Physical Illness and Schizophrenia

A Review of the Evidence

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This book provides the first comprehensive and systematic review of current research evidence on the prevalence of physical diseases in people with schizophrenia, a disorder afflicting approximately 1% of the global population, and a group with mortality rates twice as high as the general population. The evidence presented will support programmes aiming to increase awareness of these problems and improve treatment. This is the first in a series of books addressing an issue emerging as a priority in the mental health field: the timely and proper recognition of physical health problems in people with mental disorders. It should be read by policy makers, service managers, mental health professionals and general practitioners.

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CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE UNIVERSITY PRESS
Cambridge, New York, Melbourne, Madrid, Cape Town, Singapore, São Paulo

Cambridge University Press
The Edinburgh Building, Cambridge CB2 8RU, UK
Published in the United States of America by Cambridge University Press, New York
www.cambridge.org
Information on this title: www.cambridge.org/9780521882644

First published in print format 2007

ISBN-13 978-0-511-36813-4 eBook (Adobe Reader)
ISBN-10 0-511-36813-5 eBook (Adobe Reader)

ISBN-13 978-0-521-88264-4 paperback
ISBN-10 0-521-88264-8 paperback

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Preface

This is the first of a series of volumes addressing an issue which is emerging as a priority in the mental health field: the timely and proper recognition of physical health problems in people with severe mental disorders.

It is now well documented by research that people with severe mental disorders have a higher prevalence of several physical diseases and a higher mortality from natural causes than the general population. They seem not to have benefited from the recent favourable trends concerning mortality due to some physical diseases, in particular cardiovascular illness. Their access to physical healthcare is reduced and the quality of the physical care they receive is worse as compared with the general population. If we are really concerned about the quality of life of people with mental disorders and wish to protect their civil rights, we cannot ignore the fact that physical health is a crucial dimension of their quality of life, and that access to a physical healthcare of the same quality as that available to the rest of the population is one of their basic rights as human beings and as citizens.

The initial trigger for the preparation of this series of books has been a personal communication to one of us from a physician working with the Médecins sans Frontières in a Central Asian republic. He felt desperate because he was unable to get sufficient resources to deal with the very high mortality of people with schizophrenia admitted to the central mental hospital in the country: according to his account, one person out of two admitted for schizophrenia was likely to be dead at the end of the year in which he/she was admitted for treatment. Some of the excess mortality would be due, like in other countries, to suicide, but a large proportion of those who would die would have a physical disease (e.g. tuberculosis) as the main cause of death.

Indeed, mental hospitals in many countries are often lacking equipment that could help in making the diagnosis of physical illness as well as medications and other material that would make it possible to recognize and treat physical illness. Psychiatrists are reluctant to treat physical illness, perhaps as frequently as doctors in other medical specialties fail to recognize that their patients also suffer from a mental disorder or refuse to provide treatment for it.

Why people with mental illness are more likely to have a physical illness than the rest of the population is only partially known. Part of the answer to this

question may be that some people with mental illness do not pay sufficient attention to their bodies and do not follow elementary rules of hygiene and disease prophylaxis. The fact that they often live in conditions of poverty and are exposed to considerable dangers of violence and abuse might also explain some of the excess morbidity and mortality from physical illness that they have. The fact that people with mental illness may be abusing alcohol or taking drugs and that they are therefore exposed to the health consequences of substance abuse and diseases related to the manner of use of drugs (e.g. hepatitis) may also play a role. There remains, however, a substantial proportion of excess physical morbidity that is not explicable by the above-mentioned factors, and it is therefore necessary to suppose that there are factors that facilitate the occurrence of physical illness and are inherent in people who have mental disorders. Changes in the immune system and hormonal imbalance have been mentioned as being among those factors, but it is obvious that more research will be necessary to unravel the puzzle of high rates of physical illness in people with mental disorders.

In many countries psychiatrists have taken off their white coats, shed the symbols of being physicians, forgetting that they are medical doctors – with a particular interest in mental symptoms but still essentially practitioners of a medical discipline. The creation of the specialty of liaison psychiatry is a sad testimony to the fact that only a small proportion of psychiatrists have an interest in dealing in a comprehensive manner with people struck by illness. There are no liaison internists, liaison dermatologists nor liaison surgeons: when invited to consult other colleagues, they simply do that without creating a subgroup that will be specially trained to do this. The existence of liaison psychiatrists is an unwise message to the rest of medicine: despite having a medical diploma, only a few among the psychiatrists are sufficiently well trained in medicine to be able to deal with patients who have a mental and a physical disease at the same time.

What should be done about this? The first step is raising awareness of the problem among mental healthcare professionals, primary care providers, patients with mental illness and their families. Education and training of mental health professionals and primary care providers is a further essential step. Mental health professionals should be trained to perform at least basic medical tasks. They should be educated about the importance of recognizing physical illness in people with severe mental disorders, and encouraged to familiarize themselves with the most common reasons for underdiagnosis or misdiagnosis of physical illness in these people. On the other hand, primary care providers should overcome their reluctance to treat people with severe mental illness, and learn effective ways to interact and communicate with them: it is not only an issue of knowledge and skills, but most of all one of attitudes.

Another essential step is the development of an appropriate integration between mental health and physical healthcare. There is some debate in the

literature about who should monitor physical health in people with severe mental disorders. However, the crucial point is that there should always be 'somebody' in charge of this problem (i.e. a well-identified professional should be responsible for the physical healthcare of each patient).

Finally, further research in this area is needed. Physical illnesses should not be always regarded as confounding variables in studies dealing with mental illness. Physical comorbidity should be studied systematically, so that the interaction between the various mental disorders and the different physical diseases – in inpatients as well as in outpatients, in women as well as in men, and in young people as well as in the elderly – can be better understood.

This series of books aims to contribute to several of the above steps, by providing a comprehensive review of current research evidence on the prevalence of the various physical diseases in people with the most common mental disorders, and by identifying possible targets for future research. We hope the volume will be useful not only to policy-makers and mental health professionals, but also to primary care practitioners and at least to some extent to those who receive care from mental health services and their families.

Acknowledgements

We wish to thank Professors and Doctors A. de Leon, A. H. Friedlander, D. Lawrence, K. Hatta, D. Lawrence, K. Hatta, D. Templer, R. McCreadie, D. Perkins, P. B. Mortensen, J. K. Rybakowski, I. Steiner, M. U. Mondelli, R. Oken, J. Newcomer and F. Cournos for reviewing parts of this review. Evelyn Dass is thanked for her help with the literature search and the Association for the Improvement of Mental Health Programmes for its support. Eli Lilly provided an unrestricted educational grant to the latter association.

Thanks to John Langerholc for his correction of the draft.

Abbreviations

AD	Alzheimer's disease
ADH	antidiuretic hormone
AHA	American Heart Association
AIDS	acquired immundeficiency syndrome
AMI	acute myocardial infarction
AML	amyotrophic lateral sclerosis
AP	angina pectoris
ARA	American Rheumatism Association
ASA	arylsulphatase A
ASA-CS	arylsulphatase A cerebroside sulphate
ASA-NCS	arylsulphatase A nitrocatechol sulphate
ATP	Adult Treatment Panel (definition of metabolic syndrome)
BDV	Borna disease virus
BMC	bone mineral content
BMD	bone mineral density
BMI	body mass index
CATIE	Clinical Trials of Antipsychotic Treatment Effectiveness
CI	confidence internal
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CPK	creatinine phosphokinase
CSF	cerebrospinal fluid
D2	dopamine 2
DEXA	dual-energy X-ray absorptiometry
DM	diabetes mellitus
DMFT	decayed, missing and filled teeth
DNA	deoxyribonucleic acid
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, 3rd revision
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th revision
ECG	electrocardiogram
EEG	electroencephalogram

EFT_4	estimated free thyroxine
ESR	erythrocyte sedimentation rate
EPS	extrapyramidal side-effects/symptoms
ESS	euthyroid sick syndrome
FEV_1	forced expiratory volume
FSH	follicle-stimulating hormone
FT_3I	free triiodothyronine index
FT_4I	free thyroxine index
FVC	forced vital capacity
GBV-C	GB virus-C (GB, initials of the first patient)
GRH	gonadotropin-releasing hormone
HBV	hepatitis B virus
HbsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HDL	high-density lipoprotein
HDL-C	high-density lipoprotein cholesterol
HGV	hepatitis G virus
HIV	human immunodeficiency virus
HTLV-1	human T-cell lymphotrophic virus type 1
IBS	irritable bowel syndrome
ICD-10	International Classification of Diseases, 10th revision
IFG	impaired fasting glucose
IgE	immunoglobulin E
IGT	impaired glucose tolerance
IHD	ischaemic heart disease
IRR	incidence rate ratio
i.v.	intravenous
LDL	low-density lipoprotein
LH	luteinizing hormone
MEDLINE	Online database of 11 million citations and abstracts from health and medical journals and other news sources
MI	myocardial infarction
MeSH	Medical Subject Headings
MLD	metachromatic leukodystrophy
MS	metabolic syndrome
n	number
NAD	nicotinamide/ nicotine acid
NDWG	normalized diurnal weight gain
n.s.	not statistically significant
NTI	non-thyroidal illness
OR	odds ratio
OSA	obstructive sleep apnoea
p	significance level

PBCs	pregnancy and birth complications
PCR	polymerase chain reaction
PD	polydipsia
PU	polyuria
QTc	rate-corrected QT interval
RA	rheumatoid arthritis
RateR	rate ratio
RR	relative risk
RRBP	Riva Rocci/blood pressure
s.	statistically significant
SAD	schizoaffective disorder
SIDS	sudden infant death syndrome
SIR	standardized incidence rate
SMR	standardized morbidity ratio
SPGU	specific gravity of urine
STEP	Schizophrenia Treatment and Education Program
T_3	triiodothyronine
T_4	thyroxine
TBE	tick-borne encephalitis
TBG	thyroxine-finding globulin
TCI	transient cerebral ischaemia
TMD	temporomandibular disorder
TRH	thyrotropin-releasing hormone
TSH	thyroid-stimulating hormone
TTV	TT-virus (TT, initials of the first patient)
URI	upper respiratory infections
VA	ventricular arrhythmia
WI	water intoxication

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Introduction

Schizophrenia is a chronic disease that afflicts approximately 1% of the population worldwide (Freedman 2003). It usually afflicts people at a young age and, according to a report of the World Health Organization, it is among the seven most disabling diseases in the age group between 20 and 45, far surpassing diabetes, HIV or cardiovascular diseases (World Health Organization 2001). A number of reviews have shown that there is an excess mortality in people with schizophrenia, the overall mortality being twice as high as that in the general population (Allebeck 1989, Brown 1997, Colton and Manderscheid 2006, Harris and Barraclough 1998), so that schizophrenia has been called a 'life-shortening disease'(Allebeck 1989). Suicide and accidents account for about 40% of this excess mortality (Baxter and Appleby 1999, Black *et al.* 1985, Palmer *et al.* 2005, Tsuang *et al.* 1999); the rest is due to physical illness. Despite this excess mortality due to physical diseases, the concern for the somatic well-being of people with schizophrenia has been neglected for decades. A number of reasons account for this neglect, one of them being the stigma related to psychiatric disorders (Sartorius and Schulze 2005). A recent population-wide study in Australia (Lawrence *et al.* 2003) showed that although people with schizophrenia suffer more frequently from cardiovascular problems than the general population, they receive revascularization procedures less frequently than the general population. People with mental disorders were also reported to be less likely to be placed on HbA1c and cholesterol monitoring (Jones *et al.* 2004), to have a retinal examination if they have diabetes (Desai *et al.* 2002), to be treated for osteoporosis (Bishop *et al.* 2004) or to receive medical visits (Cradock-O'Leary *et al.* 2002, Folsom *et al.* 2002); and they are treated for a physical disease only if it is life-threatening (Munck-Jorgensen *et al.* 2000).

While the excess mortality of people with schizophrenia has been well established (Allebeck 1989, Brown 1997, Harris and Barraclough 1998), no comprehensive review of the comorbidity of schizophrenia with physical illness is available to date. Such data would be useful, because a review of the excess rates of *comorbidities* rather than excess *mortality* assesses the problem at a

stage when interventions are still possible. The main aim of this book was to fill this gap by providing a comprehensive review of the epidemiological literature on the association between schizophrenia and comorbid medical illnesses. Hypotheses explaining excess or reduced rates are also listed. The review may thus serve as a basis for projects for improving the physical health of people with schizophrenia.

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Method

A search in MEDLINE (1966 – last update May 2006) was made to find epidemiological studies on the association between schizophrenia and physical illnesses. A broad search strategy had to be used to ensure that no physical illness had been missed. For this reason the MeSH term for schizophrenia was combined with the 23 MeSH terms for the general disease categories of physical diseases. If the search had been performed for each individual physical disease alone, some diseases could have easily been missed. These MeSH terms were:

- Bacterial Infections and Mycoses
- Virus Diseases (+ HIV)
- Parasitic Diseases
- Neoplasms
- Musculoskeletal Diseases
- Digestive System Diseases
- Stomatognathic Diseases
- Respiratory Tract Diseases
- Otorhinolaryngologic Diseases
- Diseases of the Nervous System: autoimmune diseases of the nervous system, autonomic nervous system diseases, central nervous system diseases *(brain diseases*, *CNS infections, encephalomyelitis, high-pressure neurological syndrome, meningitis, movement disorders, ocular motility disorders, pneumocephalus, spinal cord diseases)*, chronobiology disorders, cranial nerve diseases, demyelinating diseases, nervous system malformations, nervous system neoplasms, neurocutaneous syndrome, neurodegenerative diseases, neurologic manifestations, neuromuscular diseases, neurotoxicity syndromes, sleep disorders, trauma, nervous system
- Eye Diseases
- Urologic and Male Genital Diseases
- Female Genital Diseases and Pregnancy Complications
- Cardiovascular Diseases
- Hemic and Lymphatic Diseases

- Congenital, Hereditary and Neonatal Diseases and Abnormalities
- Skin and Connective Tissue Diseases
- Nutritional and Metabolic Diseases
- Endocrine Diseases
- Immune System Diseases
- Disorders of Environmental Origin
- Animal diseases
- Pathological Conditions, Signs and Symptoms.

All abstracts found were read, and potentially relevant articles were ordered for more detailed inspection. The first search was made in autumn 2004; an update search was made in May 2006. The search was complemented by relevant articles mentioned in the studies and other reviews identified. In addition, the drafts of each thematic chapter were sent to experts with the request for information on studies that were missed by our search (see Acknowledgements).

At the beginning of each section we indicate how many references were found by the MEDLINE search and how many references were added from other sources (mainly cross-referencing). These numbers relate solely to the epidemiological studies included in the various sections, not to references for e.g. definitions, hypotheses etc. The aim of this description was to provide some information about the search and on how many studies were found for each category.

There was no restriction as to language.

The focus was on comorbidity studies rather than on mortality studies, since, on the one hand, mortality studies had already been well summarized in other reviews (Allebeck 1989, Brown 1997, Harris and Barraclough 1998). Furthermore, the interest in doing a review of comorbidity studies lies in these studies which assess the associations at a stage when interventions are still possible. Studies that were concerned with mere side-effects of antipsychotic drugs rather than true comorbid diseases were also excluded. Sometimes, however, this distinction was difficult. For example, weight gain is a side-effect of antipsychotic drugs, but the resulting obesity and its potential consequences are major health problems.

Given that the general quality of the studies identified varied substantially from one disease category to another, it was not possible to apply the same inclusion and exclusion criteria for all disease categories. For example, while there are many high-quality, population-based studies on the association between schizophrenia and cancer, the literature on bacterial infections in schizophrenia is much more limited. The aim of the review was not only to find out for which areas compelling evidence is already available, but also whether according to preliminary evidence there are areas of potential importance that could be the focus of future research. Therefore the inclusion criteria such as e.g. 'only population-based studies' or 'only controlled studies' could not be applied to all

chapters. Rather, in well-researched areas (such as that of comorbidity of cancer and schizophrenia), we included only the high-quality studies (in particular, population-based studies with a control group), whereas in areas where only very few studies were available, studies of lower quality such as case series were also included.

When the same study was found several times in different searches, it was described only once in the best fitting category. On the other hand, some studies examined more than one comorbid condition. They were then reported in different chapters. Due to the heterogeneity in terms of quality and designs, meta-analytic calculations were not possible, but rather the results were described in a narrative way. Potential explanations for increased or decreased rates of some physical illnesses are also summarized. Finally, informations on the country of origin of the studies are presented, so as to address the question of whether the results can be generalized to all patients with schizophrenia or are limited only to specific populations.