Mental Health International

The 5th US/Canada Forum on Mental Health and Productivity:

Reference Report of

Presentations and Proceedings

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MENTAL HEALTH INTERNATIONAL

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Thanks to all of the Forum participants and organizers for their assistance in making the forum event a success and in the preparation of this report.

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PART 1 – Protocols

About this Report

This report provides detailed information on the content of the 5th US/Canada Forum on Mental Health and Productivity.

The full-text of each of the presentations delivered at the Forum is included here in this report as edited transcripts based on the audio recording of the event. Other content is presented concerning the key themes from the discussion that occurred during the meeting and select ideas captured in the comments and interviews obtained after the meeting from the panel of experts.

Other related source material from the Forum is also provided in the appendices to this report concerning: the Forum Sponsor (Appendix A), the Forum Host and Report Sponsor (Appendix B), the full roster of the invited presenters, discussants and members of the executive panel (Appendix C), a brief review of the four previous US/Canada Forums on Mental Health and Productivity (Appendix D) and highlights of the 2011 Final Report from the Roundtable (Appendix E).

BRIEF NARRATIVE REPORT ALSO AVAILABLE

We have also prepared an executive report of the 5th Forum that is written in more of a journalistic narrative style. It is much shorter and focuses on the general themes of the presentations and the main ideas generated from the discussion. It also presents a unifying strategy and plan of action for the future that addresses the opportunities of greatest interest to the participants. As we publicize the report and distribute it widely, we hope to encourage business, government and science to come together around the common cause of promoting workplace mental health.

PART 2 – Prologue

Context for the 5th Forum

This invitation-only meeting was held on November 20th, 2013 in Toronto, Ontario, Canada. It was hosted by the Canadian Imperial Bank of Commerce in its global corporate headquarters located in the heart of Toronto's financial district. The host venue of the beautiful CIBC executive boardroom on the 56th floor of the building symbolized both the high level of respect afforded to the participants and the high goals of the Forum agenda.

The meeting featured a pair of keynote addresses, presentations by ten other distinguished speakers and open discussion from over 30 participants representing different areas of business and science who hailed from Canada, the United States and the UK. Also in attendance as observers were an executive panel of a dozen experts and analysts from the US and Canada who were tasked with providing insights and advice after the Forum.

The first four Forums in the series were held in 2007 and 2008 and were organized by the Global Business Economic Roundtable on Addiction and Mental Health. The Roundtable was active between the years of 1998 to 2011. Sponsoring the Forum series was one of many of the Roundtable's contributions. Its' goal was to translate, interpret, seek-out and study scientific data from the world's great research institutions and leading scientists and to learn from the real-life workplace experience of employees. This body of work was summarized in a Final Report published by the Roundtable in 2011 and highlighted here in Appendix E.

The Forum series began in Washington DC in 2007 and was launched by Canada's Ambassador to the United States, Mr. Michael Wilson, and the US Ambassador to Canada, David Wilkins. Another Forum was held later that same year in Ottawa and two more in 2008 in Boston and Toronto. Each Forum succeeded in bringing together business executives, politicians and researchers to address topics of mental health and the workplace.

A new non-for profit organization, Mental Health International, founded in 2013 is the successor to the Roundtable. Bill Wilkerson, Executive Chair, Joseph Ricciuti, President and CEO, Helen Lackey, Corporate Secretary and board members Dr. Mark Attridge and Dr. Roger McIntyre are the company's founders. It has the aim of building alliances between business and brain science, researchers and workplaces, trading partners and economic sectors. Mental Health International was the sponsor and main organizer of the 5th Forum and is also the author of this report.

The Centre for Addiction and Mental Health (CAMH), based in Toronto, also assisted in planning certain aspects of the 5th Forum. The support of CAMH is appreciated and in particular, Dr. Bruce Pollock and Dr. James Kennedy, who were instrumental in selecting speakers for the Forum. Also, a CAMH Foundation special reception celebrating the Campbell Family Mental Health Research Symposium was held the day before the 5th Forum and featured several of same internationally renowned presenters, including Dr. Daniel Weinberger, Dr. Thomas Insel and Dr. Anthony Phillips.

Going forward, a 6th US/Canada Forum is now in the planning stages to be held later in 2014 in Denver, Colorado. The theme of this meeting will be to examine suicide prevention and depression.

Purpose of the 5th Forum

The primary purpose of the 2013 Forum was to develop a strategic international agenda for mental health in the workplaces of nations through a business-science partnership to accelerate ultimate remission or cure scenarios for depression and allied conditions.

The Honourable Michael Wilson also placed his influence behind the genesis of the 5th Forum, providing the opening presentation and personally mandating Mental Health International to develop a strategy for responding to the Forum theme of creating a Business-Science Partnership. The science and business co-chairs of the Forum were, respectively, Dr. Bruce Pollock, Vice-President, Research, Centre for Addiction and Mental Health and Rupert Duchesne, Group CEO, Aimia Corporation and Chairman, Brain Canada. Others involved in planning the meeting including the following past co-chairs of the Forum series:

Past Co-Chairs of the US/Canada Forum Series on Mental Health and Productivity

- Colum Bastable, Chairman, Cushman-Wakefield Real Estate
- John Hunkin, former Chairman and CEO, Canadian Imperial Bank of Canada (CIBC)
- Dr. Ron Kessler, Professor of Health Policy, Harvard University Medical School
- Dr. Thomas Insel, Director, National Institute of Mental Health (NIMH), United States
- Dr. Anthony Phillips, Scientific Director, Canadian Institute of Neuroscience, Mental Health and Addiction, Canadian Institutes of Health Research (CIHR)
- Dr. Rémi Quirion, Chief Scientist, Province of Quebec
- Joseph Ricciuti, President and CEO, Mental Health International
- Honorable Michael Wilson, Chairman, Barclays Canada
- Bill Wilkerson, Executive Chairman, Mental Health International (Forum General Chairman)

Proposal for Discussion at the 5th Forum

The presenters and participants were asked to consider the following general proposal, which was distributed in advance of the meeting.

International Business-Science Partnership for Mental Health and Productivity

On a number of fronts, Canada has effectively canvassed for – and made happen – international cooperation and collaboration as the bookends for strategic action to reduce the global impact of major mental disorders. This outreach has been, largely, science-to-science. Expanding this to include business as a strategic partner of science across borders would seem to make sense. There is much to leverage, build on and bring together for this purpose. A Business-Science Partnership – by way of example – would not only be an advocate for scientific data sharing and joint-effort but such a partnership could:

• Build a business and economic case for strategic investments in science to accelerate improved care and treatment across borders, institutions and projects;

• Make the case for barrier reductions and political support to accelerate the transfer of new scientific discovery into clinical innovation and improved care;

• Recruit workplaces and employee groups as accessible sites and volunteer subjects for clinical trials to reduce the cost and time needed to bring new knowledge and new therapies to market; and

• Create an information service to translate business-to-science and science-to-business to report on trends and to interpret the meaning of what research means what to employers and their people, this as a guide to corporate investments in research.

Final Agenda for the 5th Forum

WELCOME and OVERVIEW
Forum Host: John Hunkin, Former Chairman and CEO, CIBC
Forum Sponsor: Bill Wilkerson

BRAIN HEALTH IN A BRAIN-BASED ECONOMY
Facilitator: Joseph Ricciuti
Forum Co-Chair Business: Rupert Duchesne
Forum Co-Chair Science: Dr. Bruce Pollock

RE-THINKING MENTAL ILLNESSES AND BRAIN RESEARCH IN A BRAIN ECONOMY
Invited Panel Presentations:
- A Global Brain Economy - Honorable Michael Wilson
- Brain Health Research in Canada - Dr. Anthony Phillips
- Brain Health Research in the United States - Dr. Thomas Insel

Supplemental Presentation:
- Brain Capital in the Canadian Military - Col. Dr. Rakesh Jetly

KEYNOTE ADDRESS: Finding a Cure for Mental Illnesses: Is this a Possibility or a Pipe Dream?
Dr. Daniel Weinberger

BREAKTHROUGHS IN TREATING MENTAL DISORDERS: Historic Beginnings of Personalized Medicine
Personalized Medicine Based on Genetic Testing - Dr. James Kennedy & Dr. Nicholas Voudouris
Personalized Medicine Based on Brain Wave (EEG) Testing - George Carpenter, IV & Dr. Gary Hasey

FORGING A NEW ERA OF COLLABORATION: Halting the Progression of Human Suffering and Economic Losses
Facilitator: Bill Wilkerson

KEYNOTE ADDRESS: The Five Principles of Transformation for a New Era of Collaboration
Don Tapscott

DISCUSSION: Forging A New Era of Collaboration

PART 3 – Introduction to the Forum

The FORUM HOST

John Hunkin

Former Chairman and Chief Executive Officer, Canadian Imperial Bank of Commerce
Toronto, Ontario, Canada

JOHN HUNKIN: Ladies and gentlemen, I am John Hunkin. I am a member of the board of the CAMH Foundation and previously I was chairman and chief executive officer of the Canadian Imperial Bank of Commerce - and once in a while they lend me the room. So, on behalf of Gerry McCaughey, CEO of CIBC, who couldn't be with us today, I want to welcome you all to CIBC and to the 56th floor boardroom.

The FORUM'S SPONSOR

Bill Wilkerson

Executive Chairman, Mental Health International
Toronto, Ontario, Canada

Bill Wilkerson is the Executive Chairman of Mental Health International and was a Co-Founder of the Global Business and Economic Roundtable on Addiction and Mental Health. In addition, he also served as a sworn civilian adviser to the Royal Canadian Mounted Police 2008-2011. He is a strong proponent for mental health strategies in policing, military service, teaching and nursing as well as the private sector workplace. Wilkerson draws upon his extensive experience in various fields spanning business, journalism, the arts and government service.

WELCOME

BILL WILKERSON: This is our 5th US/Canada Forum on Mental Health and Productivity. The first Forum was held in 2007 and was hosted by the Honourable Michael Wilson, when he was our ambassador to the United States in Washington. The second Forum was held later that same year in Ottawa, with Mrs. Harper as our guest of honour. The third Forum was held in 2008 at Harvard University, where Professor Ron Kessler, the famed epidemiologist, hosted us. Our last Forum occurred back in Toronto in the fall of 2008, where we discussed mental health in the law enforcement and military communities. So, we've had a few years' delay since the last forum in 2008.

For today, we're hoping by the end of the morning that we will have some sense of whether or not is a good idea to develop an ongoing business-science relationship or partnership - not to duplicate or replace anything that's currently existing, of course - but to provide a vehicle through which information moves more regularly and has a strategic touch to it.

PART 4 – Brain Health in a Brain-Based Economy

FACILITATOR: Joseph Ricciuti

FORUM CO-CHAIR for BUSINESS

Rupert Duchesne

Group CEO, AIMIA Inc. & Chairman of Brain Canada
Montreal, Quebec, Canada

Rupert Duchesne, MBA, is CEO of Aimia Inc. In this role he presided over a decade of rapid growth of the organization from its carve-out as a division of Air Canada in 2002, the initial public offering as the Aeroplan Income Fund in 2005, the conversion to corporate status as Groupe Aeroplan, Inc. in 2008 and the re-branding of the Corporation as Aimia in 2011. In 1996, he joined Air Canada as Vice President, Marketing, and in 1999 was promoted to Senior Vice President, International. Mr. Duchesne also has experience in strategy and investment consulting with other firms around the world. Mr. Duchesne holds a MBA from the University of Manchester and a Bachelors degree with Honours in Pharmacology from the University of Leeds, both in England. He is Chair of the executive boards of the NeuroScience Canada Partnership and of the Brain Canada Foundation.

Mr. Duchesne is also Chair of Brain Canada. Brain Canada is a national non-profit organization that develops and supports collaborative, multidisciplinary, multi-institutional research across the neurosciences. Brain Canada connects the knowledge and resources available in this area to accelerate neuroscience research and funding and maximize the output of Canada's world-class scientists and researchers. Brain Canada was created to address the twin challenges of increasing the scale of brain research funding in Canada and widening its scope to encourage interdisciplinary collaboration to produce insights for treating multiple disorders.

FORUM CO-CHAIR for SCIENCE

Dr. Bruce Pollock

Vice President, Centre for Addiction and Mental Health & Professor at the University of Toronto
Toronto, Ontario, Canada

Bruce Pollock, **MD, PhD, FRCP(C), DFAPA, FCP,** is Vice President of Research and Director of the Campbell Family Mental Health Research Institute, and Senior Scientist with the Geriatric Program at the Centre for Addiction and Mental Health (CAMH) & Professor and Director of Geriatric Psychiatry at the University of Toronto. Dr. Pollock has authored more than 300 published articles and is internationally recognized for his work in geriatric clinical psychopharmacology. He is a Distinguished Fellow of the American Psychiatric Association, a Fellow of the American College of Clinical Pharmacology and a Fellow of the Canadian Psychiatric Association. His most recent honours include the William B. Abrams Award in Geriatric Clinical Pharmacology (with Distinction) from the American Society for Clinical Pharmacology and Therapeutics and the Jack Weinberg Memorial Award (with Distinction) from the American Psychiatric Association. He holds a PhD in pharmacology from the University of Pittsburgh and a MD and BSc from the University of Toronto.

INTRODUCTORY REMARKS

RUPERT DUCHESNE: I'm the business co-chair for the 5th US/Canada Forum on Mental Health and Productivity.

Let me give you a brief overview of Brain Canada. Just a year ago, the Government of Canada and Brain Canada embarked on the biggest single private partnership in brain research, $100 million from the government over five years to be matched by the private sector. We're about a third of the way towards that match, so it's going very well and built on the strong foundation of the brain repair program in the late 2000s, which had a substantial and significant outcome. I think this demonstrates the critical importance of and the necessity for the government, business and science to come together in a common cause to have meaningful impact not only on mental health, but obviously also on the disabling and utterly often deadly effects of brain illness and injury.

This Forum demonstrates the same point with an added dimension. It's about cooperation and partnerships that have to reach across borders. The problems we're grappling with really know no boundaries. In fact, at the CAMH research symposium yesterday, the brain was rated as being second in complexity and difficulty to understand, behind only the cosmos, and with a clear view that eventually understanding the brain may actually may be harder. So, we really have to search very hard to find a solution without the common borders with which we are so familiar. This Forum by definition already stretches across those borders as we have presenters and participants from Canada, from the United States and from other places as well.

Today we are going to discuss the ways and the means to promote that sense of common cause across geographic borders, across disciplinary borders, across organization sectors and across scientific disciplines. That is at the core of what this is about – why we are having this meeting. A formal cooperation between business and science is really critical, if we're going to bring a better understanding and better outcomes to this area of brain health.

DR. BRUCE POLLOCK: I want to thank Bill [Wilkerson] and his team for a really spectacular job in putting this together and in being able to bring all this talent from multiple spheres into one room. In just in the first part we have the directors of the US National Institutes of Mental Health and the Canadian equivalent and then a keynote address from Danny Weinberger, who really is, without any exaggeration or hype, one of the - if not the - preeminent scientist in the field today working in schizophrenia.

So, we are going right to the speakers. Thank you.

PART 5 – Re-Thinking Mental Illnesses and Brain Research in a Brain Economy

FACILITATOR: Joseph Ricciuti

Presentation 1 - The Honourable Michael Wilson, Chairman, Barclays Canada

Presentation 2 - Dr. Anthony Phillips, Scientific Director, Canadian Institute for Neuroscience and Mental Health, Canadian Institutes for Health Research (CIHR)

Presentation 3 - Dr. Tom Insel, Director, National Institutes of Mental Health (NIMH), United States

Supplemental Presentation - Dr. Rakesh Jetly, Canadian Forces Psychiatry and Mental Health Advisor to Surgeon General Directorate of Mental Health, Canadian Forces Health Services Group Headquarters

PART 5 – Re-Thinking Mental Illnesses and Brain Research in a Brain Economy

PRESENTATION 1 – OPENINING REMARKS:

"A Global Brain Economy - Looking Backward and Looking Forward"

Honourable Michael Wilson
Chairman, Barclays Canada
Toronto, Ontario, Canada

Mr. Wilson, PC, CC, LLD (Hon.), is currently Chairman of Barclays Capital Canada, Inc. Mr. Wilson had prior executive leadership positions in the banking industry at UBS Canada and RBC Financial Group and in business as a director of BP Canada and director of Manulife Financial. He served as Canada's Ambassador to the United States from 2006 to 2009 and as Canada's Finance Minister from 1984 to 1991 with later government appointments as the Minister of Industry, Science and Technology and as Minister of International Trade. He is co-chair of the Canadian Institutes of Health Research (CIHR) and is the former Senior Chairman of the Global Business and Economic Roundtable on Addiction and Mental Health. He is also active in supporting the NeuroScience Canada Partnership, the Centre for Addiction and Mental Health, the Canadian Cancer Society, the Canadian Council for Public-Private Partnerships and the Canadian Coalition for Good Governance. He has received a number of awards for his work in these fields, as well as from the Conference Board of Canada, the Public Policy Forum and the Rotman School of Business. Mr. Wilson is a Companion of the Order of Canada and has honorary degrees from the University of Toronto, York University and Trinity College at the University of Toronto.

Let me make some brief opening remarks. But before I do that, let me just make an observation: This session today is a continuation of many years of collaboration and dialogue focused on the importance of dealing with mental health and mental illness in the workplace. At the centre of all of this activity throughout that period of time has been and continues to be Bill Wilkerson. So let me say at the outset of my remarks how much we all appreciate the vision, the energy and the commitment of Bill and give him a round of applause to demonstrate our support.

This morning we'll hear from some of the top figures in science. They will discuss the future direction in brain science. We'll also examine how business and science might strike a strategic partnership and agenda to accelerate new knowledge and its transfer into clinical care. Tony Phillips, Tom Insel and I will create some context for this, framed by an equation that we created for the Roundtable's final report [from 2011], which I think you all have at your place. And that equation is:

Brain Science + Brain Health = Brain Capital

That's a formulation which is quite appropriate to unite the agenda of business, the economy and science for the following three reasons: One, we all know this, that it's an economy where most new jobs demand cerebral and not manual skills, where the minds and not the backs of workers do the heavy lifting for business. Two, this is also an economy where brain-based mental disorders such as serious

depression have emerged as the fastest growing cause of workforce disability. But, more than that, this brain-based mental disorder is also on track with heart disease to become the leading cause of work years lost due to disability and premature death, a key factor in our collective fight to improve productivity. There's a significant convergence here of significant trends.

As you may know, Mental Health International is the successor to the Global Roundtable. Bill is chairing a new and European corporate initiative called Target Depression in the Workplace. Peter [Hongaard] Andersen, who is here, and Tony Phillips were instrumental in bringing this project to life and I'm pleased that my bank, Barclays, is one of several major global employers who are part of that work. The theme driving the project is a roundtable concept and which we now propose to export in a brain-based economy. I should say that I didn't write this, but:

"Human cognition is the ignition of workplace productivity."

The brain economy is based on having healthy minds in the workplace. In my judgment we must now move beyond awareness raising to concrete action in order to reverse the prevailing mental health trends in the workplace.

I'm delighted that George Cope is here as the CEO of Bell Canada. I hope that he will take the opportunity to talk about what he has done with Bell to tackling these workplace issues. I am told that there's a dashboard of indicators of what is happening to mental health in his company. George, I hope that you can expand on that because I'm sure people in this room would be interested to see how you are bridging that gap, bringing that practical knowledge into business decision making.

In this context the question presents itself of how best to bring business and brain science together, to promote and protect the vital assets across borders. In the Roundtable's final report in 2011, we also made recommendations, which I hope merit your consideration this morning. Let me close by recapping those points:

Recommendations from the Global Business and Economic Roundtable on Addiction and Mental Health's 2011 Final Report:

- One, that Canada, US, Europe and other nations unite in a brain health and brain science free trade agreement not through government in this case, except as employers in their own right, but between business and science.

- Two, that an international workplace-centered, 10-year business-science dialogue be undertaken to reverse the tides of brain-based disorders including mental illness in working families with specific aims to reduce economic costs.

- Three, for these purposes we create an international business science partnership consisting of international corporations and the institutes and practitioners of brain science. The purpose, to create a straight line of two-way information from business to science and back again, to accelerate the transfer of new knowledge into clinical innovation and reduce workplace-based risks.

- Four, that the years 2014 to 2023 be designated, as a galvanizing measure, the workplace decade of the brain.

Now, I'd recommend that Mental Health International, already taking the lead in Europe, be duly resourced to develop this strategy and develop a detailed business plan.

One final point: With all this in mind, let me ask Tony Phillips and Tom Insel to comment on these matters from the perspective of brain health and brain science.

PART 5 – Re-Thinking Mental Illnesses and Brain Research in a Brain Economy

PRESENTATION 2:

"Brain Health Research in Canada"

Dr. Tony Phillips

Scientific Director, Canadian Institutes for Health Research and Director, UBC Institute of Mental Health
Vancouver, British Columbia, Canada

Tony Phillips, PhD, is the Scientific Director for the Institute of Neurosciences, Mental Health and Addiction for the Canadian Institutes of Health Research (CIHR). He is also the Founding Director of the UBC Institute of Mental Health and Professor of Psychiatry and Senior Scientist in the University of British Columbia / Vancouver Coastal Health Brain Research Centre. He joined the Department of Psychology at the University of British Columbia in 1970, was appointed Full Professor in 1980 and served as Head from 1994-1999. He subsequently joined the Department of Psychiatry, Faculty of Medicine at UBC in 2000 and became Founding Director of the UBC Institute of Mental Health in 2005. Dr. Phillips' research interests are broadly based within the field of preclinical neuropsychopharmacology and systems neuroscience. He has published over 300 peer-reviewed articles and book chapters. Dr. Phillips has also played an important role in the evolution of the biotechnology industry in Canada, having been a Founding Director of QLT, which is a biotechnology company dedicated to the development and commercialization of innovative ocular products that address the unmet medical needs of patients with inherited retinal diseases. He is a Fellow of the Royal Society of Canada and has received awards from the Canadian Psychological Association and the Canadian College of Neuropsychopharmacology. In 2013, the UBC Faculty of Medicine awarded him a Lifetime Achievement Award. He holds a PhD in Psychology from the University of Western Ontario.

In trying to frame the comments that I'm going to share with you, I couldn't resist being influenced by where we are. Here we are in the headquarters of one of the most impressive banks in the world and we're surrounded by the success of what I would call "responsible capitalism."

Canada's Brain Science Balance Sheet

I've really prepared sort of a "balance sheet" of where we stand in Canada with respect to both the assets that we have to bring to bear to this international collaborative effort. I also want to point out - and I think Tom Insel will build on this - the liabilities in the form of the mental health challenges that currently exist and that have to be faced. Both in the context of the stress of the workplace that many people are feeling and also the fact that we have an aging population which brings with it its own health challenges, many of which relate to how the brain functions.

Let me begin by laying out what I think is actually not as well understood in the country as it should be. This is the tremendous asset that we've already created in Canada over the last 75 years or so as we've built a very strong asset base in the health and brain sciences.

I'm a scientific director of one of the 13 institutes in the Canadian Institutes of Health Research (CIHR) and that's our counterpart to Tom's organization, the NIH [National Institutes of Health] in the United States. In Canada, ours is a virtual organization, as we don't have large campuses with our internal scientific staff to address issues of national importance. But we have built a wonderful collaboration with all of the research-intensive, health-oriented universities and many of the teaching hospitals, especially in this city [Toronto].

A Proud History of Brain Science Research in Canada

Going back to the time of Wilder Penfield at McGill University in the 1930s, Canada has established itself on the international stage of neuroscience and brain sciences. I can't overemphasize the impact that Wilder Penfield and his colleagues at McGill have had, not only in shaping opinion about the brain sciences and really emphasizing the fact that the brain is really the most precious organ that we each possess – but also in recognizing the vulnerability and complexity of the brain.

By addressing the challenge of understanding the brain better, as Penfield was trying to do, to understand the genesis of epilepsy and how it could eventually be controlled, he set the stage for a broad understanding of the brain from a systems perspective and also very early on he urged us to always think about brain science in the context of its impact on patients. And I think that's a theme that, in Canada, we've taken to heart.

Penfield was lucky to have other colleagues in Montreal. Here I'm thinking of Donald Hebb, who became the chancellor of McGill University, eventually, but at the time when he had his major influence he was the head of psychology at McGill. Donald Hebb established many, many years ago – 60 or 70 years ago – the whole concept of cognitive neuroscience and the fact that our psychology is brain based, that our ability to think and move and interact in a complex world originates in specialized systems in the brain.

Hebb also made another contribution that we've only just begun to realize and to appreciate. He saw, long before we had the data, that the brain is a highly adaptable and plastic and changing organ. When I was taking my training, we were told that the brain that we received at birth was fixed and we were going to lose a certain amount of brain cells every year. If we were really lucky, we would maintain most of our function before we passed on. Well, that turns out not to be true. The brain has the capacity in certain regions to regenerate itself but, more importantly, it has the ability to change and adapt and, by integrating into its synaptic weights, it can embed experience. This is now called brain plasticity.

So we have the capacity in our brains to generate new experiences and to remember these experiences. And Hebb pointed the way in studying synaptic plasticity and how the brain generates memories that form the basis of cognition.

Brain Research Centres of Excellence Across Canada

Over the following 50 or so years since Hebb's pioneering research, Canada has invested very, very heavily in ensuring that it has nodes of excellence across the country, whether it be in Dalhousie University, Newfoundland, or in Montreal, where we still have some wonderful resources with the University of Montreal being a world-recognized leader in neurosciences paralleling the contributions of McGill. And there are tremendous resources here in Toronto, you just have to walk down University Avenue, past Sick Children's Hospital, CAMH is in the vicinity. Then you can move into the western part of Canada, into Manitoba, and Saskatchewan and Alberta.

One of my dearest friends, Sam Weiss, is the head of the Hotchkiss Brain Centre in Calgary, at the University of Calgary. Alberta is really being very innovative in creating a province-based partnership. Neuroscience Alberta now links the universities located in Lethbridge, Calgary and Edmonton, all with a uniform curriculum in brain research and with common and non-overlapping areas of focus in research. At CIRH we have established a very effective partnership with the Hotchkiss Brain Centre and also with the Ontario Brain Institute and the Ontario Neurotrauma Foundation to lead the way in a scientific examination of traumatic brain injury.

I couldn't conclude these remarks without also saying that British Columbia is blessed with great strength in the neurosciences, both at Simon Fraser University and also at my home university, the University of British Columbia. At UBC we're about to open the Djavad Mowafaghian Centre for Brain Health, in a new $100 million edifice – it's a beautiful building - that will integrate all of the health sciences as it is related to brain research at UBC.

Interdisciplinary Research and Treatment in Academia

I also want to describe a few examples of the partnerships that are happening within academia in Canada.

The UBC Centre for Brain Health is set up to have clinical expertise spanning psychiatry, neurology, and neuropathology, so a patient can come in to that facility and be seen with the unique symptoms that they're displaying, not just somebody who has movement disorder but someone who may be a Parkinson's patient who also has clinical depression. So the patient can get an integrated approach to treatment in one place. Also, in the research labs below at the same facility, they are exploring the study of genetics and brain imaging. We can now start to integrate these together in one unified approach to using our knowledge about the brain to address issues of major importance to patients. By building a facility such as this, it's expressing a new concept of how we can integrate across disciplines to really gain new insights into how the brain works but also to apply that, when appropriate, to the treatment of major disorders.

We have a lot on our asset sheet in Canada. I think the CIHR - which my colleague, Michael Wilson, co-chairs - is an underappreciated asset in this country. Canada is spending, through CIHR, close to a billion dollars a year on health research. It's not health services delivery; it's health research. But it's health research that's really quite unique in the world, because the approach that we are taking is an integrated approach that places as much emphasis on the knowledge about the social, environmental and health determinants of health research as it does on the twin disciplines of basic neuroscience and clinical neuroscience.

Canada's International Influence

CIHR is working at the service of Canadians and also for many international efforts. For example, we've been working – at the same time as the government was working for many years to establish a free trade agreement with Europe – behind the scenes with our counterparts in the EU that fund health research in that part of the world. We've also, for many years going back much further, had similar relationships with our colleagues at the NIH in the United States.

But our recent European initiatives have borne a lot of fruit. I can think of about five or six major initiatives that we're involved in now, the sum total of which is in the hundreds of millions of dollars collectively, in which Canada sits at a table like this as an equal partner with all of the EU, in programs such as one can ERA-NET Neuron. "ERA" means European Research Area. So there's a whole integrated

approach within Europe to try to build an international collaboration in neuroscience. Canada has been a partner in that group now for five years.

We have championed early on and Remi Quirion, who sadly can't be here, when he was in my post as director of our institute began discussions about how Canada could become involved in something called epigenetics. We now have something called the International Human Epigenome Consortium. This is a $200 million initiative in which we're going to collectively understand a thousand epigenomes. This will give us greater insight into understanding how the genetic code is read and the implications of that for understanding disease. We heard firsthand about the importance of this issue yesterday at the Campbell Family Symposium at CAMH.

But the point I'm making is that Canada sits at that table, a Canadian is the chair of that body and collectively, we're putting $50 million of Canadian money towards this effort to stand alongside the NIH effort, which really got this started with $160 million effort. Then every other nation that is part of this has pledged at least $10 million to this effort. It very quickly becomes a $250 million international effort in a leading edge of science, in which Canada has a quiet investment; nobody in this room knows about it. Maybe we should also be investing in better communications.

Dementia and Neuro-degeneration

On another area, which is going to relate to our liabilities, is the impending crisis of age-related dementia. The Europeans have organized something called a joint program in neuro-degeneration. Twenty-seven countries in Europe are part of that program. Canada is the only international country that's an equal partner and sits at that table, and I'm one of the two representatives on that body.

In the area of dementia-related research we're realizing two things: One is that when we're trying to understand how our knowledge of the brain can inform better patient care. We have to recognize that this is a lifelong study. We have to look at the brain from a neuro-developmental perspective because the insults and events that happen throughout the course of life can be quite influential in how well we manage our later years. So that's one point to make.

The other sad commentary is that many of these insults set the stage for different aspects of neuro-degeneration. Alzheimer's is used in the popular vernacular to talk about a disease of the brain that leads to cognitive impairment but, really, it's just one of many, many different disorders that are all neuro-degenerative in nature. We have to understand the process of neuro-degeneration in the context of disease if we're really going to get a handle on dementia.

In Canada, CIHR has led the way in creating something called the Canadian Consortium on Neuro-Degeneration in Aging. And this is turning out to be a public-private partnership because CIHR is putting on the table close to $30 million, and we've already found matching partners in the country with esteemed organization such as the Alzheimer's Society of Canada and many others to provide a matching sum of $30 million. We have now launched this initiative with $60 million of funding behind it.

Considering all of these investments, I would argue, allows us to address the liability side of this balance sheet. In an article that Tom co-authored recently, he reminded us that brain-related injuries right now cost the world's economy over $2.5 trillion. Furthermore, by year 2030, it's estimated that that sum will more than double to exceed $6.5 trillion. My point here is that the liability side of this balance sheet is really daunting. It affects individuals at every stage of their development.

Youth Mental Health

One of the other partnerships that we're very proud of at CIHR is the partnership with the Boeckh Foundation. This also has a public-private partnership model that has put together a new network for youth mental health. It is now in its final stages of peer review and we hope to announce the successful team early in 2014. This is a $25 million initiative, which is going to transform the way in which we think about youth mental health and, hopefully, set examples that we can share with our colleagues on the international stage.

The negative impact of brain health disorders occurs mostly in youth. Indeed, upwards of 75 percent of mental illnesses, are diagnosed in youth and many of them are chronic illnesses that start in young adulthood and continue to the grave. Some forms of later neurodegeneration occur in the fourth and fifth decade of life, but it's a trajectory that's very daunting and we need collectively to put all of our efforts together if we're going to crack this problem. Opportunities for early identification and intervention also come with the young adult onset of many of these brain disorders.

Conclusion

Canada is amazingly well positioned to have a partnership with the NIH, to have a partnership with the Europeans and to do our bit to really collectively understand the brain at a deeper level. We always need to also keep in mind that this effort has to be translational and it has to be put at the service of patients. That's how we think at CIHR. I know that's how they think at the NIH and at the European commission. I'm actually very optimistic. We can always do with more money and a better partnership between science and business could be very fruitful for both sides of the equation.

I hope I've convinced you in these few remarks that achieving brain health for Canadians not an empty dream. We bring a lot to this table and we have established relationships that go back decades that are built on individual friendships and individual reputations. Everybody that I know in the Canadian neuroscience community is committed to making a difference in this area. With your support and with your partnership, I think we can really see this decade of workplace mental health through to a successful conclusion.

PART 5 – Re-Thinking Mental Illnesses and Brain Research in a Brain Economy

PRESENTATION 3:

"Brain Health Research in the United States"

Dr. Tom Insel

Director, National Institute of Mental Health, US Department of Health and Human Services
Rockville, Maryland, USA

Tom Insel, MD, is director of the National Institute of Mental Health (NIMH), the component of the US National Institutes of Health charged with generating the knowledge needed to understand, treat, and prevent mental disorders. His tenure at NIMH began in 2002 and has been distinguished by groundbreaking findings in the areas of practical clinical trials, autism research, and the role of genetics in mental illnesses. Previously, he was Professor of Psychiatry at Emory University in Atlanta, Georgia, where he was founding director of the Center for Behavioral Neuroscience and also the Director of an NIH-funded Center for Autism Research. From 1994 to 1999, he was director of the Yerkes Regional Primate Research Center in Atlanta. He has published over 250 scientific articles and four books, including the *Neurobiology of Parental Care* (with Michael Numan) in 2003. He is a member of the Institute of Medicine, a fellow of the American College of Neuropsychopharmacology, and is a recipient of several awards including the Outstanding Service Award from the US Public Health Service. He graduated from the combined BA-MD program at Boston University.

I'm just delighted to be here. Part of the reason is what you just heard from Tony. I think for us, in the States, we were looking to Canada to see the kinds of innovations and the partnerships that are developing here. You're able to do that in a way that we're finding sometimes a little more challenging. It is pretty exciting to see the number of programs that are launching here in Canada, all of which have as a major focus this issue of putting brain science and brain health together for brain capital. I think it's a great driver in terms of an overall principle.

Today, I will provide some numbers and use this as a framing device for the conversation to follow with all of you. Most of you have some sense of the challenge in front of us but it's worth trying to get a sense of what do we really need to fix - just what's the problem statement here. In the answer, I will use data that has been collected, either internationally or in North America.

Clinical Issues

Disability: For most of us, I think if you said what are the major health challenges that face us you'd probably think about cancer, heart disease, AIDS and certainly cancer, heart cancer and stroke are the major sources of mortality. But when the World Health Organization looked at disability as opposed to mortality, the leading indicator there was none of the ones I just mentioned. It was actually brain disorders, what are called neuropsychiatric illnesses, especially depression.

Early Onset: Unlike the big killers like cancer and heart disease, brain disorders, the neurodegenerative disorders occur late in life, but most of them – such as depression, schizophrenia, autism, ADHD, a whole range of very common problems – begin in childhood. We've begun to understand that these are the chronic disorders of young people. If you add substance abuse to that, you get the whole package of what we have to contend with as a society, where the big disability drivers are. If you actually look at the numbers, 75 percent of adults with a mental illness will say that they had onset before age 24. It's a very different picture than what you have for a cancer or heart disease or, in this case, neurodegenerative diseases which are a huge issue as well but which occur much later in life.

Suicide: It's not just what we would call disability or morbidity, but mortality as well. And this is one of those what Dr. Weinberger likes to call inconvenient truths. Suicide, which is most commonly associated with a serious mental illness, is a huge public health challenge that has not received very much attention. In Canada, last year, there were approximately 3,900 suicides, which is six times the number of homicides. It's more than the number of deaths from most all of the forms of cancer. It's extraordinary that this is such an enormous public health problem. And yet we aren't talking about this in the way that we talk about so many other issues. What makes this data particularly striking is that many of these cases are preventable because these are due to a brain disorder that just isn't being detected and it's not being treated or, if it is being treated, it's not being treated well enough.

I think the challenge for us is to embrace both the morbidity and mortality and understand those numbers to make sure the public understands that challenge, and also to recognize that it's not just a public health issue, but also very much an economic one.

Depression

Depression is one of the most prevalent of mental disorders. It is certainly the leading, single source of disability when one looks across all preventable causes, particularly in people under the age of 49. The prevalence is enormous. About 16 percent lifetime and, within any given year, about 6 percent of people will meet the criteria of depression.

For those of you who don't have personal experience with it, depression is a terrible name to put on this brain disorder because it doesn't begin to capture what this experience is like. It actually has nothing to do with sadness. When you're depressed, you hope you can feel sad. That would be an improvement. There is a sense of, sort of, really anguish or severe anxiety that comes with it. For many people, it's a feeling of deadness. It's a complete lack of feeling. And perhaps the descriptions that most people give, sort of falling into a dark place, falling down a well – an extraordinary description from Andrew Sullivan, who's probably written the best book on depression called, "Noon Day Demon", talks about a great oak tree that's covered with vines, so much so that you can't see the tree through the vines. It's like the tree is dying, but it's just the vines, which is this terrible illness that is keeping it up. That is sort of what depression feels like. There's nothing left of you. You think you've been overtaken by this illness that saps your energy completely and yet you can't sleep because often you're so anxious. You have no appetite. You have no sex drive. You have a sense of having some like influenza and yet there's no actual viral illness. There's no fever, but it has that same effect of a complete sapping of your energy and complete sense of hopelessness and worthlessness.

Economic Issues

Tony mentioned that when the World Economic Forum, about a year or two ago, decided to take a look at what are the major barriers to development, globally, they of course dealt with a number of issues around sanitation and technology but they put a special group together to say, "What are the challenges

in terms of health?" And they did what I think any of us would do. They said, "It's no longer so much acute infectious diseases. The challenge today is to think about chronic, non-communicable diseases," and that is very much the mantra that you'll get from the Gates Foundation and from WHO. That's kind of the buzz term, is the chronic non-communicable diseases. The ones they were thinking about were the ones that any of us would think about: cancer, heart disease, AIDS, pulmonary disease in this case because they were concerned about smoking. And with diabetes used as a control, they also threw in mental illness.

To their amazement, mental illness turned out to be the largest cost of all of those chronic non-communicable diseases, $2.5 trillion in 2010. This group of mental disorders, because they start early and because they are global and because they are so prevalent and because they are disabling, actually cost more and will become a bigger barrier to development, globally, than cancer, diabetes, pulmonary disease and one other thrown in there as well. Heart disease was excluded from the analyses but the others all put together. So this was a huge challenge for us to think about. And it is part of the reason why we see now a global awareness and an increased interest in trying to figure out how to cope with the problem.

Depression and the Workplace

This plays out perhaps most dramatically in the workplace, and we've heard over the previous roundtables some of the numbers. I just wanted to walk through those with you very quickly to give you a feeling for how one disorder, depression, plays out in terms of the business case that we all have to face.

It's an extraordinary experience that 16 percent of people will go through having depression at some point and six percent a year, and many of them will be employed. We have some sense of the cost of that in the workplace and the best estimate of the cost of depression overall, at least in the United States, is about $53 billion a year.

The cost of work impairment is $33 billion of that $53 billion total. When we break that down, and there are ways to do this with a surprising amount of precision, about $24 billion is related to absenteeism. There's another piece called presenteeism. This is when people do show up for work but they simply can't function as well as they usually do. They sit, and they are drained and they may try but there is nothing that they can try with. There is just no substance. There's no vigour with which they can attack any kind of problem at work. The presenteeism cost is about another $8 or $9 billion from lost revenue in the United States. To break that down and make it a little more understandable, the best estimates we have is that for a company that employs a thousand people, depression costs, on average, about $250,000 a year.

So this is a serious economic challenge. It's not just depression that we deal with in the workplace. It's attention deficit hyperactivity disorder, which does affect particularly men. It's also eating disorders, which has a huge impact on women and has a very high mortality rate. It's a range of other anxiety and mood disorders, which we know are far more prevalent than the number of people actually getting treated for it.

Need for More Effective Identification and Treatment

So what do we need? What's the real important challenge going forward? One is we have to figure out a way to help more people to seek treatment and to get treatments that work. We can do much, much better. We know we live with what we have, a "law of halves" in the treatment of depression: about

half the people who have it will get a diagnosis and get treated. About half of those who get treated will get a treatment that has a scientific basis and has any real hope of being effective. And, unfortunately, with the current treatments we have, about half of those who receive treatment will respond sufficiently well enough to be able to go back to work at full force.

That's not a great recommendation for where we are, but it's the best we do now and we can certainly make that much better if we simply increase the fractions at each level.

At NIMH, where I work, is a research institution. So we're mostly focused on that final level. Could we come up with treatments that are just much more effective so that when people seek out help they will be much more likely to quickly recover? And one would think that if you had such treatments to offer, there would be people who would be much more likely to seek out help because they would realize that the hope was there.

I do think we have to be honest and admit that the treatments we have aren't good enough for too many people, but they are terrific compared to what we had even decades ago. But we have put a lot of energy into thinking about how to do this better and we do actually have some very promising new interventions, some that instead of taking six to eight weeks will work within a matter of hours, some that don't involve medications.

There was a front-page article in the New York Times yesterday about treating depression using cognitive behaviour therapy for sleep. That's very promising. So there are a whole range of new opportunities coming out of the science that are very, very promising.

The Genomic Revolution in Brain Science

The last thing I'd like to say about this is that as we learn more about how to do better on the treatment of mental illness, it really forces us to recognize that we need to know much, much more about the brain. These are, as you've heard from Michael, ultimately best thought of as brain disorders, which is something that we haven't really been that aware of until the last decade or so.

Medicine has progressed over the last century because we've been able to get beyond symptom-based diagnosis. There was a time when as a medical student much of what I learned about how to diagnose heart disease was based on symptoms. And then we became much more intelligent about going beyond symptoms, listening very carefully to what patients are experiencing but also collecting biomarkers such as measuring cholesterol and looking at perfusion of the heart and a whole range of other things that help us to make a diagnosis often much earlier than when somebody has a heart attack.

The unfortunate thing is that psychiatry is one of the very few specialties that has not made that transition. Psychiatry is still focused on making a diagnosis based on presenting symptoms and there are no biomarkers. And we don't even use cognitive tests that could be a kind of biomarker. So I have been on the record saying that diagnostic schemes, whether it's ICD or DSM or any of the ones that are in wide use, are essential for giving us a common language. But isn't it sad that, in 2013, we can't do better than that? It is time to bring in the biology, bring in cognitive science, understand more about the social determinants of mental illness, all of those kinds of factors that we use in every other branch of medicine but that, for some reason, we have not been able to bring to bear here and we need to figure out how to do that. But we are in the middle of a revolution in how we approach and how we study, how we understand the brain and this revolution has gotten a lot of new energy because there are brain initiatives popping up all over the place.

Investing in Brain Science Research

The European Union has announced the Human Brain Project this past year as one of its flagships for technology innovation. It is a $1.5 billion effort over 10 years. It is a public-private partnership to create simulations but also to have some impact on mental health care.

President Obama, on April 2 of this year, announced a US Brain Initiative, which launched with a $110 million commitment in just the first year. It's supposed to grow to a figure much larger over at least a decade. In a really remarkable speech that he gave at the White House with some 200 neuroscientists present, he explained that in his second term as President he wanted to do a major science initiative, a signature project, and struggled with whether that should be climate change or clean energy. But he decided instead that this really was the time to make this next decade about exploring the brain and about making this, as he called it, the next Great American Project. He compared it to the Apollo program to get a man on the moon, or the human genome project. He challenged both public agencies, ours at the NIMH as well as a couple of others in the US, and the private partners, to get engaged in this effort. It is starting to take place already with the recent announcement of a range of initiatives, some of which will be public, some of which will be private, some of which will be partnerships, to move forward in a much deeper understanding of this great mystery which does compare to the cosmos, as Dr. Weinberger spoke about yesterday at the CAMH conference.

I think this project is going to be a really special opportunity for us to capitalize upon, along with Brain Canada, along with what's going on in the EU, along with a Chinese brain project, a Japanese brain project, an Israeli brain project and a Hungarian brain project that's now launching as well. Indeed, this is becoming a global effort as people around the world begin to understand that this is where both the opportunity and the needs are going to be, based on the economic challenges in front of us and the disability and mortality burden I've talked about.

This is an extraordinary time. I think we are at a moment where because of this global awareness we can make real progress. There is a global unmet medical need that is going to require this kind of a partnership and this kind of a large a large effort to meet the challenge.

When we think about research, we tend to talk about the costs that we have to incur to do the studies. But consider, as it has been said many years ago by Mary Lasker, who was one of the great advocates of mental health research, that, "If you think research is expensive, try disease." It's worth remembering that when we're talking about science and research costs, these are really investments against the much larger costs that are currently incurred by not knowing enough about the problem, not understanding what the problem is or not understanding enough about what to do about it. It will be absolutely essential for us to get better science if we're going to get better public health outcomes.

Conclusion

I'll finish with what Michael Wilson started with, and that is that I think for us this equation of "brain science plus brain health equals brain capital" is really a great driver. It's a great way to define where we need to go and what we should think about as the outcomes.

PART 5 – Re-Thinking Mental Illnesses and Brain Research in a Brain Economy

SUPPLEMENTAL PRESENTATION

"Brain Capital in the Canadian Military"

Col. Dr. Rakesh Jetly
Mental Health Adviser, Directorate of Mental Health, Canadian Forces Health Services Group Headquarters
Ottawa, Ontario, Canada

Colonel Rakesh Jetly, OMM, CD, MD, FRCP(C) is a Canadian Forces Psychiatrist and Mental Health Adviser to the Surgeon General, Directorate of Mental Health in the Canadian Forces Health Services Group Headquarters. He is also an Assistant Professor in the Department of Psychiatry at Dalhousie University in Nova Scotia. Colonel Jetly, who started as a General Duty Medical Officer in 1989, is now a Canadian Forces psychiatrist. He was a part of the Canadian Humanitarian mission to Rwanda in 1994, has been deployed twice to Kandahar twice, and continues to contribute to Post Traumatic Stress Disorder research and as a mental health advisor to the Canadian Forces Surgeon General.

I give thanks for this opportunity to speak on what the Canadian Forces are doing in this arena for our men and women in uniform. It is very heartening to me, as a psychiatrist, to hear some of the business examples and about the science that's moving forward.

Canadian Military as an Employer Organization

In Canadian Forces we have 70,000 people, so we're not as big as the US military, not by any stretch. We have some interesting conditions that make the military different from the private sector, because the labour code doesn't apply. Our people have signed up for unlimited liability. We send them where they go; they have no choice in terms of deployments and thus they have to go wherever the government sends them for military service. We have no union, so good or bad; it's kind of a little bit different in that way from other large organizations that do have a unionized workforce.

The other advantage that we have in the military – sort of the elephant in the room as nobody has really mentioned it right now for Canadians – is that the public health system is really broken in Canada for its inability to work effectively for mental health. We don't have an effective public treatment system for mental health in most of our provinces.

In the Canadian Forces, we are out of our own private health system. We look after our soldiers from entry to release. So our employer pays for equipment, pays my salary and pays the soldiers' salaries. So this is a really clear advantage to this kind of workplace for how it affects workplace mental health.

Occupational Medicine Approach

In the private sector, when someone goes to see the family doctor, what often happens is that he or she gets a script that says the patient has severe stress and can't work and then it turns into a disability claim. In the military, we've made an effort to establish an occupational mental health approach. This approach is needed because even though the medical schools, the psychology PhD programs, and the psychiatry programs all teach about how to do care, but they don't usually teach about how to do occupational medicine and how to serve the workplace.

For example, when somebody walks in and you ask them, "What do you do for a living in medicine?," that's usually an icebreaker. But in the military, that's the No. 1 thing: "What do you do?" This immediately means this is the task the person does, this is what we expect of them, this is when recovery occurs and this is what they want to do. For example, if he is an infantry soldier, he needs to charge towards the enemy and fight, so let's think about what he has to do in this kind of work. It is the occupational mental health approach to determine what it is that person needs to do.

Stress Management Training

At a lot of companies, a mental health briefing is just somebody from HR who comes down, gives you a talk about your entitlements and then puts the employee assistance program (EAP) number in front of people. I think corporations can do more. What we have done and what I challenge people here to do with this is to consider that most of your people who are off work, are off work because of stress. I do review of disability claims for insurance companies and a lot of the cases don't even meet the criteria for a diagnostic psychiatric illness. Mental health education and training is really needed and not just for leaders (like George [Cope] talked about at Bell) but for everybody. Also, treatment and training programs can borrow concepts from sports psychology and performance psychology to help employees be better prepared to respond to the day-to-day stresses of life. Our research has shown these approaches can increases people's resilience and confidence to cope with stressful situations – all from participating in a one or two-day interactive workshop. Interestingly enough, it also increases their confidence to deal with stressful situations. It also reduces stigma and increases help seeking, if they need it.

Leadership and Organizational Climate

The other part of our approach is trying to have authentic, caring leadership that creates the moral climate for people to seek help. In the military, leadership is a big thing but there's research – a lot of good American research and Canadian research – that the leadership affects the mental health outcomes of troops' and that the soldiers themselves also acknowledge this relationship.

Timely Access to Effective Mental Health Care

Another key is timely access to evidence-based care. We realize the 50 percent of people who don't even seek care. And among those who do, many do not get the right treatment. But if we can get 40 percent of people to have access to evidence-based care instead of the typical 20 percent, then we've made great inroads. I think that issue [lack of access to effective care] is more the vulnerability for your organizations and not so much for the military because we basically pay for the care and we get the care for our soldiers.

Return-to-Work/Stay-at-Work Programs

The other absolute key is to have an effective return-to-work program with people that are trained in vocational rehabilitation. With our return-to-work program, I like to think of it more as keep them working. Why even send people off for two or three months or two or three weeks and then come back? We should be able to instead modify their workplace with the advice of clinicians that have occupational medicine training. In this way, the person can stay at work during their recovery, if it is appropriate to their clinical progress.

Conclusion

I think these are the important elements of adopting a positive approach to brain health in the workplace that we can do right now. And we have done that in the Canadian Forces. If I'm going to get ill with a mental illness, right now, in Canada, I'd rather be in the Canadian Forces than not. Thank You.

Comment from BILL WILKERSON: Thank you, very much, Rakesh. There are two things I want to add. Firstly, Canada's forces were the innovator of providing a peer-support program. And secondly, through a number of predecessors at the lieutenant-general level, post-traumatic stress and PTSD went from becoming regarded as a weakness to being seen as an injury and a wound from which one can eventually return to the field. This was a tremendous change. Our soldiers who were in the Afghanistan conflict, said, "You mean, I can go back into action?" after being treated for PTSD. It was just an incredible turn-around. And thirdly, we got them to talk about PTSD as a "concussion from the inside out" – to consider it a normal reaction to an abnormal event. That shifted a lot of the family consideration of what their loved one was going through. Thank you for your presentation today and thank you for your continuing leadership in this field.

PART 6 – Keynote Address

"Finding a Cure for Mental Illnesses: Is this a Reality or a Pipe Dream?"

Dr. Daniel Weinberger
Director and Chief Executive Officer, Lieber Institute for Brain Development
Baltimore, Maryland, United States

Daniel R. Weinberger, MD, became the Director and CEO of the Lieber Institute for Brain Development in the summer of 2011 after leaving the National Institute of Mental Health (NIMH) where he was head of the Genes, Cognition and Psychosis Program. Dr. Weinberger is regarded worldwide as perhaps the preeminent scientist in schizophrenia research, having been at the forefront of scientific investigation of this illness and related disorders for a generation. He is board certified in both psychiatry and neurology. He was instrumental in focusing research on the role of abnormal brain development as a risk factor for schizophrenia. His research lab identified the first specific genetic mechanism of risk for schizophrenia and the first genetic effects that account for variation in specific human cognitive functions and in human temperament.

In 2003, *Science* magazine highlighted the genetic research of his lab as the second biggest scientific breakthrough of the year, second to the discovery of the origins of the cosmos. He is the recipient of many honors and awards, including the K. J. Zulch Neuroscience Prize of the Max Planck Society in Germany, the NIH's Directors Award, The William K. Warren Medical Research Institute Award, the Adolf Meyer Prize of the American Psychiatric Association, the Gold Medal Award of the Society of Biological Psychiatry, the Foundation's Fund Prize from the American Psychiatric Association, and the Lieber Prize of the National Alliance for Research on Schizophrenia and Affective Disorders (now the Brain and Behavior Research Foundation). He is past president of the Society of Biological Psychiatry, past president of the American College of Neuro-psychopharmacology, and has been elected to the Institute of Medicine of the National Academy of Sciences.

Dr. Weinberger received his MD degree from the University of Pennsylvania and his BA degree from Johns Hopkins University and did residencies in psychiatry at Harvard Medical School and in neurology at George Washington University.

Good morning, everybody. I was asked to tackle a provocative question, one in which we all have an interest around this table, a question that could signal a future direction of brain research and science problem. And that question is:

Is finding a cure for major mental illnesses a possibility or simply a pipe dream?

For many years I've been part of what I call the pro-neuroscience tour. I've been to many meetings, but to have a gathering of local and national business leaders all focused on this question of mental health and mental illness, I've never seen anything quite like this. I must say this is an extraordinary experience to stand here in this room, which reminds me of that scene from Dr. Strangelove. I can't say I've ever had an experience of addressing a gathering like this. I think it's an extraordinary development and my hope is that I can make some comments that might be interesting, informative and maybe help direct your thinking a little bit.

What is the plausibility of curing mental illness? My guess is this is a highly plausible prospect. I think it's more than realistic to imagine that cures are there and they will be discovered. People have said this for a hundred years that these cures are just around the corner. But the difference between where we are now and where we were at any previous time in the last century is that today we have learned more about the causes of mental illness in the last 10 years than we have known in all of the past history. Actually, we now have the first objective evidence that there has ever been in all of history of what mental illnesses actually represent at the medical-biological level.

Investment in Research

The secret to success in this endeavour is an investment in research. Let me just start off by saying how critical the private sector is in making this investment. There's no other roadmap that's going to get this done.

I stand here today as a representative of a historic, recently established institution called the Lieber Institute for Brain Development. It was established by two families in the United States who made the largest, by a very significant margin, single investment in biomedical research focused on mental illness in all of history. It was an extraordinary personal investment. It was based on the idea that there are certain things that private money can do that the public sector cannot do. And this is what you people here from the business community just do intuitively, which is to create an environment that is efficient, flexible and expects deliverables. The concept of deliverables exists in the real world but is not necessarily true in the academic world. At the Lieber Institute, we define deliverables as "something that has impact beyond your own career."

This is something that private investment can focus on and that the public funding sector has a harder time being preoccupied with. This focus on deliverables is something that's generally missing in many areas of scientific exploration. Few scientists have the expectation that their work will actually matter outside their laboratory or university or personal academic position. It is because of this context that I don't believe that the progress needed to find cures is possible without major private investment in this goal.

State of Neuroscience Research

Let me talk a little bit about the status of the field. Today we stand on this unique precipice. We have insights about mental illnesses that we never had a decade ago. There's a general perception out in the basic mainstream of biomedical science that mental illness research has finally moved out of the backwaters of science. *Science* magazine, which is the publication of the American Association for the Advancement of Science, about 10 years ago began to recognize that insights about the causes and mechanism of mental illness were emerging, and they were emerging from the new developments in neuroscience and the dramatic availability of the human reference genome sequence. What they claimed was that the implications of understanding genetic causes of mental illness, which were clearly now foreseeable and realistic, represented the second biggest scientific breakthrough of 2003, second to the origins of the cosmos.

Old Phenomenological Approach. The reason this statement was made was because it was clear that prior to the development of these tools and these capabilities to understand the causes of mental illness, we had no idea what mental illness really was. We knew what it looked like. We knew what it felt like. We knew what it sounded like. But we had no idea what it really was and the genetic discoveries represented the first absolute objective clues to what these illnesses are at a very, very basic cellular level. A consequence of following such an approach is that there is no treatment, whether it is talk

therapy, electricity, pharmacology, magnetism, or any of the treatments used in psychiatry today – that was discovered based on an understanding of the causes of mental illness. Not one. Now that we have some clues to these causes there has to be a better way to find treatments.

New Genetic Approach. In all of the rest of medicine, the *Holy Grail* is to understand the cellular origins of medical illnesses. We had no clues to this in psychiatry. And in fact, if you think about schizophrenia, for a hundred years people had identified many, many factors that seemed to be associated with risk of schizophrenia. The trouble was that the same set of risk factors also applied to depression, autism, attention deficit hyperactivity disorder or substance abuse. Thus, many of the same characteristics that seemed to be related to the likelihood that somebody would manifest one of these illnesses in their lifetime. The problem with all this phenomenology, this sort of soft science that kept psychiatry in the backwater of biomedical research, is that it was impossible to know what's the chicken and what's the egg. The only thing that can't possibly be the chicken is the genes. The genes, by definition, are the egg.

I often say that if you think of life as a Monopoly game, genes will never determine how many railroads you own or whether you have a monopoly on Boardwalk and Park Place. The roll of the dice actually determines a lot of what happens to you. But genes are the only square on the board that you ever know with absolute certainty because genes are the "Go" square. They are the toolbox that you play the game with. They are the biological resources that you have to interact with your environment.

Genes Provide Clues to the Causes of Mental Illness

As they do in cancer and Alzheimer's disease and heart disease and all common medical illness, genes represent the clues to causation. Not just clues to how thinks look, how they feel and how they act, but to what causes them. Genes cause illnesses at a very basic biological level. This is an example of why we study and why we want to understand the role of genes in mental illnesses.

We've known for a hundred years that all major mental illnesses run in families. We learned in the last 50 or 60 years that the reason they run in families is not the same reason religion or language runs in families. It's not something you're taught from your parents. Mental illnesses run in families for the same reason that most other medical illnesses run in families; it's genes that are inherited. Genes transcend all this phenomenology or what something looks like, sounds like, and feels like. Genes represent mechanisms of disease. By definition, they are mechanisms of disease. They're not necessarily the only mechanisms. They may not even be the mechanisms that you can most easily remediate, but they are the first objective clues to what causes these conditions.

The Environment. Genes also finally allow us to clarify the role of the environment. We've always known that the environment is very important in the expression of mental illness and their emergence and probably something of their causation. However, the problem with the environment is, as Bob Dylan said, one man's ceiling is another man's floor. Everybody experiences their environment, even if it looks somewhat similar, with their own individual biological toolbox and people don't necessarily experience the environment in the way. For example, for some people stress is challenging and very invigorating. Yet, for other people, it's disabling. We can't really understand the role of the environment at an individual level until we understand what the genes and the biological tools are that people bring to this.

At-Risk Status. Genes identify at-risk populations. Today you can send your saliva sample to a company called 23andMe. You will get back a printout of all the illnesses that you're supposedly at risk for. I'm not going to get into the potential value of all that – that rabbit hole that you go down when you do something like that – but nevertheless, there all these algorithms suggesting that we can predict

people's risk status for a variety of conditions where genes contribute to them. Certainly in mental illness, this is the first objective clue that we've ever had by which we can begin to imagine that we might be able to predict people's individual risk status.

Let me just mention where we are right now in psychiatric genetics. Research has begun to identify the areas of the human genome where certain genes are a risk factor for mental illness. This is work that has emerged with great momentum and fanfare in the last few years. The result is that we now have discovered hundreds and hundreds of genes across different populations in the world that are risk factors for schizophrenia.

Risk Does Not Mean Cause. Genes do not cause hallucinations and illusions. They don't cause depression. They don't cause panic attacks. They don't cause anxiety. They can be associated with those manifestations. It's very important to realize that mental illness – whether it is autism, schizophrenia, or ADHD – genes do not give you these conditions. Rather, they establish how at risk you are and how much risk you have, as you accumulate other risk factors, such that you're likely to fall off the edge and then actually manifest the illness. It's the same story as for heart disease or for stroke or for diabetes. Genes do not cause heart attacks. Genes do cause biological changes like elevated cholesterol or changes in inflammation of blood vessels that contribute to the biology of risk.

The first point to understand about the causal role of genes is that all common medical disorders – mental illness, diabetes, heart disease, and stroke – are multifactorial conditions and they're very heterogeneous conditions. Every person that has the exact same diagnosis does not necessarily get there with the exact same set of risk factors. Nobody has an illness because they've only accumulated one risk factor. They must have multiple risk factors and they have to fit together in a lawful, biologically relevant way. The accumulation of risk factors for heart disease all combine to increase the biology that makes your heart fail. It doesn't contribute to a biology that makes your kidneys function better. It contributes to a biology that makes your heart function worse.

The second point is that every individual with the same illness does not have the same risk factors. You can get there with different combinations of risk factors. This is what's called polygenic, or in genetic terms, multifactorial and heterogeneity. Everybody is not exactly the same, even though they may have the same diagnosis.

Finally, even some people with all the risk factors may not manifest the condition because they have other factors – what are called protective factors. These could be genes that nullify some of the other risk genes or maybe certain environmental factors.

But this is the complexity of the genetics of all common medical disorders. They are illnesses that are based on genes that determine your risk, not your fate. This gives us great opportunity to try to reverse the probabilities of risk.

Genes Affect Cell Biology

Genes affect the biology of cells. Genes do this in two primary ways. They are responsible for these fixed lifelong traits that we have. For example, how tall we are, what colour hair we have, or what colour eyes we have. They also are the blueprints for the moment-to-moment function of all the cells in our body. Genes encode all these proteins, which allow cells to grow, to divide, to communicate with other cells, to store information, to build a brain. Genes build your brain. Your brain processes information. It processes emotional information. It processes sensory information, vision, touch, and taste. It processes cognitive information, thinking, and problem solving. And the genes that affect the

biology of cells translate ultimately in the function of these brain systems that have the emergent properties of behaviour.

What we see as the abnormal behaviours linked to genes have something to do with how these cells are affected in their early programs and how they build a brain that has a problem, environmental information processing. The hope is that filling in these different steps along the road from a gene to behaviour will provide clues for the development of the next generation of treatments.

The metaphor that I like to use for thinking about how genes can relate to psychiatric illnesses is to think about what happens in an orchestra. Think of the behaviour as the music and the musical score as the DNA. The musicians, who are the cells, are trying to decode the score embedded in the DNA. Individual instruments in the orchestra represent different systems, such as the woodwinds, percussion, brass, and strings. Altogether the music they create is the behaviour. And we understand now that problems in the score have manifestations. These problems in the score create difficulties for certain individual musicians, who cannot work efficiently as part of the orchestral systems that produce the music.

This is our increasing understanding of the levels of problems that are related to mental illness that we're trying to intervene upon. We're wondering how far are we going to get with the genetic revolution in mental illness. How far can genes take us? Will they change how we diagnose people? Will they allow us to prevent the emergence of these conditions? Will they inform us of what the mechanisms of these illnesses are? We will predict outcomes better. Will this work? Will it lead to new therapeutic targets?

These are all the areas in which there's a very active research effort and we still don't know the answer to where all of these things will lead us. I think it's very clear that in some areas we will see real progress in the next five to 10 years.

Personalized Medicine in Psychiatry

The evidence is that genes represent mechanisms of disease. We have to understand how genes affect the biology of cells. This will give us a much better understanding of why, as Tom Insel mentioned, only about half of the people have reliable responses to some antidepressant drugs. Why do some people respond better than others to the same drugs? Some of the reason for this will be genetic. And then there's no question that we will identify a new way to remediate these conditions because we have this new biological information.

This is an historic opportunity for the discovery of mechanisms and novel targets. Genetic association is an entry point into the molecular mechanisms of illness. Most of biomedical research that's focused on finding cures is focused on understanding the mechanisms to try to reverse that disordered biology. The molecular mechanisms will inform basic models for target discovery. By understanding these mechanisms, we can create the models, which will be the basis for the deliverables that can be used to test for new treatments. Then the next generation of therapies will grow out of this much deeper understanding of what these conditions were.

What makes this moment in time so historic is that 10 years ago, we had none of the information that we have now. We couldn't even think this way 10 years ago. It was a true "pipe dream" that we could ever be in a place where we could imagine we had enough information about what these conditions represented at a very basic biological level that we could dream of the possibility of curing them.

Both Tony and Tom mentioned that we've become increasingly aware of the early age range at which many people begin to get psychiatric disorders. We've known for years that autism and ADHD and dyslexia and certain childhood-onset psychiatric disorders clearly must have something to do with how the brain is coming online and assembling itself. These are brain-building processes that occur very early in childhood. But it has become increasingly clear that even the major adult-appearing psychiatric disorders are not really about only the adult brain and it's functioning in the adult world. It's about how this brain gets started on a path.

I like to say that it's a little bit like the Federal Reserve banking system in the United States. When the Federal Reserve changes an interest rate, even a very small change in the interest rate, it has ripples effects throughout the entire economy and the entire society. Think of the same ripple effect for genetic influences in brain development. Slight genetic glitches very early in the life of a cell have effects throughout the development of these cells and ultimately the development of the brain and how an individual interacts and manages his environmental experience in a lifetime. As an example, we certainly know that emotional temperament is very much present in children very early in life. We've increasingly come to appreciate that manifestations of brain function that ultimately are associated with later-onset psychiatric illness also appear very early in life.

Stand Up Study. Let's consider one of the many studies that have looked at individuals who are hospitalized as adults for psychiatric illnesses. The question was if there was any evidence that even though these people did not have a psychiatric illness earlier in their life, was their brain somehow not quite getting online—or developing —in a perfectly normal way. Consider that the average human being first can stand unassisted at about nine months of age. A large study from Finland showed that the probability of somebody in their lifetime being hospitalized with the diagnosis of schizophrenia is about 0.5 percent if they had stood at nine months of age. This figure is about the average rate of schizophrenia incidence in the Finnish population. But among the male children who had stood three months later, at the age of 12 months (which is certainly within one standard deviation of normal) they had almost three times the probability of being hospitalized with a diagnosis of schizophrenia later in their lifetime. The important point of this study was not to suggest that people who stand at 12 months develop schizophrenia. Most people who stand at 12 months are perfectly normal, but among the population who do manifest schizophrenia later in their life, there's evidence that even very early in their lifetime, the programs that build the brain and get it to mature appropriately are slightly on tilt. They're slightly disorganized.

Another example is that about 25 percent of people who later manifest schizophrenia as adults, were enuretic [urinating while asleep; bed-wetting] as children. That's about three times the rate found in the general population. And there are many other examples of this. It's really quite remarkable how consistent this kind of scientific research has been on early indicators of later development of psychiatric disorders. This kind of research shows how there can be clues from very early in life that the brain is having difficulty getting the music to play in the right way.

Other research shows that many of the genes that have been linked to schizophrenia also seem to be particularly relevant to assembling the fetal brain. Certain genes that are linked to psychiatric illnesses are much more abundantly "turned on" during fetal life than during adult life. We think this pattern is representative for many of the genetic factors linked to psychiatric illnesses. They are about building the brain, not necessarily about controlling the function of the brain at the time that the illness is first diagnosed.

All of this suggests that we can look at the very first cells and identify glitches in how these cells get started. The evidence is emerging that when you look at these clues to the causative factors of mental illness by examining the set of genes, which dictate the first and earliest behaviour of cells, we find that these cells are making subtle mistakes in the very first things that they do.

Stem Cell Research. Another area of study involves stem cells. These are the first cells that build the body and that build every organ and build the brain. We've looked at stem cells that build the brain that were taken from people with psychiatric illnesses. What we find is that their cells are making small mistakes from the very first days of their life, compared to the same types of cells from normal adults. The early growth patterns for the stem cells from parts of body other than the brain are much less likely to show a difference between those with psychiatric disorders and normal controls.

So this is now a whole new world of trying to take these genetic clues into actual human cells to see if we can see where these glitches start, where does the interest rate first get changed in this lifetime of changing the economics of brain growth, development and function. This kind of understanding may be a whole new way to find remediation. The technology exists now to take cells from real people that have real genomes and real genetic glitches that relate to the conditions that we're interested in and control the behaviour of these cells exclusively and to be able to explore them at critical moments when that change in the interest rate first starts to affect the biology of that cell, because this may be a way to discover new strategies for discovering new treatments that we could never do by studying people long after the illness has manifested itself. This is the promise of cures in a whole new realm of scientific exploration that was science fiction only a few years ago.

Roadmap to a Cure

I want to revisit how private investment can change the landscape of psychiatric research. Because of the technological advances, discoveries and the insights that have emerged in the last decade based on causes of mental illness, I think we can decipher a roadmap that is highly likely to be successful in finding much more effective treatments for these conditions than we 've ever had. This roadmap is not some great proprietary secret. It's really in the minds of many scientists. The problem is that it's very difficult to marshal a concerted effort to have all of us follow this roadmap. What tends to get us derailed from the roadmap is that there are too many individual agendas, and the individual agendas make it hard for the community to stay on the roadmap. This is a roadmap that will produce new therapies. The roadmap starts with clues to etiology, clues to causation, which are genes that comes from other places. It looks in the human brain to understand how these genes are affecting the development and function of the brain. It identifies the mechanisms, very specific mechanisms, that those genes are doing to the human brain and then it builds models in these stem cells and ultimately in animals based on those specific mechanisms, which cannot be identified unless you move through the various stages of this roadmap.

These are exactly the same strategies being taken in cancer and other areas of medicine where molecular mechanisms can be specifically extracted from all this complex biology and made the focus of the next generation of discovery. What private money can do is say, "We're going to make this roadmap the plan of how we define the deliverables that are necessary." I don't believe this can be done any other way. No one group can do this by themselves. The government can't do it by itself. Private investment can't do it by itself. So it has to be a partnership, but it's only private investment that can stick to the principle of getting to the bottom line.

I want to thank you very much for your attention. It has really been a great privilege for me to have a chance to interact with you.

Comment from PETER HONGAARD ANDERSEN: I was particularly interested in what kind of environmental or social factors are influencing the risk level of your gene set. Could you comment on how far you are in this understanding and how do you see a balance in research going for preventive factors versus how we can treat these diseases?

DR. DANIEL WEINBERGER: That is a very important question. Of course there are many socio-environmental factors that contribute to all aspects of how we think about psychiatric illness. Environmental factors contribute undoubtedly to people's risk, they contribute to the age of onset, to the severity, to disability, and also probably to the manifestations. There are many clues for this kind of external influence. For example, we know that severe adverse childhood experience is a strong risk factor for a child for adult psychiatric illnesses. I think there's enough epidemiological data that is consistent and robust enough that it's impossible to dismiss this relationship. However, the problem in doing research in that area is that there's tremendous variability in how people respond to these experiences. It's difficult to quantify the experiences. Scientific research is challenging in that area. The hope is that by putting genetics, which is much more objective, quantifiable, bounded, into the equation of understanding the role of environment that the environmental factors will become much more apparent and know with more confidence how they represent risk factors. I think the problem with where we currently stand with our understanding of social environmental risk factors is we know they're important and we have a lot of data in population-based studies showing they're important. What has been difficult is to translate them at an individual subject level into a meaningful prediction of an algorithm for individuals. In order to do that, we're going to have to take the objective genetic information and add that to the equation of trying to understand individual liability.

PART 7 – Breakthroughs in Treating Mental Disorders: Historic Beginnings of Personalized Medicine

PRESENTATION 1:

"Personalized Medicine Based on Genetic Testing"

Dr. James Kennedy

Director, New Tanenbaum Centre for Pharmacogenetics, Centre for Addiction and Mental Health (CAMH) and Professor of Psychiatry, the University of Toronto
Toronto, Ontario, Canada

James Kennedy, MD, MSc, FRCP(C) is the Director of the New Tanenbaum Centre for Pharmacogenetics at the Centre for Addiction and Mental Health (CAMH) and he is the I'Anson Professor in the Department of Psychiatry and the Institute of Medical Science at the University of Toronto, where he is also the Director of the Neuroscience Research Department and Head of the Psychiatric Neurogenetics Section. Dr. Kennedy's research is dedicated to finding genes involved in the cause of mental illness. He has published pioneering findings relating gene variants in the dopamine, serotonin, and neurodevelopment systems to psychiatric disorders, and to treatment response. Dr. Kennedy has published close to 400 papers and his research has led to several discoveries. Dr. Kennedy is currently applying molecular genetic technology to investigate genetic factors that may predict response and side effects to psychiatric medications (pharmacogenetics). He is a nationally board certified psychiatrist and a fellow of the Royal College of Physicians and Surgeons of Canada. He is a member of the Neuroscience and Mental Health Board of the Medical Research Council in the UK, the Scientific Council of NARSAD: Brain and Behavior Fund and was recently appointed to the European OPTiMiSE Schizophrenia Study Advisory Board. His awards include the University of Calgary Medical School Research Alumnus Award, NARSAD Distinguished Service Medal, and the Novartis Endowment for Molecular Genetics Education. He holds an MD from the University of Calgary and both a masters of science and a bachelors of science from York University.

& Dr. Nicholas Voudouris

Family Physician, Thornhill Medical Centre
Thornhill, Ontario, Canada

Nick Voudouris, MD, EMBA, joined the Thornhill Medical Centre in 1990 as a family doctor. Prior to his role at Thornhill, he spent three years providing medical care in small communities in Ontario and the Northwest Territories. His undergraduate education was at Trinity College, University of Toronto and he completed his MD at the University of Calgary and then interned at North York General Hospital and Sunnybrook Health Sciences Centre. He is also a graduate (with distinction) of the Executive MBA program at the Ivey School of Business at the University of Western Ontario. He is the past Chairman of the Mackenzie Health Richmond Hill Foundation where he helped to raise $35 million for the hospital's redevelopment. He is also currently Medical Director for Seniors and Chronic Medical Illnesses at Mackenzie Health in Richmond Hill, Ontario.

DR. JAMES KENNEDY: I am going to discuss how Dr. Voudouris and I are delivering genetics to the people in a preventive fashion at the Thornhill Medical Centre in Ontario. This is the first ever genetic testing for depression medications in primary care.

Stress and Exercise

The recent research has shown how the epigenetic mechanisms interact with DNA when a person is under stress. To illustrate this for you I have a metaphor to consider. What happens when a person gets under stress is similar to when you had a handset on a coiled phone cord, well, the DNA isn't actually a coil of course, but the coil gets super-coiled. It coils upon itself and gets bound up and all tangled together. And this is like what happens when we are under stress. The stress hormones, including cortisol in the adrenal glands, gets into the DNA and tells the DNA, it modifies it so that it coils on itself and the genes go into what I would call a coil bunker. In most circumstances this is a protective mechanism. But with chronic stress, if your genes are not expressing themselves in a well-organized way, this leads to a stress-induced mental illness.

In terms of doing something about mental health in the workplace, I wanted to make an opening comment about how prevention efforts can be done in corporations. My prescription, as a clinical psychiatrist, to the workers of the world is to simply do more exercise, because physical exercise creates these growth factors, which go into the brain. One of them Dr. Weinberger and I have studied is called brain drive neurotrophic factor, which is stored inside the blood cells, in platelets. The more exercise you get, this more that this factor gets released. It then bathes the brain and also it works against the cortisol effect to uncoil this coiled bunker that the genes are hiding in. It helps the person open up and respond in a flexible way to the stresses of the environment. This exercise brain benefit relates to the knowledge-based jobs that we're all in. We're sitting around at a desk. We're thinking, but we're not moving. But as humans, we are designed as a beautiful machine to have brain and body interaction. And you'll see articles coming out about preventing depression through exercise programs. So that's my simple prescription today for all of us sitting and not moving around the table.

CAMH Research on Personalized Medicine for Depression

At the Centre for Addiction and Mental Health we are delivering genetics to psychiatrists and to family doctors in a way that cuts through the complexity. When patients come to see their doctor with depression or other mental disorders the doctor starts to think what kind of medication this patient should get. With depression the doctor has a choice of more than 20 different antidepressant medications. But the way that doctors have made this decision up until now, is through a process of trial and error by trying different medications – or the doctor just picks his or her favourite antidepressant. What's been cut out of this picture is the patient. This is troublesome when it's the patient who has to take the medication and who suffers the side effects. We contend that the patient's characteristics should determine which drug should be prescribed.

As Dr. Weinberger discussed, our genetic blueprint goes a long way to telling us how people are different. DNA is an exquisitely individualized source of information about people. What we're doing at CAMH is measuring that individuality and we do this through examining the genes in the body that break down common psychiatric medications. Given the large databases that exist of past research on differential patterns of clinical treatment efficacy due to genetic profiles, it is now possible to use this wealth of clinical information in a more prescriptive fashion to predict which medications are most likely to be a good match for an individual patient.

Genetic Testing. Based on a genetic test, we can score people as to whether they're very fast at getting rid of medications out of their body, or normal or very slow. People who are very slow tend to have the medication accumulate in their bloodstream. If it's an elderly person and they take the Prozac on Day One, they feel okay. But by Day Three, after taking three doses, they try to get up in the morning and take a step towards the bathroom and fall over and either break their hip or hit their head and then they're hospitalized and it's a huge cost to the health care system.

That kind of scenario could be prevented by a simple genetic test saying, "This person is going to get rid of this drug slowly and they need a much lower dose, one quarter of the dose." For example, if the standard dose of Prozac is 20 milligrams; then this particular patient should get only 5 milligrams. So we are sorting people into three groups, which are color coded as green, yellow and red. The genetic test sorts people into a green column of medications where those medications are good for that patient. The red column is for medications that are genetically not well matched to the person; they are either too fast or too slow. In the yellow group are medications that we are unsure about the match.

Potential Cost Savings. A study done through the Mayo Clinic in Minnesota by Joel Winner and colleagues examined the monetary implications of this kind of testing and improved outcomes it yields. They used this same genetic test to sort people into red, yellow and green types and then compared the groups in terms of the costs for their psychiatric visits, medication costs, costs of days absent from work and costs of disability claims. The results show that the savings in a patient with depression was $5,188 per patient, if they had this genetic test done and the red column of adverse-matching medications was avoided.

In Ontario, we have about 100,000 people with depression at any given time. If every one of these cases in Ontario were to see this kind of savings, after subtracting out the $1,200 cost of the test, it would be a potential total cost savings in just one year of $400 million for just one year. If you multiply it by three to go Canada-wide, that's a savings of $1.2 billion dollars. For the United States, that figure goes to $12 billion dollars in potential cost savings. If we go global, to the three billion total population in world, that's over $120 billion dollars in savings. And that's all with a simple genetic test that we deliver in 48 hours after the patient has seen the doctor.

So how does this new testing process exactly work? Well, I'm going to show you now a two-minute video of how Dr. Voudouris and I have launched this test in primary care. Here's how we're delivering these genetic tests to primary care patients.

[Video Plays]

DR. NICHOLAS VOUDOURIS: A lot of people have asked me, "So what's happened since the 10 months that we've started? What are the most important things that you've learned?" For my answer, I can boil it down into two things. The first point is that is we're making an incredible difference. When our patients get that yellow, green, red list of medications, it's really a wonderful thing because they can understand it. People laugh at a little bit at the metaphor of the stop sign colored lights, but it really works. They also really like on the second page of their testing report where it lists all scientific research studies on the genetics of it all. They say, "Wow, this is real science. I can believe this. This is going to make a difference."

Case Example:

I want to share with you the case of a certain patient of mine, a woman who I've been taking care of for 20 years. She's now 35 years old. When I first started taking care of her at age 15 she was a star at school. She was a valedictorian, wanted to go to university and be the biggest businesswoman in the entire world. Well, she went to the University of Toronto and after two years she got sick, she got depressed. She came to me. I tried her on two different medicines, neither of which worked. So I naturally referred her to a psychiatrist who tried her on two more different medicines and they didn't work either, which resulted in the psychiatrist saying that she didn't want to get better and she was gaming the system. She took that to mean that she was never going to get better because there was no medicine that worked because she had tried four of them. So she changed her life and became a low-level administrative assistant in a corporation here in Canada. She knew her limits. She couldn't go to any social functions outside of work. She just went to work, did her job, and went home. When we did the genetic test on her, we found that there were 12 red medicines that she should not take. More significantly, all four of the medications that she had been put on in the past were those red medicines. So she wasn't gaming the system. We just didn't know which medicine to give her. So we switched and gave her one of the green medicines. After seven months of taking the matched medicine she is doing very well and she's even thinking of going back to school. So that's just a great example of just one person making a difference.

University Research Partnership

The other thing that I've learned concerns our initial expectations on how the private-public partnership would work. For this project, the Thornhill Medical Centre has worked in partnership with the researchers at CAMH and the University of Toronto. We were taking patients who were "normal" and healthy, who were required then to go on a medicine, and we were telling them that they had to participate in a research study. We thought that they'd head to the hills because they wouldn't want to be involved with a research project and that they'd instead just go on to the Internet-based resources for genetic testing, which was easy, anonymous, and which was in the Zeitgeist of the times.

What we found was the exact opposite. Our cases really wanted to be involved with the university and with CAMH. They wanted a credible and structured program. They wanted to be looked at person-to-person because they felt that the researchers were looking after their best interests and that whatever they were going to be told was going to be true. On the other hand, they were very afraid of sending their genetic material to companies all over the world, not knowing what was going to happen. So this patient response was a real eye-opener for us at the Centre. The other thing that's important to keep in mind is that the family doctors are the frontline troops in this issue and a lot of them didn't want to deal with some of the genetics companies either.

What this experience has taught us is that yes, we need the financing, we need the service, we need the ability that big money brings. But we have to be very careful to recognize that the patients involved in this research are people and that they are giving this information to us as sort of a sacred trust in order to try to help them. Therefore, we have to move forward in a way that allows them to be protected, that allows it to be scientific, and that allows it to work.

So I think that we are making a real difference. Although, is still in the early days of the project plan, I feel there's a tremendous potential for it.

PART 7 – Breakthroughs in Treating Mental Disorders: Historic Beginnings of Personalized Medicine

PRESENTATION 2:

"Personalized Medicine Based on Brain Wave (EEG) Testing"

George Carpenter, IV

Chief Executive Officer, CNS Response Inc.
Orange County, California, USA

George Carpenter, MBA, is Chief Executive Officer of CNS Response Inc. CNS Response is a neuroscience company focused on improving the quality of treatment for patients with brain disorders, by providing objective information to prescribers of psychiatric medications. His primary responsibility involved developing strategy and commercializing the rEEG technology. From 2002 until he joined CNS in October 2007, Mr. Carpenter was the President and CEO of WorkWell Systems, Inc., a national physical medicine firm that manages occupational health programs for Fortune 500 employers. From 1990 to 2001, Mr. Carpenter founded and served as Chairman and CEO of Core, Inc., a company focused on integrated disability management and work-force analytics. From 1984 to 1990, Mr. Carpenter was a Vice President of Operations with Baxter Healthcare. Mr. Carpenter began his career at Inland Steel where he served as a Senior Systems Consultant in manufacturing process control. He holds an MBA in Finance from the University of Chicago and a BA with Distinction in International Policy and Law from Dartmouth College.

& Dr. Gary Hasey

Associate Professor of Psychiatry at McMaster University and Chief Medical Officer for Digital Medical Experts, Inc.
Toronto, Ontario, Canada

Gary Hasey, MD, is an Associate Professor in the Department of Psychiatry and Behavioural Neurosciences at McMaster University. He is the director for the electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS) clinics at St Joseph's Hospital. With his engineering collaborators, he has developed computer-based machine learning algorithms capable of analyzing electroencephalogram (EEG) and clinical data to determine psychiatric diagnosis and to predict response to TMS, ECT, antidepressant medication, antipsychotic medication and cognitive behaviour therapy. This technology is being commercialized through Digital Medical Experts Inc., where he serves as Chief Medical Officer. Previously, he was a consulting psychiatrist for 12 years at the Centre for Addiction and Mental Health (CAMH). He holds a MD from the University of Alberta.

GEORGE CARPENTER, IV: I have what I think is a really interesting story and I think one that you're going to understand in the context of genomics. We study a phenotype, a phenotype as expressed by a functioning brain and measures using one of the oldest tests we have, which is electroencephalography (EEG). We're actually measuring how well do people with a certain kind of brain respond with some of the oldest and most well-normed data that we can find on psychiatric medication outcomes.

Later on I am going to let the science of our work be discussed by my colleague Dr. Gary Hasey. But first, let me tell you who we are at CNS Response and how we've look at radically reframing the problem of poor medication outcomes by adding testing based on genomics.

But to start, I'm going to offer you a challenge. The challenge is that I won't over-claim the technologies we use and you, in turn, as the doctors, will not hold our technology to a higher standard than you hold trial-and-error pharmacotherapy. I say that because that is the dominant treatment today and it hurts people. We can do better. We can do it better with the genotype and we can do better with the phenotype. But the best part of this is that we can do it today. These tools exist today.

About CNS Response

Who are we? CNS Response is a private, for-profit capitalist company. There has been about $30 million invested into it. We've never made any money. We lose gobs of money and yet we're still going. We're still going because there is a really good idea here. We are a public-private partnership with the United States Department of Defense and we currently doing a 2,000-soldier trial of this technology. The technology actually has over 80 research clinical trials behind it and a dozen of them are our own studies.

It's kind of like we are under a cooperative research and development agreement with the military. It's kind of like Craig Venter with the genomics approach. We're not actually trying to split the atom or come up with a new molecule. We're just trying to use computers to do a better job. What we do is algorithms. You probably haven't heard of us, but you've probably heard of the Cloud and the Internet. And if you don't believe in algorithms, then you should stop driving your car or stop shopping online because these all use algorithms.

A Brief History of the Company

One of the doctors who founded our company is a pathologist. He went into psychiatry with a group practice in Los Angeles over 20 years ago. Back then he said, "Why don't we measure anything?" So we started measuring three things: 1) the date and dose and type of medication; 2) the patient's presenting EEG (which is the basic measure of electrophysiology); and 3) and outcomes in terms of global clinical improvement. It turns out that these three things correlate together very well. They correlate to the extent that they reduce the number of drugs needed to get to the right answer. His point was, "We have a hundred psychotropic drugs. We don't need three more. We need to know how to use the ones that we have."

CNS Response and the Walter Reed Trials Research

All we did was use the drugs that we have already that are used in personalized medicine based on the phenotype of the individual patient. If our work was expanded, we would have a remarkable impact on medication outcomes and potentially even on suicide. In the 2,000-soldier trial that we're doing at

Walter Reed Medical Center, we're looking at primary efficacy endpoints and all of our trials have been successful on that outcome. We're also looking at suicidality and reducing severe adverse events because we think fewer shots on goal with better accuracy equals a better outcome.

A problem today is that most doctors are still practising medicine in silos. Where has that happened before? Well, it happened in pediatric oncology in the 1960s. Back then a diagnosis of cancer was a death sentence for a child. But then the doctors got together and they said, "You know what? We shouldn't practise in our silos. We do great, great work as individual - hero diagnosticians - but, at the end of the day, the secret dies with us. We don't share. We don't get out of our silos." So they networked. And now you cannot be treated in the United States now if you're a kid with cancer without being part of a clinical trial. As a result, we're now at a 90 percent cure rates for pediatric cancer.

Networking works. Algorithms works. Math works.

We're just the higher primate standing in between DNA, which is a binary information system, and algorithms, where our car is now smarter than we are. What we're trying to do is cut the distance to the goal and make these algorithms available, understandable, tractable, and usable by doctors today.

General Peter Chiarelli

Let me also offer a kind of radical reframing of the problem. I don't know if you've already seen the video we are about to play, but General Peter Chiarelli is my hero. He retired just a couple of years ago, after being given the job of managing the suicide and PTSD problem for the United States military. Over the course of his tenure, the number of suicides increased, in one of the most frustrating jobs in the world. And one of his frustrations was all that of the experts disagree. He couldn't get a community consensus around how to improve the success that we have with these therapies.

Audio from the Video:

> "General Pete Chiarelli served two tours as a combat commander in Iraq, but admits he was clueless about brain injury when he became the No. 2 man in the army in 2008.
>
> "I went to visit eight installation in seven days and when I got to the fourth one, I realized that the problem was much bigger than that. It was a problem about the health and well being of the entire force. I talked to soldiers who told me that they felt that doctors were throwing bags of pills at them. I talked to doctors who basically said they had soldiers lined up outside their offices, and they really only had an RVU of about 20 minutes to spend with each one of them.
>
> "Like a dummy, I thought back then the drugs that we were going ahead and prescribing those soldiers were all drugs that had been developed for the treatment of post-traumatic stress and traumatic brain injury. In my new job, I found out that that's not necessarily the case. In fact, it isn't the case at all.
>
> "I had expert after expert come into my office and explain to me, and the thing I found most frustrating was that expert after expert told me something different. They could not agree. I had 15 of the finest minds in there and I got 16 different answers. It was the most frustrating thing I had ever done."

I apologize for the dramatic music in the video, but you get the point. We need something practical, today, that can solve a problem. We've had a 682 percent increase in psychotropic medications in the military in the United States over the last six years. That's not because the drugs work so well. Much of the problem is because we're giving more medications to the same people. The doctor says: "You didn't respond on two medications, so let's try three." Part of our protocol is we actually wash you out of medications [stop taking all drugs] before you have the EEG test. That was something that is very controversial. Doctors don't like to wash patients out of medications for five half-lives. But we found a remarkable surprise when people wash out - in most cases, they get better. In fact, we've had 10 percent of people in previous trials actually not go back on medication after being washed out. So there's a lot to be said for a very limited claim: give doctors information; they will reduce trial and error. And that's all we really claim.

I want to focus now on what CNS Response is doing at Walter Reed Medical Center in the United States. Located in the Washington, DC area, Walter Reed is the premier medical research teaching hospital for the United States military.

I'm just going to give you a couple of examples and describe how the trial is designed. I think it's helpful if you look at the great work that Helen Mayberg has done at Emory University in Georgia using PET scan to predict medication response or response to cognitive behavioural therapy. There's a great editorial written in Nature about the virtue of this for reducing stigma. And as Dr. Insel said, half of people who need care for mental health disorders never seek treatment. The stigma around the lack of efficacy of treatments and the personal costs of going into treatment is very high and it can also be lethal. Tom Brennan, who's a friend of ours, wrote an excellent suicide note and published it a few weeks ago. He is a military journalist, so he writes a wonderful note. Fortunately, he did not kill himself. He got better and he got better based on an EEG-based therapy.

The reason I say that is because he's a marine and he actually wrote the note because he was thinking of killing himself because, as he writes in his note, once he was diagnosed, once that DSM label was applied to his condition, he was no longer a marine. He was literally on a different career track and he identified himself as a marine.

We often think of these things with kind of a New Yorker cartoon view of what psychiatry is. It's cute. It's subjective. It's fluffy. But it is not these things. There are real hard clinical endpoints to psychiatric disorders and suicide is certainly one of them. We know that stigma is a contributor to not getting treatment. The paradox is that these medications work profoundly well in the right brains, but they don't work well on the average and so they don't work two-thirds of the time when actually applied – because the drugs are not being matched to the brain of the patient. Dr. Insel's "rule of halves" is quite true and it really is the guiding light behind these very inexpensive, simple approaches to data mining, which offers a way to get better data in front of the doctor at the point of care when that moment of writing that first script can be dramatically improved.

It's not perfect, but it's two to three times better than trial-and-error pharmacotherapy. We think the machine-learning algorithms are a key part of this. I don't personally look it as data mining so much as data fracking. We are forcing huge amounts of data through what we already know are known phenotype markers and doctors armed with this kind of data-driven tool can do much better.

We really need that support for the doctor because we don't have enough evidence. The pace of evidence development from clinical research is slow. We get it either from large drug studies or from

large research universities. How much money is going into either source? Well, many large pharmaceutical folks are getting out of the CNS category of drug development research because it's so hard to beat placebo.

The doctors who founded this company 20 years ago said, "There's not going to be more randomized control trials. Let's just make our own. Let's actually have the data inform us and learn every time we touch the patient. Let's do a better job generating our own evidence." As a result, they have built what is one of the largest phenotype databases of medication response and it is built according to what actually works in real humans.

Consider another example. "The Medicated Child" is a 2008 "Frontline" TV documentary. It did a great job explaining that, in fact, most of the medications prescribed to children are off-label and have little or no evidence for their effectiveness in pediatric populations [because they were tested on adults and not on children]. So, we're not going to get evidence by waiting for the next RCT [randomized controlled trial]. We really do have to build it ourselves.

Now, the military is a leader in the adoption of this kind of machine learning technology. Colonel Bradley originally had us into Walter Reed when he was running the psychiatry program. We are now working with Dr. Brett Schneider who has done a fantastic job. We are a for-profit company but we're also open source. We build these machine-learning tools and we also publish our data.

We had a hard time when the FDA looked at this and they said, "Wait a minute. You are agnostic to diagnosis? Why?" Well, as Dr. Insel has pointed out, there isn't a lot of scientific validity behind symptom clusters. We're just looking at the biology and the electrophysiology and saying, "Here's what was associated with an improvement." Often the results we have found are counterintuitive. But more importantly, often the results are very positive. We had a researcher come up at Walter Reed a few months ago who was very upset. He had worked at the NIH [National Institutes of Health] for years. He said, "I don't understand. I've been working with functional MRI and PET scans for 10 years at NIH and we have not found these biomarkers that you seem to claim you have found." Again, we make no claim other than clinical utility and reduced trial and error.

But what's surprising is that we're using a tool that's very old and inexpensive to use – we charge $540 for this test at Walter Reed. There is something great about a very old tool. It has large databases of both clinical patients and of asymptomatic controls and all of this normative data. Because of all of this old data on EEG we can characterize pathophysiology by using EEG. This kind of EEG testing utility is also deployable to a battlefield. It is simple, cheap, easy. In the future, as we build bigger databases of PET and functional MRI treatments, these tools can be used as well.

The power of this approach to solving clinical problems comes from the application of crowd-sourced outcomes. Every time a doctor sees a patient and we get an outcome, that data then improves the predictiveness of these algorithms and the patients are getting better. So in the worst case, as we keep collecting more data at least we're learning. And if you don't think your car's learning and the Internet's learning and every other algorithm around you is learning about you, they are. Let's actually harness that same process of machine learning to improve mental health.

That's our story at CNS Response. Thank you. Now I'd like to introduce Dr. Hasey. His team at McMaster University is doing exactly the same kind of research on EEG phenotype medication response predictions that we are doing at CNS Response.

DR. HASEY: We are a team of psychiatrists and engineers who have worked independently for decades. In the last five years we've combined our knowledge and come up with an interesting technology that I think might hold some promise. We have learned that if we want to have our technology make any kind of significant clinical impact, we need to have business people in the engine room and at the helm to drive this forward. With McMaster University's help and encouragement, we've created a company called Digital Medical Experts and we've recruited Bruno Maruzzo, who's in the corner here today, as our CEO.

I'm going to be talking about improving and personalizing the treatment of depression using machine learning, also known as data mining or artificial intelligence. The current state of the art for prescribing psychiatric medication is quite poor, as you've heard. Physicians who are confronted with depressed patients typically select a drug in a randomized fashion or they go through serial trial and error, much as you would in a shoe store where the clerk's favourite shoes are lined up and you try one after another until you find a fit. Not surprisingly, but typically, the drug that is prescribed the first time around is not correct in two out of three instances. That's a failure in over 60 percent of cases.

What is Machine Learning?

Machine learning is a possible solution to that uncertainty. It's a technology that allows one to classify based on very large amounts of data. For example, let's ask a computer to determine whether a photograph of a particular person is a male or a female. What is done first is that the computer is trained and then it's tested. The training phase involves collecting a large number of known males and a large number of known females and then, from those people, you extract features or attributes and large numbers of variables that you think might conceivably have some relevance to distinguishing the sex of the person.

It turns out that most of these variable are actually not relevant; the number of fingers, for example. Other variables are more productive in classifying male or female sex and we instruct our algorithms to go through those thousands of variables and to choose those few variables that seem to have some individual power in classifying. Through this process, we end up with a much smaller set of features or variables and then those are put into a multi-dimensional matrix. In this instance, we have hair length, voice pitch and muscle mass that are plotted in three dimensions. We take an individual person and plot their attributes into that matrix and if the predictive model works correctly then we find that all the females are clustered in one spatial area, all the males in another, with only a small area of uncertainty or overlap. Once you've developed this kind of an algorithm, you go on to test it. Our studies show that we're correct in about three out of four instances with this particular machine-learning model.

Predicting Psychiatric Diagnosis from Brain Wave Data (EEG)

In the real world, we actually use brainwaves or EEGs as our dataset from which we extract the features and we ask the computer to classify according to different clinical needs. Let me first explain about the EEG or brainwaves, this is an example of an EEG. We extract from the data obtained of thousands of different variables and we process those to eliminate most of them, leaving only a few remaining elements which we then use for classification purposes.

If we assign the computer the task of differentiating patients by clinical diagnosis, we get the following kinds of results. In one of our early pilot studies we have 195 persons, 64 who had major depressive disorder, 40 who had schizophrenia and 91 who were normal or healthy and used as reference group.

Using the machine learning process we were able to identify about 86 percent of the depressed patients, 87 percent of the schizophrenics and about 88 percent of the healthy individuals without actually seeing them. We just look at their brainwave pattern.

A more challenging task is to separate depression that's due to bipolar disorder from other kinds of depression. In another study, we had 76 persons, 64 of whom had major depressive disorder and 12 who had bipolar disorder. We were able to correctly identify 94 percent of the depressed and 92 percent of the bipolar patients using machine-learning algorithms employing EEG as their dataset.

Predicting Psychiatric Treatment Effectiveness from Brain Wave Data (EEG)

Moving on to treatment was our next objective. We hope to build a catalogue where we can tell treatment by treatment whether a person would respond based on their EEG profile. The first drug we tested was sertraline. We found that we could identify and separate — and this is from data collected before we treated them — about 88 percent of the people into responder or non-responder groups.

We then tried this approach with another technology called transcranial magnetic stimulation, which is the next step after electroconvulsive therapy – sometimes called electric shock therapy. But it's a more user-friendly technology. In any case, we were able to identify in advance whether a person would respond to TMS with about 84 percent level of confidence.

We had some data drawn from the schizophrenic population treated with a very powerful drug called clozapine. This drug works when other drugs in the class fail in many instances. It's a very dangerous drug. It can suppress your bone marrow and people can die of infections. You must have a blood test every month forever as long as you're on this drug and people remain on it for a lifetime. So it would be important to know whether this dangerous drug is going to work or not before a treatment phase is started. We applied our machine-learning methodology, analyzing the EEG brainwave signals of the patients and we were able to identify with about 84 percent confidence whether they would respond or not to this medication.

Next Step of Science-Business Partnership

We hope to take this research-based technology, with the assistance of business, and commercialize it for more general use. Imagine being able to take it into the local medical clinic where a patient appearing at his physician's office would be sent for an EEG test. The EEG test would be analyzed and, within a few minutes, a report would be returned to the physician her giving an estimate of the probability of various psychiatric diagnoses and better still, a list of treatments with a probability of response attached to each treatment.

I thank Mr. Carpenter for the opportunity to address this group.

PART 8 – Forging A New Era of Collaboration: Halting the Progression of Human Suffering and Economic Losses

FACILITATOR: Bill Wilkerson

Keynote Address

"The Five Principles of Transformation for a New Era of Collaboration"

Don Tapscott
President and CEO, The Tapscott Group
Toronto, Ontario, Canada

Mr. Tapscott is one of the world's leading authorities on innovation, media, and the economic and social impact of technology and advises business and government leaders around the world. Over the past 30 years he has introduced many groundbreaking concepts that are part of contemporary understanding. He is President and CEO of The Tapscott Group, a member of the World Economic Forum, Chancellor of Trent University (Peterborough, Ontario), adjunct professor of management at the Rotman School of Management and fellow at the Martin Prosperity Institute (both at the University of Toronto). He has authored or co-authored 15 books, including the 1992 international best seller *Paradigm Shift: The New Promise of Informatics Technology*. Some of his other books that focus on the influence of the Internet include *The Digital Economy: Promise and Peril in the Age of Networked Intelligence* (1995), *Growing Up Digital: The Rise of the Net Generation* (2000), and *Digital Capital: Harnessing the Power of Business Webs* (2000). Two of his most influential management books are *Wikinomics: How Mass Collaboration Changes Everything* (2007) and *Macrowikinomics: Rebooting Business and the World* (2011). In 2013, Thinkers50 ranked him fourth among the world's most influential management thinkers and he was awarded the Global Solutions Award for launching and leading the Global Solutions Networks program, which is based at the Rotman School of Management at the University of Toronto.

As many of the speakers have said, this is an extraordinary time in mental health research and, I think, more broadly in human history. Tom Insel said we're in the middle of a revolution in how we study the brain and in mental health research.

For many years, I've been investigating how collaboration and the digital revolution really changes business, the economy and society. What I'd like to do today is to stand back and try and describe this change that we're going through, not in science, but in how science is conducted. I think that this change has big implications for the business community and I'm going to argue to you that this is a very important meeting and initiative that we're talking about today for some reasons that they may not be totally clear to you.

Like most people, I have a personal connection to the issue of mental illness. My brother, Dave, was diagnosed with schizophrenia decades ago. Consequently, Ana Lopes – my wife of 30 years, who is sitting here – and I have invested a lot of time over the years in trying to find funding for mental health research. Ana more than me, as she is recently is the Chair of the CAMH Foundation. We're also very happy to say that the Tapscott Chair in Schizophrenia Studies is Art Petronis, who is working in the area of epigenetics.

I can skip the obligatory discussion about the importance of this issue because I think that that has been covered. And I can also skip the economic costs because that has been covered as well. But I would like to comment on this issue of the knowledge economy because it's true that we create wealth and prosperity and innovations through brain today rather than through brawn. But there are some sides to this that are also important.

Increasingly, brains don't work in isolation. They work through collaboration and, in many ways, we're starting to connect brains together and teams, increasingly, do many, many things. Michael [Wilson] talks about in the mining industry we have a focus health and safety. Well, we also need health and safety for the brain.

Furthermore, brains need to develop their knowledge, lifelong. When I graduated many years ago, I thought I was pretty much set for life and all you had to do was have a field and you kept up in your chosen field. Well, today you're not set for life. You're set for, I don't know, 15 minutes. And if you took a technical course in the first year of university, half of what you took is obsolete by the time you get to your fourth year. So brains and their knowledge are sort of are like a milk carton. They have a time stamp on them and they're going to go sour unless they're constantly being rebuilt. This new generation coming into the workforce needs to collaborate in new ways in order to stay fresh. They are a generation that will reinvent their knowledge base many times throughout their lives.

What's the state of the art today in mental health research? Well, there's an extraordinary report that was done recently that's called the, "CAMH Task Force, Enhancing Discovery, Creating and Sharing New Knowledge: The Research Renaissance in CAMH." Included in this report is this staggering statement that significant breakthroughs have not occurred in mental health research for decades. A number of people have alluded to that today. Dr. Insel talked about how we have soft science, psychiatry is based on studying symptoms, medications are based on treating symptoms and, when you think about today's psychotropic drugs, they're pretty much derivatives of the drugs that existed decades ago. Dr. Weinberger talked about the growing recognition that the field needs to identify the fundamental common neural pathways, the cellular origins, the genetic score which cut across disorders and we need this roadmap, as Dr. Weinberger called it.

So why has this occurred? How can this be that there haven't been significant developments in decades? Is the brain too hard to understand? Or is it possible that our model for doing research has been wrong? What has our model been?

The Current Ineffective Mental Health Research Model

Well, as Dr. Weinberger said, we have too many individual agendas and that's a way of coating a whole modus operandi of how not just health research but scientific research has been done during the Industrial Age. In the private sector, we have companies, biotech pharmaceutical companies and so on that compete with each other and so they do not work in collaboration. They do not share data and

they conduct their own clinical trials, which are often then duplicative of what others are doing.

When it comes to the public sector, academics and research conducted by hospitals and so on, you have individual scientists that compete for grants to fund the research. That's the way the granting model works. The scientists work on research projects often in relative isolation. There is only limited collaboration and sharing of data and sometimes, later on when they come up with some results, those results are peer-reviewed and they are published by a whole separate industry called the publishing industry that charges the academic institutions that funded the research in the first place to buy the publications. And those publications are often behind a firewall.

This entire model has some big flaws. A lot of people are coming to the conclusion that we need a fundamental change in the way that together, as a society, we investigate these important problems. Dr. Bruce Pollock, for whom I'm a huge fan, says real breakthroughs in discovery and into the causes and effective treatments of mental illness will occur when the silence within and between institutions doing research falls. We need to do more. We need to move more to a new era of collaboration and the sharing of data and knowledge.

Trevor Young, who is the chair of the Department of Psychiatry at the University of Toronto, points out that there has been a long tradition of sharing data and international collaboration to move patient care ahead. He basically argues, "Why can't we do the same thing when it comes to research?"

So let me sort of stereotype, a bit, the model we have now. If there were some implicit principles in this model, it would be that we have competition, that there's a lack of transparency, that data is hoarded, that people work in institutions – often, these silos exist within institutions and people don't even share data within them. The people act with integrity, of course, but the integrity is parochial in that you're trying to do the right thing for your institution, for your project, for your silo as opposed to doing the right thing for human health.

The Internet Ushers in the Age of Collaboration

This approach is all changing, right now. What's going on in this room today is a description of that change. We have a new age of collaboration and, among other things, the Internet radically drops transaction and collaboration costs in our economy. It's not about hooking up online or creating a gardening community or websites or government online or anything like that. It's a global computational platform that reduces the costs of collaboration. Humanity is building a machine that enables us to work together, to share data and to have a new modus operandi for many of our institutions.

If you look around today, most institutions in society are changing. Old models of the corporation, of the financial services industry, the media is being transformed. The last newspaper in Canada will be published in the year 2030 and I guarantee that when that happens your newspaper won't be delivered to your door in the morning.

Our universities are also being transformed. The university is losing its monopoly over higher education. More young people will be studying university courses on MOOCs (massively open online courseware) in five years from now than there will be in all of the university on-campus courses combined.

So it's logical that these tectonic forces transforming our institutions would affect research as well. Let me give you five principles that are sort of the antithesis of the principles that I've described, that we've been operating under.

Principle 1: Collaboration

The first is collaboration. Tom Insel says networking works. And this is rolling out throughout all of our institutions in our economy. Procter & Gamble gets 60 percent of its innovations from outside of the company now. They have 9,000 chemists inside their boundaries, but they have 1.8 million chemists outside that they can now get to. If they're looking for a molecule to do something, let's say take red wine off a shirt, there may be a grad student in Taipei or a researcher in Toronto that comes up with a molecule and Procter & Gamble pays them. It's a different model. Rather than, "We grant you money. Go figure out a problem," it's that, "We have a problem. Who can figure it out?" and the person who figures it out gets the funding. Now, there are some issues with that but it's a change and it reflects a change that's underway.

The next step is that you don't go to InnoCentive that has a million chemists on it. You build your own innovation and research ecosystem using tools like Inno360. Eighty percent of the web is the deep web. You don't get access to it through Google, but you can go create an ecosystem using tools like Inno360, where you find the uniquely qualified minds out there to solve a specific problem. But talent is outside your boundaries. It's not necessarily inside. These are huge changes.

There are 275,000 amateur astronomers who are mapping the heavens right now and an astrophysicist that I've been working with said this would take all the professional astronomers in the world 120 years to do. This group, Galaxy Zoo, will have it done in a year because it turns out that amateur astronomers can categorize and use a taxonomy to name galaxies with approximately the same success rate as professionals.

So what does this mean for mental health research? Well, a good starting point is the structural genomics consortium that is based here in Toronto and tied in with MARS. This is a group that understands that a rising tide lifts all boats and we need to get together. We created a human genome. Now we can create all kinds of other things – as mentioned, the human epigenome, for example.

The Ontario Brain Institute is in the business of fixing the research paradigm on brain research and it's driving collaboration. It's a very powerful and wonderful initiative. We've got the Toronto Dementia Research Alliance, another initiative that's working to bring about collaboration amongst different researchers in organizations. We have The Organization for Human Brain Mapping. This goes on and on. There's a tidal wave now of people saying, "The old model doesn't work. We need to break down the silos."

Just some of the organizations that came up today: The Canadian Consortium on Neurodegeneration and Aging, the International Epigenome Consortium, and the Canadian Institute for Mental Health.

Principle 2: Openness

The second principle is that rather than opacity we can have openness. When people think about transparency, they often think about WikiLeaks, where transparency is a force or a negative thing. But to me, WikiLeaks is really just the tip of the iceberg because transparency is now such a powerful new

force in the economy. What my research shows is that when people communicate or when institutions communicate pertinent information with their partners, employees, customers, and with the communities within which they operate, society and so on, that is when all kinds of good things happen.

Another benefit is that you drop transaction and collaboration costs in a research consortium. You build trust. You build loyalty. You get less office politics or political activity. It's just about opening the kimono. And increasingly, institutions need to do this and it's a wonderful thing because sunlight is the best disinfectant. We're all, as institutions, becoming naked and if you're going to be naked there are some corollaries that flow from that.

One of them is that being fit is no longer optional – it's required. If you're going to be naked, you've got to get buff. That's a great thing, because there's a lot of disinfecting to do in our institutions in this society. There are all kinds of wonderful initiatives happening around transparency. For example, there is the open access and open science initiative the University of Leicester in the UK.

Principle 3: Sharing

The third principle for transformation is sharing. This is different than transparency. Transparency is about the communication of pertinent information. Sharing is about assets, about intellectual property, about data, and about giving up these assets. There's a revolution happening across many institutions on this front.

The computer industry used to compete on the basis of their operating systems. DEC had a better operating system than IBM, they would say, an operating platform. But then along comes Linux, which is a computer operating system that's in the commons. Originally in the computer industry, some people said, "This is communism. Products should be developed by companies, not by collaborations." And IBM actually was the first to figure out, "No. This is going to be a good thing for the computer industry." IBM embraced Linux. They gave away $400 million of software. In doing so, they saved themselves $900 million a year developing their own proprietary operating system. IBM created a platform on which they built a multi-billion dollar hardware and services business and they also got to change the whole dynamics of the industry. They kept Microsoft out of the high-end enterprise marketplace.

So in terms of sharing, it turns out that sharing isn't communism. It's sort of like capitalism in this new era of collaboration that we're entering into.

Take the case of the pharmaceuticals, which this year are falling off the patent cliff. Many of you know about this. "Big Pharma" in North America and in other countries, like the UK, these companies are losing a quarter of their revenue in a single year. This is a shocking thing. So what are you going to do? Cut back on your paper clips or something? No. The industry needs to change its whole modus operandi and the big opportunity is to share clinical trial data. Now there are already steps underway to share pre-competitive research, comparator arm data. You're testing a compound. You have a placebo in a comparative arm. You can share those really easily without sharing the results of the test group.

The failed results of clinical research are another thing that's already being shared. Led by GSK and Andrew Witty, who's the CEO there and someone I've been working with, the industry is going to place clinical trial research in a commons. That's ultimately what will be done and it will compete on a higher

level. They'll compete on delivery systems, on services, on packaging, on customization of medications and this is going to lead to important breakthroughs in human health.

And by the way, when it comes to mental health research the pharmaceuticals have pretty much stopped doing mental health research. I think the reason is what I'm talking about. It's not that the brain is too hard to figure out. Rather, it's that they just can't do it by themselves. Until they change their model, they're just giving up and this is a terrible thing. Having made billions of dollars on these drugs over the years, they're just saying, "It's not profitable anymore."

So other big collaborations: We have the Smart Foundation. It's a global non-profit organization devoted to realizing the promise of translational biomedical research through the development of a smart, knowledge management platform. We have the Wellcome Trust in the UK. It is committed to ensuring that the outputs of research it funds, including research data, are managed and used in ways that maximize public benefit. Wow, what a change.

Principle 4: Interdependence

The fourth principle of transformation is interdependence. The idea is that we have a number of pillars of society that increasingly need to work together and that's, in many ways, what this meeting is all about. But in the past these pillars have not cooperated well, in general, and specifically around health research and specifically around mental research.

Let me explain: We have the state, pillar No. 1. We have the private sector, markets. We have the civil society, which includes academia and public research institutions and so on. And there's a new pillar, individuals now – because of the Internet, can now be pillars of society. So a retired chemist somewhere can discover an amazing new molecule by participating on the InnoCentive Network.

I'm normally working with business executives and business audiences and it's very popular, especially in the United States, to say, "The best thing governments can do is get out of the way." And to me one of the great tragedies of what's happening with our municipal politics in Toronto is not just the current bad behaviour of the mayor but the attitude that that the best thing government can do is to have less government. Well, this is just an inappropriate and dangerous attitude for this new age of interdependence. We need to work together.

Consider the whole subprime mortgage crisis and how the banks in the United States were affected so badly by that. And yet he Canadian banks were not. In fact, they did really well. If you look at the safest banks in North America today, the top six are Canadian. Of the strongest banks in North America today, most of the top group are Canadian. Why is this? Were the Canadian executives just stronger, just smarter? I was talking to Gord Nixon, who runs RBC, and I said, "Boy, you must be pretty proud of yourself." And he said, "Not really. I mean, the structure of the mortgage market is different in Canada." It was regulation in Canada and government involvement that prevented this terrible situation from happening.

We need to have these different pillars of society now work together. Dr. Weinberger was talking about no group can do this by themselves. George [Cope at Bell Canada] says there's a role for government intervening. We're probably going to need some legislation around workplace safety. George Carpenter also talked about building public-private partnerships. We need a new era of interdependence.

There are lots of wonderful initiatives that are just starting now. This is one that I came across. This is a proposed partnership between private philanthropic donors, pharmaceutical companies, government and academia with the sole focus of bringing neuroscience drugs to market. It involves the University of Toronto, the Centre for Addiction and Mental Health (CAMH), the pharmaceutical companies, the Canadian government, philanthropists and so on. Now this is just a proposal now, but it's the kind of thing that's in the spirit of what I'm talking about and which kind of brings me to my final thought.

The Global Business and Economic Roundtable on Addiction and Mental Health that Bill [Wilkerson] initiated many years ago was in the spirit of interdependence. I think it made some real progress. The proposal before you today from MHI, to consider forming an international business-science partnership for mental health and productivity, to me, is on the money. We need to orchestrate capability from all of society in an integrated and collaborative way to overcome these challenges.

Principle 5: Integrity

The final principle for transformation is integrity. This is about being honest, being considerate of the interests of others and being accountable. This is the foundation of building trust. Trust is the expectation that another party will be honest, that they'll care about your interests, and that they'll abide by their commitments. To build a trust and to move forward on this, we need to behave with integrity. Not just doing the right things for our own research department or our patients, our own hospital or our own university or our own city or our own institutions, but for humanity. So there's an opportunity to change the paradigm around integrity.

As Dr. Weinberger said, we've got too many individual agendas. Peter Anderson and Dr. Jetly also both talked about bringing authentic leadership. To me, that is what's required, is to have authenticity and integrity driving everything we're doing.

We have something like this now in the transformational research that is being done in adolescent mental health. This is a program that's trying to drive and change behaviour and to get people cooperating together to do the right thing. I think the big new initiative of President Obama that Dr. Insel noted is another example and it ha $100 million of funding to get it started. Of course, that's not a drop in the bucket, but it's certainly not sufficient to attack this problem properly. It's about doing the right thing and getting started. These are the kinds of initiatives, of course, that we all need to support.

Conclusion

These five principles are kind of antithetical, in some regards, to the ways that things have been done. This is not something that I'm proposing. Rather, I'm just describing what I see happening today in the world. It's a very exciting time. I've never been more optimistic about making great breakthroughs.

My final thought is what I've just described is a new paradigm in doing research and in mental health research in particular. When you get a paradigm shift, you get a new paradigm. You get dislocation and conflict and these things are nearly always received with coolness or worse, and vested interests fight against change. Recall that in Thomas Kuhn's book, *The Structure of Scientific Revolutions*, he described how the leaders of Newtonian physics initially fought against Einstein's general theory of relativity. It's not going to be easy to make this shift. Grants are still given according to the old paradigm, where people compete for grants.

How do we find the leadership for change? Well, it's going to come from everywhere basically and the people sitting around this table here today is an inspiring case in point about how we can do this if we find the will to do it.

We have seen many decades with not a lot of real progress in mental health treatment. We can move to a new period where there is a lot of progress. I think that if we build a new paradigm in global collaboration around these principles of transformation then maybe, to paraphrase Dr. Weinberger, we can change the score and build a better human symphony.

Can we be hopeful here? To me, I think the future is not something to be predicted - it's something to be achieved. I hope that all of you will be very determined to achieve a different future around a new paradigm in research.

Thank you very much.

PART 9: Comments and Ideas from Forum Participants

PRINCIPAL FINDING OF THE 5TH US/CANADA FORUM ON MENTAL HEALTH AND PRODUCTIVITY: Support for the development of a formal business plan to support the creation of a new international business-science partnership for the promotion of brain health and brain capital in a global brain economy.

This part of the report presents the key themes from the discussion that occurred during the meeting and select ideas captured in the comments and interviews obtained after the meeting from the panel of experts.

GENERAL COMMENTS FROM FORUM PARTICIPANTS:

MICHAEL WILSON: All of the discussion today is a terrific example of the recognition of a problem by a broad range of people. I think the initiative that we've been talking about at the Forum has ways of internationalizing it or "globalizing" it.

This Mental Health International proposal is precisely what Don Tapscott has been talking about. To the extent that you can take what we have done here in Canada, what we've done in collaboration with the United States, and some of these other examples and build on these in a global approach, I think it sets a very clear vision of where we want to go.

This is precisely the challenge: taking the Roundtable idea, research being accomplished by the institutions represented by people around this table, putting this all together and taking that next step. Going from North America to Europe offers great promise of doing that.

There's a certain like-mindedness of approach (around this table). And that may set the stage for something to be done more globally through WHO [The World Health Organization] or other international organizations like that. To accomplish this I think we look to Bill [Wilkerson] and Joe [Riccuiti] – and people around this table – to identify next steps are to make this business-science partnership happen in North America and Europe. We've got a great opportunity here.

ANTHONY BOECKH: At the Boeckh Foundation, four years ago we began collaborating with NIMH [the US National Institutes of Mental Health], Province of Alberta, Canadian Institutes for Health Research, and the Rand Organization in Cambridge, England. Mental health must be a team game, we need a lot more players on the team, and we need a level playing field. International collaboration among funders can really bring lots of things together to really push the agenda, learn from each other and really improve patient outcomes.

DON TAPSCOTT: I love the term "business-science partnership" because it gets us beyond that old paradigm of business's narrow interest in reducing costs – which is important – but it's insufficient. Business can be a driver for change. Is it conceivable that there could be a global collaboration in critical areas of psychiatric and brain research with the goal of breaking the logjam and achieving breakthroughs. Through global collaboration could we create the equivalent of Linux of the brain?

What would such collaboration look like? What kind of information could be shared?

MIKE SULLIVAN: How does one use the network assembled here in this room? How do we work together to improve the efficiency of the health care treatment system? To the extent that there are solutions in the genomic science breakthroughs, we need to make sure we can operationalize them.

PETER HONGAARD ANDERSEN: For the past seven years, I've been chairing the industry side of the largest public-private partnership in the world. The project costs over two billion euros for five years. And the biggest chunk of the funding goes to brain diseases. I can tell you that it has taken a few years for industry and academia to understand that we actually can work together.

The biggest roadblock I have seen in this (process of collaboration) occurs at the political level. Diseases are everywhere in the world and diseases have no borders. But politicians just don't appreciate – just don't get it – that we need to collaborate across continents, in fact, all over the world, to exchange ideas and data to bring us to the next level. Therefore, I really encourage everybody to use influence at the political level to (reinforce) how important this goal is.

DR. REMI QUIRION: The Forum has served a unique purpose. But (workplace mental health) is always hard to keep it on the Front page and (sustain) as a top priority for business and governments. One possible way to achieve that goal, however, is to go global. Mental health research – and mental health in the workplace – must become a top priority for everyone on the globe and not just for a few countries. We must aim to put mental health in the workplace on the agenda of the G8, United Nations, and the WHO.

DR. SALLY-SPENCER: Convening such high level of leadership around this critical public health issue is inspiring. I am now fully dedicated to replicating this effort in Colorado where our rates of suicide among working-aged men are very high. The emphasis on global collaboration among public, private and non-profit sectors is the future for our cause. I was so encouraged to see such promising models of this at the Forum.

MELINDA HEAD: The challenge for MHI is to get some focus from all of the great ideas and presentations at the Forum. MHI has to decide on a *focus* for the future. We need to be clear on what our *vision* is. This is a leadership issue. We need a sharp focus. The academic/science world is more tactical whereas the business world is more strategic and responsive to a *brand*. MHI must brand itself now.

MIKE SCHWARTZ: The concept of creating a vehicle where business and science actually communicate in an orderly, strategic way across borders is phenomenal. So, the challenge is how do you bring that about? (Using the symphony analogy) do we need a conductor? What's the mechanism, catalyst or agency to really make this to happen and to move it forward?

MICHAEL WILSON: Mental Health International is the successor to the Global Roundtable, and Bill is chairing a new and European corporate initiative called Target Depression in the Workplace. I'd recommend that Mental Health International, already taking the lead in Europe, be duly resourced to develop this strategy and a detailed business plan.

IDEA 1: Mental Health International serving as a champion of the cause and direct the scope of activities in the formative phase of the new partnership.

Development of a single online source for collecting and sharing the international wealth of information, resources, organizations and people involved with the new business-science partnership. This website could facilitate the connections to a great many partners and other existing organizations interested in the partnership goals.

The resources could be identified through several action steps, including the many resources already discussed by the presenters and discussants at the 5th Forum; these and other resources could be collected via a follow-up survey to all of the people involved with 5th Forum and through extension to their professional networks.

The types of resources could include: profiles and contact information for people, leading organizations, specific reports and printed documents, websites, and so on. Ongoing communication around the nature of the resources available and new additions could be done through a regular e-mail notification process and perhaps some kind of regular brief newsletter.

DON TAPSCOTT: Such sharing, collaboration and cooperation is occurring in many parts of the economy. In Toronto, a not-for-profit collaboration called the Structural Genomics Consortium has been formed to determine the three dimensional structures of proteins of medical relevance and place them in the public domain without restriction.

The Transformational Research in Adolescent Mental Health (TRAM) partnership aims to catalyze fundamental change through building a pan-Canadian network that unites patients, family representatives, policy makers, service providers and community organizations.

The Toronto Dementia Research Alliance – established by the Toronto Academic Health Science Network, to pioneer a "new paradigm for collaborative research … and an effective platform for consistent collection and interpretation of clinical data across member institutions."

ALYSIA DAVIES: While at the Forum, I was struck by the fact that I was privy to information about (a) the latest developments in mental health treatment and (b) corporate executives' interest in supporting it. I suspect most employees of organizations, and the general public, are not as likely to know about such information.

My suggestion is that the contents of this dialogue between experts and executives become more public in some ongoing way – not just in terms of a report about what happened – but regular updates. I think Dr. Insel's blog at the NIMH website is a good example of how to bring this kind of information to the general public in an accessible and regularly updated format.

MHI could create something similar for multiple bloggers involved with this initiative on the same platform. This would also be an easy way for the parties involved to keep updated on what everyone in the field is doing to move things forward and to identify opportunities to work together.

This would also offer some hope to people who are frustrated by (the lack of) mental health access and treatment in the health care system, letting them see what (opportunities and improvements) are coming down the pipeline and the high-level interest in supporting it.

DAVID BLODGETT: One of Canada's historic companies, Great-West Life, made an explicit commitment to the public interest in forming and funding the Great-West Life Centre for Mental Health in the Workplace. Other members of Canada's insurance industry also have demonstrated support for mental health in the workplace.

LOUISE BRADLEY: The standard for psychological health and safety in the workplace is almost a year old now. We've put a call out for businesses and organizations to step up to the plate to be evaluated among those who have adopted the standard. And we've had a tremendous response to that. As an organization [The Mental Health Commission of Canada], we partner and collaborate with everybody. Today is a really good opportunity to take a step further and certainly we'd be very happy to continue to be involved in bringing other stakeholders.

Dr. QUIRION: Bring in the Youth. We must bring in young minds (Under age 30) so that they get involved and so us how to package our message in 144 characters! There is potential for lots of innovative ideas from those guys on how best to attack the problem of MH in the workplace and MH research. If we want to collaborate –then we need to actually collaborate. So need a resource and staffing to do this.

IDEA 2: Return to Work/Stay at Work for Mental Health Cases – Best Practices for Collaborative Care and Fast Tracking of Science to Practice for Brain Health Clinical Innovations We need to see more rapid transfer of new genomic advances for brain health treatments from science to practice and employee benefits access = science to practice in the are of bringing to market the new medication testing matching procedures and also for the best practices in RTW for mental health issues.

EDWARD SELLERS: One major issue is translating discovery into practice that makes a difference. Genomics promises a lot but having it make a difference will be a real challenge. So the problem is how to get doctors to adhere to best practices.

GEORGE WEBBER: Of concern to me is the gap between some promising research results and the understanding and knowledge level of these results among the clinical practitioners - the age-old knowledge transfer issue. We can't keep basing our diagnosis solely on described symptoms with no support from biomarkers.

CYNTHIA JOYCE: There is a disconnect between the discovery research and the health services delivery and occupational health areas. It would be interesting and powerful if we could identify the threads shared by each. That may be a place where my company, MQ: Transforming Mental Health, can help – together with the Tony Phillip's and Tom Insel's of this world. It speaks volumes that they have been a continuous presence in these discussions.

DAVID BLODGETT: We in the insurance sector need to work harder as carriers and with our clients to make sure that we're educating employers and those employee populations better, that we work harder to encourage modified return-to-work programs so that they're not in fear of losing those disability benefits, that they'll venture forward and come to the table and try to get back to work into the workplace.

JOSEPH IANNICELLI: If all the insurers could have all of (people who made a depression-based disability insurance claim) receive the genetic-testing to get the proper drug the first time, just imagine what that will do – that one small step – to improve the resolution rates of depression?

BILL WILKERSON: There is a horror story a day from people who have been put in a vicious circle around various elements of the so-called return-to-work process. I get most of those phone calls just because my name is out there. And it's a breakdown with case management. It would seem to me we must design case management models within the larger partnership proposed to improve measurably the grassroots management of the return to work and return to function process. MHI is working on a "functionality model" for this process because functional recovery lags clinical recovery.

MELINDA HEAD: Let's get examples of (best practices of this) from Canada, the United States and the UK, brand these and get them into hands and minds of business people. We need to involve business people in creating the new workbook and contributing their own case studies – using a standard format reporting and interview tools created by researchers at MHI.

IDEA 3: International Brain Capital Scorecard and Business Case ROI Modeler Tool. The Forum produced a mandate for creating a detailed business case/plan to create an International Business/Brain Science Partnership for Brain Health and Brain in a Brain Economy.

Leaders in businesses need training and tools to demonstrate the importance of the spending more on brain health treatment services and the resulting longer-term ROI it yields in avoided disability claims and turnover costs and shorter-term ROI in work productivity and absence.

One of the most important elements to developing and maintaining organizational efforts to promote improved mental health in the workforce is to be able to know what kinds of program and polices are most useful to put in place and then to track the outcomes of these programs and policies.

But interpreting the progress in each phase is often difficult due to a lack of standard guidelines on what constitutes relevant best practices and then what kind of comparative experience is there concerning how a particular organization, industry or even county is doing on the level of implementation success and in achieving outcomes.

Given the recent advances in the applied social sciences on the development of business scorecards and dashboard type metrics, it is possible to now create an external benchmark or standard that can be used for comparative purposes. The specific elements of the scorecard can be drawn from an existing research and grey literature that has many good examples of validated business drivers of the organizational factors and health care system factors that lead to better brain health can be specified and assessed for each employer or organization.

Update the 2007 Research Gap Analysis Literature Review Report that was done for the Roundtable and major Canadian insurers, gaps reduced, case studies of employers doing leading edge policy and practices including outcomes.

This calls for a scorecard of metrics in workplace brain health for international use by businesses to relevant programs and associated costs and outcomes.

JOSEPH RICCUITI: We need to create a meaningful tool and International Performance Scorecard which builds the business case and supports targeted investments in workplace mental health initiatives and measures the relative business success to the organization against their industry and country peers.

DR. BOB FRANCIS: We need to profile how different business organizations have done better job of addressing and supporting brain health issues? I believe that Bell Canada has really set the pace, set the standard-bearer in this whole mental health piece. But I would like to see is a meeting of other CEOs and ask them what are they going to do for their own employees.

DAVID BLODGETT: The Canadian Health and Life Insurance Association, in 2007, adopted a strategy to establish benchmarks for mental health in the workplace – for their own members. The centre-piece was a set of guiding principles to improve the industry's knowledge and awareness of these issues.

MIKE SULLIVAN: I think one of the most powerful aspects of the Forum on Mental Health & Productivity is that the team at Mental Health International was able to bring together not only some of the brightest minds on the planet in the area of Mental Health, but also the business leaders that can help operationalize some of the ideas and then *measure* the returns.

The real issue in Canada is that we do not have decent data that is readily available to measure key metrics in this area and the ROI to business leaders of addressing the issues head on. The data is disparate and the classification tools are inconsistent and not easily integrated. On top of that, vendors that administer plans are not concerned with health outcomes.

If groups like Mental Health International don't take the lead in Canada, who will? We rely on US data, but the US metrics are not necessarily relevant in Canada because of the differences in our systems, and what is/is not funded by employers north of the border. There would be real power in a dashboard of metrics along these lines:

- Prevalence of depression, anxiety, sleep disorders and psychoses among employees and employee spouses/partners/dependents), and changes in prevalence over time.

- Adherence rates by employees to antidepressant therapies, prioritized reasons for non-adherence

- Prevalence of treatment-resistant depression to prioritize additional resources for needed in these cases and integrated drug-STD and drug-LTD data sets to measure:

    - Changes in the number and average duration of STD claims related to Depression or another form of mental illness and how that compares to dollars for therapies.

    - Changes in the number and average duration of LTD claims related to depression or another form of mental illness.

    - Cumulative number of days lost in a given year among employees with mental Illness and direct costs to employers.

    - Spending on chronic conditions co-morbid with depression and assessment of on how investments/spending on employee services have reduced the impact.

- Appropriateness of therapies (i.e., how many plan members are started on low doses of antidepressants and not titrated to higher doses as needed)

- ROI on case management.

IDEA 4: Create online calculator for businesses to do a customized analysis of projected cost burden of brain health problems among their employees at their company and potential savings from better policy and service programs.

DAVID BLODGETT: From the health insurance industry perspective, big employers need to become more engaged in the ROI for doing more with mental health in the workplace. Business needs to see the investment value in paying for more medication treatments along with talk therapy counseling. Research shows greater clinical benefit for both Rx and talk therapies.

Stigma (of mental illness) will (recede) when greater numbers of employees seek (and receive timely) care. So we need more (not less) spending on mental health benefits and insurance program (will prove cost-effective). A mandate for MHI is to reach the chief and senior executives with this message. Maybe start with business schools.

IDEA 5: learn from International AIDS Anti-stigma Campaign and Its Public-Private Partnership Requirement of A Results-Oriented Approach to Change for Improving Mental Health in the Workplace

DR. ROGER MCINTYRE: The metaphor that really stands out as inspiring for us is what has happened in HIV and AIDS, probably more so than most of the non-communicable disorders. When I was a medical student in Halifax on a 8-week rotation on a general in-patient unit, if someone came in with HIV/AIDS, they likely would not see the end of my rotation. They wouldn't last six to eight weeks.

And now the CDC [Centers for Disease Control in the US] has declared it a chronic disease. That is a remarkable statement about a health condition that's obviously very much stigmatized. And there's so much to learn about what HIV/AIDS did in the last two, three decades. Its success is clearly a statement about the focus on a results-oriented deliverable.

And they did it through collaboration between a variety of sources, including private, NGOs [non-government organizations], public, academia, and advocacy. I would add results-oriented collaborations as our goal and urgency for deliverables. And that's exactly the wake-up call psychiatry and the brain sciences need - to be more accountable and provide deliverables. We have an opportunity to inject results-oriented collaboration to brain science, which hitherto has been missing from the place.

DR. CATHERINE ZAHN: What is gratifying for someone like myself, who's only four years into that mental illness world – as opposed to the physical illness world – the words that are being used like illness, disability, mortality and brain disorders, are new to this sphere. We have a tendency to talk in euphemisms, and I'm glad to see that (change).

GREG DURANT: Everybody is concerned about the growth of mental illness as a causation of LTD because it has skyrocketed over the years such that today 40 to 50 percent of disability is diagnosed as being related to or having causations of mental illness.

My completely unscientific theory is that in fact it hasn't grown. It has always been there. It's just that the work that this roundtable and these forums have done to mitigate the stigma and this make it more acceptable has just allowed it to emerge and be properly diagnosed. Today, employee benefit costs are now about 7 percent of payroll.

But, if we don't look at these things and affect them, in a working lifetime I think these costs could dramatically increase and eventually become equal to payroll. But, I'm really excited about some of the opportunities that will be coming in the next 10 years from the advances in treatment we heard about at the forum.

MARY ANN BAYNTON: Stigma and unnecessary suffering can cause even those with mild mental illness to feel hopeless. Stigma including judgment, criticism, and isolation can lead to feelings of hopelessness. Hopelessness has led to suicide. Unnecessary suffering can be a result of months or years of ineffective treatment approaches.

What we heard at this forum is hope – hope for a reduction in stigma as the biology of mental illness changes minds of those who mistakenly believe mental illness is a character defect. Hope for a reduction in unnecessary suffering as effective treatment is more likely to happen with the first attempt. Through international collaboration we can accelerate these advances and end stigma as well as unnecessary suffering for those around the world who live with mental illness.

LINDA QUATTRIN: What is different about mental health (compared to cancer, HIV, diabetes – other chronic illnesses that are much better funded) is patient advocacy for research (vs. for better services, which our patients advocate for). How can we build a popular movement advocating for mental health research to force greater political engagement?

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PART 10 – Epilogue

The Pathway Forward

The outcome of the dialogue contained in this verbatim/edited Reference Document is a new pathway for the advancement of "Brain Health in a Brain Economy."

The 5th US/Canada Forum on Mental Health and Productivity brought leaders in business and science together to answer one question –"Is the search for a cure fort mental illness a plausible objective?" – and tackle another: "Can business+science form a new partnership to accelerate the transfer of new knowledge about the brain into clinical care for people?"

As noted in the Narrative Report appearing elsewhere on the MHI web site, scientific investigation of the mysteries, functions, disorders and diseases of the brain is every bit as complex and significant to humankind as the exploration of outer space.

It is safe to say not everyone has a stake in a machine's visit to Mars, but we all have a stake in the new technology of brain science, in the innovations of treatment that will one day emerge from scientific discovery.

The proposed business+science partnership for brain health in a brain economy which emerged from the 5th US/Canada Forum, will benefit not merely two sectors whose leadership is called for, but the wider public, working populations, families and children who represent, in many, respects the demographic of greatest vulnerability.

In a global economy where new jobs demand cerebral skills more than manual ones, brain health assumes well-defined economic value and significance. The dialogue that follows brings leaders in business and science together to examine these matters.

There are dramatic revelations in this transcript. But, there is also disappointment that new scientific knowledge of the human brain, in the form of new treatments for brain disorders, reaches everyday people too slowly, too seldom, and, too frequently, never at all.

This must change. And the roadmap for bringing that change to fruition runs across the map of the world. No one nation, scientific discipline, corporation, government or research institution can achieve this alone.

The 5th US/Canada Forum underscored that point emphatically. Canada's former Ambassador to he United States, Michael Wilson, out it this way: "Like all the great issues of the day, solutions for brain health will be found only through international consultations"

In this light, the world just became more interdependent. And maybe a bit smaller.

PART 11 – Appendices

Appendix A: About the Forum Sponsor: Mental Health International

Appendix B: Acknowledgement of the Forum Host and the Report Sponsor: CIBC and Lundbeck Canada Inc.

Appendix C: Roster of Attendees

Appendix D: Summary of Past US/Canada Forums of Mental Health and Productivity

Appendix E: Highlights of the 2011 Final Report from the Roundtable

APPENDIX A: About the Forum Sponsor

Mental Health International was as Sponsor of the 5th US/Canada Forum on Mental Health and Productivity

Founded in in 2013, Mental Health International is the trade name of Mental Health Insights and International Advisory Group Inc. and operates as a Canadian-based not for profit organization. It is the successor to the Global Business and Economic Roundtable on Addiction and Mental Health. Drawing on the Roundtable's nearly decade and a half of unprecedented, pioneering work, Mental Health International will:

- Serve as an adviser to employers to be innovative and transparent in promoting and protecting mental health in their workplace;
- Help employers do now what we know now about containing the disabling impact of mental disorders on the performance of individuals and whole organizations; and
- Connect research and innovation for real progress in workplace mental health.

The goal for Mental Health International is to help usher in a new era of collaboration, across borders within and between the scientific and business communities as the greatest hope we have to real answers to the human suffering and economic costs imposed by major mental disorders.

The Team at Mental Health International:

- Bill Wilkerson, **Executive Chairman**
- Joseph Ricciuti, **President and CEO**
- Helen Lackey, **Corporate Secretary**
- Mark Attridge, PhD, MA, **Board Member**
- Roger S. McIntyre, MD, FRCP(C), **Board Member**
- Ian M. F. Arnold, MD, MSc, **Network Partner**
- Alysia Davies, LLB, **Network Partner**
- Lyn Garrett, CACII, **Network Partner**
- Sandra Routledge, BNSc, **Network Partner**

The 5th Forum Management included: Bill Wilkerson, Joseph Ricciuti and Helen Lackey, with research and legal support from Alysia Davies, host venue coordination support from Melanie North (CIBC Corporate Events and Public Affairs) and on-site volunteers Olga Cwiek and Jennie Ryan.

APPENDIX B: Acknowledgement of the Forum Host and Report Sponsor

1. CIBC hosted the venue for the meeting.

2. Lundbeck Canada Inc. sponsored the publication of the 5th US/Canada Forum Report.

The Canadian Imperial Bank of Commerce generously provided an elegant venue for holding the 5th Forum. The meeting was held in the Executive Boardroom on the 56th floor of the CIBC world headquarters building in Toronto.

Special recognition goes to former CEO of CIBC, John Hunkin and to current CEO, Gerry McCaughey as well as to their administrative staff and the technical support team at CIBC.

About The Canadian Imperial Bank of Commerce

CIBC is a leading Canadian-based financial institution that employs over 43,000 people. Through its three main business units – Retail and Business Banking, Wealth Management and Wholesale Banking – CIBC provides a full suite of financial products and services in Canada and around the world. The corporate headquarters are located in Toronto.

~~2.~~ Lundbeck Canada Inc. sponsored the publication of the 5th US/Canada Forum Report.

We offer a s~~S~~pecial note of thanks to Patrick Cashman, President and CEO, and Daniel McCarthy, Senior Director, External Relations at Lundbeck Canada Inc. for their support and generous contribution to fund the publication of the 5th Forum Report.

About Lundbeck

Lundbeck is a global pharmaceutical company highly committed to improving the quality of life for people suffering from Brain Diseases. Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy and Huntington's, Alzheimer's and Parkinson's diseases. Lundbeck is one of Denmark's most research-intensive enterprises, employing more than 1,200 highly-trained specialists in its research and development units. Each year, Lundbeck re-invests about 20% of its revenue into further research and development in order to discover new pharmaceuticals that can improve treatment options for neurological disorders.

Lundbeck Canada is a subsidiary of H. Lundbeck A/S, an international research-based pharmaceutical company, which focuses on diseases of the Central Nervous System and most recently, oncology. Based in Montreal, Lundbeck Canada has been part of the Canadian pharmaceutical industry for more than a decade and markets products for the treatment of many neurological disorders, including: depression, anxiety, Alzheimer's Disease, schizophrenia, bipolar disorders, and chronic lymphocytic leukemia and non-Hodgkin lymphoma.

APPENDIX C: Roster of Attendees

- Presenters
- Discussants
- Executive Panel

PRESESENTERS

George Carpenter, IV, MBA
CEO, CNS Response, Inc.
Orange County, California, United States

Rupert Duchesne, MBA
Group CEO, AIMIA Inc. (parent of Aeroplan) and Chairman, Brain Canada
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Daniel Weinberger, MD
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Honorable Michael Wilson, PC, CC, LLD (Hon.)
Chairman, Barclays Canada
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Copenhagen, Denmark

David Blodgett
President and CEO, Group Medical Services and GMS Insurance Inc.
Regina, Saskatchewan, Canada

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APPENDIX D: Summary of Past US/Canada Forums on Mental Health and Productivity

* Reprinted from the 2011 Final Report of the Global Economic Roundtable on Addiction and Mental Health

The Boardroom Series culminates in an extraordinary four-part series of US/Canada Forums on Mental Health and Productivity. Held in 2007 and 2008, these meetings are convened by the Ambassadors to Canada and the United States and bring business leaders together with a 'common cause.' In fact, the Forum brought science and business together in a unique way. The Co-Chairs of the series included the distinguished humanitarian and business leader, Edgar Kaiser and Roundtable founding member, Colum Bastable, as well as senior US and Canadian scientists. Brief summaries of these Forums follow below:

The 1st US/Canada Forum, hosted by Ambassador Michael Wilson at the Canadian Embassy, held in Washington, DC, United States, on February 15, 2007

Famed epidemiologist Dr. Ron Kessler of Harvard University unveils his landmark, 4-country '**Depression and Work Performance Study**' to identify the cost/benefits of the early and effective treatment of depression in the workplace.

John Wright, Senior Vice-President of Ipsos-Reid, reveals the results of an opinion survey commissioned by Great-West Life. He finds the stigma of mental illness receding 'a bit' but the number of people suffering mental illness still staggering: 'a country within a continent.'

As host, Ambassador Wilson sets a future direction: *"Every significant challenge we face - economic, demographic, security, energy and health - has international dimensions. I would absolutely include mental health in this.'* He calls on business and science to find a 'cure' for mental illness — a term he uses 'very deliberately."

Moya Greene, President and Chief Executive Officer of Canada Post Corporation, and now CEO of the Royal Mail in the United Kingdom, says, "Solving the problems of early onset, finding cures and achieving remission – that gives people hope."

The 2nd US/Canada Forum hosted by the US Ambassador to Canada, David Wilkins, held in Ottawa, Ontario, Canada, on November 14, 2007

Special Guest: Laureen Harper, wife of Prime Minister Harper

At this 2nd Forum, Colum Bastable, then President and CEO – now Chairman – of Cushman and Wakefield LePage unveils the Roundtable's '**New CEO Guidelines for Mental Health and Productivity**.'

Mr. Bastable then undergoes a 'depression screening' interview back-stage with prominent psychiatrist Dr. David Goldbloom to demonstrate that the process is 'blameless and shameless' –and also 'very useful.' He received a standing ovation from the 200 participants present.

The Roundtable's CFO Task Force delivers a '**CFO Framework**' to stimulate measure and manage investments in the mental health of the working population.

Harvard's Dr. Ron Kessler delivers 'Part II' of his 'Depression and Work Performance Study.' His 'profit of care' report states that screening employees for depression and ensuring access to appropriate care will save employers money.

John Wright, SVP, Ipsos Reid, and Mike Schwartz, Senior Vice-President, Group Benefits, of Great-West Life and head of the Great-West Life Centre for Mental Health in the Workplace, reveal the results of pioneering research funded by Great-West Life surveying 6,000 US and Canadian employees on their opinion of the impact of depression in the workplace.

A principal finding: 84 percent of this huge sample believes CEOs should make helping employees with depression a key human resource priority. Based on the CEO survey noted earlier, CEOs seem to agree.

3rd US/Canada Forum hosted by Dr. Steven Hyman, Provost, Harvard University and Dr. Ron Kessler, Harvard Medical School, held at Harvard Medical School, Cambridge, Mass., United States, on May 29, 2008

The New England-Canada Business Council joins the roster of business leaders supporting bilateral cooperation in the international advancement of mental health in the workplace.

This Forum focuses on the 'mental health of working parents and their children' and a panel of parents and children re-live vivid experiences that for the business leaders present are evocative, instructive and unforgettable.

High-level diplomatic representation continues with Canada's Consul-General in Boston, Neil LeBlanc, as he underscores the complexities facing working parents caring for troubled children merits employers' attentions on both sides of the border.

Dr. Mary Jane England, former President of the American Psychiatry Association and now President of the prestigious Regis College, outlines plans for a study by US Academies of Science into the links among early child development, childhood depression and parenting.

University of Portland researchers report that parents of children suffering mental illness often quit their jobs due to employer inflexibility in work hours at this time of family crisis. Parents, they found, sometimes feel blamed for the mental health problems of their kids.

The 4th US/Canada Forum hosted by Robert McLellan, Executive Vice-President, TD Bank Financial Group, held at TD Centre, Toronto, Canada, on November 19, 2008

The fourth and final Forum is 'Mental Health in the Workplace of Heroes.' Police and military personnel attend in full uniform talking about mental health problems in their own ranks and in their own lives. Individuals tell their personal stories as participants are completely enthralled.

The Deputy Commissioner of the RCMP, Steve Graham, sees this Forum as a time for the military and police to finally go public with their serious concerns about mental illness in their own ranks.

The Chief of Police of York Region in Ontario, Armand LaBarge, said "mental illness has been a taboo subject in law enforcement but that is now changing. This topic is especially relevant for those of us that have chosen the profession of policing."

Major General Walter Semianiw, then Chief of Military Personnel, now the Commanding Officer of the Army in Canada, makes a clear commitment to the mental health of his people by declaring "mental health and mental illness are a major strategic priority for the Canadian Forces." He says:

> *"The Forces aim to maximize the psychological fitness of service members throughout their service career, while aiding members who develop psychological injuries and illness. Getting people back to work is clearly the foundation of our program."*

In short, military people are not 'damaged goods' as a result of PTSD and depression. They can continue to serve their country. Civilian employers need to hear this message.

Law enforcement and the military recognize – more naturally, perhaps, than civilian employers – that non-medical mental health support and care are just as important as medical care.

In both law enforcement and the military, peer support training is critical to the success of any kind of mental health program. "Not only must the Chain of Command facilitate support and care, we need the 'buddy system' to do the same." General Semianiw said.

When queried by Justice Edward Ormston, Ontario Superior Court and chair of the 4th Forum, Major-General Semianiw responded:

> *"We do not distinguish between physical and mental military injuries when it comes to compensation or recognition – even in the awarding of The Sacrifice Medal."*

The 4th Forum also features a briefing on clinical studies led by Harvard and McGill researchers to find 'a cure' for PTSD.

APPENDIX E: Highlights of the 2011 Final Report of the Roundtable

* Adapted from the ~~2011~~ Final Report of the Global Economic Roundtable on Addiction and Mental Health

This appendix an overview of the key ideas and facts from the 2011 Final Report and the Grey Paper of the Roundtable that was included in the report.

The full 72-page report can be downloaded as a PDF from the Mental Health International website.

Citation: Wilkerson, M., & Wilkerson, B. (2011). *Brain Health + Brain Skills = Brain Capital: Final Report of the Global Business and Economic Roundtable on Addiction and Mental Health*. Toronto, ON: Global Business and Economic Roundtable on Addiction and Mental Health.

A. Review of Key Content from 2011 Final Report

Comorbidity and the Depression Matrix

Large-scale research studies conducted in the United States by Dr. Ron Kessler of Harvard University and in other countries have consistently shown that people suffering from major depression tend to also have higher rates of many other chronic and disabling health conditions. For example, the largest worldwide study ever to compare the health decrements of depression and other chronic conditions (250,000 people in 60 countries across all regions of the world) found that between 9 percent and 23 percent of those living with some form of chronic illness also suffer depression. In 2006, the European Union's Consultative Report concluded that *"evidence of co-morbidities is persuasive"* and all health services and research institutions should reach out and cooperate with the mental health scientific community.

The 'co-morbidity crisis' is a network of conditions allied within what we have called "The Great Depression MATRIX." With depression being at the center of the matrix, there are conceptual and empirical links to: cardiovascular disease, diabetes, asthma, arthritis and pain disorders, cancer, obesity, head trauma and concussions, anxiety and other mental illnesses, addictions, and suicide. The Great Depression MATRIX – in its entirety – is susceptible to the trigger-like effects of chronic stress and social environments in the workplace that can affect healthy brain function.

One implication of the Depression Matrix approach is the '*re-positioning'* of depression as a 'physical disorder' with physical and psychological symptoms to distance the concept of depression from the stigma of 'mental illness' but simply to represent it more accurately. Indeed, Dr. Carmine Pariante of King's College in London, England, says depression can result in such drastic hormonal changes that it becomes an 'endocrine illness or immune disorder' such that: "*depression can no longer be described as a simple disorder of the brain, but rather must be understood to be a series of biological changes that span mind, brains, genes and body – affecting both psychology and physical health*." Dr. Roger McIntyre says depression should be re-classified medically from a mood disorder to a metabolic disorder and that research into the co-morbidity of depression is needed to uncover new and novel approaches to treating depression. For example, Dr. McIntyre is testing insulin as a treatment for depression.

The Rise of Chronic Diseases

Across the globe, non-communicable diseases are now the major cause of death and disability, even in the developing world. The fact that chronic diseases pose a far greater risk and cost burden to society than do infectious diseases is at odds with the long-standing focus of the United Nations and many governments on attempting to control the outbreak and spread of infectious diseases at the expense of devoting more resources to the prevention and management of chronic diseases – including depression and addiction.

Research Advances Slow to Reach Clinical Practice

In a 2011 report, the Canadian Institutes for Health Research (CIHR) says that investments in biomedical discoveries have produced only 'limited uptake of these results into clinical practice.' Critical data for the development of preventative, diagnostic and treatment interventions are routinely lost in two 'Death Valleys:' One 'Death Valley' is Canada's failure to transfer basic research into clinical knowledge at a sufficient clip, and volume, and the second 'Death Valley' is a similar 'failure to transfer' clinical science and knowledge into clinical practice and health care decisions on the front lines. As a consequence, Canada has 'significant deficits' in the leadership and coordination of clinical research directly related to patient needs and is '*rapidly falling behind other industrial countries,*' according to the CIHR.

The Enormous and Increasing Cost of Mental Health

The World Health Organization (WHO) expects depression 'to lead the pack' of chronic disorders that pose the greatest risk to historic gains in life expectancy, child mortality and occupational health and safety. A special analysis of the North American Free Trade Area and the European Community was commissioned for the 2011 Report based on the assumption that the economic costs of mental disorders are representatively distributed as 4 percent of the Gross Domestic Product (GDP). Using 2009 data from the International Monetary Fund, 4 percent of GDP attributed to mental health in Canada was over $51 billion dollars; over $570 billion in the United States; and over $488 billion in the Economic Union as a whole – with $85 billion in just the United Kingdom alone.

Prevalence of Depression and Disability

The disability incidence of depression is stubbornly high. The landmark Kessler Co-Morbidity Study found that 17-21% of the working population with depression went on short-term disability in a given year. Commissioned by the Roundtable and sponsored by Great-West Life, Ipsos Reid polled 6,000 Canadian and US employees and found '*a country within a continent*' of depression in the workplace. Some 30% of those surveyed knew someone who was diagnosed with depression, 18 percent were themselves diagnosed. A 2005 report by the European Economic Commission found that nearly 30 percent of adult Europeans experience at least one form of mental ill health during any given year. Data published by the US Centers for Disease Control (CDC) estimates that 1 in 4 US adults will experience a mental illness in a given year and one half of the population will do so over a lifetime. The disability incidence of depression is stubbornly high. The landmark Kessler Co-Morbidity Study found that 17-21 percent of the working population with depression went on short-term disability in a given year.

Suicide

The financial impact is just one measure of the cost of mental disorders. The loss of human lives is another. Depression has long been recognized as a contributing factor in the majority of suicides. Historical rates of the incidence of suicide have recorded over 3,000 suicides per year in Canada, over 25,000 suicides per year in the United States and over 40,000 suicides per year in the EU. Of course, many more people are damaged in their attempts at suicide that are non-lethal. What's even worse is that suicide occurs so often among the young in our society. Worldwide, suicide is one of the three leading causes of death among young people 15-24 years of age.

B. Review of the 'Grey Paper'

Also included in the Final Report was a companion report called:

The Grey Paper: NEW Workplace of 21st Century – Toward a Productivity Revolution Through Mental Health & Innovation.

This report had seven areas of focus, of which the basic points are described below.

End of Depression

With the recent advances in the scientific understanding of the human genetic code, the end of depression is now a realistic goal for future, offing a new chapter for the advancement of mental health in the workplace – a way to neutralize depression as a principal source of disability and premature death. It is the workplace where the early signs of both substance abuse and depression most evidently occur and co-occur. It is also through the workplace where employer-sponsored counselling resources – called employee assistance programs (EAPs) – can provide workplace screenings and early intervention to employees and their families in these matters.

Global Corporate Leadership

The World Health Organization articulated the mantra –(there can be no health without mental health) – and we recognize that this fact must be appreciated and acted upon by those in corporate leadership positions. The 2011 report called on leaders to designate 2012-2022 as the '**Workplace Decade of the Brain'** to galvanize business and public awareness of this campaign and to seek applications of the ground breaking discoveries of the 1990s 'Decade of the Brain'. The 'Workplace Decade of the Brain' will focus on the transfer of known and new brain knowledge into clinical practice and workplace applications.

Road to Remission Runs Through the Workplace

The search for a cure for depression is best channeled through the dynamics of its co-morbidity with chronic illnesses, and through workplaces where working populations are vulnerable to wide panoply of environmental risk – which is a key feature of neuro-genetic inquiry. Several disciplines will be needed for this international campaign of research, education and prevention and this assembly might best be described as an expression of '*neuro-economic research'*, which relates brain function to economic decision-making and organizational behaviour. The research we have in mind will define the experience of depression not only in terms of the individual who is suffering the condition but, more broadly, the

attitude and response of co-workers and managers to the circumstances in which that individual is placed. We also visualize workplaces being used as venues for what Dr. Insel describes as 'practical clinical trials' and one objective of the campaign will be to help clinicians find alternative methods to diagnose those brain disorders that we call mental illnesses.

Unraveling the Great Depression Matrix

The National Institute of Mental Health seeks 'gains in neuroscience and genetics that are key to understanding the complexities of mental disorders' and funds brain discoveries that fuel research into the causes of mental disorders. The NIMH believes greater emphasis must be placed on measuring the 'functional outcomes' of clinical research, which is all-important to employers and employees alike.

The NEW Neuroeconomic Workplace

The *NEW* or *NeuroEconomic Workplace* is the workplace of the future. This *NEW* Workplace – as a venue for research, prevention and education – must be designed, managed and sustained to promote and protect the mental health of working populations as a straightforward duty of asset management. There is ample evidence that brain health and brain skills will define the competitive edge that corporations doing business in the global economy will need. The *NEW* Workplace will be based on the tenets of a socially and psychologically healthy environment in which people not only earn their pay-cheque but earn and exchange respect as a defining feature of this environment.

Therefore, we suggest this: the next stage of development for mental health in the workplace is focused on innovation as a deliverable of psychologically healthy workplaces and employee mental health as the facilitator of employee-based competitive advantage. We see the principal focus of the workplace-based, international campaign of research, education and prevention proposed here to focus sharply on 'innovation in psychologically healthy workplaces' as a principal deliverable.

The NEW Workplace as a Venue for Suicide Prevention

The ***NEW*** Workplace will be a home for information, education and support for employees dealing with questions of suicide in their own lives or in the workplace itself.

Tana Nash, one of Canada's most effective suicide prevention advocates provided some comments. Her efforts in her home community are remarkable evidence of what can be done when one is committed and creative. For example, she has taken suicide prevention into local high schools to train students to support each other in the face of bullying, suicide and gang violence and to heighten student awareness of suicide risk factors and warning sides. Ms. Nash has also delivered information packages to funeral homes to assist suicide survivors discuss and make the cause of death public if that's what the family wants to do.

1. The following ten common steps toward suicide were presented: Emotional isolation (malignant loss of self-esteem and usefulness);
2. Peer pressure and exclusion (deep sense of having lost acceptance, recognition, belonging);
3. Void of joblessness (deep sense of loss of identity, self-worth)
4. Emptiness of depression (pervasive loss of the energy and motivation to live);
5. Impulse (why not right now?);
6. Drugs/alcohol (desperation peaks);
7. Available means (gun, rope, drugs, locale);

8. Family history of suicide (higher risk);
9. Youth and children (altered perceptions of death and dying; loss of place);
10. Social disadvantage and grievance (the profound weariness of perpetual worry and seething).

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