



Scientific Advisory Committee (SAC) Review CIHR Annual Progress Report 2021

COMMITTEE MEMBERSHIP:

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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 24 months. (Maximum 1000 words)

The four pillars are well-designed and all have active involvement of members. The pillars encompass important research topics that impact people living in Canada.

Pillar 1 (Diagnostics):

Pillar 1 has demonstrated flexibility to reorient their research informed by patient priorities gathered by PCAC through a priority setting process. This process showed innovation and capacity to build bridges between the medical research community and patient representatives. It is positive that research objectives continue to be refined collaboratively through deliberative processes closely involving patient-partners and scientific researchers.

Pillar 2 (Prevention and Risk Reduction):

This pillar has established a robust portfolio of projects and successfully recruited students and post-doctoral fellows into the research program. Although tick surveillance during 2020 was not possible due to the pandemic, good progress was made during 2019 and if this continues throughout 2021 and 2022 it should provide excellent data.

Pillar 3 (Clinical Science and Health Services):

It is promising to see that cohort and biobank protocols, agreements, and databases are all set up and recruitment has now started. The ability to be open for enrollment for the 2021 Lyme season is a tremendous achievement which resulted in the enrollment of 18 patients this season (to date) and the biobanking of the associated blood samples.

In the recruitment process for cohort and biobank studies it was noted that cases were being missed overnight and weekends. The group has shown capacity to adapt their research practices by modifying protocols to address the problems, such as attempting to enlist local family medicine/GP offices to help with recruitment.

Pillar 4 (Patient & Community Engagement, Training, and Knowledge Translation):

A diverse and creative portfolio of projects led by both members of the faculty and patient representatives show promise. For example, the interview project with healthcare providers is very well developed from a methodological perspective. The diversification strategy used to recruit participants is thorough. The research team (Dr. Rylan Egan, Madison Robertson, Dr. Angela Coderre-Ball notably) is extremely receptive to patient partners' input. The way the research team deployed a participatory approach, notably when reviewing protocols and manuscripts, seems seamless and natural.

The brokered dialogue project is impressive and makes use of a promising innovative methodology (e.g., use of film-based content creation approaches oriented towards deliberation) and consistently with participatory-action research. This project shows promises to help bridge some of the tensions between stakeholders with diverging perspectives which is a major issue in discourses around Lyme disease. It is also notable that the project will shed light on "Lyme practices" both from multiple perspectives including patients and clinicians.

The reviews of training initiatives and grey literature materials on Lyme disease are highly relevant for clinical practice.

With the help of Pillar 4 members, the PCAC has been actively engaged throughout the 4 pillars of research and have had significant contributions and input throughout.

It is promising to see that the knowledge porthole will include nationally-available modules on contentious or uncertain topics and that each module will provide information on knowns and unknowns. It is commendable that the Network aims to highlight scientific uncertainty in modules targeting healthcare professionals. Acknowledging uncertainty as opposed to cultivating rigid ways of thinking paves the way for future research on Lyme disease.

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 24 months. (Maximum 1000 words)

SAC commends the network for the progress made within the research network despite setbacks related to the COVID-19 pandemic. Flexibility and adaptability in the face of the pandemic demonstrates strength in Network management and governance.

The Network also demonstrates effectiveness at working as an interdisciplinary team and one that encourages active involvement of student trainees and postdoctoral fellows. The active involvement at multiple members will help to ensure that research will be ongoing. In particular, the involvement of PhD students and post-docs will ensure that there is a pool of individuals who are building their career in the field, which will lead to future research projects and new groups of doctoral students.

CLyDRN involves a variety of stakeholders as evidenced in the pages 19 and 20 of the report (e.g., patients, clinicians, healthcare system managers, government representatives, industry, media, students, advocacy groups, etc.) and has shown initiative to include more stakeholders (e.g., stakeholder mapping). The Network's willingness to extend stakeholder participation beyond patient partners to include community leaders, representatives of professional associations whose members are regularly exposed to ticks, etc., is exemplary and very well aligned with the tenets of participatory research.

The Network is using a productive working model for including patients and showed progress related to patient/community engagement (e.g., framework for patient compensation). It is very promising to see data on the number of patients and community members involved in the Network and plans to involve further stakeholders. The Network shows strong efforts to ensure good patient partner representation in its events including the Annual General Meeting and Lyme Disease Awareness Month.

It is noteworthy that the Network continues to seek opportunities for funding and have been successful in obtaining funds. For example, the recent grant obtained by Dr. Rob Colautti to fund interdisciplinary research involving early-career researchers from health sciences, social sciences, and natural sciences seems to be a promising opportunity.

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 24 months. (Maximum 1000 words)

While there are many strengths of the Network and its research program, SAC would like to see certain goal achieved or progress made in these areas over the next project period:

Pillar 1:

There is concern regarding the lack of progress made within Pillar 1 and the fact that there still seems to be a lack of clarity regarding the main goals and whether it is possible for a full agreement to be achieved in a timely manner in order to fulfill its goals. It is commendable that a consultant, who has experience in working with patient groups, has been recruited to aid this process. Questions remain as to whether the consultant, while playing a valuable role, has the in-depth knowledge and expertise required to formulate the best study design and methodology.

While it is commendable that the aims of the diagnostic research will only be conducted explicitly in response to patient-identified priorities it raises questions about whether this process has become too prohibitive and whether the scientists/clinicians should be given more of an input.

There needs to be more explicit identification of which assays will be recommended for use as tier 1 and tier 2. For example, will the products be federal agency approved commercial source or a reputable laboratory in-house product? Specificity will help avoid ambiguities that can contribute to distrust of diagnostic assays.

Concern about the novelty or level of innovation within the proposed research plans of the Pillar. For example, Lyme disease can be extremely complex and involve multiple systems and organs. The Pillar does not seem to be focused on these issues, with more of a focus on early Lyme and not chronic Lyme disease.

The opportunity and arrangements in progress to obtain specimens from provincial labs has been identified and would represent a significant opportunity to proceed with research into diagnostic testing and avoid the prolonged waits for samples to be available from the cohort and biobank studies of Pillar 3. The lack of well characterized samples from patients with chronic Lyme/PTLDS is a major roadblock to the goal of an initial focus on biomarkers for this condition. Perhaps a study focusing on under-recognized sources of early misdiagnosis with accepted pathogens like *B. miyamotoi* would be a good first project that would address aspects of misdiagnosis as a risk for later complications.

It is apparent that there is some conflict and difficulty in getting consensus on research directions. The Pillar might also consider some strategic planning techniques such as Technology Roadmapping (TRM). TRM is a process where a shared vision is created and then corresponding technologies/research are identified to achieve the vision. The technologies and research are then studied and a plan is created in how to achieve them by working backwards.

Pillar 2:

Although environmental reservoir targeted applications should not interfere with human targeted applications it may be interesting to find out public sentiment on application of these measures if a Lyme disease vaccine is approved for human use.

Another opportunity is to expand the scope of testing in Pillar 2 for detection of *Borrelia mayonii*, another (less common) cause of Lyme disease in Canada. Along the same lines, it might be useful to also test for co-infections (as has been done in some studies) since we know that the presence of co-infections can have a negative impact on Lyme disease. Testing could be expanded to use 16S rRNA gene testing for broad range detection of bacteria.

Pillar 3:

It will be important to ensure that sample acquisition remains on track in order to achieve the proposed goal.

There is concern is that biobank samples are only to be taken at baseline and after 1 month and there is to be no further follow-up sample collection. The Network is going to great lengths to set up a Cohort study and biobank and may be missing out on an extremely valuable resource by not collecting follow-up samples, even if it is just clotted blood samples. Consider rethinking this strategy.

Strongly encourage CIHR to consider extending the funding available for this project. A huge amount of groundwork has been laid for this project and it would be remiss to not allow the project to reach its full potential and ensure all the activities are completed.

Pillar 4:

It would be a laudable objective to aim for 2-3 papers about the Network's approach to public involvement published in academic journals (including those focusing on patient/community engagement).

It is also notable that patient/community engagement in things like data analysis has yet to happen and this goal must continue in order to achieve engagement throughout the research process. By involving patient partners in this process care ought to be taken to ensure they are not further burdened by engaging in analysis. One suggestion is to summarize data so that time spent by patient partners on reviewing analysis is optimized.

Developing a patient/community engagement training programme for researchers may help with further engaging patients/community in research processes. This type of training program for researchers is essential if engagement is to become sustainable in the Network.

There was agreement with the report statement about the need for more diversity in patient and community engagement. Diversity needs to be a strong future focus particularly with respect to the engagement of Indigenous communities.

There appears to be ongoing struggles with reaching out to the wider Lyme Disease advocacy community and in broadening engagement across all provinces. A pragmatic approach is encouraged here. For example, it is better to see one more province on board next year than very little progress across all the provinces and better to have 1-2 advocacy groups than attempting to reach all.

The annual report highlighted problems with patient burnout and the apparent lack of interest expressed by some patient partners. This is a worrisome and should be addressed by discussing with members of the PCAC. Questions to consider: Is it a situation that patients are not valued for their contributions (compensation is not the only way to value)? Are patients being discounted (inadvertently or deliberately) by not being kept in the loop?

Comments for all Pillars in the Network:

The Network should aim to have patient partners included as co-applicants on research and as co-authors on research papers. In the least, manuscripts written by Network members ought to involve a few patient partners to review manuscripts to mitigate potential biases. This can help prevent issues where researchers affiliated with the Network publish papers that misrepresent the perspectives of patients or patient organization (e.g., Journault et al., 2020). When papers are published that reinforce the divide between patient groups and the medical community it undermines the Network's effort to build bridges between these stakeholder groups. However, the involvement of patient partners in the revision of manuscripts in Pillar IV is exemplary so the case highlighted above may be an outlier.

A potential weakness is that the Network relies significantly on volunteer efforts, and therefore progress can be limited by participant time and interest. This is somewhat offset by the involvement of academics and ongoing PhD student projects since these individuals have incentives to complete projects to adhere to grant schedules and graduate students. The use of paid consultant (e.g., for design of clinical studies) is another way to ensure that things get done (although oversight of these individuals is still needed).

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)

In summary, the research program underway represents a significant and comprehensive portfolio to address many of the important research questions of Lyme disease facing the Canadian population. To strengthen the continuation of the research programs and further develop the Network, we offer these key recommendations:

- Agreement and finalization of the research goals for Pillar 1 as soon as possible to allow the seed grants to be distributed and the research to be carried out before the end of the project term.
- Continued focused efforts on the recruitment of patients for the biobank and cohort studies of Pillar 3. And, further consideration should be given regarding the collection of follow-up samples.
- Expanding testing for *Borrelia mayonii* and at minimal consideration of other strains, such as Euro-BBsl-b.garini, b.miyamotoi. Testing for co-infections should also be considered.
- Secure alternative and additional sources of funding to ensure that current research projects can be finished. Further to this, determine methods for continuing the work of the Network if grant funding ceases (i.e., contingency plans).
- Increase diversity of patient/community engagement while prioritizing quality involvement over quantity. A focus on quantity may lead to tokenism if implemented incorrectly.
- Increase involvement of patient in full-spectrum of research practice by including them as co-applicants and co-authors.
- Invite at least one patient partner to review all manuscripts before their submission to avoid publishing analyses which perpetuate the negative portrayal of Lyme disease patient groups.
- Given the reliance on volunteers, consider methods for ensuring progress and reducing potential burnout particularly among patient partners. There may be additional opportunities for paid positions including consultant work.
- Ensure that the knowledge porthole will not be redundant with existing Lyme disease resources developed by Canadian and American medical associations and provincial organizations.

- Ensure that the support provided by the Network to professional bodies to develop Lyme disease guidelines will be timely and useful while considering recent initiatives that have already led to improved guidelines (e.g., INESSS).

5. ADDITIONAL COMMENTS

(Maximum 1000 words)

- It was helpful to see some data on the number of patient and community stakeholders involved in the Network. It would be helpful to have more data on involvement of stakeholders: Is there any diversity data available for this community? How close are you to reaching the 50% patient partners on committees, a goal cited in the governance section? This quantitative data could be helpful in telling the story, and some of it might be used to greater effect in the executive summary. Also, what is the justification for having 50% patient partners?
- With respect to the scoping review on Indigenous peoples experiences and perspectives on Lyme disease the literature on this topic may be very sparse. It might be useful to broaden the scope of this scoping review to encompass patient perspectives, more broadly, on Lyme disease care and include a section specifically on Indigenous experiences. Alternatively, PCAC could be consulted to better delineate the scope of the literature review (if these consultations have not taken place). If there is sufficient literature on Indigenous experiences the scoping review could be relevant and useful.
- More description could be provided about the causes of resistance among Lyme disease advocacy groups. Is it resistance to the Network, to research generally, to institutions, or all of the above?
- There is an opportunity within the Network to study the changing perspectives of those participating within the research Network (i.e., scientists, patients, students, etc.). For example, the Network could consider examining changes in knowledge, attitudes, beliefs, and practices of the Network participants as time passes and how these changes affect Lyme disease prevention, diagnostics and treatment.
- A BMJ Article of interest about researcher training programme in UCL London might be helpful: <http://bmjopen.bmj.com/cgi/content/full/bmjopen-2020-047995>.
- Question remains about the usefulness of the knowledge porthole and whether it will be redundant with existing clinical practice guidelines and knowledge translation tools developed by Canadian and American medical associations and provincial organizations (e.g., INESSS in Québec)?
- The methodology deployed through the priority settings exercise with patients for Pillar 1 is unique and might act as a useful reference to others involved in patient engaged research. Consider sharing/publishing about this process.

- Question: Can CLyDRN clarify their relationship with the Public Health Agency of Canada (PHAC)? Their stances on Lyme disease appear to be similar which suggests there may be influence from PHAC within the Network. This is concerning if CLyDRN's mandate is to improve what we know and address knowledge gaps.
- The report is short on recommendations or requests of the funder – what could CIHR be doing to help/support the Network further?
- At times, it can be confusing for patient partners who are sporadically involved to stay up-to-date regarding the research progress within the Network. The newsletter introduced about a year ago and sent around every four months is useful in that regard.
- Stylistic comment: The annual report executive summary provides a very comprehensive overview of all the CLyDRN achievements of the past year. However, it is dense at times. It would be helpful to have a few bullet points at the beginning which highlight the key achievements or milestones of the year.
- Stylistic comment: It would be helpful to have a statement from the PCAC included in the report, perhaps as an appendix. While the report is fulsome in discussing patient/community engagement, at times their voice is lost.
- A patient partner who is a member of SAC has expressed concerns about the leadership of Pillars 1 & 3. A report detailing these concerns can be provided upon CIHR's request.