oucru

COVID-19

RESEARCH AND ENGAGEMENT PROJECTS PORTFOLIO

Projects in Progress & Outputs | 24 February 2022

Oxford University Clinical Research Unit

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INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-Cov-2) and its disease, COVID-19, have caused unprecedented disruption globally since they were first described in China in December 2019. The OUCRU programme has felt the full force of that disruption, with severe lockdowns and waves of infection experienced repeatedly over the last 24 months in Viet Nam, Indonesia and Nepal. However, alongside the disruption has come opportunity, particularly the opportunity to conduct research that helps us understand the medical and social impact of the pandemic and improve the ways we control and treat the virus.

The entire OUCRU programme should be enormously proud of the way it has responded to the pandemic. The virus has brought us together. We have supported one another through many difficult periods when the virus seemed to threaten every aspect of our life and work, and we have found new ways to communicate and collaborate. The consequent research has been remarkable, not least because its conception and conduct has been in some of the most difficult circumstances any of us have ever experienced. We have addressed almost every important aspect of the pandemic, from its societal impact to viral genomic surveillance and COVID-19 therapy. Our work has fostered new collaborations with respective governments and their institutions that have ensured our research is relevant and impactful. These collaborations will have a lasting effect on OUCRU's standing and future work within the region.

As we update OUCRU's COVID-19 response in these pages, much has changed in the last 6 months. The large and devastating waves of the Delta variant have passed, but the Omicron variant is now on the ascendency in Asia. The problems this new variant will cause will be dependent upon the levels of population immunity that it confronts. There are grounds for cautious optimism: Indonesia is well-vaccinated, and Viet Namhas gone from low to very high vaccine coverage in 6 months of extraordinary effort (with >1 million vaccines given a day at times). Nepal seems to have gone through a recent omicron wave with low numbers in hospital and relatively few deaths. As we usher in the new lunar year of the tiger, we hope that it will be considerably better than the year of the buffalo.

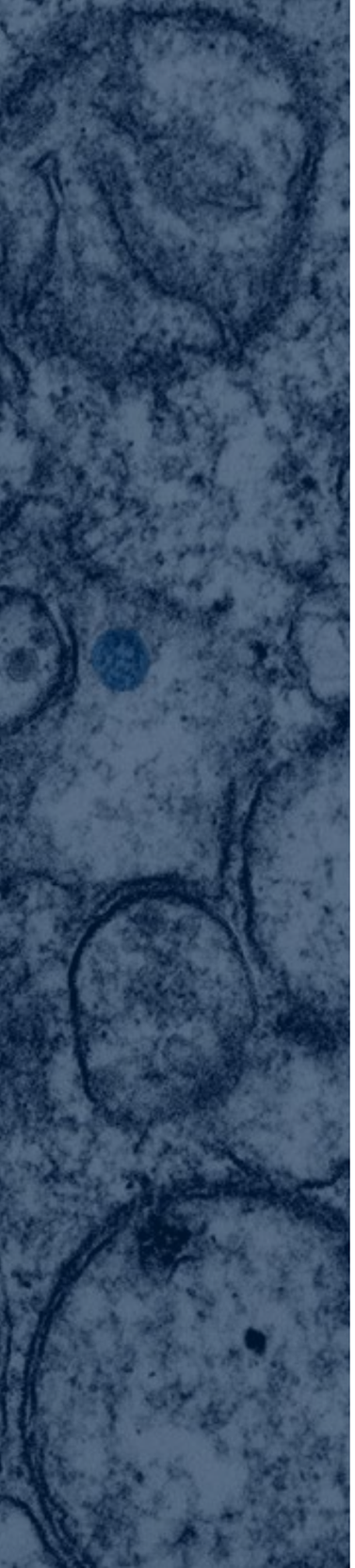
Of course, none of the work described would be possible without our key partners – The Hospital for Tropical Diseases in Ho Chi Minh City, the National Hospital for Tropical Diseases and the National Institute of Hygiene And Epidemiology in Ha Noi, Patan Academy of Health Sciences in Nepal, the Eijkman Institute and the University of Indonesia in Indonesia, and the University of Oxford, UK – and without the support from our funders, in particular the Wellcome Trust.

Professor Guy Thwaites

Director
Viet Nam Wellcome Africa Asia Programme
Oxford University Clinical Research Unit
Professor of Infectious Diseases,
University of Oxford

Acronyms

APF	Armed Police Force Hospital, Nepal
BPKIHS	B.P. Koirala Institute of Health Sciences, Nepal
CDC	Centre for Disease Control
DFAT	Australian Department of Foreign Affairs and Trade
EOCRU	Eijkman-Oxford Clinical Research Unit
FKUI	Fakultas Kedokteran Universitas Indonesia
HAMS	Hospital for Advanced Medicine and Surgery
HTD	Hospital For Tropical Diseases, Ho Chi Minh City, Viet Nam
ICU	Intensive care unit
IOCRL	Universities of Indonesia and Oxford Clinical Research Laboratory
LMICs	Low- and middle-income countries
NHRC	Nepal Health Research Council
NHTD	Viet Nam National Hospital For Tropical Diseases, Ha Noi
NIH CEIRS	US National Institutes of Health, Centers of Excellence for Influenza Research
NIHE	Viet Nam National Institute of Hygiene and Epidemiology
NIHR	UK National Institute for Health Research
NPH	Nepal Police Hospital
OUCRU	Oxford University Clinical Research Unit
OxTREC	Oxford Tropical Research Ethics Committee
PAHS	Patan Academy of Health Sciences, Nepal
PoAHS	Pokhara Academy of Health Sciences, Nepal
PBMC	Peripheral blood mononuclear cells
PCR Test	Polymerase Chain Reaction (PCR) test
PI	Principal Investigator
RSSBD	Rumah Sakit Umum Daerah Sumba Barat Daya Hospital, Indonesia
STIDH	Sukraraj Tropical and Infectious Disease Hospital, Nepal
WRH	Western Regional Hospital Pokhara, Nepal



About Us

The Oxford University Clinical Research Unit (OUCRU) is a large-scale clinical and public health research unit with site offices in Viet Nam, Indonesia, and Nepal.

Part of the Centre for Tropical Medicine and Global Health at the University of Oxford (UK), OUCRU was first established in Ho Chi Minh City in 1991, hosted by the Hospital for Tropical Diseases (HTD), Viet Nam. In 2003, OUCRU-NP was established in Kathmandu, Nepal, hosted by Patan Hospital and the Patan Academy of Health Sciences. OUCRU Ha Noi was established in 2006 in partnership with the National Hospital for Tropical Diseases (NHTD) and the National Institute of Hygiene and Epidemiology (NIHE), Viet Nam. In 2008, the Eijkman-Oxford Clinical Research Unit (EOCRU) was established in Jakarta, Indonesia, in partnership with the Eijkman Institute for Molecular Biology and Faculty of Medicine University of Indonesia.

Our vision is to have a local, regional and global impact on health by leading a locally-driven research programme on infectious diseases in Southeast Asia.

Our research programme covers clinical and laboratory research with hospital and community-based patient populations, including epidemiology, immunology, host and pathogen genetics, molecular biology, microbiology and virology, mathematical modelling, bioinformatics, biostatistics, and social science. This work is supported by an extensive clinical trials unit and data management centre compliant with national and international regulations and comprehensive management, finance, public engagement, and administrative support offices.

OUCRU receives considerable support from Wellcome as part of the Africa and Asia Programmes. Together with our partners, we have led a highly successful effort in enhancing the infrastructure and capacity to perform clinical trials and basic scientific research in Viet Nam, Indonesia, and Nepal.

Website: www.oucru.org

COVID-19 SNAPSHOT

On March 11, 2020, when WHO declared the COVID-19 outbreak a pandemic, countries in WHO South Asia and Southeast Asia Region were either responding to their first cases of importation or cluster of cases or keeping a strict vigil against the importation of the new coronavirus. Now, more than 22 months later, the pandemic is still raging on, with ongoing waves of infection sweeping through countries across the world.

By 24 February 2022, a total of 430 million cases[2] had been recorded worldwide, and 5.92 million people had died.

After a long period of relative containment, Viet Nam has experienced its first major wave of nationwide infections, starting end of April 2021, with now (24 February 2022) more than 2.97 million cases and 39,773 deaths reported. In July 2021, many parts of Viet Nam's population, including the capital city of Ha Noi[3], Ho Chi Minh City and the Mekong Delta region[4], entered lockdown due to a surge of infections. Starting from the beginning of September 2021, the total cases had started to decrease to several thousand per day, and since late September 2021, most of the cities and provinces had eased the restrictions[5]. However, since late November 2021, there has been slight increase of new cases, with over 10,000 cases per day recorded[6].

Meanwhile, as of 24 February 2022, Indonesia - the fourth most populous nation in the world - had reported 5.35 million cases, the highest in Southeast Asia[7]. A total of 147,025 deaths on 24 February 2022 marks Indonesia as second in Asia[8] in terms of death toll.

After experiencing a second wave at the end of 2021, Nepal is facing a possible third wave with the number of cases rising and trend showing infections in clusters. As of 24 February 2022, a number of 976,361 cases had been reported and 11,930 people had died.

Time of data: 24 February 2022

For updated Covid-19 data, visit Our World in Data[1]

For more information, refer to **weekly Covid-19 Situation Reports by WHO:**

Viet Nam:
https://bit.ly/WHOVietNamCovid19

Indonesia:
https://bit.ly/WHOIndoCovid19

Nepal:
https://bit.ly/WHONepalCovid19

For a full list of **SARS-CoV-2 Variants of Interest (VOIs) and Variants of Concern (VOCs), visit:**
https://bit.ly/WHOCovidVariants

For a full list of **COVID-19 Vaccines** within WHO EUL/PQ evaluation process, visit:
https://bit.ly/WHOCovid19Vaccines

Source: Our World in Data, recorded on 24 February 2022	Total Confirmed Cases (per million people)	Total Deaths (per million people)
Viet Nam	30,278	405.15
Indonesia	19,362	532.00
Nepal	32,902	402.02

Variants

During late 2020, the emergence of SARS-CoV-2 variants that posed an increased risk to global public health prompted the characterisation of specific Variants of Interest (VOIs) and Variants of Concern (VOCs) in order to prioritise global monitoring and research, and ultimately to inform the ongoing response to the COVID-19 pandemic.

The Delta variant (Pango lineages B.1.617.2), first documented in India in October 2020, has been responsible for the surge of cases in most countries in South and Southeast Asia, including Viet Nam, Indonesia, and Nepal.

First detected in multiple countries in November 2021, the Omicron variant (Pando lineages B.1.1.529) has been designated as a variant of concern by WHO on 26 November 2021[10]. Omicron is quickly replacing Delta as the predominant variant in many parts of the world.

Vaccines

As of 24 February 2022, at least 13 different vaccines (across six platforms) have been approved by WHO and administered worldwide.

In Viet Nam, people aged 12 or older[11] are eligible to get the vaccine. As of 24 February 2022, 80.99 percent of Viet Nam's eligible population (79.51 million people) have received at least one dose of the vaccine, and 78.37 percent (76.94 million people) have been fully vaccinated[12]. On 10 December 2021, Ho Chi Minh City initiated a campaign to administer third doses to adults over 50, those with weakened immune systems, and frontline workers[13]. The main vaccines used in the national vaccine rollout programme include Sinovac-CoronaVac, AstraZeneca, and Pfizer, with Moderna, Abdala, and Sputnik taking up smaller proportions.

Indonesia started vaccinating its adult population at the beginning of 2021. As of 24 February 2022, around 68.78 percent of its eligible population (190.09 million people) have received at least one dose of the COVID-19 vaccine, and 51.31 percent (141.81 million people) have been fully vaccinated[14]. The national vaccine rollout is primarily based on Sinovac-CoronaVac and AstraZeneca, with smaller batches of other vaccines becoming available.

Starting 10 July 2021, Indonesia gave nearly 1.5 million healthcare workers a third shot of Moderna's mRNA vaccine[15] to increase the protection in response to a new outbreak in the country, and the government launched a mass booster campaign for the general population in January 2022.

Nepal launched its vaccination drive on January 27[16], with an eligible population of 21.6 million[17] people. As of 24 February 2022, 72.31 percent of the country's population (21.46 million people) have received at least one dose, and 57.87 percent (17.17 million people) have been fully vaccinated[18].

RANDOMISED CONTROLLED TRIALS

Photo: Unsplash | Louis Reed

The RECOVERY Trial – A Randomised Evaluation of COVID-19 Therapy

Principal Investigators
OUCRU: Jeremy Day
EOCRU: Raph Hamers
OUCRU-NP:
Buddha Basnyat

Partner PIs:
Dr. Pradip Gyanwali (Nepal Health Research Council),
Dr. Erni Nelwan (Faculty of Medicine University of Indonesia, FKUI),
Dr. Nguyen Van Vinh Chau (Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam)

Locations of the study
Nepal, Indonesia, Viet Nam (HCMC and Ha Noi)

More information
https://www.recoverytrial.net/

Funders:
This trial is supported by grants to the University of Oxford from the National Institute for Health Research (NIHR), UK Research and Innovation, and Wellcome, and by core funding provided by the Bill and Melinda Gates Foundation, the Foreign, Commonwealth & Development Office, Health Data Research UK, the Medical Research Council Population Health Research Unit, the NIHR Oxford Biomedical Research Centre, NIHR Clinical Trials Unit Support Funding, and Wellcome Trust.

Aims:
This international clinical trial aims to identify treatments that reduce the risk of death in patients hospitalised with suspected or confirmed COVID-19. It is a large multicenter trial recruiting in hospitals in the United Kingdom, Indonesia, Nepal, Viet Nam and Ghana.

Study Design:
Well-designed, pragmatic, and easy to implement clinical trials are key to generating the evidence needed to best manage pandemic diseases, which occur essentially in emergency situations. The RECOVERY trial sets this paradigm. It is a large open-label factorial designed platform trial that enables the simultaneous testing of multiple different treatments. As particular treatments are found to be effective or ineffective, they are dropped from the trial and should form part of the standard of care.

The study is designed to have high power to deliver precise estimates of the effect of particular treatments on the risk of death. New treatment interventions are added to the trial as evidence emerges from small-scale studies of their possible value. While originally based in the UK, the extension of the RECOVERY trial to international sites, building upon well-established clinical research networks and collaborations, will ensure that the results of the trial have global relevance.

RECOVERY in Nepal

RECOVERY in Nepal is being led by the Nepal Health Research Council (NHRC) in collaboration with OUCRU-Nepal. There are currently five active sites in Nepal: Sukraraj Tropical and Infectious Disease Hospital (STIDH), Armed Police Force (APF) Hospital,Nepal Police Hospital (NPH), Hospital for Advanced Medicine and Surgery (HAMS), and Pokhara Academy of Health Sciences (PAHS).

The site Principal Investigator are:

- For STIDH: Dr. Anup Bastola and Dr. Bimal Sharma Chalise
- For APF: Dr. Roshan Kumar Jha and Dr. Binay Kumar Adhikari
- For HAMS: Dr. Hem Raj Paneru and Dr. Raju Pangeni
- For NPH: Dr. Damodar Poudel, Dr, Bibek Rajbhandari and Dr. Sumi Singh
- For PoAHS: Dr. Santosh Baniya, Dr. Sharad Baral and Dr. Sunil Pathak.

Prof. Buddha Basnyat from OUCRU-Nepal and Dr. Pradip Gyanwali from NHRC are the country investigators for this trial.

About the Nepal site:
Sukraraj Tropical and Infectious Disease Hospital (STIDH) is the only Infectious & Tropical Disease Hospital established in 1933 in Kathmandu, Nepal. This is the national referral hospital with a capacity of 100 beds inpatient service. It receives patients from all over the country and referred patients from the Valley hospitals. This is one of the main hospitals in Kathmandu valley where patients with COVID-19 are being treated.

Armed Police Force (APF) hospital is a 200-bed government hospital that was dedicated as an anti-coronavirus dedicated facility by the Ministry of Health, Nepal. Recently another police hospital (Nepal Police Hospital) has also been added for enrollment of patients. This is also a government hospital which has a capacity of 200 beds.

Hospital for Advanced Medicine and Surgery (HAMS) is a multi-disciplinary tertiary care boutique hospital with 50 beds of which 10 are ICU beds. HAMS has been providing quality and affordable healthcare for over 22 years now.

Nepal Police Hospital was inaugurated by the late king Birendra Bir Bikram Shah Dev on the 27th of Chaitra, 2040 BS with an intention to provide free health services to in-service policemen, their families and ex-servicemen and their spouses. The hospital was opened to the general public in May 2017, with 311-bed hospital set aside as 20 beds for general ward and 30 beds for post-operative wards. The hospital is providing general medicine, surgery, gynaecology, orthopaedics, dental, radiology, ENT and ophthalmology services.

Pokhara Academy of Health Sciences is the teaching wing of Western Regional Hospital Pokhara, Nepal. Western Regional Hospital (WRH), located at Ramghat, Kaski, is the second biggest hospital of Nepal and biggest hospital in the Western region with the capacity of 500 beds.

RECOVERY in Indonesia

This trial is being hosted and led by the Faculty of Medicine, University of Indonesia and supported by the Universities of Indonesia and Oxford Clinical Research Laboratory (IOCRL), a joint facility established in 2017 on the faculty's campus in Central Jakarta, that serves as a hub to support clinical trials, education and public engagement.

The study is being led by Dr. Erni Nelwan (Faculty of Medicine University of Indonesia, FKUI) as the country Principal Investigator, Prof. Raph Hamers (Oxford University, based at FKUI) as the country's responsible investigator of the trial, and Dr. Mutia Radharjani, as the Head of the Clinical Research Support Unit at the Eijkman-Oxford Clinical Research Unit (EOCRU).

There are currently five study sites: Martha Friska Hospital, Medan; Metropolitan Medical Centre, Jakarta; Hasan Sadikin Hospital, Bandung; UNAIR hospital, Surabaya; Kandou Hospital, Manado; Puri Raharja Hospital, Denpasar. Other potential sites will be added.

Outputs to Date:
Having enrolled more than 47,000 patients to date, RECOVERY has provided precise data demonstrating the efficacy of dexamethasone, tocilizumab, and a cocktail of CoV antibodies (Regeneron) in reducing the risk of death in hospitalised patients, and that hydroxychloroquine, azithromycin, lopinavir-ritonavir, aspirin, colchicine, and convalescent plasma are ineffective. These results have influenced World Health Organisation and national guidelines for the treatment of COVID19. Current treatments undergoing evaluation include high dose corticosteroids and empagliflozin.

Publications:

RECOVERY Collaborative Group. Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. medRxiv [Internet] 2021; Available from: https://doi.org/10.1101/2021.06.08.21258132

RECOVERY Collaborative Group. Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. The Lancet [Internet] 2021;397(10274):605-612. Available from: https://doi.org/10.1016/S0140-6736(21)00149-5

RECOVERY Collaborative Group. Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. [Internet] 2021; Available from: https://doi.org/10.1101/2021.06.15.21258542

RECOVERY Collaborative Group. Colchicine in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. medRxiv [Internet] 2021; Available from: https://doi.org/10.1101/2021.05.18.21257267

RECOVERY in Viet Nam

The National Hospital for Tropical Diseases (NHTD), Ha Noi, is a tertiary care centre for infectious diseases in northern Viet Nam. Unlike most hospitals, NHTD is a specialist hospital under the direct supervision of the Ministry of Health.

The Hospital for Tropical Diseases (HTD), Ho Chi Minh City, is the referral hospital for infectious diseases for all of southern Viet Nam.

RECOVERY Collaborative Group. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial. The Lancet [Internet] 2021; 397(10289):2049-2059. Available from: https://doi.org/10.1016/S0140-6736(21)00897-7

RECOVERY Collaborative Group. Dexamethasone in Hospitalised Patients with Covid-19. New England Journal of Medicine [Internet] 2021; 384(8):693-704. Available from: https://www.nejm.org/doi/10.1056/NEJMoa2021436

RECOVERY Collaborative Group. Effect of Hydroxychloroquine in Hospitalised Patients with Covid-19. New England Journal of Medicine [Internet] 2020; 383(21):2030-2040. Available from: https://www.nejm.org/doi/10.1056/NEJMoa2022926

RECOVERY Collaborative Group. Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. The Lancet [Internet] 2020;396(10259):1345-1352. Available from: https://doi.org/10.1016/S0140-6736(20)32013-4

RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. The Lancet [Internet] 2021;397(10285):1637-1645. Available from: https://doi.org/10.1016/S0140-6736(21)00676-0

The COPCOV Study

Funders
Bill & Melinda Gates Foundation,
Wellcome Trust
MasterCard
Therapeutics Accelerator

Principal Investigator
Nick White (MORU)

EOCRU PI
Raph Hamers

OUCRU-NP PI
Buddha Basnyat

Location of activity
Nepal and Indonesia. Activity suspended in Viet Nam.

Website
www.tropmedres.ac/covid-19/copcov

Background:
COVID-19 has caused nearly 4.5 million deaths. Although vaccines are being deployed, the timelines for widespread roll-out are likely to be lengthy, particularly in areas where health systems are most fragile. Many experts anticipate that smaller outbreaks may occur in the future and that the disease will likely stay with us for a considerable time.

Chloroquine/hydroxychloroquine have been in constant use for more than 60 years. They are cheap, safe, well-tolerated and, importantly, available now. However, we still do not know, a year after the emergence of COVID-19, whether they can prevent the infection. These drugs could still be of benefit while we wait for the world's population to be vaccinated. Chloroquine/ hydroxychloroquine may also be beneficial in future pandemics, where vaccines would not be instantly available, or if vaccines became ineffective in the current pandemic.

Front-line healthcare workers and other high-risk individuals are at increased risk of infection. It is crucial that they are protected against the disease. Adequate personal protection is key, but additional interventions could further lower the risk of infection. There are currently no drugs for the prevention of COVID-19. The World Health Organisation recommends that outside the clinical trial setting, we should not give healthcare workers any drugs claiming to prevent COVID-19 before we know that they are safe and effective.

About the study:
COPCOV is a randomised, placebo-controlled pre-exposure prophylaxis study to determine whether chloroquine or hydroxychloroquine prevents coronavirus disease (COVID-19).

The COPCOV study has enrolled 4,000+ vital frontline healthcare workers and staff who have close contact with COVID-19 patients to determine whether chloroquine or hydroxychloroquine effectively prevents or reduces the severity of COVID-19 infections. We expect to have preliminary results as to whether chloroquine or hydroxychloroquine can prevent COVID-19 in the middle of 2022.

COPCOV in Indonesia

The study is being managed by Dr. Erni Nelwan (Faculty of Medicine University of Indonesia, FKUI) as the country Principal Investigator, Prof. Raph Hamers (Oxford University, based at FKUI) as the country's responsible investigator of the trial, and Dr. Mutia Radharjani, as the head of the Clinical Research Support Unit at EOCRU.

About the Indonesia site:
This trial is hosted and led by the Faculty of Medicine, University of Indonesia and supported by the Universities of Indonesia and Oxford Clinical Research laboratory (IOCRL). This is a joint facility established in 2017 on the faculty's campus in Central Jakarta, that serves as a hub to support clinical trials, education and public engagement.

The trial is recruiting at five active sites: the Universitas Airlangga (UNAIR) Hospital and Husada Utama Hospital in Surabaya, Murni Teguh and Bunda Thamrin hospital in Medan, and Sardjito Hospital in Yogyakarta.

COPCOV in Nepal

The trial preparation was put on hold in Nepal due to the country's mass vaccination of healthcare workers. But it now has started enrollment and randomisation in the community adjoining the the B.P. Koirala Insititute of Health Sciences (BPKIHS) after the successful amendment of the protocol, which now includes the general public who are at risk to contract COVID-19.

Description of the team:
This study is being managed by Dr. Suchita Shrestha, a Medical doctor and an MPH graduate from Mahidol University, Thailand.

Dr. Sanjib Kumar Sharma is the site PI and will be supervising the study at BPKIHS, Dharan. He is the head of the Department of Internal Medicine in Nepal. He has been involved in various multicentre research projects related to chronic kidney disease, diabetes, hypertension, snake bites etc. and has published more than 120 articles in national and international journals in the related fields. He is also the key personnel directly involved in the management of COVID-19 patients at BPKIHS, Dharan, Nepal.

About the Nepal site:
B.P. Koirala Institute of Health Sciences (BPKIHS) was established on January 18, 1993, and subsequently upgraded as an Autonomous Health Sciences University on October 28, 1998, with a mandate to work towards developing a socially responsible and competent health workforce, providing health care and engaging in health research. BPKIHS is located in Eastern Nepal & it has extended its continued health services through teaching district concepts to Primary Health Care Centers, District Hospitals and Zonal Hospitals in six districts of the region.

This Institute is envisaged as one of the finest examples of Indo-Nepal Cooperation. This University is aptly named after Bisheshwar Prasad Koirala, Nepal's visionary leader in social upliftment and a firm believer of National Reconciliation and National Integration. Candidates from disadvantaged groups are given opportunities for admission in most of the academic programmes. While selecting candidates for postgraduate studies, the Institute has given due recognition to those medical officers who have worked in the primary health centres and district hospitals.

Outputs to date:

Schilling W, Callery J, Taylor W et al. Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; protocol for a randomised, placebo-controlled prophylaxis study (COPCOV). Wellcome Open Research [Internet] 2020;5:241. Available from: https://doi.org/10.12688/wellcomeopenres.15784.1

Schilling W, Callery J, Chandna A, Hamers R, Watson J, White N. The WHO guideline on drugs to prevent COVID-19: small numbers- big conclusions. Wellcome Open Research [Internet] 2021; 6:71. Available from: https://doi.org/10.12688/wellcomeopenres.16741.1

White N, Watson J, Hoglund R, Chan X, Cheah P, Tarning J. COVID-19 prevention and treatment: A critical analysis of chloroquine and hydroxychloroquine clinical pharmacology. PLOS Medicine [Internet] 2020; 17(9):e1003252. Available from: https://doi.org/10.1371/journal.pmed.1003252

Evaluation of awake prone positioning effectiveness in moderate to severe COVID-19 (Awake Prone Study)

Funders
Wellcome Trust

Principal Investigators
Nguyen Thanh Truong, Louise Thwaites

Location of activity
Hospital for Tropical Diseases (including other hospital belong to HTD), Ho Chi Minh City, Viet Nam

Background:
Supplemental oxygen is recommended to maintain oxygen saturations in those with COVID-19 associated acute respiratory failure. Many patients require escalation of therapy, from simple low-flow systems to higher flow methods, non-invasive ventilation or endotracheal intubation and invasive mechanical ventilation. Escalation of therapy necessitates increased utilisation of healthcare resources such as oxygen, equipment and skilled staff. Whilst already in short supply in resource-limited countries, these are even further limited in the current pandemic situation.

In patients with severe acute respiratory distress syndrome (ARDS) receiving mechanical ventilation, prone position has been shown to increase survival and respiratory outcomes.

However, it is unclear whether patients on lower degrees of respiratory support (eg oxygen via facemask or nasal canulae) also benefit, nor whether data from well-resourced healthcare environments apply in LMICs such as Viet Nam, particularly under pandemic situations when considerable resources are required to help patients maintain prone positioning.

Primary Objective:
To determine whether prone positioning of hospitalised Vietnamese patients with moderate to severe COVID-19 for ≥ 8 hours a day reduces the need for escalation of respiratory therapy compared to standard care.

Secondary Objectives:
1. To determine whether prone positioning with a protocol aiming for ≥ 8 hours a day results in reduced intubation rates, improved mortality and shorter duration of hospital stay compared to standard care.
2. To compare changes in FiO2, SpO2, respiratory rate and heart rate that occur during prone position of hospitalised Vietnamese patients with moderate to severe COVID-19.
3. To determine whether prone positioning for ≥ 8 hours a day is associated with reduced oxygen utilisation compared to standard care.
4. To determine safety of prone positioning.

A Randomised, Double-Blinded, Positive Controlled Phase IIb Clinical Trial to Evaluate the Immunogenicity and Safety of COVID-19 Vaccine (Vero Cell), Inactivated Booster Dose in Adults who have completed two doses of CoronaVac® or VaxzevriaTM in Indonesia (PRO-nCOV-2006)

Funders
SinoVac Life Sciences

Principal Investigators
Robert Sinto,
Raph Hamers

Location of activity
Jakarta

Collaborators
Faculty of Medicine Universitas Indonesia,
Jakarta Health Agency

Vaccine-induced population immunity is a key global strategy to control the COVID-19 pandemic, and to date eight COVID-19 vaccines have received Emergency Use Listing (EUL) by the WHO. Accumulating evidence shows a progressive increase in breakthrough infections after a two-dose vaccine schedule associated with diminishing humoral immunity over time. Neutralisation and vaccine effectiveness after two-dose vaccine schedules are particularly reduced for the recently emerged Omicron variant (B.1.1.529), with significant restoration after a third vaccine booster dose. CoronaVac (SinoVac Life Sciences Co Ltd, Beijing, China), an inactivated whole-virus vaccine that received WHO EUL on June 1st, 202118, is currently one of the most widely administered COVID-19 vaccines worldwide with around 2 billion in 54 countries, as per February, 2022, and the predominant vaccine in Indonesia.

Importance:
As policy makers in several countries have started implementing third or periodic boosting to protect the most vulnerable populations, and mitigate health care and economic impacts, further clinical trial data and cohort studieswill be are critical to guide decisions regarding when, which populations and what boosters should be administered. Recent trials suggested that heterologous (or "mix and match") virus-vectored or mRNA booster strategies were more immunogenic than a homologous schedule, albeit with increased reactogenicity in some combinations. There are still insufficient data on the efficacy and efficacy persistence of a CoronaVac booster immunisation after primary vaccination with CoronaVac or Vaxrevia, and whether a double-dose booster could enhance immunogenicity.

Objectives:
The present study is designed to evaluate the immunogenicity of a third booster dose of CoronaVac among adults aged 18 years and above, after primary vaccination with CoronaVac or Vaxrevia, given in a medium-dose (currently approved) or full-dose (600 SU/0.5 ml and 1200 SU/0.5 ml, respectively).

Photo: Unsplash | Steven Cornfield

Primary: To evaluate the immunogenicity of a high or medium dosage inactivated booster vaccine

Secondary:
- To evaluate immune persistence of a high or medium dosage inactivated booster vaccine
- To evaluate the safety of a high or medium dosage inactivated COVID-19 booster vaccine

Exploratory:
- To evaluate cellular immune responses of a high or medium dosage inactivated COVID-19 booster vaccine
- To evaluate incidence and genetic variants of COVID-19 breakthrough infections.

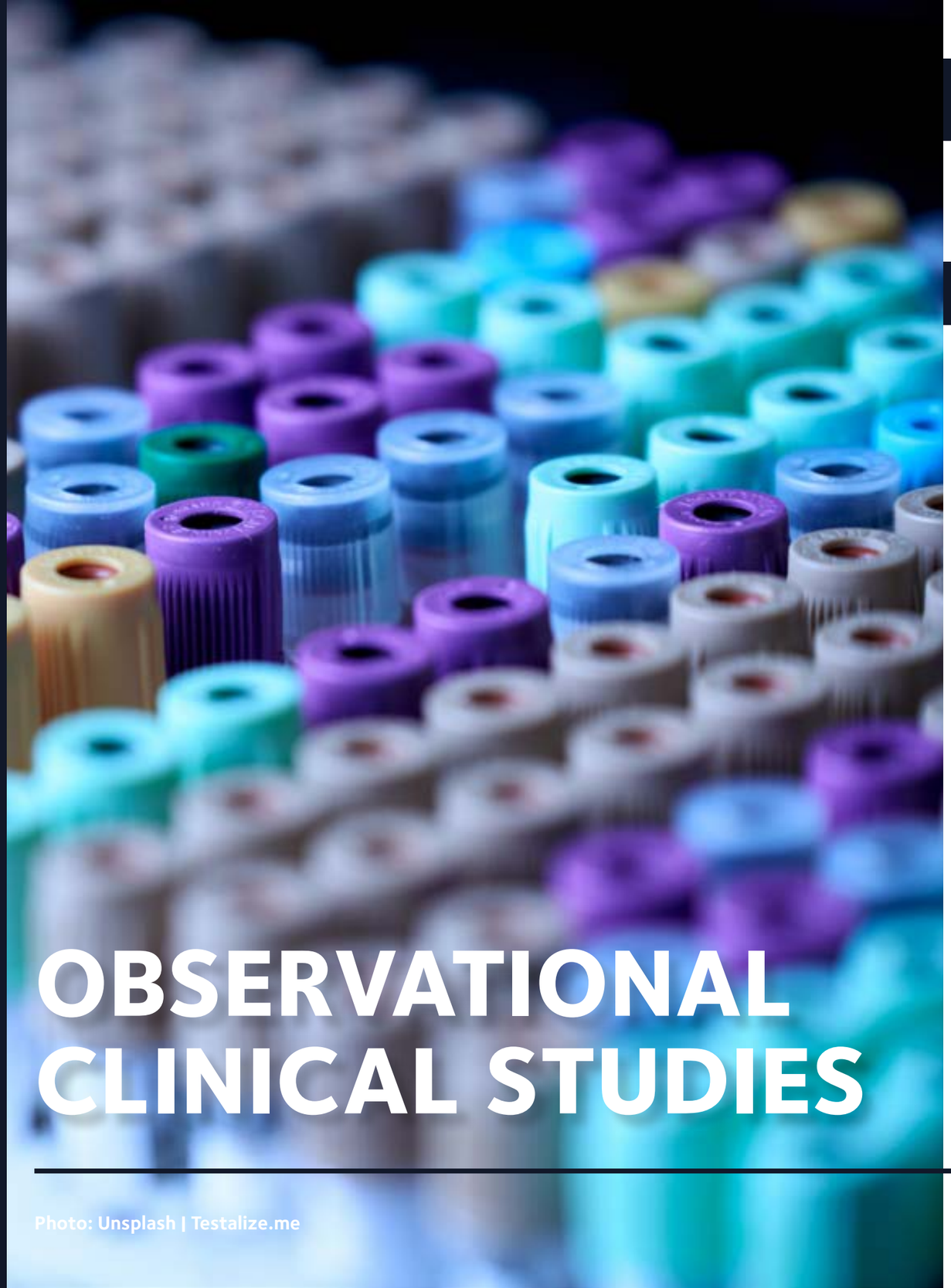


Photo: Unsplash | Testalize.me

Observational clinical studies

Prediction of respiratory failure in COVID-19 infection and understanding pathophysiological mechanisms

Funder
University of Oxford

Principal Investigator
Sophie Yacoub

Locations of activity
Ha Noi, Ho Chi Minh City, and Cu Chi, Viet Nam and Jakarta, Indonesia

Background:
In this observational study, our primary aim is to utilise the expertise we have developed in OUCRU Viet Nam to develop dynamic models that predict disease progression using real-time, longitudinal clinico-physiological data and specific blood biomarkers. Achieving this requires research in early infection and across the disease severity spectrum. In many countries, this is difficult due to the high burden of severe cases. In Viet Nam, the early identification of SARS-CoV-2 infections is routine due to a highly efficient test, trace and quarantine system.

At OUCRU Viet Nam, in collaboration with Oxford University, we are using point-of-care ultrasound and physiological monitoring via simple, low-cost wearable devices to develop artificial intelligence (AI) systems to better manage critically ill patients.

In this project, we intend to use conventional statistical techniques and AI to develop dynamic predictive models that will enable the identification of patients at risk of disease progression in COVID-19. We will build on our expertise using data from wearable devices, point-of-care heart and lung ultrasound, and specific blood biomarkers.

Status:
This study is currently recruiting in two sites in Ho Chi Minh City (Hospital for Tropical Diseases and Cu Chi Hospital) as well as in the National Hospital for Tropical Diseases in Ha Noi and the Pasar Minggu Hospital in Jakarta, Indonesia.

ISARIC Study: The natural history of SARS-CoV-2 infection in Viet Nam

Funder
OUCRU
(Wellcome funding)

Principal Investigators
Le Van Tan,
Rogier van Doorn

Locations of activity
Ho Chi Minh City and Ha Noi, Viet Nam

Background:
Most clinical research to date has been focusing on COVID-19 patients with moderately severe to severe disease because these are groups of patients that are admitted to hospitals for management worldwide. As a consequence, little is known about the natural history and transmission potential of completely asymptomatic and very mild infection with SARS-CoV-2.

We are in a unique position to study the natural history of SARS-CoV-2 infection due to the strict isolation, quarantine and contract tracing protocols enacted in Viet Nam. We are able, therefore, to recruit patients into our studies at all stages of infection, including pre- and asymptomatic carriers.

We also aim to evaluate the utility potential of wearable devices in monitoring COVID-19 patients remotely, thereby reducing the risk of transmission for healthcare workers.

Importance:
Our aim is to better understand the natural history of the infection. This is important to inform the development of intervention strategies and is highly relevant for the current global response to the ongoing COVID-19 pandemic.

Objectives:
1. To describe the clinical, laboratory and virological characteristics of SARS-CoV-2 infection;
2. To study the immune responses in SARS-CoV-2 infected patients;
3. To identify potential protein markers that can predict severe disease;
4. To unravel the evolutionary history of SARS-CoV-2 at both within the human host and population-level;
5. To evaluate the utility potential of rapid antigen tests for the diagnostics and management of COVID-19 patients;
6. To develop and sustain a research platform at key institutes and hospitals in Viet Nam to enable the country to rapidly respond to emerging infection outbreaks in the future.

Photo:
Wearable pulse oximeter device and smartphone display used for remote monitoring. Figure appeared in: Nguyen Van Vinh Chau, Ho Bich Hai, Greeff Heloise et al. Wearable remote monitoring for patients with COVID-19 in low-resource settings: case study [Internet]. BMJ Innovations. 2021. Available from: http://dx.doi.org/10.1136/bmjinnov-2021-000706

Outputs to date:

Huynh Kim Mai, Nguyen Bao Trieu, Trinh Hoang Long et al. Long-Term Humoral Immune Response in Persons with Asymptomatic or Mild SARS-CoV-2 Infection, Viet Nam. Emerging Infectious Diseases [Internet] 2021;27(2):663-666. Available from: https://doi.org/10.3201/eid2702.204226

ISARIC Clinical Characterisation Group. COVID-19 symptoms at hospital admission vary with age and sex: results from the ISARIC prospective multinational observational study. Infection [Internet] 2021; Available from: https://doi.org/10.1007/s15010-021-01599-5

Le Van Tan, Nghiem My Ngoc, Bui Thi Ton That et al. Duration of viral detection in throat and rectum of a patient with COVID-19. [Internet] 2020;Available from: https://doi.org/10.1101/2020.03.07.20032052

Le Van Tan, Nguyen Thi Thu Hong, Nghiem My Ngoc et al. SARS-CoV-2 and co-infections detection in nasopharyngeal throat swabs of COVID-19 patients by metagenomics. Journal of Infection [Internet] 2020;81(2):e175-e177. Available from: https://doi.org/10.1016/j.jinf.2020.06.033

Nguyen Van Vinh Chau, Ho Bich Hai, Greeff Heloise et al. Wearable remote monitoring for patients with COVID-19 in low-resource settings: case study [Internet]. BMJ Innovations. 2021. Available from: http://dx.doi.org/10.1136/bmjinnov-2021-000706

Nguyen Van Vinh Chau, Le Mau Toan, Dinh Nguyen Huy Man et al. Absence of SARS-CoV-2 antibodies in health care workers of a tertiary referral hospital for COVID-19 in southern Viet Nam. Journal of Infection [Internet] 2021;82(1):e36-e37. Available from: https://doi.org/10.1016/j.jinf.2020.11.018

Nguyen Van Vinh Chau, Nguyen Tri Dung, Geskus Ronald et al. Proactive response and innovative approaches to SARS-CoV-2 in Viet Nam [Internet]. 2021; Available from: http://dx.doi.org/10.1136/bmjinnov-2021-000712

Nguyen Van Vinh Chau, Vo Thanh Lam, Nguyen Thanh Dung et al. The Natural History and Transmission Potential of Asymptomatic Severe Acute Respiratory Syndrome Coronavirus 2 Infection. Clinical Infectious Diseases [Internet] 2020;71(10):2679-2687. Available from: https://doi.org/10.1093/cid/ciaa711

Ton That Thanh, Nguyen Thi Thanh Nhan, Nguyen To Anh et al. SARS-CoV-2 RNA loads in Vietnamese children. Journal of Infection [Internet] 2022 Jan 13:S0163-4453(22)00012-3. Available from: https://doi.org/10.1016/j.jinf.2022.01.010

Clinical characteristics, management and disease outcomes of COVID-19 patients in Indonesia: Clinical Characterisation Protocol (INACO study)

Funder
University of Oxford, Wellcome Trust

Principal Investigator
Raph Hamers

Location of activity
Jakarta, Indonesia

Collaborators
Anis Karuniawati, Faculty of Medicine Universitas Indonesia;
Dwi Utomo, Pasar Minggu Hospital;
Robert Sinto, Carolus Hospital;
Vera Irawany, Fatmawati Hospital;
Ayodhia Pitaloka Pasaribu, Universitas North Sumatera.

Background:
The global COVID-19/SARS-CoV-2 pandemic disproportionately affects low- and middle-income countries (LMICs), but rigorous research of its clinical management and consequences in those settings is lacking. With the fourth-largest population (270 million) globally, Indonesia is facing tremendous challenges, particularly in Jakarta and other hot zones, with the highest death toll in the region.

Systematic approaches are urgently needed to "learn-as-we-go" by characterising clinical patterns, management and outcomes of hospitalised COVID-19 patients, analysed in an international context, to improve the constantly evolving national response.

The project accrues a prospective observational cohort of hospitalised COVID-19 patients in multiple hospitals in Jakarta and Medan, with additional sites being linked in other cities in Indonesia, to generate this critically needed evidence. Clinical data have been shared with the ISARIC platform to support global data analysis. This work also establishes a research platform for ancillary studies of disease mechanisms and therapeutic intervention studies, including the use of wearable devices for patient monitoring, inflammation markers, and SARS-CoV-2 genomic surveillance.

Objectives:
1. To describe the clinical patterns, severity, and current management of COVID-19 patients, estimate the disease outcomes, and identify associated factors in Indonesia;
2. To inform local clinical practice and national policy based on this evidence and identify specific gaps in care;
3. To establish a COVID-19 clinical research platform for studies and trials.

The impact of Covid-19 on pregnancy care and outcomes (CovPreg)

Funder
OUCRU (Wellcome Funding)

Principal Investigator
Anuraj Shankar

Partner PIs
Dr. Rina Agustina (Faculty of Medicine University of Indonesia);
Ms. Annisa Dwi Utami (Summit Institute for Development)

Collaborators
Davrina Rianda (Faculty of Medicine University of Indonesia);
Yuni Dwi Setiyawati (Summit Institute for Development);
Jakarta Health Office;
District Health Office of Magelang, Banggai and East Lombok;
University of Mataram School of Medicine.

Locations of activity
Jakarta, Districts of Magelang, Banggai, East Lombok, Indonesia

Primary objectives:
1. Document gaps and impact of changes in antenatal care (ANC), delivery, and post-natal care (PNC) due to health system changes during the Covid-19 pandemic in Indonesia.
   - Estimate gaps in ANC, delivery, and PNC due to Covid-19;
   - Estimate the impact of care gaps on maternal and neonatal health: pregnancy weight gain, blood pressure, haemoglobin level, blood sugar, delivery care, gestational age at birth, birth weight.
2. Estimate the excess morbidity and mortality among pregnant women and newborns due to maternal exposure or infection with SARS-CoV-2.

Importance:
Longitudinal analysis of maternal care for ~4000 women before and after the pandemic indicates ~40% reduction in overall ANC, with the most significant reductions in ANC2 and ANC3. Longitudinal follow-up of 1100 women under routine ANC care indicates ~2% of women are swab positive and asymptomatic at the first ANC visit, with ~32% being antibody positive; and ~34% becoming antibody-positive during pregnancy. Associations with birth weight, preterm birth and other pregnancy-related morbidities are underway. The goal of the work is to guide targeted strengthening of specific high impact components of maternal care during the pandemic and to define priority for resources to mitigate the impact of SARS-CoV-2, such as maternal vaccination.

The impact of maternal COVID-19 on newborn health, immunity, and development (CovNeo)

Funder
OUCRU (Wellcome Funding)

Principal Investigator
Anuraj Shankar

Partner PIs:
Ms. Yuni Dwi Setiyawati (Summit Institute for Development)

Collaborators
Brigitta Warouw (Summit Institute for Development), Provincial Health Office of West Nusa Tenggara, District Health Office of East Lombok, University of Mataram School of Medicine, MMC Diagnostic Clinic.

Location of activity
East Lombok, Indonesia

Importance
Increased risks for poor neonatal outcomes have been reported for maternal SARS-CoV-2 and other pathogenic viral diseases including SARS, MERS, influenza; and Zika virus which has serious adverse effects on fetal growth and brain development. The COVID-19 in pregnancy (CovPreg) has observed adverse effects of the pandemic on pregnant women, and in a separate study, known as THRIVE-GEN, we are tracking early childhood development, and seeing evidence of developmental delays, and poor home environment for child development, and family stress. Given the limited knowledge of the maternal biomedical and psychosocial effects of COVID-19 on neonatal health, it is important to assess these effects, and implications may influence interventions to mitigate the effects of COVID-19 on neonatal health and development, such as more intensive vaccine policy for pregnant women and infants.

Primary objectives:
1. Measure the SARS-CoV-2 burden in newborns:
   - What is the prevalence of SARS-CoV-2 infection as assessed during the neonatal period?
   - What is the prevalence of detectable maternal antibody (Ab) to SARS-CoV-2 during the neonatal period, and what is the persistence of such Ab at 6 months of age?
   - What is the incidence of COVID-19 in infants during the first year?
   - What is the morbidity and mortality of infants of SARS-CoV-2 exposed women?
2. Measure the level of COVID-19-related social factors:
   - What is the stress in households and the nurturing and stimulation practices?
   - What are the care-seeking practiced for post-natal care for infants?
   - What is infant development at 6 months and 12 months?
3. Determine the COVID-19-associated morbidity, mortality and poor development of newborns/infants due to the above conditions.

Real-world assessment of the immunogenicity and effectiveness of COVID-19 vaccines in Indonesia (INVITE Study)

Principal Investigator
Raph Hamers

Partner PI
Dr. Erni Nelwan

Location of activity
Hospitals and primary health centres in Jakarta, Indonesia

Collaborators
Dwi Utomo, Pasar Minggu Hospital; Robert Sinto, Carolus Hospital; Jakarta Health Office.

Background:
The unprecedented speed with which COVID-19 vaccines have been developed and approved represents a major scientific achievement, and vaccine-induced population immunity is a key global strategy to control the COVID-19 pandemic. There are still many "real-world" knowledge gaps on vaccine-induced immune responses, correlates of protection and temporal changes, the clinical impact of breakthrough infections, effectiveness and reactogenicity of (heterologous) vaccine boosters. More research is warranted to understand vaccine-induced humoral and cellular immunity to SARS-CoV-2, defining detailed targets of humoral and cellular immune responses at the epitope level, characterising the B-cell receptor and T-cell receptor repertoire elicited by infection or vaccination, and establishing the long-term durability and maintenance, of protective immunity after infection or vaccination. This is particularly true for the widely used inactivated whole-virus vaccines, such as Sinovac/CoronaVac, being rolled out in many countries worldwide, including Indonesia, a populous middle-income country and one of the COVID-19 epicentres.

This research project offers a unique window of opportunity for research and learning to leverage several observational patient cohorts in Indonesian populations to conduct real-world assessments of COVID-19 vaccinations as they are rolled out to inform optimal vaccination strategies in the face of emerging SARS-CoV-2 variants. The study aims to generate essential real-world information on the immunogenicity and effectiveness of COVID-19 vaccines (based on inactivated virus, viral vector and others) in Indonesia in terms of immune responses, adverse reactions, and SARS-CoV-2 breakthrough infections.

Objectives:
1. To assess humoral and cellular immune responses following primer and booster vaccine doses, in individuals with and without pre-existing immunity;
2. To assess vaccine reactogenicity in individuals with and without pre-existing immunity;
3. To characterise SARS-CoV-2 breakthrough infections post-vaccination.

Importance:
The spread of variants of concern threatens the success of national COVID-19 vaccine programmes, with particular concerns around the potentially reduced effectiveness of CoronaVac/SinoVac against Omicron infections, although it is yet unclear what will be the impact at scale. In order to address these challenges effectively, there is an urgent need to understand the biological consequences of the mutations found in these variants and the consequential impact on their susceptibility to current control measures, including vaccines, drugs and non-pharmaceutical interventions. Measuring immune correlates of vaccine-induced protection is key for understanding COVID-19 and the development of next-generation vaccines.

Advanced analytics of Covid-19 patient data to better define infection and outcomes

Principal Investigator
Anuraj Shankar

Partner PI
Dr. Erlina Burhan, Faculty of Medicine University of Indonesia; Dr. Rina Agustina, Faculty of Medicine University of Indonesia.

Location of activity
Jakarta, Indonesia

Collaborators
Jakarta Health Office; National Disaster Relief Agency

Background:
Analyses of correlates of SARS-CoV-2 infection or mortality have usually assessed individual predictors. This study aimed to determine if patterns of combined predictors may better identify the risk of infection and mortality. This is a retrospective cohort study of 106 hospitalised patients. For the first nine days of the pandemic in Indonesia, we selected all 18 confirmed cases, all 60 suspected cases, and 28 putatively negative patients with pneumonia and no travel history. Hierarchical cluster analyses (HCA) and principal component analyses (PCA) identified cluster and covariance patterns for symptoms or haematology, which were analysed with other predictors of infection or mortality using logistic regression.

Importance:
For univariate analyses, no significant association with infection was seen for fever, cough, dyspnea, headache, runny nose, sore throat, gastrointestinal complaints (GIC), or haematology. A PCA symptom component for fever, cough, and GI symptoms tended to associate with increased risk of infection (OR 3.41; 95% CI 1.06-14; p=0.06), and a haematology component with elevated monocytes had decreased risk (OR 0.26; 0.07-0.79; 0.027). Multivariate analysis revealed that an HCA cluster of 3-5 symptoms, typically fever, cough, headache, runny nose, sore throat but little dyspnea and no GI symptoms, tended to reduce risk (aOR 0.048; <0.001–0.52; 0.056). In univariate analyses for death, an HCA cluster of cough, fever, and dyspnea had increased risk (OR 5.75; 1.06 – 31.3, 0.043). Other significant predictors of infection were age ≥ 45, international travel, contact with a Covid-19 patient, and pneumonia. Diabetes and history of contact were associated with higher mortality. Cluster groups and co-variance patterns may be stronger correlates of SARS-CoV-2 infection than individual predictors.

Outputs to date:
Burhan E, Syam A, Rahyussalim A et al. The emergence of COVID-19 in Indonesia: analysis of predictors of infection and mortality using independent and clustered data approaches. MedRxiv [Internet] 2021; Available from: https://doi.org/10.1101/2020.07.10.20147942

Clinical epidemiology of paediatric COVID-19 Delta variant cases from North Sumatra, Indonesia

Principal Investigator
Anuraj Shankar

Partner PIs:
Dr. Tryna Tania (Murni Teguh Memorial Hospital, Medan, North Sumatra, Indonesia), Dr. Ariel Pradipta (GSI Laboratory, Jakarta, Indonesia)

Collaborators
R Lia Kusumawati (University of North Sumatera, Medan, North Sumatra, Indonesia), Inke Nadia Diniyanti Lubis (Murni Teguh Memorial Hospital, Medan, North Sumatra, Indonesia), Meutia A Kumaheri (GSI Laboratory, Jakarta, Indonesia)

Location of activity
Medan

Background:
The impact of SARS-CoV-2 and it variants remains poorly understood. Moreover, few studies had reported on the presence, or the clinical relevance, of the Delta variant in children from a low- and middle-income country (LMIC).

Objective:
To examine the emergence and clinical impact and epidemiology of the Delta variant in paediatric COVID-19 patients from North Sumatra, Indonesia.

Importance:
We tracked the Delta variant among paediatric cases in North Sumatra, Indonesia, from June-July 2021. Whole-genome sequences (WGS) from 18 new COVID-19 paediatric patients showed that 6 were B.1.459 and 6 were B.1.466.2, known variants in Indonesia in Clade 20A. Six were the Delta variant B.1.617.2 of Clade 21A, with 5 on one branch, and one on a distant branch consistent with that patient's geographic separation, suggesting at least two introductions to the region. Variants tended to be spatially clustered, and four children with Delta variant had an adult infected household member, all of whom had lower real-time polymerase chain reaction (RT-PCR) cycle threshold (Ct) values compared to the child. No temporal trends were observed for Ct. These data support a paradigm shift with children being highly susceptible to the Delta variant and a priority for vaccination.

Outputs to date:
Kusumawati, R. Lia and Lubis, Inke Nadia Diniyanti and Kumaheri, Meutia Ayuputeri and Pradipta, Ariel and Faksri, Kiatichai and Mutiara, Mutiara and Shankar, Anuraj H. and Tania, Tryna. Clinical Epidemiology of Paediatric COVID-19 Delta Variant Cases from North Sumatra, Indonesia. The Lancet [Internet] 2021. Available from: http://dx.doi.org/10.2139/ssrn.3935668

Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study

Principal Investigator
Henry Surendra

Collaborator
Jakarta Health Office

Location of activity
Jakarta, Indonesia

Background:
Data on COVID-19-related mortality and associated factors from low-resource settings are scarce. Current understanding of COVID-19 mortality mostly comes from clinical epidemiological studies conducted in the early phase of the pandemic in China, and high-income countries of North America and Europe suggesting COVID-19-related mortality was associated with older age and common underlying chronic co-morbidities including hypertension, diabetes, obesity, cardiac disease, chronic kidney disease and liver disease. However, most COVID-19 cases have occurred in low- and middle-income countries (LMIC), where reliable data are scarce. In Southeast Asia, by January 26, 2021, COVID-19 case fatality rate had been reported at 2.3% (35/1551) in Vietnam, 2.0% (10,386/516,166) in Philippines, 0.5% (75/14,646) in Thailand, 0.4% (700/190,434) in Malaysia, 0% (0/460) in Cambodia, and <0.1% in Singapore (29/59,366). Indonesia has the highest number of COVID-19 cases and deaths in the region, reporting 2.8% case fatality rate (28,468/1,012,350), with the highest number of cases in the capital city of Jakarta. A preliminary analysis of the first two months of surveillance in Jakarta found that 381 of 4052 (9.4%) patients had died, associated with older age, dyspnea, pneumonia, and hypertension.

Objectives:
This study examined clinical characteristics and factors associated with in-hospital mortality of COVID-19 patients in Jakarta, Indonesia, from March 2 to July 31, 2020.

Importance:
This study of the complete epidemiological surveillance data of Jakarta during the first five months of the epidemic is one of the largest studies in LMIC and the largest in Southeast Asia to date, that analysed the characteristics and outcomes of patients hospitalised with PCR-confirmed COVID-19. Overall in-hospital mortality was lower than reported in high-income countries, which is likely explained by the younger hospital population, fewer comorbidities and less severe disease. Nonetheless, age-specific mortalities were comparable to high-income countries. Although the large majority (78%) of people who died were 50 years or older, deaths occurred across all age groups. A concerning finding was the death of 11% (7/61) of children <5 years hospitalised with COVID-19, which contrasts with previous evidence that severe disease and death among children is rare.
This study affirmed the vulnerability of elderly and comorbid COVID-19 patients. Increasing burdens of non-communicable diseases in the urban centres of developing nations will impact morbidity and mortality associated with COVID-19. Further studies are needed to understand the extent and underlying causes of death related to COVID-19 in children <5 years in LMIC.

Outputs to date:
Surendra H, Elyazar I, Djaafara B et al. Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study. The Lancet Regional Health - Western Pacifc [Internet] 2021;9:100108. Available from: https://doi.org/10.1016/j.lanwpc.2021.100108

The clinical features, epidemiology, immunology and host genetics associated with SARS-CoV-2 infection in children and adults in Ho Chi Minh City, Viet Nam

OUCRU Principal Investigator
Le Van Tan

Partner Principal Investigator
Dr. Nguyen Van Vinh Chau (Hospital for Tropical Diseases, Ho Chi Minh City),
Dr. Nguyen Thanh Hung (Children's Hospital 1, Ho Chi Minh City),
Dr. Nguyen Tran Nam (City Children's Hospital, Ho Chi Minh City)

Location of activity
Ho Chi Minh City, Viet Nam

Background:
The on-going nation-wide outbreak caused by the Delta variant in a relatively naïve population in Viet Namnecessitates a multidisciplinary research approach to better understand the clinical futures, virology, pathophysiology and associated host genetic factors of the infections, especially determinants of severe diseases. These data are critical to informing the development of appropriate intervention strategies, thereby improving clinical outcomes and mitigating the impacts of the COVID-19 pandemic.

Aims:
1. To describe the clinical features and associated laboratory findings in children and adults with SARS-CoV-2 infection
2. To understand the circulation and evolution of SARS-CoV-2 in Viet Nam
3. To describe and compare SARS-CoV-2 viral loads in children and adults
4. To gain insights into the immune responses in children and adults infected with SARS-CoV-2 infections
5. To identify potential factors (including host-genetic markers) that are associated with poor clinical outcome of SARS-CoV-2 infection.

Impact:
The study results would inform the global research agenda on clinical management and the development of intervention strategies aiming at reducing the burden posed by COVID-19 and SARS-CoV-2 infections.

Outputs to date:
Ton That Thanh, Nguyen Thi Thanh Nhan, Nguyen To Anh et al. SARS-CoV-2 RNA loads in Vietnamese children. Journal of Infection [Internet] 2022. Available from: https://doi.org/10.1016/j.jinf.2022.01.010

DIAGNOSTICS & LABORATORY STUDIES

Photo: Pexels | Chokniti Khongchum

Validation of SARS-CoV-2 diagnosis with Reverse Transcription Loop-mediated Isothermal Amplification (RT-LAMP) on FTA filter paper for remote sites in Eastern Indonesia

Funder
OUCRU
(Wellcome Funding)

Principal Investigator
Suwarti

Collaborators
Dr. Claus Bogh (Sumba Foundation),
Bonifacius (Karitas Hospital),
Yohanes Niko Santoso P. (Karitas Hosiptal),
Yacobus B. Da Costa (Pratama Rada Bolo Hospital)

Locations of activity
Karitas Hospital and Pratama Rada Bolo Hospital
Sumba, East Nusa Tenggara, Indonesia

Indonesia's island geography across more than 5000 km steeply challenges the control of the COVID-19 pandemic. Moreover, uneven laboratory diagnostic capacities in remote and sparsely populated underdeveloped eastern areas of the archipelago further complicate the problem. For example, on the eastern island of Sumba, East Nusa Tenggara, more than 30 days are required to confirm COVID-19 by RT-PCR analysis during the early months of Covid-19. The absence of RT-PCR capacity on that island forces sample delivery by now limited air transport. COVID-19 diagnostics play vital roles in support of treatment and control of SARS-CoV-2 transmission. This remarked the inequities of diagnosis that will lead to the delayed response of treatment and care for Covid-19 patients in Sumba Island and create a catastrophe of Covid-19 pandemic response in remote settings. Currently, COVID-19 RT-PCR analysis uses nasopharyngeal or oropharyngeal swab specimens as the gold standard for diagnosis. Swab collections are uncomfortable and require close interaction with patients and impose the need for specialised swabs and viral transport medium (VTM) tubes. The pandemic and this single preferred means of diagnosis have created critical supply and reagent shortages all across the globe. That already precarious supply chain is deeply exacerbated in places like eastern Indonesia, where RT-PCR capacities are nearly non-existent and technical, fiscal, and logistical limitations severely constrict access to timely COVID-19 diagnostics.

Isothermal PCR, such as loop-mediated isothermal amplification (LAMP), has been an emerging tool as a great alternative to the RT-PCR method. LAMP possesses some fundamental advantages such as amplification at a constant temperature, exclusion of a thermal cycler, a faster test result, and potentially a larger diagnostic capacity while maintaining similar sensitivity and specificity, thus making it more suitable than the RT-PCR for monitoring a pandemic.

The study aims to use RT-LAMP in the Sumba region, specifically in the Southwest Sumba district, to remedy nearly non-existent COVID-19 diagnostic services for its sensitivity, specificity, independent-logistic supply with relatively low cost per reaction ($16.5) compared to RT-PCR cost ($80 per test in Indonesia) based on our calculation. RT-LAMP platform also liberates the dependency of the supply chain by the specific vendor, so logistic supply will be under control.

Objectives:

1. Validate diagnosis of SARS-CoV-2 by analysis of saliva by RT-LAMP among patients seeking treatment for febrile illness at Southwest Sumba District, Sumba island.
2. Validate the practical diagnosis of SARS-CoV-2 by analysis of saliva specimens collected on FTA filter paper and analysed at the RT-LAMP laboratory at Southwest Sumba.
3. Describe the demographic characteristics, clinical features, risk factors for severe disease, and response to treatment among patients confirmed as having COVID-19 illness.

Establishing the Southeast Asia Serological Surveillance Network (SASSNet) in Indonesia and Viet Nam

Funder
Not yet confirmed

Principal Investigator
J Kevin Baird

Locations of activity
Indonesia and Viet Nam

The project aims to establish the Southeast Asian Serological Surveillance Network (SASSNet) and operations in Indonesia and Viet Nam. The Network will apply optimised and validated serological sampling, analysis, and reporting of exposures to emerging and endemic neglected tropical infectious diseases of regional importance.

The project leverages both robotic ELISA and Luminex multiplex high throughput platforms in order to efficiently and sustainably surveil several dozen infections/vaccinations. The sampling strategy is a pragmatic approach of age-stratified anonymised residual blood specimens from networks of 25 hospitals in Indonesia and 20 in Viet Nam, based on existing efforts active in Viet Nam since 2009 and recently expanded throughout the entire country. The project joins academic research partners from the University of Oxford's clinical research units in Indonesia and Viet Nam with researchers within the respective Ministry of Health in both nations.

The first year of effort focuses exclusively on serological surveillance of SARS-CoV-2 through three distinct workstreams:

1. Establishing routine national serological surveillance by ELISA;
2. Cross-sectional surveys for exposure to SARS-CoV-2 at selected sites; and
3. Following two longitudinal cohorts for serological assessment by ELISA over a 1-year period, where enrollment in one cohort immediately follows qPCR positivity for SARS-CoV-2, and in the other immediately follows vaccination against COVID-19.

Year 1 will also see the optimising and validation of a multiplex Luminex assay for six distinct SARS-CoV-2 antigenic targets and three distinct immunoglobulins (A, M, and G), along with Spike S1 and Spike N proteins of MERS-CoV, and four seasonal coronaviruses. The same multiplex assay will later include eight emerging infections (e.g. Nipah, Zika, and Japanese encephalitis viruses), neglected tropical infections (e.g., Dengue, malaria, filariasis, leprosy, and intestinal helminthiases), and vaccine-preventable infections (e.g. measles, diphtheria, and tetanus). That multiplex serological assay will constitute the basis of routine national serological surveillance, and the project aims to build that capacity within Ministry of Health facilities in Indonesia and Viet Nam and to turn those facilities over to the respective authorities at the end of the 5-year life of the project.

Establishing a hospital-based nationwide sero-surveillance system in Viet Nam

Funder
OUCRU
(Wellcome Funding)

Principal Investigators
Marc Choisy
Rogier van Doorn

Timeline:
Started in 2009 with 10 hospitals in southern VN, expanded with 10 hospitals in northern Viet Nam in 2019, ongoing.

Objectives:
This project aims to establish and run a nationally representative serum bank for Viet Nam, as a resource for researchers and policymakers to understand infectious disease emergence, transmission, immunity and vaccination in the population.

The serum bank periodically collects age-stratified residual serum samples from hospital labs in order to establish both a cross-sectional and longitudinal collection.

Significance:
The platform's strategic importance has been accentuated by COVID-19 and is as follows:

- It enhances OUCRU's relevance to and impact upon public health in Viet Nam, supporting outbreak responses and prevention.
- It creates a substantial long-term longitudinal research resource, allowing OUCRU to address multiple research questions concerning the epidemiology of emerging and vaccine-preventable infectious diseases, but also infectious diseases for which the transmission is difficult to understand, either because part of it is not directly tractable (e.g. TB or COVID-19), or because of complex immunological processes (e.g. dengue, influenza).
- Vaccine-preventable and emerging infections, and the serum bank itself, is a part of the strategic vision for OUCRU in the applications for bridging and core funding with Wellcome.

Output(s) to date
Studies on influenza, tetanus and measles have been completed.

We are awaiting funding for large-scale COVID-19 research in the current and future collections to study background immunity, population-level exposure and vaccine coverage.

Consortium for Surveillance of SARS-CoV-2 Sequence and Structure in LMICs: Leveraging the capabilities and networks of the Wellcome-funded International Units

Funder
Wellcome Trust

Principal Investigators
Philip Bejon,
Le Van Tan,
Anuraj Shankar

Locations of activity
Indonesia and Viet Nam

Timeline
April 2021 - April 2022

Objectives:
The goal of this Consortium is to deliver large-scale real-time SARS-CoV-2 whole genome sequencing capacity (WCS) to hospitals and local governments across Wellcome Africa-Asia programme countries. This effort, when combined with epidemiological and clinical information, will inform interventions and policy decisions during the current pandemic.

Virus genome data are combined with clinical and epidemiological datasets in order to help to guide public health interventions and policies. Subsequent analyses will enable the evaluation of novel treatments and non-pharmacological interventions on SARS-CoV-2 virus populations and spread and provide information on introductions versus community transmission and outbreaks.

These data will also allow researchers to identify and evaluate emerging genetic changes and understand how they affect the ability of the virus to transmit from person to person and to cause severe forms of the disease.

Impact:
Shared technologies, bio-informatics, experience, and funds across the Wellcome Africa-Asia Sequencing Consortium has led to better and faster SARS-CoV-2 WGS. This includes contribution of nearly 6,000 SARS-CoV-2 WGS to GISAID, comprising 20-30% of all WGS from Viet Namor Indonesia, and nearly 4x acceleration of WGS throughput, thereby enabling the first detections of the Alpha, Delta, and Omicron variants in Viet Namor Indonesia. This was possible by strengthening the WGS capacity for the national Centers for Disease Control, and the Ministries of Health in Viet Namand Indonesia, and with specific institutions in Viet Namincluding the Hospital for Tropical Diseases, and National Institute of Hygiene and Epidemiology; and in Indonesia it led to establishment of the public private partnership social enterprise known as the Genomik Solidaritas Indonesia Laboratory (GSI Lab) as the highest throughput molecular diagnostics and WGS facility in the country. Key lessons include the need for global and local partnerships across the Africa Asia Program, and to foster use of multiple technologies and skillsets, and interdisciplinary teams of scientists focused on genomics.

Outputs to date

Le Van Tan. COVID-19 control in Viet Nam. Nature Immunology [Internet] 2021;22(3):261-261. Available from: https://doi.org/10.1038/s41590-021-00882-9

Nguyen Thi Tam, Pham Ngoc Thach, Trang Dinh Van et al. Genetic diversity of SARS-CoV-2 and clinical, epidemiological characteristics of COVID-19 patients in Ha Noi, Viet Nam. PLOS ONE [Internet] 2020;15(11):e0242537. Available from: https://doi.org/10.1371/journal.pone.0242537

Nguyen Van Vinh Chau, Le Nguyen Thanh Nhan, Lam Anh Nguyet et al. Absence of SARS-CoV-2 antibodies in pre-pandemic plasma from children and adults in Viet Nam. [Internet] 2021; Available from: https://doi.org/10.1101/2021.07.12.21260379

Nguyen Van Vinh Chau, Nguyen Thi Thu Hong, Nghiem My Ngoc et al. Rapid whole-genome sequencing to inform COVID-19 outbreak response in Viet Nam. Journal of Infection [Internet] 2021;82(6):276-316. Available from: https://doi.org/10.1016/j.jinf.2021.03.017

Nguyen Van Vinh Chau, Nguyen Thi Thu Hong, Nghiem My Ngoc et al. Superspreading Event of SARS-CoV-2 Infection at a Bar, Ho Chi Minh City, Viet Nam. Emerging Infectious Diseases [Internet] 2021;27(1):310-314. Available from: https://doi.org/10.3201/eid2701.203480

Ton That Thanh, Nguyen Thi Thanh Nhan, Huynh Kim Mai et al. The Application of Sample Pooling for Mass Screening of SARS-CoV-2 in an Outbreak of COVID-19 in Viet Nam. The American Journal of Tropical Medicine and Hygiene [Internet] 2021;104(4):1531-1534. Available from: https://doi.org/10.4269/ajtmh.20-1583

Pradipta A, Kumaheri MA, Wahyudi LD, Susanto AP, Agasi HI, Shankar AH, Sudarmono P. Accelerating detection of variants during COVID-19 surges by diverse technological and public health partnerships: a case study from Indonesia. Front Genet 2022 13:801332. Available from: https://doi.org/10.3389/fgene.2022.801332

COVID-19 outbreak response in Viet Nam

Principal Investigator
Le Van Tan

Location
Viet Nam

SARS-CoV-2 Sequencing
OUCRU Viet Nam has dedicated our whole molecular diagnostic facilities and sample processing systems for COVID-19 diagnostics. A team of 15 senior research staff at OUCRU has teamed up with the diagnostic group at the Hospital for Tropical Diseases in Ho Chi Minh City to perform COVID-19 diagnostics.

As of July 2021, the lab can process some 1,500 tests per day. By July 5, 2021, the OUCRU/HTD diagnostics team had conducted PCR testing for 140,000 individuals in Ho Chi Minh City, Viet Nam.

We have been leading real-time whole-genome sequencing to inform Viet Nam's outbreak response, especially in Ho Chi Minh City. The turnaround time is 24 hours. Ho Chi Minh City is one of the few places in Southeast Asia where whole-genome sequencing of SARS-CoV-2 has been successfully applied for outbreak response.

Key milestones are:

- The Tan Son Nhat international airport outbreak in February 2021. Rapid whole-genome sequencing found that the SARS-CoV-2 variant A.23.1 was responsible for this outbreak. Therefore, the outbreak in Ho Chi Minh City at the time was epidemiologically unrelated to the ongoing outbreak in Hai Duong and Quang Ninh, which was caused by the Alpha variant (B.1.1.7).
- The ongoing citywide outbreak: Since the second week of May 2021, several clusters of symptomatic SARS-CoV-2 infection of unknown origin have been detected in Ho Chi Minh City. Using whole-genome sequencing, our team showed that while both the Alpha and Delta variants were responsible for these clusters, the Delta variant with higher transmissibility has become the dominant variant responsible for the current outbreak in the city.
- Collectively, these whole-genome sequencing data have been critical to informing COVID-19 response in Ho Chi Minh City and Viet Nam as a whole, contributing to the overall success of SARS-CoV-2 control in Viet Nam. We were recently recognised by the People's Committee of Ho Chi Minh City for our contribution to the COVID-19 outbreak response in the city.

Capacity building:
We have trained our colleagues at the Institute of Pasteur in Nha Trang on the whole-genome sequencing of SARS-CoV-2. They can now operate the sequencing platform independently with remote support from our team in Ho Chi Minh City. Similarly, the team at OUCRU Ha Noi has transferred sequencing protocols for direct sequencing to the National Insititute of Hygiene and Epidemiology (NIHE) in Ha Noi, who are applying this independently. The OUCRU Ha Noi team works with the National Hospital for Tropical Diseases and aims to sequence all epidemiologically relevant viruses weekly.

Immunogenicity and safety of COVID-19 vaccine in Vietnamese healthcare workers

Principal Investigator
Le Van Tan

Partner PI
Dr. Nguyen Van Vinh Chau (Hospital For Tropical Diseases)

Location of Activity
Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam

Status
The study was approved by the HTD Institutional Review Board and OxTREC and is currently ongoing. HTD was strongly supportive of the study, and the results will be communicated to the Vietnamese Ministry of Health and the Department of Health.

Background:
According to the Viet Nam Ministry of Health, as of 4th April 2021, Viet Nam has received nearly one million doses of the AstraZeneca COVID-19 vaccine. Accordingly, a total of 52,335 frontline healthcare workers from 19 provinces/cities across the country have received their first doses. As yet, none in Viet Nam has received a second dose of the COVID-19 vaccine.

At the Hospital for Tropical Diseases (HTD) in Ho Chi Minh City, a total of 894 members of staff received their first doses of the AstraZeneca COVID-19 vaccine during the second week of March 2021. Yet, there has been no reported data regarding the immunogenicity of COVID-19 vaccines and the associated adverse events in Vietnamese people. Likewise, it remains unknown regarding the extent to which seasonal coronaviruses might interact with the immune landscape generated by the COVID-19 vaccine and vice versa.

The emergence of variants of concerns (B.1.1.7, P1 and B.1.135) of SARS-CoV-2 emphasises the importance of active surveillance for SARS-CoV-2 variants worldwide. Of equal importance is to assess the immune escape potential of such novel variants. These are now the top priorities of the WHO and the public health authorities of countries across the globe.

Collectively, to inform the global vaccination programme, we aim to fill some important existing gaps in knowledge about the immunogenicity of the AstraZeneca COVID-19 vaccine in Vietnamese healthcare workers and the adverse events that might arise within 48 hours after vaccination. More specifically, our primary aims are to determine the development of detectable neutralising antibodies after vaccination (first and second doses) and the durability of neutralising antibodies for a period of 12 months after vaccination. Additionally, to inform the public about the safety of the AstraZeneca COVID-19 vaccine, we will also synthesisedata on the associated adverse events occurring within 48 hours after vaccination. This 48-hour window time was determined by the Vietnamese Ministry of Health.

Primary Objectives:

- To determine the development of detectable neutralising antibodies to SARS-CoV-2 at 14 and 28 days after the first dose of AstraZeneca COVID-19 vaccine in Vietnamese healthcare workers.
- To assess the durability and kinetic of neutralising antibodies against SARS-CoV-2 in Vietnamese people over 12 months after vaccination.
- To describe the adverse events arising within 48 hours after receiving the AstraZeneca COVID-19 vaccine, allied with the development of neutralising antibodies at 14 and 28 days after the first dose and 14 days after the second dose.

Secondary Objectives:

- To assess the impact of the second dose on the titers of neutralising antibodies to SARS-CoV-2 at 14 days after the administration.
- To record SARS-CoV-2 infection events (if any) and the associated clinical features in Vietnamese people after receiving the AstraZeneca COVID-19 vaccine.
- To assess the T cell response against SARS-CoV-2 in Vietnamese people after receiving AstraZeneca COVID-19 vaccine and (if relevant) the immune escape potential of new SARS-CoV-2 variants.
- To assess the cross-reactivity between immunity induced by AstraZeneca COVID-19 vaccine and common cold coronaviruses (NL63, OC43, 229E and HKU1).

Importance:
The Africa Asia Programmes (including OUCRU) have recently been funded by Wellcome to strengthen the whole-genome sequencing capacity and to conduct active surveillance for SARS-CoV-2 variants in their respective host countries. Therefore, if relevant, we will use the collected PBMC and plasma samples of the present study to assess the immune escape potential of new variants of SARS-CoV-2.

Collectively, the present study forms a part of our holistic effort on SARS-CoV-2 evolution and immunity in Viet Nam and the region. As such, the obtained data are critical to informing the local, regional and global vaccination programme and the associated COVID-19 research.

From the public engagement perspective, it is also critical to demonstrate that the AstraZeneca COVID-19 vaccine is safe and effective. This project will provide data on the common side effects of the vaccine, and we will work with the HTD and OUCRU Public Engagement team to identify the best communication channels for this important data.

Outputs to date:

Le Van Tan. COVID-19 control in Viet Nam. Nature Immunology [Internet] 2021;22(3):261-261. Available from: https://doi.org/10.1038/s41590-021-00882-9

Nguyen Van Vinh Chau, Le Nguyen Thanh Nhan, Lam Anh Nguyet et al. Absence of SARS-CoV-2 antibodies in pre-pandemic plasma from children and adults in Viet Nam. [Internet] 2021;Available from: https://doi.org/10.1101/2021.07.12.21260379

Nguyen Van Vinh C, Nguyen Thi Thu Hong, Nghiem My Ngoc et al. Rapid whole-genome sequencing to inform COVID-19 outbreak response in Viet Nam. Journal of Infection [Internet] 2021;82(6):276-316. Available from: https://doi.org/10.1016/j.jinf.2021.03.017

Nguyen Van Vinh Chau, Nguyen Thi Thu Hong, Nghiem My Ngoc et al. Superspreading Event of SARS-CoV-2 Infection at a Bar, Ho Chi Minh City, Viet Nam. Emerging Infectious Diseases [Internet] 2021;27(1):310-314. Available from: https://doi.org/10.3201/eid2701.203480

Ton That Thanh, Nguyen Thi Thanh Nhan, Huynh Kim Mai et al. The Application of Sample Pooling for Mass Screening of SARS-CoV-2 in an Outbreak of COVID-19 in Viet Nam. The American Journal of Tropical Medicine and Hygiene [Internet] 2021;104(4):1531-1534. Available from: https://doi.org/10.4269/ajtmh.20-1583

Enhancing the utility of SARS-CoV-2 antibody rapid diagnostic tests (RDTs) for disease surveillance.

Principal Investigator
Anuraj Shankar

Partner PI
Dr. Rina Agustina (Faculty of Medicine University of Indonesia)

Location of Activity
Jakarta, Indonesia (May 2020)

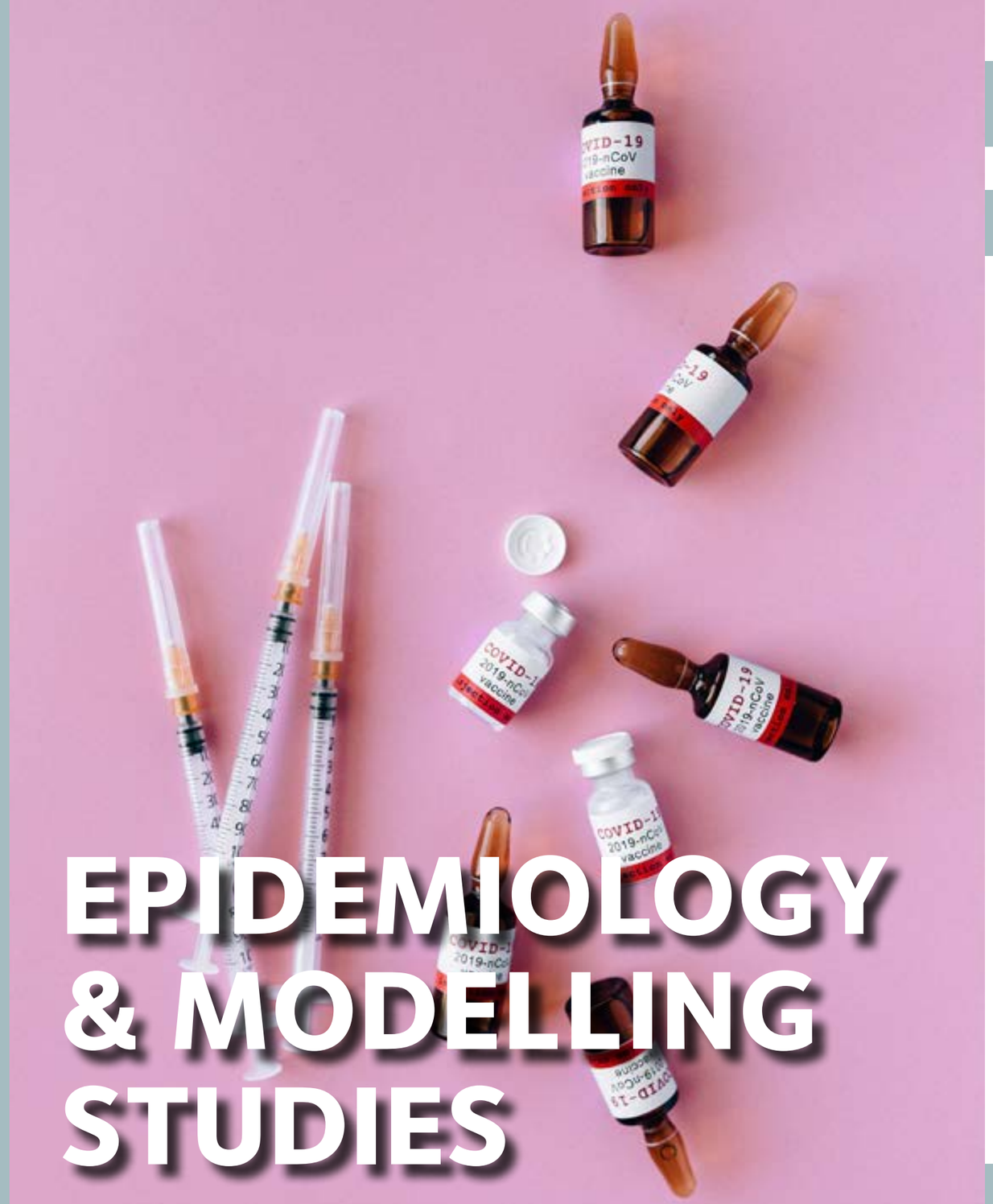
Collaborators
Jakarta Health Office, National Institute of Health Research and Development

Primary objective:
To investigate if the integration of symptomatic, demographical and diet-related comorbidities data with antibody rapid diagnostic tests (RDTs) improves their potential to assess infection rates in addition to exposure, thereby broadening their utility for surveillance.

Importance:
RDT-IgM/IgG-positive tests were associated with infection (OR 10.8, 95% CI 4.43 to 26.4, p<0.001) with an area under the curve (AUC) of 0.708% and 50% sensitivity, 91.5% specificity, 30.8% positive predictive value (PPV) and 96.1% negative predictive value (NPV). RDT results combined with age, gender, contact history, symptoms, and comorbidities increased the AUC to 0.787 and yielded 62.5% sensitivity, 87.0% specificity, 26.6% PPV and 96.9% NPV. SARS-CoV-2 RDT-IgM/IgG results integrated with other predictors increased test sensitivity by 25%, indicating the approach may be an affordable tool for epidemiological surveillance for population-based Covid-19 exposure and current infection, especially in groups with outbreaks or high transmission. This may provide an affordable option for surveillance as RT-PCR is sensitive but costly, and antigen-based RDTs are cheap but of low sensitivity, and both detect current infection but not exposure, but SARS-CoV-2 IgM/IgG RDTs detect exposure but with poor sensitivity for current infection.

Output to date:

Agustina R, Syam AF, Wirawan F, Widyahening IS, Rahyussalim AJ, Yusra Y, Rianda D, Burhan E, Salama N, Daulay R, Halim ARV, Shankar AH. (2021) Integration of symptomatic, demographical and diet-related comorbidities data with SARS-CoV-2 antibody rapid diagnostic tests during epidemiological surveillance: a cross-sectional study in Jakarta, Indonesia. BMJ Open. 11:e047763.



EPIDEMIOLOGY & MODELLING STUDIES

Photo: Pexels | Nataliya Vaitkevich

Epidemiology and Modelling Studies

Tracking all-cause mortality at the epicentre of Indonesia's COVID-19 epidemic (TREMOR)

Funder
OUCRU
(Wellcome Funding)

Principal Investigator
Iqbal Elyazar

Locations of activity
8 cities in Indonesia
(Jakarta, Tangerang, Bandung, Semarang, Yogyakarta, Surabaya, Mataram, Denpasar)

Indonesians have suffered heavily due to COVID-19. Its causative agent, the SARS-CoV-2 virus, has been confirmed to occur in all 34 provinces. Since the first reported cases in Indonesia on 2 March 2020, nearly 250,000 cases and 9,500 deaths confirmed as COVID-19 have accrued. Both numbers are seriously under-reported as a consequence of severely limited diagnostic capacities.

We know that a heavy backlog of diagnostic services for COVID-19 pushes the turnaround time to 1-2 weeks or more, and many, if not most patients who die, do so before the diagnosis can be confirmed. Those patients are referred for burial as suspected COVID-19 and the subjects of special protocols for burial, e.g., sealed plastic wrapping rather than ritual cleansing and wrapping in fabric as per religious custom.

Given the extremely limited capacity of diagnostics, we aim to develop access to records of burials and cremations, or other measures of all-cause mortality, in these cities in order to begin to analyse the extent of mortal harm caused by COVID-19 as a means of measuring the spread and impact of SARS-CoV-2 transmission. Success in doing so would lead to broader surveys of COVID-19 attributable mortality. The protocol here represents a proposed work as a means to demonstrate the utility and validity of the methods applied.

Objectives
Determine quantifiable excess mortality and understanding of deaths associated with the onset of COVID-19 epidemics among eight urban centres in Indonesia. Specifically:

- Assemble weekly data on all-cause mortality by age and gender from all eight cities from January 2015 up to the present day, with weekly reporting until March 2021.
- Assemble weekly data reporting regarding COVID-19 suspect deaths, along with confirmed COVID-19 cases and confirmed deaths, all by age and gender.
- For each city, generate a monthly calculation of excess mortality attributable to COVID-19 compared to both suspected and confirmed deaths.
- Report these findings to the government agencies managing the COVID-19 crisis.

Output to date:
Elyazar I, Surendra H, Ekawati L et al. Excess mortality during the first ten months of COVID-19 epidemic at Jakarta, Indonesia. [Internet] 2020;Available from: https://www.medrxiv.org/content/10.1101/2020.12.14.20248159v1

Impact of the COVID-19 epidemic on TB, HIV, and childhood vaccination programmes in Indonesia, and policy and health system factors fostering programme resilience (COHERE; COVID Health System Resilience)

Funder
OUCRU
(Wellcome Funding)

Principal Investigators
Iqbal Elyazar,
Raph Hamers

Location of activity
Indonesia

Collaborators
National HIV Control Program,
National Tuberculosis Control Program,
Childhood Immunisation Programme,
Arbovrus Programme,
Ministry of Health

The number of deaths from COVID-19 continues to rise globally, but data quantifying the impact of the pandemic on other major infectious disease burdens in low- and middle-income countries (LMIC) are scarce. Interruption of supply chains, diversion of resources and overwhelmed health systems could have severe collateral effects on existing public health programmes. COVID-19 control measures, such as lockdowns and patient hesitancy might limit access to and uptake of health care services, affecting diagnostic testing, disease management, vaccine uptake, among others. Models have estimated that in high-burden settings, deaths due to HIV (mostly due to antiretroviral therapy [ART] interruptions) and tuberculosis (mostly due to reductions in timely diagnosis and treatment) could increase by up to 10% and 20%, respectively, over 5 years, compared with if there was no COVID-19 pandemic. Further, reduced uptake of routine childhood vaccinations, due to temporary programme suspensions or hesitancy, could lead to excess vaccine-preventable deaths. Moreover, it is crucial to define health system factors at the district level associated with lesser or greater resilience to the COVID-19 burden, and to identify those target groups who were more or less affected.

Indonesia is a diverse, middle-income nation, with the world's fourth largest population (270 million) spread out across the vast archipelago, has unique challenges to reaching universal health coverage through a decentralised health system. Concurrent with growing non-communicable disease burdens, high infectious disease burdens persist, particularly of respiratory infections, diarrheal diseases and tuberculosis. Globally, it is ranked the 3rd high-burden TB country (~1 million new cases per year; incidence 391/100,000 pop), and it has one of the fastest growing HIV epidemics (~46,000 new cases per year; ~640,000 people living with HIV). Pre-COVID, only 58% of children aged 12-23 months were fully immunised -below the 93% government target.

Indonesia has the second highest number of COVID-19 cases (>4 million) and deaths (>145,000) in Asia, and an estimated 61% excess mortality in Jakarta. Moreover, concerns have been raised around impacts of the COVID-19 epidemic and lockdowns on government's health services, but to date no rigorous analyses have been conducted to quantify national and district-level impacts on the care cascades for HIV, TB and childhood vaccination uptake.

Primary Objectives:
To measure the impact of the COVID-19 pandemic and lockdowns within the respective national programmes in Indonesia, at the national, provincial and district levels and and identify policy and health system factors of resilience and population disparities for key risk groups:

- TB care cascades (testing, diagnosis, linkage to care and treatment)
- HIV care cascades (testing, diagnosis, linkage to care and treatment)
- Childhood vaccination uptake

Importance:
To date, there are few published data from LMIC that quantify the effects of COVID-19 on health services and patient-related outcomes of the major infectious diseases HIV, tuberculosis and vaccine-preventable diseases, which may set back individual health and broader public health goals in the long-term. There are even fewer studies seeking to learn lessons from pre-pandemic district level health policy and health system preparedness that foster resilience to major shocks such as Covid-19; lessons that would enhance robust health systems in a post-pandemic world. As Indonesia is managing the COVID-19 epidemic, the health system should be strenghtened to make efforts to catch-up with any gaps in HIV and TB testing and treatment as well as vaccination uptake with the highest priority. The study findings can help identify public health priorities and inform innovative strategies. Research into service disruptions, and the factors that impeded those services during the COVID-19 lockdown, can inform public health responses to future outbreaks.

Photo: Unsplash | Dikaseva

Pandemic inequity in a megacity: a multilevel analysis of individual, community and health care vulnerability risks for COVID-19 mortality in Jakarta, Indonesia

Principal Investigator
Henry Surendra

Location of activity
Jakarta, Indonesia

Collaborators
Jakarta Health Agency,
Faculty of Medicine
Universitas Indonesia

There are currently 33 megacities, defined by the United Nations Department of Economic and Social Affairs as cities with a population of at least 10 million persons. Megacities comprise 8% of the global population, yet account for approximately 20% of all COVID-19 deaths. Megacities often contain high levels of inequity with regard to income, housing, sanitation, transportation, population density, basic health care, and other factors. The important role of health inequity in the spread and mortality of epidemics has been known from influenza in 1918 to Ebola in 2014. The severity of illness and clinical outcomes can be affected by the concentration of comorbidities in susceptible groups in communities, and through disparities of access to health care for preventive measures or prompt diagnosis and treatment. Ensuring health equity, especially in megacities experiencing massive urbanisation and mobility is essential for the current and future global health threats.

Importance:
In the context of the ongoing pandemic, understanding community-level risk factors associated with the mortality is very important to guide policymaking and target public health and clinical interventions, particularly in the context of fragile public health systems. At individual-level, older age and pre-existing chronic comorbidities have been consistently reported as the main risk factors of COVID-19-related mortality across different settings. At the community-level, recent findings in US, Chile and Brazil suggested that COVID-19 mortality was concentrated in groups with higher socio-demographics vulnerability.

However, there is a general scarcity of data in LMICs assessing the influence of community-level socio-demographics factors on COVID-19-related mortality. Indonesia, the world's fourth most populous country (population 274 million), is a lower-middle income country (LMIC) featuring great geographic, cultural and socio-economic diversity across the archipelago. Indonesia has suffered the highest number of COVID-19 confirmed cases and deaths in Southeast Asia, second only to India in all of Asia, at 4,253,598 cases and 143,744 deaths (3·4% case fatality rate (CFR)) up to November 22, 2021, of which 20% (863,482) of cases and 9·4% (13,574) of deaths occurred in its capital Jakarta, a megacity that features stark health inequalities and socio-demographic heterogeneity.

Objective:
In this retrospective cohort study, we assessed individual, community-level and health care vulnerability among the 44 sub-districts of DKI Jakarta and how those factors were associated with COVID-19-related mortality during the first 18 months of the epidemic in that province (March 2020 through August 2021).

Photo: Unsplash | Jason Cooper

Results:
This retrospective population-based study of the complete epidemiological surveillance data of Jakarta (N=705,503 cases) during the first eighteen months of the epidemic is the largest studies in LMIC to date, that comprehensively analysed the individual, community, and healthcare vulnerability associated with COVID-19-related mortality among individuals diagnosed with PCR-confirmed COVID-19. The overall case fatality rate among general population in Jakarta was 1·5% (10,797/705,503). Individual factors associated with risk of death were older age, male sex, comorbidities, and, during the first wave, age <5 years (adjusted odds ratio (aOR) 1·56, 95%CI 1·04-2·35; reference: age 20-29 years). The risk of death was further increased for people living in sub-districts with high rates of poverty (aOR for the poorer quarter 1·35, 95%CI 1·17-1·55; reference: wealthiest quarter), high population density (aOR for the highest density 1·34, 95%CI 1·14-2·58), and low COVID-19 vaccination coverage (aOR for the lowest coverage 1·25, 95%CI 1·13-1·38; reference: the highest).

Implications:
Differences in socio-demographics and access to quality health services, among other factors, greatly influence COVID-19 mortality in low-resource settings. This study affirmed that in addition to well-known individual risk factors, community-level socio-demographics and healthcare factors further increase the vulnerability of communities to die from COVID-19 in urban low-resource settings. These results highlight the need for accelerated vaccine rollout and additional preventive interventions to protect the urban poor who are most vulnerable to dying from COVID-19.

Natural history of SARS-CoV-2 in comparison to influenza A virus: a multi-site study focused in the Southern Hemisphere and equatorial regions

Funder
US NIH

Principal Investigators
Scientific Leadership Group with representatives from 7 consortia including the 5 Centres of Excellence in Influenza Research and Surveillance (CEIRS)

OUCRU Principal Investigator
Rogier van Doorn

Locations of activity
Ha Nam and Ha Noi, Viet Nam

Status
Ongoing until May 2022

Aims:
This study aims to conduct human surveillance for SARS-CoV-2 and influenza virus at eight sites across the Southern Hemisphere and equatorial regions. Each of these sites has an established research relationship with one of the five Centers of the CEIRS Network. Each site has the clinical and laboratory infrastructure needed to support enrollment, data and sample collection, and analysis of virological and serological parameters using qPCR and ELISA assays, respectively. Each site is furthermore able to ship biospecimens to US-based CEIRS laboratories for more in-depth analyses. One of the sites is the Ha Nam community household cohort that is led by OUCRU Ha Noi and the National Institute of Hygiene and Epidemiology, Viet Nam.

Importance:
Major knowledge gaps remain around the natural history of infection, the spectrum of disease, risk factors for severe outcomes and the magnitude, quality and longevity of immune responses. To address these gaps, systematic and in-depth analyses of viral load, clinical outcomes, and immune responses of infected individuals are rapidly needed. We propose to undertake such an effort. To give context to the results obtained and better understand their implications for human health, we will examine SARS-CoV-2 and influenza virus infection in parallel.

Objectives:
- Document clinical outcomes and risk factors for severe disease in individuals with SARS-CoV-2 infection.
- Define virology features of SARS-CoV-2 infection.
- Define the magnitude, quality and longevity of immune responses to SARS-CoV-2.
- Importantly, as a reference for comparison, parallel examination of influenza will be undertaken in each of these aims.

Status:
The study aims to enroll 40 index cases with influenza and 40 index cases with COVID-19. We will follow-up patients in 12 months. According to the recommended schedule (10 sampling time points), acutely infected participants will be more intensively sampled to determine virus infection dynamics and kinetics, humoral and cellular immune responses, co-infections, and host gene expression.

Currently, the project is active. We are screening patients with respiratory illness in the cohort. At the time of writing, no patients have tested positive for influenza or SARS-CoV-2 viruses.

Strengthening Preparedness in the Asia-Pacific Region through Knowledge - SPARK

Funder
Australian Department of Foreign Affairs and Trade

Principal Investigator
Iqbal Elyazar

Location of Activity
Indonesia

Website:
www.spark.edu.au

The inter-cities mobility network plays an important role in understanding outbreaks. It serves as a proxy for the transmission network. The cities with high mobility are more vulnerable to virus infection.

Understanding the effectiveness of large-scale social distancing interventions is critical. A map that examines the impact of social distancing on population mobility will help health officials understand what policies are most effective. As governments started to introduce large-social distancing and isolation measures, we expect individuals to start adjusting their mobility behaviour. Mobility data can provide important insights into how people move and how these patterns change. This work aims to characterise people's mobility in the high burden of SARS-CoV-2 in Jakarta, the capital of Indonesia.

Objectives:
1. To assess travel behaviour changes (volume and connectivity) in Greater Jakarta over time (during the large social restriction, relaxation, second large social restriction).
2. To assess how those travel behaviour changes affected the epidemic spreading in Greater Jakarta.
3. To assess how socio-economic status affected COVID-19 burden (incidence, mortality) in Greater Jakarta.

Photo: Pexels | Tom Fisk

Covid-19 ICU burden

Funder
OUCRU
(Wellcome funding)

Principal Investigator
Marc Choisy

Locations of Activity
Ha Noi and Ho Chi Minh City, Viet Nam

Collaborators
Dr. Pham Quang Thai, Epidemiology Department, National Institute of Hygiene and Epidemiology (NIHE), Ha Noi and Ho Chi Minh City CDC.

Aims:
The purpose of this study is to develop a mathematical model of ICU burden in time and space. The model is calibrated with data collected in Viet Nam when available or with data published from other countries (in particular, what concerns risk factors of severe cases). It takes into account age contact structure and population mobility data as inferred from the analysis of Facebook data.

Importance:
Such a model of ICU burden is required by the National Steering Committee for COVID-19 response. Such a model will be used to assist fast decision making if a crisis occurs. As such, the model is an original enough piece of research to be published in itself as it allows to model in great detail the distribution of the durations in the various epidemiological states. The framework of the model is generic enough to be applied to other contexts than Viet Nam and other diseases than COVID-19.

Primary Objectives:
1. Predict the ICU burden in space and time with and without relocation of critical equipment from hospital to hospital.
2. Look for policies (including quarantine, lock-down and stay-at-home, potentially with different implementations by locality and age class) that minimise the ICU burden using Optimal Control Theory.

Outputs to date:
Richard Q, Alizon S, Choisy M, Sofonea M, Djidjou-Demasse R. Age-structured non-pharmaceutical interventions for optimal control of COVID-19 epidemic. PLOS Computational Biology [Internet] 2021;17(3):e1008776. Available from: https://doi.org/10.1371/journal.pcbi.1008776

Djidjou-Demasse R, Michalakis Y, Choisy M, Sofonea M, Alizon S. Optimal COVID-19 epidemic control until vaccine deployment. [Internet] 2020;Available from: https://doi.org/10.1101/2020.04.02.20049189

Software: R package for discrete-time non-Markovian simulations [Internet]. GitHub. 2021;Available from: https://github.com/thinhong/cpp_training

A web-based application on contact tracing questionnaire

Funder
This project is currently seeking funding

Principal Investigators
Nhat Le,
Ronald Geskus,
Marc Choisy

Locations of Activity
Ha Noi and Ho Chi Minh City, Viet Nam

Collaborator(s):
Dr. Pham Quang Thai, Epidemiology Department, National Institute of Hygiene and Epidemiology (NIHE), Vera Arntzen (Leiden University)

Purpose:
This study aims to develop a standardised format for the questionnaire on contacts and build a smart device app to collect contact-tracing information.

Importance:
The world becomes increasingly more vulnerable to pandemics of novel infectious agents. When a novel infection emerges, an efficient methodology to contain the spread is contact tracing, which aims to identify all contacts of a diagnosed case and test them for infection.

Contact tracing is generally performed in a rush and in a way that is not always carefully considered. Furthermore, the data are collected to address immediate public health questions and are rarely collected in a standard format.

We propose a system to collect contact tracing information in a safe and standardised way. Such a system fulfils immediate public health purposes like containing the outbreak and is also helpful for research purposes. For example, contact tracing data can provide information for estimating key epidemiological quantities such as the distribution of latency and incubation period. Precise and unbiased estimates of these quantities will improve the predictions from epidemiological and mathematical models and thus are extremely valuable for efficient and timely control of the disease.

Primary Objectives:
- We design an electronic questionnaire on individual contact-tracing information, which is embedded into an app. This app connects to a central database in the cloud server. The app can also detect frequent errors during data entry, such as multiple formats of dates or Vietnamese free text. We will investigate how best to structure the questionnaires.
- We write an R package that can read the raw contact data per individual into R and transform the data into a format that consists of possible sources of infection and the period of contact with each of them. The package also includes functionalities that appeared as a shiny app that visualises the transmission chain developed by Vera Arntzen.

Characterising the distribution of incubation time and latency time

Funder
Wellcome Trust (OUCRU core funding), University of Leiden (the Netherlands)

Principal Investigators
Ronald Geskus, Nhat Le, Marc Choisy (for the OUCRU COVID-19 Modeling Group)

Locations of Activity
Ha Noi and Ho Chi Minh City, Viet Nam

Collaborators
Dr. Pham Quang Thai, epidemiology department, National Institute of Hygiene and Epidemiology (NIHE); Vera Arntzen and Marta Fiocco (University of Leiden)

The time from infection to becoming infectious (latency time) and to developing symptoms (incubation time) are key characteristics of any infection. For SARS-CoV-2, data to estimate both quantities have not been collected in a systematic way. As a consequence, information is incomplete, and there is a high risk of bias. For most individuals, the exact time of infection is not known. At most, we have information on the exposure interval during which someone became infected. Also, a large percentage of individuals remains asymptomatic, and these individuals are more likely to be missed in data collection.

Study design:
From the start of the pandemic until July 2021, Viet Nam has performed active contact tracing of all community infected individuals and quarantined these "F1 contacts" in supervised locations. Since March 2020, all individuals that entered Viet Nam have been quarantined. Viet Namhas had four major outbreaks, caused by at least three different variants, the original variant, the alpha variant and the Delta variant. In collaboration with NIHE and the Ho Chi Minh City Centre for Disease Control, we combine data from different sources and outbreaks to create a unique data set with representative information on the initial stages of the SARS-CoV-2 infection and disease process.

Contact tracing data provides information on the window of exposure. For the latency time, we assume that individuals become infectious when SARS-CoV-2 RNA becomes detectable. This information is obtained from the longitudinal polymerase chain reaction (PCR) test results.

For the incubation time, we use the time when patients first report symptoms that are suggestive of SARS-CoV-2 infection; individuals that remain asymptomatic are excluded. Data on the latency time are doubly interval-censored. Not only the time origin (infection) but also the event time (detectable RNA) is at best known to lie within an interval: the presence of detectable RNA is known each time a PCR test is done. For the incubation time, we have exact information on the time of becoming symptomatic for most individuals; then, only the time origin is interval-censored. We estimate both distributions by maximising the likelihood for (doubly) interval-censored data. We compare estimates for the different variants.

Impact
The length of the quarantine period is based on estimates of the incubation time distribution because data on the latency time is lacking. Our project will fill this gap by estimating the latency time distribution. Furthermore, latency time and incubation time are important components for mathematical models that quantify and predict the spread of SARS-CoV-2.

Outputs to date:
Pham Quang Thai, Rabaa M, Duong Huy Luong et al. The First 100 Days of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Control in Viet Nam. Clinical Infectious Diseases [Internet] 2020;72(9):e334-e342. Available from: https://doi.org/10.1093/cid/ciaa1130

The probability to remain asymptomatic and its dependence on age, sex and the presence of comorbidities

Funder
Wellcome Trust (OUCRU core funding)

Principal Investigators
Nguyen Thi Minh Nguyet, Le Thanh Hoang Nhat, Ronald Geskus, Marc Choisy (for the OUCRU COVID-19 Modeling Group)

Location of Activity
Ho Chi Minh City, Viet Nam

Collaborator
Dr. Pham Quang Thai, Epidemiology Department, National Institute of Hygiene and Epidemiology (NIHE)

Many individuals that are infected with SARS-CoV-2 don't show any symptoms. However, estimates of the probability to remain asymptomatic are scarce and likely to be biased. Data are often not collected in a systematic way, and asymptomatic individuals are more likely to be missed, creating a downward bias. One of the few exceptions is the outbreak on the Diamond Princess cruise ship in February 2020.

Study design:
Since the end of March 2020, Viet Nam has performed active contact tracing of all community infected individuals and quarantined these "F1 contacts" in supervised locations. If an F1 contact tests positive, his/her contacts become F1 contacts, etcetera. In this way, individuals within such a network of infections are unlikely to be missed.

Although some (mostly asymptomatic) infection chains may still go unnoticed, this is the closest to a representative sample of infections that can be attained. We use data from the time that contact tracing was implemented in Viet Nam.

The main source of information is the data from the Ministry of Health (MoH), but we will also use data on symptom onset after diagnosis from hospitals. Data are collected and curated by the National Institute of Hygiene and Epidemiology (NIHE).

We perform a logistic regression analysis in order to investigate how the probability of remaining asymptomatic depends on age, sex and the presence of comorbidities.

Impact:
In many countries, the state of the pandemic is monitored by testing persons with symptoms only. Knowing the proportion of individuals that remains asymptomatic helps to give a better understanding of the state of the pandemic. This holds even stronger if this information is used in a mathematical model for the spread that allows for differences in infectivity by symptomatic status. It may also be an important parameter for a model that estimates the probability of ongoing transmission, given that no symptomatic cases have been found for some period of time.

Effects of the COVID-19 pandemic on vaccine uptake in Viet Nam

Funder
Vaccine Impact Modelling Consortium

Principal Investigator
Marc Choisy
Phung Khanh Lam
Du Hong Duc

Partner PI
Pham Quang Thai (NIHE)

Locations of Activity
OUCRU Ho Chi Minh City & NIHE (Ha Noi)

Status
ongoing until November 2021

Aims:
Public health crises have collateral effects. For example, the 2014 Ebola epidemic in Western Africa severely disrupted vaccine uptakes against measles and this caused major measles outbreaks in the years that followed the Ebola crisis. Following the same rationale, we aim to assess the gaps in vaccination against childhood diseases that were caused by the COVID-19 pandemic in Viet Nam in 2020 and 2021. Gaps in vaccination could be caused by imposed lockdowns during outbreaks, but also by the change in people's behaviour between outbreaks, when people tend to avoid gathering in health centres because of the fear of getting infected.

Importance:
Vaccine-preventable diseases are both potentially extremely dangerous and, in principle, very easy to prevent as long as the vaccine coverage is high enough. By detecting the formation of "pockets of susceptibility" consecutively to the COVID-19 crisis, health authorities will be able to deploy catch-up vaccination campaigns in order to mitigate the risk of outbreaks in the most vulnerable populations.

Objectives:
- Assess the number of missed vaccinations per disease, month and province in Viet Nam;
- Assess the delays in vaccination per disease, month and province in Viet Nam;
- Convert the estimated missed and delayed vaccinations into risks of outbreak per disease, month and province in Viet Nam;
- Investigate whether there are any differences between public and private clinics.

Methods:
Analysis of the data from the national electronic vaccination registry. This system was set up in 2017 and records every single vaccine shot given to any child born after January 2017. Each record contains the vaccine given, the child ID, the day of injection, the location, as well as the type of health centre where the shot is given (private clinic versus public vaccine centre).

Optimising the timing of the second dose of vaccine shot

Funder
Wellcome Trust (OUCRU core funding)

Principal Investigator
Marc Choisy

Location of Activity
Ho Chi Minh City, Viet Nam

Timeline
July 2021 - ongoing

Aims:
The number one goal of COVID-19 vaccines is to reduce as much as possible the risk of severe forms of COVID-19, and this objective is fulfilled by all the vaccines currently used. However, we also know that vaccines do not 100% prevent infections, and, in case of infection, they do not 100% prevent transmission either. There is more and more data that is published on the detailed within-host viral and immunological dynamics following infection or vaccination. This allows us to estimate, almost day by day, the degrees of infectiousness after infection and protection after vaccination and recovery. The aim is to develop a mathematical model based on these very detailed data, and that would account for both the within-host and between-host dynamics of the virus. This model will then be used in order to look for the optimal timing of the second dose of a vaccine. From an immunological point of view, the later the second dose is administrated, the higher its efficiency. However, from an epidemiological point of view, the later the second dose is given, the more time is given to the virus to spread in the population. We will use the model to find the optimal timing that trades off these within- and between-host processes.

Importance:
Vaccination is the only way to return to normal life. The better the vaccination campaign is tuned, the sooner the return to normal life will be, and the more lives can be saved. Furthermore, there are several vaccines that are now in use, and the use of one type over another one depends essentially on the availability of each vaccine. It becomes important too to understand what are the effects of mixed vaccinations that include a first dose of one type and a second dose of another type. Finally, it has also been proposed that giving half a dose to twice as many people could be an efficient strategy at the epidemiological level.

Objectives:
- Is it better to vaccinate twice as many people with one dose or twice as fewer people with two doses. The answer likely depends on the types of vaccine and the exact epidemiological situation.
- Same questions with half a dose.
- What is the optimal timing of the second dose? The answer likely depends on the types of vaccine and the exact epidemiological situation.

Evaluating mortality data to capture the dynamics of COVID-19 in Java, Indonesia

Principal Investigator
Bimandra A. Djaafara

Collaborator
Jakarta Health Office

Location of activity
Jakarta, Indonesia

Background:
As in many countries, quantifying COVID-19 spread in Indonesia remains challenging due to testing limitations. In Java, non-pharmaceutical interventions (NPIs) were implemented throughout 2020. However, as a vaccination campaign launches, cases and deaths are rising across the island.

We used modelling to explore the extent to which data on burials in Jakarta using strict COVID-19 protocols (C19P) provide additional insight into the transmissibility of the disease, epidemic trajectory, and the impact of NPIs. We assess how the implementation of NPIs in early 2021 will shape the epidemic during the period of likely vaccine rollout.

Objectives:
1. To explore the extent to which data on burials in Jakarta using strict COVID-19 protocols (C19P) provide additional insight into the transmissibility of the disease, epidemic trajectory, and the impact of NPIs.
2. To assess how the implementation of NPIs in early 2021 will shape the epidemic during the period of likely vaccine rollout.

Importance:
COVID-19 protocols burial data in Jakarta suggest a death toll approximately 3.3 times higher than reported. Transmission estimates using these data suggest earlier, larger, and more sustained impact of NPIs. Measures to reduce sub-national spread, particularly during Ramadan, substantially mitigated spread to more vulnerable rural areas. Given the current trajectory, daily cases and deaths are likely to increase in most regions as the vaccine is rolled out. Transmission may peak in early 2021 in Jakarta if current levels of control are maintained. However, relaxation of control measures is likely to lead to a subsequent resurgence in the absence of an effective vaccination campaign. Syndromic measures of mortality provide a complete picture of COVID-19 severity upon which to base decision-making. The high potential impact of the vaccine in Java is attributable to reductions in transmission to date and is dependent on these being maintained. Increases in control in the relatively short-term will likely yield large, synergistic increases in vaccine impact.

Outputs to date:
Djaafara B, Whittaker C, Watson O et al. Using syndromic measures of mortality to capture the dynamics of COVID-19 in Java, Indonesia, in the context of vaccination rollout. BMC Medicine [Internet] 2021;19(1). Available from: https://doi.org/10.1186/s12916-021-02016-2

Mortality among healthcare workers in Indonesia during 18 months of COVID-19

Principal Investigator
Lenny Ekawati

Collaborators
LaporCOVID-19, Indonesian Doctor Association, National Institute of Health Research and Development, Indonesia National Nurses Association, Indonesian Midwives Association, Association of Indonesian Medical Laboratory Technologist

Location of activity
Jakarta, Indonesia

Background:
The pandemic resulting from nearly 430 million confirmed SC2 infections (COVID-19) has caused nearly 6 million deaths globally. Healthcare workers (HCWs) serving these patients are at high risk of becoming infected.
For health and care workers (HCWs) around the world the pandemic caused a heightened risk of occupational exposure to a new fast spreading disease. Concerns over the broader impact of the pandemic on HCWs and their crucial role at the forefront of the response were recognised.

HCWs serving these patients are at high risk of becoming infected. The pandemic resulted in many deaths among HCWs and their households. The healthcare sector is one of the most severely hit by the pandemic. HCWs have been documented to have a higher risk of infection with SARS-CoV-2 than the general population.

Objectives:
The study aims to examine HCW mortality occurring during between March 2020 and July 2021 (the first 18 months) of the COVID-19 health crisis. We compared the death rate of HCWs and general population.

Methods:
The research team downloaded HCW standardised mortality data from a web-based digital funeral database dedicated to HCW. Those volunteers searched daily obituaries on online news, social media (Twitter, Facebook, Instagram) and queried the following professional medical and health associations: Association of Indonesian Medical Doctors (Ikatan Dokter Indonesia; IDI); National Association of Nurses (Persatuan Perawat Nasional Indonesia, PPNI); Association of Midwives (Ikatan Bidan Indonesia, IBI); and Association of Medical Laboratory Technologists (Persatuan Ahli Teknologi Laboratorium Kesehatan Indonesia, PATELKI). Volunteers curated essential variables from those sources and solicited testimonials from family and colleagues. Data were entered into a standardised Excel database. Mortality frequency was cross-tabulated by employment type, administrative location (province, district/city), and social demographics to present heterogeneity over time. Relative Ratio of death rate of HCWs and general population and its 95% confidence were calculated.

The COVID-19 pandemic affected severely a national healthcare resilience system. Urgent need for better health systems and preparedness is required to protect life and provide essential services to healthcare front liners during any emerging pandemic threats.

Outputs to date:
Manuscript has been been prepared.

Optimising use of routine surveillance data to investigate vaccine effectiveness on COVID-19 severity and mortality in adults diagnosed with COVID-19 in Jakarta, Indonesia: A retrospective cohort study

Principal Investigator
Henry Surendra

Collaborator
Jakarta Health Office

Location of activity
Jakarta, Indonesia

Background:
Real-world effectiveness studies are important for monitoring performance of COVID-19 vaccination programmes and informing COVID-19 prevention and control policies. To our knowleldge, there was no study assessing the real world vaccine effectivenes against COVID-19 severity and mortality in Jakarta, Indonesia that has been done to date.

Objectives:
This study aims to assess the real world COVID-19 vaccine affectiveness agains severety and mortality in adults diagnosed with COVID-19 during the first 7 months of vaccine rollout (15 January 2021 to 7 August 2021).

Methods:
This retrospective cohort included all individuals aged ≥18 years old with PCR-confirmed COVID-19 in Jakarta, Indonesia. We extracted demographic, and clinical data available from the Jakarta Health Office record and linked the individuals with vaccination status recorded in the Jakarta Health Office Vaccine Registration. We calculated the adjusted odds ratio and vaccine effectiveness against severity and mortality among the PCR-confirmed adults population. The vaccine effectiveness will be reported as (1-odds ratio) and their 95% confidence interval. The vaccine affectivenes will be adjusted by age, sex, days since fully vaccinated to test, and known comorbidity.

Importance:
This sudy will be the first study utilising routine surveillance data to povide information of the real world vaccine effectivenest against COVID-19 severity and mortality in Jakarta, Indonesia.

Photo: Unsplash | Fadil Fauzi

Outputs to date:
Data have been collected and analysis is ongoing.

SOCIAL SCIENCE STUDIES

Photo: Unsplash | Hoach Le Dinh

COVID-19 Social Science and Public Engagement Action Research in Viet Nam, Indonesia and Nepal (SPEAR)

Funder
OUCRU
(Wellcome funding)

Principal Investigators:
Jennifer Van Nuil,
Sonia Lewycka,
Mary Chambers,
Abhilasha Karkey,
Raph Hamers

Phase 1: Exploring the experiences and impacts of COVID-19 for healthcare workers and vulnerable communities

Aims:
This project draws on anthropological and participatory engagement methods to explore the wider socio-cultural context of COVID-19 and its impact on health-related workers and vulnerable communities in Viet Nam, Nepal, and Indonesia.

Primary Objectives:

- Identify and describe the experiences and perceptions of healthcare workers and other healthcare staff during/after the COVID-19 pandemic in Nepal, Indonesia, and Viet Nam.
- Explore the impact of the COVID-19 outbreak on vulnerable communities in Nepal, Indonesia, and Viet Nam.
- Identify misinformation circulating within these populations and co-design targeted evidenced-based public engagement.

Phase 1 progress:
To date, in January 2022, we have collected almost 4,000 surveys, 222 in-depth interviews, and 59 digital diaries across the sites, including participants from both healthcare workers and community members groups. The data collection phase is now completed and analysis is in progress.

Photo:
Sunita Baniya,
Digital Diary participant,
Paramedic Counsellor,
Kathmandu, Nepal.

SPEAR (Cont.)

Digital diaries:
http://www.oucru.org/digital-diary/

Media monitoring:
http://www.oucru.org/media-monitoring/

Phase 2: Exploring barriers to access and uptake of SARS-CoV-2 vaccines in Viet Nam, Indonesia and Nepal to inform national vaccine strategies

Aims:
To inform national policy and support initiatives to ensure equitable access to SARS-CoV-2 vaccines and effective public engagement through exploration of public perceptions and understanding.

Primary Objectives:
To inform national and global policymakers concerning access and acceptance of COVID-19 vaccines.

It is intended that the project will provide evidence to:
- Enable us to create targeted evidence-based public health information to counter misinformation;
- Enable partner and government organisations to strengthen their support for health workers and improve the access of vulnerable communities to public health measures;
- Contribute to global discussions and guidelines (e.g. WHO facilitated forums) about ethics, public engagement and COVID-19, and support for healthcare workers.

Phase 2 progress:
We expanded SPEAR to include additional data collection (surveys and in-depth interviews) focused on vaccine acceptance and access within the study sites. The second phase of SPEAR started in November 2021 and data collection should be completed by March 2022.

Project progress:
The SPEAR teams are embedded in multiple sites within Viet Nam, Nepal, and Indonesia, with both social science data collection and engagement activities taking place within each site. These methods include surveys, focus groups discussions, interviews, 'digital diaries' (filming of personal stories), and online forums. In addition, we have a Media Monitoring component to track the misinformation that is circulating online about Covid-19.

Outputs to date:
Jennifer Ilo Van Nuil, Dewi Friska, Aria Karika, et al. COVID-19 Social Science and Public Engagement Action Research in Vietnam, Indonesia and Nepal (SPEAR): A mixed methods study exploring the experiences and impacts of COVID-19 for healthcare workers and vulnerable communities. Wellcome Open Research, 2021(6):352. Available from: https://wellcomeopenresearch.org/articles/6-352
Chambers M, Deokota D, Dien R, Nguyen Hoang Yen. Co-production and COVID-19: Digital Diaries as a Platform for Participating in COVID-19 Research. 2021 [Internet]. In: Williams O, Tembo D, Ocloo J, Kaur M, Hickey G, ed. by. COVID-19 and Co-production in Health and Social Care Research, Policy, and Practice: Volume 2: Co-production Methods and Working Together at a Distance. Bristol: Bristol University Press; 2021. p.105-112. Available from: http://www.jstor.org/stable/j.ctv1p6hqk9.16

Principal Investigators:
Jennifer Ilo Van Nuil, Sonia Lewycka, Mary Chambers

Location of activity
Ho Chi Minh City, Viet Nam

SPEAR in Viet Nam

The SPEAR project in Viet Nam is being led by Jennifer Ilo Van Nuil and Sonia Lewycka for the social science components and Mary Chambers for the public engagement component, with project management support from Jaom Fisher. There are four main sites in Viet Nam, including the Hospital for Tropical Diseases (HTD) in Ho Chi Minh City, National Hospital for Tropical Diseases in Ha Noi, and areas with ongoing research collaborations in Nam Dinh and Dak Lak.

OUCRU's social science data collection team working in HCMC includes Nguyen Thi Hong Yen, Nguyen Thi Kim Ngoc, Nguyen Le Thao My, Tran Minh Hien, Nguyen Hoang Yen, Tran Kim Van Anh, and Hung Vu Bao, Nhung Doan Phuong, and Pham Ngoc Thanh together with collaborators from the HTD hospital including Dr. Nguyen Thanh Phong, Dr. Nguyen Thanh Truong, and Head Nurse Bui Thi Hong Ngoc.

The team in Nam Dinh and Ha Noi includes Yen Nguyen Thi Hong, Nam Vinh Nguyen, Tran Phuong Thao, Nguyen Thi Kim Tuyen, and Tran Thi Hang, Dr. Dung Vu Tien Viet and Ha Le Thanh, along with collaborators from National Hospital for Tropical Diseases. The Dak Lak team includes Nguyen Thanh Ha, and Nguyen Le Thao My. Nguyen Hoang Yen coordinates the digital diary engagement data collection within Viet Nam.

Principal Investigator
Abhilasha Karkey

Location of activity
Kathmandu, Nepal

SPEAR in Nepal

The SPEAR project in Nepal under the supervision of Abhilasha Karkey is being coordinated by Samita Rijal (social sciences research) and Summita Udas Shakya (public and community engagement). Dinesh Deokota is leading the Digital Diary component for the whole project, and in Nepal, and leading recruitment for the community-based research.

The social science research team includes Samita Rijal, Summita Shakya, Dr. Amit Gautum, Aakriti Pandey, Pratibha Thapa, and Manish Duwal. The engagement team includes Niharika Kharel. The psychology team for the study includes Dr. Rabi Shakya, Dr. Pawan Sharma, and Anup Rajbhandari, all senior practising psychiatrists at the Patan Hospital.

The study is being conducted in 4 regions: Terai region (Kapilbvastu/Biratnagar/Dharan), Urban region (Kathmandu/Bhaktapur/Patan), Hills region (Sindhulpalchowk), Mountainous region (lower Mustang).

Principal Investigator
Raph Hamers

Location of activity
Jakarta, Indonesia

SPEAR in Indonesia

The SPEAR project in Indonesia is being led by Dr. Dewi Friska, from the Faculty of Medicine, Universitas Indonesia and Dr. Raph Hamers (EOCRU). The project is being coordinated by Ragil Dien and Mutia Rahardjani from EOCRU, and advised by Dr. Aria Kekalih, from the Department of Community Medicine, Universitas Indonesia.

The EOCRU social science research and public engagement team include: Ragil Dien, Livia Nathania Kurniawan, Ida Ayu Sutrisni, Ralalicia Limato, and Diana Timoria, and Fahmi Ramadhan. Collaborations are with local hospitals and Puskesmas in Jakarta and Bandung and The Sumba Foundation in Sumba. The study is being conducted in three provinces: DKI Jakarta, West Java, and Nusa Tenggara Timur (NTT).

PUBLIC & COMMUNITY ENGAGEMENT

Photo: Pexels | Pixabay

Public & Community Engagement

Photo: Digital diary participants from West Sumba, Eastern Indonesia

Public and community engagement response to Covid-19

Funder
OUCRU
(Wellcome funding)

Principal Investigator
Mary Chambers

Location of activity
Viet Nam, Indonesia and Nepal

Objectives
Building trust in a time of public health crisis through public and community engagement, including:

- Building dialogue between public and experts;
- Listening to communities;
- Empowering communities through knowledge transfer;

Photo:
Science debates to engaging Vietnamese young people and scientists to use debate as a tool for discussing health science-related topics in Viet Nam.

Public and community engagement response to Covid-19
Outputs to date

Photo:
'Hear the Expert' - EOCRU and The Conversation Indonesia. Live stream discussion between scientists and the public. April 21, 2020.

Dialogue | 2020

- 'Online science debates' - engaging Vietnamese young people and scientists to use debate as a tool for discussing health science-related topics. Viet Nam.
- 'Hear the Expert' – EOCRU and The Conversation Indonesia. Live stream discussion between scientists and the public. April 21, 2020.
- 'How to overcome stress during the pandemic season for Healthcare Workers – Online Workshop' – OUCRU and Healthcare Improvement Research (CHIR) and Wake up Schools. Live stream workshop discussion stress factors of Healthcare Workers and introducing the practice of mindfulness to reduce their stress. April 5, 2020. Viet Nam.
- 'Ask the Scientists' – OUCRU Schools Engagement team. Online 'chats' between schoolchildren and scientists. Viet Nam.
- 'Covid-19: Truths and Myths' – OUCRU and British Embassy Viet Nam, live stream Q&A between experts and the public. June 9, 2020: Prof. Jeremy Day and Nguyen Thanh Ha. Viet Nam.
- 'Working together to beat Covid-19: engaging and involving patients and public' – Cochrane Training Webinar Series. June 11, 2020: Dr. Mary Chambers.
- Virtual Tea Talk Series 'COVID19: Truth and Myths', Interactive session with students June 20, 2020 and with communities July 7, 2020 - Nepal.
- COVID Experience sharing sessions with frontline workers of OUCRU-NP (first session on July 5, second session July 17, third session July 28, fourth session July 30) - Nepal.
- Workshops for young people exploring the avenues through which news is disseminated and developing skills for assessing the strength of the news being shared - Viet Nam:
  - "Science against fake news" Ho Chi Minh City, June 26, 2020- equipping junior students with skills to recognise fake news.
  - "Combating Covid-19 related fake news", Ho Chi Minh City, July 25, 2020 - improving health literacy for young people (facilitated by Media and Communication Officer. University of Social Science and Humanities)

Photo:
'Covid-19 Vaccine: A discussion' - a livestream session between experts and the public in collaboration with the British Embassy Viet Nam, WHO, and Unicef. April 29, 2021

Dialogue | 2021

- Webinar: 'The Lived experience of Frontline Health Workers', CONNECT/The Global Health Network Research in Focus Lecture, January 26, 2021: Sarita Pyatha (Nepal).
- Digital Diaries Video Screening at OUCRU (7th March 2021) and with Medical Doctors at Teaching hospital (March 30, 2021) Nepal.
- Tea Talks in the community about COVID-19 Vaccination Hesitancy. ('Working together to beat Covid-19: engaging and involving community and experts'). First session on April 5, 2021, second session April 15, 2021 - Nepal.
- Tea Talk Session in the community about Post Covid-19 Scenario and Vaccination along with ward members and Tole health workers. Nepal
- 'Covid-19 Vaccine: A discussion' - OUCRU, British Embassy Viet Nam, WHO, and Unicef, livestream Q &A between experts and the public. With Dr. Kidong Park, Rana Flowers, Marcus Winsley, Prof. Jeremy Day and Dr. Tu Van. April 29, 2021. Viet Nam.
- Virtual Tea Talks Series with OUCRU staff, in collaboration with the Patan Hospital Psychiatric Department: A series of programs to address mental health issues in the workplace: Tea talks (informal program) aimed at helping to reduce stress and sharing experiences, walk-in counselling sessions (formal support). May - June 2021; Nepal.
- Podcast Healthcare Wecare, in collaboration with PE Youth Science Ambassadors: A series of podcasts have developed featuring conversations between youth and health experts to support mental health of Vietnamese young people in the time of social isolation and for the new normal
- Video screening on "Understanding COVID-19 testing", 30 November 2021. Targeted audiences: Lalitpur community, Nepal

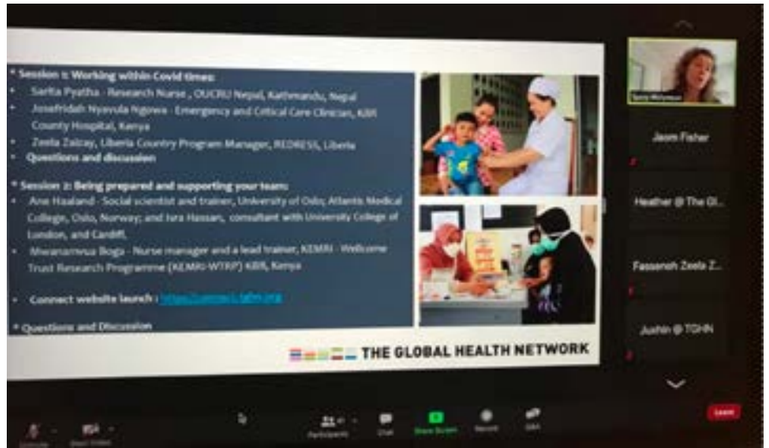


Photo:
Webinar: 'The Lived experience of Frontline Health Workers', CONNECT/The Global Health Network Research in Focus Lecture, January 26, 2021: Sarita Pyatha, Nepal.

Public and community engagement response to Covid-19
Outputs to date (cont.)

Photo:
Digital Diaries (personal stories of Covid-19 experiences): Instagram @StoriesFromTheIslands

Photo:
Podcast program. (7 episodes – November 2020 – current): A monthly podcast on Spotify aimed at accurate public health communication. Involving doctors, researchers, EOCRU experts in medical, public health, and related fields as well as external speakers.

Listening to communities | 2020
- Schools Photo Competition – Photo and caption about the learning experience in Covid-19 lockdown in Viet Nam.
- Advisory group meeting: HTD healthcare workers. June 10, 2020; Viet Nam.

Listening to communities | 2021
- 'Voice of science' - A digital youth engagement platform to put science at the heart of Vietnamese young people as well as to collect their perspectives and recommendations for good health research activities. Viet Nam.
- Digital Diaries (personal stories from health care workers and community members of their Covid-19 experiences): The process included online introductions, trainings, technical and editing support to utilise photos, scripts, and videos to share stories and reflections of some of the challenges and positive experiences during this time. Viet Nam, Nepal and Indonesia

Outputs from three countries:

http://www.oucru.org/digital-diary/
https://www.instagram.com/storiesfromtheislands/

Viet Nam:
1. Organised 04 online introductions to 04 community members from HCMC in the last 4 months
2. Developed 02 new digital stories with participants using video participatory method
3. Plan to organise 01 online screening on the 8th of January, 2022 for online community through OUCRU Facebook page.

Indonesia:
1. Participated by 13 health care workers and 23 community representatives from 3 sites (Jakarta, Bandung and Sumba)
2. Collected 151 stories with 7 themes
3. Organised 1 direct community screening in Sumba and online exhibition through Instagram platform (Stories from the Islands)
- Health Research Advisory Board: Meeting with community members about "Covid-19 research at OUCRU and community's concerns". October 20, 2021: Associate Professor Le Van Tan and Dr. Lam Minh Yen and 11 advisory community members. Viet Nam
- Hospital Radio: Broadcasting the radio in HTD with a series about "spreading the love and positivity in life" to thank the health workers and help to reduce stress amongst the health workers and patients during the lockdown. Viet Nam
- Awareness Video on "Maintaining the Physical Distance in office premises" on social media by OUCRU-NP. Nepal
- Awareness Video on "Understanding Covid-19 Testing": A video on the how results are analysed for Covid-19 test and CT value. Nepal.

Listening to communities | 2022
- Digital Diaries, Viet Nam:

1. Organised 01 online screening on 8th January, 2022 for online community through OUCRU Facebook page.

Knowledge transfer | 2020
- Articles for The Conversation newspaper - EOCRU – Indonesia.
- Poster 'How to protect yourself from Covid-19' - OUCRU NP - Nepal.
- WHO 'Myth Busters' for social media – in Vietnamese and Nepali OUCRU & OUCRU NP.
- Animations for social media: 'Coping with stress during Covid-19' In Bahasa Indonesia, Vietnamese, Nepali and English.

Public and community engagement response to Covid-19
Outputs to date (cont.)

- Khan Quang Do (Youth Magazine) Articles, Viet Nam, on the following topics:
  - Emotion Trap in Consuming News in the Pandemic September 8, 2020;
  - Nutrition Misunderstanding in the Pandemic Context, September 15, 2020;
  - Mathematical Modelling. What is it? And How can it help alleviate the Pandemic? September 22, 2020;
  - Four unknowns about Covid-19, September 29, 2020;
  - What is the smallest living organism in the world? October 6, 2020;
  - Wildlife Consumption, October 13, 2020.

Knowledge transfer | 2021

- Podcast program. (7 episodes – November 2020 – current): A monthly podcast on Spotify aimed at accurate public health communication. Involving doctors, researchers, EOCRU experts in medical, public health, and related fields as well as external speakers (Dr. Siti Nadia, M. Epid (Spokesperson for Covid-19 Vaccination from Indonesia's Ministry of Health) and Prof. Zubairi Djoerban, Sp.PD-KHOM (Head of the Covid-19 Task Force of The Board of the Indonesian Medical Association/Pengurus Besar Ikatan Dokter Indonesia).). Episode 1 - Indonesia.
- Radio program (Sumba): Aiming to disseminate significant and accurate information and engage interest in health issues amongst the public in rural areas in Sumba using easy-to-understand language in the local dialect, the program is aired on bi-weekly basis and has released four episodes. Indonesia.
- Covid-19 Related Video Interview Series (EOCRU Social Media), Indonesia: To engage and educate the public through social media about the Covid-19 pandemic – a series of 10 videos of interviews with 6 internal researchers and collaborators on the following topics:
  - Future of Covid-19 in Indonesia through mathematical modelling;
  - Covid-19 herd immunity in Indonesia: What, when, and how;
  - How effective are large-scale social restrictions and mudik (returning to hometowns) prohibitions to suppress the number of cases and the transmission rate of Covid-19 in Indonesia?;
  - The impact of mass media publication about Covid-19 toward public decision and action;
  - How we can be more careful in consuming Covid-19 related news.
  - How we can be more careful in consuming Covid-19 related news
  - Pregnancy and Breastfeeding in Pandemic situation
  - Vaccine Experiences in Youth eyes (comparing the experiences in Indonesia and overseas)
  - How does the COVID-19 works in your body?
  - COVID-19 vaccine for children, is it safe?
- 'Digital science hub' : A joint project between OUCRU and Bayer Viet Nam to develop the science literacy of Vietnamese children through online engagement and science learning activities. Viet Nam.
- World Immunisation Week: 'I'm vaccinated' social media campaign Viet Nam.
- Short film for social media: 'Q & A on Covid-19 Vaccine' – –]with Hospital for Tropical Diseases HCMC with Dr. Truong Ngoc Trung. Viet Nam.
- Providing factual information about COVID-19 and answering FAQs of communities through VIBER Group. Nepal.
- Posters: Post-vaccination advice, precaution of mental health during isolation, Difference between Covid-19 and flu symptoms, Precaution during pregnancy while Covid-19 positive, Omicron virus, Physical Distance at Vaccination Centre, Precautions during Festive season – all displayed in the hospital and within the community. Nepal
- Dissemination of Covid-19 information booklet during community response with ward members, Lalitpur, Nepal
- OUCRU Viet Namsocial media posts (from June to December 2021) responding to public concerns and interests related to Covid-19 and vaccination:
- Responding with infographic about the risks of side effects versus the benefits of the Covid-19 vaccine.
- Responding with Q&A posters addressing specific questions or misinformation about Covid-19 vaccines, such as efficacy of vaccine on variants, efficacy and effectiveness of different vaccines, vaccination for children, etc.
- Responding with informative animations on topics such as taking care of Covid-19 patients at home and addressing all common questions about Covid-19 vaccination. The development and production of these animations were led by an OUCRU researcher.
- Supporting national vaccination rollout: I'm vaccinated campaign posters of healthcare workers and community members sharing their photos and messages of getting their Covid-19 vaccines.
- Provided positivity and expressed empathy to support people's wellbeing during the Covid-19 pandemic. The posts covered topics on taking care of mental health in lockdown and for talking to children about Covid-19.
- OUCRU Nepal social media awareness (posters) from August to December 2021) responding to public concerns and interests related to Covid-19 and vaccination including:
  - Post-vaccination advice,
  - Precaution of mental health during isolation,
  - Difference between Covid-19 and flu symptoms,
  - Precaution during pregnancy while covid-19 positive,
  - Omicron virus,
  - Physical Distance on Vaccination Centre,
  - Precaution towards COVID 19 during Festive season
- Social Media Awareness: "Video Display on maintaining physical distance within office premises". Nepal

Combating Covid-19-related disinformation and fake news

Photo:
Livestream session:
Covid-19 Myths & Truth.
British Embassy in Viet Nam.
June 9, 2020.

Funder
University of Oxford

Principal Investigator
Mary Chambers

Collaborators
Nguyen Thanh Ha,
Tran Minh Hien,
Summita Udas,
Ragil Dien,
Livia Nathania Kurniawan,
Fahmi Ramadhan,
Neharika Kharel,
Katrina Lawson

Location of activity
Ho Chi Minh City, Viet Nam
Jakarta, Indonesia

Importance:
Public health and wellbeing is put at risk by disinformation and fake news, and never more seriously than in times of public health emergencies such as the current Covid-19 pandemic. While traditional news from state and commercially owned broadcasting channels and newspapers remains a dominant source of scientific information, social media platforms have become important sources of health information and sites for public discourse. However, the health and science presented on these platforms are often problematic. We propose that the antidote to this risk is a targeted and positive public engagement response delivering evidence-based news in partnership with policymakers and key public health stakeholders is a way to counter the dissemination of misinformation..

Methods:
By tracking current disinformation and fake news stories about Covid-19 and the Covid-19 vaccines on social media in Viet Nam, Nepal and Indonesia – the host countries for Oxford University Clinical Research Units, we will identify misinformation that is circulating in these communities. Our findings will be fed back to national policymakers and public health stakeholders to enable them to tailor their Covid-19 related public health messaging. We will bring working groups together to develop evidence-based, locally appropriate public engagement media and open discussion forums to positively counter the trending misinformation, thereby increasing understanding, safe behaviour and public/expert trust.

Ouputs to date:
- Workshops:
  - Media literacy workshops for young people – developing tools to recognise fake news on social media and online media (2020), Viet Nam;
  - Science Against Fake News Workshop for high school students to equip with skills of analysis and evaluation of information on the Internet (2020), Viet Nam;
- Posters: "Myth buster" information about Covid19 (2020), Nepal;
- Leaflets: Covid-19 information (2020), Nepal.
- Online discussions:
  - 'The health of pregnant and breastfeeding mothers during the pandemic'. Instagram Livestream discussion (6 February 2022), Indonesia.
- Online engagement:
  - Social media: Facebook and Instagram animations and health education materials to counter identified misinformation content within the media about Covid19 and Covid19 vaccines. e.g. Myth busters (2020), Viet Nam, #Iamvaccinated campaign (2021), Viet Nam;
  - Viber: Q & A of specific health information to community disseminated via community health worker Viber networks (2021), Nepal;
  - Podcasts: Monthly podcast with medical and scientific experts providing accurate health information (November 2020 - current), Indonesia;
- Youtube videos:
  - Coping with stress during the COVID-19 pandemic' (April 21, 2020), Indonesia. Available at: youtu.be/9FodSAYpI4A
  - How to quarantine F0 at home' (August 10, 2021), Viet Nam. Available at: youtu.be/4dP770XaCl4
  - Sharing personal experiences of Covid-19 pandemic - a medical worker (2021), Viet Nam. Available at: youtu.be/oIykoCkC_bk
  - Answering questions about the Covid-19 Vaccine with Dr. Truong Ngoc Trung (HTD) (May 2021), Viet Nam. Available at: youtu.be/t3xGkqTHSuw

Photo:
#IAmVaccinated
campaign (2021),
Viet Nam

POLICY ENGAGEMENT

Photo: Unsplash | Florian Wehde

Policy Engagement

Covid-19 and the Gendered Research Gap

Funder
OUCRU
(Wellcome funding)

Team members
Evelyne Kestelyn,
Katrina Lawson,
Ngo Thi Hoa,
Louise Thwaites

Locations of Activity
Viet Nam, Australia

Among the many extraordinary responses to the COVID-19 pandemic globally, has been the response in the research community, with thousands of new collaborations, projects and publications being rapidly developed and implemented. These have been supported by funding schemes, many of which have been modified or expanded. While these initiatives have led to breakthroughs in COVID-19 prevention, treatment and control, the gendered impacts on the health and medical research workforce cannot be ignored.

Early in the pandemic, transition to home working, and innovations such as online meetings were hailed as breakthroughs in research culture, addressing many of the barriers female scientists had experienced to progressing careers. However, as women still hold the majority of primary caring roles globally, the shift to working from home, coupled with school closures, left many women juggling caring and career responsibilities[12]. Studies conducted since early in the pandemic have demonstrated that women are underrepresented in journal submissions and publications[13]. How this may impact women's long-term careers is unknown, although journal publications remain key academic outputs and prerequisites for future funding.

The OUCRU Women in Science Group is collaborating with the George Institute in Australia, and NAFOSTED in Viet Nam to explore these issues more deeply. Initial findings from looking at publicly available data in Australia, the UK and Viet Nam have shown that inequitable distribution of research funding impacts the feasibility and sustainability of women in health and medical research careers. Work needs to be done to assess and address factors contributing to this, to ensure that the gendered gaps don't continue to widen as the pandemic progresses.

Publication
[Internet]. Covid and Society. 2021; Available from: https://covidandsociety.com/how-covid-19-widened-gender-research-gap-women-juggling-caring-career-duties/

Engaging with policymakers in the COVID-19 pandemic through the creation of an Outbreak Advisory Board

Funder
OUCRU
(Wellcome funding)

Project Lead
Katrina Lawson

Team members
Nghiem Nguyen Minh Trang, Nguyen Kim Ngan, Ngo Phan Bao Tran

Location of Activity
Viet Nam

In order to ensure that OUCRU's COVID-19 research is locally-driven and is best able to achieve local, regional and global impact, we have established an OUCRU Outbreak Advisory Board (OAB).

The goals of the OAB are to:

- Provide a forum to discuss, share and understand activities and priorities in the context of infectious disease outbreaks.
- Ensure that OUCRU's outbreak response projects are useful for key stakeholders' policy needs.
- Strengthen the networks between researchers and policymakers focused on outbreak response at national and international levels.

Board members come from multiple levels in the Vietnamese COVID-19 response: national and regional, domestic and international – to ensure broad perspectives are included. The OAB was established in response to COVID-19 but will exist in perpetuity and in future will be able to advise on work relating to general epidemic preparedness and acute outbreaks.

During the pandemic, the board convenes quarterly, using Zoom. Meetings are short, structured and planned in advance. To date, two meetings have been conducted, one in October 2020 and another in March 2021. The third meeting, which should have been organised in June, was cancelled due to the complicated situation of the outbreak happening nationwide. This meeting will be rescheduled as soon as practical. The first meeting focused on understanding each member's concerns and their activities related to COVID-19 while the second meeting was specific to vaccination strategies, post-vaccination immunology and testing strategies. Establishing the OAB had its challenges, but once set up, it is easy to maintain, and serves as a forum for researchers and policymakers to connect regularly across a wide range of interest areas.

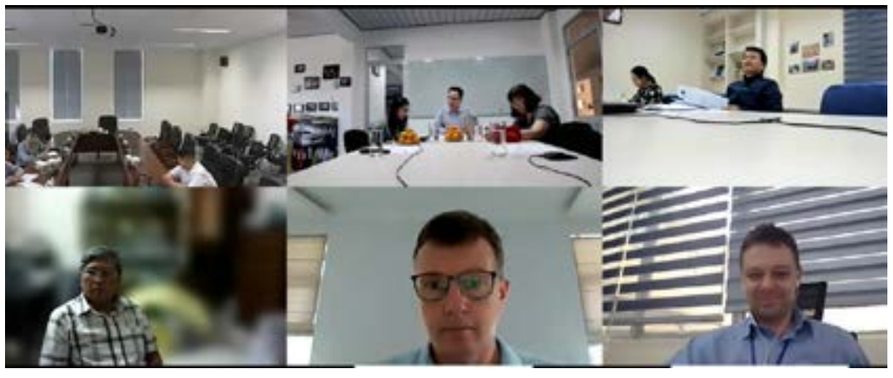


Photo:
An OAB meeting taking place via Zoom

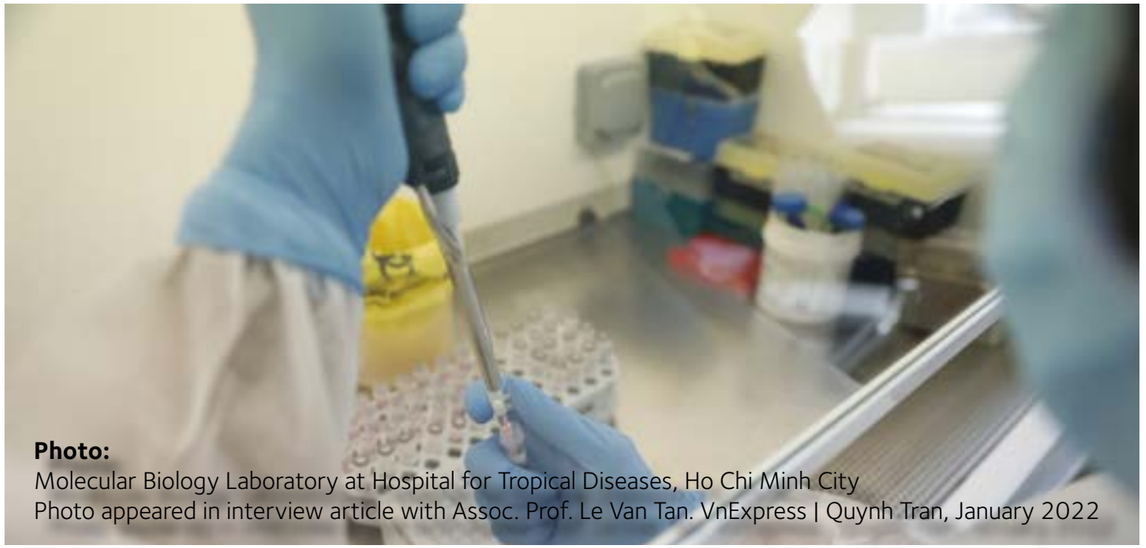


Photo:
Molecular Biology Laboratory at Hospital for Tropical Diseases, Ho Chi Minh City
Photo appeared in interview article with Assoc. Prof. Le Van Tan. VnExpress | Quynh Tran, January 2022

Summary of Covid-19 press outputs

Funder
OUCRU
(Wellcome funding)

Project Lead
Katrina Lawson

Team members
Ngo Huyen Chi, Nguyen Kim Ngan, Ngo Phan Bao Tran

Locations of Activity
Viet Nam, Indonesia and Nepal

The Covid-19 pandemic has elevated OUCRU's position as an expert in infectious diseases. Because of our involvement in various Covid-19 projects and our works in supporting governments to manage Covid-19 outbreaks in Viet Nam, Indonesia, and Nepal, we have received a substantial volume of interview requests and press mentions.

More specifically:

From 1 July 2020 to 24 February 2022, OUCRU has received a total of 80 interview requests, including 25 requests from Vietnamese publications and 55 requests from international news networks.

During this period, our experts have given 66 interviews with prominent news outlets and networks, including the Associated Press, Business Insider, BBC News, The Economist, ChannelNewsAsia, Le Figaro, and Vietnamese publications such as VTV News, VNExpress, Zing News, VTC News, etc.

The issues mentioned can be divided into three large categories:

1. Management of Covid-19 outbreaks in Viet Nam;
2. OUCRU's works in sequencing the SARS-CoV-2 virus;
3. Covid-19 vaccinations and Covid-19 vaccine efficacy;

The full list of articles is available upon request.

OUR PEOPLE

*In order of appearance

Prof. Guy Thwaites	Director
Assoc. Prof. H Rogier van Doorn	Director of OUCRU Ha Noi
Prof. J Kevin Baird	Director of EOCRU
Prof. Buddha Basnyat	Director of OUCRU Nepal

In collaboration with:

Prof. Nicholas White	Professor, Mahidol University, Thailand
Dr. Nguyen Van Vinh Chau	Deputy Director, Ho Chi Minh City Department of Health, Viet Nam
Dr. Nguyen Thanh Truong	Deputy Director, Hospital For Tropical Diseases, Ho Chi Minh City, Viet Nam
Dr. Pham Ngoc Thach	Director, National Hospital for Tropical Disease, Ha Noi, Viet Nam
Dr. Nguyen Thanh Hung	Director, Children's Hospital 1, Ho Chi Minh City, Viet Nam
Dr. Nguyen Tran Nam	Head of Infectious Diseases Department, City Children's Hospital, Ho Chi Minh City, Viet Nam
Prof. Philip Bejon	Director, Wellcome-KEMRI-Oxford Collaborative Research Programme, Kenya
Dr. Pham Quang Thai	Deputy Head, Epidemiology Department, Viet Nam NIHE
Vera Arntzen	PhD Candidate, Leiden University, the Netherlands
Dr. Marta Fiocco	Professor, Leiden University, the Netherlands
Damien Philippon	PhD Candidate, University of Hong Kong, Hong Kong
Dr. Quentin Richard	Post-doctoral Scientist, MIVEGEC, CNRS-IRD-University of Montpellier, France
Ramsès Djidjou-Demasse	Research Scientist, MIVEGEC, CNRS-IRD-University of Montpellier, France
Christian Selinger	Research Scientist, MIVEGEC, CNRS-IRD-University of Montpellier, France
Samuel Alizon	Director of Research, MIVEGEC, CNRS-IRD-University of Montpellier, France
Dr. Dewi Friska	Lecturer, Department of Community Medicine, Universitas Indonesia
Dr. Aria Kekalih	Lecturer, Department of Community Medicine, Universitas Indonesia
Claus Bogh	Health Program Director, The Sumba Foundation, Indonesia
Dinesh Deokota	Director, Media for Development, Nepal
Dr. Rabi Shakya	Senior Practicing Psychiatrist, Patan Hospital
Dr. Pawan Sharma	Senior Practicing Psychiatrist, Patan Hospital
Anup Rajbhandari	Senior Practicing Psychiatrist, Patan Hospital
Dr. Nguyen Thanh Phong	Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam
Dr. Nguyen Thanh Truong	Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam
Bui Thi Hong Ngoc	Head Nurse, Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam
Dr. Mai Thi Phuoc Loan	Dak Lak CDC
Prof. Dr. Ari Fahrial Syam	Dean, Faculty of Medicine University of Indonesia
Prof. Dr. Badriul Hegar	Director, Indonesia Medical Education and Research Institute
Dr. Erni Juwita Nelwan	Lecturer, Faculty of Medicine University of Indonesia
Dr. Anis Karuniawati	Vice Dean Faculty of Medicine University of Indonesia
Dr. Rina Agustina	Head, Human Nutrition Research Center, Indonesia Medical Education and Research Institute, Faculty of Medicine University of Indonesia
Dr. Vera Irawany	Anaesthesiologist, Fatmawati Hospital
Dr. Robert Sinto	Infectious Disease Physician, Carolus Hospital
Dr. Dwi Utomo Nusantara	Pathology Specialist, Pasar Minggu Hospital
Dr. Ayodhia Pitaloka Pasaribu	Lecturer, Faculty of Medicine, University of Sumatera Utara
Dr. Mutiara	Director of Murni Teguh Hospital
Dr. Beni Satria	Director of Bunda Thamrin Hospital
Prof. Dr. Nasronudin	Lecturer, Faculty of Medicine Universitas Airlangga
Dr. Franciscus Ginting	Infectious Disease Physician, Adam Malik Hospital
Dr. Yanri Wijayanti Subronto	Infectious Disease Physician, Sardjito Hospital
Dr. Uun Sumardi	Infectious Disease Physician, Hasan Sadikin Hospital
Dr. Claus Bogh	Director of the Sumba Foundation
Bonifacius	Physician, Karitas Hospital
Yohanes Niko Santoso P.	Director, Karitas Hosiptal
Yacobus B. Da Costa	Pratama Rada Bolo Hospital
Annisa Dwi Utami	Summit Institute for Development
Yuni Dwi Setiyawati	Summit Institute for Development
Dr. Erlina Burhan	Lecturer, Faculty of Medicine Universitas Indonesia, Persahabatan Hospital

OUCRU

Dr. Sophie Yacoub	Head of Dengue Research Group
Prof. Jeremy Day	Head of CNS and HIV Infections Research Group
Assoc. Prof. Le Van Tan	Head of Emerging Infections Group
Assoc. Prof. C Louise Thwaites	Senior Clinical Research Fellow, Emerging Infections Group
Assoc. Prof. Ronald Geskus	Head of the Biostatistics Group
Dr. Marc Choisy	Head of Mathematical Modelling Group
Dr. Le Thanh Hoang Nhat	Postdoctoral Scientist, Biostatistics Group
Dr. Du Hong Duc	Postdoctoral Scientist, Biostatistics Group
Dr. Phung Khanh Lam	Postdoctoral Scientist, Biostatistics Group
Dr. Nguyen To Anh	Postdoctoral Scientist, Emerging Infections Group
Dr. Thomas Kesteman	Clinical Microbiologist, OUCRU Ha Noi
Dr. Nguyen Thi Tam	Postdoctoral Scientist, OUCRU Ha Noi
Dr. Dung Vu Tien Viet	Postdoctoral Scientist, OUCRU Ha Noi
Trinh Son Tung	Research Assistant, OUCRU Ha Noi
Ong Phuc Thinh	Research Assistant, Mathematical Modelling Group
Tran Thi Bich Lieu	Research Assistant, Mathematical Modelling Group
Duong Thuy Trang	Research Assistant, Mathematical Modelling Group
Nguyen Duc Manh	Research Assistant, Mathematical Modelling Group
Nguyen Thi Minh Nguyet	Research Assistant, Biostatistics Group
Dr. Jennifer Van Nuil	Researcher in Global Health Ethics, CTU
Dr. Sonia Lewycka	Senior Epidemiologist, OUCRU Ha Noi
Evelyne Kestelyn	Head of the Clinical Trials Unit
Dr. Celine Pascale Vidaillac	Head of Research Operations – CTU
Dr. Nguyen Thi Phuong Dung	Head of Research Governance – CTU
Dr. Nguyen Than Ha Quyen	Senior Clinical Research Associate – CTU
Nguyen Bao Tran	Senior Clinical Research Coordinator – CTU
Nguyen Thi Huyen Trang	Clinical Research Monitor – CTU
Dr. Mary Chambers	Head of Public Engagement with Science
Jaom Fisher	Research Enrichment Manager (PCE)
Nguyen Thi Hong Yen	Social Science Research Assistant (Social Sciences - CTU)
Nguyen Le Thao My	Social Science Research Assistant (Social Sciences - CTU)
Nguyen Thanh Ha	Social Science Researcher (PCE)
Nguyen Thi Kim Ngoc	Public Engagement Coordinator (PCE)
Tran Minh Hien	Public Engagement Coordinator (PCE)
Nguyen Hoang Yen	Graphic designer (PCE)
Tran Dong Thai Han	Public Engagement Communications Coordinator (PCE)
Tran Kim Van Anh	Public Engagement Administrator (PCE)
Pham Ngoc Thanh	Psychological advisor (PCE)
Doan Phuong Nhung	Social Science Research Assistant (Social Sciences - CTU)
Nguyen Vinh Nam	PhD Student

OUCRU (cont.)

Tran Phuong Thao	Research Assistant
Nguyen Thi Kim Tuyen	CTU Coordinator
Tran Thi Hang	Research Assistant
Assoc. Prof. Ngo Thi Hoa	Head of Zoonosis Group
Katrina Lawson	Grants and Communications Manager
Nghiem Nguyen Minh Trang	Policy Engagement Researcher
Nguyen Kim Ngan	Policy Engagement Coordinator
Ngo Phan Bao Tran	Policy Engagement Coordinator
Ngo Huyen Chi	Senior Communications Officer
Vu Bao Hung	Communications Officer
Ha Le Thanh	Data Science/Statistics Officer

EOCRU

Assoc. Prof. Raph Hamers	Head of Clinical Research Programme
Dr. Suwarti	Postdoctoral Laboratory Scientist
Dr. Anuraj Shankar	Head of Community Research Programme
Dr. Iqbal Elyazar	Head of Spatial Epidemiology Programme
Dr. Decy Subekti	Senior Laboratory Scientist
Dr. Henry Surendra	Epidemiologist
Bimandra A. Djaafara	Mathematical modeler
Cindy Natasha	Clinical Trial Coordinator
Fitri Wulandari	Clinical Trial Administrator
Khairunisa Puspatriani	Clinical Trial Pharmacist
Ragil Dien	Public Engagement Officer
Livia Nathania Kurniawan	Public Engagement Officer
Mutia Rahardjani	Clinical Research Operational Senior Manager
Ida Ayu Sutrisni	Junior Social Science Researcher
Ralalicia Limato	DPhil student - Social Science Researcher
Diana Timoria	Public Engagement Project Officer (PCE)
Fahmi Ramadhan	Public Engagement Officer (PCE)

OUCRU-NP

Assoc. Prof. Abhilasha Karkey	Vice Director of OUCRU Nepal
Summita Udas	Public Engagement Officer
Dr. Suchita Shrestha	Program coordinator
Samita Rijal	CTU Officer (CTU)
Dr. Amit Gautum	Research Coordinator (CTU)
Aakriti Pandey	Research Coordinator (CTU)
Pratibha Thapa	Research Coordinator (CTU)
Niharika Kharel	Media Monitoring Assistant
Manis Duwal	Research Coordinator

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The Oxford University Clinical Research Unit
Website: oucru.org
For more information, contact us at: communications@oucru.org

oucru