BC COVID-19
STRATEGIC RESEARCH
ADVISORY COMMITTEE

BC COVID-19 Strategic Research Framework: An Evolving Guide for Decision-Makers and Researchers

Issue 2 – Adaptive Research Response
December 2020

Table of Contents

Purpose

Responsive research, particularly in the time of crisis, requires a systematic approach to understanding both the needs for research and the capabilities to fulfill them. Over the last ten months, British Columbia has seen the mobilization of a range of enabling structures and considerable funding intended to deliver meaningful evidence to inform the management of the COVID-19 pandemic. With promising vaccine candidates now under review at Health Canada, our research response must pivot to include priority questions in support of an efficient, timely and safe immunization program.

Within this context, this "living document," the second issue of a research framework, has been developed by the BC COVID-19 Strategic Research Advisory Committee (SRAC) to:

- Describe efforts in BC, to-date and current, to support a robust research response to COVID-19
- Describe SRAC's activities to align and coordinate the actions of the research community, especially as we move into a period where wise use of vaccine may help fundamentally impact viral transmission
- Update COVID-19 research priorities within the rapidly evolving BC context to support the ongoing identification of outstanding research needs

Like the first issue, this document will be used by SRAC to advise the Province on COVID-19 research related issues. SRAC also encourages use of the framework by BC organizations, teams and individuals to ensure as much cohesion as possible in BC's research response to the pandemic. This work is necessarily reflective and iterative; community participation through review and feedback as well as ongoing communication with SRAC is welcomed and encouraged. Questions or comments for SRAC can be directed to SRAC@msfhr.org.

The BC COVID-19 Strategic Research Advisory Committee

Provincial coordination for COVID-19 research is critical to:

- Best utilize resources (human, capital) for the benefit of the patients and public
- Ensure that key evidence required by the public, the health systems, and communities to respond to the pandemic are not overlooked
- Reduce duplication and waste
- Promote harmonization of processes that enable timely and relevant research

Supported by the Michael Smith Foundation for Health Research, the BC COVID-19 Strategic Research Advisory Committee was formed to provide strategic alignment among the Provincial Health Officer, government, the health system, the public, and the BC research community. To that end, on April 30, 2020 the SRAC published issue one of the BC COVID-19 Strategic Research Framework.

SRAC is now moving into a new phase of work, informed by community feedback and emerging evidence from BC and around the world, and with a clearer picture of the research planned and underway and some of the impediments to these efforts. It is important to acknowledge that much effort so far has contributed to greater understanding of the pathogen, its transmission and effects on people and populations. Now that there are new tools with which to address prevention and transmission, SRAC must help assure that front line staff and health leaders have the answers they need to put an end to the worst phases of the pandemic. An historic immunization effort will require deliberate attention to implementation science.

SRAC will now focus on:

1. Continuing to advise the Provincial Health Officer, the Ministry of Health, the research community, and the public on COVID-19 related research plans and initiatives. These include the enabling mechanisms for COVID-19 related research (by for example the BC Academic Health Science Network [BC AHSN], PopulationData BC, the COVID-19 Clinical Research Coordination Initiative), the health sector plan for COVID-19 response, the unintended consequences work led by the Ministry of Health, and the Michael Smith Foundation for Health Research (MSFHR) BC COVID-19 knowledge translation plan and other COVID-19 related research response activities, including most recently BC's vaccine rollout strategy.

2. Specific priority areas with respect to BC-specific COVID-19 research: SRAC working groups will support the research efforts in these areas. Supported by MSFHR, approaches include developing or supporting collaborations, information sharing events, detailed discussion papers, and advice with respect to funding. The following have been identified as initial priority areas where, based on review of

feedback to SRAC from the research community, the public and decision makers, more detailed collaborative work is required to coordinate and inform the research response in BC:

- Long term care (LTC) - integrating research on disease transmission risks with the longstanding policy and program issues in congregate care settings in collaboration with the planned LTC quality improvement initiative at BC AHSN
- Allying the broader BC research effort with Indigenous-led and governed efforts
- Research-informed risk- and public communication
- Disease characterization and subpopulation risk – coordinating the utilization of the data from the evolving cohort of COVID-19 patients
- Applying learning from pandemic experience so far to advise on retooling BC's pandemic response research capabilities for this and future emergencies.

The list of priorities will evolve as other areas of focus are identified. It is evident that informing optimized COVID-19 immunization activity across the above themes must be a priority.

What We Have Learned

It became clear as the work of SRAC proceeded that there was a significant challenge, not just in tracking all of the COVID-19 related research, but keeping it in context. How do you compare the value of basic science work with harm mitigation? How much distribution of impact is based on underlying structural social and economic inequities? How should you assess the quality of research that is released under accelerated and abbreviated processes? How can you adapt funding processes quickly enough to respond to evolving needs? Is there a risk of duplication of research in some areas and significant gaps in others, and should this be a concern?

Thanks to provincial, national and international research efforts, we have learned a great deal about COVID-19 since the last issue:

- The virus is well characterized, and its pace of evolution is being tracked through genomics.
- Transmission is highly dispersed, meaning that many people will not transmit, but that some people and settings contribute large numbers of infections. Understanding of these settings is key to public health action.
- Best practices in the care of the critically ill, including the use of dexamethasone, can reduce mortality; many more treatment options do not work while others are under evaluation.
- Large, collaborative, adaptive clinical trials are essential for pandemic response.
- Methods for direct detection and serological assays have been developed or evaluated. Using these methods, we know that population exposure is still relatively low and that we are a way off from herd immunity.
- People can develop neutralizing antibody responses to the virus, but how long-lived these are is an open question.
- Many vaccine preparations are safe and immunogenic, and many have made it to Phase 3 trials, with preliminary evidence of high short-term efficacy for three vaccine candidates at the time of writing. These candidates are under review with regulatory bodies and the prospect of launching immunization programs in 2021 is very real.
- Public health responses (isolation, contact tracing and follow-up) together with public action (reducing contacts, using non-medical masks in crowded settings, staying home when sick, good hygiene) can drop transmission but are hard to sustain when opening up activities and businesses. Moreover, public health workforces may need to find ways to pivot to vaccine delivery.
- Pandemics do not affect all people equally: a number of populations suffer a higher burden of illness, due to both biological factors and imbalances in social, economic and health equity. In addition, public health measures impact some populations and communities more than others and perpetuate inequities.

As this research from around the world unfolds at an unprecedented pace, SRAC appreciates that there is a continued need for strong emphasis on high quality research that is:

- Supporting decision-making in BC and not available from research from other jurisdictions
- Based on initiatives that specifically exploit the strengths and capabilities of BC-based research
- Readily useable by those who need to make decisions: individual citizens, organizations, clinicians, public health leaders and government leaders
- A substantial contribution to the global body of research

Research areas in context

SRAC recognized that, in a competitive research environment traditionally fragmented by discipline, an overview is required to understand the range of research necessary to respond to an emerging disease and the relationships of this research to health system actions and outcomes. A framework was developed to highlight the interdependence of efforts across the full array of health research from basic science to social science and to help navigate some of the important questions about relative priorities (Appendix 2: A Framework for Research and Action in an Emerging Disease).

The tasks of the research response to COVID-19 in BC continue to be the ongoing development of the knowledge in these areas, to identify the gaps, opportunities for collaborative and expedited research efforts and the mobilization of the emerging knowledge to support the decisions required (Appendix 3: Principles and Assumptions for Rapid Response Research).

BC's Research Response

The funding for research worldwide has been significant. In BC government, funding agencies, foundations and industry provide substantial investment in research (Appendix 6: BC's Research Response to COVID-19). In April the BC Academic Health Science Network made available and continues to update and enhance an inventory of funded research projects, developed by the MoH, that has been invaluable resource connecting researchers and decision-makers.

The research community in BC has very rapidly mobilized a remarkable array of supports and efforts to better coordinate and facilitate the research response (Appendix 4: Structures and Processes supporting Rapid Research Response in BC). This is a testimony to the thoughtful investment in these supporting structures prior to the pandemic.

One of the most notable efforts in the coordination of basic research, clinical trials, and the clinical care is the work centering on patients with COVID-19 (Appendix 5: BC's Post COVID-19 Recovery Clinic and Interdisciplinary Clinical Care and Research Network). These linked initiatives provide a fascinating case-study in the opportunities and challenges of innovative,

cross- disciplinary research, particularly when it is associated with the direct clinical care of patients in a regionalized health system.

With a view to ongoing support and improvement, MSFHR is undertaking an evaluation of the research response to COVID-19 in BC. This will focus on the importance of coordination and collaboration between health researchers and research users. The approach will be strengths-based and identify insights and opportunities to build these functions. The ongoing plans for SRAC will support and extend these efforts and continue to identify opportunities for innovations and collaborative work (Appendix 7: Evaluation of BC's Research Response to COVID -19).

SRAC also gathered input and feedback on the work of the committee. The public, the research community, practitioners, public health and health care practitioners and decision-makers at all levels continue to see the need for enhanced communications and the importance of strategies that support thoughtful knowledge translation (Appendix 8: MSFHR CoVID-19 Knowledge Translation Plan). Trust in the research enterprise requires transparency and responsiveness. Risk communication has a strong evidence-base. This is increasingly important as people are required to comply with a wide range of public health measures over the coming months to minimize the burden of this disease on our society. It is therefore a key focus of SRAC moving forward to undertake actions to support these efforts.

The Management of COVID-19: Health Sector Plan for Fall/Winter 2020/21 from the BC Ministry of Health lays out the health system plans for the upcoming months, and there are key areas where research can support these efforts. The health system in BC has also learned a great deal about the strengths, resiliencies, and gaps in the research environment. The Ministry has an ongoing process through its Partnerships & Innovation Division, Ministry Research Advisory Committee, and senior executive to identify and satisfy long term and emerging priorities for research in this response. BC-specific research is required to inform: protection of vulnerable seniors in long term care, protection of higher-risk patients in community with primary and specialist care, improved transportation and access in rural and remote areas, increased assessment and laboratory testing capacity, strengthening hospital capacity and services, adequate personal protective equipment, and mental health impacts and management in healthcare workers and vulnerable individuals in communities. With almost 450 documented COVID-19 research projects in BC, there are ample opportunities for meeting these needs, supporting patient-oriented research and undertaking participatory action research.

The emergence of promising vaccine candidates has had no small contribution from BC. The lipid nanoparticle delivery systems invented here are critical to the function of some mRNA vaccines, yet we lack domestic drug development and manufacturing capacity, leaving us vulnerable to the potential for vaccine nationalism. This must be remedied: the strength of BC's biotechnology industry makes it imperative that we contribute to a national solution.

BC COVID-19 Research Priorities

The initial issue of the BC COVID-19 Strategic Research Framework outlined a series of potential research questions associated with timelines of the pandemic. Laying out priorities in this way provided an important focus of engagement and discussion with the community, and SRAC received a great deal of feedback. We solicited input from the research community, decision-makers and the public prior to the development of this issue, and these research areas are included. The Ministry of Health has recently undertaken an extensive internal exercise to identify the research needs, and these too have been reflected in this summary.

With the continually increasing volume of individually funded research projects, it is a challenge to identify where new initiatives are filling these needs and where gaps remain. Widespread use of the BC AHSN inventory of BC COVID-19 research and broader communication of the needs and projects will continue to make links between researchers and decision-makers. The additional knowledge translation approaches detailed in the MSFHR plan will emphasize these important connections and will contribute to the process of mutually developed priority projects.

The following are presented as revised lists of questions and are not comprehensive lists of specific research topics. The intention is to cover the full range of needed research (specific to health and health system research) based on the important questions that have arisen in the management and response to the pandemic in BC. It is provided as a resource for a provincial response and will inform SRAC's ongoing identification of gaps and opportunities. The community's participation in the ongoing process of identifying research areas is appreciated.

Current situation and research questions to aid response present to vaccine deployment

Assumptions and considerations

- It is not anticipated that herd immunity will bring the epidemic to a natural end in BC anytime soon. There is also the possibility that immunity to COVID may not be sufficiently long-lived to provide population protection.
- Ongoing control measures including appropriate testing, contact tracing and follow up need to continue.
- Clusters and outbreaks will continue to occur, and control efforts will focus on mitigating the risks based on community factors.
- Schools, community and health services, and many aspects of daily life have resumed and will continue with physical distancing and other controls as feasible.
- Specific additional protection for the most vulnerable will continue.

- Vaccination programs require BC-specific research with respect to considerations for administration, ongoing outcome assessments and communication strategies to support deployment decisions in the context of federal processes.
- Diagnostic and treatment approaches to COVID-19 related disease will continue to improve as they are emerging from experience around the world and here in BC. Recent progress on alternative methods of specimen collection and rapid testing options are notable.
- The understanding of the clinical and immunological outcomes of COVID-19 disease is evolving and this knowledge is key to planning appropriate actions in the health care system and the community.
- With ongoing planning and monitoring, the health system will continue to have the capacity to meet the need for care.
- Models of health care have changed and require monitoring and evaluation.
- Workplace adaptation requires a strong evidence base.
- Communications efforts will be required to combat misinformation and maintain a coherent societal response. Misinformation has been identified as a serious risk.
- Control measures have secondary impacts on the health and well-being of the population, social determinants of health and the delivery of health care services. People have been differentially impacted by both the disease and the control measures:
    - Underlying health and socioeconomic disparities are amplified.
    - Impacts include psycho-social effects.
    - Mitigation of these effects requires ongoing surveillance and targeted action.
- The unique geography and culture of BC requires special attention to remote, rural, and First Nations communities.

Examples of relevant research questions

SARS-CoV-2 Pathogen and Immune Response

- How is the SARS-CoV-2 virus changing as it spreads through the population? How do we undertake surveillance to identify significant shifts if they occur?
- How can we best deploy genomic analysis to the understanding of general spread and cluster analysis?
- What are the BC-specific interests and areas of exploration in the context of the serological studies underway nationally and internationally?
- Are there differences in infection and immune responses among specific population subgroups (age, gender, ethnicity)? How does this impact our approach to vaccine development and deployment?
- What is the variability in viral load in infected people (between people and across time) and how does this affect transmissibility?
- What are the physical properties of the virus that need to inform disinfection and infection control practices? What is the best approach to the testing of these?

- How do immune responses to each new vaccine platform compare with natural immunity? Are there important host factors governing efficacy?

COVID-19 disease prevention and treatment

Diagnosis and prognosis

- How do we balance (and then communicate) the considerations of sensitivity, specificity, timeliness, scalability, and cost when assessing and then deploying new diagnostic tests?
- How do we navigate the territory between diagnostic testing and screening? What is the value of testing asymptomatic people?
- What is the appropriate array of clinical investigations post-diagnosis and pre-treatment?
- Are there early indicators of severe disease?
- What are the most important pre-existing conditions, including medication use, that impact clinical course? Can we use BC linked data to continue to characterize this?

Infection control

- Can we devise "clinical trials" from the components of infection control practice now that we have more information about the pathogen and the disease?
- What are the characteristics of facilities, workplaces, community settings, and family arrangements that successfully control outbreaks within BC and across other jurisdictions?
- How well do practitioners, patients and the public understand the principles and best practices of infection control? What are the best ways to communicate these?

Prevention

- How well does current contact tracing and follow up work? Are there variabilities in communities and populations with respect to the needs?
- What are the best methods for assessing the effectiveness of public health measures in a variety of settings across BC? In real time? Over longer periods?
- What information is required to better target interventions to avoid unnecessary restrictions? How can we improve the specificity of the monitoring and surveillance to allow for more tailored community approaches?
- How well do people understand the basic principles of the prevention of the spread of respiratory diseases? Does social media help or confuse, and how do we manage its effect? How widespread is misinformation and its uptake?
- In times of uncertainty, can we set up action research to rigorously compare different policy and practice approaches in real time? Examples could include schools, congregate care settings, community services, and workplaces.
- What is the best approach to determining priorities for vaccine deployment? What public education, information and engagement is required?

Treatment

- How do we support the best use of clinical trials in BC? What are the unique strengths of our system that can be leveraged? What are we learning from successful COVID-19 clinical trials around the globe, and what are the implications for clinical trials infrastructure, preparedness, and organization in BC?
- Can BC-linked data be systematically deployed to inform clinical care in an emerging disease?
- What are the specific care needs for the BC population, including those in remote and rural settings?
- How do we better integrate specialized care for individuals, especially over the long term in follow up?
- Has primary health care been optimally deployed in the care of these patients? Is it adequately linked to specialists and public health?
- How has mental health, addiction, and social care been provided to patients (and their families) with COVID-19?
- How has palliative care been deployed for patients with COVID-19 in long term care and other settings?

Impact

On patients with COVID-19

- What are the care needs for patients over time across the spectrum of illness?
- What are the health and other outcomes? What are the costs?
- How do we assess the burden of illness associated with COVID-19 relative to other important preventable health conditions? How does this influence future action and response?

On patients needing other care

What are the impacts on the patterns of care and the outcomes for patients with:

- Chronic conditions requiring longitudinal care (cancer, heart disease, diabetes, neurological conditions, mental illness, addictions, etc.)
- Conditions requiring acute and urgent intervention, including injuries, other infections, cardiac conditions, strokes etc.
- Need for diagnostic examinations or scheduled treatment (including surgery)
- Need for health maintenance interventions such as screening and immunization
- Need for palliative and end of life care
- How have these impacts been mitigated in BC? How do our results compare with other jurisdictions and what are the determinants of these differences?
- Can COVID-19 immunization reduce the risk of nosocomial infection?

On the health system

- How is the provision of care shifting over this period? What are the changes to access to care, provider and patient satisfaction, and health outcomes? What are the changes that need to be sustained?
- How has this impacted health authorities with respect to redeployment of resources?
- Has the health authority structure itself helped in supporting an appropriate response (for example in comparing BC to other jurisdictions)? What lessons can be learned from successes?
- What has the impact been on health practitioners outside of the health authority structure? Have structures as the Division of Family Practice contributed to the response?
- Were pandemic preparedness plans adequate to prepare for the health system response?
- How have health workers been impacted by the disease itself and by other factors such as workload and stressors?
- What specific health policies have helped or hindered responses?
- How do we reflect societal values in the health system response to an emerging disease?
- Which health care workers should be prioritized for early immunization if supplies are limited?

On the public

- How well have we characterized risk as evidence emerged? How has it been communicated?
- How has the mental health of the public been affected by the pandemic?
- Have health behaviours been affected? Substance use? Exercise? Diet? How are differences distributed?
- What are the impacts on other preventable conditions such as unintentional injury, violence and suicide?
- Do these impacts differentially impact different populations and communities?
- Specifically, what are the impacts on children? How can we monitor and mitigate this?
- What are the variations in impact related to family and community structures including extended families?
- How do structural issues such as poverty, racism, gender issues, and other inequities influence outcomes?

Research questions to aid longer term response (vaccine deployment and onwards)

Assumptions and considerations

- Vaccine mediated immunity in BC and elsewhere is the goal.
- COVID-19 disease will continue to require surveillance and management.

- Should vaccine-mediated immunity not be readily achieved, ongoing risk management will be required in the full context of disease impact relative to overall population health outcomes in BC and globally.
- There will be ongoing disparity in the impact of the disease and associated control measures based on structural inequities and this will require thoughtful examination.
- There will be long term impacts on the health and functioning of society.
- Current public health systems need reinvestment and retooling to better prevent and respond to emerging threats.
- Health services need plans that provide for timely and adequate response to surges based on a wide range of hazards and emergencies.
- Positive lessons can be learned from our adaptations.
- An important goal is the integration of a learning health care system with our research response to any present or future emerging threat.

Examples of research questions:

- Are we supporting the research to identify emerging pathogens at the animal/human interface? Is BC optimally deploying a "One Health" approach to this research? One Health is a collaborative, multisectoral, and transdisciplinary approach with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.
- Can we build on our strengths in disease detection and characterization, biotechnology, and clinical trials to better integrate pandemic response research with a learning health care system? Can we help to grow Canada's domestic scientific and industrial response to pandemics?
- What are the best approaches to communicable disease surveillance in BC? Is this supported by linkage to analysis of the determinants of risk in BC? What is the role of syndromic surveillance? Can novel information sources such as data from wide-scale information platforms be integrated?
- How do we better engage frontline workers in the research enterprise to enhance capacity?
- How can we better assess the values held by our communities to inform health interventions in the time of crisis?
- What changes to health service delivery need to be maintained? How will these be monitored?
- What are the important gaps in public knowledge about the risks and prevention of preventable health conditions, particularly communicable disease?
- How do we best continue population health surveillance to support the mitigation of long-term health effects? How do we better understand and correct health disparities based on structural inequities including gender issues, poverty and racism?
- What innovations in immunization program delivery could expedite our historic effort to deploy COVID-19 vaccine across populations?

Appendix 1: The BC COVID-19 Strategic Research Advisory Committee: Terms of Reference

1. Purpose

Given the urgency to find solutions to accelerate an end to the pandemic and mitigate its effects, the BC COVID-19 SRAC is convened to advise the Province on the priorities, funding, coordination, and dissemination of research projects and their results. The focus is on the BC-specific research needs and strengths in the context of national and global research initiatives.

2. Membership and Leadership

2.1. Members in the committee will be appointed by the BC Ministry of Health (MoH) and the Michael Smith Foundation for Health Research (MSFHR)

2.2. The committee will be comprised of:

- **2.2.1.** Co-chairs: one appointed by the Office of the Public Health Officer (PHO) and one from the MSFHR
- **2.2.2.** At least three subject matter experts from diverse health research backgrounds including biomedical ethics and the Network Environments for Indigenous Health Research
- **2.2.3.** Chief Scientific Officer MSFHR
- **2.2.4.** Members to provide the perspective of health system decision makers including the BC MoH and Health Authorities
- **2.2.5.** Members of the public

3. Mandate and Duties

3.1. The committee reports to the BC MoH Associate Deputy Minister and the PHO through the Chairs

3.2. The committee has the responsibility to advise on:

- **3.2.1.** The understanding of provincial COVID-19 research needs and questions (including those across the healthcare system) as they are being defined
- **3.2.2.** The development of provincial COVID-19 research frameworks as necessary
- **3.2.3.** The identification of emerging research issues and responses
- **3.2.4.** The coordination of research resources and infrastructure to support COVID-19 research
- **3.2.5.** The development and implementation of a provincial knowledge translation strategy to support the translation of COVID-19 research evidence into practice

4. Operations and Documentation

4.1. The committee's work will be defined and guided by a project plan and communications plan

4.2. The committee will meet by teleconference at the call of the co-chairs

4.3. Every effort will be made to schedule meetings to facilitate full attendance by all members

4.4. Decisions will be made by consensus

4.5. The committee may convene working groups to inform specific tasks

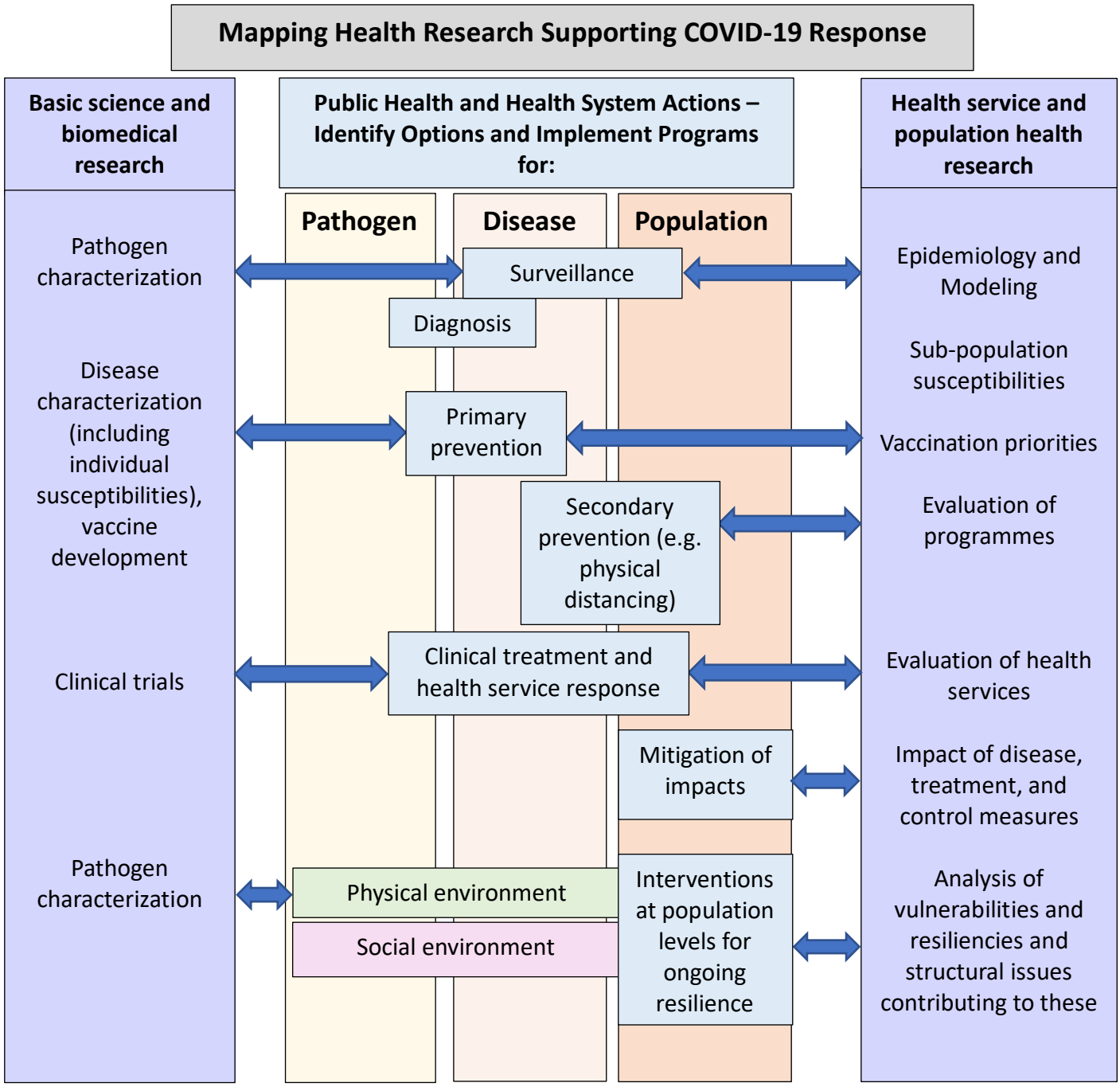
4.6. Administrative support for the committee, including recording of meeting notes, and the development of reports and communication materials, will be provided by the MSFHR secretariat

Appendix 2: A Framework for Research and Action in an Emerging Disease

The diagram below maps the interconnections and dependencies across the range of necessary research in the response to an emerging disease that spans all domains of health research. It is intended to support the researchers, funders, and the public in understanding where the wide-ranging research efforts fit where there are opportunities for coordination and creativity in the approaches to research needs. Based on the widely used communicable disease framework of pathogen, host, and environment, this overview documents the relationships between the areas of research that may appear to be independent but clearly do depend on each other. This is always the case – understanding the biology and medical science are necessary to the understanding of the epidemiology, health service needs, and societal impact of a condition, and the priorities for basic science research can be informed by the human and societal impacts. In an emerging disease, this is even more evident. Planning interventions such as public health control, infection control, treatments, and follow up, all require a detailed understanding of the properties of the infective agent, the vulnerabilities of people (and variations in this), and the social environments where the disease is manifest. An example of this is seen in the ongoing search for evidence-based approaches to personal protective equipment and other environmental interventions that must be informed by the findings first in the laboratory (what should work?) but then in the community (what does work, how well, in which groups, and at what cost?)

The all-important ongoing assessment of balance between the risks mitigated by treatment and public health response, and those created by them requires a detailed understanding of the consequences of both the disease itself and the control measures used. The Ministry of Health has undertaken a program of work to better delineate some of the unintended consequences in BC. This work sits at the interface between the health system processes of ongoing health and health system surveillance and the important specific nuances that can only be drawn through the detailed research needed to inform that surveillance. The response to this pandemic has highlighted the need for detailed and community-specific ongoing monitoring of health risks, determinants, behaviours, services and outcomes.

Research to minimize the impact of this pathogen through prevention of the spread of infection and optimal clinical treatments are immediate primary goals, however equally important is research to understand the factors that have resulted in preventable variability in impact.


Mapping Health Research Supporting COVID-19 Response
Basic science and biomedical research
Public Health and Health System Actions – Identify Options and Implement Programs for:
Health service and population health research
Pathogen
Disease
Population
Pathogen characterization
Surveillance
Epidemiology and Modeling
Diagnosis
Sub-population susceptibilities
Disease characterization (including individual susceptibilities), vaccine development
Primary prevention
Vaccination priorities
Secondary prevention (e.g. physical distancing)
Evaluation of programmes
Clinical trials
Clinical treatment and health service response
Evaluation of health services
Mitigation of impacts
Impact of disease, treatment, and control measures
Pathogen characterization
Physical environment
Social environment
Interventions at population levels for ongoing resilience
Analysis of vulnerabilities and resiliencies and structural issues contributing to these

Appendix 3: Principles and Assumptions for Rapid Research Response

In the first issue of the framework, we identified the following principles and assumptions. These still pertain and serve as an important checklist as we continue to plan our support for the research response.

1. Research efforts should build on BC strengths as a component of the national and global contribution and leverage resources where possible.
2. Research efforts should address BC-specific needs that cannot be otherwise met (for example: BC population serology studies, surveys of the population, and analysis of health care organizational structures in the context of response).
3. Identification of research needs must be based on as wide a range of information and input as possible, including patients and the public, without causing delays in the research response.
4. First Nations in BC have articulated approaches to research that must be embedded in the research enterprise. These address the fundamental concerns of First Nations ethics, cultural safety, trauma informed care, and indigenous approaches and worldviews in the conducting of research and the translation and implementation of research findings.
5. Fostering collaboration will avoid unnecessary duplication of research efforts.
6. Wider use of cross and multi-disciplinary teams, including sequential projects, is needed to address complex questions that cross traditional boundaries of expertise. Where possible, research efforts should be integrated into the health delivery system. Innovative approaches should be considered such as the direct funding of COVID -19 specific research teams in addition to individual research projects.
7. Processes such as data access, ethics approvals, institutional approvals, and access to biobanking should be linked and streamlined to accelerate projects.
8. Diverse methodologies and perspectives, including those with lived experiences, will be required to understand impacts on marginalized and/or vulnerable communities and individuals, including social and cultural impacts. There is an opportunity to build on current strategies for patient-oriented research.
9. Access to participation in research must, where appropriate, include British Columbians who live outside the major urban areas.
10. Expanded sharing of methodologies, materials and data are needed.
11. Existing long-term research initiatives and mechanisms can be mobilized to support some of these specific needs (existing surveys, disease registries, cohort studies).
12. There is an increased need for the synthesis and dissemination of research results in a global environment of emerging evidence.
13. Rapid knowledge mobilization is required.
14. Existing research and innovation support structures in BC should be leveraged.
15. The capacity of research teams may be impacted by the control measures themselves and this must be considered in resource allocation.
16. Diversion of research resources from other critical areas of health research must be monitored and managed.

Appendix 4: Structures and Processes Supporting a Rapid Research Response in BC

The research system in BC is characterized by a number of strengths that position it well for response to the pandemic. Across BC important structures including the BCCDC, the BC Academic Health Science Network, the Michael Smith Foundation for Health Research, Genome BC, the academic institutions and the horizontally integrated health authorities themselves, all supported by clear governance from the BC Ministry of Health, have been able to mobilize and respond to the research needs of the pandemic.

Feedback has indicated that ongoing work is required to monitor and manage these efforts as there is still the perception that there may unnecessary delays related to burdensome administrative processes for researchers. As always, the balance between efficient processes and the necessary attention to accepted research standards requires care and open communication.

Endeavoring to support the coordination of research efforts, new structures have been developed including:

- The BC COVID-19 Clinical Trials Network
- The Clinical Research Coordination Initiative

Existing groups have mobilized and adapted to the needs for responsive research:

- PopulationData BC
- Research Ethics BC
- BC SUPPORT Unit

Several successful virtual research symposia have been convened with BC researchers including:

- BC Centre for Disease Control
- BC COVID-19 Research and Collaboration Symposium: Public Health, Populations, Health Services, and Impacts
- BC COVID-19 Symposium Summary
- Ethical Implications of COVID-19

Appendix 5: BC's Post COVID-19 Recovery Clinic and Interdisciplinary Clinical Care and Research Network

There have been remarkable efforts to organize the researchers themselves in some areas – most notably in the coordination of basic research, clinical trials, and the clinical care of patients who have recovered from COVID-19. These linked initiatives provide a fascinating case-study in the opportunities and challenges of innovative cross disciplinary research, particularly when it is associated with the direct clinical care of patients in a regionalized health system. It has proven difficult to coordinate the interconnected research and clinical activities that must necessarily inform each other. BC has significant strengths in the pre-existing connections between public health and health services in regional health authorities and the provincial coordinating role inherent in the Provincial Health Services Authority. However, this work has also highlighted how very difficult it is to rapidly mobilize innovative work in the setting of a research system based on a competition at every level; between individual researchers, institutions and funding agencies themselves, situated in a regionalized health care system that is based on the same competitive stance for public resources and associated with a complicated commercial research environment. The understanding and management of conflicts are important considerations and require ongoing thought and open discussion. Patients are at the centre of these complex research and clinical environments and coordination of effort will not only improve the efficiency and richness of research output, but it will improve the quality of care.

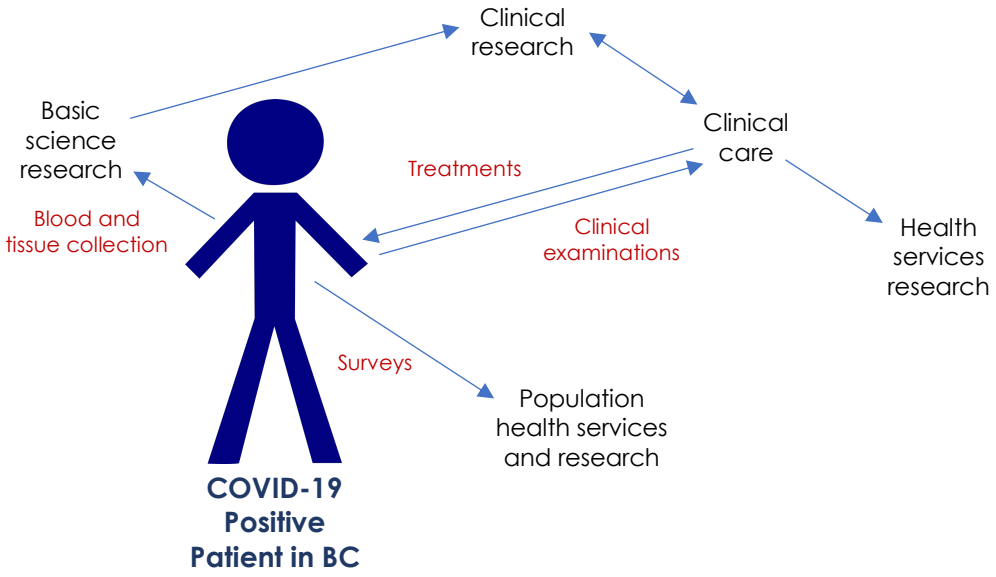


Figure 1. COVID-19 Positive Patients - relationship to research and clinical care

The full environment, however, becomes very complex when considering all of the interconnected administrative, research, and clinical structures and processes that surround the patients. A key component of this system ensuring the appropriate contact of patients who test positive for COVID-19 in order to seek their consent to be contacted for participation in research projects. This has commenced through a number of different channels, including BCCDC , and the REACH platform.

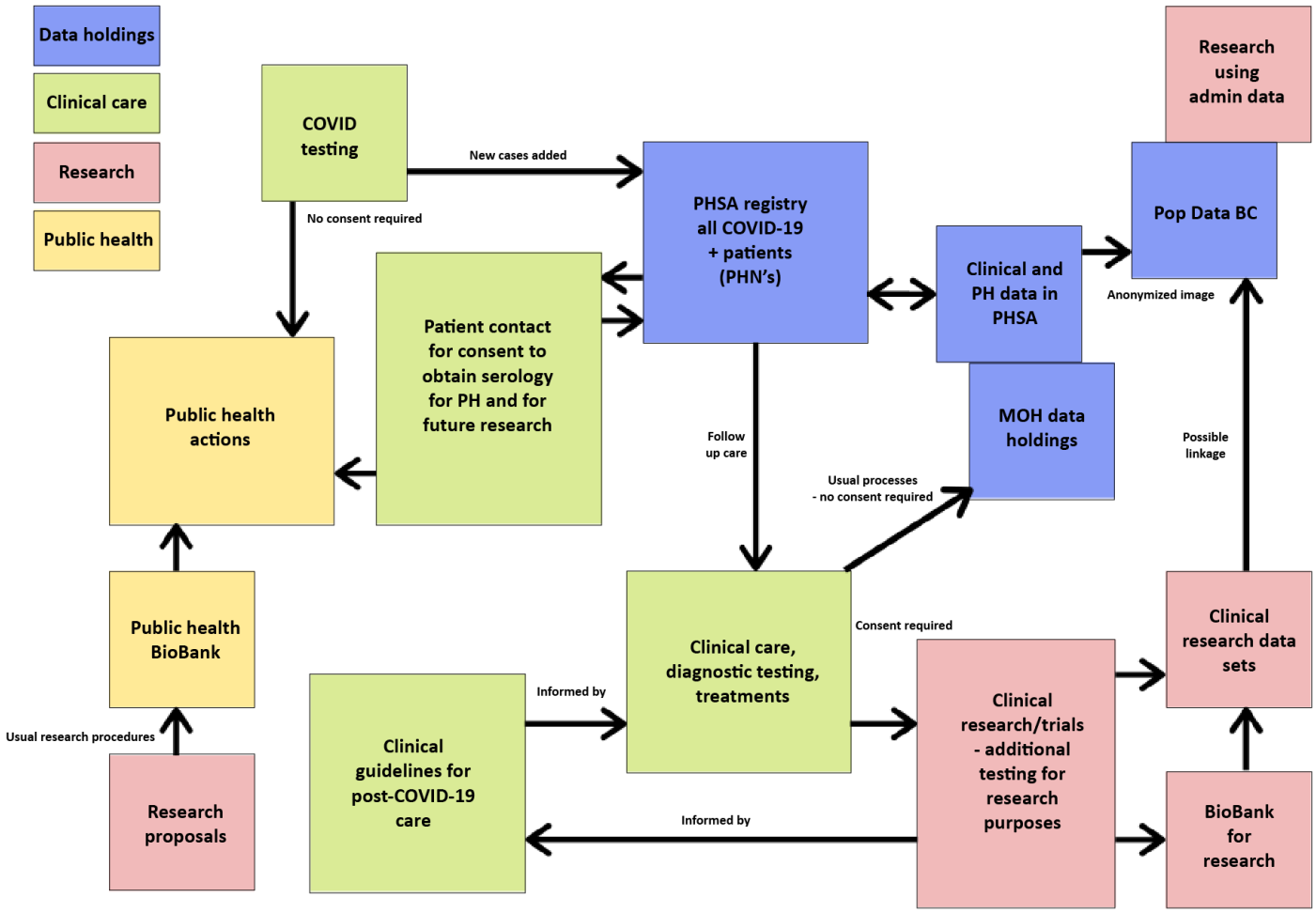


Figure 2. Systems view of COVID-19 patients in BC: follow up for care, research and public health action

Early in the spring, as the care needs for patients with and recovering from COVID-19 became more evident, clinicians and researchers recognized the need to coordinate their interactions with these patients with the view to:

- Delivering evidence-based multidisciplinary follow up care
- Generating evidence to inform this care through clinical research
- Streamlining the process for research participation for patients

These efforts have been supported by other processes such as the BC COVID-19 Clinical Trial Network, the REACH initiative, and others outlined in Appendix 3.

Specific proposals are currently under development and consideration for the creation of a provincial network of post-COVID interdisciplinary health clinics and associated supporting structures.

Still to be determined is a specific approach to the full incorporation of remote, rural, and Indigenous perspective. This cannot rely on multi-disciplinary clinics and the usual approaches to clinical research, but must build on different local strengths, including community-based care. There is an opportunity for a more creative approach to the inclusion of rural practitioners and patients in clinical research to improve care and the applicability of research evidence in these settings.

Activities to date include:

- Launching of the core elements of the network within existing clinics (Respiratory at PHC and VCH, morphed into Integrated PCRC Clinic at PHC, and being developed at VCH and Surrey; Post-Critical Illness Virtual Clinic in FHA; PCP and ER pathways of care; despite engaging medical professionals in the other HA, there are no existing specified clinics or care pathways in Island Health, IH, or NHA).
- The initial 'structure' to enable this coordinated network development, a small executive committee and two working groups: Research Coordination and Clinical Care Coordination Working Groups, have been working to identify this coordinated approach. This structure grew out of the combined recognition by the clinical and research community of the problem from multiple meetings with a large interdisciplinary group (BCCDC, MOH, HA, Universities, researchers, clinicians).

The Executive Committee for this initiative offers the following summary:

"The network would embody key values and principles central to health care: true partnership to include patients as full and respected team members from the outset, with a wide range of clinical specialties, including primary care, research, and public health. We can create a culture of patient-partnership from the ground-up, an approach that will inform all future care of this disease and other novel systemic diseases. The value of the network could enable best outcomes for patients and the health care system as well as potential cost savings. It would also

enable and catalyze research across and between disciplines, enabling discovery and implementation of best therapies and strategies in real time."

From a public health perspective, this model is scalable/adaptable to other diseases, thus whilst initially “post-COVID health clinics” at this stage, these would be adaptable to new novel pathogens, syndromes, and epidemics of public health importance (e.g., opioids, vaping), if appropriate. Given issues related to jurisdictional independence, and unique circumstances of specific HA (including variable burden of diseases), this model of an integrated network is not particularly onerous on any one health authority.

Appendix 6: BC's Research Response to COVID-19

- Currently there are more than 500 COVID-19 research projects underway involving BC researchers over 118 surveys provincially and nationally. These can be accessed and searched through the AHSN Research and Survey Inventories: a comprehensive source that also includes some unfunded and proposed projects. These projects are funded to a value of over $200 M.

- The province is well positioned to coordinate COVID-19 research activities in the province and to derive value from the provincial, federal, and philanthropic COVID-19 research investments.

- Key organizations, such as the Michael Smith Foundation for Health Research (MSFHR), the BC Academic Health Sciences Network (BC AHSN), and the COVID-19 Provincial COVID Strategic Research Advisory Committee (SRAC), are working with the Ministry of Health, other funders, university partners, and health authorities to ensure that BC's health research enterprise is working collaboratively to provide a coordinated, strategic approach to COVID-19 research.

- The MSFHR launched a COVID-19 Research Response Fund worth $2.0 million to support research related to COVID-19.

- Genome BC has responded to the need for research on COVID-19 by launching the COVID-19 Rapid Response Fund. Thirteen projects are currently underway, each awarded up to $250,000 for a total of $1.78 million in funding.

- BC Researchers are also receiving funding for COVID-19 related research from the BC Academic Health Sciences Network, the Canadian Institute for Health Research (multiple funding opportunities), the BC Support Unit, the Natural Sciences and Engineering Research Council (NSERC), the Social Sciences and Humanities Research Council of Canada (SSHRC), Community Living British Columbia, the Bill and Melinda Gates Foundation, Canada's Digital Technology Supercluster COVID-19 Program, and many internal funding opportunities for researchers at BC Research Universities, and other for profit and non-government organizations.

- Private sector and US government investment in BC Biotechnology companies has been considerable.

Appendix 7: Evaluation of the BC Research Response to COVID-19

There has been an unprecedented mobilization of COVID-19 research worldwide resulting in an avalanche of studies, methodologies, and results. BC's health research community has initiated a number of COVID-19-related research and initiatives to contribute to the COVID-19 research response in BC, as well as to contribute to the global research effort. Early on in the pandemic, the COVID-19 Strategic Research Advisory Committee (SRAC) identified a need to bring these individual efforts together through a coordinated COVID-19 research response.

The pandemic has underscored the importance of effective coordination and collaboration between health researchers, decision makers, healthcare professionals, patients, and the public to see that research evidence is used to inform health system response for maximum benefit to patients and the public. Discussions among SRAC, Ministry of Health (MoH), Michael Smith Foundation for Health Research (MSFHR), and BC Academic Health Science Network (BCAHSN) are underway to determine what further actions are required to strengthen coordination of the COVID-19 research response across BC.

The COVID-19 Strategic Research Framework was developed early to guide the research response, with the intention of being regularly renewed as the COVID-19 pandemic and response unfolds. However, it is unclear how well the framework covers the full spectrum of research, how well it is being used to shape the response of the many partner organizations and affiliated researchers, and the extent to which all the necessary partners and stakeholders are engaged in its evolution to ensure a comprehensive, coordinated research response for BC. Evaluation is needed to provide ongoing guidance to MoH, SRAC, MSFHR, and AHSN to strengthen the coordination aspects of the provincial research response, and thus the impact of the response overall.

The evaluation is envisaged to unfold in three phases:

1. **Rapid review and synthesis** to provide an early "snapshot" of actions to date, and learning about the implementation, outcomes, and gaps in the coordination of the research response to date. The rapid review and synthesis will also inform the development of an evaluation framework for the coordination aspects of the response.
2. **Development of an evaluation framework** to provide a clear structure for measuring the success of the coordination aspects of the response (i.e. how, and how well coordination activities are supporting the effectiveness and efficiency of the research response).
3. **Evaluation implementation** to implement and report on the results of the evaluation.

Scope

The focus of the evaluation is on coordination aspects of the research response: how, and how well the coordination supports the impact of the research in provincial priority areas. The impact of the research itself is out of scope, as this will be separately evaluated as part of funders' ongoing monitoring and evaluation programs. The scope will be clarified and confirmed as part of the evaluation framework development.

Guiding questions

The rapid review and synthesis will involve a comprehensive document review and semi-structured interviews guided by the following high-level questions:

1. ***What actions*** have been undertaken to support a coordinated research response?
2. ***What does success look like*** for a coordinated research response? How will we know when we get there?
3. In what ways has a coordinated research response approach ***created or supported the conditions*** for research to influence health care policy and practice? What are some key examples of where policy and / or practice have been influenced because of coordination (e.g. health research + collaboration + shared infrastructure)? What factors made these successful?
4. In what overall areas of research, or research groups, is ***coordination strongest or weakest*** and why? What are the key enablers and barriers to coordination in these areas?
5. Where does ***duplication*** in the system to support COVID-19 research exist, and how might this be reduced through increased coordination?
6. What is ***missing*** from the system that is needed to support better coordination, and how might it be addressed?
7. What is the ***role (actual and potential) of the strategic research framework*** in supporting more effective coordination?
8. Are there any ***unanticipated outcomes*** (positive, negative, neutral) from the coordination work to date?

Key participants

Key participants in the evaluation of the coordination elements of the research response include: Ministry of Health, Office of the Provincial Health Officer, MSFHR, academic leaders, health authority leaders, health research funding agencies, health system leaders, researchers, healthcare professionals, patient partners, and shared platform providers. All these groups will contribute to the rapid review, development of the evaluation framework, and evaluation implementation.

Appendix 8. MSFHR COVID-19 Knowledge Translation Plan

The COVID-19 pandemic has underscored the importance of quickly translating knowledge produced from research to inform public health action. Critical to this is the coordination and collaboration between health researchers, decision makers and healthcare professionals. Knowledge produced from COVID research must be integrated within public health plans and services to accelerate the benefits that can make a real difference to the public and patients. As part of a coordinated BC research response to COVID-19, a range of province-wide knowledge translation[1] activities are taking place to enable the use of COVID-19-related evidence – for example:

- *Planning*: SFU Knowledge Mobilization Hub, UBC Knowledge Exchange Unit, Health Authority Research Departments, University Research Services
- *Collaborating*: BC SUPPORT Unit Regional Centres, University Community Engagement Offices, Ministry of Health, MSFHR and funding agencies
- *Disseminating*: BCCDC Language Guide, AHSN Inventory of Research, MSFHR KT Pathways Provincial COVID-19 Resource Hub, BC COVID-19 Clinical Trial Network, CanCOVID, COVID-END, University Communications offices

MSFHR will facilitate the translation of COVID-19 research evidence in partnership with the BC COVID-19 Strategic Research Advisory Committee and other provincial partners to achieve the following objectives:

1. Directly connect researchers, research users including public and patients, and funders for action on BC research priorities.
2. Strengthen opportunities for knowledge exchange between researchers and researcher users including public and patients.
3. Enhance active dissemination[2] of research evidence produced as part of BC's response.
4. Enhance implementation of research evidence in BC priority areas through researcher/research user partnerships including with public and patients.

[1] Knowledge translation is defined broadly as activities that improve the use of research evidence in practice, policy and further research. They include knowledge synthesis, exchange, dissemination and implementation.
[2] Active dissemination involves identifying key messages from research evidence per target audience (e.g., patients/public; other researchers; media; policy makers), for specific goals (e.g., to inform policy; to generate behavior change; to raise awareness) using appropriate KT strategies (e.g., educational outreach; mass media campaign; IT decision supports).