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Professor
Merete
Nordentoft

2020

The Novo Nordisk Prize

Nomination of Merete Nordentoft

The Novo Nordisk Foundation is awarding the 2020 Novo Nordisk Prize to Professor Merete Nordentoft for her remarkable clinical social psychiatric studies and pioneering clinical epidemiological research on suicide and other mortality risks experienced by people affected by mental disorders. Her empirical findings and discoveries on this topic have practical implications for the care and management of the people being treated for these disorders and provide guidance for pre-discharge planning to prevent suicide and other premature mortality risks experienced by newly discharged patients with mental disorders.

Merete Nordentoft graduated as a medical doctor from University of Copenhagen in 1982 and obtained her PhD degree from University of Copenhagen in 1994 with a thesis entitled *Homelessness, social integration and quality of life among psychiatric patients in Denmark*. In that periode, she conducted remarkable field studies on homeless people, especially those with mental illness, a topic which at that time was not given much attention.

In parallel with her clinical training in psychiatry, she continued her research, both with clinical studies and elegant use of Danish patient registries, and in 2007 Merete Nordentoft became Doctor of Medical Science with a thesis entitled *Prevention of suicide and attempted suicide in Denmark*. In her thesis and in an extensive number of publications, Merete Nordentoft contributed impressively with high-class clinical and excellent epidemiological studies regarding suicide as well as very important intervention studies in selected high-risk groups, including people with

schizophrenia. She investigated risk factors and possibilities for preventing suicide and suicide attempts during hospitalization and shortly after discharge from a department of psychiatry. She also studied mortality and life expectancy among people with various mental disorders and proved that the life expectancy of people with schizophrenia is 15–20 years shorter than in the general population. In addition to the very important studies providing fundamental insight into suicidal patterns among people with schizophrenia, she also led numerous groundbreaking studies using Danish registry data to explore other negative outcomes among people with mental disorders. Moreover, Merete Nordentoft has consistently delivered impressive cost-effective research approaches to understand the impact on long-term disability and develop clinical interventions to improve the outcomes for people with mental disorders. Her research is characterized by a unique clinical focus on the patient, and her pioneering contributions have paved the way for increasing attention from society on mental disorders. Her

research has addressed some of the most marginalized people in society who experience some of the greatest health inequalities. As such, mental health has long been a neglected area within society in general and within health care, medical research and public health in particular. Based on Merete Nordentoft's tireless efforts and longstanding scientific contributions, this view is now changing, with important implications for the status of these disorders in society.

Merete Nordentoft has contributed numerous highly original studies in psychiatric epidemiology and large clinical trials. Her work has covered a range of hugely important areas within mental health research, especially in schizophrenia. Impressively, her work includes studies of aetiology, prognosis and effective treatments of a range of mental disorders and outcomes, including psychosis, major depressive disorder, autism and suicide.

Her innovative use of Danish registry data has led to multiple discoveries regarding the long-term outcomes of mental health problems and the aetiology of these disorders, which could not be studied with primary research or trials. Merete Nordentoft's studies often directly indicate the relevance of early identification and intervention in first-episode psychosis patients and the relevance of suicide identification and prevention. This work led to the development and testing of numerous intervention programmes. The impact of her work on psychiatric research and clinical practice has been of enormous importance. This is especially evident for

schizophrenia and other psychotic disorders. Merete Nordentoft has initiated numerous clinical trials involving psychotic patients and importantly, she initiated already in 1998 the OPUS trial: early intervention in first-episode psychosis, which evaluated the effect of assertive specialized early intervention compared with standard treatment for 547 people with first-episode psychosis. This treatment had remarkable effects on psychotic and negative symptoms, substance abuse, user satisfaction, adherence to treatment and use of bed-days. The concept has been confirmed over a longer period and has now been transformed into permanent clinical service. Since then, she has been the principal investigator for many other clinical trials, which has contributed to evidence and changed clinical practice.

Professor Merete Nordentoft has extensive collaboration with colleagues in Denmark and is a leading role model in Danish clinical psychiatry. Merete Nordentoft has been honoured with several national and international prizes and awards. In recognition of the enormous international impact of her research, the Association for Education and Research in Suicide Prevention named an annual prize for suicide prevention after her. In 1997, Merete Nordentoft was appointed chair of the task group on suicide mortality under Denmark's Ministry of Health, demonstrating her exceptional scientific expertise and clinical efforts to prevent suicide from very early in her career. Merete Nordentoft has attracted impressive external funding for her clinical research. She has shown great leadership and mentored a large number of young scientists and

PhD students. She has an impressive scientific output of more than 500 original publications, many published in leading high-impact journals including *The Lancet*, the *Journal of the American Medical Association*, *Nature* and *Nature Genetics*. She has also authored multiple review articles in her field, and many of her reviews and original articles are frequently cited. Merete Nordentoft's research has contributed on the international scene in a leading role and with important clinical impact. She collaborates intensively with international research consortia on many major questions, including the significance of genetic and environmental factors for schizophrenia, affective disorders and the interaction between a person's genes and environment such as drug abuse or suicidal behaviour. As an expert in epidemiology, suicidal behaviour, psychopathology and early clinical intervention in psychosis, Merete Nordentoft has definitively been successful in taking her research findings far beyond scientific publications. This is truly remarkable.

In summary, the Committee on the Novo Nordisk Prize finds that Professor Merete Nordentoft is clearly a worthy recipient of the 2020 Novo Nordisk Prize based on her systematic and highly original international clinical research on suicide and other mortality risks experienced by people with mental disorders. The impact of her work on psychiatric research and clinical practice has been enormous. Based on her pioneering research, awarding Merete Nordentoft the 2020 Novo Nordisk Prize is therefore well founded.

The 2020 Novo Nordisk Prize was awarded on Friday, 27 March to Merete Nordentoft, Clinical Professor, University of Copenhagen and Preben Bo Mortensen, Professor and Scientific Director, iPSYCH, Aarhus University.







**The quest
to save
people from
the voices
that kill**

Voices that talk to you. They encourage you to kill yourself, stab somebody or contemplate how to kill yourself. This is reality for 1 of 100 people. Most often they do not know that the voices are not real, and 1 in 4 actually try to commit suicide. 2020 Novo Nordisk Prize recipient Merete Nordentoft has dedicated her life to studying suicide prevention and schizophrenia. Merete Nordentoft hopes for the future that the people at risk can be identified and helped when they are still children.

It seems unbelievable. Do people really hear these violent and terrifying threats about persecution and death? And do they really think anyone will poison them or kill their loved ones? The most unimaginable aspect, however, is that any one of us can develop schizophrenia, and when it strikes, it arrives surreptitiously like a slow distortion of the reality we think we know and have control over. However, people with schizophrenia can get help, and if they receive it early enough, they can learn to live with schizophrenia.

“Schizophrenia reduces people’s lives by 15–20 years on average. They have excess mortality from both unnatural causes of death such as suicide and accidents and natural causes, since they have an increased risk of dying from every somatic disease. The good news is that early treatment can help people with schizophrenia. We hope that in the future we can find the children at risk and their families, because early intervention could enable these children learn to cope early so they do not need to be removed from the home later on,” explains Merete Nordentoft.

Fascination with the brain

Mental disorders such as schizophrenia are common and extremely challenging for the people who have them and for their families and society. However, little was known 20 years ago about the increased suicide risk and general comorbidity that severely impair the quality of life and increase mortality.

Although Merete Nordentoft already knew at a young age that she wanted to become a doctor, she was not aware of this scary and fascinating illness.

“It was almost a coincidence. I thought I might become a neurologist, but then I got this first position in psychiatry. The first 6 months of my first employment in a day hospital was very calm. I was almost bored, but then they opened an acute department where we had all the severe disorders such as first-onset psychosis, and that caught my attention, because I was really attracted to understand how the brain creates these symptoms and how these people perceive the world.”

Merete Nordentoft’s fascination with the brain led her to start a research project in her first job to explore the clinical issues she encountered in her work. She consulted the people who had attempted suicide and inventoried them as her first project. A few years later, she carried out a PhD project at Bispebjerg Hospital, examining what happened when community mental health centres were implemented in the mental health services in Copenhagen.

“At that time, I thought that the people who would be most vulnerable to these changes, by which they are supposed to become more independent, would be those who used many services already. But we realized that the most vulnerable people



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were those who had their first contact with the mental health services, whereas almost nothing negative happened to those who had been in treatment for 10 years. So I became aware that the early phase of psychosis is a very vulnerable period in which many bad things can happen.”

An action plan

The study also made Merete Nordentoft realize that, if people are left untreated in the early phase of psychosis, many negative things can happen. For example, the risk of suicide is higher in the early years than later on.

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In 1993, she published a 10-year follow-up study of people who had attempted suicide in the prestigious *British Medical Journal*. The study showed that most people who attempted suicide were at high risk of succeeding because the risk factors were not very specific. A national strategy to prevent suicide was needed.

“In 1997, it was decided that we should have a national suicide prevention plan, so it was developed during 1997 and ready in 1998. In that connection, Preben Bo Mortensen was doing most of epidemiological studies to demonstrate which groups were most important. This work formed the basis for the actual action plan targeting the majority of the people who attempt suicide. I was chairing the committee preparing the action plan and so our collaboration began then.”

The rate declined

The epidemiological studies of Preben Bo Mortensen and Merete Nordentoft on the risk factors for suicide among young people were supposed to inform the work of the committee preparing the action plan, but the groundbreaking results also helped to change the views of both researchers and health professionals on suicide and on mental illness. A 2002 article in the *British Medical Journal* both affirmed and confirmed this hypothesis.

“Basically, the conclusion was that recognizing mental illness among young people and dealing with it appropriately could help prevent suicide. Further, we found that the high relative risk of suicide associated with low socioeconomic status of the parents seemed overestimated.”

The effect of the parents' socioeconomic status decreased after the researchers adjusted for the family history of mental illness and suicide, which strongly affects the children's suicidal tendencies. Denmark's suicide rate had been extremely high in the 1980s, and when the action plan was adopted the number was 700–800 per year. It then declined to 600 and has been stable for years.

“We still need to do more work, because 600 is still far too many. People with schizophrenia have a 20 times higher risk than the general population. One quarter of the people with schizophrenia attempt suicide, and ultimately 5–8% die from it.”

Less focus on the disorder

The epidemiological studies had clearly shown that suicide rates can be reduced. A 2004 article in the *British Medical Journal* showed that the suicide rate declined among people with schizophrenia in Denmark from 1981 to 1997.

“Our theory was that this may have resulted from better psychiatric treatment, reduced access to means of suicide or improved treatment after suicide attempts. People admitted to hospital with schizophrenia had the highest risk of suicide in the first year after their first admission.”

Alongside the suicide studies, Merete Nordentoft had already started the OPUS study in 1998, in which 547 young people with schizophrenia had 2 years of very intensive treatment versus 2 years of standard treatment and then were followed up after 1 year and 2 years.

“We named it OPUS because we wanted to express that instruments should play together and need a conductor, so we needed things to be coordinated. The people with the disorder meet a more interdisciplinary team consisting of psychologists, psychiatrists, occupational therapists and social workers. In

this way, you coordinate the efforts to solve the challenges the people with the disorder have in their everyday lives instead of just focusing on the disorder.”

And it worked. The group that received the OPUS treatment had fewer hallucinations and delusions and fewer negative symptoms such as social withdrawal, passivity and lack of expression compared with standard treatment. There was also less substance abuse and fewer bad days.

“The very general picture was that the people with the disorder were more satisfied with the treatment, as were their parents, because they learned more about their children's symptoms. They spent less time hospitalized in psychiatric wards and spent less time in institutions, so they learned how to organize themselves and manage their symptoms and their situation. I think that the long-term effect was more about improving social functioning.”

International impact

The OPUS studies were such a great success that the researchers got funding for follow-up 5, 10 and 20 years afterwards and for another trial investigating which interventions are needed to sustain the positive effects. So today the participants can be used as a cohort to show the prognosis of schizophrenia and related disorders in a modern context, and the researchers do not have to rely on old textbooks from when treatment was completely different. But more importantly, the OPUS treatment became standard all over Denmark.

“We had to push when we had the initial results, but all the public authorities were very positive, so they wanted us to keep the staff members who were trained and they wanted to transform it into a permanent service. Later on, through state funding, it was disseminated in several waves to implement it further. Further, some of the patients were actually able to explain how this has

meant a difference. They were really great spokespeople for themselves.”

In 2005, the experiences in working with intensive early intervention even led to a set of international clinical guidelines for early psychosis. The experiences from Merete Nordentoft’s OPUS trial were key to the guidelines, which mentioned the importance of early identification and treatment.

“The longer you live with untreated or poorly treated psychotic conditions, the worse is the outcome and the higher is the risk of unwanted outcomes, such as suicide. Other undesired outcomes include homicide, although this is seldom, attacking somebody, social isolation and deterioration of social conditions. So many negative things can happen if you do not treat early, and treating somebody who has had a psychotic disorder for many years is much more difficult.”

Voices and the cannabis link

Merete Nordentoft’s group recently initiated a new trial aiming to help people who hear voices. The idea is to test whether simulation training in a virtual environment can reduce auditory hallucinations and distress. With a voice-transforming program, the voice of the therapist can be modified so it sounds similar to the voice the person with schizophrenia used to hear. The therapist can interact with this person by switching between acting as the nasty voice and the supportive therapist. Hopefully this will help the person with schizophrenia to stand up against the voices, be able to stop listening to them and stop believing that they are omnipotent.

An example of some of the possible consequences of untreated psychosis came from Merete Nordentoft’s study of homeless people in Denmark from 1999 to 2009. Of the 32,711 registered homeless people (23,040 men and 9671 women), 14,381 men and 5632 women had mental disorders. The life expectancy of

these homeless people was 22 years lower for men and 17 years lower for women than for the general population. Substance abuse disorder was the most frequent mortality risk.

“I also went around to identify homeless people with schizophrenia and interviewed them. They were so convinced that their delusions were real that they would never even think of seeking help, so they were convinced that they were being followed and they had many conditions. The women were the most visible ones, so that was why the study was called shopping bag ladies. Fourteen of the 15 interviewees had schizophrenia with massive delusions and hallucinations.” For the men, substance abuse disorder was one of the main reasons for their mental disorder, and substance abuse is one of the main risk factors for schizophrenia. Merete Nordentoft’s group has carried out several studies examining the risk of transitioning from being diagnosed with cannabis abuse to developing psychotic disorder.

“Several of our studies have shown that substance abuse, especially cannabis abuse, is associated with a higher risk of developing schizophrenia, and we also demonstrated within this OPUS study that those who continued using cannabis had a higher risk of continuing to have severe psychotic symptoms than those who stopped.”

Lifespan reduced by 15–20 years

With the OPUS trials, the importance of early intervention became the gold standard, so today people with schizophrenia are treated with both antipsychotic medication and psychosocial interventions in which they learn about the symptoms and warning signs, and their families are also involved.

“Many things can improve the prognosis. Maybe they can stay get more targeted support from their parents. And also some measures can help the treatment to become more effective, such



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as having more knowledge about their own symptoms and knowing more about what to do with the symptoms. Our data showed that, after 1 year, half the people with schizophrenia do not have psychotic symptoms anymore, so that is a really positive outcome.”

Despite the improvements, there is still much to be done. This was demonstrated by a 2013 study showing that women with mental disorders have about 15 years’ lower life expectancy than the general population and 20 years lower for men. Mortality from somatic diseases was increased two- to threefold, and excess mortality from external causes ranged from three- to 77-fold.

“Mortality from suicide was highest among people with affective disorders and personality disorders. The effects of schizophrenia on the number of years of potential life lost and life expectancy seem to be substantial and not to have lessened over time. So even though much has happened with the OPUS development, interventions and initiatives to reduce this mortality gap still urgently need to be implemented.”

A genetic factor

Today Merete Nordentoft heads a research unit of more than 60 researchers, with 40 employed in clinical studies and more than 20 working on epidemiological research. Since 2012, she has also been one of the six principal investigators in the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH). As part of iPSYCH, she initiated the major Danish High Risk and Resilience Study VIA 7 – a cohort study of 522 7-year-old children with 0, 1 or 2 parents with schizophrenia or bipolar disorder.

“There has been a logical track in my research career. I started by studying people with mental disorders who already used considerable mental health services. Then we examined people with their first psychotic episode, and now we are starting an effort for these children who are at risk of developing mental disorders later in life because their parents are sick. In other words, we are trying to determine whether we can intervene at an earlier stage than when everything has gone so wrong that people end up homeless on the street.”

The aim is to identify new and targetable biological and clinical markers of the early risk of psychosis. Today, both genetic and environmental factors are known to be involved. Up to 15% of the genetic risk has been explained. In the studies, the strongest factor inversely related to poor outcome is the polygenic risk for educational attainment.

“Your genes partly explain the likelihood of completing a long educational programme. Of course, you can influence this yourself, but people can be genetically predisposed to being able to complete a long educational programme. This is less likely for the children who have early symptoms of mental disorder, but this is related to the home environment and how well functioning their parents or other caregivers are, so genes and environment also interact.”

A big surprise

Early intervention has proved to be crucial in combating schizophrenia and other mental disorders. Given the many environmental risk factors – responsible for 60–70% of the total risk – much can be done. Even though Merete Nordentoft and her colleagues are still exploring new risk factors, such as infections, the most important current focus is the children and their parents.

“This started out with epidemiology, in which we found out that the children of people with severe mental disorders, including schizophrenia, bipolar disorder and others, had a higher risk of developing a mental disorder. So this is an important high-risk group, because we can prevent mental disorders but we could also maybe improve in intervening in the social conditions.”

The researchers also showed that these children were less likely to complete primary and lower-secondary school and were more likely to be removed from the home and placed outside, so they knew that this is a vulnerable group.

“We called the project the Danish High Risk and Resilience Study – VIA 7 because the children were 7 years old when we started, and they were recruited if their parents had either schizophrenia or bipolar disorder. We assessed them very thoroughly and interviewed both their parents. We got many data showing that the children whose parents had schizophrenia were more likely to have neurocognitive deficits, social cognitive deficits, poorer motor function, poorer language, poorer quality of life and a less optimal home environment.”

Nevertheless, the researchers examined the numbers more closely and found to their great surprise that half the children with parents with schizophrenia were not affected and were at the same level as the control group, whereas 25% of the children were affected on all domains. The researchers aim to invent a tool that more easily can identify the children at higher risk and provide treatment earlier.

“Our experiences from interviews with the parents of these children is that they experience that they cannot get the support they need, so I think more thorough mapping would enable us to find families in which early intervention could prevent removal from the home later. Through early support for these families, I think it is possible to prevent them from starting to develop delusions, hallucinations and the poor self-confidence often seen among people with schizophrenia.”

The Novo Nordisk Prize Committee

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