Brain and Cognitive Health Program

Request for Expressions of Interest

Context

This document presents a program that is currently under development at Snow Medical. We invite you to submit an Expression of Interest. We encourage researchers to put forward their best and most ambitious ideas – it is entirely acceptable to identify capabilities that are not yet in place.

This concept call is intended to inform the development of a new 2027 Snow Medical funding opportunity.

The aim is to identify opportunities that we believe is likely to have strong translation potential and real world impact, aligned with Snow Medical principles and from which one or more funding programs will emerge.

A **Snow Medical Brain and Cognitive Health Program seeks to unlock scientific or technical capability that**:

- Has the potential to catalyse social and economic returns
- Changes the perception of what's possible
- Underexplored relative to its potential impact
- Unlikely to be achieved through traditional funding mechanisms
- Sits at an opportunity inflection point

Summary

Cognitive function depends on a wide range of interacting biological systems – vascular, metabolic, immune, endocrine and neural – many of which change across the lifespan and are, in principle, modifiable. Dementia is one consequence of failure across these systems, preceded by a long biological runway that creates a broader opportunity to intervene in cognitive health, not only in dementia.

This program will investigate three complementary opportunities: modifiable brain-body mechanisms; mechanisms that enable cognitive resilience despite neuropathology; and scalable non-invasive approaches to predict and alter cognitive trajectory.

The goal is to accelerate the capacity to **predict, understand and deliberately modify cognitive trajectory.**

We are currently seeking expressions of interest for research funding between $3-6 million over 3 years. Snow Medical seeks to fund 4-6 programs in 2027 with potential for renewed funding pending outcomes and review.

Applicants are asked to submit a concise description of the scientific opportunity they propose to address. **EOI submission deadline is Sunday 1 November 2026.**

Who should apply

This call is not restricted to researchers who already identify as dementia specialists. We also encourage applications from researchers whose primary expertise lies in adjacent fields, including **immunology and immunometabolism, endocrinology and metabolic disease, vascular biology, sleep and circadian science, gut-microbiome research, computational modelling, and engineering of non-invasive technologies**, where that expertise could be redirected toward understanding or modifying cognitive trajectory.

Projects that use other disease models, healthy-ageing cohorts, or non-human systems as an entry point are welcome, provided there is a credible plan to link findings back to cognitive or brain-health outcomes in humans. Where useful, Snow Medical can help connect applicants with complementary dementia and clinical expertise during Program Development – you do not need to already have this in place at the EOI stage.

Program background

Dementia represents a major and increasing challenge to population health as life expectancy increases. Globally, the number of people living with dementia is projected to rise substantially over the coming decades [1]. In Australia, dementia is already a major contributor to mortality, disability and health-system burden. The associated societal costs extend beyond direct healthcare expenditure to include informal care, loss of independence and reduced workforce participation.

Despite substantial advances in the molecular characterisation of neurodegenerative disease, options for preventing or substantially delaying dementia remain limited. The recent development of anti-amyloid therapies represents an important advance in Alzheimer's disease treatment and provides evidence that modification of disease-associated biology can alter clinical progression [2,3]. However, the effects observed to date are modest, treatment is currently restricted to individuals with early symptomatic disease and confirmed amyloid pathology, and delivery requires substantial diagnostic and monitoring infrastructure. These therapies therefore address only one component of the broader challenge of maintaining cognitive function across an ageing population.

A further limitation is diagnostic delay. The biological processes underlying Alzheimer's disease and related dementias develop over many years before clinical diagnosis. Longitudinal biomarker studies indicate that amyloid, tau and neurodegenerative changes may be detectable well before substantial cognitive impairment becomes apparent [4,5]. Consequently, by the time dementia is clinically expressed, considerable pathological and neural change may already have occurred. Prevention therefore requires approaches capable of identifying vulnerability and modifying cognitive trajectory substantially earlier in the disease course.

This program is based on the premise that preserving cognitive function will require a broader scientific strategy than targeting established neuropathology alone. Two complementary opportunities are particularly important: targeting modifiable biological processes that contribute to cognitive vulnerability, and identifying mechanisms that allow cognitive function to be maintained despite ageing and neuropathological burden. Advances in biomarkers, longitudinal phenotyping and non-invasive technologies increasingly provide the capability to investigate and ultimately manipulate both processes before substantial functional impairment occurs.

Dementia is used throughout this document as the clearest and most urgent motivating case, but the mechanisms of interest are shared across neurodegenerative, psychiatric and healthy-ageing contexts.

From modifiable risk factors to causal mechanisms

A substantial body of epidemiological evidence indicates that dementia risk is influenced by modifiable factors across the life course. The 2024 Lancet Commission identified 14 potentially modifiable risk factors and estimated that, at a population level, a substantial proportion of dementia may be associated with these exposures [6]. These include cardiovascular and metabolic health, physical activity, sensory impairment, education, social factors and other environmental and behavioural influences.

Intervention studies provide increasing evidence that some of these factors are amenable to modification. Multidomain prevention trials have reported benefits on cognitive outcomes in selected populations, and the Australian *Maintain Your Brain* trial in over 6000 participants demonstrated that a personalised, digitally delivered multidomain intervention can produce measurable cognitive benefit at large scale [7].

However, associations between cognition and exercise, vascular health, sleep, metabolism or diet may arise through multiple interacting pathways, and the relevant mechanisms are likely to differ between individuals and across stages of ageing. This limits the ability to identify optimal intervention targets, determine appropriate timing and dose, or establish whether an intervention has engaged the biological process responsible for benefit.

The scientific opportunity is therefore to move from risk-factor identification toward causal and characterisation of modifiable mechanisms.

Increasing evidence supports a systems-level view of cognitive ageing in which brain function is influenced by physiological processes throughout the body. Vascular and neurovascular dysfunction, metabolic and energy regulation, endocrine signalling, immune and inflammatory processes, sleep and clearance mechanisms, autonomic regulation and other peripheral signals may influence neuronal function and susceptibility to neurodegeneration [8,9,11–15]. This program is designed to bring together multidisciplinary expertise.

This creates a broad but experimentally tractable research opportunity space - to identify the underlying biological pathways through which systemic physiology modifies brain function. Establishing causality, target engagement and cognitive consequence would allow these pathways to become candidates for direct intervention.

This rationale underpins our Research **Node 1: Brain–Body Mechanisms of Cognitive Ageing**, which seeks to identify modifiable systemic mechanisms that contribute to cognitive decline and determine whether their manipulation can alter cognitive function.

Cognitive resilience as a complementary therapeutic target

Variation in cognitive outcome cannot be explained fully by the extent of neuropathology. Neuropathological studies have long demonstrated substantial heterogeneity in the relationship between pathological burden and clinical expression. Some individuals retain relatively preserved cognition despite levels of Alzheimer's, vascular or other pathology that are commonly associated with cognitive impairment.

This discrepancy is increasingly conceptualised in terms of cognitive resilience: cognitive performance that is better than would be expected given an individual's burden of age-related brain disease [10]. While genetic influences are likely to contribute, the extent to which resilience is mediated by endogenous mechanisms that are themselves modifiable remains an important unresolved question.

This forms the basis of our Research **Node 2: Mechanisms of Cognitive Resilience**, which asks whether the biological and neural mechanisms associated with preserved cognition can be identified and harnessed to modify vulnerability to cognitive decline.

Earlier prediction and scalable intervention

Currently, dementia diagnosis occurs after substantial functional and, in many cases, biological change. A prevention-oriented strategy therefore requires measures capable of identifying changes in cognitive, behavioural or biological trajectory before conventional diagnostic thresholds are reached.

Rapid advances in passive digital behavioural monitoring, blood-based biomarkers, neuroimaging, digital phenotyping, and cognitive measurement are increasing the feasibility of detecting such changes. Their value within this program will lie in their capacity to enable identification of individuals or periods of increased vulnerability, stratification of likely intervention response, longitudinal assessment within individuals, and measurement of target engagement.

Non-invasive interventions provide an increasingly important route to translation. Digital intervention programs, repurposing of existing medications, focused ultrasound, transcranial magnetic stimulation and other emerging modalities will be considered based on their potential to scale with minimal risks and delivery constraints. Scalability does not necessarily exclude interventions that currently require specialist infrastructure, but it does require a credible pathway toward broader accessibility if efficacy is established.

These considerations underpin our Research **Node 3: Scalable Non-Invasive Predictive Markers and Interventions**, which combines the capacity for earlier risk detection and developing scalable interventions capable of modifying cognitive trajectory.

Why this opportunity is timely

Australia has produced some of the strongest causal evidence globally that interventions targeting modifiable factors can improve cognitive outcomes [7], providing a robust evidence base for intervention and establishing risk modification as a practical starting point for action. Concurrent advances in biomarkers, wearable technologies and AI-supported data integration are enabling increasingly sophisticated phenotyping of individuals and populations, creating new opportunities for precision prevention and intervention. In parallel, breakthroughs across vascular biology, metabolism, immunology and neuroscience are revealing the interconnected mechanisms through which whole-body physiology shapes brain health across the lifespan. Collectively, these advances are transforming the field from one focused primarily on describing decline to one capable of predicting risk, targeting underlying mechanisms and delivering scalable interventions through non-invasive technologies, repurposed therapeutics and digital platforms.

Australia has substantial research capability across each of these areas. Relevant strengths include large longitudinal and trial-ready cohorts; established expertise in dementia prevention, vascular cognitive impairment and cognitive resilience;

scalable digital intervention platforms; biomarker and precision-phenotyping capabilities; strong neuroscience, metabolic and immune-health research; and expertise in emerging non-invasive technologies. However, these capabilities are often advanced in parallel rather than in concert, creating a significant opportunity to integrate expertise, platforms and data within a shared framework capable of linking mechanisms, measurement and intervention.

What we expect to fund

This opportunity seeks to identify three complementary research nodes:

- **Node 1. Brain-Body Mechanisms** – discovery science – causal validation of modifiable systemic mechanisms of cognitive decline.
- **Node 2. Mechanisms of Cognitive Resilience** – discovery science – why cognitive function is maintained in some individuals despite neuropathology and whether these protective mechanisms can be deliberately enhanced.
- **Node 3. Scalable non-invasive predictive markers and interventions** – translational and clinical implementation science – develop non-invasive tools capable of detecting and altering cognitive trajectory at population scale.

We anticipate supporting multidisciplinary teams across academic research, clinical research, engineering, technology and other relevant sectors. Each Node is envisaged as a cross-disciplinary research community operating within a common framework and supported by harmonised platforms that accelerate the translation of research into evidence-based interventions. The objective is not simply to fund excellent science, but to create dynamic and evolving scientific communities that integrate expertise, technologies, datasets and capabilities around a shared challenge. Nodes should provide a focal point for collaboration, attract new partners and collaborators as the science develops, and generate connections both within and across Nodes that may not otherwise occur through traditional research structures. Through these interactions, the program aims to catalyse new scientific directions and accelerate the translation of discovery into impact.

We are interested in programs across the risk continuum, including cognitively healthy adults in midlife and older age, individuals at elevated risk, people with evidence of preclinical disease and people with mild cognitive impairment, and programs involving animal models, where there is a credible link to human clinical data and cognitive outcomes.

Indicative funding is in the range of $3-6 million (AUD) per program over 3 years, with potential for further funding pending outcomes that require scale and acceleration.

Program-wide expectations

Although projects may enter the program at different stages of maturity, four principles will apply:

1. Cognitive outcomes matter

The program's north-star outcome is the preservation of meaningful cognitive function.

2. Scalability should influence intervention design from the beginning

Technologies requiring specialist resources such as focused ultrasound or transcranial magnetic stimulation may be appropriate where there is a plausible pathway toward accessible delivery.

3. Measurement should allow us to see change before dementia

Within-subjects measurement, computational modelling, digital phenotyping, biomarkers and precision stratification may operate as enabling capabilities across all three Nodes rather than as a standalone program Node.

We are unlikely to support

- Conventional pharmaceutical development programs (e.g. lead optimization, formulation programs) but will consider discovery of novel targets and mechanistically informed drug repurposing.
- Epidemiology or observational studies without a credible pathway to causal validation

- Preclinical mechanistic studies with no credible plan to establish a cognitive, behavioural or brain-relevant readout (a plan is sufficient at EOI stage)
- Invasive interventions without a compelling rationale

NODE 1 - BRAIN-BODY MECHANISMS OF COGNITIVE AGEING

What systemic processes can we leverage to resist cognitive decline?

We start from the observation that the evidence linking dementia risk and factors such as cardiovascular and metabolic health and other aspects of lifestyle-affected systems is increasingly compelling, though the causal mechanisms driving these links remains obscure.

We believe this creates an opportunity toward a mechanistic science of modifiable cognitive ageing.

Approaches may include, but are not limited to, investigation of:

- vascular and neurovascular mechanisms;
- metabolic and energy regulation pathways (e.g. GLP-1);
- immune and inflammatory pathways (neuroimmune axis);
- sleep, clearance and glymphatic biology;
- exercise-induced systemic signals;
- autonomic and interoceptive pathways;
- stress-response;
- microbiome- or other gut-brain signalling;
- interactions between multiple systemic mechanisms that may determine cognitive trajectory.

Preclinical mechanistic studies are encouraged where they enable mechanistic insights with potential to parallel human clinical studies.

By the end of a successful Node 1 project, potential outcomes may include:

- identified a modifiable brain-body mechanism for modulation of cognitive function
- established measurable indicators of target engagement
- defined when, in whom and under what conditions the mechanism is likely to matter
- demonstrated a credible pathway toward a human intervention or provided an early human signal where feasible.

The objective is to reveal new biological levers that can be pulled to alter cognitive trajectory.

NODE 2 - MECHANISMS OF COGNITIVE RESILIENCE

Why do some people maintain cognition despite ageing and neuropathology - and can we reproduce that resilience in others?

We start from the observation that some individuals show substantially better cognitive function than would be expected given the amount of disease-related change present in the brain. This is driven in part by genes, however other endogenous mechanisms remain unknown.

The primary goal of Node 2 is therefore to identify the mechanisms that distinguish a resilient brain from a vulnerable one, determine whether those mechanisms are causal, and test whether resilience can be deliberately increased.

Where appropriate, projects should move from identification of a resilience signature to experimental manipulation.

Preclinical mechanistic studies are encouraged where they enable mechanistic insights with potential to parallel human clinical studies.

By the end of a successful Node 2 project, potential outcomes may include:

- identified a biological mechanism that preserves cognitive function beyond expected based on pathological burden
- demonstrated that engaging the mechanism improves resilience or alters vulnerability to a relevant challenge
- identified measurable signals that could be used to stratify individuals

The program seeks to move resilience from something we observe to something we control.

NODE 3 - SCALABLE NON-INVASIVE PREDICTIVE MARKERS AND INTERVENTIONS

Where can we intervene at scale?

We start with the observation that intervention programs require scalability.

The primary goal of Node 3 is to develop non-invasive interventions capable of reliably engaging mechanisms that protect cognition, increase resilience or restore healthy brain function, while retaining a credible pathway to use at meaningful population scale.

We are interested in both new technologies and existing clinical and community platforms. Approaches

may include intervention development or clinical trials involving but not limited to:

- lifestyle modification programs
- specialised technology - focused ultrasound, transcranial magnetic stimulation
- drug repurposing
- biomarkers
- screening platforms

By the end of a successful Node 3 project, potential outcomes may include:

- established a controllable intervention and characterised an appropriate dose-response relationship
- demonstrated meaningful downstream biological, cognitive or functional consequences
- shown an improvement in capability over existing interventions, rather than an incremental variation of current technology
- established an explicit pathway toward human use and increasing accessibility
- where maturity permits, demonstrated target engagement or proof of mechanism in humans

The objective is to enable controllable, non-invasive ways of altering cognitive trajectory rather than simply measuring it.

Program Development and Selection Process

Snow Medical will use a two-staged process to identify ambitious scientific opportunities, develop the strongest concepts and assemble a complementary portfolio of programs capable of advancing the objectives of the Cognitive Healthspan Program.

In Stage I, applications are assessed for both **the strength of individual concepts** and **how those concepts could contribute to a coherent overall portfolio**. In Stage II, invited applicants will participate in a co-design process intended to strengthen the scientific strategy and identify where resources can create the greatest additional value.

Snow Medical may work with shortlisted teams to identify missing capabilities, facilitate collaborations, define milestones and adjust program scope before final funding decisions are made.

Stage 1 — Expression of Interest

The EOI is intended to identify ambitious scientific concepts that warrant further development with Snow Medical. Applicants are not expected to submit a fully developed research program at this stage.

Format

Part A — Scientific Concept (maximum 2 pages, size 12 font, excluding references)

- alignment with one or more Program Nodes;
- the scientific problem or opportunity and why it matters;
- the central hypothesis, mechanism or capability to be tested or developed;
- the critical limitation in current knowledge or capability that prevents progress;
- why the proposed approach could produce a substantial advance over the current state of the field;
- the proposed pathway from mechanism to meaningful cognitive outcome;
- the key experimental or translational uncertainties;
- why Snow Medical support could enable progress unlikely to occur through conventional funding mechanisms.

Part B — Team and Capability Summary (maximum 1 page, size 12 font, excluding references)

- the proposed multidisciplinary team, collaborators and capabilities represented;
- capabilities, collaborators or infrastructure that may still be required;

Applicants are not expected to have assembled the complete multidisciplinary team at EOI stage.

In completing the Expression of Interest, we encourage applicants to consider a bold and ambitious vision: if given the opportunity to pursue the ideal version of their research program, what capabilities are needed? It is entirely acceptable to identify capabilities, collaborators or infrastructure that are not yet in place – missing capabilities will not disadvantage an application, and Snow Medical may help address these gaps for selected concepts during Program Development.

Assessment

EOIs will undergo an initial assessment of scientific opportunity, strategic alignment, plausibility and potential impact. Snow Medical may seek targeted expert advice where specialist expertise is required.

EOIs will be assessed on:

- scientific significance and originality;
- transformative potential;
- strength and testability of the central hypothesis;
- leadership capability; and
- **Snow Medical additionality** – including the value of bringing fields adjacent to dementia research (e.g. immunology, metabolism, sleep science, computational neuroscience) to bear on cognitive trajectory, not only novelty within the existing dementia field.

Shortlisted teams will be invited to a **Program Development stage**, during which concepts, teams and program architecture may be further developed before submission of a Full Proposal.

EOI Submission Deadline: 11:59pm Sunday 1 November 2026

Stage 2 — Program Development

Program Development is a co-design process with Snow Medical intended to develop promising concepts into a Full Program.

Shortlisted teams will engage with Snow Medical to refine the scientific architecture of the proposed work. This may include consideration of:

- the central hypothesis and assumptions on which the program depends;
- potential overlap or capability gaps;
- opportunities to strengthen causal inference;
- opportunities to exploit existing partnerships, platforms, datasets or infrastructure;
- potential milestones and decision points.

Concepts may evolve substantially between EOI and Full Proposal.

Shortlisted teams notified for commencing Program Development: November 2026

Full Program design will undergo independent assessment by national and international experts with relevant scientific, clinical, technological and translational expertise. Funding recommendations will be submitted to the Snow Medical Board for final approval with expected program establishment to commence in **Q3 2027.**

Timeline

Activity	Indicative Date*
Call for Expressions of Interest Opens	8 September 2026
Expression of Interest Deadline	1 November 2026
Applicants Notified and Invited to Participate in Program Development	November 2026
Stage II Program Development to Full Program	November 2026 - March 2027

**dates are subject to change as required*

Active Program Management

Snow Medical intends to remain actively engaged throughout the duration of funded programs. Where results materially change the scientific opportunity, Snow Medical and research teams may agree to accelerate promising work or discontinue approaches that are no longer justified. This approach is intended to preserve the flexibility required for ambitious research while maintaining clear accountability for scientific progress and the responsible allocation of program resources.

Eligibility Requirements

Applications must be submitted through an Australian university or Medical Research Institute.

Lead Applicants are expected to be **independent investigators with demonstrated scientific leadership** (minimum level: Level C / Senior Lecturer).

Further details are provided on our website under “How to Apply”.

Questions

We welcome any questions regarding this Program. Please contact info@snowmedical.org.au.

References

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