



Scientific Advisory Committee (SAC) Summative Evaluation Review CIHR Annual Progress Report 2022

COMMITTEE MEMBERSHIP:

- **Dr. John Aucott** (Johns Hopkins University, Baltimore, Maryland)
- **Dr. Alan Barbour** (University of California Irvine, California)
- **Dr. Simon Denegri** (Academy of Medical Sciences, London, United Kingdom) [*Note: Dr. Denegri regrets not being able to provide feedback for this reporting year*].
- **Dr. Maria Gomes-Solecki** (The University of Tennessee Health Science Center, Memphis, Tennessee)
- **Dr. Sally Mavin** (Raigmore Hospital, Inverness, Scotland)
- **Dr. Jean Tsao** (Michigan State University, East Lansing, Michigan)
- **Sarah Merkley** (Patient Partner)

1. STRENGTHS OF RESEARCH PROGRAM

Please comment on the strengths and achievements of the research programs implemented under the Network's Pillars and Committees over the past 12 months. (Maximum 1000 words)

An overall strength of CLyDRN is the all-inclusive approach to research on Lyme disease with each of the Pillars having a unique focus. In the past year, progress was made in all four of the Network's research Pillars. It is promising to see that most of the planned work appears to be back on track following disruptions of the COVID-19 pandemic.

A significant achievement within the past year for **Pillar 1** is that the top three patient priorities and research goals were successfully identified. These priorities seem very attainable to achieve once rolled out. The work undertaken with a consultant appears to have had a positive effect and helped the Pillar to move forward. Despite the delay in Pillar 1's progress, the process that Pillar members (i.e., patients and scientists) persevered through is a success story that can be learned from for all other Pillars and other future endeavors on how stakeholder groups with different values and perspectives can be brought together to make forward progress.

One of the greatest achievements and strengths of the Network in the past year involves the work completed within **Pillar 2** related to surveillance and modelling particularly the advanced development and implementation of surveillance activities. This is especially important as Canada faces increased northern expansion of the range of human-biting *Ixodes* ticks along much of its southern border. This Pillar has shown excellent execution of their program resulting in significant publications. Surveillance in 115 sites all over the country and future expansion of sites in 2022 and 2023 is a major strength. Integrating a One-Health approach,

Veterinary surveillance (ticks and disease) allows for projection of new areas of expansion of Lyme and other tick borne diseases. Another strength in the Epidemiology Working Group was the connection to Pillar 3 and using cases from the Cohort study. Using one resource in multiple ways is a strength and a benefit to the research program.

Within **Pillar 3** there have been nationwide effort to launch the Biobank. The clinical research activity of collection, curation, and storage of human specimens from patients for the Biobank undertaken within this Pillar in the last year, although not fully realized, is a major achievement. The availability of these specimens collected from different locations and over time will be an essential and unique resource for ongoing research in Canada and, potentially, internationally.

Some projects, particularly in **Pillar 4**, have made an effort to include patients throughout the research process, such as the Brokered Dialogue study that involved collaboration with patients at the outset of study design. The Brokered Dialogue project itself is impressive and much progress has been made with Phase 1 of the study. This Pillar was also able to produce a systematic review of research regarding knowledge translation and training of healthcare providers, which is a huge strength. Dissemination and knowledge translation efforts are important to ensure this research gains more traction among those who can benefit the most from this knowledge. This Pillar was able to develop a partnership with eTick, which is a great success and allows for continued partnerships in the future.

The Network continues to demonstrate its strength by incorporating and maintaining meaningful patient engagement. For example, the Network's inclusion of patient representatives throughout the Network's pillars and committees. Further, the Network's focus on the importance of tick-borne diseases addresses many of the issues important to patients. Engaging Indigenous communities in Lyme disease research is very positive and it is important to document and publish Indigenous peoples' experiences and perspectives regarding Lyme and other tick-borne diseases.

Lastly, the Network was successful in creating an online forum during May 2022 that engaged researchers, patients, Lyme disease advocates and other concerned citizens in Lyme disease research. It is commendable that the online forum included presentations not only by CLyDRN scientists and trainees but also by researchers outside the Network. It was a well-attended event and there were also many new stakeholders that attended which has helped encourage new participation within the Network.

2. STRENGTHS OF NETWORK

Please comment on the strengths of the strategies related to the Network's management and governance that have been developed over the past 12 months. (Maximum 1000 words)

Over the past year, the Network underwent a significant transition in their leadership and it is apparent that the transition was effectively executed. During this transition, the Network was able to maintain their focus on important issues.

The progress made in **Pillar 1** reflects positive leadership and organization. The tensions that were evident this time last year within this Pillar seem to have resolved with the recruitment of a consultant to facilitate the setting of research priorities and consensus building.

Management of the Network appears to be running effectively as the Network continues to keep different stakeholders engaged and they maintain regular committee meetings. For example, **Pillar 3** members met monthly over the past year which is a strength as this allows for continuous discussion, evaluation, and communication of the Cohort study and the Biobank study. It is clear that regular meetings are occurring across all Pillars and Committees. This shows that Network members are dedicated and spend time actively engaging in their Pillars and with one another.

The way that the Network has fully embraced the involvement of patient partners within each Pillar and Committee by utilising the framework with which to engage, induct, and manage these partnerships is impressive and should be held up as a model to other such initiatives. It appears that improvements were made in compensation of patient partners and this has helped encourage participation. The orientation of new members to the Network and its research program is well organized and practical. It is also encouraging to note that there has been wider stakeholder engagement during this last reporting period, which can only help strengthen the Network and help drive the work forward in the future.

It is noteworthy that the Network's research program is moving forward despite the challenges inherent in the approach they have undertaken (i.e., patients and scientists working together). It is commendable that the Network is thinking about and initiating plans on how to sustain a future program. The amount of external funding obtained by the Network is commendable. Obtaining funds and the forward planning that is now evident will help ensure the work continues beyond the scope of this Network.

Note: A few SAC members expressed that they could not adequately comment on the Network's management and governance. One member expressed that while they cannot comment on this area, through their observations, there is nothing comparable to the Network in terms of scope and representation of government, academic institutions, and patients in the United States.

3. OPPORTUNITIES FOR IMPROVEMENT

Please comment on the weaknesses and opportunities for improvement of the research programs and the Network's development over the past 12 months. (Maximum 1000 words)

To preface, SAC acknowledges the ongoing COVID-19 pandemic continues to impact the time and personnel that can be applied to achieving CLyDRN's goals. Some areas for improvement listed below may have been part of the initial objectives of the Network and may have experienced pandemic related delays in implementation.

It is noted that **Pillar 1** will no longer use stored bloods to investigate their research priorities and that work on the research objectives will not commence until 2023. There is concern that the protocol decision to use prospectively collected samples further delays the start of the research component of this Pillar. If the proposed research aims to collect their own human samples this should be gathered under the Biobank. Without a well-maintained clinically characterized Biobank, development of diagnostics is not possible.

For **Pillar 2**, maintaining a backbone of surveillance for ticks is important and taking advantage of the Veterinarian surveillance option as they will continue to maintain records of clinical Lyme disease in their area, which is a good sentinel for human Lyme disease.

For **Pillar 3**, activation of the Lunenburg site biorepository was delayed due to equipment delays. This will result in missing the majority of the 2022 Lyme disease season. Because of the seasonal nature of participant recruitment it is essential that equipment and personal are in place prior the recruitment season in the spring and summer of each year.

Another area for improvement under **Pillar 3** is the collection of specimens from a control group. While the collection of specimens from individuals with Lyme disease for the biobank is progressing, it seemed that there are as of yet no specimens from suitable controls. If this reflects a challenge in recruiting controls, there may need to be rethinking of the incentives, including cash rewards, for people to serve as controls. It is also possible that research sites (i.e., those with extensive clinical research activities and resources) are better prepared, staffed, and equipped for recruitment and collection of specimens from healthy controls are at other locations than the sites of highest incidence of Lyme disease. It may be preferable to have, as controls, individuals at geographically low risk of Lyme disease. The problem with controls in a Lyme disease endemic area is they may already have had Lyme disease that was undiagnosed. This Pillar might consider using commercial sources, like BioIVT, where controls can be recruited from areas that are non-endemic for Lyme. Work undertaken in this Pillar may also consider increasing sequence-based genotyping (for example, the *OspC* gene amplified by PCR) of *B. burgdorferi* organisms that have been identified in patients either by PCR or culture. There could also be selective genotyping of organisms identified in ticks and reservoir hosts during the surveillance activities.

It is imperative to secure funding to keep the Biobank operating. The Network should prioritize securing future funding for this work. This is a foundational resource that is essential to future research on diagnostics and detection systems for Lyme and other tick-borne disease. The continued operation of the Biobank can also be leveraged to establish international collaborations.

In **Pillar 4**, the Knowledge Translation Porthole is currently on hold. It is important that valuable communication initiatives are developed to help disseminate information about completed and ongoing projects, both nationally and internationally. Another opportunity for improvement is in the healthcare practitioner study. Increasing the number of interviews with national healthcare practitioners as well as including international healthcare practitioners for comparison could help increase engagement and generate new kinds of knowledge.

Overall, there is opportunity and a need for the Network to define specific milestones for moving forward within a timeline (e.g., securing future funding, wrap-up of current funding, etc.). The Network also has opportunity to improve their fundraising efforts beyond traditional research grant funding. One example is to engage with new potential stakeholders that will donate to the Network. Another possibility is to create partnerships with other researchers internationally that can generate new opportunities for funding while offering avenues for data sharing and comparison. This could increase the relevance and sustainability of the Network's research program.

In terms of community outreach and the inclusion of new stakeholders in the Network, it is recommended that the Network engage vector control associations. Additionally, while Veterinarians are a part of CLyDRN and surveillance activities, it seems there is opportunity to engage the Veterinarian profession as a stakeholder group (e.g., through outreach, education,

and surveillance opportunities). The Network could increase their work with universities and colleges nationwide such as providing information to share with these academic institutions, presenting lectures to students, or having more students involved as participants or researchers.

Additionally, the Network can improve their external communications. For example, a web page could be added to the CLyDRN website for a list of Network-associated publications including hyperlinks (i.e., URLs) to the publications, preferably to open-access versions of the articles that would promote public access and engagement to research. The Network could benefit from making a more accessible and dynamic website. Having more resources available on the website for the general public, such as information regarding LD clinics nationwide, places to drop off ticks for testing, and guidance on accurate LD testing. There is also opportunity to create more online presence via social media (e.g., Facebook, Instagram). Social media could facilitate awareness campaigns to support fundraising and increase public awareness. Securing additional funding for communications is recommended. Funds could be used to hire a Communication Specialist to help manage the website and social media as well as support partnership building with companies or individuals to launch awareness campaigns.

Related to the organization of SAC members, we recommend increasing opportunities for SAC members to ask questions, engage with CLyDRN members, and provide input. In particular, it would be helpful to increase the time allotted for the annual meeting between the Executive Committee and SAC. One suggestion is to have the meeting occur over a 3-hour period to allow time for more questions and discussion. Another suggestion is to include a mid-year check-in.

4. SUMMARY OF PRIORITY RECOMMENDATIONS

Please provide a summary of your review and recommendations for the research programs and the Network's development to address over the next fiscal year. (Maximum 1000 words)

Recommendation 1: Maintaining the momentum that **Pillar 1** has established during this reporting period is important. It is noted that research work is not planned to commence until 2023, presumably because they need to collect sufficient prospective samples. Stored blood and serums, although potentially biased, can still be a very useful resource for such studies and if utilised, could help maintain this momentum.

Recommendation 2: COHORT and Biobank recruitment should continue to be pushed, including the recruitment of controls. As mentioned earlier in our review the data and samples resulting from this work will be invaluable and will help attract further funding.

Recommendation 3: It is important that the Network continues to work on their forward planning and fundraising to ensure the longevity of this work. Future work could be more streamlined and focused as the scope of the initial plan was ambitious especially with the four different Pillar areas. Prioritize the areas that need to be completed within the next few years and allocate funding as appropriate. Strategic planning could be led by a professional facilitator (perhaps one of the social scientists in the network can fill this role or hire someone from the outside the Network). This planning would be helpful not only in supporting the identification of funding opportunities but for prioritizing efforts and coming up with alternative ways to carry out the network's goals and objectives.

Recommendation 4: Improving external communications to allow for the dissemination of the incredible work carried out by this Network to national and international audiences should be a priority. Continuation of the Knowledge Porthole work might support improvement of knowledge translation and communications more broadly. Increasing knowledge translation to the general public through multiple methods (e.g., social media, universities/colleges, general public, researchers nationwide/internationally, educating health care providers) is worthwhile. Creation of social media sites can support increased public awareness of the Network and the development of a more dynamic website that allows the public to access and engage with research and resources developed by the Network.

Recommendation 5: If resources are an issue and survival of the Network is at stake a recommendation is made to focus on publishing all data acquired on surveillance in Pillar 2 (and other pillars) and securing funding to keep Pillar 3 running to establish a Canada-wide Biobank that can be accessed by the research community at large. This could be major accomplishment of this Network.

5. ADDITIONAL COMMENTS

(Maximum 1000 words)

- A major success of the CIHR funded program has been the establishment of the patient cohorts and biorepository under **Pillar 3**. Measures of this success include both significant recruitment at the initial site in Ontario and the ability to obtain positive cultures of *B. burgdorferi* from patient samples. It is imperative that this significant work continue and for an ongoing multi-year funding to be secured. It would be a tragic loss of investment of the substantial upfront costs if this program were to shut down at the end of its CIHR funding.
- The network has the opportunity to conduct some formal scholarship on patient-scientist engagement. For example, is the Brokered Dialogue film going to be the only product or will there be an analysis conducted on the Brokered Dialogue process? Analysis of the brokered dialogue process is an interested opportunity.
- With respect to **Pillar 3**, recovery of isolates of *Borrelia burgdorferi* from human cases is especially important because of the association of strain genotypes with invasiveness of the infection, with certain reservoir hosts, and with different geographic regions. While eventually the strain typing could be done with a single PCR target with sequence, characterization of a certain number of humans isolates of *B. burgdorferi* infection acquired in Canada provides a solid foundation for future studies with higher throughput capacity. Isolation in culture would also be important if there is further evidence of other species of *Borrelia*, like *garinii*, in Canada.
- Another comment related to **Pillar 3**, Biobank: there is a minimal number of participants so far in the Biobank study and this is understandable due to there only being two sites accepting participants. The two sites are hospitals, which in my perspective as someone with Lyme disease, may be a con to the success of this study.

Not many diagnosed LD patients go to the hospital. Most LD patients have positive test results from the USA or Germany so will be viewed as someone with not legitimate test results (not a Canadian positive). There is a generous portion of ER physicians and nurses that lack education, understanding, and respect towards LD patients. Positively diagnosed LD patients infrequently visit the ER due to our test results always showing as “normal”, and the physicians not being able to figure out what is the cause. It is easier for a LD patient to seek help from their Lyme Literate Medical Doctor, Lyme Literate Naturopathic Doctor, or their Family Doctor. The ER may see more newly diagnosed LD patients, or patients that do not know they have LD yet. Expanding to more sites in different cities, provinces, and diverse locations (LD clinics, naturopathic offices, universities/colleges, urgent care clinics, family doctor offices, chronic pain clinics), would allow for more accuracy and diversity among patients.

- A strength of the Network is that the Pillars are solely focusing on Lyme disease, with the goal of expanding to all tick-borne diseases. There is opportunity to expand and include vector-borne diseases, but this may take away from the original outlook of the Network. Lyme disease is a huge public health threat in Canada, and the Canadian government fails to realize the epidemic of Lyme disease and coinfections. If the Network built upon this and focused on vector-borne diseases or other diseases as well, it would take away from how under-recognized and dismissed tick-borne disease is in Canada. Using Lyme disease and other tick-borne illnesses anchors the focus of the Network. For now, the Network should continue to focus on sticking with tick-borne diseases only, so that more funding is directed to this area to allow for more understanding, education, and expertise.