diaMentis

Brief submitted to the House of Commons
Standing Committee on Finance
Parliament of Canada
diaMentis, Normand Tremblay, CEO

A healthy population means a healthy economy

Development of a support tool for the diagnosis of mental illness (schizophrenia (SZ), bipolar disorders (BP), major depression (MD) and anxiety)

Mental health: A problem that affects us all

The knowledge economy, innovation and entrepreneurship are powerful drivers of economic growth and prosperity. In this regard, a population will be most productive when it is in good health. Health care is a key sector of economic development (for Canada and the world) and a fundamental value for Canadians. Mental health is a global priority, since, according to the World Health Organization (WHO), it affects nearly 450 million people. In a statement for World Health Day on April 7, 2017, Prime Minister Trudeau said, "One in three Canadians will experience a mental illness during their lifetime, but these serious health problems are not always visible. By talking about depression and mental health openly and honestly, we can help end the stigma that too often acts as a barrier for those who want and need help."

In Canada, one person in five, or about 6.7 million people, are dealing with a mental health problem. For the sake of comparison, 2.2 million people have type 2 diabetes, and 1.4 million people have cardiovascular disease. Mental health disorders show up early in life. Every year, more than 28% of people aged 20 to 29 have a mental illness, and by the age of 40, one of every two people has, or will have had, a mental illness. If you include families and caregivers, almost everyone is affected by the disease in one way or another. It is the second-leading cause of hospitalization in the 15-to-34 age group and the third-leading cause in the 35-to-44 age group, all diseases combined.

A serious diagnostic problem

Diagnosing mental illnesses is quite complex and presents many challenges, since the various diseases share a number of symptoms.

Diagnosis depends on observation of the symptoms and on the patients' ability to answer clinicians' questions satisfactorily. Thus, all that clinicians have to work with in making a diagnosis and selecting a medication is their observation of clinical signs and symptoms. The absence of quantitative, biological diagnostic tools makes their work much more difficult.

diaMentis

A trial-and-error period of uncertain length is often necessary; in some cases, it can take years. About 50% of patients will their diagnosis changed in the first seven or eight years of their illness and will not receive the best possible treatment. During this phase, many patients get discouraged, go off their medication and find themselves in a downward spiral leading to job loss, family break-up, homelessness and, all too often, suicide. Ninety percent of suicides are associated with mental illness, and no decrease has been observed in the last 50 years.

Major economic impact

According to the Mental Health Commission of Canada, the estimated total cost of mental illness in Canada was at least $50 billion in 2012, not counting the costs associated with the care provided by caregivers and most of the other costs unrelated to the health care system and mental health support services, such as justice system costs. That is equivalent to 2.8% of Canada's gross domestic product in 2011.

The impact of mental illness is particularly serious in the workplace and in the working-age population. Mental illness accounts for nearly 30% of short-term and long-term disability claims in Canada.

In 2010, mental health disorders were responsible for 47% of approved disability claims in the federal public service, almost double the proportion 20 years ago.

Many studies demonstrate the clinical and economic value of better mental health diagnosis. Stabilizing the patient in the first five years is closely linked to a better long-term prognosis.

The diagnostic support tool developed by diaMentis

None of the diagnostic support tools described in the literature meet the desired performance criteria with regard to predictive value, non-invasive technology, ease of use and low cost.

diaMentis is currently developing an initial differential diagnostic support tool for schizophrenia and bipolar 1 disorder. The frequent and simultaneous presence of psychotic symptoms in bipolar 1 patients results in a high risk of confusion with schizophrenia. Other indications such as major depression and anxiety will be added as further data and research become available.

Scientific basis

During the embryo's development, the retina is formed from the same cells as the brain and is therefore part of the central nervous system (CNS). As a result, effects or anomalies in the structure and/or functioning of the neurons in the brain are also observable in the retina's neurons. Changes in retinal function may reflect poor neurological functioning associated with mental disorders. This information in the retina is analyzed to identify characteristics specific to certain mental illnesses: biomarkers.

diaMentis

Initial proof of concept

The initial proof of concept is based on work carried out between 2011 and 2014 at the research centre of Laval University's Institut universitaire en santé mentale de Québec (CRIUSMQ). Using data obtained through a simple eye examination, an electroretinogram (ERG), researchers identified biosignatures specific to certain mental disorders in the retina.

ERG examinations, which are based on a non-invasive technology used in ophthalmology for more than 45 years, were conducted on nearly 1,000 patients suffering from schizophrenia, bipolar disorders and major depression. With this data, algorithms were developed with the aim of creating predictive models, thereby confirming the approach's commercial potential as a diagnostic support tool. This simple, non-invasive, inexpensive test provides quantitative measurements of various parameters specific to those diseases. This initial diagnostic support tool will help clinicians arrive more quickly at a more accurate diagnosis, thus preventing the patient's condition from deteriorating.

A patent application (Canada, the United States and Europe) based on this work has been filed (cf. *PCT/CA2014/050233: Use of electroretinography (ERG) for the assessment of psychiatric disorders*).

Savings for society

Schizophrenia, bipolar disorders and major depression affect about 9% of the non-American adult population, or about 25 million people.

A recent study by Cloutier et al. (2016) provided a fairly accurate picture of the economic burden due to schizophrenia in the United States. The authors estimated that in 2013, the economic burden of schizophrenia was US$155.7 billion.

- **Direct health costs** (medication, hospitalizations, medical care, follow-ups, etc.) accounted for **25%** of the costs.

- Indirect costs (unemployment, loss of productivity, suicide, caregivers) and **non-health-related costs** (justice system costs, homelessness, etc.) made up the remaining **75%**.

The data from this study was used to extrapolate data for Canada, whose population is 11% of the size of the U.S. population. On the basis of these assumptions, the total cost of schizophrenia in Canada is probably $17 billion a year.

The following are the biggest costs:

1. Unemployment: 37.9%
2. Care provided by the family: 33.7%
3. Hospitalization costs: 9.8%

If the diaMentis tool reduced the indirect costs by just 5%, the potential savings for Canada would be $645 million a year.

An additional reduction of 20% in hospitalization costs, for example, would result in further annual savings of $335 million.

diaMentis

Financial partners to date

Since 2015, diaMentis has received $3.25 million in private capital from investors selected specifically for their expertise, and it has received support from the National Research Council's Industrial Research Assistance Program ($477,000). These investments made it possible to carry out the following activities:

- Complete its spin-off through the transfer of data from Laval University;
- Begin hiring a multidisciplinary team;
- Consolidate the intellectual property;
- Carry out a comprehensive risk analysis;
- Validate the regulatory process;
- Select the researchers (Canadian and American) to do the feasibility study, purchase the ERG equipment and perform the study design.

Significant challenges

Consolidation of the previous data in an industrial context as well as the studies and research on the Canadian and American markets are needed:

1. **Feasibility study:** The goal is to consolidate the algorithms that are part of the initial predictive models developed at Laval University in relation to the directives of health regulatory agencies (Health Canada, Food and Drug Administration, European Agency for the Evaluation of Medicinal Products). To that end, a study involving 300 subjects (SZ, BP, control) will be carried out at three clinical sites (Canada and the United States). The objective is to develop an effective, robust, well-tested diagnostic support tool.

2. **Pivotal study:** This study will validate the performance of the algorithms (fine-tuned through the feasibility study) in an actual use context with a view to their commercialization. It will be conducted at various clinical sites (Canada and the United States).

3. **Regulatory approval and commercialization:** Following the pivotal study, we hope to have our first SZ-BP1 differential diagnostic support product licensed by the health regulatory authorities with a view to commercializing it initially in Canada and the United States and subsequently in other parts of the world.

Preparation of new partnerships for commercialization on world markets

The experts associated with the project (physicians, psychiatrists) are convinced of the high potential of this technological platform. The development of simple, non-invasive, inexpensive biomarkers is highly important in view of the costs associated with the lack of a quantitative diagnostic tool and the disease's medical and social consequences. Over the next three years, diaMentis will bring in international experts to assist in the development of its technology and thus create an innovative business that is well positioned on the world market. We want to build a thriving Canadian company that addresses a global problem, and to create a hub of expertise that is unique in the world.

diaMentis

The next development stages will generate significant value for the company. To achieve this, however, financing is a major challenge, and introducing the product on the various markets will depend on how quickly the company can be capitalized. There is every reason to believe that this new approach may improve the productivity of people suffering from mental illness while saving money for the health system and society.

Statistics show that 21.4% of the Canadian labour force currently has a mental health disorder that may be lowering productivity. People who are at the beginning or the peak of their working lives are among the most seriously affected. By allowing early intervention, the product will reduce the period during which the illness is untreated and thereby diminish its severity.

The faster the company is able to generate revenue, the sooner it will be able to support the development of other indications and become more competitive internationally. Access to adequate, appropriate funding is essential for the advancement of priority projects for the Canadian economy and the health of Canadians.

diaMentis is currently in funding negotiations with the Government of Quebec. It is working closely with the Ministère de l'Économie, de la Science et de l'Innovation.

We are confident that the various levels of government, like our private investors, have a great interest in providing as much assistance and support as possible to continue the development of this diagnostic support tool.

diaMentis

APPENDIX

A problem that affects us all

Globally, more than 450 million people have mental health problems.

Mental illness is one of the leading causes of hospitalization in the United States and Canada.

The annual loss of productivity is more than 15%.

Mental disorders and substance abuse are the world's leading causes of disability.

A problem that affects us all

One person in five will have mental problems during his/her lifetime.

Mental illness is an important risk factor for other diseases (e.g., HIV, cardiovascular problems, diabetes).

Mental illness has a major economic impact on society and health care.

THREE OF THE TOP 15 INCAPACITATING DISORDERS ARE MENTAL PROBLEMS

1. DEPRESSIVE DISORDERS: 10.9%
2. Visual disorders: 4.6%
3. Hearing loss: 4.4%
4. Involuntary injuries: 4%
5. Alcoholism-related disorders: 3.7%
6. [Illegible]: 3%
7. SCHIZOPHRENIA: 2.7%
8. Arthritis: 2.6%
9. BIPOLAR DISORDERS: 2.4%
10. Anemia: 2.2%
11. Perinatal conditions: 2.2%
12. Asthma: 2%
13. Falls: 1.9%
14. Pulmonary disease: 1.9%
15. Malnutrition: 1.7%
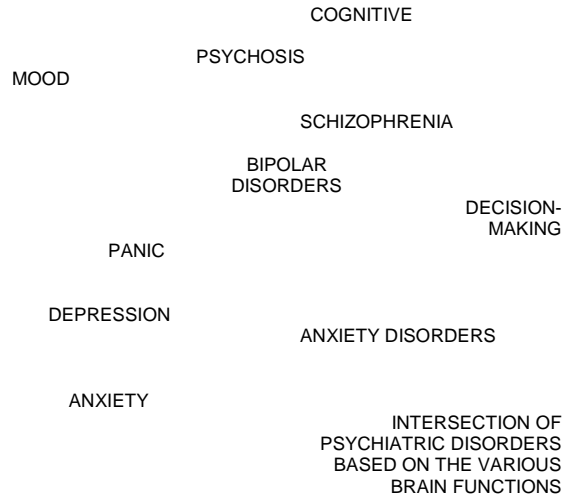
diaMentis

The root of the problem

Diagnosis depends primarily on observation and clinical identification of symptoms and the patient's ability and willingness to answer the physician's questions satisfactorily.

The symptoms are not always fully present at the onset of the disease.

The various diseases share certain symptoms.

There is a very high level of difficulty in diagnosing mental disorders.

There are currently no diagnostic tools on the market.

COGNITIVE

PSYCHOSIS

MOOD

SCHIZOPHRENIA

BIPOLAR DISORDERS

DECISION-MAKING

PANIC

DEPRESSION

ANXIETY DISORDERS

ANXIETY

INTERSECTION OF PSYCHIATRIC DISORDERS BASED ON THE VARIOUS BRAIN FUNCTIONS

THE CONSEQUENCES
of misdiagnosis

Medical uncertainty	Discouraged patients	Wrong or late diagnosis can lead to substance abuse and/or suicide	30% to 40% of patients with SZ or BP have their diagnosis changed in the first 3 to 5 years (40% to 50% after 7 or 8 years)	Up to 70% of bipolar disorders are not diagnosed

90% of suicides are associated with a mental illness, and no decrease in suicide has been observed in the last 50 years.

diaMentis

VALUE ADDED

Many studies demonstrate the clinical and economic value of better diagnosis.

Stabilization of the patient in the first five years is closely linked to a better long-term prognosis.

diaMentis offers

- Reliable biomarkers
- A non-invasive test
- Low cost
- Easy deployment
- Fast results through a web service

SEVERITY

Normal diagnosis
Treatment

Rapid diagnosis
Treatment

TIME

Trigger Inflammation Effects on tissues Symptoms of disease

SOLUTION
(value proposition)

| Faster, more accurate diagnosis | Right choice of treatments and psychotherapy | Greater acceptance of the disease by the patient; better follow-up on treatments |
| Faster return to work (reduction of disability premiums and family pressure) | Decrease in number and length of hospitalizations | Fewer relapses |

= BETTER RESULTS for the patient, the family, the clinicians, the health system and society

diaMentis

Scientific advisory committee

- Stuart C. Coupland, Ph.D., Eye Institute, University of Ottawa (Canada)
- Claude Hariton, Ph.D., Advanced Accelerator Applications S.A. (France)
- Steven M. Silverstein, Ph.D., Rutgers University (United States)