2020

The Novo Nordisk Prize

Professor
Preben Bo Mortensen
Nomination of Preben Bo Mortensen

The Novo Nordisk Foundation is awarding the 2020 Novo Nordisk Prize to Professor Preben Bo Mortensen for his remarkable pioneering registry-based studies combining data from biobanks and population registries demonstrating key causes for developing severe mental disorders and for the impact this research has had on medical science.

Preben Bo Mortensen graduated as a medical doctor from Aarhus University in 1986 and did clinical training in psychiatry and neurology. Since 2000, he has been a professor at Aarhus University and headed the National Centre for Register-based Research at Aarhus University. Professor Preben Bo Mortensen has provided an internationally outstanding and exceptional contribution to understanding the epidemiology of mental disorders, which are very frequent disorders and often with a serious clinical course. He began his scientific career already as a medical student and was awarded Aarhus University’s gold medal for his research on relationships linking cancer with schizophrenia. In his first years as a medical doctor, Preben Bo Mortensen continued this important work, further establishing the Danish registries as a unique asset for his work by exploring the complex and paradoxical association between cancer and schizophrenia. This work was compiled in his doctoral thesis entitled *The epidemiology of cancer in schizophrenic patients*, and he became Doctor of Medical Science in 1995. In his thesis and in an extensive number of publications from the late 1980s and early 1990s, Preben Bo Mortensen contributed remarkably to understanding the comorbidity among patients with schizophrenia.

Throughout his career, Preben Bo Mortensen has contributed in particular to understanding important causes for schizophrenia and other mental disorders, including both environmental and genetic causes, course of the disorders, comorbidities and mortality. In addition, Preben Bo Mortensen has contributed exceptionally to understanding the causes of suicide, which exemplifies highly original scientific contributions, and in 1997 he became member of the task group on suicide mortality under Denmark’s Ministry of Health. In parallel with his outstanding scientific career, Preben Bo Mortensen has had multiple positions of trust. He has collaborated internationally throughout his career, starting with a WHO fellowship in 1988 at Johns Hopkins University, the United States National Institute of Mental Health and Columbia University, and since 1999 he has been Adjunct Professor at the Department of Mental Health, School of Hygiene and Public Health, Johns Hopkins University. During the past more than 20 years, he has extended his international collaboration documenting the impressive asset of the National Centre for Register-based Research at Aarhus University at the international scale for exploring complex mental disorders.
Preben Bo Mortensen’s research on suicide is highly unique and truly original. Using Danish registry data, he demonstrated that completed suicide and mental disorders in relatives were confirmed risk factors for suicide, and the effect of family suicide history is independent of the familial clustering of mental disorders. Family history of suicide should be established in the assessment of suicide risk. Further, he established risk factors for suicide by analysing all suicide events in Denmark, integrating psychiatric, demographic and socioeconomic risk factors. These studies showed that suicide prevention aimed at people hospitalized with mental disorders and improved detection and treatment of mental disorders in the general population may be the most efficient strategy to decrease the risk of suicide. Reports of high relative risk and attributable risk associated with unemployment and other socioeconomic risk factors may be confounded and overestimated owing to the lack of adjustment for the association with mental disorders. These studies clearly are of definitive superior quality and frequently cited contributions in medical research.

In a series of studies, Preben Bo Mortensen established that schizophrenia is not only affected by family history but also by place
and elsewhere. He has had a leading international role in high-impact research identifying causes for mental disorders and has been the driving force for establishing a multifaceted pioneering set of investigations that have harvested remarkable epidemiological and clinical evidence by combining data from multiple registries.

Preben Bo Mortensen has been honoured with several national and international prizes and awards. He has attracted considerable external funding for his research. In 2000, he received substantial funding from the Danish National Research Foundation to establish the National Centre for Register-based Research and is currently heading the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH). He has shown great leadership and mentored a large number of young scientists and PhD students. He has an impressive scientific output of nearly 700 original publications, many published in leading high-impact journals including the *New England Journal of Medicine*, *The Lancet*, the *Journal of the American Medical Association* and *Nature*. He has also authored multiple review articles in his field, and many of his reviews and original articles are frequently cited. Preben Bo Mortensen’s research has contributed on the international scene in a leading role and with important clinical impact. Thus, Preben Bo Mortensen stands out as a preeminent scientific researcher in psychiatric research, and his scientific work has influenced the understanding not only of mental disorders but far beyond documented his scientific importance for other medical fields including pharmacology, genetics, clinical psychology and internal medicine.

In summary, the Committee on the Novo Nordisk Prize finds that Professor Preben Bo Mortensen is clearly a worthy recipient of the 2020 Novo Nordisk Prize based on his systematic, comprehensive and highly original international research combining registry-based data with biological data, which has outstanding impact for understanding the causes for development of serious mental disorders in general and in particular for understanding the causes for schizophrenia, bipolar disorders and suicide.
The 2020 Novo Nordisk Prize was awarded to Preben Bo Mortensen, Professor and Scientific Director, iPSYCH, Aarhus University and Merete Nordentoft, Clinical Professor, University of Copenhagen.
Searching for patterns that can save lives
This might look like the same old story about genes and the environment, but not really. For most diseases, discussing whether the cause is genes or environment makes little sense. Instead, Preben Bo Mortensen and his colleagues attempt – using registry data – to understand the dynamics of how we move through life. This has led to the creation of the world’s largest study within psychiatric genetics: iPSYCH. The ultimate goal is to help doctors to improve the chances of making decisions that can ultimately help save the lives of people with mental disorders. For his longstanding efforts, Preben Bo Mortensen is receiving the 2020 Novo Nordisk Prize.

It is not fair. Some people can smoke like a chimney all their lives, while others die from lung cancer despite never smoking. Although statistics rarely do justice to each individual, the current use of big data and registry research is generating some of the great new opportunities in the treatment of people with diseases. Preben Bo Mortensen's fascination with numbers and patterns, and his ability to ask the right questions, has resulted in him playing a key role in treatment for people with mental disorders worldwide.

“In the late 1990s, I got to be part of a committee, chaired by my co-recipient of this Prize, Merete Nordentoft, to come up with an actual national action plan for preventing suicide. To inform the committee, we did a study that showed that severe mental illness is a really dominant cause of suicide and that there are particularly vulnerable periods. This led to more systematic suicide prevention and that intervention at least coincided with a drop in Denmark's suicide rates,” explains Preben Bo Mortensen.

The link with schizophrenia
Already from a very young age, Preben Bo Mortensen was deeply fascinated by how the human body functions, so he decided to study medicine, but the high degree of rote learning required was not exactly his cup of tea.

“It was a bit like reading telephone directories: a stack of them every term, learn it by heart, throw it all away, take the next term, repeat, repeat. And, honestly, it was a bit boring. So that drew me towards research.”

During medical school, Preben Bo Mortensen also realized that getting a job would be difficult because unemployment among doctors was high at the time. So he decided that doing some research might improve his chances and happened to end in a situation that later created his career path.

“I stumbled into something called a prize thesis at Aarhus University. I had no idea that such tasks usually targeted a specific researcher, so I just gave it a shot, and I was lucky, because the researcher who was targeted decided not to do it. This became my opportunity to get into a whole new and exciting field.”

The topic was to study whether individuals diagnosed with schizophrenia, counterintuitively, have a lower risk of developing cancer than other people.

“It was like a total revelation. For the first time, I thought, during medical school, I was asked to think, come up with ideas, pursue goals I found interesting, read about topics that I chose
because I thought they were useful and so on. And usually when people ask me: ‘How did it start?’ Well, I got into research while I was a medical student and then I sort of never left.”

Preben Bo Mortensen got a WHO fellowship and travelled to prestigious Johns Hopkins University in Baltimore, Maryland, where he was asked to give his first lecture.

“A registry-related revelation
Preben Bo Mortensen not only won the Aarhus University gold medal for his thesis but also documented a special link. Today, cancer still stands out among people with schizophrenia as one of the few causes of death that is not hugely elevated. The reason is still unknown, but this work had triggered Preben Bo Mortensen’s interest in this field and made him realize that he was crazy about numbers.

His degree as a medical doctor in psychiatry from Aarhus University with a gold medal thesis led to a position at the Department of Psychiatric Demography of Aarhus University led by Annalise Dupont. Denmark had introduced universal social security numbers (Denmark’s Civil Registration System) in 1968, and Annalise Dupont’s task was to create an electronic Psychiatric Central Registry based on the social security numbers. The Registry recorded data electronically already from 1969 – laying the groundwork for Danish epidemiological research on psychiatry to later take a leading international position.

“For my gold medal thesis, I was given the opportunity to work on a cohort going back 30 years with more than 6000 people with schizophrenia. At that time, I think I just took these registries for granted. I got many questions: ‘Oh, are you still sitting up there watching numbers?’ and ‘Are you ever going to get out into the real world?’ And I certainly intended to start focusing on clinical work, which I actually also enjoyed very much. But Annalise Dupont told me that I should go out and see how they do stuff in other places before I decided whether to leave research altogether.”

Strange seasonal phenomena
The potential of registry-based research was soon realized. In 1993, Preben Bo Mortensen published landmark results in the British Journal of Psychiatry, reporting, for the first time, statistics on mortality and causes of death for people diagnosed with their first episode of schizophrenia. The figures showed that people newly diagnosed with schizophrenia had a very highly elevated risk of suicide, especially in the first year.
“But we actually also saw more than a 50% increase in this already very high risk of early suicides during the 1970s and 1980s when half of the psychiatric beds had been closed down, so we speculated that the increasing suicide risk indicated some adverse effects of deinstitutionalization, which was also an early indication that something could be done about this problem.”

The study also confirmed markedly elevated all-cause mortality among people with schizophrenia and higher death rates from natural causes, except for cancer and cerebrovascular diseases.

At about the same time, Preben Bo Mortensen had the good fortune to meet two United States researchers, E. Fuller Torrey and Robert Yolken. They not only could see the potential in his work on registries but could also, with funds from the Stanley Medical Research Institute, enable new, more ambitious projects looking more closely for patterns related to who developed this chronic and severe mental disorder. This required a struggle, but the big breakthrough came in 1999.

“The most well-established risk factor for schizophrenia is to have a parent or sibling with the disorder, and ideally it would be great to be able to construct a psychiatric family history for everybody living in Denmark to get the denominators right. That is a tall order. I had been thinking that we could use Denmark’s Civil Registration System to actually link with relatives and then look up the relatives in the Psychiatric Central Registry, but back then getting these data was also extremely expensive. Then I was at a meeting about something related to registries where Mads Melbye from Statens Serum Institute was present and he had already done that, so we made an agreement that I could pay for a statistician who could work with him on their data.”

For the first time, the research could begin to quantify in a total nationwide population what had been said to be the causes of schizophrenia, and the researchers demonstrated the influence of genetics but also suggested that environmental factors have an unexpectedly large role.

“Although a history of schizophrenia among a parent or sibling is associated with the highest relative risk of developing the disease, curiously, we also showed that growing up in the city led to a twofold elevated schizophrenia risk. And people born in late winter or early spring also had a significantly higher risk.”

A very direct suggestion
At almost the same time, Preben Bo Mortensen joined a committee chaired by another expert in mental disorders, Merete Nordentoft. The task of this committee was to develop an action plan for preventing suicide.

“It was really curious that many experts in this field were saying: ‘This population group is very important, and it’s the young women, it’s the immigrants or it’s something else.’ At that time, no study in the world had been able to, at the same time, look closely at risk-factors such as mental illness, income and employment and demographic factors such as whether you are married or not, whether you have children or not.” This was necessary to get some idea of the relative importance of the risk factors.

To optimally inform the suicide prevention committee, Preben Bo Mortensen and his team performed a registry-based study that became the largest and most thorough ever. The study showed very clearly that mental illness is the predominant contributing cause of suicide in the population.

“However, it is not like you get a diagnosis and then you are doomed to a very high risk. There are phases: sometimes you feel better, sometimes you feel worse. You often go to a hospital when you feel worse, so actually suicidality increased more during
Giving doctors and politicians new facts
The study, which was published in *The Lancet*, led to a very direct suggestion from the committee: that one aspect of preventing suicide should be more systematically asking people who are discharged from hospital whether they have suicidal thoughts but also closer follow-up just after discharge.

“It looks like this may have worked. Suicide rates stopped growing, but of course we will never know whether that was the cause. But I think that was probably the most direct example during my career where I thought that, just looking at the numbers, you can actually hope that this worked.”

The work of Preben Bo Mortensen and colleagues in building registry-based research infrastructure in Denmark really began to pay off in the following years. It resulted in many innovative studies, led by the many talented people working with him, proving existing hypotheses based on this infrastructure, whereas other hypotheses turned out to be wrong.

For example, concern had been expressed about whether having an induced abortion potentially harms women’s mental health. Using Danish registry data, his team estimated the rates of first-time psychiatric contact for any type of mental disorder within the 12 months after the abortion or childbirth compared with the 9-month period preceding the event.

“We confirmed that the incidence of psychiatric contact was similar before and after a first-trimester abortion, so this did not support a hypothesis of an increased risk of mental disorders after abortion. Studies like this are important, regardless of whether they prove or disprove a connection. Ultimately, what we can do is give doctors and politicians new facts and possible tools to act on these facts.”

Treatment not effective enough
Other studies established important hypotheses about associations, such as an association between autoimmune diseases and subsequent risk of mental disorders, and the registry-based analysis also confirmed that mental disorders affect the subsequent risk of developing cardiovascular disease. People with severe mental disorders had a threefold risk of dying from heart disease 5 years after being diagnosed with it and also had a reduced likelihood of undergoing invasive procedures related to heart disease within these 5 years.

“Of course, these are just associations and numbers, but given the excess mortality and lower rates of invasive procedures, as well as fewer prescriptions of modern drugs for high cholesterol or blood pressure, we concluded that the treatment was not sufficiently effective. So we thought: maybe we can do something by paying more attention to whether we take blood tests and whether we actually try to implement state-of-the-art treatment.”

John McGrath, a good friend of Preben Bo Mortensen, found another possible association connected to the previous study showing that people born in the winter more often develop schizophrenia, suggesting that the reason could be that people in northern Europe lack vitamin D from the sun in the winter. An initial study did not find the expected relationships, but since the numbers were small and complex, the researchers did a larger and more rigorous study. This was possible because of another unique resource for research in Denmark: the Danish Neonatal Screening Biobank had been created by Bent Nørgaard-Pedersen and his successor David M. Hougaard at Statens Serum Institut, collecting and storing tiny amounts of blood on the filter papers used for neonatal screening of all children born in Denmark.
Preben Bo Mortensen started working with them, first on studies of early infections as risk factors for schizophrenia and then on John McGrath’s vitamin D study.

“That study, as well as a subsequent replication, showed that low concentrations of neonatal vitamin D are associated with increased risk of schizophrenia. Of course, you should always remember the low baseline rate of the disease, so most people will never be affected, but nevertheless we concluded that this could contribute to a sizeable proportion of cases in Denmark.”

The purpose of iPSYCH is to find the causes and create the basis for improving treatment and prevention related to five of the most serious mental disorders: autism, attention-deficit/hyperactivity disorder, schizophrenia, bipolar disorder and depression.

“I had had a dream for years of not only predicting and finding associations based on social and environmental markers, such as season, place of birth, nutrients and the like but also doing proper genetics. Of course, this was a moving target in 2000, because it was back when genomic technology was immensely more difficult and expensive and required higher input of DNA. Plus, I did not know anything about molecular genetics or laboratory work. Luckily, I knew people who did.”

In 2012, with the emergence of new genomic technologies, the time had come to realize that dream. With the largest grants ever awarded for psychiatric research in Denmark, the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH) was established by an interdisciplinary team of six principal investigators, including this year’s two Novo Nordisk Prize recipients.

The world’s largest study within psychiatric genetics
Similar to many of Preben Bo Mortensen’s other registry-based studies, John McGrath’s vitamin D study also stimulated the careers of many young researchers and kick-started new studies to understand how vitamin D status affects brain development and mental health. However, the many studies and associations linking mental disorders had also kick-started an idea in Preben Bo Mortensen’s head.

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So far, the project has resulted in more than 740 publications. Progress in psychiatric genetics today is driven by international collaborations such as the Psychiatric Genetics Consortium, and iPSYCH has from its beginning been engaged in this. One of the first major successes was a 2014 article in *Nature* about schizophrenia-associated genetic loci, describing the largest genome-wide association study. The researchers analysed almost 37,000 cases of schizophrenia and identified 108 conservatively defined loci – 83 of which had not been reported previously. Also, importantly, the population-based data from Denmark could be used to document the ability to begin to measure genetic liability meaningfully with biological data instead of being limited to using family history. Since then, the iPSYCH project has contributed importantly to the vast majority of the new major international studies unravelling the genetic underpinnings of major mental disorders.

Preben Bo Mortensen generally sees his work as an attempt to identify useful patterns in a complex web – a combination of biological building blocks plus the cumulative sum of life experiences. In his view, lifelong quarrels about genes and environment are therefore not very fruitful.

“I think if you come from any other university background, you are perhaps interested in finding scientific truth in a more ideal sense. But, in my opinion, if you are a doctor, that is not what you do. Your goals are in a way more modest but not less important. When you work with treatment or prevention, you decide ‘would it be better to do this, do that or do nothing?’. So the purpose of my work is just to, in a world of uncertainty, help improve the chances of making the best decision possible.”
The Novo Nordisk Prize

The Novo Nordisk Prize, which was first conferred in 1963, is awarded to recognize unique medical research or other research contributions that benefit medical science. The Prize is awarded for a predominantly Danish contribution.

The Prize is awarded annually and is accompanied by DKK 3 million – of which DKK 500,000 is a personal award, with the remaining amount as an allowance for research purposes within the Prize recipient’s field of expertise. The Prize may not be awarded to members of the Board of the Novo Nordisk Foundation or members of committees or to members of boards, directors or employees of the Novo Group.

The Novo Nordisk Foundation’s Board of Directors appoints the members of the Prize Committee. The 2020 Committee comprised the following seven members:

» Jørgen Frøkiaer, professor, chair
» Marja Jäättelä, professor
» Henrik Toft Sørensen, professor
» Anne Tybjærg Hansen, professor
» Lars Fugger, professor
» Liselotte Højgaard, professor
» Birgitte Nauntofte, CEO, Novo Nordisk Foundation

Candidates for the Novo Nordisk Prize can be nominated by the Prize Committee and former Prize recipients. In addition, a call for nominations is published in the spring, and candidates can be nominated based on this call.

The Committee meetings thoroughly discuss the nominated candidates with regard to their research contribution and impact, and a comprehensive bibliometric report is produced. A few candidates are then selected for thorough international peer review. Based on the international peer reviews, the Committee reaches a decision about the year’s Prize recipient. The award event takes place in the spring at the Novo Nordisk Foundation Prize Celebration, at which the Novozymes Prize is also awarded.

In addition, in celebration of the award, the recipient gives a lecture lasting about 1 hour at his or her workplace. Before the end of the year, the recipient and the Foundation arrange an international symposium within the scientific field of the Prize recipient.
Previous recipients of

The Novo Nordisk Prize 1963–2019

1963  Professor, dr.med. Erik Warburg
1964  Chief physician, dr.med. Claus Brun
1965  Professor, dr.med. J. C. Skou
1966  Professor, dr.med. Jørn Hess Thaysen
1967  Professor, dr.med. Knud Lundbæk
1968  Chief physician, dr.med. Niels A. Lassen
1969  Professor, dr.phil. Erik Zeuthen
1970  Professor, dr.med. Poul Astrup
1971  Professor, dr.med. Mogens Schou
1972  Chief Physician, dr.med. J. Chr. Siim
1973  Professor, mag.scient. K. A. Marcker
1974  Professor, dr.med. Michael Schwartz
1975  Director, dr.phil. Georg Mandahl-Barth
1976  Professor, dr.med. Niels Tygstrup
1977  Professor, dr.med. Erik Amdrup
1978  Chief physician, dr.med. Margareta Mikkelsen and
     Professor, dr.med. Villy Posborg Petersen
1979  Chief physician, dr.med. Gerhard Salomon
1980  Professor, dr.med. Bent Friis Hansen
1981  Professor, dr.med. Flemming Kissmeyer-Nielsen and
     chief physician, dr.med. Arne Sveigaard
1982  Professor, dr.med. Jens F. Rehfeld
1983  Professor, dr.med. Christian Crone
1984  Head of Department, med.dr. Staffan Magnusson
1985  Professor, dr.phil. Hans Klenow
1986  Chief Physician, dr.med. Hans Henrik Holm
1987  Professor, dr.phil. Hans H. Ussing
1988  Professor, dr.med. Gunnar Bendixen
1989  Associate professor, med.dr. Ove B. Norén and
     Associate professor, med.dr. Hans G. Sjöström
1990  Professor, dr.med. Morten Simonsen
1991  Professor, dr.med. Peter Leth Jørgensen and
     Professor, med.dr. Arvid Maunsbach
1992  Chief physician, dr.med. Jan Fahrenkrug and
     Professor, dr.med. Jens Juul Holst
1993  Professor, dr.med. Niels E. Skakkebæk
1994  Professor, dr.med. Hans Jørgen G. Gundersen
1995  Research professor, dr.med. Niels Borregaard
1996  Professor, chief physician, dr.med. Henrik Kehlet
1997  Research professor, dr.scient. Peter E. Nielsen
1998  Professor, dr.med. Michael J. Mulvany and
     Professor, dr.med. Christian Aalkjær
1999  Professor, med.dr. Bengt Saltin
2000  Research professor, dr.med. Peter Aaby
2001  Professor, dr.med. Thue W. Schwartz
2002  Professor, dr.med. Jørgen Gliemann
2003  Professor, PhD Jiri Bartek and
     Senior researcher Jiri Lukas
2004  Professor, PhD Matthias Mann and
     Professor Peter Roepstorff
2005  Professor, dr.med. Mads Melbye
2006  Professor, dr.med. Henning Beck-Nielsen
2007  Professor, med.dr. Marja Jäättelä
2008  Professor, director, PhD Kristian Helin
2009  Managing director, professor, dr.med. Søren Nielsen
2010  Professor, dr.odont. Henrik Clausen
2011  Professor, dr.med Peter Lawætz Andersen
2012  Professor, dr.med. Erik A. Richter
2013  Professor, dr.med. Soren Kragh Moestrup
2014  Professor, PhD Søren Molin
2015  Professor, dr.med. Jens Bukh
2016  Professor, dr.med. Christian Torp-Pedersen
2017  Professor, PhD Poul Nissen
2018  Professor, PhD Jørgen Kjems
2019  Professor, Hans Bisgaard