Written Submission for the Pre-Budget Consultations in Advance of the 2020 Budget

By: ALS Society of Canada

August 2019

RECOMMENDATION:

That the Government of Canada invests $35 million over five years to fund CAPTURE ALS, a Canadian-led open science platform of comprehensive biological data from 1,000 Canadians living with ALS that will enable the study of ALS heterogeneity to strengthen clinical trials and accelerate therapeutic development.

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An Urgent Need

Released in June 2019, *A Dementia Strategy for Canada* outlines the importance of urgent investment in brain health, particularly in diseases that commonly occur in an aged population. As Canada's population continues to live longer, the prevalence of neurodegenerative diseases, where aging is a major risk factor, will continue to rise and represent a growing economic challenge[1].

One of the most prominent neurodegenerative diseases is amyotrophic lateral sclerosis (ALS). ALS is a terminal disease that paralyzes people because the brain is no longer able to communicate with the muscles that we are typically able to move at will. Over time as the living wires that connect our brain and muscles, called motor neurons, break down, someone living with ALS will lose the ability to walk, talk, eat, swallow, and eventually breathe. Approximately 3,000 Canadians are living with ALS at any given time.

With no cure for ALS, and few treatment options available, 80% of people with ALS will die within two to five years of diagnosis. Each year approximately 1,000 Canadians will learn that they have ALS, and another 1,000 Canadians will die from the disease. ALS affects individuals and families in the prime of their lives. Anyone can develop ALS regardless of gender, socioeconomic status, geography, or race.

Moreover, ALS results in many broader societal and economic impacts. People diagnosed with the disease are ultimately forced to leave the workforce due to their progression. The same is often true for family caregivers who commonly take leave from work to provide needed care to those living with the disease. Families living with ALS often face a $150,000 to $250,000 financial burden over the course of the disease due to expenses for treatment, care, and equipment needs as well as lost income[2]. This does not include the cost to the healthcare system when people living with ALS experience lengthy hospital stays due to a lack of appropriate home or community care.

Translating Discovery into Treatment

The most common genetic cause of ALS, called C9ORF72, was discovered in 2011. Since then, research discovery has accelerated at an unprecedented pace, and we are getting significantly closer to understanding how ALS is caused. While we have come a long way in developing animal models of ALS, there is still more to be done in understanding human ALS; not enough is known about the disease in people to translate many of the recent laboratory discoveries into effective treatments and therapies.

This is primarily due to the fact that ALS is a heterogeneous disease, meaning that the site of onset, rate of progression, cases of frontotemporal dementia (50% of people with ALS), and potential environmental triggers differ from person to person.

Current mechanisms for biological sampling and data collection from people diagnosed with ALS are very limited. When a person living with ALS dies, so too does our ability to learn from their unique form of the disease. Better data collection is needed to understand why ALS is different in each person and to develop personalized medicine that will align with different prognoses.

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[1] GBD 2015 Neurological Disorders Collaborator Group. Lancet Neurol. 2017 Nov;16(11):877-897

[2] Economic burden of amyotrophic lateral sclerosis: A Canadian study of out-of-pocket expenses," by Matthew Gladman, Celina Dharamshi and Lorne Zinman, published in Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2014.

CAPTURE ALS

CAPTURE (Comprehensive Analysis Platform to Understand, Remedy, and Eliminate) ALS will address the heterogeneity of ALS. It is an innovative initiative that will leverage a $35 million research investment over five years for a national collaborative effort to tackle the most important remaining hurdle in the ability to develop new treatments – and possibly cure – ALS.

Led by a group of world-renowned Canadian ALS experts, CAPTURE ALS will be driven academically at four existing ALS centres of excellence across Canada -- Edmonton, Toronto, Montréal, and Quebec City – with the principal investigator located in Alberta. The platform will merge existing research programs into a singular and powerful resource for studying ALS data, supporting the collaboration that already exists within the Canadian ALS research community and connecting into other international initiatives to create a global network of human ALS resources and information, shared freely through open science.

Collaborative research through open science is critical to studying ALS due to the limited global patient, financial and human resources to solve the disease in any one place. CAPTURE ALS emphasizes the international sharing already demonstrated within the ALS research community, creating a potential model for how other unsolved diseases can accelerate their impact and discovery.

Leveraging state-of-the-art technology, CAPTURE ALS will build on current ALS research to collect and use biological, environmental, genetic, clinical, and imaging data of 1000 Canadians living with ALS to create individual "fingerprints" or biosignatures of the disease. These comprehensive biosignatures will be contributed to open science, enabling researchers across Canada and internationally to dive deeper into the heterogeneity of ALS.

To truly understand the effectiveness of potential therapies and which individuals might benefit from certain experimental therapies, ALS researchers must be able to differentiate patients based on how their ALS progresses. This is critical to creating a future where each person diagnosed with ALS can receive treatment that responds best to their specific disease variation.

Understanding the heterogeneity of ALS will not only accelerate the development of therapies for ALS; it will also help clinicians and researchers create stronger clinical trials. Being able to identify how ALS will manifest and progress in one person compared to another will enable researchers to design clinical trials that no longer amalgamate everyone with ALS into one data set. The ability to take a different approach to clinical trials based on disease heterogeneity will provide the means for researchers to understand how disease progression is being altered, delayed, or even stopped by a potential therapy. Moreover, pinpointing whether a potential therapy is more effective for a particular patient group will also quicken the pace at which therapies move towards market approval.

CAPTURE ALS involves four main stages:

1) **Data Collection:** Over multiple visits, biological samples such as blood, urine, cerebrospinal fluid, and stem cell samples will be taken to monitor disease progression. Information on other variables such as risk factor exposure, socioeconomic status and race will also be collected.

2) **Creation of Biosignatures**: Using a combination of established and cutting-edge scientific experiments, the biological samples will be analyzed. Modern machine learning techniques will then be used to create a "fingerprint" or biosignature for each individual participant. The biosignature samples will be de-identified for privacy.

3) **Open Science Contributions**: The ALS biosignature data will be made available through an open science database to aid in collaboration with international ALS initiatives. Global scientists will be able to analyze the biosignatures further and add to our understanding of ALS.

4) **Promotion of Future Research**: The collection of the samples and data from each participant effectively creates a permanent resource to study individual human cases of ALS. The remaining samples will be stored in a national ALS biorepository network to enhance future studies and harness emerging technology for future research.

Ultimately, by deciphering heterogeneity in ALS, CAPTURE ALS will lead to the discovery of new therapies, enhance the success of clinical trials, reveal who is ideal for specific treatment regimens, and accelerate market approval and access of effective therapies. These outcomes will see the burden of ALS significantly decrease, resulting in people living longer and contributing more productively to society.

A Community that is Ready

ALS is a disease that cannot wait, and the patient and research community is ready for answers. The ALS community measures time not by months or years, but by loss – loss of function and loss of life. Every week that goes by without a cure or effective treatment, approximately 20 Canadians die of ALS.

Moreover, parliamentarians witnessed firsthand the tremendous impact of ALS following the diagnosis of the Honourable Mauril Bélanger. On April 5, 2017, the House of Commons unanimously adopted Private Members Motion M-105, which called on the government to *"play a leadership role in supporting ALS research, and to support national efforts to find a cure for ALS at the earliest opportunity."*

Furthermore, Canada's ALS research community is a credible and well-connected network of some of the world's most respected academics, clinicians, and scientists. The community collaborates and innovates through the Canadian ALS Research Network (CALS) and at the annual ALS Canada Research Forum, as well as internationally through initiatives like Project MinE. Through the Canadian ALS Neuroimaging Consortium (CALSNIC), a project funded through the ALS Canada Research Program in partnership with the Brain Canada Foundation, the ALS research community is experienced in conducting multi-site research initiatives. As well, since 2014, the ALS Canada Research Program has been a partner to the Brain Canada Foundation. This collective experience demonstrates that Canada's ALS research community is well-positioned for the next landmark medical discovery and to lead the next generation of global ALS research.

Current Challenges in the Funding of Canadian Health Research

In 2014, $11.5 million of funds donated by Canadians through the ALS Ice Bucket Challenge were directed to the ALS Canada Research Program, with an additional $10 million matched by the Brain Canada Foundation (supported by federal funds from Health Canada) for a total of $21.5 million in dedicated ALS research investment over five years. The investment of those funds is now complete and has resulted in building the foundation of scientific resources and discovery that makes CAPTURE ALS possible.

Furthermore, mechanisms for funding networked health research in Canada through CIHR and Tri-Council (CRCC) tend to prioritize investing in research projects focused on broader health issues, such as neurological disease instead of ALS. Additionally, the grants awarded tend to support disease areas that are considered more prevalent than ALS and also have other fundraising capacities and resources to develop grant applications and partnerships. This has resulted in an environment where a disease like ALS cannot successfully compete for resources through traditional funding pockets.

Consider that from 2012 to 2017, CIHR invested just under $16 million in research related to ALS, which included funding for research projects examining many related diseases, such as Parkinson's disease, and other neurodegenerative disorders. Just over $10 million was invested in research directly related to ALS, an amount that is far less than the annual commitment to many other diseases. Additionally, when comparing this amount to the total CIHR funding profile from 2012 to 2017, less than two-tenths of one per cent (0.19%) was invested in grants directly related to ALS research. For a terminal disease like ALS, less than 0.2% of overall federal health research funding is not enough – nor does it demonstrate the government is holding itself accountable to the commitment of M-105.

Budget Request:

An investment of $35 million over the next five years to the principal investigator's academic institution to fund CAPTURE ALS, a ground-breaking Canadian led open-science platform of comprehensive biological data from 1,000 Canadians living with ALS, enabling the study of ALS heterogeneity to strengthen clinical trials and accelerate therapeutic development.

This critical funding will be leveraged to support impactful and evidence-based research directly focused on developing effective treatments that will have a meaningful impact for those living with ALS.