Welcome to the first edition of The SPREAD

Dear readers, the MCID has just recently entered its third year of operations, having been founded in January 2021 as a strategic center of the University of Bern, in response to a generous donation by the Stiftung Vinetum.

To keep MCID Members and those interested in the MCID up-to-date with center activities, as well as to provide contents related to infectious disease research at a multi-disciplinary level, we have launched The SPREAD. This newsletter, to be released quarterly, is available to download from the MCID website, where one can also register to receive it by email. The SPREAD will feature articles on ongoing MCID research as well as spotlight articles, interviews and a section dedicated to MCID news, upcoming events and highlighted publications. We would like to thank everybody who has contributed to this first issue.

Make sure you keep up-to-date on MCID news and activities by visiting our website, following us on twitter (@MCIDBern) and signing up to receive future copies of The SPREAD.

Yours sincerely,
Rebecca Limenitakis (MCID Managing Director)
Anita Hochuli (MCID Teaching and Outreach Coordinator)
Sequence Sleuthing: How SARS-CoV-2’s mutations can help us track it

Article by: Dr. Emma Hodcroft (Institute of Social and Preventive Medicine (ISPM), University of Bern / Department of Medicine, University of Geneva)

Keeping track of variants has become tricky – recently, it can seem like there’s a new one every week. On the other hand, everything is still called Omicron. So - are these new variants different or not? How can scientists tell? And what is a variant anyway?

It might be a surprise to hear that there’s no hard definition of ‘variant,’ ‘clade,’ or ‘lineage,’ even though we’ve heard so much about them in the past three years. Historically, these terms mean roughly the same thing: they refer to clusters of samples that share a genetic ancestor and thus have shared genetic code, and are worth distinguishing from others. But how ‘recent’ that ancestor may be, how similar the sequences within groups are, and why they’re considered worth naming, varies widely across pathogens. When it comes to SARS-CoV-2, the ‘why’ has become somewhat standardized – scientists want to give labels to groups of viruses that may change how much the virus spreads, what treatments might work, and whether their severity is changed.

A lot of this depends on viral sequences – the genetic material of SARS-CoV-2 that can be extracted from PCR tests and analyzed to tell how a new sample fits into the larger SARS-CoV-2 phylogeny. For example, an increase in the proportion of sequences that carry a novel set of mutations may be a sign that these changes allows faster transmission, or more reinfection. Additionally, from studying SARS-CoV-2 in the lab and through modelling, we know what areas of the virus are associated with possible changes in how the virus behaves, like avoiding immune recognition. However, our ability to predict exactly how much impact a new variant will have is not perfect: many variants get basic names (via a scheme known as Pango – the XBB and BQ.1 you may have seen), but the vast majority will never make it into a news article, and even fewer will become dominant regionally or globally.

These general methods to identify variants worth keeping an eye on have been in use for most of the pandemic, so why do things feel a little different now? One reason is that scientists are currently seeing the same mutations appearing again and again in different parts of the SARS-CoV-2 family tree. Called ‘convergent evolution,’ this is often interpreted in evolutionary terms as a sign that something is beneficial – the fitness advantage for having that change is large enough that it’s selected for independently in many places. In SARS-CoV-2 currently, many of these convergent mutations are associated with immune escape.
This makes sense – most people around the world have now been vaccinated, infected, or, increasingly, both, and so their immune systems are well-primed to recognize SARS-CoV-2 variants that have come before. Thus, any change that allows infection of those with immunity will offer a clear advantage. However, with so many different clusters of sequences sharing the same sets of mutations that have the potential to increase transmission, many groups have been given variant names – hence the ‘variant soup’ we see today.

With so many differences, why are we still in the ‘Omicron era’? The “Greek letters” are designated separately from the more fine-grained lineages. Nowadays these are designed to highlight variants that could significantly change our pandemic response – like Omicron did with its change in disease severity and its ability to reinfect. Even though the Omicron sub-lineages (which we hear about today) have significant numbers of changes, and continue to pose a global challenge through driving new waves of infection and reinfection, our response to reducing transmission and handling these waves hasn’t significantly changed.

A schematic diagram showing all the variants of SARS-CoV-2, named by the Nextclade nomenclature and the corresponding Greek letter and Pango names. Credit: Nextstrain.org

And this is something to be cautiously optimistic about. While SARS-Cov-2 continues to evolve, and waves of cases have been driven by recent variants, these variants have not put as much pressure on our health-care systems, nor lead to the steep increases in deaths, that we previously saw – thanks largely to the high levels of immunity we now have. Through continued global sequencing, we can ensure we have our eyes on the horizon for new variants, and try to predict what impact they may have, as we navigate our way cautiously through the end of the pandemic.
The Covid-19 pandemic posed and still poses many unprecedented challenges to health care systems and public health efforts worldwide: According to which criteria should severely ill patients in hospitals be treated? How to distribute and ensure access to vaccines? Which groups were especially affected by Covid-19 policy responses? And how to apply contact tracing technologies in a fair and privacy-preserving way? These questions, among others, were discussed in the past years and entailed a wide range of ethical issues to be solved. It could also be observed that policy making, science and ethics were deeply intertwined with ethical considerations and underlying values being at the core of political decision-making.

Effectively tackling infectious diseases therefore requires an examination of the values and the value trade-offs that underlie and guide political action. The Ethics & Policy Lab (EPL) conducts research and offers support to MCID researchers in the fields of ethics and policy. Precisely, the EPL has two main aims:

1) To analyse the ethical dimensions of research and policy responses on infectious diseases and to develop constructive solutions for dealing with related ethical conflicts.
2) To feed MCID research outcomes into public policy and to facilitate political decisions that are based on scientific evidence.

With regard to ethics, the EPL supports MCID members in receiving ethics approval for their research projects. Often, their research entails further interesting questions related to ethics, which we help to systematically assess. In doing so, we employ different methods of evaluation: We start by assessing the needs of MCID projects in terms of ethical aspects and tailor an ethical analysis according to these needs. This usually involves clarifying and analyzing the values assumed in specific research designs, and its consequences in practice considering the broader societal context. Theoretical frameworks are employed to analyze the ethical issues at stake and to develop recommendations and implications for practice. We support projects, for example, in the study design for assessing infections with communicable diseases, what to take into account when planning longitudinal studies involving genetic information and how to communicate risks. We also support MCID researchers by providing trainings in ethics, in translating their research into policy making and support in drafting ethics-based policy recommendations.

Besides supporting MCID-funded projects, we also conduct own research on ethical aspects of infectious diseases and its management. One objective of our research is to elucidate the ethical challenges related to the Covid-19 pandemic, the underlying values in political decision-making, as well as the use of digital health technology and health data and to prepare for future public health crises. More specifically, we currently focus on the following research themes in our research at the Ethics & Policy Lab (this is not exclusive and may shift according to current developments and political advances):
Ethical dimensions in policy making and ethical policy advice

The objective of this research stream is to explore policy makers' and scientists' views on the ethical challenges during policy making on Covid-19 related measures, the role ethical considerations played in policy making during the pandemic, what kind of ethics assistance would be useful in policy making, and advice to tackle future public health crises. During a previous explorative interview study that we conducted in 2015 on ethical issues during policy making, policy makers explicitly expressed the need for ethical tools and assistance in line with policy advice for reaching morally sustainable decisions. The study furthermore distilled and proved that ethical concepts and values frequently come into play in health policy making, which need better dissection, analysis and recommendations for more value-based policy making. We are currently extending the results of this study.

Preparedness for future public health crises – ethical issues arising in distinct challenge areas

While the Covid-19 pandemic is still ongoing, it is vital to already prepare for future public health crises. Drug resistance, referred to as antimicrobial resistance (AMR), and the consequences of climate change on health represent major future threats, for which better preparedness, also from an ethical perspective, is needed. The global and national action plans on AMR, for instance, have not received much attention from an ethical perspective even though the proposed actions require changes in society which yield various ethical challenges. We therefore aim to assess the ethical challenges of action plans on AMR to ensure that strategies to tackle this issue are ethically responsible. One example is that higher drug prices as a result of efforts to limit antibiotic use pose a threat to equitable access.

Ethics in data-driven digital health and public health

In the field of health, the digital dimension is ever increasing, and in the last few years, digital health initiatives received much interest and increasing investments from public and private sources. The purposes and utilizations of digital health, such as apps, wearables and other digital solutions, are to monitor, prevent, screen, diagnose and treat health-related issues. In a previous paper, we outlined the chances and challenges of digital health from an ethical perspective, taking a justice view. To provide better guidance on how to govern digital health technologies, we would like to develop and propose an ethical framework for developing and implementing digital health technologies. During the recent Covid-19 pandemic digital health technologies, such as contact tracing and certificate apps, were employed to contain the pandemic spread. It will be interesting to assess whether the Covid-19 pandemic will have accelerated the uptake of digital health in general, as for many, Covid-19 related apps were the first interaction with digital approaches to health and healthcare and what this implies for willingness to share data.

With regard to transferring relevant findings of MCID research into the policy-sphere, we collaborate with public administration and political decision-makers to design ethical and evidence-based policy solutions. We also work together with policy makers and conduct applied research projects, policy evaluations from an ethical perspective, advice on feasible, ethics-based and socially accepted policy measures, on ethical aspects of infectious disease management, and on preparedness for future public health crises.

Contact the EPL if you are interested in collaboration or have questions about your work or our research projects: Dr. Caroline Brall, ethics-related matters, Dr. Caroline Schlaufer, policy-related matters.

References

Airtracker: monitoring viral transmission in the classroom

Article by: Dr. Rebecca Limenitakis (MCID), on behalf of Prof. Dr. Lukas Fenner, Dr. Nicolas Banholzer, Dr. Kathrin Zürcher (Institute of Social and Preventive Medicine (ISPM)), Dr. med. Philipp Jent (University Hospital Bern), Dr. Pascal Bittel (Institute for Infectious Diseases (IFIK)) and Prof. Dr. Tina Hascher (Institute of Education Science (IES))

The COVID-19 pandemic, caused by the SARS-CoV-2 virus has brought back into focus the modes of transmission of respiratory viruses and how viral spread can be minimized by preventative measures. While this is a topic that is critical to society as a whole, surprisingly few studies have been conducted that address this subject area, in part due to difficulties in detecting air-borne viral particles. The SARS-CoV-2 virus, influenza viruses and other respiratory viruses are transmitted by exhaled, infectious droplets and there is growing evidence that long-range transmission by fine aerosols (respiratory particles < 5 µm) may play a role in SARS-CoV-2 viral particle spread, in addition to transmission via larger aerosols, more recently defined as respiratory particles > 100 µm\(^1\,^2\).

Fine aerosols are thought to be particularly problematic for transmission as they persist in the air longer than larger aerosols, accumulating in indoor spaces. Fine aerosol transmission may be of particular relevance in confined spaces such as school classrooms, where individuals are often with poor ventilation. How high is the transmission of respiratory viruses in school classrooms? Does mask-wearing or air-cleaning impact this transmission rate? What are the effects of such intervention measures on the mental well-being of school students?

In January 2022, an MCID-funded project was initiated by a multi-disciplinary team of University of Bern researchers: Institute for Social and Preventive Medicine (ISPM), Department of Infectious Diseases (Inselspital Bern), Institute for Infectious Diseases (IFIK), and the Institute of Educational Science (IES). The aim of the project was to understand better the transmission of SARS-CoV-2 in school rooms and the extent to which schoolroom transmission is reduced by the wearing of masks and by air cleaners. Determining the extent to which such measures can reduce viral transmission is highly important. There is a strong wish for schools to be kept open even during periods of high viral transmission, with concerns that school closures can negatively impact student well-being and mental health, particularly in adolescents. Measures that are demonstrated to limit viral transmission while allowing students to continue in-person teaching may thus prove valuable in specific instances or as standard procedure during peaks of respiratory virus transmission.

The aim of this study, now entering a second phase of sampling, is to provide data to inform decision making by educational and public health authorities. Required ethical approval for this project was acquired before its commencement and students/parents gave their permission for involvement in the study, by way of providing saliva samples and being assessed for emotional well-being. All data collected was anonymized.
The project team collected data in two secondary schools over a seven-week study period. Epidemiological data were collected in five classes, and environmental and molecular data were collected in two classrooms. Data collected included confirmed/suspected cases of respiratory infections, air quality data (including CO2 levels and aerosol concentrations) and detection of viral particles in saliva and aerosol samples. The above parameters were assessed in conditions without any transmission prevention measures, as well as during a phase of government-mandated compulsory mask-wearing and in the presence of air cleaners.

The transmission model based on collected data revealed an average risk of becoming infected with SARS-CoV-2 in the school classes analysed of 3% during the mandated mask-wearing period compared to 14% when no intervention measures were in place, aside from regular window-opening. In the presence of air cleaners, the risk was reduced to 11%, reflecting a significant but modest effect of air cleaning on transmission. Molecular analysis of saliva and airborne samples detected SARS-CoV-2 throughout the study and occasionally other respiratory viruses. Aerosol and particle matter mass concentrations were significantly reduced by both mask wearing and air cleaning. These findings mirrored similar observations made in a previous artificial simulation study3.

This data strongly suggests that both mask-wearing and air cleaning can reduce viral transmission in a classroom setting. While it is not proposed that such measures are adopted on a continuous basis in schools, this study suggests that the wearing of masks and cleaning of air in classrooms may be beneficial in periods of high viral transmission.

While this can be assessed to some degree by country-wide or more local data on current respiratory virus infection rates, an ideal situation would be the regular monitory of environmental factors in sentinel classrooms that may reveal poor air quality or even significant viral load in respiratory particles and would trigger adoption of prevention measures on a temporary basis. Results of this study will be submitted to a peer-reviewed journal and sampling is underway to provide a second dataset for further analysis.

An additional aspect of this MCID-funded project involves the assessment of the emotional well-being of school students during a pandemic situation and the associations of different control measures on this well-being status. This data, collected using a questionnaires on student habitual well-being in school and a series of standardized items assessing daily affective experiences, is currently being analysed. Preliminary results do suggest that student well-being was neither negatively affected by wearing masks nor air cleaning.

References
Revision of EpiA, the Swiss Epidemics Act

A multidisciplinary research team including five MCID Members has written a thesis paper on the escalation model as input for the ongoing revision of the Swiss Epidemics Act.

The Swiss Epidemics Act regulates the detection, monitoring, prevention, and control of infectious diseases in Switzerland. The act came into force in 2016 after its approval by 60% of Swiss voters in a referendum. The act defines the measures that can be taken by cantons and the Confederation to limit negative effects of infectious diseases on public health. It also defines the responsibilities of cantons and the Confederation in an infectious disease outbreak. To do so, the act defines a three-stage escalation model with three epidemiological situations: a normal situation, a special situation, and an extraordinary situation. While cantons are responsible for disease control in a normal situation, the Federal Council may take measures for the whole of Switzerland after consulting the cantons in a special situation. In an extraordinary situation, the Federal Council may decide alone upon mandatory measures for the whole country.

The revision process

Six years of implementation of the Epidemics Act and experience gained during the COVID-19 pandemic have highlighted several needs for optimization. The Federal Council therefore mandated the Federal Office of Public Health (FOPH) to prepare a revision of the Epidemics Act. The revision should include all lessons learned from the COVID-19 pandemic, allowing improvement of preparedness for future crises. The revision comprises the following topics, among others:

- strengthening prevention
- clarifying responsibilities of cantons / the Confederation
- the escalation model
- digitalization
- vaccination or other control measures
- compensation schemes for future disease outbreaks
The FOPH launched the revision project at the end of 2021. Expert opinions were collected and stakeholder workshops conducted to gather input for the revision. In early 2023, a draft of the revised act will be prepared and from mid-2023, the draft will be open for comment for all concerned actors in a consultation process. The draft law is expected to be submitted to parliament by the Federal Council in 2024.

The contribution of the MCID
A group of MCID and ISPM researchers was mandated by the FOPH to write a thesis paper critically examining the implementation of the three-stage escalation model in the past with a specific focus on the COVID-19 pandemic. Led by Christian Althaus (ISPM) and Caroline Schläufer (KPM), the team concluded that the escalation model has overall proven its worth. They formulated six recommendations for the further development of the escalation model:

i. Clear and operationalizable epidemiological criteria that define when the epidemiological situation changes (from the normal to the special situation and from the special to the extraordinary situation and back) need to be developed.
ii. An efficient process of assessing the epidemiological situation needs to be defined.
iii. A group of experts needs to be involved in the risk assessment on the basis of the predefined criteria.
iv. During the special situation, an efficient process of consulting the cantons needs to be defined.
v. The Confederation should play a leading role in the special situation.
vi. A predefined crisis management body is needed to coordinate measures during the special and extraordinary situations.

Considering these recommendations in the revision of the Epidemics Act should facilitate the application of the escalation model, significantly improve its utility, and thus enable timely decision-making and early control of infectious diseases.

Reference

MCID Co-Chairs look back on two years of the MCID

Interview with: Prof. Dr. Carmen Faso (MCID interfaculty lecturer) and Prof. Dr. Volker Thiel (Institute of Virology and Immunology (IVI) / Vetsuisse)

What have been some of the key tasks for the center since it was launched in January 2021?

Carmen: establishing the MCID as a fully-fledged strategic center of the University of Bern has taken up most of our time, ranging from providing the legal framework for our activities, all the way to defining corporate identity-compliant visuals. At the same time, we began defining the MCID’s scientific direction as part of a community-driven effort. This is a work-in-progress which I am very excited to pursue.

What has been your highlight so far in the life of the MCID?

Volker: seeing all MCID members for the first time in “real life” at the MCID opening event. Until then we had only been interacting virtually because of COVID measures. It was great to see everyone in person for the first time and to not only discuss research but also get to know each other outside of an online meeting setting.

Carmen: seeing colleagues from disparate disciplines join forces and engage in scientific exchange and research on a common topic. To observe, support and mediate this process is a priceless experience for me.

What has the biggest challenge been in getting the MCID up and running?

Carmen: we were tasked with establishing a transparent, reliable and accountable funding allocation procedure, mindful of the Stiftung Vinetum’s goals and our own community’s needs, in a very short amount of time and in extraordinary working conditions. None of this would have been possible without the outstanding work and dedication of our colleagues Dr. Rebecca Limenitakis and Dr. Usha Sarma, both staff members of the MCID.

What are your primary roles as Co-Chairs of the MCID?

Volker: I think our main roles are to think ahead and provide ideas as to how the MCID should move forward. We gather feedback, collect ideas from MCID Members, navigate options and landscapes and present possibilities for future growth to the MCID Directorate, the decision-making body of the MCID. The synthesis of our collective thoughts can then be brought to action with a lot of hard work done in the background by the management office.
What exciting opportunities do you see for the MCID in the future?

**Carmen:** there are two very exciting goals ahead of us. The first is the development of a full teaching and outreach portfolio. The Ethics & Policy lab marked the very first EPL MCID workshop led by Dr. Caroline Schlaufer. This first teaching activity will be followed by several others in 2023 thanks to the efforts of MCID Staff member Dr. Anita Hochuli. The second is expanding the MCID’s reach beyond Switzerland by engaging with similar institutions and initiatives in Europe and perhaps beyond.

**Volker:** It will be great to follow the work within the MCID-funded research projects and to see an growing community at the University of Bern that is interested in infectious diseases, pandemic preparedness, and inter/multidisciplinary work. Another aspect of the MCID is the fostering of young talents, and with the teaching and outreach activities it will be interesting to see how we can increase awareness, expertise, and knowledge amongst students and young researchers in this area.

What does “multidisciplinarity” mean to you?

**Carmen:** I learned that the potential for multidisciplinary research is often underestimated because we are (perhaps too) preoccupied with our achievements in one specific field of inquiry. Multidisciplinarity in research is a precious opportunity to expand one’s horizons and formulate innovative research questions to spark new fields of inquiry. To me, it begins with the ability to communicate ones’ scientific passion and interests on topics that are, by their very nature, multifaceted.

**Volker:** I thought I knew what multidisciplinary means, but I had to learn that in practice there’s much more to learn. Every discipline has its own way of working and thinking, and accordingly, scientific structures are adapted to this. The MCID provides a great opportunity to learn from each other.

How does your own research fit with the mission of the MCID to study and provide strategies to mitigate health, healthcare, societal, ethical, and economic risks from infectious diseases?

**Volker:** The research in my group is in the biomedical, veterinary and microbiology field, fitting well with the Microbiology cluster, which I’m a member of. As we have been working on coronaviruses for many years, our work fits very well with the mission of the MCID, and has been particularly relevant during the pandemic. However, since the pandemic threat affected essentially all aspects of our society, a lot of attention was given to the interfaces between science, society and politics, something I felt very strongly during my time as a member of the Swiss National COVID-19 Science Task Force and which lies at the heart of the MCID with its emphasis on multi- and inter-disciplinarity.

**Carmen:** I am fascinated by how pathogens and hosts communicate on a molecular level and how this exchange impacts a host’s health and a pathogen’s chances of survival and dissemination. Understanding the basis of this communication is essential to mitigate or downright abolish infection and detrimental consequences for the host. My focus is on single cell parasites of the gastrointestinal tract that infect humans and other animals. Although millions of people globally are affected, the illnesses they cause are often neglected since treatment options are scarce and effective vaccines have not yet been developed.
MCID-funded Early Career Research Grants for Women (ECRG-W) projects begin
Six projects have been awarded MCID ECRG-W funding and began running in January 2022 on topics ranging from pathogen surveillance in garden wildlife to governmental blame deflection during the COVID-19 pandemic.

MCID Member, Emma Hodcroft, awarded SNSF starting grant
MCID Member Emma Hodcroft has been awarded an SNSF starting grant and in Autumn 2023 will begin her own research group at the SwissTPH focusing on the phylogenetics and evolution of enteroviruses.

MCID Co-Chair, Carmen Faso, takes on role of Co-President of the SCNAT Biology Platform
MCID Co-Chair and interfaculty lecturer, Carmen Faso and Irene Adrian-Kalchhauser, head of the Institute for Fish and Wildlife Health (FWI), Vetsuisse, take on co-presidency of the Swiss Academy of Sciences Biology Platform.

MCID Co-Chair, Volker Thiel, to act as member of the Swiss Covid-19 Scientific Advisory Panel
Volker Thiel will provide coronavirus expertise as a member of the Swiss Covid-19 Scientific Advisory Panel, formed to provide independent analysis and advice on behalf of the Swiss government.

MCID researchers awarded Charles C. Shepherd prize for work on the SARS-CoV-2 spike protein
MCID Members Fabien Labroussaa, Jenna Kelly, Ronald Dijkman, Jörg Jores, Charaf Benarafa, Volker Thiel and collaborators awarded the Charles C. Shepherd award for their work on the SARS-CoV-2 spike protein.

Events
MCID Ethics and Policy Lab workshop on research ethics
On 7th March 2023, the EPL will hold a workshop for MCID Members on the topic of research ethics with the title “Reflecting on the ethical dimensions of your research and obtaining ethics approval.”

European Mucosal Immunology Group (EMIG) meeting 2023, Bern
Registration is now open for the 12th European Mucosal Immunology Group Meeting, to be held in Bern from 12th-14th July 2023. Early registration closes on 28th February.

The XVIth International Nidovirus Symposium 2023, Montreux
Registration is now open for the 16th International Nidovirus Symposium to be held in Montreux, Switzerland from 14th-18th May 2023.

Highlighted publications
Nicola Low et al. on mpox transmission
Nicola Low, MCID Epidemiology cluster chair, and collaborators, identify unanswered questions on the role of sexual contact in mpox transmission, providing a framework for cross-national research studies involving existing cohorts and multi-disciplinary teams to address these questions.

Georgia Salanti et al. on mental health during the Covid-19 pandemic
MCID Member, Georgia Salanti, and MHCVID team publish a paper on the effect of the COVID-19 pandemic and associated control meaures on mental health.

Jenna Kelly et al. on host responses to influenza virus A infection
MCID Members Jenna Kelly, Volker Thiel and Ronald Dijkman, together with others at the University of Bern publish on host responses to infection by influenza A virus using a comprehensive single-cell analysis approach.

Johanna Hornung, Fritz Sager, Caroline Schlauffer et al. on scientific policy advise in crisis situations
MCID Society and Law cluster members Johanna Hornung, Fritz Sager and Caroline Schlauffer, together with collaborators conducted a study on policy advice during times of crisis, including the Covid-19 pandemic.
The Multidisciplinary Center for Infectious Diseases (MCID) is a strategic center of the University of Bern, Switzerland, founded through the generous support of the Vinetum Foundation.

Register here to receive future copies of the newsletter by email and visit the MCID website to read more about MCID activities and news.

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