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CIHR-SUPPORTED RESEARCH ON DEMENTIA

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NEED MORE EVIDENCE?

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WELCOME TO THE FALL 2014 ISSUE OF **SHOW ME THE EVIDENCE**

The statistics are well known: our population is getting older, and dementia diagnoses are on the rise. With no effective treatments available, the outlook for people with dementia, their families, and the public in general is discouraging. But underneath all the bleak headlines, there are glimmers of hope. Through more collaborative research, we are learning new things about dementia every day, and networks of researchers are working together to turn this knowledge into better outcomes for dementia patients and their caregivers.

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's health research investment agency. CIHR provides support for investigator-driven health research, but also sets strategic investment priorities to respond to key health and health system challenges. In identifying areas for strategic investment, we carefully consider where Canada can capitalize on its research strengths and have the greatest possible impact. To date, CIHR has developed several Signature Initiatives to help us make strategic investments in promising areas of health research.

In this issue of *Show me the Evidence*, we profile CIHR's national research strategy on dementia, also known as the International Collaborative Research Strategy for Alzheimer's Disease. Dementia is a growing health care challenge in Canada. As people enter their senior years, their risk of developing dementia climbs. Statistics Canada projects that by the year 2036, approximately 25% of Canadians will be over the age of 65, up from 14% in 2009. And as our population ages, the rate of Alzheimer's disease and other dementias will also climb. While experts predict that other high-income countries will experience similar increases, low- and middle-income countries could see a 250% surge in dementia during the same period. CIHR is working closely with national and international partners to identify and invest in the research projects with the greatest potential.

The CIHR-supported research highlighted in this issue has not only helped improve our understanding of dementia, it's also created new possibilities for improved diagnosis, treatment and quality of life for patients and their families. The stories describe:

- An improved understanding of shared risk factors for vascular health and dementia;
- Improved support for dementia caregivers; and,
- Advances in diagnosis crucial to the prevention of disease

CIHR-funded research and researchers have delivered:

- **A POTENTIAL NEW APPROACH TO PREVENTING OR SLOWING THE ONSET OF DEMENTIA;**
- **AN ASSESSMENT TOOL TO HELP HEALTH PROFESSIONALS UNDERSTAND THE NEEDS OF DEMENTIA CAREGIVERS; AND,**
- **AN INTERNATIONALLY-RECOGNIZED DIAGNOSTIC TOOL FOR IDENTIFYING THE EARLY SIGNS OF COGNITIVE IMPAIRMENT.**

PREVENTABLE DEMENTIA: A RADICAL RETHINK OF THE CAUSES OF DEMENTIA

Two veteran stroke and dementia researchers say the evidence points to a common, treatable origin

AT A GLANCE

WHO: DR. SANDRA BLACK, UNIVERSITY OF TORONTO; DR. VLADIMIR HACHINSKI, WESTERN UNIVERSITY

ISSUE: THE INCREASE IN THE NUMBER OF ELDERLY CANADIANS WITH DEMENTIA, INCLUDING ALZHEIMER'S, IS DRIVING THE NEED FOR AN UNDERSTANDING OF THE PROCESSES BEHIND DEMENTIA THAT WILL LEAD TO IMPROVED TREATMENTS. THERE'S COMPELLING RESEARCH EVIDENCE THAT STROKES AND DEMENTIAS HAVE A COMMON ORIGIN, AND INTERACT, THROUGH THE HEALTH OF BRAIN BLOOD FLOW, OR CEREBROVASCULAR HEALTH. THIS INSIGHT HAS PROFOUND TREATMENT IMPLICATIONS SINCE THERE ARE KNOWN PREVENTATIVE AND TREATMENT OPTIONS TO IMPROVE VASCULAR HEALTH.

PROJECT: DR. HACHINSKI'S CIHR-FUNDED BASIC RESEARCH HAS LAID THE GROUNDWORK FOR AN UNDERSTANDING OF THE LINKS BETWEEN STROKES, DEMENTIA AND OVERALL BRAIN VASCULAR HEALTH. DR. BLACK'S SUNNYBROOK DEMENTIA STUDY HAS HELPED VISUALIZE THE LINK BETWEEN THESE DISEASES THROUGH THE COLLECTION AND ANALYSIS OF BRAIN SCANS OF MORE THAN 1,000 DEMENTIA PATIENTS.

RESEARCH EVIDENCE: THROUGH HER NEUROIMAGING RESEARCH, DR. BLACK IS EXPLORING THE USE OF IMAGING AS AN EARLY DETECTION AND SCREENING TOOL FOR DEMENTIA-RELATED VASCULAR CHANGES.

EVIDENCE IN ACTION: DRS. BLACK AND HACHINSKI'S RESEARCH IS LEADING TO A FUNDAMENTALLY NEW APPROACH TO DEMENTIA TREATMENT: EARLY PREVENTION BASED ON ADDRESSING RISK FACTORS FOR VASCULAR HEALTH, SUCH AS HYPERTENSION, DIABETES AND SMOKING. THEIR RESEARCH WAS INSTRUMENTAL TO THE DEVELOPMENT OF THE FIRST DEMENTIA SCREENING PROTOCOL THAT COMBINES STROKE, DEMENTIA AND OVERALL VASCULAR HEALTH.

SOURCES: VLADIMIR HACHINSKI & LUCIANO SPOSATO, "DEMENTIA: FROM MUDDLED DIAGNOSES TO TREATABLE MECHANISMS," *BRAIN*, 136 (2013):2652–2656.

SANDRA BLACK, "VASCULAR COGNITIVE IMPAIRMENT: EPIDEMIOLOGY, SUBTYPES, DIAGNOSIS AND MANAGEMENT", *THE JOURNAL OF THE ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH*, 41 (2011):49–56

Dr. Sandra Black is pointing to one of a dozen tiny black dots on an elderly patient's brain scan.¹

"These are literally tiny little holes in the brain," says Dr. Black of the pen-nib-sized dots.

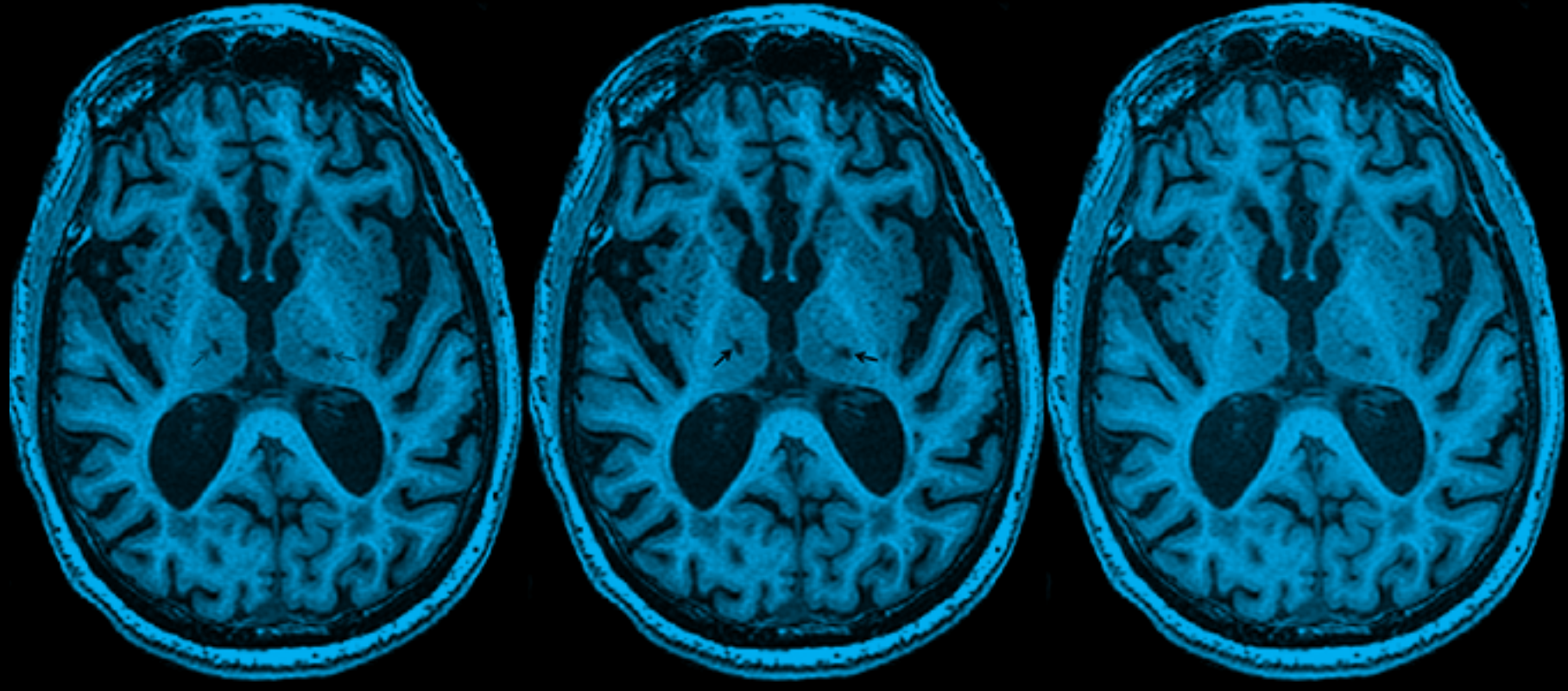
The holes are the result of silent, or covert, strokes, when a lack of blood has caused localized brain tissue death, or, in medical language, an infarct. But this brain scan wasn't done to study strokes. It was part of the landmark CIHR-funded brain imaging study known as the Sunnybrook Dementia Study.²

Dr. Black, and her Western University colleague, Dr. Vladimir Hachinski, are world-leading veterans of stroke and dementia research, as well as clinical care, and they both see overwhelming evidence that the two conditions are intimately linked. Both strokes and dementia, their research shows, are issues of cerebrovascular health – the condition of blood flow through brain arteries and veins.

Their insight points to a dramatic shift in perspective on the treatment of dementias, including Alzheimer's: that they can be prevented by reducing vascular risk factors, such as hypertension and lack of exercise.³

"All dementias have a vascular component," says Dr. Hachinski, who's the current president of the World Federation of Neurology. "Of all the things that we know, the only main thing we know for sure is that we can treat vascular disease."

During his more than 40-year career, Dr. Hachinski has pioneered the study of vascular-related dementia, cognitive impairment due to the effect of strokes and brain vascular disease. He developed the Hachinski Ischaemic Score,⁴ a widely used clinical test to differentiate between Alzheimer's-type dementia and vascular dementia.⁵



“These are literally tiny little holes in the brain,”
says Dr. Black of the pen-nib-sized dots.

TYPES OF DEMENTIA DEMENTIA IS A TERM THAT REFERS TO THE IMPACT ON COGNITION AND BEHAVIOUR OF SEVERAL DIFFERENT DISEASES CAUSED BY DIFFERENT PHYSICAL CHANGES TO THE BRAIN. ALZHEIMER’S DISEASE, A NEURODEGENERATIVE CONDITION, IS THE MOST COMMON FORM OF DEMENTIA. IT IS TRADITIONALLY DIAGNOSED BY THE PRESENCE OF AMYLOID AND TAU PROTEIN CLUMPS, OR PLAQUES, THROUGHOUT THE BRAIN. VASCULAR DEMENTIA, ON THE OTHER HAND, IS CAUSED BY LOSS OF BLOOD FLOW TO PARTS OF THE BRAIN. BUT DR. HACHINSKI SAYS THIS DISTINCTION IS BEING OUTDATED BY A DEEPER UNDERSTANDING OF THE COMMON VASCULAR COMPONENTS TO BOTH CONDITIONS.



DELAY, DELAY, DELAY
ONE KEY TO PREVENTING DEMENTIA IS TO DELAY ITS ONSET, SAYS DR. VLADIMIR HACHINSKI. “IF YOU CAN DELAY DEMENTIA BY ONE YEAR YOU WILL CUT THE PREVALENCE BY 20 PERCENT. IF YOU CAN DELAY IT BY FIVE YEARS YOU REALLY CUT IN HALF THE PREVALENCE BECAUSE PEOPLE WILL DIE FROM OTHER THINGS OR MULTIPLE CAUSES,” HE SAYS. REDUCING VASCULAR RISK FACTORS TO DELAY THE ONSET OF DEMENTIA CAN THUS HAVE A PROFOUND IMPACT ON THE QUALITY OF LIFE OF A PERSON’S FINAL YEARS.

EVIDENCE IN ACTION: A MORE COMPREHENSIVE VIEW OF DEMENTIA

DRS. BLACK AND HACHINSKI'S RESEARCH AND LEADERSHIP WERE INSTRUMENTAL TO THE DEVELOPMENT OF THE FIRST DEMENTIA SCREENING PROTOCOL THAT COMBINES MEASURES OF COGNITIVE IMPAIRMENT AND VASCULAR RISK FACTORS. THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND CANADIAN STROKE NETWORK VASCULAR COGNITIVE IMPAIRMENT HARMONIZATION STANDARD IS THE CURRENT CLINICAL GOLD-STANDARD ASSESSMENT OF THIS TYPE.¹⁰

Alzheimer's-type dementia is traditionally diagnosed by the presence of amyloid and tau protein clumps, or plaques, throughout the brain. But Dr. Hachinski says this is a distinction that's been superseded by a deeper understanding of the common vascular components.

"Most dementias are mixed dementias," he says, with both a vascular and Alzheimer's-like protein component.

In an analysis of data from the Canadian Study for Health and Aging, which contains detailed medical information on 12,000 Canadians, Dr. Hachinski and colleagues found that people over 65 who had experienced a stroke also had some cognitive impairment.⁶ Then, in a lab mouse model he co-created, he demonstrated that induced strokes in the presence of amyloid deposits resulted in much greater brain damage than in the absence of amyloid.⁷

"It's a two-way street," says Dr. Black of the links between strokes and dementia. "I always shock people at conferences when I say that Alzheimer's is a cause of stroke because it causes hemorrhaging from the amyloid that goes into the vessels."

VISUALIZING VASCULAR BURDEN

Through the ongoing Sunnybrook Dementia Study, started in 1995, she's collected standardized MRI and SPECT-scan (Single Positron Emission Computed Tomography) images of more than 1,000 patients with dementia. In addition, she's led the development of an "analytical pipeline" for correlating patients' brain scans with their cognitive and behavioural profiles, and comparing them to scans of healthy aging brains.

"We've done scans in a way that's enabled us to measure the brain changes in a way that's very objective," says Dr. Black of the study, which has produced more than 140 scientific papers.

These scans have revealed the widespread nature of silent strokes.

"A quarter of Canadians 65 and older have these tiny areas of dead brain tissue," says Dr. Black. Unlike major strokes which result in dramatic, almost immediate paralysis or loss of speech, silent strokes cause gradual, cumulative cognitive decline.

But these silent strokes are not the only source of decline. The scans have also revealed that as many as 9-in-10 elderly Canadians' brain function is slowed by some level of white matter disease, named for the lobe-shaped white patches that appear on brain scans.⁸

"We think those white regions are water on the brain," explains Dr. Black. The cerebral equivalent of swollen ankles, these white regions are the result of the pooling of cerebrospinal and interstitial (between cells) fluid in the brain. Dr. Black believes this is caused by a thickening of the veins that drain blood from deep in the brain, creating "vascular resistance." These thickened veins act like a partially blocked drain, preventing the cerebrospinal and interstitial fluid from being reabsorbed into the veins, thereby slowing the brain's ability to flush-out "garbage" such as amyloid and tau proteins.

White matter disease "may be very important in the etiology (cause) of Alzheimer's," says Dr. Black. She's testing this hypothesis through a current CIHR-funded study looking at amyloid build-up over time in patients with white matter disease.

A NEW APPROACH TO DEMENTIA

Taken together, Dr. Hachinski's and Dr. Black's findings are prompting them to call for a new clinical approach to dementias of all kinds: one focused on delaying, or even preventing, the disease by reducing vascular risk factors long before the appearance of dementia.

"Roughly speaking, the molecular mischief of Alzheimer's disease takes about 20 years to develop, so by the time you exhibit symptoms there is a lot of pathology in the brain that you're not going to solve with a silver bullet," says Dr. Hachinski. "If we are going to make any difference we'll have to start earlier, and we'll have to treat the risk factors that we know we can treat."

Under this new approach, one of the main challenges will be learning to reliably spot the early signs of dementia. With Western University colleague Dr. Manuel Montero-Odasso, Dr. Hachinski has recently shown that changes in gait (walking) in elderly patients may be an early warning sign of "brain failure." Gait changes are thus a possible screening tool for those who'd benefit from treating reversible vascular risk factors, including obesity, lack of exercise, and unhealthy diet.⁹

Similarly, Dr. Black's neuroimaging research has laid the groundwork for the possibility of using brain imaging, including the tiny black dots that are indicative of brain tissue death, as an early detection and screening tool for dementia-related vascular changes. Inspired by the major successes with cardiovascular and stroke treatment achieved in the past 20 years, Dr. Black says her focus is now seeing these vascular gains transferred to dementia prevention.

"I find myself to be involved in system change with respect to dementia because I have a sense of urgency about the future," says Dr. Black. "We need to find ways to set up care to prevent this disease."

BRIDGING RESEARCH SILOS

DRS. HACHINSKI AND BLACK ARE REACHING OUT TO COLLEAGUES IN BOTH THE STROKE AND DEMENTIA COMMUNITIES AND BUILDING COMMON GROUND ON THE ISSUE OF BRAIN VASCULAR HEALTH. THEY'RE BOTH ON THE EXECUTIVE COUNCIL OF THE INTERNATIONAL SOCIETY FOR VASCULAR BEHAVIOURAL AND COGNITIVE DISORDERS. THIS INTERDISCIPLINARY RESEARCH BRIDGE-BUILDING HELPED PAVE THE WAY FOR THE NEW CIHR CANADA-WIDE VASCULAR HEALTH NETWORK, DEDICATED TO BREAKING DOWN BARRIERS BETWEEN DISCIPLINES AND VASCULAR DISEASES.¹¹

FOR MORE INFORMATION

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Canadian Vascular Network website: <http://www.cihr-irsc.gc.ca/e/48014.html>.

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C.A.R.E. FOR CAREGIVERS: AN INNOVATIVE PSYCHOSOCIAL TOOL ASSESSES THE NEEDS OF CAREGIVERS

As Canada's ageing baby boomers increasingly care for a spouse or parent with dementia, family caregivers need support to avoid becoming patients

AT A GLANCE

WHO: DR. JANICE KEEFE, MOUNT SAINT VINCENT UNIVERSITY

ISSUE: AS THE NUMBER OF CANADIANS WITH DEMENTIA GROWS, THE BURDEN OF THIS INCREASE WILL FALL LARGELY ON FAMILY CAREGIVERS. HOWEVER, WHILE FAMILY CAREGIVERS ARE KEY TO THE CANADIAN HEALTH CARE SYSTEM, THEY AREN'T VIEWED AS CLIENTS BY MANY HEALTH SERVICE AGENCIES. NEW ASSESSMENT TOOLS TO ACCURATELY IDENTIFY CAREGIVER NEEDS ARE NEEDED TO INFORM THE DEVELOPMENT OF CAREGIVER SUPPORT PROGRAMS.

PROJECT: SINCE 2001, DR. JANICE KEEFE HAS CO-LED THE DEVELOPMENT OF THE C.A.R.E. TOOL, A PIONEERING PSYCHOSOCIAL QUESTIONNAIRE THAT CAPTURES FAMILY CAREGIVERS' DIVERSE AND COMPLEX NEEDS.

RESEARCH EVIDENCE: IN A RECENT CIHR-FUNDED STUDY, KEEFE AND COLLEAGUES IDENTIFIED BEST-PRACTICE GUIDELINES FOR THE TIMING OF CAREGIVER ASSESSMENT FOR THOSE CARING FOR ELDERLY SPOUSES WITH DEMENTIA.

EVIDENCE IN ACTION: DURING THE PAST DECADE, THE C.A.R.E. TOOL HAS PROMPTED A GROWING PARADIGM SHIFT IN HOW NATIONAL, PROVINCIAL AND LOCAL HEALTH SYSTEMS THINK ABOUT WHO THEY SERVE: THAT IN THE CASE OF DISABLED AND ELDERLY PERSONS BEING CARED FOR AT HOME, THE ELDERLY SPOUSAL CAREGIVER ALSO REQUIRES CARE AND SUPPORT. ALBERTA'S CAREGIVER AND ENHANCED RESPITE PILOT PROJECT USED THE C.A.R.E. TOOL TO IDENTIFY AT-RISK FAMILY CAREGIVERS, AND GUIDE POLICY DEVELOPMENT FOR CAREGIVER SUPPORT PROGRAMS.

SOURCES: KEEFE, JANICE, ET AL., "CAREGIVERS' ASPIRATIONS, REALITIES, AND EXPECTATIONS: THE C.A.R.E. TOOL," *JOURNAL OF APPLIED GERONTOLOGY*, 27, 3(2008):286–308.



SHARING INSIGHT TO IMPROVE CARE FOR THE ELDERLY

INSIGHTS FROM C.A.R.E. TOOL RESEARCH ARE SHAPING A NEW GENERATION OF HEALTH PROFESSIONALS. “PART OF WHAT I DO NOW IS I SPEAK TO THE SECOND-YEAR MEDICAL STUDENTS ABOUT ISSUES RELATED TO CAREGIVING AND HOMECARE,” SAYS DR. KEEFE, WHO IS ALSO THE HEAD OF POLICY DEVELOPMENT WITH THE CANADIAN DEMENTIA KNOWLEDGE TRANSLATION NETWORK. “I GIVE THESE FUTURE PHYSICIANS A PERSPECTIVE ON WHAT’S HAPPENING OUT IN THE COMMUNITY AND WHAT IS THE EVIDENCE THAT WE HAVE LEARNED FROM FAMILY MEMBERS WHO ARE CARING FOR OLDER PEOPLE WITH DEMENTIA.”

From her office at Mount Saint Vincent University in Halifax, Dr. Janice Keefe is co-leading a webinar for 200 health care providers working at nursing homes, hospitals, Alzheimer’s societies and seniors’ health organizations across Canada and the United States.¹ The webinar’s accompanying text chat buzzes with enthusiasm.

“This is just what I’ve been looking for,” types one participant representing a national mental health agency.

What’s unusual is that Dr. Keefe’s not talking about patients, the traditional “clients” of these organizations. She’s talking about their at-home, family caregivers.

“These caregivers are the backbone of our current health system,” says Dr. Keefe. “Yet we don’t treat them this way. One of the big challenges we face is that caregivers aren’t viewed as a client or eligible for services in and of themselves.”

She’s working to change this situation. For the past twenty years, Dr. Keefe and her team have been at the forefront of an international movement focused on assessing the health needs and challenges of family caregivers – predominantly daughters and spouses – who are caring for elderly loved ones with disabilities, cognitive impairments and dementia.

The research comes at a critical juncture. With the number of elderly Canadians on the rise, we are set to see an increase in the rate of Alzheimer’s disease and other dementias. This growing health burden will fall largely on family caregivers.²

At the heart of Dr. Keefe’s research is her co-creation of the Caregivers’ Aspirations, Realities and Expectations (C.A.R.E.) Tool. It’s a pioneering assessment tool for developing an evidence-based understanding of the support services that family caregivers need.

“We wanted to give caregivers a voice, to really let caregivers tell their story in their own words,” says C.A.R.E. Tool co-creator Nancy Guberman, now a retired University of Quebec in Montreal professor of social work, who co-presented the webinar.

EVIDENCE IN ACTION: STARTING A CONVERSATION

THE CAREGIVERS' ASPIRATIONS, REALITIES AND EXPECTATIONS (C.A.R.E.) TOOL IS HELPING HEALTH CARE PROVIDERS UNDERSTAND THE DIVERSE AND COMPLEX NEEDS OF FAMILY CAREGIVERS. AT ITS CORE, THE C.A.R.E. TOOL IS A CONVERSATION STARTER, BOTH BETWEEN CAREGIVERS AND HOME SUPPORT PROFESSIONALS, AND AMONG HEALTH POLICY OFFICIALS. "IT'S AN AWARENESS ISSUE," SAYS C.A.R.E. TOOL CO-CREATOR JANICE KEEFE. "THE C.A.R.E. TOOL IS FUELLING A DIALOGUE ABOUT THE NEEDS OF FAMILY CAREGIVERS."

STARTING A CONVERSATION ABOUT C.A.R.E.

Dr. Keefe, Professor Guberman and colleagues started C.A.R.E.'s development in 1998 after conducting a global survey of existing caregiver assessment tools and not finding a single, comprehensive tool. The C.A.R.E. Tool fills this gap. For caregivers, the C.A.R.E. Tool provides the chance to sit down for an hour or more, either in a single session or several, and talk about their situation.

"For two-thirds of them, it was the first time they'd been able to talk about their experiences as caregivers," says Dr. Keefe of the 168 caregivers in Quebec and Nova Scotia who took part in the tool's initial research and development.

But it's more than just a chance to talk. The C.A.R.E. Tool also offers a detailed framework for a structured conversation between health care providers – including social workers, nurses and other health care professionals – and caregivers about the caregivers' challenges, concerns and hopes. Critically, it helps link these needs to potential caregiver support services, such as respite support.

The C.A.R.E. Tool has also helped reveal important details about today's spousal caregivers. A recent C.A.R.E. study found that three-in-four were women between the ages of 65 and 90, caring for an elderly spouse, one often in cognitive decline. The vast majority of these caregivers perform their role out of love and a sense of spousal obligation, often not even thinking of themselves as "caregivers", says Dr. Keefe. However, through the C.A.R.E. Tool conversation process, what's clear is that more than half feel exhausted and overwhelmed, and more than 70% are frustrated and discouraged.

C.A.R.E. CHANGING POLICY

During the past decade the C.A.R.E. Tool has prompted a growing paradigm shift in how national, provincial and local health systems account for who they serve.³

"All the research says that if you focus on caregivers enabling them to continue caring for as long as possible it's more beneficial to the caregiver, the client and the health system as a whole," says Jamie Davenport, Director, Home Care Development, Seniors Health, Primary and Community Care with Alberta Health Services (AHS). Ms. Davenport recently authored a report on an AHS pilot project that used the C.A.R.E. Tool to assess the needs of 79 home caregivers, 80 percent of whom were elderly female spouses caring for a husband with a cognitive impairment. The result, says Ms. Davenport, altered policy so that at-risk caregivers throughout the province are assessed.

For Dr. Keefe, the next stage of the research involves developing evidence-based best practices for caregiver assessment. For example, in the recent "Timing of the C.A.R.E. Tool Project," Dr. Keefe and colleagues explored when, in the case of caregivers of spouses with dementia, it was best to provide caregiver assessment. The study group of 100 spousal caregivers in Nova Scotia and Prince Edward Island was equally divided into three groups: those caring for a spouse with mild, moderate or severe cognitive impairment.⁴

"The interesting thing is that some of the people caring for moderately and severely cognitively impaired spouses felt that it would be better to have the assessment earlier because it would have prepared them for some of the things they were now experiencing," says Dr. Keefe. The researchers concluded that in an ideal situation every caregiver should be assessed once they're identified as a caregiver to provide a baseline assessment.

There's evidence that the C.A.R.E. Tool and the process of caregiver needs assessment has a positive health impact in-and-of itself.

"Caregiver assessment really helps to maintain the health and well-being of caregivers," says Professor Guberman. "It does this by allowing caregivers to talk through their issues and start considering their own needs."

Ms. Davenport agrees: "There is definitely a therapeutic impact of the C.A.R.E. Tool for caregivers. We had situations in which as soon as our project nurse walked into a home and sat at the table the caregiver broke down."

As Dr. Keefe and her research team prepare to write a synthesis report on lessons learned from the C.A.R.E. Tool's past fifteen years, Dr. Keefe is also reflecting on her personal experience. Last summer, her mother passed away after five years of cognitive decline. Her mother was able to spend those final years in her own PEI home thanks to the coordinated efforts of her nine children who shared daily care for her.

"I really am committed to improving the lives of caregivers," says Dr. Keefe. "At the same time we have to watch the balance between advocacy and evidence so that we're always coming back to what [the] data tells us."

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A LIGHTER LOAD

FOR THOSE CARING AT HOME FOR AN ELDERLY SPOUSE WITH COGNITIVE IMPAIRMENT, THERE'S OFTEN A HEAVY, IF INVISIBLE, PSYCHOLOGICAL BURDEN – ONE THAT CAN GRADUALLY ERODE A CAREGIVER'S MENTAL HEALTH. ALBERTA'S CAREGIVER AND ENHANCED RESPITE PILOT PROJECT DEMONSTRATED THE C.A.R.E. TOOL CAN HELP LIGHTEN THIS EMOTIONAL LOAD. CAREGIVERS COMPLETED EITHER THE CAREGIVER RISK SCREEN OR THE ZARIT BURDEN TEST (A STRUCTURED VERBAL INTERACTION USED TO EVALUATE LEVELS OF STRESS IN CAREGIVERS OF ALZHEIMER PATIENTS) BEFORE AND AFTER RECEIVING ADDITIONAL HOURS OF IN-HOME RESPITE SUPPORT AND THE C.A.R.E. ASSESSMENT. "THERE WAS A REDUCTION IN PEOPLES' SCORES ON THE CAREGIVER RISK SCREEN AND THE ZARIT BURDEN," SAYS MS. DAVENPORT, NOTING THAT THIS WAS ATTRIBUTED TO THE COMBINATION OF THE C.A.R.E. PROCESS AND RESPITE SUPPORT. "IT WAS ENOUGH TO SHOW US THAT WE MADE A SMALL IMPACT ON THE PARTICIPANTS. THEY FELT A LITTLE BETTER."

FOR MORE INFORMATION

C.A.R.E. Tool primary website: http://www.msvu.ca/en/home/community/Centres_Institutes/centreonaging/projects/caregiverassessment/default.aspx.

Canadian Caregiver Coalition website: <http://www.ccc-ccan.ca/>.

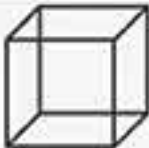
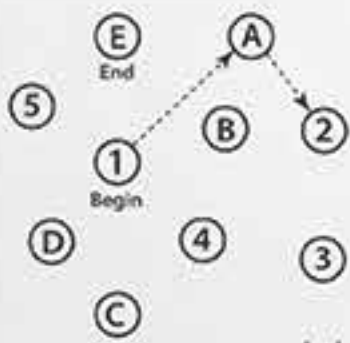

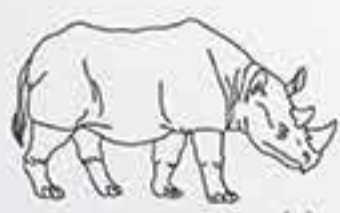
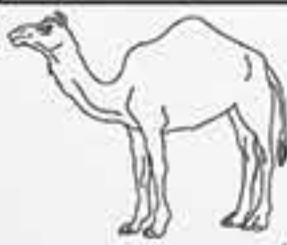
Canadian Dementia Knowledge Translation Network website: <http://lifeandminds.ca/>.

Statistics Canada, Portrait of Caregivers: 2012. Available at: <http://www.ccc-ccan.ca/media.php?mid=378>.

Janice Keefe's TEDx lecture What to do about mom?: <http://www.youtube.com/watch?v=BkoDNKsosc>.

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME: _____
Education: _____
Sex: _____ Date of birth: _____
DATE: _____

VISUOSPATIAL / EXECUTIVE			Copy cube	Draw CLOCK (Ten past eleven) (3 points)			POINTS		
				<input type="checkbox"/> Contour <input type="checkbox"/> Numbers <input type="checkbox"/> Hands			___/5		
NAMING									
						___/3			
MEMORY		Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	No points
		1st trial							
		2nd trial							
ATTENTION		Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order.		[] 2 1 8 5 4					___/2
		Subject has to repeat them in the backward order.		[] 7 4 2					
		Read list of letters. The subject must tap with his hand at each letter A. No points if > 2 errors.		[] FBACMNAAJKLBAFAKDEAAA JAMOF AAB					___/1
		Serial 7 subtraction starting at 100		[] 93	[] 86	[] 79	[] 72	[] 65	___/3
				4 or 3 correct subtractions: 3 pts. 2 or 2 correct: 2 pts. 1 correct: 1 pt. 0 correct: 0 pt.					
LANGUAGE									
		Read the following sentence: "John is the one to help to..."							___/2
		Name maximum number of words in one minute that begin with the letter F.							___/1
		Similarity between words (e.g., banana - orange = fruit)							___/2
		Read the following sentence: "The cat was under the couch when..."							___/5
		Read the following sentence: "The cat was under the couch when..."							___/5
Optional									
ORIENTATION		[] Date: _____ [] Month: _____ Year: _____		Place: _____ City: _____					___/6
		© Nasreddine M... www.mocatest.org Normal: > 26		TOTAL					___/30

MOCA HELPS CLINICIANS

NEUROLOGY JOURNALS SKEPTICAL AT FIRST
THE TEAM'S GROUNDBREAKING STUDY WAS INITIALLY REJECTED BY SEVERAL WELL-RESPECTED NEUROLOGY JOURNALS. AS OF FEBRUARY 2014, NINE YEARS AFTER BEING PUBLISHED IN THE *JOURNAL OF THE AMERICAN GERIATRICS SOCIETY*, THE STUDY HAD SURPASSED 1,800 CITATIONS. IT WAS ALSO RECOGNIZED AS THE MOST-CITED ARTICLE ON MILD COGNITIVE IMPAIRMENT BETWEEN 2006 AND 2009.¹

MoCA test page sample used in photo courtesy of Ziad S. Nasreddine.

NO TIME TO WASTE: DETECTING THE EARLY SIGNS OF DEMENTIA

The Montreal Cognitive Assessment helps clinicians around the world quickly identify mild cognitive impairment

AT A GLANCE

WHO: DR. ZIAD S. NASREDDINE, CENTER FOR DIAGNOSIS AND RESEARCH ON ALZHEIMER'S DISEASE (CEDRA); DR. NATALIE PHILLIPS, CONCORDIA UNIVERSITY; DR. HOWARD CHERTKOW, MCGILL UNIVERSITY

ISSUE: CLINICIANS CAN DIAGNOSE MILD COGNITIVE IMPAIRMENT (MCI) WITH A NEUROPSYCHOLOGICAL EXAM, BUT IT IS A LENGTHY PROCEDURE. THE MINI MENTAL STATE EXAMINATION (MMSE), IS COMMONLY USED TO DETECT DEMENTIA AND IS RELATIVELY SHORT, BUT IT ISN'T SENSITIVE ENOUGH TO DETECT MCI.

PROJECT: BETWEEN 1996 AND 2005, USING A COMBINATION OF CLINICAL EXPERIENCE, RESEARCH INFRASTRUCTURE AND INSIGHTS FROM NEUROPSYCHOLOGY, RESEARCHERS DEVELOPED THE MONTREAL COGNITIVE ASSESSMENT (MoCA), A TOOL TO SCREEN FOR MCI IN 10 MINUTES.

RESEARCH EVIDENCE: THE MoCA DETECTED 90% OF SUBJECTS WITH MCI, WHILE THE MMSE FOUND ONLY 18%. THE MoCA ALSO DETECTED 100% OF SUBJECTS WITH ALZHEIMER'S DISEASE COMPARED TO 78% FOR THE MMSE.

EVIDENCE IN ACTION: THE MoCA HAS NOW BEEN TRANSLATED INTO AT LEAST 43 LANGUAGES AND DIALECTS, AND IS USED BY CLINICIANS IN 100 COUNTRIES.

SOURCES: JULAYANONT, P., ET AL. "THE MONTREAL COGNITIVE ASSESSMENT (MoCA): CONCEPT AND CLINICAL REVIEW." FORTHCOMING IN A.J. LARNER (ED.), *COGNITIVE SCREENING INSTRUMENTS: A PRACTICAL APPROACH*. SPRINGER-VERLAG.

THE MoCA WEBSITE: WWW.MOCATEST.ORG.

In 1996, just two weeks into his new job on the south shore of Montreal, Dr. Ziad Nasreddine couldn't find time for all his work. Cognitive assessments for mild cognitive impairment (MCI) at the Neuro Rive-Sud Clinic were taking at least 90 minutes per patient. Either he had to develop a tool to speed up these assessments or abandon his cognitive neurology practice before it had even begun.

Fast forward to 2014: a tool he pioneered known now as the Montreal Cognitive Assessment (MoCA) is not only helping Dr. Nasreddine manage his own work, it's enabling clinicians all over the world to screen patients for MCI with remarkable sensitivity in about 10 minutes and detect the early signs of dementia.

The MoCA – pronounced "mocha" – features 11 sub-tests that assess several mental processes: attention and concentration, executive function (planning, organizing, flexibility), memory, language, visuoconstructional skills (drawing a three-dimensional cube and a clock), conceptual thinking, calculations and orientation. A score of 26 out of 30 is considered normal, and scores are adjusted based on the patient's level of education.

A free, paper-and-pencil tool, the MoCA has now been translated into at least 43 languages and dialects, and is used by clinicians in 100 countries around the world.

"I get emails from neurologists around the world thanking us for giving them this test," says Dr. Nasreddine. "A lot of clinics don't have anything between a comprehensive neurological assessment and the Mini Mental State Examination (MMSE). It's filling an important niche."

EVIDENCE IN ACTION: A SENSITIVE AND TIMELY COGNITIVE ASSESSMENT TOOL

THE MoCA HAS BEEN ENDORSED BY THE CANADIAN STROKE CONSORTIUM AND THE NATIONAL INSTITUTES OF HEALTH (NIH) IN THE U.S.¹ IN THEIR CLINICAL TRIAL, USING BOTH ENGLISH- AND FRENCH-SPEAKING SUBJECTS, THE TEAM FOUND THE MMSE IDENTIFIED MILD COGNITIVE IMPAIRMENTS ONLY 18% OF THE TIME, WHILE THE MoCA IDENTIFIED 90% OF CASES. EVEN FOR DEMENTIA, THE NEW TOOL WAS MORE EFFICIENT: THE MMSE IDENTIFIED 78% OF ALZHEIMER'S CASES, WHILE THE MoCA IDENTIFIED 100%.²

BEFORE THE MoCA

Since the mid-1970s, the MMSE had been the gold standard for cognitive screening. While this 10-minute test was designed to detect cognitive impairment in dementia, it was not sensitive enough to pick up signs of milder cognitive deficits, which sometimes lead to dementia, or to evaluate executive function. Thus, family members might notice the mental decline in a loved one, but the person might still easily pass the relatively simple test items on the MMSE, leaving impairment undiagnosed.

“It can sometimes take two years to convince family doctors who use the MMSE to acknowledge the mild cognitive impairment in their patient,” says Dr. Nasreddine. “This is valuable time lost because a lot can be done during the MCI period. The doctor can follow the patient more closely, and the family can keep an eye on issues like driving, medications, vascular risk factors and legal matters like power of attorney in case of incapacity.”

Taking a cognitive test is not only useful for detecting cognitive deficits: it can also reassure subjects who pass the test that their memory lapses are normal, and not dementia. Scoring high on simple questions in the MMSE, however, did not calm the jitters of Dr. Nasreddine's patients. “I couldn't reassure them there was nothing to be worried about with just the MMSE,” he says.

While in residency at Sherbrooke University, Dr. Nasreddine had developed a one-hour screening test for MCI, an innovation that helped him land a fellowship at the University of California Los Angeles (UCLA). After starting a practice at the Neuro Rive-Sud Clinic in Montreal, however, he quickly discovered that a one-hour test absorbed too much time in his busy schedule. Between 1996 and 2000, while at the clinic, he continued to fine-tune the test based on his clinical experience. An initial scientific trial with French-speaking subjects using a 10-minute version yielded promising results.

The desire to develop an English version of the tool and publish research findings brought two new partners on board in 2003 who further enhanced the tool. Dr. Howard Chertkow, director of the Jewish General Hospital Memory Clinic and a professor of neurology at McGill University, brought two decades of research experience in memory and Alzheimer's disease. Dr. Natalie Phillips, a psychology professor at Concordia University who directs the Cognitive Aging and Psychophysiology Lab, brought academic and clinical expertise in neuropsychology, language, working memory and executive function.

“The three of us sat down and looked at the preliminary data – which items could help discriminate older adults with normal cognition from those with MCI and mild Alzheimer's,” says Dr. Phillips.

Ultimately, the team kept the most useful items and added a few new ones. Dr. Phillips, for example, helped find the “sweet spot” in memory retention: the number of words to remember that would be demanding enough to catch a memory difficulty without stumping a healthy older adult. They settled on five words, one fewer than an earlier version of the MoCA.

Dr. Chertkow drew on his own CIHR-supported research that showed people with Alzheimer's disease quickly lose the ability to identify unfamiliar animals. “So instead of naming a watch and a pen [as in the MMSE], which is not a challenge, people have to name a lion, rhinoceros and a camel,” he says.

THE MoCA IN PRACTICE

While MoCA has been validated as a screening tool, the researchers point out that it has clinical limitations. Dr. Nasreddine uses the test cautiously. “If the results are normal, you reassure patients,” he says. “If it's abnormal, we don't jump to conclusions. Anything can affect performance. You have to be vigilant as a clinician, and try to interpret results correctly.”

In her neuropsychological research, Dr. Phillips uses the MoCA all the time to screen out older adults with cognition problems. “It's an entry point into the lab,” she says. “Then we do more extensive testing.”

Dr. Serge Gauthier, who directs Alzheimer's research at the McGill Centre for Studies in Aging, agrees other tools than just the MoCA are required. “It's a fantastic tool, but once you find abnormalities, you need to probe deeper,” says Dr. Gauthier, who was part of a working group studying how to validate the MoCA for people with lower levels of education.

Will the MoCA stand the test of time? “Cognitive tests don't last forever,” says Dr. Chertkow. “An efficient computerized test may eventually replace the MoCA.” For her part, Dr. Phillips cautions about any approach relying solely on computers. “Nothing replaces the information an experienced clinician gets from seeing a patient taking a cognitive test in person,” she says.

Whether on its own or in conjunction with other tests, the work of Drs. Nasreddine, Phillips and Chertkow will likely play a future role in the field. “Once there is better treatment for dementia, early diagnosis will be key for therapy,” says Dr. Chertkow. “That's exactly what the MoCA was designed to do.”

1 Nasreddine, Ziad, MoCA News (2010). Available at: http://www.mocatest.org/moca_news.asp.

2 Nasreddine, Ziad, et al. “The Montreal Cognitive Assessment (MoCA): A brief screening tool for mild cognitive impairment,” *Journal of the American Geriatrics Society* 53(2005):695-699.

TRANSLATING THE MoCA

YOU CAN TEST VERBAL FLUENCY USING PHONEMIC (LETTERS OF THE ALPHABET) AND SEMANTIC (CATEGORIES) CUES. ONE OF THE MoCA'S SUB-TESTS ASKS SUBJECTS TO NAME AS MANY WORDS THAT START WITH THE LETTER “F” AS POSSIBLE WITHIN ONE MINUTE. HOWEVER, THIS TEST PRESENTED A CHALLENGE WHEN THE MoCA WAS ADAPTED FOR PATIENTS IN HONG KONG. “IN THE CHINESE LANGUAGE, WE DON'T USE AN ALPHABET SO WE CAN'T TEST PHONEMIC FLUENCY,” SAYS DR. ADRIAN WONG, A CLINICAL PSYCHOLOGIST AND NEUROPSYCHOLOGIST AT THE HONG KONG INSTITUTE OF EDUCATION. “WE TEST SEMANTIC FLUENCY BY ASKING SUBJECTS TO NAME ANIMALS. THERE ARE PSYCHOLOGICAL DIFFERENCES, BUT IT'S THE BEST WE CAN DO.” THE HONG KONG MoCA, WHICH HAS BEEN VALIDATED FOR USE IN THAT POPULATION, ALSO ADAPTS OTHER SUB-TESTS INVOLVING LETTERS.

FOR MORE INFORMATION

The MoCA test (Copyright Z. Nasreddine MD) is freely available for clinical, educational and academic research use, at www.mocatest.org. The training kit includes a video of test administration, neuro-anatomical correlation, and clinical interpretation. Contact ziad.nasreddine@cedra.ca or info@mocatest.org.

Cognitive Aging and Psychophysiology Lab (CAP) website: <http://psychology.concordia.ca/fac/phillips/>.

McGill Centre for Studies in Aging website: <http://aging.mcgill.ca/index.html>.

An interview with Dr. Ziad Nasreddine: How to treat Alzheimer's. Video: <http://fr.video.canoe.tv/video/divertissement/cinema/2045312001/le-dr-ziad-nasreddine/1180121103001/page/3>.



MoCA GOES DIGITAL

AN ELECTRONIC VERSION OF THE MoCA (VERSION 8.1), WHICH INCORPORATES AUTOMATIC SCORING OF THE TEST, PROCESSING SPEED AND THE CALCULATION OF A NEW MEMORY INDEX SCORE (MIS), WILL BE AVAILABLE IN 2014. THE MoCA-MIS HELPS CLINICIANS AND RESEARCHERS DETERMINE WHICH MCI SUBJECTS ARE MORE LIKELY TO CONVERT TO ALZHEIMER'S DISEASE IN THE NEXT 18 MONTHS.



CIHR'S INTERNATIONAL COLLABORATIVE RESEARCH STRATEGY FOR ALZHEIMER'S DISEASE

Since it was founded, CIHR has been a strong supporter of dementia research. Over the past decade, CIHR has awarded more than \$236 million to researchers exploring the causes and possible treatments of Alzheimer's disease and other forms of dementia.

The organization has invested in research exploring all aspects of dementia, from identifying the genetic roots of the condition to understanding its impact on the quality of life of patients and caregivers. While it is important to study the many facets of this complex group of diseases, it's vital that we do so in a coordinated way that maximizes our country's research strengths.

Recognizing this need for a coordinated approach to dementia, CIHR created the International Collaborative Research Strategy for Alzheimer's Disease in 2009 as its first Signature Initiative. The Strategy is led by CIHR Institute of Aging and co-led by CIHR Institute of Neurosciences, Mental Health and Addiction. The Strategy has three main areas of focus:

1. **Primary Prevention** – Prevent dementias from occurring by identifying the underlying mechanisms responsible for the neurodegenerative processes that lead to Alzheimer's disease and related dementias.
2. **Secondary Prevention** – Delay the progression of disease through diagnosis and early intervention.
3. **Quality of Life** – Improve access to quality care and enable the health care system to deal more efficiently with the rising number of individuals with dementia.

The Strategy consists of a national component and an international component. In 2013, CIHR launched a call for expressions of interest for the Canadian Consortium on Neurodegeneration in Aging (CCNA) – the national component of CIHR's Dementia Strategy. The CCNA will bring together more than 340 researchers in a new collaborative space to work with clinicians, patients, caregiver associations, health charities, policy makers and industry partners from across the country and around the globe. By bringing together the leading experts in various sectors touching dementia, the CCNA will help increase the speed at which we generate the knowledge that is essential in the pursuit of new ways to delay the onset of the disease, prevent it from occurring, and also improve the quality of life of those affected and their families.



The consortium will be supported by CIHR and 14 partners in both the public and private sectors. CIHR held the first CCNA partners' forum in the summer of 2013, where participants were invited to share their ideas and perspectives on how to build an innovative and collaborative research agenda for the final CCNA application.

On the international front, CIHR has helped Canada secure partnerships with dementia research programs in other countries, including the Alzheimer's Disease Neuroimaging Initiative (ADNI) in the U.S., the Wellcome Trust-MRC-Canada partnership in the U.K., the France-Québec-Canada partnership, the Network of Centres of Excellence in Neurodegeneration (COEN) with seven partner countries in Europe, the Joint Programme in Neurodegenerative Disease Research (JPND) with 27 partner countries in the EU, and a Joint Program with the National Natural Science Foundation of China.

These international partnerships are essential in bringing together the complementary expertise of researchers and are aiding the development of methods, technologies and research platforms to spur further advances in the field. For example, CIHR is an active member of JPND and its COEN associated initiative in order to support the inclusion of Canadian researchers in collaborative efforts on priority topics such as comparing the different mechanisms underlying the different neurodegenerative diseases causing dementia.

Through both the CCNA and international partnerships, CIHR aims to support transformative research that will lead to preventive, diagnostic and treatment approaches to Alzheimer's disease and related dementias.

FOR MORE INFORMATION

CIHR's International Collaborative Research Strategy for Alzheimer's Disease:
<http://www.cihr-irsc.gc.ca/e/43629.html>.

CIHR Strategic Initiatives:
<http://www.cihr-irsc.gc.ca/e/12679.html>.

NEED MORE EVIDENCE?

Thank you for reading the Fall 2014 issue of *Show me the Evidence*. We hope that you enjoyed learning more about the impact of Canadian health researchers and encourage you to visit CIHR's website (www.cihr-irsc.gc.ca) and social media sites (www.cihr-irsc.gc.ca/e/42402.html) to learn about other CIHR-funded success stories.

IN THE SPRING 2015 ISSUE OF *SHOW ME THE EVIDENCE*, WE WILL BE LOOKING AT CIHR AND PARTNER-FUNDED RESEARCH SUCCESSES IN THE AREA OF EPIGENETICS RESEARCH.

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EVIDENCE IN THE MAKING

www.cihr-irsc.gc.ca/e/44921.html

EVIDENCE MAKERS

www.cihr-irsc.gc.ca/e/47688.html

FEEDBACK FROM THE COMMUNITY

www.cihr-irsc.gc.ca/e/44922.html