MAGAZINE
2014–2015

Lundbeck PROGRESS IN MIND

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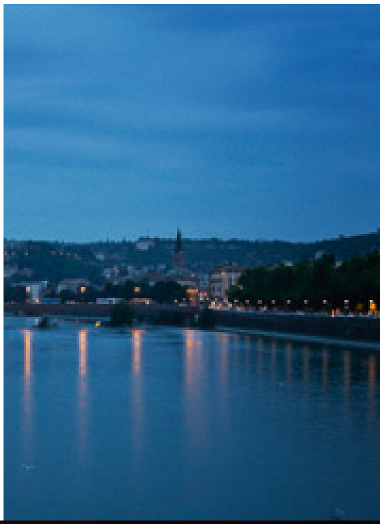

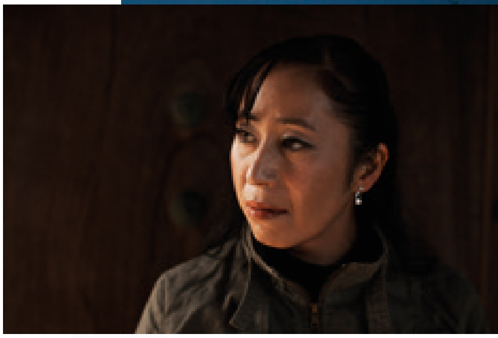

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PROGRESS IN MIND

Brain disease represents an enormous burden first and foremost to patients and their families, but also more broadly to society. The global magnitude and impact of problems related to brain disease have been largely underestimated over the years. Not until 2011, did the United Nations recognize brain disease as a global health problem which requires global action – and a global solution.

According to the World Health Organization (WHO), 700 million people worldwide suffer from brain disease. Despite treatment advances and increased efforts to improve early recognition, WHO characterizes the field as a "hidden human rights emergency"[1] emphasizing that a profound stigmatization surrounding patients with brain disease still exists.

Joining forces

As a global pharmaceutical company specialized in brain disease, Lundbeck recognizes that we have a vital role to play when it comes to addressing this challenge. We work to put brain disease on the international agenda and contribute with what we do best: Conducting pioneering neuroscience research and developing new and improved medicines.

However, more needs to be done. In order to address the global health problem and to create lasting results, a multifaceted approach with cooperation between stakeholder groups is required. Only by joining forces across sectors, will it be possible to tackle the challenge and the immense human and economic burden it represents. We therefore encourage policy makers, patient organizations and health care professionals to contribute by prioritizing the concern.

Our foundation for progress

In this issue of the Lundbeck Magazine, we focus on the foundation, which enables us to address the global health problem that brain disease represents today: Our continuous patient focus and our aspiration to find new and improved treatments that can make these patients' lives better. We call this *Progress in Mind*.

Through three honest portraits, we let you into the worlds of three patients who have each experienced the difficulties of being diagnosed with a serious brain disease, but who have also learnt to deal with it. Kazuko from Japan lives with depression, Gary from the US suffers from schizophrenia and Bente from Norway struggled with alcohol dependence for many years.

I would like to thank each of them for sharing their stories. Every time, we get the opportunity to encounter stories like these, we become wiser and understand more. To Lundbeck, these stories represent valuable knowledge which we take back to our laboratories with the purpose of developing tomorrow's drugs and treatments. Further, the knowledge is beneficial to the public's awareness and understanding of brain disease, and helps to increase the necessary joint efforts and global action.

I hope you will find this issue of the Lundbeck Magazine interesting, and that the features and portraits will provide you with insight into what drives us towards the overall goal of making a difference to people living with brain disease.

Ulf Wiinberg

Ulf Wiinberg
President and CEO

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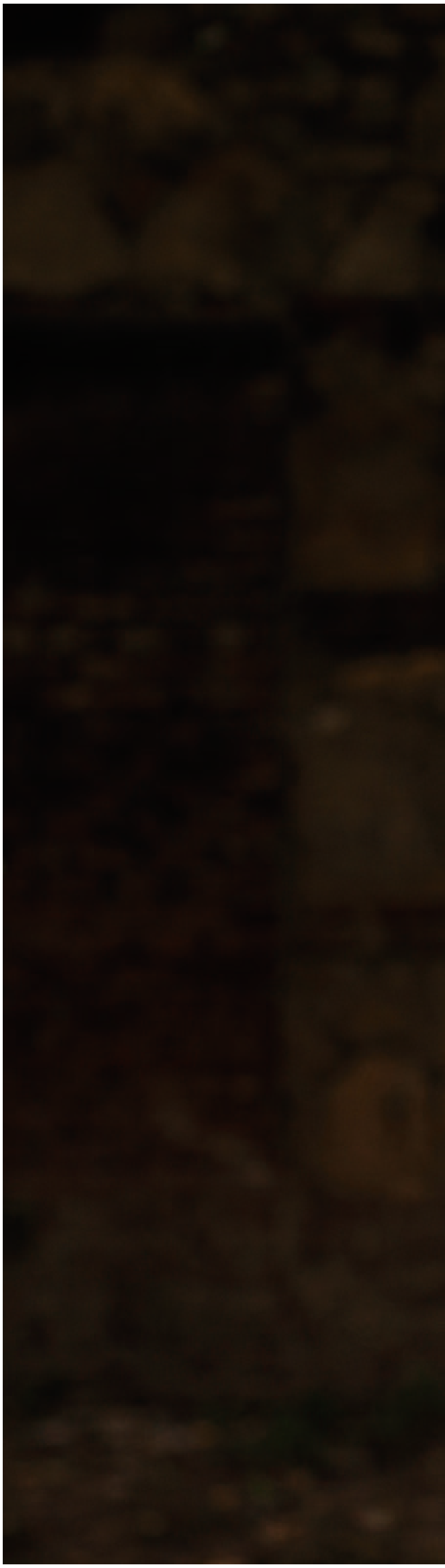
[1] WHO Quality Rights Project – addressing a hidden emergency, 2011.

A HIDDEN HUMAN RIGHTS EMERGENCY

The number one obstacle to better mental health care is the stigmatization of people with mental illness. And stigmatization occurs on every level of society, according to psychiatrist Norman Sartorius, who has been a leading figure in the international promotion of mental health for half a century.



One hundred and seventy-five million years. That's how many years of human life were affected by mental illness in 2010, representing a vast blighting and blunting of individual experience.

That makes mental and substance-use disorders the world's leading contributors to years lived with disability.[1] But the principle of "global solutions for global problems" hasn't applied to mental illness in the same way it has to other widespread illnesses – as psychiatrist Norman Sartorius can attest to with numerous examples.

After a long international career fighting for better prevention and treatment of mental and neurological disorders – most notably as the first director of WHO's Division of Mental Health – Dr. Sartorius is now active in NGOs and as a consultant and lecturer. He recounts the story of a UN summit that recently convened to put global action on non-communicable diseases on the international agenda.[2] Cancer, heart disease, COPD and diabetes were all included as matters of "profound concern" to the General Assembly. But mental illness didn't appear on the list. He says it wasn't until later, in response to pressure by several national delegations, that the summit inserted a sentence in its declaration acknowledging that mental and neurological disorders also contribute to the global burden of disease. "It was really shameful that mental illness hadn't been included," he says. "And this happened in 2011."

Even one penny is too much

It's a paradox. Mental illness constitutes a staggering burden of disease, yet it isn't a priority. The reasons are many. Dr. Sartorius points to the entrenched distance between psychiatry and other medical disciplines. ➔

He underscores the fact that for a long time, there weren't any effective treatment options. But he identifies the chief cause not in any lack of knowledge or treatments, but in the stigmatization of mental illness. The stigma of mental illness marks not only people who suffer from it, but also their families and the people who provide them with care and mental health services. And it leads to discrimination that affects people in all walks of life. WHO recently characterized the stigmatization of the mentally ill as "a hidden human rights emergency."[3] To illustrate the problem, Dr. Sartorius says that even when inexpensive medicines are available, it doesn't guarantee that governments and health care providers will supply them. Why? "Because the mentally ill patient is considered by them as having no value," he explains. "And if he is of no value, then any treatment is too expensive. Even one penny is too much."

Dr. Sartorius maintains that the number one obstacle to effective treatment, buried deep within governments, public health agencies, health services and the general public, is stigmatization. He asks rhetorically, "Who wants to help a person with schizophrenia? If he dies sooner, that's a decrease in cost."

Among health care providers, stigmatization leads to discrimination in treating the physical illnesses that commonly affect those suffering from mental illness. For instance, mentally ill heart patients are offered coronary bypasses and angioplasties only half as often as ordinary heart patients. Dr. Sartorius says that generally speaking, people with mental disorders who come seeking help for a physical illness may find that non-psychiatric health care personnel don't believe them, give them substandard care, use insulting language and treat them without empathy. "You would never say about somebody that he is a *pneumonic*. But the mentally ill patient – he is no longer Mr Smith. He is a *schizophrenic*."

I would select depression

What can be done to help? Dr. Sartorius doesn't put much stock in short-term anti-stigma campaigns that target the general public. Efforts to combat stigma must be a routine part of mental health services. In addition, he says, roundabout ways can sometimes be used to obtain better care for mental illnesses. People who are mentally ill are often subject to a range of other conditions such as heart disease and diabetes. Health decision makers across the world are becoming increasingly aware of the need to address these conditions because of their epidemic growth. This situation can be turned to good account, says Dr. Sartorius. One can lobby decision makers to do something about mental illness – because treating them will reduce the costs and complications of chronic physical illnesses.

These days, Dr. Sartorius is involved in a multi-country project that uses this very approach. It works like this: diabetes has been exploding in most parts of the world, consuming large portions of national health budgets. The long-term complications of diabetes, such as eye and nerve damage, are particularly costly. At the same time, there is evidence that patients with diabetes who also suffer from depression develop long-term complications twice as often as other diabetic patients. The project's strategy is quite simple, Dr. Sartorius explains: "We said, 'Let's deal with depression so as to reduce the complications of diabetes.' They answered, 'Oh! Treating depression will reduce complications of diabetes? We should certainly do *that*.'"[4]

If Dr. Sartorius were permitted to choose one – and only one – thing to lobby for in order to improve global mental health, he knows what it would be. "I would select depression. Because of its eminent treatability, because it is often co-morbid with other illnesses, and because of the large number of people it affects."

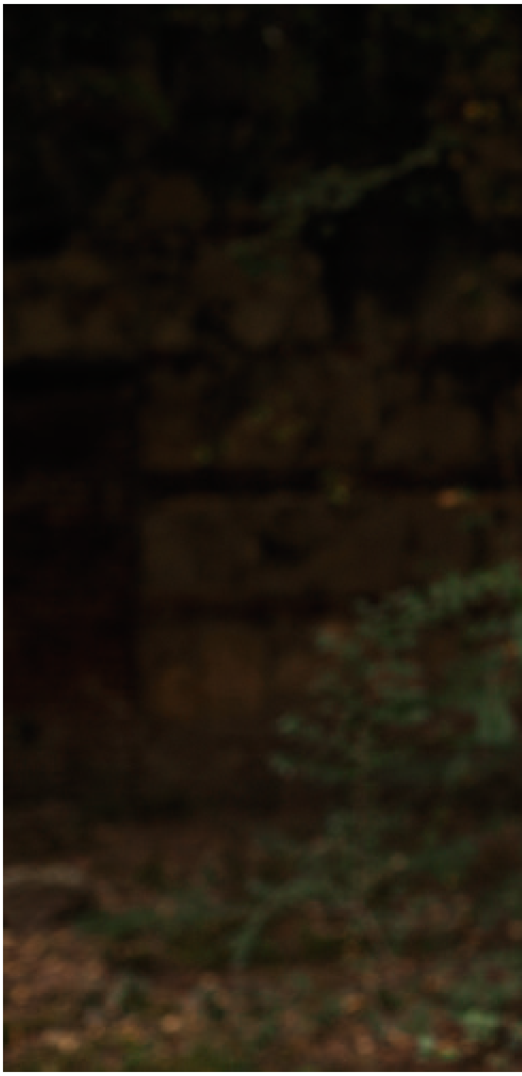
He pauses briefly.

"And then I would insist that we start taking measures to *prevent* mental illness."

The friend of the elderly

Dr. Sartorius' calendar is booked solid with work-related activities around the world. Half a century of effort, in a field that offers many frustrations, has made him an optimist about the long term. Time is on the side of everyone who works to improve the state of mental health, he believes. And if you question his faith in progress, he'll remind you of where things stood in the old days. The mentally ill had few legal protections, and there was little sense of moral obligation to look after people with mental illness, especially since there were no effective treatments for it at that time.

Take senile dementia, for instance. In the not-so-distant past, there were institutions that left their windows open in winter so that those with dementia would contract pneumonia. "This happened in Europe, and it happened in my time. They used to call pneumonia 'the friend of the elderly.' "



Such behaviour is no longer acceptable. Humanity is evolving, insists Dr. Sartorius, and people are improving as moral beings all the time. "Today, we offer these patients food, shelter, warmth. The money for that is spent out of moral obligation."

Enlightened opportunism

People who work in mental health promotion have to be indefatigable; achieving goals in this field sometimes takes decades. When Dr. Sartorius first assumed responsibility for mental health at WHO in the 1970s, few countries had a national mental health policy.

Norman Sartorius

M.D., Ph.D.

PREVIOUS POSITIONS (SELECTED)

- Director, Division of Mental Health, WHO
- President, World Psychiatric Association
- President, Association of European Psychiatrists

CURRENT POSITIONS (SELECTED)

- Professorial appointments at universities in several countries, including the UK, the US and China
- President, International Association for the Promotion of Mental Health Programmes
- Co-editor and advisory board member, various scientific journals

RESEARCH INTERESTS

- Public health
- Stigmatization and its consequences
- Co-morbidity of mental and physical illness
- Cross-cultural and epidemiological psychiatry

In time, such policies became common, even if the process was often drawn out for decades. For instance, China took the first steps towards formulating a mental health law in the early 1980s, yet the law still wasn't in place when Dr. Sartorius left WHO in 1993. It wasn't until 2013, after some thirty years of effort, that the law was finally adopted. Of course, adoption does not always guarantee implementation, but Dr. Sartorius predicts that the law will succeed in China, thanks to one key circumstance.

"This law has been passed with substantial budgetary support, which shows us that the Chinese government really means it," he notes. Time and again, he has heard decision makers assure him that they recognize the importance of mental health. "But that is not enough," Dr. Sartorius smiles. "Their statements have to be supported financially."

On a more personal note, Dr. Sartorius thinks that people who are working for better mental health should not rely too much on long-range programmes in which everything is planned from A to Z. A long working life has taught him another rule to live by: sometimes, in addition to good planning, you have to rely on luck and adopt a strategy of what he calls "enlightened opportunism."

But how? Dr. Sartorius explains that you must keep yourself in a state of watchful preparation and look for opportunities. Understand your local surroundings and their needs, and stand ready with the best tools. Opportunities will arise; luck will come. "And then…," he says, and makes a sudden gesture, "you pounce!" Ⓛ

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1) Whiteford H et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010, The Lancet Epub, 2013.
2) NCD Alliance. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, 2011.
3) WHO Quality Rights Project – addressing a hidden emergency, 2011.
4) Sartorius N, Cimino L. The Dialogue on Diabetes and Depression Initiative: Origins and achievements. Journal of Affective Disorders, 2012, 142S1: 4-7.

DISEASE AREAS

PSYCHIATRY

Alcohol dependence

Alcohol dependence is a brain disease, characterized by a pattern of alcohol consumption potentially leading to physiological, psychological and social impairment. Excessive drinking increases a person's risk of developing more than 60 other diseases. Excessive alcohol consumption is also associated with a large cost to society due to accidents, violence, lost productivity and healthcare costs.

Anxiety

Anxiety is a normal response to stress, worry or threat – but when it is very severe, long-lasting, or out of proportion to the circumstances, it becomes known as an anxiety disorder. There are several different types of anxiety disorder: e.g. generalised anxiety disorder, social anxiety disorder, panic disorder and obsessive–compulsive disorder. By affecting a person's mood, thoughts and behaviour, an anxiety disorder can make it difficult to cope with daily life at home, at work or school, and when socialising.

Bipolar disorder

Bipolar disorder is a severe mental illness, previously called manic-depressive psychosis. It is characterised by periods of altered mood, which may be manic, depressive or mixed (i.e., alternating rapidly between mania and depression). These intense moods often lead to problems with daily functioning, ruined personal relationships and suicide attempts. The first manic episode, necessary for making a diagnosis of bipolar disorder, is frequently preceded by one or more depressive episodes.

Depression

Depression is a serious medical condition that is associated with a series of symptoms including melancholy, loss of energy, difficulty in concentrating and suicidal thoughts. These symptoms can have a great impact on daily life. Due to chemical changes in the brain, people with depression may experience long-lasting feelings of sadness and anxiety, have unexplained aches and pains, and suffer from poor quality of sleep and/or lack of interest and energy.

Schizophrenia

Schizophrenia is a psychotic disorder, often life-long, which may lead to marked changes in a person's perception of reality. It carries a notable 'stigma' and is often misunderstood. People with schizophrenia experience disturbed thoughts, emotions and behaviour. Schizophrenia is caused by an imbalance in the chemicals that send signals to the brain, leading to the perception (seeing/hearing/thinking) of things that are not real.

Lundbeck is a specialist in brain diseases. We research, develop and market treatments for a number of brain diseases within psychiatry and neurology.

NEUROLOGY

Alzheimer's disease

Alzheimer's disease is a progressive brain disease, in which the brain gradually degenerates. It most frequently occurs in people aged above 65–70 years. People with Alzheimer's disease develop distressing changes in memory, thought, function and behaviour, which worsen over time. These changes increasingly impact upon the person's daily life, reducing their independence, until ultimately they are entirely dependent on others.

Epilepsy

Epilepsy, also known as 'seizure disorder', is a medical condition in which the brain experiences intense surges of electrical activity. This produces seizures which affect a variety of mental and physical functions, such as consciousness, body movements or actions. People with epilepsy can generally live a full life span; however, they must take precautions to reduce the risk of injuring themselves during seizures.

Huntington's disease

Huntington's disease is an inherited disorder in which the brain slowly degenerates. Over a number of years, a person with Huntington's disease may experience a triad of behavioural, cognitive and motor symptoms. Ultimately, people with Huntington's disease become completely dependent on a caregiver. This places a huge burden on the caregiver, who is usually a family member.

Parkinson's disease

Parkinson's disease is a long-term and progressive brain disease that most commonly affects those over the age of 60. People with Parkinson's disease have difficulties controlling their body movements, and symptoms become worse as the condition progresses. Ultimately, Parkinson's disease impairs the patient's ability to function in daily life situations.

Stroke

A stroke is a very serious acute (short-term) event, caused by a sudden impairment in the blood supply to the brain, which can damage the brain tissue. A stroke (also called 'brain attack') occurs when a blood vessel that brings oxygen and nutrients to the brain either bursts or is clogged by a blood clot or some other mass. When a stroke occurs, it kills brain cells in the immediate area. This usually happens within a few minutes.

IN A GHOSTLY WORLD

When Kazuko Shiraishi was severely ill with depression, she stopped being able to see colour – and then to taste or smell. With her senses shutting down, she longed to let go entirely.

Kazuko Shiraishi hides in the toilet. She weeps as soundlessly and quickly as she can, so that her colleagues won't notice her absence. But in a small office, everyone is aware of everyone else's moods. And the urge to cry overwhelms her often in the course of a day.

The year is 1999, the location a suburb of Tokyo. Kazuko is 32 years old, an office clerk – and a newly-wed. She dries her eyes with toilet paper and slips back to her desk.

Before Kazuko got married, three things were important to her. Work. Friends. And a fiancé. But after she wed, she broke off all contact with her friends. It was her own choice, and it was necessary, she thought, if she were to fulfil her obligations as a wife. "I decided that from now on, there should be only two things in my life: work and marriage. I intended to be a perfect wife."

Kazuko told her family doctor about her crying jags and insomnia, figuring that he would no doubt diagnose her with "accumulated fatigue." But her affliction turned out to be something else entirely. An illness that, at the time, seemed to have nothing to do with her at all.

She didn't tell her husband. He knew quite well how she was doing, and in his eyes, she was a great disappointment. He too had expected a flawless wife – and one who would earn money until she became pregnant. But when Kazuko came home from work, he felt she wasn't quick enough in getting dinner on the table. If he came home before his wife, he would calculate his waiting time from when he himself had arrived. Kazuko raced through her days: late home from work, get dinner underway, do laundry, crawl in bed at 12:30 and lie there awake, then up again before 5 and get going with her domestic chores before hurrying off to the office. And then that evening, repeat the whole cycle all over again.

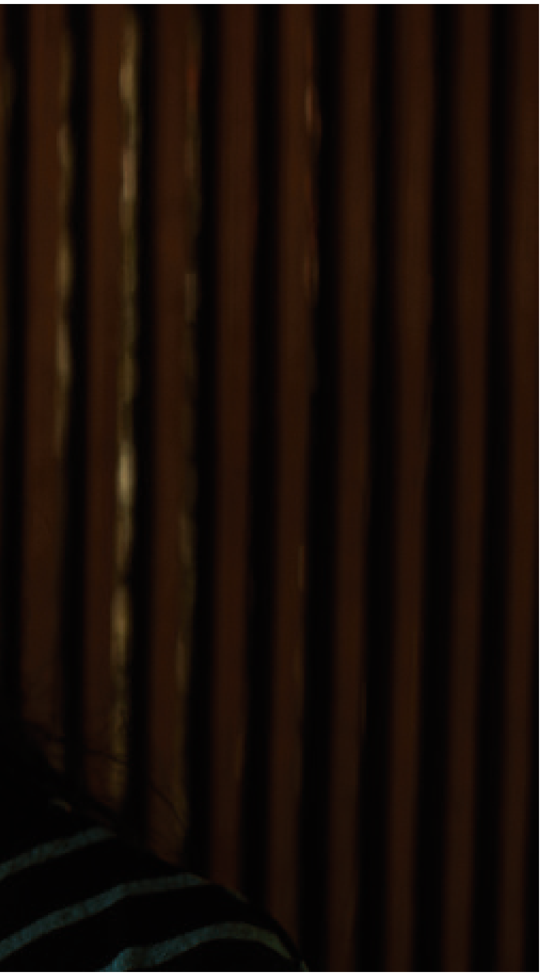
A recent Cabinet Office survey shows that at least one in every three Japanese women has experienced physical harm or psychological harassment in the home.[1] Kazuko became one of these women. Her husband shouted words at her that she still can't repeat. He hit her. Although Kazuko's mother and older brother urged her to move back in with them, and her doctor had diagnosed her with *major depressive disorder*, Kazuko remained where she was. "I could not admit my marriage was a failure," she says today.

Nevertheless, after five months of marriage, the violence and the harsh words became too much, and she left her husband. But that didn't make her feel any better.

In the bathroom mirror

Only one thing remained that could rescue her – to be the perfect employee. It was critical to her that she appeared clear and composed at the office, but the medicine a psychiatrist had prescribed made her dizzy. She felt she had to stop taking it. "I had failed as a housewife. I could not fail as an employee too. That would mean: *You are nobody.*"

One night, she got up to go to the bathroom. When she looked in the mirror,



she noticed something that made her wonder, but she was too exhausted to react. In the morning, the strange thing was still there. "I looked in the bathroom mirror and there was no colour at all. Not behind me, not anywhere. All gone."

It was the last morning of the New Year's holidays, and Kazuko's first thought was for her next day at work. At the office, she had to manage documents that were organized by colour – but what now? She wrote the names of the colours on small sticky notes and set them on her papers. In this way she was able to cope; she could still "save face" at work.

But from then on, she lived in her own ghostly world. Everything was greyish, black and white. Kazuko compares it to a black-and-white film. Was it hot or cold? Her senses couldn't tell her that either. Every morning, she asked her mother about the weather so that she could dress appropriately. The loss of colour had appeared suddenly. Then bit by bit, other sensory losses began to infiltrate her life. Kazuko enjoyed sweet things, pastel cream cakes and candy in bright colours. The tempting colour had already drained out of her treats. But now they also began to lose their taste and smell.

She attempted to find foods that gave her some suggestion of their prior pleasure, but gradually her senses of taste and smell faded entirely. "I realized that all food would fail me. And then I became scared of food. I became scared of even looking at food because of the disappointment."

This once-athletic woman grew skinnier and skinnier. No one at work asked what was wrong. "My colleagues knew, but couldn't say anything," explains Kazuko. "They were all junior employees and couldn't speak to a senior colleague. So they pretended that nothing was wrong."

She couldn't help but mention to a couple of colleagues that she no longer could taste or smell anything. She still remembers a senior colleague's reply. "Is that so," he said. ➔

> "I had failed as a housewife. I could not fail as an employee too. That would mean: You are nobody."
>
> – *Kazuko Shiraishi*

Split in two

Kazuko strove to work calmly and efficiently. Yet she was often a hairsbreadth away from snapping when colleagues' work routines frustrated her. Only once did her composure crack. No, she didn't raise her voice; she says she couldn't do that. But she found herself throwing her computer keyboard on the floor. Everyone witnessed her loss of control.

For a long time, her thoughts had been circling around a particular action, and now, a short time after the incident with the keyboard, she finally gave notice.

But that didn't make her feel any better. Kazuko had been living with her mother, brother and sister-in-law for a couple of years, and her situation had just gone from bad to worse: "I had failed as a housewife. I had failed as an employee. I was useless now. Of no value at all." Her family had opened up their home to her, and she, a grown woman, had become completely dependent on them. An urge swelled inside her, an urge to liberate her family from the deep disappointment that she must have been for them. "I felt so sorry for them," she says.

It would be simple enough. The remedy she would use was already there in the house; she just needed a cup and a bottle of disinfectant. One morning, Kazuko went into her room, closed the door and poured the disinfectant into a cup. She drank. She couldn't taste the fluid, but it burned her throat. Again she drank from the cup.

The lamp was amber

Kazuko's mother and brother found her unconscious on the floor. After she was admitted to the casualty ward, they persuaded her to let herself be transferred to a psychiatric hospital. Kazuko was gravely ill with depression and remained at the hospital for several months. Since that first hospital stay in 2001, she has had another three stays of two to three months each.

During the period of several years that Kazuko remembers as "the bottom," she spoke frequently with her family doctor about her longing to die. "I was split in two," she explains. "I wanted to survive, and I wanted to escape from the suffering." She wavered back and forth between these two impulses. Her doctor always managed to convince her to hang on, telling her that life still had much to offer her; She just needed to wait and see. His energy would succeed in lifting her spirits for a few days, and then she would slide back to the bottom again. Kazuko attempted suicide several times, and for a while she also engaged in self-harm.

> "Maybe one advantage of having this illness is that I can now feel compassion for other sensitive people."
>
> – *Kazuko Shiraishi*

Her last hospital stay was in 2009. She still doesn't feel fully recovered, but her body has told her that she's getting better. The same way the ability to see colour had abandoned her, it returned. One morning she awoke and looked at her lamp. It was no longer pale grey. "The lamp was amber. And my body felt so alive." She hurried out to the kitchen to test whether she could also taste again. Years before, when she had clung to her waning sense of taste, she sought to rouse it with spicy foods. Not now. "I drank some milk," Kazuko recalls. And she was able to taste it.

In her power

In Japanese culture, vulnerability can present itself as a pitiful failing and trigger a sudden plunge in your worth in the eyes of those around you. Better to hide your suffering behind an expressionless face. Better to endure loneliness in private, rather than in the glare of public disapproval. A few years before, Kazuko had despised and punished herself harshly for not being able to control her tears. She is no longer that woman, she says now. She allows herself to accept help from her family, her family doctor and the local psychiatric day care centre. She goes there regularly, several days a week, joining other people with brain disease. Here she's found new friends – people she laughs with, plays volleyball with, listens to without judging. "Maybe one advantage of having this illness is that I can now feel compassion for other sensitive people."

She didn't undergo this transformation because anyone demanded it from her. One reason it occurred was simply because she took note of how her family doctor spoke to her. She made up her mind. The way that her doctor dealt with her – she could deal with herself in that way too. It lay in her power.

"I decided to be kind to myself," Kazuko says.

1) http://www.japantimes.co.jp/opinion/2012/05/13/editorials/married-women-as-abuse-victims/#.UpR2wr57yQM

More about Kazuko Shiraishi

AGE
46

MARITAL STATUS
Divorced, no children.

RESIDENCE
Tokyo, Japan.

MOST RECENT HOSPITALIZATION
2009

FAMILY
Kazuko lives with her mother, older brother, sister-in-law and their two young daughters.

OCCUPATION
Former office clerk, now supported by her family.

DIAGNOSIS
Major depressive disorder.

CAREGIVERS
Kazuko goes to a psychiatric day care centre and sees her family doctor regularly.

HOW WOULD PEOPLE LIVING WITH DEPRESSION LIKE OTHER PEOPLE TO DEAL WITH THEM?

“

We would like you to be
patient with us. It may take
us many years to recover.
And maybe the illness
will be lifelong.

“It’s good if you keep an eye on us –
but without too much intervention
and demands. Sometimes those
things can trigger a worse outcome.
Just sit next to us instead.
Stay with us.

”

– Kazuko Shiraishi

MORE ABOUT DEPRESSION

Depression is a serious medical condition that is associated with a series of symptoms including melancholy, loss of energy, difficulty in concentrating and suicidal thoughts. These symptoms can have a great impact on daily life. Due to chemical changes in the brain, people with depression may experience long-lasting feelings of sadness and anxiety, have unexplained aches and pains, and suffer from poor quality of sleep and/or lack of interest and energy.

Depression knows no boundaries and it can present itself in a multitude of ways. Each patient experiences a cascade of physical and psychological sensations that he or she will understand and communicate through a particular cultural lens. Broadly speaking, Western cultures tend to emphasize psychological symptoms – feeling blue or moody – while Asian cultures tend to emphasize physical symptoms.

350

MILLION WORLDWIDE

Estimated number of patients[1]

3

WORLDWIDE

Rank according to WHOs disease burden[2]

30%

PATIENTS

Fewer than 30% of patients with depression have access to appropriate treatment[3]

---

1) http://www.who.int/mediacentre/factsheets/fs369/en/index.html
2) http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
3) http://www.who.int/mental_health/management/depression/who_paper_depression_wfmh_2012.pdf

SOLVING THE PUZZLE OF THE BRAIN

In recent years, researchers have taken important steps towards understanding how brain diseases develop and why they evolve the way they do. This knowledge may lead to new and improved treatments – which gives renewed hope to patients and their families.

The human brain is one of our most important organs. At the same time, the brain is extremely complex. It consists of more than 100 billion nerve cells, and each individual cell may be connected to as much as 10,000 other nerve cells.

It is a difficult task to develop drugs for brain diseases such as schizophrenia, depression, Alzheimer's and Parkinson's disease. A successful drug requires highly specialized competencies, many resources and a long-term, dedicated effort.

According to WHO, the societal burden of brain diseases is just as high as those of heart diseases and cancers combined. Over 700 million people suffer from brain diseases[1] and in the EU alone these diseases cost society EUR 350 billion in lost productivity.[2] The illnesses have great implications for the patients, whose life expectancy is 10-20 years shorter than for non-sufferers.[3]

"We know that innovation is the key, when solving the puzzle of the brain and in order to succeed bold decisions have to be made. We seek to develop completely new types of treatment which will enable us to treat brain diseases at an earlier stage of the illness, and also make it possible to treat patients who are currently untreatable," says Kim Andersen, head of Lundbeck's research.

Researchers are optimistic, not least due to the last 10 years which have seen considerable scientific breakthrough in the understanding of brain diseases.

Great ambitions

Researchers are currently fighting on two fronts. They are trying to refine medications which attack already known neurotransmitters – such as serotonin, dopamine and norepinephrine – in order to make medications more focused and cause fewer side effects. At the same time, they are also trying to identify new approaches which can be used to develop new drugs.

One of the great ambitions is to influence the underlying disease biology and slow down the progression of diseases, which currently can only be treated on the basis of their symptoms.

"The research in neurological diseases such as Alzheimer's and Parkinson's disease is where cancer research was 20 years ago. And just like cancer has progressed from being a death sentence to often being treatable and in some cases curable, the next few decades will see far more effective treatments for a variety of neurological diseases," explains Kim Andersen.

The key to treatment

Researchers have identified a number of specific gene mutations which predispose for Alzheimer's and Parkinson's disease, respectively. This insight into some of the underlying causes of the diseases can be used to develop new drugs that influence the underlying disease biology. Furthermore, knowledge of the activities of several specific proteins can lead to new therapeutic angles in the treatment of the two diseases.

"The proteins are both natural and essential, but when you get older, the brain's capacity to process 'waste products' may begin to fail, resulting in the proteins accumulating and spreading into the nervous system. The process begins many years before the disease can be observed in the patients, so an understanding of the proteins may be the key to treating patients earlier and more effectively," says Kim Andersen.

For more than 100 years, scientists have been aware that patients with Parkinson's disease develop insoluble lumps consisting of the protein alpha-synuclein in the brain as the disease progresses. And it has long been assumed that by influencing this protein, the progression of the disease may be slowed down. Lundbeck has now identified a number of antibodies which can bind to alpha-synuclein, and one of these antibodies has shown a positive effect on Parkinson's disease in animal testing.

"By influencing alpha-synuclein with an antibody, we may be able to delay the disease and prevent it from spreading to the nervous system. In this way, we can prevent the emergence of secondary symptoms and at best stop the progression of the disease," says Kim Andersen.

The project is so innovative that it has attracted both attention and research funding from the Michael J. Fox Foundation, which is one of the world's leading centers for Parkinson's research.

Similarly, tau- and beta-amyloid accumulate in the brain of Alzheimer's patients. These proteins form insoluble compounds over time, which create a poor environment in the brain.

In partnership with one of the world's leading experts in tau-research, Professor Einar M. Sigurdsson from New York University, the Danish researchers are trying to develop a therapeutic antibody against the tau-protein. As part of this process, they are also working on finding a diagnostic marker, which enables them to evaluate at an early stage whether a given antibody has an effect or not. It will make the otherwise expensive and time-consuming studies more focused and hence shorten the path to a possible treatment.

Schizophrenic mice

Researchers are also finding new ways in terms of psychiatric disorders such as depression and schizophrenia. An international research collaboration, which includes Lundbeck, has recently shown that certain variations in the human genome have a direct impact on the brain and are associated with impaired intellect and functional ability in people with these variants.

> "In place of the current one-size-fits-all treatment, a sharper biological classification of patients will enable us to increasingly provide tailor-made treatment of specific patient subgroups."
>
> – *Kim Andersen*

The findings are interesting, because the genetic variations increase the risk that carriers develop the debilitating and life-threatening brain disease schizophrenia. This means that the new research is a breakthrough in the understanding of the causes of developing schizophrenia, and the results have been published in the renowned scientific journal Nature.[4]

"Our research gives hope that in the future we can develop medications which might reduce some people's risk of developing schizophrenia, and we can also develop treatments for the so-called cognitive symptoms, which deal with functional capacity and are associated with the disease," says Kim Andersen.

The research team behind the findings have been joined as part of the comprehensive European Innovative Medicines Initiative (IMI) – NEWMEDS cooperation, where universities and pharmaceutical companies are working together to provide a greater understanding of depression and schizophrenia. Without this unique collaboration, the new knowledge would never have been generated.

Lundbeck has for several years been doing research into the importance of gene variations in schizophrenia and have in this context for example developed mice with these genome variations. Hence, these mice have the same basic biology as humans suffering from schizophrenia, and are therefore very useful in studies of the disease.

"Within the foreseeable future, the diagnosis of brain diseases will be defined on the basis of biological characteristics. A sharper biological classification of patients will enable us to increasingly provide tailor-made treatment of specific patient subgroups," says Kim Andersen.

Anesthetic against depression

Existing treatments of depression are effective by influencing so-called neurotransmitters in the brain. More than 50 years of research has resulted in great progress, but it remains a challenge that around one third of patients do not respond to their given treatment. Helping this patient population requires alternative thinking.

Research has shown that ketamine, which is a known anesthetic, has a remarkably efficient and rapid effect on severely depressed patients. The use of ketamine has many adverse side effects, such as hallucinations, agitation, nausea and possible addiction. Hence, there is a need to develop new drugs with the same effect, but without the adverse side effects.

Ketamine works through the neurotransmitter, glutamate, which is one of the key neurotransmitters in the brain. With a better understanding of how this signaling agent is imbalanced in depressed patients, the goal is to develop new treatments for both depression and anxiety.

In recent years, researchers have also found that depression is associated with neuroinflammation, which is an 'inflammatory condition' in the brain involving the so-called microglial cells. The normal function of microglial cells is that they are activated by brain injury such as stroke or trauma, where they contribute to eliminate dead cells and infectious microorganisms.

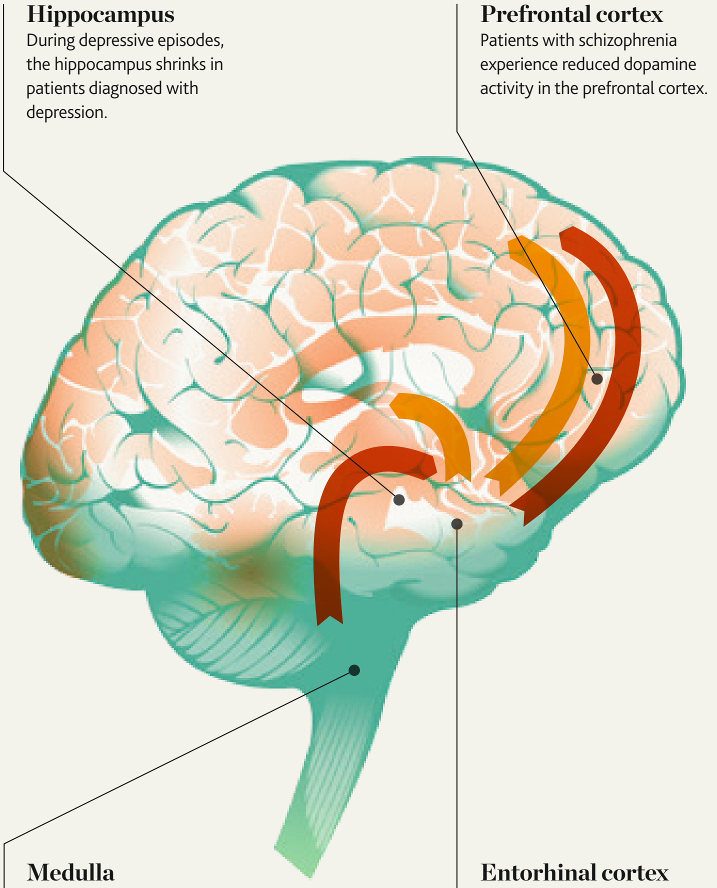
In various disease-induced imbalances, the activity of microglial cells is not correctly regulated, and it can worsen the medical condition. Studies have shown that patients suffering from depression have an upward regulation of inflammatory components in both the brain and body. Early-stage research projects are trying to determine whether patients, who cannot be treated with conventional antidepressants, are suffering from such inflammatory conditions, and whether influencing these can lead to a new type of treatment.

Big questions necessitate cooperation

Due to the great complexity of the brain, scientists all over the world have realized that it requires new ways of cooperation, if we are to achieve results in brain research. Just 10-15 years ago, the industry guarded its research activities and results with absolute secrecy. But this attitude led to a waste of resources and hindered innovations. It was unthinkable to share knowledge with each other, and different research teams were at risk of reproducing the same negative result over and over again. At the same time, the researchers' questions only managed to build on their own core competencies. It made it difficult to ask fundamental questions about the biology of brain diseases such as: Is schizophrenia one single disease? Or does it consist of several diseases? In order to find such answers, researchers need to integrate a wide variety of disciplines such as genetics, chemistry, molecular pharmacology and clinical psychiatry.

To increase the understanding of the biology behind these diseases and develop new effective drugs, Lundbeck's researchers cooperate with universities at the basic research level and enter strong industrial partnerships.

"Some questions are so comprehensive that they cannot be asked separately, and the answers cannot be found by individual players alone. Cooperation is necessary," concludes Kim Andersen. L



Hippocampus
During depressive episodes, the hippocampus shrinks in patients diagnosed with depression.

Prefrontal cortex
Patients with schizophrenia experience reduced dopamine activity in the prefrontal cortex.

Medulla
The accumulation of the protein alpha-synuclein in patients with Parkinson's disease originates in the brainstem and spreads first to the basal ganglia and later to the cerebral cortex.

Entorhinal cortex
The accumulation of the protein tau in patients with Alzheimer's disease originates in the entorhinal cortex and later spreads to hippocampus and the cerebral cortex.

R&D at Lundbeck

- More than 1,200 employees work in Lundbeck's R&D units. In 2013, approximately 20 percent of Lundbeck's revenue was invested in research and development.
- It takes 12-15 years from the researchers get a great idea until a finished drug is ready.
- The average cost of developing a new drug is DKK 10 billion.

Strategic partnerships

Lundbeck's partners come from many different parts of the global scientific community:

- Academic partners: King's College (UK), New York University (US), Mayo Clinic (US) and Heidelberg University (Germany) among others
- Foundations: The Michael J. Fox Foundation (US), The Danish National Advanced Technology Foundation (DK) among others
- Biotech companies: Vernalis plc. (UK), Genmab A/S (DK), Ossianix, Inc. (US) among others
- Pharmaceutical companies: Otsuka Pharmaceutical Co., Ltd. (JP), Takeda Pharmaceutical Company Limited (JP), Merck & Co., Ltd. (US) among others

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1) http://www.who.int/mediacentre/factsheets/fs220/en/index.html http://www.who.int/features/qa/55/en/index.html
2) Gustavsson et al. Cost of disorders of the brain in Europe, 2010. European Neuropharmacalogy, 2011. Wittchen, H.U. et al. The size and burden of mental disorders and other disorders of the brain in Europe, 2011.
3) http://alert.psychiatricnews.org/2011/07/people-with-serious-mental-illness-have.html
4) http://www.nature.com/nature/journal/v505/n7483/full/nature12818.html

WHY DO YOU KEEP LOOKING AROUND, GARY?

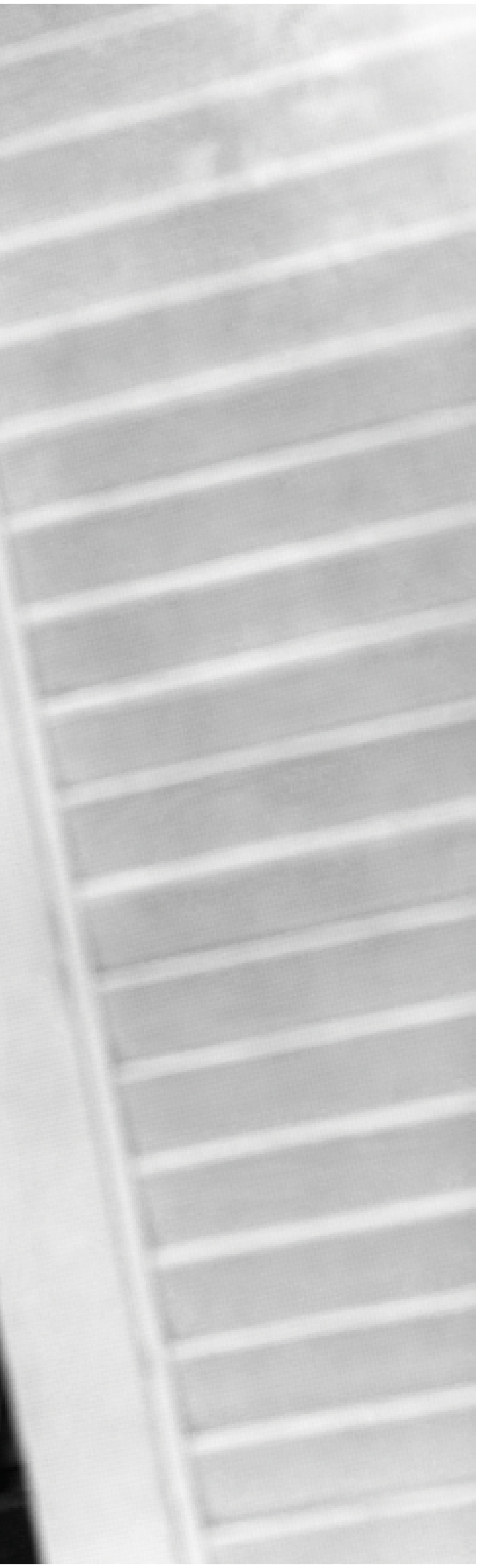
Ever since he was young, Gary Chanco has been able to hear a malevolent voice that speaks to him. Gary's mind is a painful place to be – and often, the outer world feels just as threatening to him as his inner one. Yet he has found some places of refuge.

Gary Chanco turns on the hot water. He enjoys taking long showers, especially if he feels a panic attack approaching. Suddenly he hears a voice speaking. Is it a stranger's? Is it part of himself?

He knows the voice intimately. It has spoken to him since he was a teenager, and now, at the age of 59, he hears it a couple of times a week. On this November morning, it suggests to him, in its usual conversational tone, that he turn the hot water all the way up so that he will scald himself.

A conservative family in an archconservative Florida city: that's where Gary grew up. His father was the pharmacist in the local hospital and Gary's parents kept a certain precarious health condition of his father's well hidden from the surrounding world. Already in kindergarten, Gary felt he was different. "I would wonder: *Why are the kids looking at me funny?* I suffered from insomnia problems even then, and could never take a nap with the other kids on the mat."

A few years later, Gary was the chubby boy in class who loved to watch cartoons on television; a stuffed Huckleberry Hound lay in his room. The exterior world was an unsafe place. *Why do you keep looking around, Gary?*



> "I kept it to myself. I figured maybe everybody hears voices. Or maybe this is a voice from beyond the grave?"
>
> – *Gary Chanco*

his classmates would ask. That question had two answers, and he was unable to say either one. The first was that he was afraid of being beaten up by the bigger boys. As an adult, Gary still remembers distinctly the words that one bully shouted at him after giving him a thrashing. The second answer was that he was becoming more and more convinced that someone might stab him from behind with a knife. Anybody. He had to look over his shoulder to check who might be lying in wait. And then check again.

I kept it to myself

The first time the voice spoke to Gary, he was 12 or 13 and out biking. As he remembers it, the voice simply ordered him to bike home. After that, its message was always the same, albeit with endless variations. *Gary?* the voice said. *Why don't you slash your wrists. Shoot yourself in the head. Jump in front of the train.*

Gary had always been a quiet boy, and now, as he sought to accustom himself to the voice, he grew almost mute. "I kept it to myself. I figured maybe everybody hears voices. Or maybe this was a voice from beyond the grave." At home, there might go several days during which he didn't say anything other than *Pass the mashed potatoes, please.* In school, he sat in the back row to make himself invisible. And at night he lay awake while everyone else slept. But it became harder and harder to slip under everyone's radar. To wheel around to avoid the raised knife. To not know when the voice might speak to him again. In the end, Gary forced himself to ask his parents if he could talk with a psychiatrist. But they resisted. Couldn't he just think of something else? Gary's father was especially opposed. If it became known that his son was mentally ill, what good did it do for him to conceal his own illness? For Gary's father suffered from severe chronic depression, which was being treated with electroshock therapy at another hospital than his own.

Nonetheless, Gary ended up with a psychiatrist, who decided to admit him to a psychiatric ward. Gary remained there for five months and celebrated his 16th birthday with some fellow patients as guests. Each of them got a slice of chocolate birthday cake with chocolate frosting. ➔

A prison for patients

Gary has been in and out of mental hospitals ever since; he himself guesses that he's had 15 hospitalizations. Until his early forties, he managed to support himself with jobs as a dishwasher and janitor; one treasured memory is the few good years he worked as an assistant in a computer lab. "I was able to hide my illness and was never fired from any job. But usually I'd quit after a year or so. It's hard to do a good job and fight mental illness at the same time."

Many Americans suffering from severe mental illness find themselves receiving less than adequate care at some point. Particularly in Florida, which ranks 49th among the 50 states in terms of per capita mental health funding.[1] For Gary, it happened in the middle of the first decade of the 2000s, when after several tumultuous years he landed in an assisted-living facility. The place was situated in a dangerous neighbourhood, and he had to share a room with three other men who also suffered from severe mental illness. Each of them watched the others suspiciously; were his roommates planning to steal his sparse belongings?

In the mornings, Gary sometimes woke to a cockroach scurrying up his arm. The management skimped on residents' food, and his diabetes grew worse. He still remembers the woman who distributed medicine throwing his pills on the floor. *Why'd you drop them?* she smirked as he gathered them up.

For Gary, rescue arrived in the form of his outpatient case manager at the local mental health centre. She managed to wangle him a place on the waiting list for a better-funded, more secure residential facility. Almost two years later, it was finally his turn, and Gary was able to leave the place he remembers as "a prison for patients." After his numerous moves over the years, he says that most of his belongings have been scattered. One of the few things he took with him that time was Huckleberry Hound. And a photo album.

A few weeks one summer

These days, Gary's life has achieved a fragile peace, though his health has been compromised by decades of mental and physical illness. He manages to look after his small apartment, and he is surrounded by a network of caregivers – including a life coach who comes every Wednesday from the mental health centre to see him.

A new person entered Gary's life in 2012. Not a treatment provider, and not a new acquaintance either. But a boyfriend. He's the first boyfriend that Gary's ever had, and the relationship has helped draw him out of his shell. "I've been lonely for most of my life. Looking back, I feel sad about my failure to commit to a relationship."

Here's what Gary's parents often said to him: *Don't look at boys like that.* Here's what the bully from school shouted after beating him up: *That's for being a faggot.* And here's what he keeps hidden in his photo album: two pictures of himself with another boy. They're teenagers. He seldom looks at these pictures, for they need to be protected from yellowing. But he thinks of the boy in the picture often. "We can call him Bob, even though that's not his name. We were close for a few weeks one summer, and I think it's the deepest connection I ever had in my life. We hugged and he wanted to take it further. I was afraid to. And I've regretted it ever since."

A stable point

Every Sunday morning, Gary can be found in a low white building on a residential street close to the ocean. Here, he joins a community that he first discovered 35 years ago, a community that has functioned ever since as a stable point in an otherwise turbulent life. "These people are largely what keep me going. They all accept me for who I am."

He's referring to the Unitarian Universalist Church, which has its roots in liberal Christianity. On Sundays, Gary operates the sound system during the service. And on every fourth Thursday, a good 250 people show up at the church's soup kitchen for a free meal. Gary oversees a team of up to eight volunteers, who serve food and drinks to the hungry crowd. Many of the guests are homeless, many mentally ill.

He could well have been one of the people who stand in the food line, Gary says. "Without the love and support of the church, I'd probably be homeless." He smiles a little. "I would be the one receiving food, rather than the one handing it out."

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1) Florida Council for community mental health; http://www.fccmh.org/news/docs/Press%20Release2-5-13.pdf

More about Gary Chanco

AGE
59

MARITAL STATUS
In a relationship, no children.

RESIDENCE
Florida, USA.

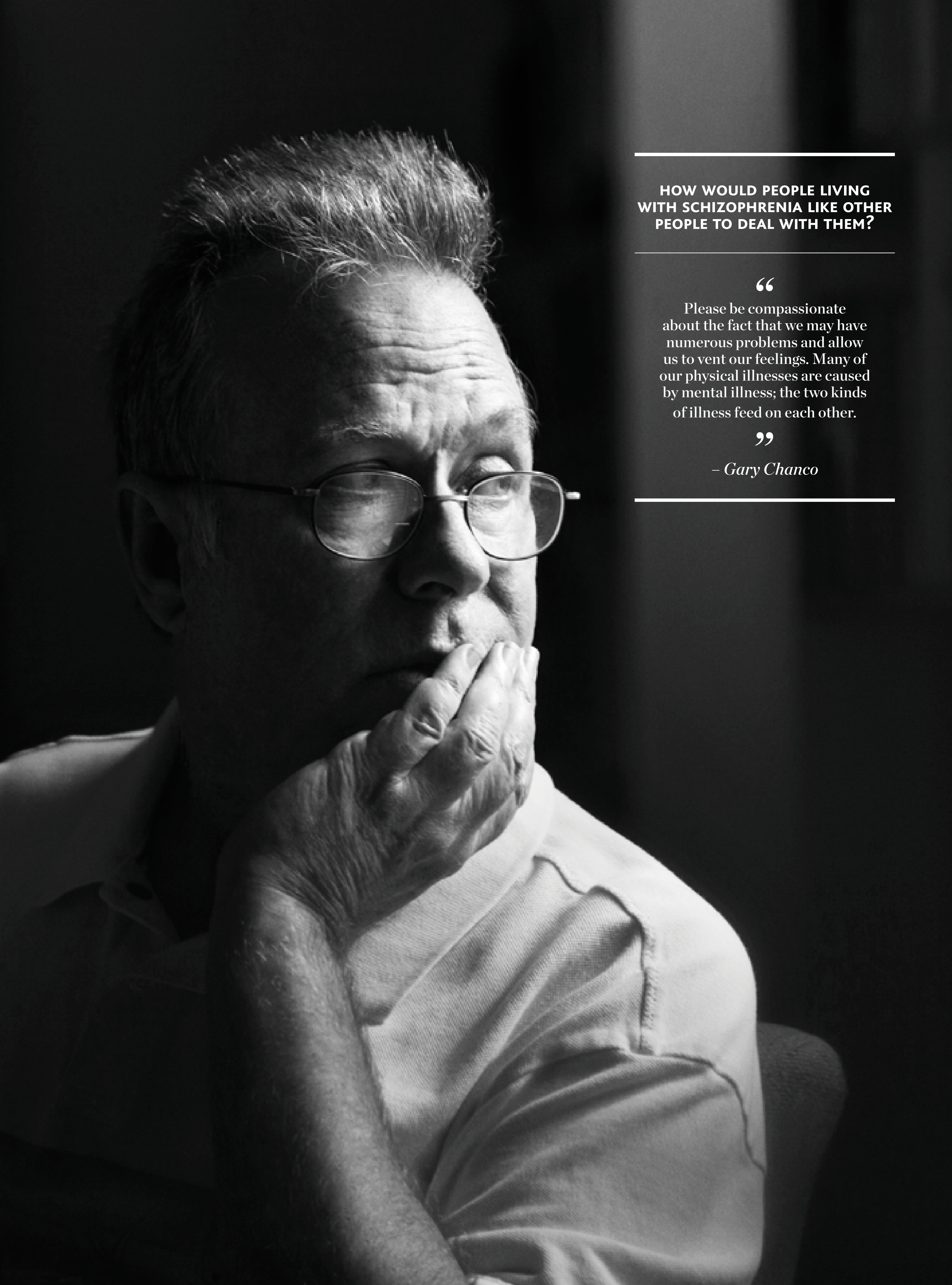
MOST RECENT HOSPITALIZATION
2011, for depression.

FAMILY
Gary's parents and older brother are deceased. His contact with the rest of his family is very sporadic.

OCCUPATION
Menial jobs until 1995, after which he began receiving a disability pension.

DIAGNOSIS
Schizophrenia with various co-morbidities, including bipolar disorder, obsessive-compulsive disorder, panic disorder, diabetes and hypertension.

CAREGIVERS
Gary receives assistance from the local mental health centre and from Volunteers of America, a charitable organization that provides help to the mentally ill. Since 1979, he's also received a great deal of support from the local Unitarian Universalist Church.



HOW WOULD PEOPLE LIVING WITH SCHIZOPHRENIA LIKE OTHER PEOPLE TO DEAL WITH THEM?

> “Please be compassionate about the fact that we may have numerous problems and allow us to vent our feelings. Many of our physical illnesses are caused by mental illness; the two kinds of illness feed on each other.”

– *Gary Chanco*

MORE ABOUT SCHIZOPHRENIA

Schizophrenia is a psychotic disorder, often life-long, which may lead to marked changes in a person's perception of reality. It carries a notable 'stigma' and is often misunderstood. People with schizophrenia experience disturbed thoughts, emotions and behaviour. Schizophrenia is caused by an imbalance in the chemicals that send signals to the brain, leading to the perception (seeing/hearing/thinking) of things that are not real.

Oral atypical antipsychotics are the most commonly used treatments for schizophrenia, but many patients are not adherent to their treatment. Poor insight is considered to be one of the main factors that predisposes an individual to problems with adhering to treatment. Since non-adherence is a major risk factor for relapse, there is a significant unmet need for treatments that can improve adherence and maintain functioning with fewer side effects.

26

MILLION WORLDWIDE

Estimated number of patients[1]

12

OVERALL

Rank according to WHOs disease burden[2]

60%

PATIENTS

Patients with schizophrenia is non-adherent to their treatments[3]

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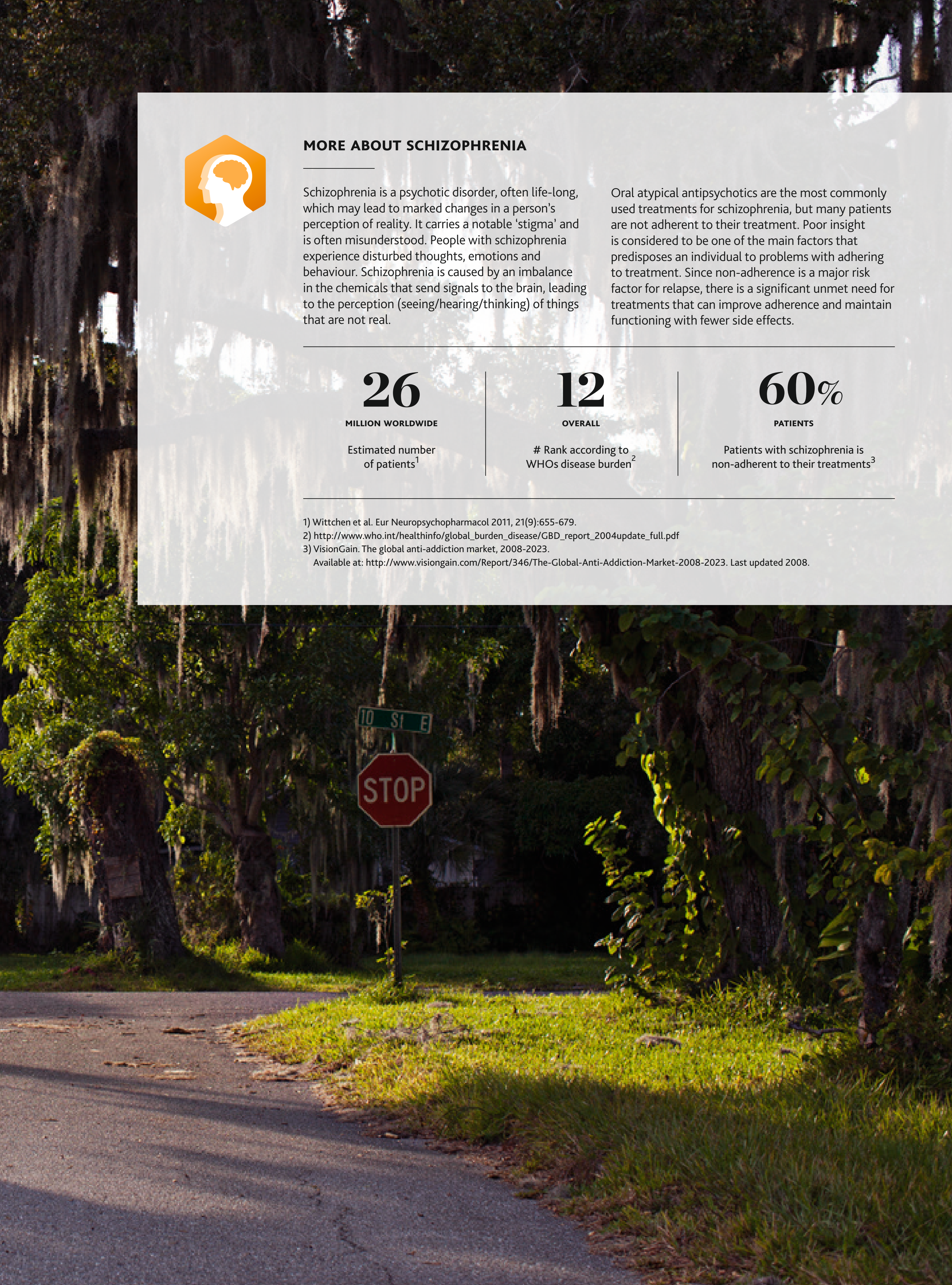
1) Wittchen et al. Eur Neuropsychopharmacol 2011, 21(9):655-679.
2) http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
3) VisionGain. The global anti-addiction market, 2008-2023.
Available at: http://www.visiongain.com/Report/346/The-Global-Anti-Addiction-Market-2008-2023. Last updated 2008.



FROM IDEA TO PATIENT

1 700 MILLION IN THE WORLD

According to the World Health Organization (WHO), 700 million people worldwide live with brain diseases. These are serious and life-threatening illnesses that affect not only patients' quality of life, but also that of their families and friends. For society in general, brain diseases also have major economic consequences. During the past 50 years, novel drugs have revolutionized the possibilities of treatment. However, there is still a huge unmet need. The development of new and innovative drugs is pivotal.

2 FROM IDEA TO DRUG CANDIDATE

Lundbeck has research units in Denmark, China and in the US. The basis for developing a new drug is deep insight into the disease itself, and into the unmet needs of patients. The process from an idea to a drug candidate is complicated. Researchers work to identify where in the human organism a new drug must act and to test substances for efficacy, side effects and toxicity. If a substance passes all of these tests, it becomes a drug candidate. This process typically takes between three and five years.

3 FROM CANDIDATE TO APPROVED DRUG

Lundbeck conducts the development activities that are necessary for a drug to be approved in some 40 countries around the world. First, a substance is tested in healthy persons for its tolerability, assimilation and distribution in the body. Following this, its efficacy and side-effect profiles are tested in a small group of patients. In the third and decisive phase, the drug is tested in a large group of patients. Developing a new drug is very demanding, and normally takes between eight and ten years.

4 PRODUCTION AND PACKAGING OF DRUGS

A drug must be safe and efficacious. It must also be possible to produce it in large amounts and in a manner that enables patients to take the drug and assimilate it optimally in the body. Lundbeck manufactures its own drugs in Denmark, China, France and Italy. Lundbeck also collaborates with a number of other companies on various phases of the production process, ranging from supply of raw materials and semi-finished products to pharmaceutical production and packaging of the drugs.

5 MAKING A DIFFERENCE TO EACH PATIENT

Lundbeck's drugs are registered in approximately 100 countries. As the products are prescription drugs, doctors decide when patients will benefit from them. Lundbeck's own representatives are in charge of spreading the knowledge of our products to doctors in 57 countries. Further the knowledge is spread through publications in scientific journals, participation in scientific conferences, and through meetings with doctors and specialists.

BOTTLES HIDDEN IN THE LAUNDRY BASKET

Alcohol played many roles in the life of Bente Karlsen Røstad. But an alcoholic? Surely not. And so she didn't need to ask for help.

On her 25th birthday, Bente goes downtown with a bunch of girlfriends, and a giddy mood seizes her. Yes! she says when the men come over and ask her to dance. Wine and beer stand on the table.

An evening on the town – it's something most young women know well. But Bente is savouring it for the first time. She's a novice when it comes to drinking alcohol and flirting. The mother of three small children, she's only recently broken free from a difficult marriage. Tonight she feels how, when she's in a group, a gentle buzz can elevate her. She becomes a Bente who dares to speak with others, a Bente who's no longer shy. "I thought: Why haven't I done this before?" she says today of that birthday evening in 1992.

A reliable sleeping aid

Things kept getting better: she started seeing a childhood friend who was affectionate to her and the kids. Bente considers John the first adult she seriously bonded with. But after they had been together for five years, he died of cancer at the age of 30.

Red wine now assumed a role in Bente's life as a reliable sleeping aid. "It was then I began to drink," she explains. "To avoid crying, and to be able to sleep." She never spoke of her grief. Her efforts were directed toward suppressing emotions so that she could be strong.

In time, it worked for her. Bente was a certified cosmetologist, took care of her children, and after a few years fell in love again. Her new boyfriend's drinking habits fascinated her. "He drank openly every day! I envied him his freedom to be up front about it. Right on! I thought. And so I began to drink like him." He enjoyed drinking a couple of beers while he made dinner; Bente would sit and watch him, and it felt very cosy.

Some things were not so cosy. "We thought of ourselves as an ordinary couple," Bente relates. "But in Norway, alcohol is expensive, and we did whatever we could to be able to drink. We stopped doing things with the children, didn't go on holiday, didn't buy new things." And she continued to drink secretly – though now she had switched over to 120-proof liquor.

She was diagnosed with depression in 2001, but that didn't change her drinking habits. Instead, she used the diagnosis to justify her use. "I'd had a tough life and was having a hard time psychologically – and so perhaps I drank a bit much."

"We did whatever we could to be able to drink. We stopped doing things with the children, didn't go on holiday, didn't buy new things."

– Bente Karlsen Røstad

Not an alcoholic

Today, Bente estimates that she abused alcohol from 1996 to 2003. At the end of this period, she could consume up to an entire litre of liquor a day. If a social worker had made an unannounced visit, he or she would have found a spotless home, food in the fridge and the children's clean clothes folded neatly. Bente's bottles were well hidden, one in the laundry basket and another on the top shelf behind her woollen jerseys. "So during the course of a day, I'd walk back and forth between the bottles 8 or 10 times. No one would give it a second thought if Mom went out to the laundry room."

The children might not have seen her drinking from the concealed bottles, but they did see a mother with tears sliding down her face while she vacuumed. They tried to cheer her up the best they could. They never bugged her for more pocket money. They kept their rooms perfectly tidy. And they begged, again and again, to put on "shows" for her, to try and entertain her by singing and dancing. Sometimes she told them that she didn't have time. Other times, she would sit down and play audience – and stare right through them. "I was completely elsewhere," she says now. "They couldn't get me to be present."

In all these years, Bente didn't consider herself an alcoholic. Alcoholics? They lived on the street, they stank, they drank without shame. No one could point a finger at her home; she smelled good, and the subject of "Mom's drinking" wasn't a subject at all. Her children and her boyfriend didn't mention it, and she certainly didn't either. And that's the way it had to go on being. Bente remembers that once in a while, someone around her would make a comment that she would pointedly ignore. And when on one occasion a teacher reported the family to the child protection agency, saying there must be something wrong at home, she managed to get herself out of that scrape as well.

A lovely evening

The front she put up would hold. Yet everything else was in pieces. "I had promised myself that I'd be a mother who put her children first," Bente says. "Now I was failing them, and I didn't even think of asking for help. I thought: How long can I keep it up?"

One September day in 2002, she felt her spirits lift. That evening they would enjoy themselves, she decided; the kids' favourite food was shrimp, and that what they ➔

would have. That day, she didn't drink, and it did turn into a lovely evening – and in their eyes too, they later told her.

When everyone had gone to bed, she poured a splash of liquor in her coffee and began to write the letters she'd planned, one addressed to each child. As she did, she drank coffee and swallowed the drugs she had set aside: some sleeping pills and John's cancer medications, which she'd saved without quite knowing what she would use them for. But she knew for what now.

Outside it was drizzling. She had on her nicest pants, and she walked down to Svarttjønn, a small lake a 10-minute walk away. Her plan was to be just boozed up and drugged enough to execute the deed. When her legs began to buckle beneath her, Bente was able to glimpse the water through the darkness, and she broke into a trot to reach it in time.

Joining the drunks

A few weeks later, Bente sat knitting in the day room of a psychiatric ward. Her suicide attempt had failed. She couldn't remember a thing, but had been told that she'd been found unconscious just by the water. One thighbone was broken. Otherwise, she'd come to no harm. Bente was dumbfounded: "I couldn't even manage to do that! How could that be?"

While she was hospitalized on the closed ward, she pleaded for extra drugs. And as soon as she'd been transferred to the open one, she went out to buy liquor. The bottle she kept hidden in her knitting. "How did you dare? people asked me later. But what could they do to me there? Throw me out? I couldn't care less."

The staff didn't confront her about the bottle in her knitting. But they must not have been deaf and blind. One caseworker began to prod her about her drinking habits; would she consider a transfer to a detox clinic? Bente's temper flared – there was no reason for that whatsoever. Not in the least! Didn't her daughter agree that the suggestion was ridiculous? But the girl merely said, "Mom, you do need help."

So Bente relented – reluctantly. Good thing no one can see me now, she thought. For now I'm joining the drunks. But there wasn't anything revolting about the other patients: housewives, young women, a banker. One group in particular caught Bente's attention. They all sat together at meals, and they looked completely ordinary. She could often hear them laughing. Who were they? They turned out to be the alcoholics in the long-term treatment group.

On her last day in clinic, Bente turned over a leaf as a new woman – a woman who wished to ask for help. When the doctor made her rounds, Bente was ready with a question. "I asked her if I could start group treatment with the others. I had no idea what I was getting into, yet I asked if I could anyway." The doctor gazed at her. "You surprise me," she told Bente. "But I really think you should."

> "I asked her if I could start group treatment with the others. I had no idea what I was getting into, yet I asked if I could anyway."
>
> *– Bente Karlsen Røstad*

More about Bente Karlsen Røstad

AGE
46

FAMILY
Three grown children,
three grandchildren.

MARITAL STATUS
Widow.

OCCUPATION
Bente worked previously as a cosmetologist, among other things. Today she is a project manager for a drug-abuse organization and a night duty officer at a shelter for people with substance abuse problems. She's also trained as a gestalt therapist.

RESIDENCE
Kristiansand, Norway.

DIAGNOSIS
Between 1996 and 2003, Bente slid into a pattern of growing alcohol abuse. In 2001, she was diagnosed with depression, an illness that she has subsequently recovered from. In 2002, she was diagnosed with alcohol dependency. She hasn't drunk alcohol since 2003.

TREATMENT
In 2002, Bente was admitted to the drug and addiction clinic at her local hospital and entered group therapy in connection with her hospitalization. She remains active in Narcotics Anonymous and meditates regularly.

HOW WOULD PEOPLE LIVING WITH ALCOHOL DEPENDENCY LIKE OTHER PEOPLE TO DEAL WITH THEM?

> “
> Speak up if you get the sense that something is wrong. Try to say it gently without accusing. Risk saying what you actually are afraid to! Risk that the person you talk to will get upset! I only wish that people had dared to be more direct with me. I wish they had thought more about my kids than about me.
> ”

– Bente Karlsen Røstad

MORE ABOUT ALCOHOL DEPENDENCE

Alcohol dependence is a brain disease, characterized by a pattern of alcohol consumption potentially leading to physiological, psychological and social impairment. Excessive drinking increases a person's risk of developing more than 60 other diseases. Excessive alcohol consumption is also associated with a large cost to society due to accidents, violence, lost productivity and healthcare costs.

Extensive research over the past 20 years has contributed to our understanding of alcohol dependence as a brain disease. However, many patients with alcohol dependence remain under-diagnosed and under-treated. This is partly due to the fact that alcohol dependence still suffers from the general perception of being a personal weakness and character flaw rather than a treatable brain disease.

14

MILLION IN EUROPE

Estimated number of patients[1]

17

OVERALL

Rank according to WHOs disease burden[2]

80%

PATIENTS

Patients with alcohol dependence remain undiagnosed, and less than 10% receive treatment[3]

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1) http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
2) http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
3) Byerly M et al., Psychiatry Res., 2005 Feb 28;133(2-3):129-33.

LUNDBECK AT A GLANCE

REVENUE

15bn

Our 2013 revenue reached DKK 15,258 million.

EMPLOYEES

6,000

We are approximately 6,000 employees.

GLOBAL PRESENCE

57

We are headquartered in Denmark and located in 57 countries.

RESEARCH AND DEVELOPMENT

20%

In 2013, approximately 20% of our revenue was reinvested in research and development of new and innovative pharmaceuticals for the treatment of brain diseases.

LUNDBECK FOUNDATION

OWNERSHIP

70%

Our largest shareholder is the Lundbeck Foundation, which holds approximately 70% of the shares. The Foundation annually grants between DKK 400-500 million to support medical research and educational and communication activities.

HISTORY

1915

Lundbeck was founded by Hans Lundbeck almost 100 years ago in 1915. The company was listed on NASDAQ OMX Copenhagen in 1999.

OUR FOCUS

We are a specialized pharmaceutical company engaged in developing new and innovative treatments for brain diseases on the basis of in-house research and external partnerships.

VISION

Our vision is to become a world leader in psychiatry and neurology.

MISSION

Our mission is to improve the quality of life of people suffering from psychiatric and neurological disorders.

VALUES

Imaginative – Dare to be different
Passionate – Never give up
Responsible – Do the right thing

PRODUCTS AND DISEASE AREAS

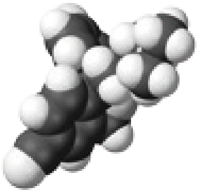
ABILIFY MAINTENA®	*Schizophrenia*
AZILECT®	*Parkinson's disease*
BRINTELLIX®	*Depression and anxiety*
CIPRALEX® **LEXAPRO®**	*Depression and anxiety*
EBIXA®	*Alzheimer's disease*
ONFI®	*Lennox-Gastaut Syndrome*
SABRIL®	*Epilepsy*
SELINCRO®	*Alcohol dependence*
XENAZINE®	*Huntington's disease*

COMPANY & PRODUCT MILESTONES

The history of Lundbeck dating
from 1915 to 2014

1980-1999

Intensified business focus



At the close of the 1980s, Lundbeck further intensified its business strategy focus. In future, Lundbeck would dedicate its efforts to development, manufacturing and commercialization of drugs for the treatment of brain diseases.

Lundbeck expanded rapidly in the 1990s, due to the success of Cipramil® for the treatment of depression and anxiety. Cipramil® got registered in more than 70 countries. To ensure its continued success, Lundbeck intensified its research activities and began in-licensing drugs from other pharmaceutical companies. This enabled Lundbeck to launch new drugs to take over when the patents on other drugs expired. In 1999, Lundbeck got listed on the stock exchange NASDAQ OMX Copenhagen.

1960-1979

The foundation of expertise

Lundbeck's success with Truxal® for the treatment of schizophrenia increased the need for additional production capacity. In 1961, Lundbeck purchased a former creamery in Lumsås, Denmark, and soon began production of active compounds. Between 1960 and 1970, the number of employees doubled to 680, of whom approximately 100 were employed abroad. Lundbeck was becoming an international company.

After 60 years of growth and development based on a wide assortment of products, Lundbeck decided at the end of the 1970s to phase out its existing agencies and cosmetics departments. After that, the company would focus only on development and commercialization of drugs.

1915-1919

The first years

Hans Lundbeck founded a trading company in Copenhagen on 14 August 1915. The company dealt in everything from machinery, biscuits, confectionery, sweeteners, cinema equipment and cameras to photographic paper and aluminium foil, besides renting out vacuum cleaners.

1920-1939

New portfolio

During its first years, the business was operated as a trading company, and from the mid-1920s, pharmaceuticals were added to its range of products. Eduard Goldschmidt was hired in 1924, bringing into the company's portfolio a number of new agency contracts for drugs: suppositories, painkillers, etc. as well as cologne and creams.

2010-2014

Global presence and new products

Geographical expansion and new product launches characterized this period. Lundbeck established a new research centre and a new production facility in China. And a historic agreement was made with Japanese Otsuka Pharmaceutical Co., Ltd. to deliver innovative medicines targeting psychiatric disorders.

In 2011, patients in the US suffering from Lennox-Gastaut syndrome were given access to a new treatment option, with the launch of Onfi®. In 2013, Lundbeck took its first steps into a new area, launching Selincro® for the treatment of alcohol dependence. Further in 2013, Abilify Maintena® was launched in the US for the treatment of schizophrenia.

Early in 2014, a new antidepressant developed in Lundbeck's own laboratories, Brintellix®, was launched in the US for the treatment of depression. At the beginning of 2014, Lundbeck employed 6,000 employees in 57 countries.

2000-2009

Expansion propelled by Cipralex®/Lexapro® success

In 2002, Cipralex®/Lexapro® was launched for the treatment of depression and anxiety. It was made available in about 100 countries worldwide and grew to account for the major share of Lundbeck's business operations. In 2003, Lundbeck acquired the US-based research company Synaptic, thereby establishing a research unit as a bridgehead in the US.

In 2009, Lundbeck furthermore acquired Ovation Pharmaceuticals, Inc., establishing Lundbeck's own commercial platform in the US, the world's largest market for pharmaceuticals. Lundbeck also acquired Elaiapharm in France, thereby increasing the company's production capacity. Sabril® was launched in the US for the treatment of epilepsy.

1940-1959

A niche in psychopharmaceuticals

Hans Lundbeck died in 1943, and Poul Viggo Petersen was employed to build up Lundbeck's pharmaceutical research. Thanks to his efforts, Lundbeck was able to create a niche for itself in psychopharmaceuticals.

During the years following World War II, Lundbeck intensified its research, laying the foundation stone for the drugs which would later make Lundbeck world famous. In 1954, Grete Lundbeck, the widow of Lundbeck's founder, established the Lundbeck Foundation for the purpose of ensuring and expanding Lundbeck's business operations, as well as for providing financial support for primarily scientific objectives and the fight against diseases.

In the 1930s, Lundbeck began production and packaging of pharmaceuticals in Denmark. To ensure sufficient manufacturing capacity, the company moved to the Copenhagen suburb of Valby in 1939, where the Lundbeck headquarters is situated today.

Product launches

2014

Brintellix® is launched for the treatment of depression.

2013

Abilify Maintena® is launched for the treatment of schizophrenia.

2013

Selincro® is launched for the treatment of alcohol dependence.

2012

Onfi® is launched for the treatment of Lennox-Gastaut syndrome (epilepsy).

2011

Saphris®/Sycrest® is launched for the treatment of schizophrenia and manic episodes associated with bipolar disorder.

2009

Sabril® is launched for the treatment of epilepsy.

2008

Xenazine® is launched for the treatment of chorea associated with Huntington's disease.

2003

Azilect® is launched for the treatment of Parkinson's disease.

2003

Ebixa® is launched for the treatment of Alzheimer's disease.

2002

Cipralex® is launched for the treatment of depression.

1996

Serdolect® is launched for the treatment of schizophrenia.

1989

Cipramil® is launched for the treatment of depression.

1959

Truxal® is launched for the treatment of schizophrenia.

1940

Lucosil® is launched for the treatment of urinary tract infections.

1937

Epicutan® is launched for the healing of wounds as Lundbeck's first original drug.

Disclaimer:
Not all products are marketed in all countries.

OUR GLOBAL REACH

Headquartered in Denmark, Lundbeck employs 6,000 people in 57 countries, and markets its products in approximately 100 countries. We have competencies and activities throughout the value chain: research, development, production, marketing and sales.

HEADQUARTERS / Denmark
RESEARCH / Denmark, China, USA
PRODUCTION / Denmark, China, France, Italy

SALES
EUROPE / Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, UK

INTERNATIONAL MARKETS / Argentina, Australia, Brazil, Canada, Central America, Chile, China, Colombia, Egypt, Hong Kong, India, Indonesia, Israel, Japan, Korea, Malaysia, Mexico, Pakistan, Philippines, Russia, Saudi Arabia, Singapore, South Africa, Turkey, Ukraine, United Arab Emirates, Venezuela

USA / United States of America

The Lundbeck Foundation

The Lundbeck Foundation is the largest shareholder of Lundbeck, owning 70% of the company. The objective of the Foundation is in part to maintain and expand the activities of Lundbeck as well as of the Foundation's other subsidiaries and portfolio companies through active value-adding ownership, and in part to provide grants for scientific research of the highest international quality in order to make a significant difference to human health and life. The Foundation annually grants between DKK 400-500 million to support medical research and educational and communication activities.

For further information, please visit www.lundbeckfonden.com.

The Lundbeck Institute

The Lundbeck Institute is an international education forum whose mission is to improve the quality of life for persons affected by psychiatric and neurological diseases.

The Institute has an associate faculty of 80 highly respected psychiatrists and neurologists from around the world.

Since it was founded in 1997, more than 4,300 specialists from 65 countries have participated in Lundbeck Institute seminars in Denmark. In addition, seminars are currently offered locally in countries worldwide.

For further information, please visit www.cnsforum.com.

THE LUNDBECK STORY

All over the world brain disease is a growing burden, not only for individuals but for families and societies as well.

An estimated 700 million people worldwide are living with brain disease and far too many suffer due to inadequate treatment, discrimination, reduced number of working days, early retirement and other unnecessary consequences.

Lundbeck is a specialized pharmaceutical company focusing on brain disease. For more than 50 years, we have been at the forefront of research within neuroscience and our development and distribution of pioneering treatments continue to make a difference to people living with brain disease.

We are recognized for having helped hundreds of millions of people suffering from brain disease, such as depression, alcohol dependence, schizophrenia, epilepsy, and Alzheimer's, Parkinson's and Huntington's disease. However, there is still a massive need for help.

Every day, we strive for improved treatment and a better life for people living with brain disease – we call this Progress in Mind.

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