Amyloidosis Research

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Cardiac amyloidosis research at UBC

- Industry-sponsored trials
  - ATTR-ACT OLE
  - ATTRibute and ATTRibute OLE
  - CardioTTRansform
  - Novo Nordisk Phase II
- Investigator-initiated funded research
  - Amyloid diagnostic study
  - HF hospitalizations in amyloidosis
- Local amyloid database
  - Anemia in amyloidosis
- Canadian Registry for Amyloidosis Research

Canadian Registry for Amyloidosis Research

APRIL, 2023

CANADIAN REGISTRY FOR AMYLOIDOSIS RESEARCH

lumiio

Rationale for a Canadian Registry for Amyloidosis Research

- Much of clinical practice driven by anecdotal data, small case series, extrapolation of findings in other populations
- Low prevalence of diagnosed disease limits size of single-centre studies and rate of recruitment to clinical trials
- Existing registries focused on one subtype, one aspect of disease management, or single centre
- A multi-institutional registry can collect data to adequately power observational studies and help identify patients for prospective trials, addressing important knowledge gaps
- Can also facilitate decision making in resource-limited health care system
- Canada is well-suited for the development of a national registry due to relatively small number of academic centres and high level of established collaboration

CRAR: Primary Objective

- Improve outcomes of amyloidosis patients through enhanced understanding of optimal diagnostic and management strategies in Canada

CRAR: Secondary Objectives

- Foster collaboration across centres that provide multidisciplinary care for amyloidosis patients
- Advance our understanding of the natural history of amyloidosis and its response to conventional and disease-modifying therapies
- Understand current variations in clinical care setting and disease management in Canada
- Attract international trial opportunities by making Canada more congruent with the international amyloidosis community
- Allow observational studies of large numbers of patients in a multi-centre setting
- Enable clinical trial development with rapid patient accrual
- Raise awareness of amyloidosis and its management through engagement with partner organizations

CRAR: Study Design

Study design:

- Prospective multicentre patient registry

Inclusion Criteria

- Confirmed diagnosis of amyloidosis based on one of the following:
  - Tissue biopsy demonstrating amyloid deposition
  - Nuclear scintigraphy consistent with ATTR amyloidosis
  - Genetic testing revealing a disease-causing mutation in the TTR gene or another gene associated with hereditary amyloidosis (e.g. ApoA1)
- Resident of Canada

Exclusion Criteria

- Failure to provide signed informed consent by subject or designated decision maker

Study sites

- Initially 6 academic centres across Canada, plans to expand to 12 or more centres

Data collection

- Baseline and annually for duration of consent

CRAR: Data Collected

Demographic information	Diagnostic procedures performed	Results of investigations (laboratory, imaging, genetic testing)
Therapies received	Current and ongoing health status (including mortality)	Patient-reported QOL measurements

Project Operations

01

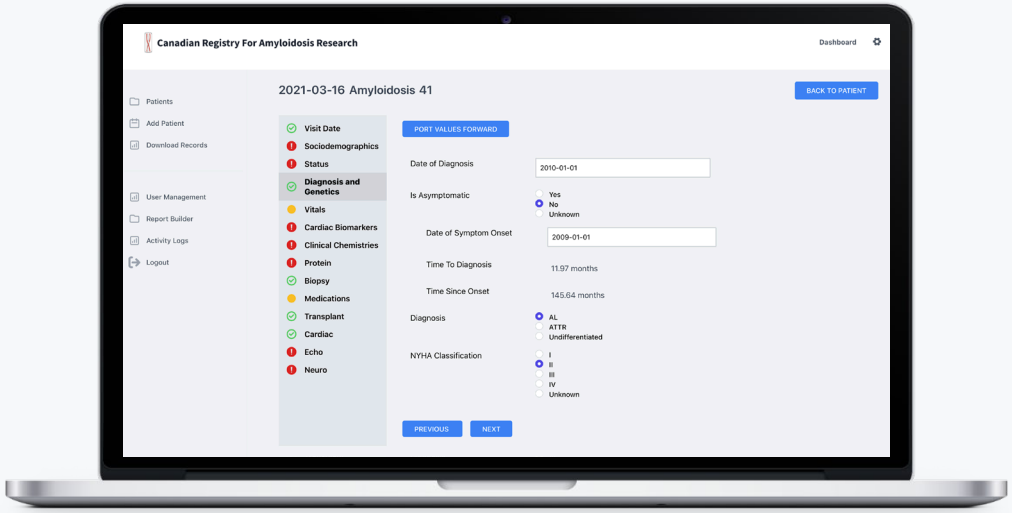
CLINIC-REPORTED COMPREHENSIVE DATA

Data on the real-world care of amyloidosis patients. Define the impact of treatment on clinical symptomology, co-morbidities and mortality.

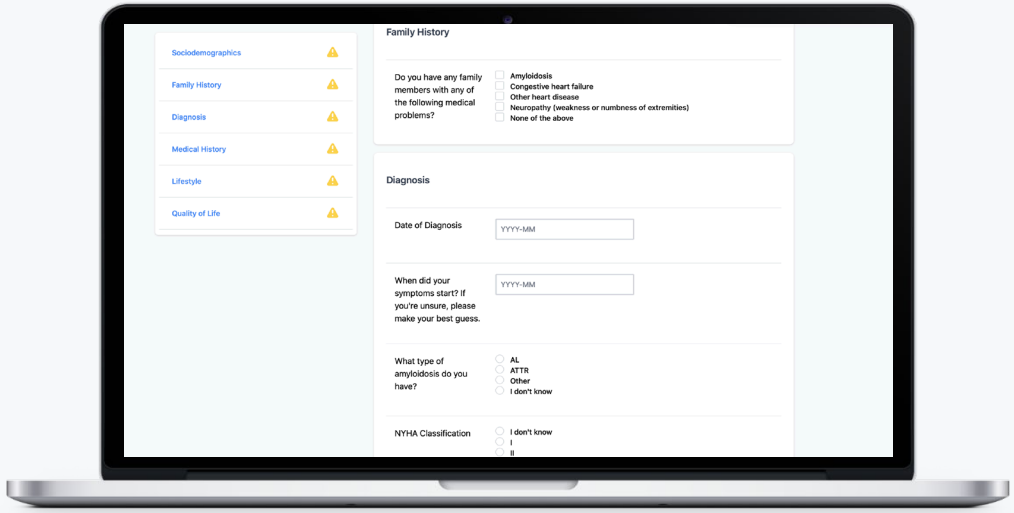
02

PATIENT-REPORTED OUTCOMES

Impacts of living with amyloidosis on activities of daily living and quality of life. Empower patient community to contribute to research.



CURRENTLY ENGAGING 10 CLINICAL SITES



PATIENTS RECRUITED VIA CLINICS AND PATIENT ORGANIZATIONS

Project Leadership

Dr. Nowell Fine, M.D.
University of Calgary

Dr. Margot Davis, M.D.
University of British Columbia

Multi-disciplinary Steering Committee

Hereditary Amyloidosis Canada
Amyloïdose Héréditaire Canada

CASN
The Canadian Amyloidosis Support Network

APRIL 2023 OVERVIEW

Registry Site Updates

- **Calgary** – Active
- **Edmonton** – Active
- **Vancouver** – Active
- **CHUQ** – Awaiting approval of central ethics
- **CHUM** – Awaiting approval of central ethics
- **McGill** – Central ethics submitted, contract signed and returned to site
- **McMaster** – Contract signed and returned to site
- **Toronto** – Ethics and contracting in progress
- **Ottawa** - Ethics submitted, awaiting approval, contract signed and returned to site
- **Halifax** – Active

- **D2P** - Active

Knowledge Translation

- ASH December 10-13, New Orleans LA
  - Published in *Blood*
- AAN April 22-27, 2023, Boston MA
- CNSF June 6-9, 2023, Banff AB

Planned Research Projects

01 Patient baseline characteristics

02 Modern history of ATTR

03 Outcomes in amyloidosis

04 Methods of diagnosis across Canada

05 Diagnostic timeline depending on first symptoms

06 Patient-reported questionnaires

Current projects

01 Tafamidis 85

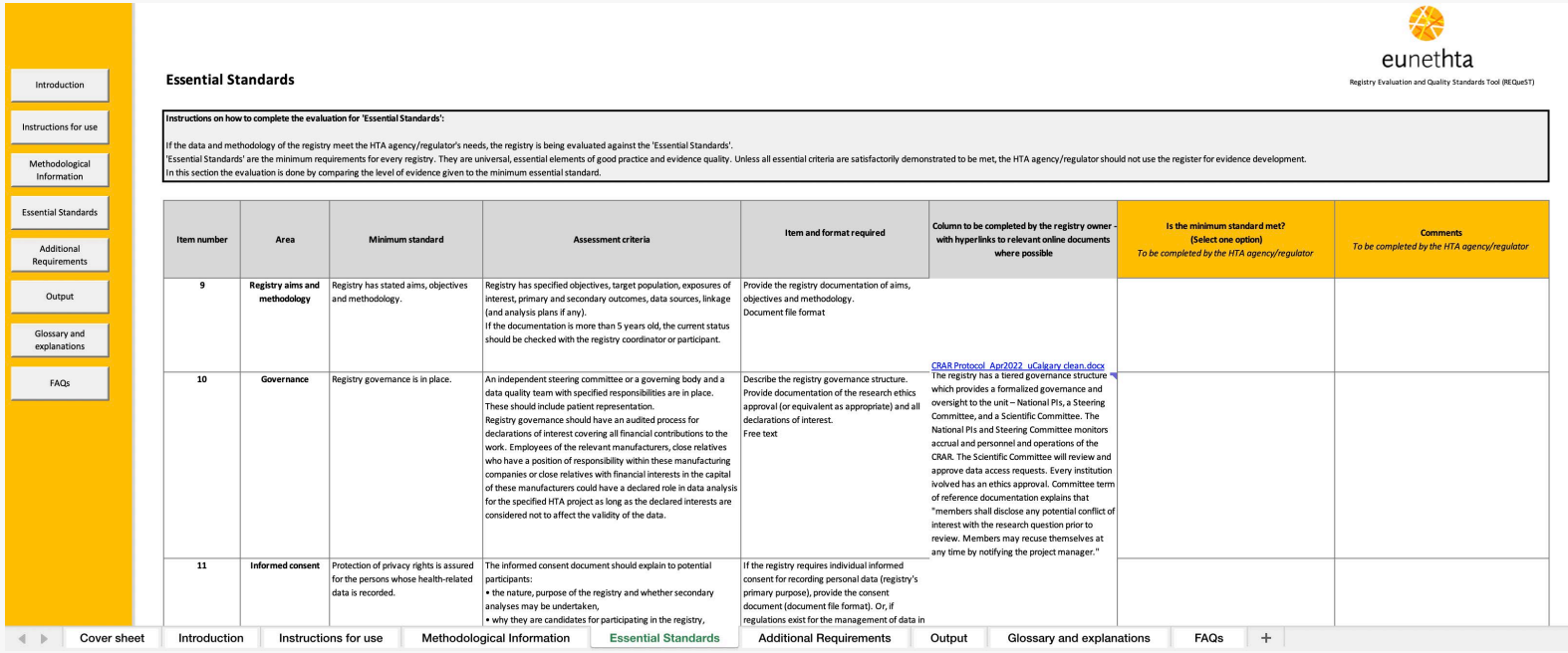
02 Linkage to admin datasets

Industry Collaborations

01	Retrospective patient journey
02	Patient mapping
03	Clinical trials feasibility
04	Clinical trials recruitment

Regulatory Engagement

- Completion of EUnetHTA REQueST Tool for CADTH Assessment



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eunethta
Registry Evaluation and Quality Standards Tool (REQueST)

Essential Standards

Instructions on how to complete the evaluation for 'Essential Standards':

If the data and methodology of the registry meet the HTA agency/regulator's needs, the registry is being evaluated against the 'Essential Standards'.
'Essential Standards' are the minimum requirements for every registry. They are universal, essential elements of good practice and evidence quality. Unless all essential criteria are satisfactorily demonstrated to be met, the HTA agency/regulator should not use the register for evidence development.
In this section the evaluation is done by comparing the level of evidence given to the minimum essential standard.

Item number	Area	Minimum standard	Assessment criteria	Item and format required	Column to be completed by the registry owner – with hyperlinks to relevant online documents where possible	Is the minimum standard met? (Select one option) *To be completed by the HTA agency/regulator*	Comments *To be completed by the HTA agency/regulator*
9	**Registry aims and methodology**	Registry has stated aims, objectives and methodology.	Registry has specified objectives, target population, exposures of interest, primary and secondary outcomes, data sources, linkage (and analysis plans if any). If the documentation is more than 5 years old, the current status should be checked with the registry coordinator or participant.	Provide the registry documentation of aims, objectives and methodology. Document file format	CRAR Protocol_Apr2022_uCalgary clean.docx		
10	**Governance**	Registry governance is in place.	An independent steering committee or a governing body and a data quality team with specified responsibilities are in place. These should include patient representation. Registry governance should have an audited process for declarations of interest covering all financial contributions to the work. Employees of the relevant manufacturers, close relatives who have a position of responsibility within these manufacturing companies or close relatives with financial interests in the capital of these manufacturers could have a declared role in data analysis for the specified HTA project as long as the declared interests are considered not to affect the validity of the data.	Describe the registry governance structure. Provide documentation of the research ethics approval (or equivalent as appropriate) and all declarations of interest. Free text	The registry has a tiered governance structure which provides a formalized governance and oversight to the unit – National PIs, a Steering Committee, and a Scientific Committee. The National PIs and Steering Committee monitors accrual and personnel and operations of the CRAR. The Scientific Committee will review and approve data access requests. Every institution involved has an ethics approval. Committee term of reference documentation explains that "members shall disclose any potential conflict of interest with the research question prior to review. Members may recuse themselves at any time by notifying the project manager."		
11	**Informed consent**	Protection of privacy rights is assured for the persons whose health-related data is recorded.	The informed consent document should explain to potential participants: • the nature, purpose of the registry and whether secondary analyses may be undertaken, • why they are candidates for participating in the registry,	If the registry requires individual informed consent for recording personal data (registry's primary purpose), provide the consent document (document file format). Or, if regulations exist for the management of data in			

Cover sheet | Introduction | Instructions for use | Methodological Information | Essential Standards | Additional Requirements | Output | Glossary and explanations | FAQs

- Request to CADTH for CIHI Data Review

Ongoing work and challenges

- Addition of new sites
  - London
  - Oakville
  - Laval
  - Winnipeg
  - St. John
- Slow onboarding of sites
  - Ethics
  - Resources
- Technologically challenged population
- Site reimbursement
- Authorship policy
- Policy for relationships with industry