, testing and vaccination history
- Safe, simple home dried blood sample (DBS) which takes 10 min
- Mail (safely) to central lab
- Quality control: humidity & storage
- Test for antibodies to determine how many Canadians infected in ongoing waves





Representativeness of online poll

Companicon group	Census 2016	Survey sa	Survey sample		
Comparison group	distribution	Phase 1	Phase 6		
Education					
Some college or less	45%	33%	34%		
College graduate/some university	32%	33%	32%		
University graduate	23%	34%	34%		
Visible minority	22%	15%	24%		
Ever smoking	54%	51%	51%		
Indigenous	5%	8%	9%		
Obese (≥ 30 kg/m ²)	27%	27%	28%		
Diabetes	9%	10%	11%		
Hypertension	23%	26%	30%		

Tang et al, JAMA Network Open, 2022

Cumulative incidence, numbers of infected adults, cumulative deaths, and period COVID mortality rate in Canada during various SARS-CoV-2 viral waves

Time period	Cumulative incidence* % (95% CI)	No of adult (age 18+) infections in millions	Cumulative no of deaths†	per million per week during the relevant period
Pre-Omicron				
2020-2021	12.7 (11.2-14.1)	3.9 (3.5-4.4)	30 149	8.6
Omicron				
BA.1/1.1				
JanMar. 2022	35.7 (34.0-37.4)	11.3 (10.7-11.8)	37 750	16.6
Omicron BA.2/5				
AprDec. 2022	77.7 (75.7-79.6)	24.6 (23.9-25.2)	49 674	7.7

CANADA: Levels of antibodies to the spike protein stratified by infection and number of vax doses



Infection only or with 1 vaccine dose

Uninfected

2 vaccine doses

3 vaccine doses

4 vaccine doses

Infected

2 vaccine doses

3 vaccine doses

4 vaccine doses

(A) By age group

CANADA: Age-specific trends to nine months in levels of antibodies to the spike protein among adults vaccinated with 3-4 doses, stratified by infection > or < 6months ago



CANADA: Cumulative incidence in each stratum of infection and vaccination in the pre-Omicron wave and during the Omicron BA.1/1.1 wave, and BA.2/BA.5 waves by age



Mid-time point of respective phases

Sub study on cellular immunity

- Population: convenience sample (n=54), from Ab-C survey participants in Greater Toronto Area
- Whole blood samples drawn April-May 2022
- SARS-CoV-2 Interferon Gamma Release Assay for T-cell activity

Subgroup	No. of participants	No. of positive	No. of negative
Vaccinated + infected	30	30 (100%)	0
Vaccinated + uninfected	3	3 (75%)	0
Unvaccinated + infected	2	1 (50%)	1 (50%)
Unvaccinated + uninfected	5	2 (40%)	3 (60%)
Total	40	36 (88%)	4 (10%)

Proportions of respondents with 1+ or 2+ symptoms lasting 12+ weeks during Omicron BA.1/1.1wave



Proportion with any long COVID symptoms

Serology Viral test result (symptoms around test)		Percent with ≥1 symptom		
Positive	Positive (with symptoms)	13.1		
Positive	Positive (asymptomatic)	5.1		
Positive	Negative or missing	5.7		
Negative	Negative or missing	4.3		

Average number of symptom weeks

Age group	Serology	Viral test result	Average no. of symptom weeks		
(years)		(symptom around test)		Female	
	Positive	Positive (with symptoms)	6.5	11.4	
19 50	Positive	Positive (asymptomatic)	3.5	0.2	
10-39	Positive	Negative or missing	3.1	3.7	
	Negative	Negative or missing	1.5	2.8	
	Positive	Positive (with symptoms)	5.0	8.7	
60 and above	Positive	Positive (asymptomatic)	1.9	2.8	
	Positive	Negative or missing	2.3	1.2	
	Negative	Negative or missing	1.0	2.7	

INDIA: Excess mortality from June 2020 to June 2021 during the COVID pandemic (from <u>uncontrolled</u> transmission)

Jha et al., Science 375, 667–671 (2022) 11 February 2022

CORONAVIRUS

COVID mortality in India: National survey data and health facility deaths

Prabhat Jha¹*, Yashwant Deshmukh², Chinmay Tumbe³, Wilson Suraweera¹, Aditi Bhowmick⁴, Sankalp Sharma⁴, Paul Novosad⁵, Sze Hang Fu¹, Leslie Newcombe¹, Hellen Gelband¹, Patrick Brown¹

Excess mortality studies in India during uncontrolled transmission

- COVID was the main contributor to India's substantial excess of deaths in the peak pandemic months of 2020 and 2021
- 2. India's actual cumulative COVID deaths about 3 million, 7-8 times higher than the officially reported
- India accounted for ~ 3-4M of the "missing" total of ~9M COVID deaths globally

India's COVID cases, deaths, and vaccination March 2020-Sept 2021



Coronavirus.app, Sept 12, 2021

CVoter survey design

- Random digit dialing (computer assisted telephone interview)
- 90% + mobile phone coverage
- Adults 18+ in 2100 randomly selected areas (300/day rolling sample) drawn from 4000 local electoral areas
- Overall margin of error + 3% nationally, weighted distribution like Census or NSSO data
- Main study 140,000 adults but with less exact question about household deaths
- Substudy of 57,000 adults from July 1-Sept 15, 2021 with exact household deaths

Adjusted percentages of adults reporting daily death in household, expected percentage in 2020 and daily confirmed COVID deaths in India, June 2020-June 2021



COVIDtracker deaths (red line, left vertical scale) represent COVID deaths reported daily (smoothed for rolling 7-day averages) at age 35 or older, adjusted for possible overreporting (see text). Expected all-cause deaths (grey line, left vertical scale) per year of 3.16% applies the UN estimated total deaths in 2021 (10.0 million) to the number of households in India (316.3 million, based on the average household size of 4.6 in the 2011 census). The daily variation in this percentage applies the variation observed among 480,000 deaths in the Million Death Study. Confirmed COVID deaths (blue bars, right vertical scale) are daily reports from Covid19india.org.

Sub-survey of 13,500 households (~57,000 people)

Who was alive in Jan 2019? Who died since and when?

- Year All cause mortality <u>rate/1000</u>
- **2019 7.0** (vs UN/SRS rates of **8.1/6.2**)
- 2020 10.5
- 2021 18.4

Sub-survey of 13,500 households (~57,000 people)



Overall, ~4.5% of households reported a COVID death vs 3.5% expected from all causes. Sub-study consistent with main poll result showing ~doubling of overall death rates for ~3 months

Reported deaths from all causes in India's Ministry of Health and Family Welfare covering 0.2 M health facilities nationally, 2020 and 2021 versus average of 2018-19, by month



Summary estimates of excess deaths in India

	Reference		Excess deaths mid (LL,UL) in	Excess as percentage of UN estimated deaths; mid
Data source	period	Months	000s	(LL,UL)
National Surve	ey			
	June 2020- July 2021	13	3325 (3159, 3491)	30.3 (28.8, 31.9)
Facility-based	deaths, national			
	July 2020- May 2021	11	630 (531 <i>,</i> 730)	27.4 (23.1, 31.7)
Civil registrati	on deaths in 10 s	tates		
	July 2020- May 2021	12	1247 (1002, 1491)	25.8 (21.3, 30.8)

Examination of 6 million rural facility deaths in 8 states in India, 2020-22



Kumar et al, submitted

Number of emergency cases (all ages), inpatient cases (ages ≥ 18 years), health facility deaths ages ≥ 10 years in rural health facilities and confirmed COVID cases (all ages) India, 2018-2021



Kumar et al, submitted

Deaths at ages ≥ 10 years in rural health facilities 2018-2021 from causes likely related and unrelated to SARS-Cov-2



Deaths at ages ≥ 10 years in rural health facilities 2018-2021 from causes likely related and unrelated to SARS-Cov-2

Cause of deaths	% Excess deaths due to Delta wave			
	vs. non peak periods	vs. Pre-COVID deaths in		
		2018-2019		
Causes likely related to SARS-CoV-2				
Respiratory	322	612		
Fever related	461	1016		
Known acute	103	354		
Known chronic	49	275		
Heart disease/ Hypertension	59	195		
Stroke	33	143		
Causes weakly related to SARS-CoV-2				
Diarrhoea	29	59		
Tuberculosis	10	-2		
HIV/AIDS	33	32		
Cancer	19	95		
Causes likely unrelated to SARS-CoV-2				
Accidents/Burns	0	21		
Animal bites/stings	24	136		
Suicide	6	75		
Unknown causes	52	315		
Total deaths	60	270		

Kumar et al, submitted

Government of India data corroborate estimates of excess deaths for 2020 (1)

- India has 10M annual deaths not 8.3M as GOI claims
- Civil Registration Data (covers about 71% of all deaths, NOT 95% as GOI claims)
- CRS average deaths in 2018-9: 7.30M vs 8.12M in 2020 or **11%** relative excess or 0.83M absolute excess.
- CVoter polling: 9% relative excess or 0.6M absolute excess in June 20-Jan 21 (8 months) vs earlier months
- WHO estimate for 2020: **9%** relative excess or 0.8M absolute excess versus earlier years

Government of India data corroborate estimates of excess deaths for 2020 (2)

- Medically Certified Cause of Death in urban hospitals (covering about 1.8M deaths out of 10M national total)
- 2020: COVID=9% of MCCD deaths, same proportion as CVoter national poll for COVID deaths and WHO's estimate for excess deaths
- COVID proportion higher in Maharashtra (**18%**), consistent with much bigger 2020 COVID wave in that state
- Absolute MCCD COVID deaths in 2020=160,000 which is greater than confirmed COVID deaths of 150,000
- Life Insurance Claims: ~3M claims, and estimate of ~4 million <u>additional</u> deaths in 2021 versus 2019

China's mortality during the COVID era

Mortality rates per 1000 at ages 60 years or older and 15-59 years in a nationally representative survey in China from 2020-23 compared to United Nations estimates for earlier years



Figure legend:

Peak viral periods in March-April 2022 and Dec 2022-Jan 20231 are shown in the black rectangles. The numbers of study deaths are shown in the text below the figure. Study deaths use rolling three-month averages. The annual mortality rates are per 1,000 person-years.

SARS-CoV-2 infection and mortality in Sierra Leone

Ahmed Osman, Ashley Aimone, Rashid Ansumana and many others



https://healsl.org/

Ministry of Health Njala University, University of Toronto

HEAL-SL Supported by the Bill and Melinda Gates Foundation, Queen Elizabeth Scholarships and Mastercard Foundation and University of Toronto, Canada







Conclusions (1)

- Sierra Leone appears to have widespread SARS-CoV-2 transmission, but relatively low levels of excess mortality from COVID.
- Cumulative seroincidence, approached 70% by July 2021, and nearly 85% by April 2022, mostly prior to vaccines.
- About half of the infections generated neutralizing antibody response.
- Despite high levels of prior infection, the Omicron viral wave managed to infect about 20% of adults, and age patterns were consistent with widespread household transmission.

Conclusions (2)

- Despite very high and rapid transmission, excess deaths from COVID appear to have been remarkably low in Sierra Leone, mostly concentrated at older ages.
- During the peak viral weeks, excess mortality was 22% at ages 30-69 years and 70% at ages 70 or more.
- Observed excess deaths were notable for respiratory infections, but did not differ greatly across specific causes that would, a priori, be strongly associated with COVID, nor among those with or without chronic disease risk factors.
 - Is there a "West African" Paradox? Correlates that protect against disease but not SARS-CoV-2 infection?

Reported COVID infections and cumulative number of people who received two SARS-CoV-vaccine doses in Sierra Leone



80% of ~7500 reported cases are in Western Area Urban (Freetown) and Rural, and incoming passengers; Vaccinated- by April 2022- **1.3 M/total pop 8M**

SIERRA LEONE: SARS-2-CoV Serosurvey in urban Bo

- COMSA DBS study covered about 4200 adults age 18+ randomly selected from about half of Bo urban areas
- Field work was first done July-Aug 2021 (during malaria/rainy season): not a COVID survey but a "healthy lifestyle" survey.
- 224 of 4200 randomly selected for COVID antibody testing
 - High quality chemiluminescence ELISA at Sinai Labs, Toronto
 - 3 antigens- RBD, Spike and Nucleocapsid (to reduce false positives)
 - Sub-set underwent neutralizing antibody assays at University of Ottawa labs
- Follow up survey in April 2022 of same cohort

SARS-CoV-2 Serosurveys in urban Bo, Sierra Leone

Assay	Delta wave: July 2021 N = 227 [*]	Omicron wave: April 2022 N=114	
Antigens on sensitive/specific ELISA			
RBD AND Spike positive	69% (157)	84% (96)	
RBD OR Spike positive	91% (207)	98% (112)	
Nucleocapsid positive	67% (153)	74% (84)	
Neutralizing antibodies (subset)	43% (97)		
Seroconversion from July 2021 to April 2022	2		
No change		64% (73)	
Became positive	21% (24)		
Became negative		15% (17)	

Age-specific mortality rate per 100,000 in HEAL-SL (top panel) and registered deaths from NCRA (bottom panel)



Osman et al, CGHR under preparation

RBD seropositivity by age in Sierra Leone



Neutralizing antibody in Sierra Leone



RBD "titers" versus Neutralization "titers"



Age-specific mortality rate per 100K population in Sierra Leone 2020-2022 from HEAL-SL (top) and registered deaths from NCRA (bottom)



Excess mortality in Sierra Leone: death rates (per 100,000) from HEAL-SL and death registration

	Peaks	Non-peaks	Excess risks, based on regression (95% CI)
HEAL-SL (media	n deaths/week)		
≥70 years	96	63	1.70 (1.23,2.35)
30-69 years	15	14	1.22 (0.93,1.61)
NCRA (median	deaths/month)		
≥70 years	400	272	1.22 (1.16,1.28)
30-69 years	715	587	1.10 (1.05,1.14)

Excess mortality by cause of death

	Weekly average deaths per 100,000 (number of deaths)				Excess mortality RR (95%CI) [†]	
	Pe	aks	Non-	peaks		
COVID-associated	8.2	139	6.0	336	1.38 (1.14,1.69)	
Vascular	5.3	90	4.2	234	1.29 (1.01,1.64)	
Respiratory	2.3	39	1.2	66	1.97 (1.33,2.93)	
Fever and infection	0.6	10	0.6	36	0.93 (0.46,1.87)	
Possibly COVID associated	10.9	184	8.8	496	1.24 (1.05,1.47)	
Not COVID associated	2.3	39	1.9	106	1.23 (0.85,1.78)	
Unknown	0.6	10	0.4	24	1.39 (0.67,2.91)	
All-cause mortality	22.1	372	17.1	962	1.29 (1.15,1.46)	

Comparisons of SARS-CoV-2 excess mortality, Africa

Setting and age group	Average per 100,000	(Lower, upper
Excess death rate per 100.000 by age	population	boundsy
Excess dealinate per 100,000 by age	~ -	
WHO estimate for Sierra Leone for 2020-2021, all ages	95	(6, 192)
Sierra Leone for 2020-2022, ages ≥30 years, present study	262	(59 <i>,</i> 576)
The Gambia for 2020, ages ≥18 years [*]	197	-
Coastal Kenya for 2020-21, ages ≥45 years ⁺	407	-
South Africa for 2020-2021, all ages [‡]	497	-
Lusaka, Zambia, burial grounds for 2020-June 2021, all ages§	153	
Namibia, national mortality report for 2021	197	
Total excess deaths		
Total ≥30 years in Sierra Leone for 2020-2022	6,900	(1,500, 15,000)
WHO estimate for Sierra Leone, all ages for 2020-2021	7,900	(480, 15,700)
Excess as percent of deaths ≥30 years in Sierra Leone for 2020-2022	5.8%	(1.3%, 12.8%)

Worldwide excess and reported COVID deaths, 2020-2022

Cumulative reported COVID-19 deaths
Cumulative excess deaths



Cumulative ~15M excess deaths vs 6M reported Likely ~20M by 2023, including ~1M in China

Of ~9 million "Missing" deaths by 2022, ~ 3-4M were in India

Overall conclusions

- Hugely variable SARS-CoV-2 pandemic globally, with different patterns of hybrid immunity (vaccine plus infection) across settings
- Canada mostly spared large excess deaths, except for nursing home populations
- Substantial excess deaths from COVID in India and China but surprisingly little excess deaths in Sierra Leone
- Reliable mortality data and rapid serosurveys are central for future pandemic response

www.cghr.org (Don't buy my books)







Disease Control Priorities Project







UNITY HEALTH TORONTO

