MORTALITY OF THE DEPRESSED ELDERLY

TUULA PULSKA

Department of Public Health Science and General Practice, University of Oulu
Unit of General Practice, University Hospital of Oulu

OULU 2001
TUULA PULSKA

MORTALITY OF THE DEPRESSED ELDERLY

Academic Dissertation to be presented with the assent of the Faculty of Medicine, University of Oulu, for public discussion in the Auditorium of Kastelli Research Center (Aapistie 1), on March 12th, 2001, at 12 noon.

OUUN YLIOPISTO, OULU 2001
Pulsk, Tuula, Mortality of the depressed elderly
Department of Public Health Science and General Practice, University of Oulu, P.O.Box 5000, FIN-90014 University of Oulu, Finland, Unit of General Practice, University Hospital of Oulu, P.O.Box 22, FIN-90221 Oulu, Finland
2001
Oulu, Finland
(Manuscript received 15 February 2001)

Abstract

The present study was conducted to describe and analyse the mortality of depressed elderly Finns. A special interest was attached to different subgroups of depressed people: those suffering from major depression, those suffering from dysthymic disorder, those who were depressed in two measurements separated by a five-year interval and those who had been depressed in the first measurement but had recovered. The prognostic value of individual symptoms of depression is poorly known and they were studied as predictors of mortality.

The material consisted of two cross-sectional studies performed in Ähtäri, in western Central Finland. The first cross-sectional study comprised those aged 60 years and over and was performed in 1984-85 (N=1529). The second cross-sectional study was performed in 1989-90 and comprised those aged 65 years and over (N=1225). The data were collected by means of postal questionnaires and clinical interviews and examinations. Depression was determined according to the DSM-III criteria.

Mortality data were derived from Statistics Finland.

The survival of the depressed elderly was poorer than that of non-depressed elderly subjects in both cohorts. In the second cohort depression also predicted death when the other predictors of mortality were controlled, but not in the first one. The factors that explain these differences include the higher mortality in the second cross-sectional study, the intensive intervention made during and after the first cross-sectional study and the somewhat different methodologies used. People with major depression had higher mortality compared to non-depressed people even after the other predictors of mortality had been controlled. The increased mortality of those suffering from dysthymic disorder was explained by their poor physical health and lowered functional abilities. Those who were depressed in both studies (i.e. suffered from long-standing or recurrent depression) had higher mortality rates compared to non-depressed people even when the other predictors of mortality were controlled.

It was notable that the mortality rate of those who had recovered from depression (depressed in the first study, but not in the second) did not differ from that of non-depressed ones. Of the individual depressive symptoms, weight loss appeared to predict mortality among depressed people, whereas gastrointestinal symptoms and dissatisfaction were more general markers of increased mortality.

Keywords: depression, aged, mortality, depressive disorder
Acknowledgements

I wish to express my sincere gratitude to my supervisor Professor Sirkka-Liisa Kivelä, M.D., Ph.D. She suggested the idea of this work and gave me an opportunity to work on a doctoral thesis in the Ähtäri project, which was a comprehensive project conducted in Ähtäri from the year 1984 to 1990. She inspired me to take up the scientific work. I will always remember her encouragement and enthusiasm.

I am deeply grateful to Docent Kimmo Pahkala, M.D., Ph.D., for his warm support. He participated in the research project at the planning and data collection phase already. He always had time for discussion on the phone, which was of great help.

I sincerely thank my co-author, Professor Pekka Laippala, Ph.D, for his patient advice and guidance in the field of statistics. Without him, these complicated analyses would have been much more difficult and time-consuming.

My warmest thanks go to my colleague Elisa Karjalainen, M.D., Ph.D. I have shared with her the life of a researcher in every phase. I am deeply grateful to Docent Heikki Luukinen, M.D., Ph.D., who helped me a lot as a senior researcher during my work. I also thank the other colleagues working in the Department of Public Health Science and General Practice at the time of my work, Keijo Koski, M.D., Ph.D., and Petteri Viramo, M.D., Ph.D., for giving their help when needed. It has been a great opportunity to participate in the versatile research training programme in the Department of Public Health Science and General Practice and to share the problems of research work together with many other colleagues, e.g. Mika Herala, M.D., Aino Laukkanen, M.D., and Anna-Maija Päivärinta, M.D.

I wish to express my gratitude to the official reviewers, Professor Esa Leinonen, M.D., Ph.D, and Professor Raimo Sulkava, M.D., Ph.D, who had time to take interest in the manuscript and to give constructive criticism at the final stage of preparation.

I owe my warm gratitude to Mr. Paavo Soini, programme designer, for his careful and quick work when performing the statistical analyses. I will always remember his empathetic and supportive attitude.

I wish to thank all those who have helped me during these years. To mention just a few, Mr. Jukka Saukkoriipi, programme designer, helped me to make many posters and slides. Professor Sirkka Keinänen-Kiukaanniemi, M.D., Ph.D, head of the Department of
Public Health Science and General Practice, as well as the other personnel, especially Mrs Aino Räinä, Mrs Ritva Mannila, Mr Mikko Katiska, Mrs Seija Martinoja and Mrs Jaana Manninen, have helped in many ways. There are too many to mention them all.

I also want to thank the researchers who collected the research material, Raija-Riitta Tervo, M.D, Päivi Köngäs-Saviaro, M.D. and Erkki Kesti, M.D. I am grateful to all those who were living in Ähtäri at the time of the project and participated in the study. Without them, this doctoral thesis would not exist.

I want to thank my brother-in-law Mr. Matti Täppinen, localization specialist, who helped me with the english language. I am also grateful to Sirkka-Liisa Leinonen, authorized translator, who revised the language of the articles and finalized the manuscript.

Finally, I am very happy to have a sweet family and supporting mother and sisters and brothers. I give my warmest thanks to my mother, Mrs. Hilja Remes, for all her self-sacrificing work for me and my family. I am grateful to my dear husband, Kari, for his everlasting love and support, which has encouraged me. My work on this doctoral thesis has demanded lots and lots of patience from him. Thanks to my daughters, Laura and Pola, for bringing a lot of joy and welcome variety to my life. I also thank my friends who have persevered in keeping up contacts despite my lack of time.

The research was financially supported by grants from the Academy of Finland, the Signe and Ane Gyllenberg Foundation, Uulo Arhio Foundation, the Finnish Medical Foundation and the University of Oulu.

February 2001  
Tuula Pulska
Abbreviations

APA        American Psychiatric Association
BMI        Body mass index
CES-D      Center for Epidemiological Studies Depression Scale
CI         Confidence interval
CNS        Central nervous system
CRF        Corticotrophin releasing factor
CT         Computerized tomography
DIS        Diagnostic Interview Schedule
DSM        Diagnostic and Statistical Manual of Mental Disorders
EURODEP    European Concerted Action on Depression of Older People
GHQ        General Health Questionnaire
GDS        Geriatric Depression Scale
HDRS       Hamilton Depression Rating Scale
HR         Hazard ratio
ICD        International Classification of Diseases
MMPI       Minnesota Multiphasic Personality Inventory
MRI        Magnetic resonance imaging
N          Number
RR         Relative risk
SADS       Schizophrenia and Affective Disorders Schedule
SD         Standard deviation
SH         Signal hyperintensity
SMR        Standardized mortality ratio
WHO        World Health Organization
ZSDS       Zung Self-Rating Depression Scale
List of tables

Table 1. Results from previous studies on mortality among depressed elderly psychiatric or psychogeriatric inpatients.
Table 2. Results from previous studies on mortality among depressed medical inpatients or institutionalized elderly.
Table 3. Results from previous community studies on mortality among depressed elderly.
Table 4. Results from previous community studies on mortality and depressive symptoms among depressed elderly.
Table 5. Results from previous studies on mortality among depressed psychiatric patients.
Table 6. Results from previous community studies on mortality among depressed all-aged populations.
Table 7. Results from previous community studies on mortality and depressive symptoms among all-aged populations.
Table 8. Formation of the study population in the first cross-sectional study.
Table 9. Formation of the study population in the second cross-sectional study.
Table 10. Characteristics of participants in both cross-sectional studies according to gender and depression.
Table 11. Comparison of participants to non-participants in the second cross-sectional study.
Table 12. Predictors of mortality according to the Cox models in the first and second cross-sectional studies in the population consisting of non-depressed and depressed people.
Table 13. Predictors of mortality according to the Cox models in the second cross-sectional study in the population consisting of non-depressed and major depressed people.
Table 14. Predictors of mortality according to the Cox models in the first and second cross-sectional studies in the population consisting of non-depressed subjects and ones suffering from dysthymic disorder.
Table 15. Predictors of mortality according to the Cox model in the population consisting of the non-depressed, the recovered and those suffering from long-standing depression.

Table 16. Distribution of depressed and non-depressed people who died during the follow-up periods in the first and second cross-sectional studies by causes of death.
List of figures

Fig. 1. Kaplan-Meier survival estimates for non-depressed and depressed in both sexes in the first cohort.
Fig. 2. Kaplan-Meier survival estimates for non-depressed and depressed in both sexes in the second cohort.
Fig. 3. Kaplan-Meier survival estimates for non-depressed subjects and those with major depression in the second cohort.
Fig. 4. Kaplan-Meier survival estimates for participants and non-participants in both sexes in the first cohort.
Fig. 5. Kaplan-Meier survival estimates for participants and non-participants in both sexes in the second cohort.
List of original articles


Some previously unpublished results have been added.
Original articles are referred to in the text by Roman numerals I-V.
### Contents

Abstract
Acknowledgements
Abbreviations
List of tables
List of figures
List of original articles

1 Introduction .......................................................... 19
2 Review of the literature ........................................... 20
   2.1 Depression among the elderly ............................... 20
       2.1.1 Concept of depression .................................... 20
       2.1.2 Classification of depression .............................. 21
           2.1.2.1 DSM classification ................................. 21
           2.1.2.2 Criteria of depression in DSM-III .................. 22
           2.1.2.3 Other classifications of depression subtypes in the elderly .... 23
       2.1.3 Etiology of depression .................................... 24
           2.1.3.1 Psychosocial factors and theories .................. 24
           2.1.3.2 Biological factors and theories ..................... 24
       2.1.4 Diagnosis of depression .................................. 26
           2.1.4.1 Symptoms of depression .............................. 26
           2.1.4.2 Diagnostic procedures .............................. 27
           2.1.4.3 Diagnosis of depression in general practice .......... 28
2.2 Mortality in depression ....................................... 29
   2.2.1 Mortality among the depressed elderly ................... 29
       2.2.1.1 Mortality among depressed elderly psychiatric
           or psychogeriatric inpatients .............................. 29
       2.2.1.2 Mortality among depressed elderly medical inpatients or
           institutionalized people .................................... 31
       2.2.1.3 Mortality among community-dwelling elderly people
           diagnosed as depressed ..................................... 32
       2.2.1.4 Mortality among elderly people with depressive
           symptoms in the community ................................. 33
   2.2.2 Mortality among all-aged depressed populations .......... 35
       2.2.2.1 Mortality among all-aged depressed patients .......... 35
5.3.2 Population with major depression .......................... 60
5.3.3 Population with dysthymic disorder .......................... 61
  5.3.3.1 First cohort ......................................... 61
  5.3.3.2 Second cohort ...................................... 61
5.3.4 Population recovered from depression and those with long-lasting depression .................. 62
5.4 Causes of death .................................................. 62
5.5 Depressive symptoms predicting mortality in the depressed elderly .................. 63
  5.5.1 Self-assessed depressive symptoms .................................. 63
  5.5.2 Interview-based depressive symptoms ............................... 64
6  Discussion .................................................... 65
6.1 Study population .............................................. 65
6.2 Methods ....................................................... 65
  6.2.1 Postal questionnaires, interviews and examinations .................. 65
  6.2.2 Measurement of factors and their use ......................... 66
  6.2.3 Statistical methods ........................................ 68
  6.2.4 Results .................................................. 68
  6.2.5 Cumulative survival of the older population .................... 69
  6.2.6 Depression as a predictor of mortality ......................... 69
    6.2.6.1 Results in two cohorts ................................ 70
    6.2.6.2 Results in depression subgroups ......................... 71
    6.2.6.3 Increased mortality in depression ......................... 73
  6.2.7 Depressive symptoms predicting mortality ..................... 74
6.3 Strengths and limitations of the study .................................. 74
7  Conclusions .................................................. 75
8  References .................................................. 76
1 Introduction

Very old descriptions of depression can be found in the Old Testament in the Bible. It is said there in the Book of Job: *Month after month I have nothing to live for; night after night brings me grief. When I lie down to sleep, the hours drag; I toss all night and for dawn...*” (Job 7:3-11). As described in these verses, depression causes a lot of personal suffering, impairs the quality of life and causes disability (Kivelä & Pahkala 2001, Wells et al. 1989). Depression has also been associated with significant morbidity and mortality in many studies (Fawcett 1993, Wulsin et al. 1999), although the results concerning mortality in depression differ in different studies. The populations as well as the measures and follow-up times have differed in those studies. Many studies lack control of other factors predicting mortality.

A good population-based material concerning depression among the Finnish elderly was collected in Ähtäri in 1984-1990. The Ähtäri study specifically reported the prevalence, symptoms, predictors and prognosis of depression (Kivelä et al. 1988; Pahkala, 1990). Because this material was available, it was interesting to describe and analyse the mortality of depressed elderly Finns, especially since the previous findings are insufficient and partly contradictory. Mortality risks in mental patients are of interest in several respects. First, they may point to etiological links between mental disorders and physical illnesses (Häfner & Bickel 1989). The differences in epidemiological behavior between two subgroups may suggest that such subgroups should be regarded as separate disease entities for purposes of etiological investigation (MacMahon & Pugh 1970). Second, they may have implications for treatment and provide clues for prevention (Häfner & Bickel 1989).

This doctoral thesis concentrates on reporting the results of a mortality analysis adjusted for other factors predicting mortality. At the beginning of the literature review, the definitions and ways of measuring of depression are discussed briefly. After that, the previous studies concerning mortality in depression among elderly and all-aged people are reviewed.
2 Review of the literature

2.1 Depression among the elderly

Generally speaking depression is the most common psychiatric disorder among the elderly, and only among the oldest old do organic disorders prevail as the most common psychiatric disturbances (Regier et al. 1984). In a review of population studies concerning the prevalence of late-life depression of clinical significance (major and minor depression) Beekman and colleagues (1999) found an average prevalence of 13.5%. The prevalence of major depression is approximately 2% among the elderly, whereas pervasive depressive syndromes which do not fulfil rigorous diagnostic criteria (minor depression) are more common (Weissman et al. 1988, Blazer 1994b, Beekman et al. 1995, Pahkala et al. 1995, Beekman et al. 1999, Penninx et al. 1999). The range of significant depressive symptoms among community populations has been estimated to be between 10% and 25% (Blazer 1994c). The figures are even higher among the hospitalized and institutionalized elderly, ranging up to 30–40% (Blazer 1994b,c).

Depression does not only involve with a lot of personal suffering and an impaired quality of life but also causes disability (Wells et al. 1989, Kivelä & Pahkala 2001) and results in excessive use of non-mental health services (Beekman et al. 1997). In addition to this, it seems that adequate treatment is not administered often enough (Copeland et al. 1992, Beekman et al. 1997).

2.1.1 Concept of depression

How should the concept of depression be defined? In a Finnish consensus meeting concerning depression it was concluded that the concept of depression is used in many contexts and its definition is contractual. Depression can mean 1) a normal reaction of mood in response to changes and losses in life, 2) a symptom, 3) a syndrome or 4) a serious, even life-threatening disease. (Suomen Akatemia & Suomalainen lääkärisura Duodecim 1995).
Hamilton (1989) describes the concept of depression in the following way: Depression is (a) a particular mood associated with a reaction to a (real/potential) loss or failure. Depression of this kind is a normal human reaction clearly related to the events that have produced it, not only in time but also in intensity. (b) Depression is also used to refer to a pathological mood present in many mental disorders and even as a consequence of somatic disease. The simplest distinction between normal and abnormal depressed mood is that the latter is unrelated to external events or out of proportion to them. (c) Depression is also used to signify a syndrome, i.e. a collection of symptoms that constitute a coherent pattern, sometimes called depressive illness. It has an identifiable, usually recurrent course, and distinct intervals between each phase. It is known to have a genetic component, and there is reasonably good evidence of an underlying biochemical disturbance.

Kielholz (1971) defined depression as a syndrome which consists of a sad mood, inhibited thinking and disturbances in psychic and psychosomatic actions. Depression is one of the affective disorders, and Blazer (1994a) describes them as follows: The mood or affective disorders are a group of disorders characterized by disturbance of mood and accompanied by a partial or complete change in mood or affect that is either manic (or hypomanic) or depressed (or mildly dysphoric) (Blazer 1994a).

### 2.1.2 Classification of depression

The International Classification of Diseases (ICD) produced by World Health Organization (WHO) is used as a uniform basis for the classification of diseases. In the beginning, it did not have a separate section for mental disorders. In the sixth revision (WHO 1948), however, chapter V was devoted to psychiatric disorders. Parallel to ICD, a diagnostic system in the field of psychiatry has been developed by American Psychiatric Association (APA), called the Diagnostic and Statistical Manual of Mental Disorders (DSM).

#### 2.1.2.1 DSM classification

The first version was published in 1952 (APA 1952) following ICD-6. The second version of DSM (APA 1968) was published simultaneously with ICD-8 (WHO 1967). Later, DSM-III (APA 1980) and ICD-9 (WHO 1977) were published simultaneously and in a fashion that permitted cross-reference.

DSM-III included three methodological innovations: the classification of mental disorders according to shared descriptive clinical features, the use of specific diagnostic criteria, and the multiaxial system (Skodol & Spitzer 1982). It was meant to be neutral with regard to etiology and usable across different theoretical orientations. The classification of disorders is based on the quantity and severity of symptoms rather than on etiology.

After DSM-III, three revisions have been published: DSM-III-R (APA 1987), DSM-IV (APA 1994) and DSM-IV-TR (APA 2000).
When DSM-III was translated into Finnish in 1983, Finnish psychiatrists unofficially gave up the ICD classification. Later, when ICD-9 (Lääkintöhallitus 1986, 1988) was officially introduced, an additional third part to the classification was produced. It consisted of the classification of mental disorders based on DSM-IIIR (Lääkintöhallitus 1989). When ICD-10 (WHO 1992a) was translated and adopted into use in Finland, psychiatrists also resumed its use because of international commitments. WHO published two diagnostic guidelines with ICD-10: ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines (WHO 1992b) and Diagnostic Criteria of Research (WHO 1993). These two diagnostic aids have been translated into Finnish and published in a combined edition (STAKES 1997).

The trend during the last few decades has been towards a non-theoretical, descriptive definition of mental disorders. Etiological thinking has been largely abandoned as non-relevant. The classification based on predominant clinical features makes the diagnostic terminology equally acceptable to both clinicians with behavioral or biological views of etiology and ones with psychoanalytic views and increases the diagnostic reliability of these disorders (Skodol & Spitzer 1982). Based on increasing knowledge, the classification of mental disorders has also developed from the few very rough classes available at first into a complex system of numerous categories and subcategories in the latest versions of the classifications.

2.1.2.2 Criteria of depression in DSM-III

At the time of the Ähtäri-project, psychiatric journals had started to use DSM-III. It was practical to use DSM-III criteria in the study, and the same criteria were used later in the follow-up study to maintain the consistency of the results, though the revised criteria (DSM-IIIR) had already been published. In DSM-III, affective disorders have been divided into major depressive disorders (bipolar disorder and major depression), other specific disorders (cyclothymic disorder and dysthymic disorder) and atypical affective disorders (atypical bipolar disorder and atypical depression).

Major depression and dysthymic disorder are defined in DSM-III as follows. Major depression is characterized by at least five symptoms lasting for a minimum period of two weeks. One of the symptoms should be either depressed mood or a loss of interest or pleasure in all or almost all activities. The other symptoms are significant weight loss or weight gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness, diminished ability to think or concentrate and recurrent thoughts of death. These may not be associated with schizophrenia, schizophreniform psychosis or paranoia. The diagnosis of major depression is made only if it cannot be established that an organic factor initiated and maintained the disturbance, and that the disturbance is not a normal reaction to the loss of a loved one. (APA 1980)

Dysthymic disorder involves symptoms characteristic of the depressive syndrome (not of sufficient severity and duration to meet the criteria for a major depressive episode) for most or all of the time during the past two years. During the depressive periods, there is either prominently depressed mood or a marked loss of interest or pleasure in all, or almost all, of one’s usual activities and pastimes. In addition to this, three of the following
associated symptoms are present: insomnia or hypersomnia, low energy or chronic fatigue, feelings of inadequacy, loss of self-esteem, self-deprecation, decreased effectiveness or productivity, decreased concentration, social withdrawal, loss of interest or enjoyment of pleasurable activities, irritability or excessive anger, inability to respond with apparent pleasure to praise or rewards, psychomotor retardation or agitation, pessimism, tearfulness, recurrent thoughts of death and suicide. Psychotic features may not be present. (APA 1980)

2.1.2.3 Other classifications of depression subtypes in the elderly

At the beginning of the 20th-century, the concept of involutional melancholia was first introduced by Kraepelin (Kraepelin 1907, see Brown et al. 1984). Classically, involutional depression has been defined as a disorder of gradual onset occurring during the involutional years, with symptoms of marked anxiety, agitation, restlessness, somatic concerns, hypochondriasis, occasional somatic or nihilistic delusions, insomnia, anorexia and weight loss (Brown et al. 1984). After careful consideration, this concept was no longer included in DSM-III. There was not enough evidence to show that menopausal depressed patients have a depressive disorder that could be separated as a distinct subtype (Weissman 1979).

Depressive disorders in the elderly may also manifest as resembling dementia. This condition is called pseudodementia. In a Finnish study, pseudodementia had a prevalence of 24% among elderly people suspected by general practitioners to have dementia (Koskinen 1991). It is important to diagnose pseudodementia correctly, because it is a treatable condition (Yesavage 1993).

Diagnosis is difficult in the case of “masked depression” (Kielholz 1973). Masked depression is a case of depressive state in which psychosomatic symptoms are so marked that it is difficult to recognize the actual psychopathological symptoms. This term is explanatory. The presence of depression should be kept in mind in association with a physical complaint with neither objective findings nor any response to somatic treatment. (Luban-Plozza & Pöldinger 1985).

The division of depression into early-onset and late-onset depression and the possible differences between them have been a matter of interest during the past decade. Late-onset depression may be linked with the vascular disease. It also seems to be a predictor of Alzheimer’s disease (Jorm et al. 1991b, Speck et al. 1995). Late-onset depression has been proposed to be a heterogenous entity, including a subgroup of patients with neurologic disorders that may not be clinically evident when the depression is first manifested. More neuroradiological and neuropsychological abnormalities, greater disability, and less frequently a positive family history have been found to be characteristic of the late-onset type (Alexopoulos et al. 1993, Alexopoulos et al. 1997a,b), though not all studies have been able to reveal differences between the early- and late-onset groups (Burvill et al. 1989).
2.1.3 Etiology of depression

There are many theories and explanations of depression in psychiatry. Different schools (e.g. cognitively oriented, psychoanalytic, existentialist etc.) have their own approaches to the phenomenon as well as specific methods of treatment. The aetiology of depression in the elderly is assumed to be multifactorial (Blazer 1999, Isometsä 1999, Lovestone & Howard 1996), and it is important to take the different factors into account in both diagnostics and treatment. Both psychosocial and biological factors are of considerable importance in the aetiology of depression at old age, but they may have different roles in preceding, precipitating and maintaining depression and in preventing recovery from it.

2.1.3.1 Psychosocial factors and theories

Losses are common in old age. Depression in the elderly has even been perceived as a predictable, understandable response to the losses and declines of the last period of life. (Murphy 1986) Serious life events (e.g. death of a spouse or child), major social problems (e.g. poor health of family members and friends) and marked chronic personal health problems contribute to the onset of depression at old age. Vulnerability to depression increases if the subject does not have a confidant. (Murphy 1982)

In the Gospel Oak Project (Prince et al. 1998), disablement (handicap) was the most important predictor of the onset of depression in the elderly. Several variables concerning health as well as many changes in health during the follow-up predicted depression in the Ähtäri study (Kivelä et al. 1996a). Certain changes in social life were also predictors of depression (including a deteriorated relationship with one’s neighbours and a decline in social participation). Even losses experienced in childhood predicted the occurrence of depression in old age, namely the loss of mother in men and the loss of father in women while under 20 years of age predicted depression in the elderly. (Kivelä et al. 1996b)

The most important psychosocial theories that have produced efficient treatment practices, are psychoanalytical theories (Mendelson 1990), cognitive theories (Rehm 1990) and interpersonal theories (Klerman 1984).

2.1.3.2 Biological factors and theories

Several biological abnormalities have been found to associate with depression. The monoamine hypothesis suggests that endogenous depression is caused by a reduction of monoamine neurotransmitters in the brain (vanPraag 1982). This is the basis of modern pharmacotherapy. Many compensatory mechanisms in the central nervous system are associated with these alterations, the neurochemistry of depression being a complicated system. Ageing may predispose the elderly to depression, because many of the neurobiological changes associated with ageing are similar to those that occur in depression (Veith & Raskind 1988).
A modified monoamine hypothesis has also been suggested. Farrar and Blair (1994) suggest that the primary defect in depression is a reduction in monoamine biosynthesis, possibly secondary to a folate deficiency or other mechanisms. On the other hand, the catabolism of catecholamines increases with aging, whereupon monoamine oxidase activity increases (Bridge et al. 1985).

Another theory of depression suggests that a disorder in the hypothalamic-pituitary-adrenal axis (HPA axis) causes an increase in the secretion of corticotrophin–releasing factor, which stimulates adrenocorticotropic hormone and cortisol release (Bateman et al. 1989). Depression is associated with hyperactivity and dysregulation of the HPA axis across the age range. This is characterized by elevated plasma and urinary cortisol, increased corticotrophin-releasing hormone (CRH), a blunted corticotrophin response to CRH, and resistance of cortisol to suppression by dexamethasone. Increased cortisol secretion is probably the most consistently observed physiological abnormality in patients with major depression. (Schneider 1994) Hormonal imbalance that also affects other hormones (e.g. thyroid-stimulating hormone, growth hormone) may result from a stress reaction and/or compensatory mechanisms in the central nervous system due to disturbed neurotransmission (Salokangas 1997).

The development of imaging techniques has led to active research of brain structure and function in depression. Depressives have been found in both computerized tomography and magnetic resonance imaging (MRI) examinations to have ventricular enlargement and an increased ventricle/brain ratio (Jacoby et al. 1981, Videbach 1997). In addition to the studies of the measurement of cerebral atrophy, some interest has been shown in “signal hyperintensities” (SHs), also known as white matter lesions, which are more frequent than expected in depressed patients (Videbach 1997). SHs might be a risk factor preceding depression and causing it by an unknown pathogenesis, but it is also possible that SHs are caused by depression or its treatment, or that this relationship is mediated through a non-related factor (O’Brien et al. 1996). Furthermore, MRI and positron emission tomography studies have indicated abnormalities in both the structure and the functioning of basal ganglia.

Imaging findings are the basis for the vascular depression hypothesis introduced by Alexopoulos and colleagues (1997a). They hypothesize the development of depression as follows: 1) Small lesions disrupting critical pathways may precipitate vascular depression. A minority of vascular depression cases may be caused directly by lesions, mainly those developing after stroke. 2) Accumulation of lesions exceeding a threshold predisposes to depression. This hypothesis is most applicable to patients with neurologically silent lesions or an old stroke. This presupposes vulnerability that may be caused by the lesions themselves or by a more widespread cerebrovascular disturbance that compromises pathways relevant to depression. Nonbiological factors may be required to trigger depression in patients thus predisposed.

Genetic factors also contribute to old-age depression, although they are more important in early-onset depression. Genetic studies of mental disorders comprise 1) studies of familial aggregation, 2) twin studies, 3) adoption studies and 4) genetic linkage studies. Most of the studies concerning the heredity of affective disorder are familial (Breitner 1994, Sham 1996). Kendler et al. (1992, 1993) have shown in twin studies that genetic influences contribute more strongly than environmental factors to the familial aggregation of major depression. In one Dutch study concerning late life depression, the
family history of mental health problems was associated with all the subtypes of depression under study (van Ojen et al. 1995a,b).

2.1.4 Diagnosis of depression

2.1.4.1 Symptoms of depression

In order to recognize depression, the physician must be acquainted with the psychic, psychomotor and psychosomatic elements of the syndrome. The psychic symptoms include depressed mood, indecisiveness, inhibition of thought, apathy or inner unrest, anxiety, depressive thought content, loss of feeling and inner emptiness. Psychomotor symptoms include either psychomotor inhibition (hypokinesia, hypomimia or animia, inhibition of vocal expression) or psychomotor agitation (physical restlessness, compulsive behaviour, unnecessary activity). Psychosomatic symptoms include loss of vitality and autonomic disturbances in a narrower sense (dizziness, cardiac arrhythmia, dryness of the mouth, constipation, respiratory complaints) or in a wider sense (sleep disturbances, sensations of pain, pressure and cold, loss of appetite, loss of weight, menstrual disorders, impotence). (Luban-Plozza & Pöldinger 1985).

The symptoms of depression among the elderly differ somewhat from those seen among younger and middle-aged adults. Old people have been found to underreport affective symptoms compared to younger ones (Lyness et al. 1995) Depression at old age is often hidden behind somatic symptoms, possibly because of somatization or because of accentuation of symptoms of concurrent illnesses (Gottfries 1998). Differing presentations may be the result of concurrent medical conditions and dementia, which are more likely to occur in older depressed patients. Evidence supporting this has been provided by Blazer and colleagues (1987), who compared depressive symptoms in a group of middle-aged (35–50 year old) and older (more than 60 years) inpatients with melancholic depression. The symptom profiles of these patients were markedly similar, with the elderly differing only in their more frequent reporting of weight loss and less frequent suicidal thoughts.

In the Ähtäri study, the most common symptoms in depressed Finnish elderly men were general somatic symptoms, initial insomnia, loss of interest in work and activities, middle insomnia and depressive mood on the Hamilton Depression Rating Scale (HDRS). Among depressed Finnish women, the most common symptoms were psychic anxiety, general somatic symptoms, initial insomnia, loss of interest in work and activities and depressive mood. (Kivelä & Pahkala 1988a) According to a semi-structured interview, the most common symptoms in both men and women were sleep disturbances, fatigability, loss of interest, depressed mood, loss of activity, pains, pessimism and feelings of uselessness (Kivelä & Pahkala 1988b). These results support the view that subjective physical complaints are part of the core depressive syndrome among the aged. This makes the diagnosis of depression challenging.
2.1.4.2 Diagnostic procedures

Research work requires elaborate and exact instruments for diagnosing depression. Many instruments have been developed for measuring depression at old age, but the choice of instrument depends on the purpose of data collection. One may wish to screen a population to identify those at high risk of depression or to make a psychiatric diagnosis. It is important to have a research instrument that is valid (it measures what it is intended to measure) and reliable (yields repeated measures that are consistent). Validity may be assessed in terms of correlation with an established instrument (convergent validity) or with clinicians’ judgements (criterion validity). (Katona 1994b)

Different strategies chosen for counting symptoms for the diagnosis of depression will result in quite different rates (varying from 27% to 46%) (Koenig et al. 1997). In the EURODEP (European Concerted Action on Depression of Older People) study, the different methodologies used to collect depressive symptoms also seemed to account for some or all of the differences in the prevalence of depression between the research centres (Prince et al. 1999).

There are scales meant to be filled in by the patients themselves. One of the most widely used self-rated depression scale is the Zung Self-Rating Depression Scale (ZSDS; Zung 1965). It contains 20 items constructed on the basis of the clinical diagnostic criteria commonly used to characterize depressive disorders. In their review of the reliability and validity of ZSDS, Hedlund and Vieweg (1979a) suggest that the evidence on validity supports the use of ZSDS as a screening instrument and as an adjunctive clinical tool, but not as an independent measure of depression. Other self-rated scales used to measure depressive symptoms include the Beck Depression Inventory (Beck et al. 1961) and Center for Epidemiological Studies Depression Scale (CES-D; Radloff 1977).

The most widely used interview–based rating scale is the HDRS (Hamilton 1960, 1967). It was originally developed as a tool to help to establish the severity of depressive symptoms. The first papers by Hamilton (1960, 1967) identified 21 rating variables, but only 17 of these are included in the official HDRS scale. The scale can be administered by a psychiatrist or any adequately trained person. Its validity and reliability have been verified in a number of investigations (Hedlund & Vieweg 1979b), and its factor structure reflects the presentation of depressive illness and symptomatology even in the community-dwelling elderly (Onega & Abraham 1997). The Montgomery-Åsberg Depression Rating Scale is another commonly used scale (Montgomery & Åsberg 1979).

Depression scales that contain somatic symptoms are sometimes difficult to interpret. Rapp and Vrana (1989) substituted the clearly somatic symptoms in the Research Diagnostic Criteria with nonsomatic symptoms in their study among elderly male medical patients. The sensitivity and specificity, when using substituted symptoms, were very good compared to the current system. These results give a possibility to substitute physical symptoms, whose origin is sometimes difficult to determine in medically ill patients. The EURODEP study did not give any reason to avoid somatic symptoms in diagnosing depression in old age. The number of somatic symptoms did not significantly increase among those aged 85 years with more physical illnesses when compared to those aged 65–84 years. (Copeland et al. 1999)

One remarkable development in the field of diagnostic procedures in psychiatry is the use of computerized diagnostic algorithms to generate diagnoses from responses to a

2.1.4.3 Diagnosis of depression in general practice

The recognition of depression in primary care is correct in about 30–40 % of the cases, the rate of accurate diagnosis ranging from 7% to 70% according to a review by Docherty (1997). According to a Finnish study of primary care patients aged 18–64 years, general practitioners identified about one quarter of the depressions they came across during their office hours, the experienced doctors being better in detecting the signs of depression than the inexperienced ones (Poutanen 1996). Male patients, who were married, or handicapped, had poor vision or had had less than 9 years of formal education were more likely not to be recognized as depressed by general practitioners in another study (Crawford et al. 1998). The severity of symptoms, the presence of physical illness and old age did not influence the recognition of depression in older people (Crawford et al. 1998). About half of those having “probable pervasive depression” according to the Short Comprehensive Assessment and Referral Evaluation were recognized by their GPs (Crawford et al. 1998). Even higher recognition figures have been reported (MacDonald 1986, Turrina et al. 1994). Unfortunately, effective recognition of depression was accompanied by a low rate of prescription of antidepressants and referrals for psychiatric evaluation (MacDonald 1986). In the consensus development conference arranged by the National Institute of Mental Health, it was stated that no further research is needed to document the underdetection of depression; rather, efforts should be directed towards improving the detection of depression (Reifler 1994).

Diagnosis of depression may be especially difficult among the elderly. Many people consider depressive symptoms a natural part of aging. There are different criteria for childhood depressions but not for elderly people. Should there be different criteria for depression among the elderly? The subtyping of depression using concepts derived from younger populations is unsatisfactory according to some researchers, and it has been pointed out that the most promising approach to subclassify depressions in elderly people could be the late/early onset division (Katona 1994a). For example, when the dysthymic disorders seen in the elderly have been compared to those in younger people, it has been suggested that they are two different disorders. In a series of elderly patients with dysthymic disorder, the gender distribution was found to be almost equal (Devanand et al. 1994), although a female predominance is usually reported (Weissman et al. 1988). The findings further include a high frequency of life stressors that preceded the onset of dysthymia, a predominance of primary dysthymia, late age at the onset of the disorder by DSM-III-R criteria (after 21 yrs of age), a relatively low prevalence of a history of major depression at an earlier time during the course of dysthymia and a low frequency if personality disorders. (Devanand et al. 1994) These findings are clearly different from those obtained in prior studies of young adults, in which most patients have had an early onset, double depression being rather the norm than the exception and comorbid axis I and axis II diagnoses being exceedingly common (Angst & Wicki 1990).
2.2 Mortality in depression

The review of the literature concerning the mortality of the depressed among elderly and all-aged people began with a Medline search with the subject headings “depressive disorder/mortality” and “depression/mortality”. Publications from 1966 till 1999 were included. The results of the search were completed by reviewing the references of the publications found as well as the bibliographies of the review articles. All publications addressing the question of whether depressed people have an increased mortality in old age and possibly adjusting for other mortality-increasing factors were selected. Specific interest was focused on the publications concerning the mortality of depressed people in old age, and the mortality studies are here divided into ones where the study population consisted of elderly people only and ones where also younger people were included in the population. The focus of the review is on the studies reporting all-cause or natural mortality.

2.2.1 Mortality among the depressed elderly


In these studies, different diagnoses and measures of depression have been used, ranging from psychiatric interviews to computer-based diagnoses and from the older ICD-classifications to DSM-III-R. The follow-up times vary from 1 to 15 years. The study populations also vary in many ways; they have different age compositions, and some have been drawn from the home-dwelling elderly and some others from the psychogeriatric or psychiatric inpatients. There are also differences in the adjusted factors when mortality has been studied. All these differences make it difficult to mutually compare the results.

Below, the studies have been divided by the populations into ones concerning (a) depressed psychiatric or psychogeriatric patients, (b) depressed elderly medical inpatients or institutionalized elderly, (c) people diagnosed as depressed in the community and (d) ones suffering from depressive symptoms in the community.

2.2.1.1 Mortality among depressed elderly psychiatric or psychogeriatric inpatients

Convincing results of an increased risk of death have been obtained in the studies concerning depressed psychiatric or psychogeriatric patients (Rabins et al. 1985, Murphy
et al. 1988, Burvill et al. 1991, Brodaty et al. 1993, Burvill & Hall 1994, Zubenko et al. 1997) (Table 1). Only in the study by Brodaty and colleagues (1993) was no increased risk of death found among women, although it was found among men.

Table 1. Results from previous studies on mortality among depressed elderly psychiatric or psychogeriatric inpatients.

<table>
<thead>
<tr>
<th>Author(s) and year</th>
<th>Cases and area</th>
<th>Controls</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabins et al. 1985</td>
<td>62 psychiatric inpatients with major depression, U.S.</td>
<td>Mortality statistics of U.S.</td>
<td>1 year</td>
<td>DSM III</td>
<td>The mortality rate of the depressed people was 2.6 times higher than expected (1.9 when suicides were excluded).</td>
</tr>
<tr>
<td>Murphy et al. 1988</td>
<td>124 psycho-geriatric inpatients and 29 depressed from community sample ≥ 60 yrs</td>
<td>168 sex and age-matched controls from community</td>
<td>4 yrs interview, Feighner criteria</td>
<td></td>
<td>The depressed people had a higher mortality rate even after controlling physical illnesses.</td>
</tr>
<tr>
<td>Burvill et al. 1991</td>
<td>103 inpatients (≥60 yrs) with major depression, Australia</td>
<td>Mortality statistics of Australia</td>
<td>1 year</td>
<td>DSM-III</td>
<td>Depressed men had a three-fold and depressed women a twofold mortality rate.</td>
</tr>
<tr>
<td>Brodaty et al. 1993</td>
<td>61 inpatients (≥60 yrs) with unipolar major depression, Sidney, Australia</td>
<td>Mortality statistics of New South Wales</td>
<td>1 and 3.8 yrs</td>
<td>DSM-III</td>
<td>Depressed men had a significantly greater mortality than expected, whereas women did not.</td>
</tr>
<tr>
<td>Burvill and Hall 1994</td>
<td>103 inpatients (60-88 yrs) with major depression, Australia</td>
<td>Mortality statistics of Australia</td>
<td>5 yrs</td>
<td>DSM-III</td>
<td>Depressed men and women had higher mortality than expected.</td>
</tr>
<tr>
<td>Zubenko et al. 1997</td>
<td>322 elderly psychogeriatric inpatients with mood disorder (mean age 71.0 yrs), U.S.</td>
<td>Mortality statistics of Pennsylvania</td>
<td>23–69 months</td>
<td>DSM-IIIR</td>
<td>Those with mood disorders (major depression, bipolar disorder or other) had a standardized mortality ratio (SMR) of 1.5.</td>
</tr>
</tbody>
</table>

All these studies consist of patients suffering from major depression according to the DSM-III/IIIR or similar criteria. The follow-up times were quite short, mostly 1 year, but in some cases almost six years. The number of deaths is very small in some studies, but the results are parallel in all of the studies. All of these studies except the one reported by Murphy and colleagues (1988) have used age-specific mortality statistics as reference. In Murphy’s study, sex- and age-matched controls were used and it was possible to control for physical illnesses. Despite this, depressed people had an increased mortality rate. The number of deaths in these studies does not allow relevant death cause analysis, but suicides contributed to the increased mortality in all of them.

It can be concluded that depressed psychiatric/psychogeriatric patients have an increased mortality rate compared to the general population. The extent to which the poor physical health of depressed people explains the increased risk of death cannot be reliably concluded because only one study has addressed this question.
2.2.1.2 Mortality among depressed elderly medical inpatients or institutionalized people

There are two mortality studies of depressed elderly medical inpatients (Koenig et al. 1989, Ganzini et al. 1997) and two of institutionalized elderly (Parmalee et al. 1992, Rovner 1993) (Table 2). In all of these studies, the cases are people suffering from major depression and the controls are non-depressed subjects in the same institutions. The follow-up times are short (from 2 months to 2.5 years).

Table 2. Results from previous studies on mortality among the depressed medical inpatients or institutionalized elderly.

<table>
<thead>
<tr>
<th>Author(s) and year</th>
<th>Cases and area</th>
<th>Controls</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koenig et al. 1989</td>
<td>41 male medical inpatients with major depression ≥65 yrs, North Carolina, U.S.</td>
<td>41 inpatients (matched by age, functional status and illnesses)</td>
<td>2–12 mo.</td>
<td>GDS, DSM-IIIR</td>
<td>People with major depression had a 1.4 times higher mortality rate compared to controls.</td>
</tr>
<tr>
<td>Parmalee et al. 1992</td>
<td>116 residents with major depression, 271 with minor depression in old people’s home</td>
<td>511 non-depressed residents in old people’s home</td>
<td>1.5 yrs.</td>
<td>SADS, GDS, DSM IIIR</td>
<td>Depression was associated with higher mortality due to its connection with somatic illnesses.</td>
</tr>
<tr>
<td>Rovner 1993</td>
<td>136 admissions to nursing homes (with depressive disorder or severe depressive symptoms), Baltimore</td>
<td>315 non-depressed admissions to nursing homes</td>
<td>1 yr.</td>
<td>DSM III</td>
<td>Occurrence of depression was associated with higher mortality in univariate analysis.</td>
</tr>
<tr>
<td>Ganzini et al. 1997</td>
<td>50 (male) veterans, medical inpatients with major depression, aged ≥65 years, U.S.</td>
<td>50 (male) veterans, medical inpatients</td>
<td>2.5 yrs.</td>
<td>GDS, DSM III</td>
<td>Depression was an independent predictor of mortality and the severity of medical illness.</td>
</tr>
</tbody>
</table>

In both studies performed among depressed elderly medical inpatients the depressed people had higher mortality than the non-depressed even after controlling for the severity of medical illnesses (Koenig et al. 1989, Ganzini et al. 1997). In the studies among the depressed institutionalized elderly, the results concerning the relationships between physical health and mortality are controversial. In one study (Parmalee et al. 1992), the higher mortality of depressed people was due to the connection between depression and somatic illnesses while the other study failed to show any connection (Rovner 1993).

Most of the quoted studies support the conclusion that depression increases the risk of mortality in elderly medical patients or institutionalized people irrespective of their physical health. Some mortality studies made among exclusive populations, e.g. stroke patients (e.g. Morris et al. 1993), myocardial infarction patients (e.g. Frasure-Smith et al. 1993), chronic dialysis patients (e.g. Numan et al. 1981) and patients with life-threatening diseases (e.g. Silverstone 1990), also support the view that comorbid depression increases the risk of death.
2.2.1.3 Mortality among community-dwelling elderly people diagnosed as depressed

Among community-dwelling elderly people, the association between the increased risk of death and depression is not as clear as among inpatients (Table 3). The findings are controversial to some extent. Many of these studies are large, including the one performed among 66-year-old Stockholmers (Enzell 1984; n=9541). Follow-up times differ from 15 months to 15 years.

Table 3. Results from previous community studies on mortality among the depressed elderly.

<table>
<thead>
<tr>
<th>Author(s), year</th>
<th>Population and area</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kay &amp; Bergmann 1966</td>
<td>N=292, ≥65 yrs, UK</td>
<td>4 yrs</td>
<td>Psychiatric interview</td>
<td>Functional psychiatric disorder was associated with an increased mortality rate, probably due to physical illnesses.</td>
</tr>
<tr>
<td>Nielsen et al. 1977</td>
<td>N=994, ≥65 yrs Samso, Denmark</td>
<td>15 yrs</td>
<td>ICD7</td>
<td>Functional psychoses, neuroses, character disorders and other mental disorders did not affect life expectancy.</td>
</tr>
<tr>
<td>Persson 1981</td>
<td>N=392, 70 yrs Gothenburg, Sweden</td>
<td>5 yrs</td>
<td>ICD8</td>
<td>Functional psychiatric disorders did not increase mortality.</td>
</tr>
<tr>
<td>Enzell 1984</td>
<td>N=9541, 66 yrs Stockholm, Sweden</td>
<td>9 yrs</td>
<td>Psychiatric examination</td>
<td>Depressed people had a higher mortality rate compared to nondepressed ones.</td>
</tr>
<tr>
<td>Davidson et al. 1988, Sharma et al. 1998</td>
<td>N=1070, ≥65 yrs, Liverpool, UK</td>
<td>3 yrs / 5 yrs interview, AGECAT</td>
<td></td>
<td>Depressed people had an elevated mortality rate.</td>
</tr>
<tr>
<td>Bruce &amp; Leaf 1989</td>
<td>N=3007, ≥55 yrs, New Haven, U.S.</td>
<td>15 mo</td>
<td>Interview (DIS), DSM-III</td>
<td>Affective disorders were associated with increased mortality independently of sex, age and physical health status.</td>
</tr>
<tr>
<td>Fredman et al. 1989</td>
<td>N=1622, ≥60 yrs, North Carolina, U.S.</td>
<td>2 yrs</td>
<td>Interview (DIS)</td>
<td>Depression and mortality had no correlation.</td>
</tr>
<tr>
<td>Jorm et al. 1991a</td>
<td>N=274, ≥70 yrs, Hobart, Australia</td>
<td>5 yrs</td>
<td>DSM-III + Rational Scale of Depression</td>
<td>Depressive disorder was associated with higher mortality, due to its relationship with physical illness.</td>
</tr>
<tr>
<td>Engedal 1996</td>
<td>N=397, (334) ≥75 yrs, Oslo, Norway</td>
<td>3 yrs</td>
<td>DSM-III-R</td>
<td>Depressed people had a higher mortality rate than non-depressed ones.</td>
</tr>
<tr>
<td>Penninx et al. 1999</td>
<td>N=3056, (55–85 yrs), Amsterdam, Netherlands</td>
<td>4 yrs</td>
<td>interview, CES-D, DSM-III (DIS)</td>
<td>Major depression in men and women and also minor depression in men increased the mortality risk even after adjustment of sociodemographics and health status.</td>
</tr>
</tbody>
</table>

In three studies, with quite different follow-up times and different numbers of study subjects, no association between depression and mortality was found (Nielsen et al. 1977, Persson 1981, Fredman et al. 1989). Two of them used ICD diagnoses of functional
psychiatric disorders/psychoses and neuroses, which apply to depressive people partly, but not fully. All the other studies show an increased mortality rate among depressed elderly people (Kay & Bergmann 1966, Enzell 1984, Davidson et al. 1988, Bruce & Leaf 1989, Jorm et al. 1991a, Engedal 1996, Sharma et al. 1998, Penninx et al. 1999). All except one (Fredman et al. 1989) of the later studies using DSM-III/IIIR criteria (Bruce & Leaf 1989, Jorm et al. 1991a, Engedal 1996, Penninx et al. 1999) have found an association between depression and mortality. In the only differed study, the number of deaths was very small.

The role of physical health in the higher mortality rate of community-living depressed people has not been studied very much. In three of these studies, physical health was taken into account as an explanatory variable. In two studies (Bruce & Leaf 1989, Penninx et al. 1999), affective disorders, namely major depression, were associated with higher mortality independently of physical health status. In the latter study, minor depression in men was also related to an increased mortality rate regardless of health status. In the third study, depressed people had a higher mortality rate due to physical illness (Jorm et al. 1991a). In the study by Kay and Bergmann (1966), those with functional psychiatric disorders tended to obtain higher ratings for physical disability than their normal counterparts. Because there was a good correspondence between the original physical ratings and mortality, the authors conclude that the physical disability was mainly responsible for the higher mortality of those suffering from functional disorders (Kay & Bergmann 1966).

Most of the findings, especially in the later studies, support the conclusion that depression increases mortality even among the community-dwelling elderly. The role of physical health in explaining the increased mortality remains unclear.

### 2.2.1.4 Mortality among elderly people with depressive symptoms in the community

Studies reporting associations between depressive symptoms and mortality are presented in Table 4. In some studies (Enzell 1984, Persson 1981, Takeida et al. 1997, Whooley & Browner 1998), high numbers of depressive symptoms were related to a higher mortality rate, and in one study reported by Anttila (1989), even a low number of depressive symptoms was associated with higher mortality. Contradictory findings have been reported in three studies (Thomas et al. 1992, Callahan et al. 1998, Fredman et al. 1999). In the last mentioned studies, the Center for Epidemiologic Studies Depression Scale (CES-D) was used with a low cut-off point, which leaves many clinically non-depressed people in the depressed group and might weaken the depression-mortality association. The population in the study by Callahan and colleagues (1998) was selected, as it consisted of people making regularly scheduled primary care visits. About two thirds of the study population consisted of African Americans, but race was controlled in the multivariate model. Although the CES-D score was also used as a four-point scale (0–5, 6–15, 16–24 and >24 CES-D points), the high CES-D scores had no independent relation to mortality (Callahan et al. 1998). This study also failed to show cognitive impairment to predict mortality.
Table 4. Results from previous community studies on mortality and depressive symptoms among the depressed elderly.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Population and area</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzell 1984</td>
<td>N=9541, 66 yrs, Stockholm, Sweden</td>
<td>9 yrs</td>
<td>5 items indicating depressive symptoms</td>
<td>The people with severe depressive symptoms had a higher mortality rate compared to the nondepressed ones.</td>
</tr>
<tr>
<td>Anttila 1989</td>
<td>N=982, ≥65 yrs, Kuusamo, Finland</td>
<td>10 yrs</td>
<td>GHQ (12-item version)</td>
<td>Minor psychiatric illness was a significant predictor of death, when the effects of age and the diseases relevant for the mortality analysis were controlled for.</td>
</tr>
<tr>
<td>Persson 1981</td>
<td>N=392, 70 yrs, Gothenburg, Sweden</td>
<td>5 yrs</td>
<td>psychiatric interview</td>
<td>High scores for depressive symptoms were associated with an increased mortality rate among males.</td>
</tr>
<tr>
<td>Thomas et al. 1992</td>
<td>N=1855, ≥65 yrs, Bronx, U.S.</td>
<td>1 and 3 yrs</td>
<td>CES-D</td>
<td>Depressive symptoms did not correlate with higher mortality.</td>
</tr>
<tr>
<td>Takeida et al. 1997</td>
<td>N=2623, (60–74 yrs), Hokkaido, Japan</td>
<td>4 yrs</td>
<td>ZSDS</td>
<td>The highest SDS score (≥2.40) was associated with an increased mortality rate. After adjustment for age, sex, number of current diseases and smoking status, the SDS score remained significant (cont. variable).</td>
</tr>
<tr>
<td>Callahan et al. 1998</td>
<td>N=3767 ≥60 yrs, Indianapolis</td>
<td>5 yrs</td>
<td>CES-D</td>
<td>Depressive symptoms did not correlate with higher mortality.</td>
</tr>
<tr>
<td>Whooley &amp; Browner 1998</td>
<td>N=7518 women ≥67 yrs</td>
<td>7 yrs</td>
<td>GDS</td>
<td>A high score of depressive symptoms correlated with an increased mortality rate even after adjusting for many diseases, smoking, perceived health and cognitive function.</td>
</tr>
<tr>
<td>Fredman et al. 1999</td>
<td>N=764 women ≥65 yrs, Baltimore, U.S.</td>
<td>6 yrs</td>
<td>CES-D</td>
<td>Depressive symptoms did not correlate significantly with higher mortality.</td>
</tr>
</tbody>
</table>

The study reported by Thomas and colleagues (1992) had an interesting design. It was a longitudinal study, and depressive symptoms were measured at the baseline and again 24 months later. After that, the respondents were divided into four groups: 1) no threshold level symptoms of depression either at the baseline or at 24 months (N-N); 2) emergent symptoms, meaning no symptoms at baseline, but symptoms present at 24 months (N-D); 3) remission group having symptoms at the baseline but not at 24 months later (D-N); and 4) persistent symptoms of depression, both at the baseline and again 24 months (D-D). The relative risk of mortality was highest in the D-D group and lowest in the N-N group, yielding no significant differences. The relative risk for each symptom group was calculated in relation to the other three groups, which may decrease the differences compared to a situation where the risk of each group would have been compared to the N-N group.

In three of these studies, the role of diseases was controlled for. Adjustment for the number of current diseases among the other variables did not explain the higher mortality of those suffering from a high number of depressive symptoms in Japan (Takeida et al. 1997). In Finland (Anttila 1989), the diseases associated with mortality were included in
the multivariate model together with age and the General Health Questionnaire (GHQ) score, and ten-year mortality was significantly higher among the high-scoring men and women. In the study by Whooley and Browner (1998), too, the high score of depressive symptoms was associated with an increased mortality even after adjusting for many diseases, smoking, perceived health and cognitive function.

It can be concluded that the findings concerning depressive symptoms and increased mortality are contradictory, and that the role of other mortality-explaining factors – especially the role of physical diseases – is poorly known.

2.2.2 Mortality among all-aged depressed populations

Many studies reporting mortality in all-aged community populations have used different clinical measures, a high level of depressive symptoms (different depression scales), self-reported depression or the use of antidepressant medications in determining depression (Tables 5–7). Although clinical diagnoses are not always made, which causes some loss of diagnostic accuracy, it is possible to study very large populations. This gives more statistical power for the associations. The age scale has varied quite a lot in these studies, and many of them lack information of the age range or mean age of the population.

2.2.2.1 Mortality among all-aged depressed patients

In these previous patient studies of all-aged depressives, clinical assessments of depression have been used. The follow-up times have been very long in many studies, lasting for up to thirty years. The determination of depression has varied from specific research criteria to ICD and DSM classifications (Table 5). Excess mortality among depressed people compared to age- and sex- (and possibly race-) specific mortality statistics has been reported in almost all of them (Tsuang & Woolson 1978, Black et al. 1985a,b, Martin et al. 1985a,b, Weeke & Vaeth 1986, Berglund & Nilsson 1987, Newman & Bland 1991, Buchholtz-Hansen et al. 1993, Allgulander 1994, Surtees & Barkley 1994). Although both genders were studied, three studies have reported an increased mortality rate only among depressed men (Evans & Whitlock 1983) or women (Black et al. 1987, Brodaty et al. 1997). In one study only men were studied, and depressed men were reported to have higher mortality than controls (Lönnqvist & Koskenvuo 1988).
Table 5. Results from previous studies on mortality among depressed psychiatric patients.

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>Population and area</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsuang &amp; Woolson 1978, Tsuang et al. 1980</td>
<td>225 psychiatric inpatients, (mean age 44) Iowa, U.S.</td>
<td>30 yrs</td>
<td>specific research criteria</td>
<td>Depressed people showed an increased mortality rate.</td>
</tr>
<tr>
<td>Evans &amp; Whitlock 1983</td>
<td>114 psychiatric hospital admissions (aged 40+ yrs), GB</td>
<td>5 yrs</td>
<td>Depression as a prominent symptom</td>
<td>Depressed men showed a significantly increased mortality rate.</td>
</tr>
<tr>
<td>Black et al. 1985a,b</td>
<td>1431 psychiatric patients with affective disorder, 243 with depressive neurosis</td>
<td>10 yrs</td>
<td>ICD9</td>
<td>Those suffering from affective disorder had a significantly higher mortality rate than expected.</td>
</tr>
<tr>
<td>Martin et al. 1985a,b</td>
<td>139 outpatients with primary, 93 with secondary unipolar affective disorder (15–84 yrs), Washington, U.S.</td>
<td>6–12 yrs</td>
<td>Feighner criteria</td>
<td>Patients with a history of depressive episodes had an increased mortality rate in the group of secondary affective disorders (due to unnatural causes of death), but not in the group of primary affective disorders.</td>
</tr>
<tr>
<td>Weeke &amp; Vaeth 1986</td>
<td>2168 psychiatric hospital admissions, (15– yrs) Denmark</td>
<td>6 yrs</td>
<td>ICD8</td>
<td>Those suffering from affective disorders had an increased unnatural mortality, men having also increased natural mortality.</td>
</tr>
<tr>
<td>Berglund &amp; Nilsson 1987</td>
<td>1206 psychiatric inpatients with severe depression/melancholia</td>
<td>14–27 yrs</td>
<td>multidimensional diagnostic schedule</td>
<td>Depressed people had an increased mortality rate.</td>
</tr>
<tr>
<td>Black et al. 1987</td>
<td>1007 people with major depression, Iowa, U.S</td>
<td>2–14 yrs</td>
<td>DSM-III, Feighner criteria</td>
<td>Depressed women had an increased all-cause mortality rate.</td>
</tr>
<tr>
<td>Lönnqvist &amp; Koskenvuo 1988</td>
<td>783 male patients with neurotic depression or affective psychosis (aged 35–64 yrs), Finland</td>
<td>3 yrs</td>
<td>ICD 8</td>
<td>Males with neurotic depression and those with affective psychosis had a higher mortality rate than the control cohort.</td>
</tr>
<tr>
<td>Newman &amp; Bland 1991</td>
<td>4022 psychiatric patients with affective disorder (6–94 yrs, median 39yrs)</td>
<td>10 yrs</td>
<td>Clinical modification of ICD9</td>
<td>People with major depression had a SMR of 2.6 for all causes of death and a SMR of 35.3 for suicide.</td>
</tr>
<tr>
<td>Buchholtz-Hansen et al. 1993</td>
<td>219 major depressed inpatients (19–67yrs), Denmark</td>
<td>3–10 yrs</td>
<td>DSM-III</td>
<td>People with major depression had an increased mortality rate, mostly due to the high suicide rate among women.</td>
</tr>
<tr>
<td>Allgulander 1994</td>
<td>38529 patients with depressive neurosis (aged 15–93 yrs), Sweden</td>
<td>up to 17 yrs</td>
<td>ICD 8</td>
<td>Patients with depressive neurosis had a more than tenfold SMR for suicide. The rate of nontraumatic deaths was slightly increased among men but not among women.</td>
</tr>
<tr>
<td>Surtees &amp; Barkley 1994</td>
<td>80 people (aged 21–65) referred to hospital for treatment of depression</td>
<td>12 yrs</td>
<td>ICD 8</td>
<td>Depressed people had an almost twofold mortality rate compared to the expected value.</td>
</tr>
<tr>
<td>Brodaty et al. 1997</td>
<td>212 patients with depression (mean age 41.4, SD 16.4)</td>
<td>25 yrs</td>
<td>ICD 8</td>
<td>Depressed women had a significantly higher mortality rate than the general population.</td>
</tr>
</tbody>
</table>
Suicides explain the most of the increased mortality rate (Tsuang & Woolson 1978, Tsuang et al. 1980, Martin et al. 1985a,b, Berglund & Nilsson 1987, Buchholz-Hansen et al. 1993, Brodaty et al. 1997). In the Finnish study the mortality rate for natural causes was about twofold, whereas the risk of suicide (among these patients with neurotic depression or affective psychosis) was more than thirty times higher than among the controls (Lönnqvist & Koskenvuo 1988). Some studies have shown that the excess mortality appears most clearly during the initial years of follow-up (Tsuang & Woolson 1978, Black et al. 1985b, 1987, Surtees & Barkley 1994, Brodaty et al. 1997). It is possible that during a long follow-up more risk factors for death emerge. None of these studies controlled any other confounding factors than sex, age and sometimes race.

2.2.2.2 Mortality among all-aged community-dwelling people diagnosed as depressed

The mortality of depressed people has been studied more extensively among psychiatric patients than among community-dwelling people. Studies performed among people living in the community are presented in table 6. In all of these studies, depressed people had increased mortality (Rorsman et al. 1982a,b, Murphy et al. 1987, Bruce et al. 1994, Kouzis et al. 1995), although in one study the mortality rate was increased among males only (Zheng et al. 1997). In one study, only deaths due to unnatural causes were increased (Rorsman et al. 1982a,b).

Table 6. Results from previous community studies on mortality among depressed all-aged populations.

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>Population and area</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rorsman et al. 1982a,b</td>
<td>3563 people, Lundby, Sweden</td>
<td>25 yrs psychiatric interview</td>
<td>Neurotics had an increased mortality rate by unnatural causes but not by natural causes.</td>
<td></td>
</tr>
<tr>
<td>Murphy et al. 1987</td>
<td>1003 people, Stirling County Study, Canada</td>
<td>16 yrs interview, depressive symptoms</td>
<td>Depression increased the mortality rate although the effects of age, sex and self-reported physical disorders were controlled.</td>
<td></td>
</tr>
<tr>
<td>Bruce et al. 1994</td>
<td>3560 people (&gt;40 yrs.) in New Haven, U.S.</td>
<td>9 yrs DSM III, DIS</td>
<td>Recent major depression (adjusted for age and sex) increased the mortality rate even when other comorbid psychiatric disorders were controlled.</td>
<td></td>
</tr>
<tr>
<td>Kouzis et al. 1995</td>
<td>15567 people (&gt;18 yrs.), ECA-study areas, U.S.</td>
<td>1 year DSM III</td>
<td>Those with major depressive disorder had a mortality increase.</td>
<td></td>
</tr>
<tr>
<td>Zheng et al. 1997</td>
<td>57897 people (&gt;25 yrs), participants of National Health Interview Survey, U.S.</td>
<td>2.5 yrs self-reported major depression</td>
<td>Those with major depression had a higher mortality rate than those without depression. The adjusted (age, sex, education, marital status, BMI, proxy respondent) HRs for men with MD were 3.1 (2.0–4.9) and those for women 1.7 (0.9–3.1).</td>
<td></td>
</tr>
</tbody>
</table>
Three of the studies included only major depressed people or concluded that only those suffering from major depression had an increased risk of premature death (Bruce et al. 1994, Kouzis et al. 1995, Zheng et al. 1997). Past episodes of major depression and chronic dysthymia were not associated with mortality (Bruce et al. 1994).

Physical disorders were controlled in two studies (Murphy et al. 1987, Kouzis et al. 1995), and they did not explain the excess mortality. When psychiatric comorbid disorders were also controlled in addition to age and sex, the mortality rate of those suffering from recent major depression was increased (Bruce et al. 1994).

### 2.2.2.3 Mortality among all-aged people with depressive symptoms in the community

Table 7 lists community studies on mortality and depressive symptoms in all-aged populations. In the majority of these studies, a large number of depressive symptoms correlated with all-cause mortality (Markush et al. 1977, Roberts et al. 1990, Huppert & Whittington, 1995, Bingefors et al. 1996), although in the study reported by Shekelle and colleagues (1981) this was the case only with the risk of death from cancer (not from other causes).

**Table 7. Results from previous community studies on mortality and depressive symptoms among all-aged populations.**

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Population and area</th>
<th>Follow-up time</th>
<th>Measure of depression</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markush et al. 1977</td>
<td>Alachua County study, 647 people (≥45 yrs), U.S</td>
<td>4 yrs</td>
<td>Scale describing depression</td>
<td>A high depression scale score correlated significantly with the mortality rate.</td>
</tr>
<tr>
<td>Shekelle et al. 1981</td>
<td>3012 (67.1% agreed) men from Western Electric health study, Chicago, U.S.</td>
<td>17 yrs</td>
<td>MMPI depression scale</td>
<td>The degree of depression had a graded correlation with the risk of death caused by cancer.</td>
</tr>
<tr>
<td>Roberts et al. 1990</td>
<td>8023 people (≥20 yrs), Alameda County Study, U.S.</td>
<td>9 yrs, 18 yrs</td>
<td>18 items of depressive symptoms</td>
<td>Marked and moderate depressive symptoms predicted mortality.</td>
</tr>
<tr>
<td>Huppert &amp; Whittington, 1995</td>
<td>6317 people (≥18 yrs)</td>
<td>7 yrs</td>
<td>GHQ (30-item version)</td>
<td>High GHQ scores and mortality had a positive correlation, both among people without limiting disease and those with limiting disease.</td>
</tr>
<tr>
<td>Bingefors et al. 1996</td>
<td>456 users of antidepressant medications, reference group 912 people, (age 15-), Sweden</td>
<td>9 yrs</td>
<td>Prescription of antidepressant</td>
<td>Depressive problems increased mortality risk.</td>
</tr>
</tbody>
</table>

In three studies physical health was controlled for. A high depression scale score correlated significantly with increased mortality, though age, sex and self-reported health problems were adjusted (Markush et al. 1977). Antidepressant treatment as a marker for depression predicted mortality after adjusting for age, sex and pre-existing medical...
conditions (Bingeefors et al. 1996). Marked and moderate depressive symptoms predicted mortality even when age, sex, education and chronic physical conditions were controlled, but when functional abilities and self-perceived health, which might also reflect depression to some extent, were added to the model, the mortality-predicting effect of depression disappeared (Roberts et al. 1990). These studies support the view that depression increases the risk of death to some extent irrespective of physical illnesses.

The study conducted by Roberts and colleagues (1990) had an interesting design and results. Depressive symptoms were measured twice of a 9-year interval, and mortality was recorded during nine years after the second measurement. The lowest mortality rates were found in the group of respondents who moved from marked depression to low depression, which suggests that a reduction of depressive symptoms, rather than an absence of a history of depression, has the greatest impact on mortality. The highest mortality rates were found among those who moved from moderate to marked depression, remained at the marked level or moved from marked to moderate depression, which suggests that chronicity and high levels of depression have a significant impact on mortality.

2.3 Causes of death

Because the greater physical morbidity of depressed people cannot be indisputably shown to explain their excess mortality, could the increased mortality of depressed people be explained by specific causes of death? The findings of lowered immune function among depressed people have led to suggestions that depressed people might have an increased risk of immune-mediated diseases, such as cancer, infections and auto-immune diseases (Herbert & Cohen 1993). There also seems to be a connection between cardio- and cerebrovascular diseases and depression (Roose et al. 1991, Aromaa et al. 1994, Musselman et al. 1998), which may cause depressed people to be more vulnerable to cardio- and cerebrovascular diseases and deaths thereof and, on the other hand, also those having vascular diseases to be more vulnerable to depression and an increased risk of death. In one study, depressed people with adequate treatment of depression had lower overall mortality, and lower mortality due to myocardial infarction than depressed people not treated or having inadequate treatment (Avery & Winokur 1976). In this chapter, the findings of specific causes of death among depressed people in the literature will be described.

2.3.1 Natural mortality

Differences in the causes of death between depressed and non-depressed people have not been extensively sought for. One reason may be that a great number of deceased (with and without a diagnosis of depression) is needed to show differences between different groups. Especially mortality studies performed among elderly depressives have consisted too few people to allow relevant death cause analyses.
2.3.1.1 Natural mortality among depressed elderly people

The most important causes of death among both depressed and non-depressed elderly are cardio- and cerebrovascular, neoplastic and respiratory diseases (Murphy et al. 1988, Zubenko et al. 1997).

There are some findings to support the role of cardio- and cerebrovascular diseases in the higher mortality of depressed elderly people. Kay and Bergmann (1966) have reported a slightly higher incidence of cerebrovascular accidents among males with functional psychiatric disorders than among normal males (13% vs 5.7%). In the study reported by Rabins et al. (1985), eight elderly people suffering from major depression died, six of them from cardiovascular causes and two by suicide. In that a discharge diagnosis of cardiovascular diseases distinguished between the survivors and the deceased. Six of the eight deceased patients (75%) had a diagnosis of cardiovascular diseases, while only 3 of 54 (6%) of those alive at follow-up had such a diagnosis (Rabins et al. 1985).

Some evidence has also been found of increased mortality from cancers among depressed elderly people. As high proportion as two-thirds of major depressed cases had cancer as a cause of death in the study reported by Koenig and colleagues (1989). A high number of depressive symptoms was also associated with higher mortality not only from cancer but also from pneumonia in one study (Takeida et al. 1997).

2.3.1.2 Natural mortality among depressed all-aged people

A mortality analysis among all-aged populations would be good material for death cause analyses because of the greater study population sizes and longer follow-up periods in many studies, but on the other hand, mortality among younger and middle-aged people is low.

Excess mortality from cancer has been found in some studies among all-aged depressed people (Kerr et al. 1969, Shekelle et al. 1981), but in other studies, no relations between cancer and depressive symptoms have been reported (Kaplan & Reynolds, 1988, Zonderman et al. 1989).

2.3.2 Unnatural mortality

Suicides are rare, and most of the discussed mortality studies among the elderly were unable to assess their proportion in the excess mortality of depressives. A large population is needed to study suicide mortality prospectively. Many studies concerning suicide mortality are retrospective and have used the psychological autopsy method or purely official statistics. According to a review, suicides accounted for 12–60% of deaths among patients with affective disorders, the suicide risk being over thirty times greater than that of the population without affective disorders (Guze & Robins, 1970). It has also been shown that, after a depression training programme for general practitioners, the
frequency of suicides and especially the rate of depressive suicides among all suicides, decreased significantly (Rihmer et al. 1995).

2.3.2.1 Unnatural mortality among depressed elderly people

Affective disorder is the most important risk factor for suicides (Conwell & Brent, 1995a). When one hundred elderly (aged 65+ yrs) suicides were retrospectively investigated, a total of 61% of the subjects could be considered to have had a clinically recognisable depressive illness before they died (Cattel & Jolley, 1995). In the previously quoted study of psychogeriatric patients, as reported by Zubenko et al. (1997), all the three suicides occurred among elderly people whose psychiatric diagnosis during their index psychiatric admission had been major depression. The rates of suicide among old people have been reported to be higher than those among younger people (Conwell & Brent 1995a). The extent to which neurobiologic changes related to aging predispose to suicide is a topic of active research (Conwell & Brent 1995b).

2.3.2.2 Unnatural mortality among all-aged depressed people

Unnatural causes of death have explained the excess mortality among depressives in many studies conducted among all-aged populations (Allgulander 1994, Berglund & Nilsson 1987, Black et al. 1985b, Buchholtz-Hanzen et al. 1993, Martin et al. 1985b, Rorsman et al. 1982b, Tsuang & Woolson, 1978). In the study reported by Rorsman et al. (1982b), the age-standardized suicide rate among men with a background of psychiatric disorders was 4 times and the accident rate about 2½ times higher than that of the general population. Depression at the time of death was present in 50% of suicides and 4% of accidents (Rorsman et al. 1982b). In another study, suicides accounted for 9.3% of the deaths among depressives as compared to 1.9% among surgical controls (Tsuang & Woolson 1978).

When the autopsy findings of people (aged 50+ yrs) who had committed suicide were compared to the findings of controls (matched for age and sex) who had died violent deaths (mainly road accidents), significantly more cancers were found among those committing suicide. The study was conducted retrospectively and based on post-mortem records, and there was no reliable knowledge of depression among all of the suicide victims. But the authors conclude that most of the suicide cases were profoundly depressed and some of them had had diagnosis of depression even before their cancer. (Whitlock 1978) Depression as a precursor of suicide seems to be a well established fact.

In view of a change in depressive symptoms, an increased risk of "unnatural" deaths was seen among depressive subjects, whose symptoms increased from moderate to marked levels of depression (Roberts et al. 1990). Patients scoring as nonendogenously depressed have been found to have a significantly higher suicide rate than endogenously depressed patients (Jorgensen & Mortensen 1990, Buchholtz-Hansen et al. 1993).
2.4 Summary of mortality in depression

In conclusion, many of the mortality studies among depressed elderly people show an increased mortality rate, but a possible publication bias in favor of positive studies should be borne in mind. Many studies have concentrated on those suffering from major depression, and the different subtypes of depression have been studied poorly. Among all-aged depressed people, many studies have reported an increased mortality risk for depressives, mostly due to suicide and other unnatural causes of death. However, to a lesser extent, these studies have also reported excess mortality from natural causes.

The role of other factors explaining mortality has been taken into account in only a few studies. Age and sex are usually controlled for. Adjustment for physical health has only been made in some studies, and the results do not give a definite answer to the question of whether poor physical health among the elderly explains the possible increased mortality of depressed people.
3 Aims of the study

1. To describe the survival of depressed people generally and in the subgroups of depression, such as major depression and dysthymic disorder (I, II, III)
2. To analyse the associations between depression, mortality and certain predictors of mortality (sex, age, marital status, educational level, smoking, physical health and functional abilities) (I, II, III)
3. To describe and analyse the survival of those suffering from longstanding/recurrent depression and those recovered from depression (IV)
4. To describe and analyse individual depressive symptoms predicting mortality (V)
4 Materials and methods

4.1 Study population and design

The material was based on the longitudinal epidemiological research on depression among the aged conducted in Finland from 1984 onwards. The first cross-sectional study was performed in 1984–1985 among all residents aged 60 years or older and living in Ähtäri, a semi-industrialized municipality in western Central Finland. Five years later, a second cross-sectional study was performed on a population consisting of all those aged 65 years or over in Ähtäri. The research project also included a one-year follow-up of those diagnosed as depressed after the first cross-sectional study. This included interviews by the researcher four times during the first year after the diagnosis of depression. After the first cross-sectional study also individual and community-based therapy was also provided. Individual therapy included supportive psychotherapy and medications in primary health care. Physiotherapy and acupuncture were given on an individual basis. The community-based therapy was aimed to improve the living conditions of the elderly, their position in society and their social status, in order to reduce the risk of depression. Lectures concerning aging and depression were given to lay people. The staff working with the elderly were also given further education.

4.1.1 First cross-sectional study

The formation of the study population in the first cross-sectional study is presented in Table 8. The study was performed in 1984–1985 on a series consisting of the total population born in 1923 or earlier and living in the semi-industrialized municipality of Ähtäri in western Central Finland on 1 Jan 1984 (N=1529, 618 men and 911 women).

Firstly, postal questionnaires were sent to the whole population between June and July 1984. Repeat questionnaires were sent in August to all those who had not returned the first one. The questionnaires with inadequate responses were filled in during the interviews made by three public health nurses and two practical nurses from Ähtärinjärvi Health Centre between August 1984 and December 1984. The people living in
institutions were interviewed between June 1984 and January 1985 by two general practitioners and two practical nurses from Ähtärinjärvi Health Centre or by the personnel of institution.

Table 8. Formation of the study population in the first cross-sectional study.

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original study population (aged 60 years and over and living in Ähtärä on 1.1.1984)</td>
<td>1529</td>
</tr>
<tr>
<td>Those who returned the postal questionnaire</td>
<td>1365</td>
</tr>
<tr>
<td>Those who had more than two missing answers in ZSDS</td>
<td>-51</td>
</tr>
<tr>
<td>Those who died before the clinical examination Or could not be interviewed</td>
<td>-42</td>
</tr>
<tr>
<td>Study population in the mortality study</td>
<td>1272</td>
</tr>
</tbody>
</table>

Secondly, clinical interviews and examinations were performed on those who scored ≥40 raw points in ZSDS and on a random sample below the cut-off point in order to determine the occurrence of depression. There were 183 men (35% of men who filled in the ZSDS questionnaire) and 302 women (40% of women who filled in the ZSDS questionnaire) who scored ≥40 raw points in ZSDS. Of these, 11 men and 9 women died before the clinical interview and examination. Due to a poor health status or other reason, 5 men and 17 women could not be interviewed. Thus, 167 men (91%) and 276 women (91%) scoring ≥40 raw points were interviewed and examined by the general practitioners.

A random sample of people scoring < 40 raw ZSDS points consisted of 62 men (18% of men scoring < 40 raw ZSDS points) and 96 women (21%). Of these, 3 women died before the clinical interview and examination, and 4 women could not be interviewed because of a poor health status, because they had moved away from the municipality, or for some other reason. A total of 62 men and 89 women scoring < 40 raw points in ZSDS and belonging to the random sample were interviewed and examined by the general practitioners.

Those having only 1 or 2 missing items in ZSDS were included in the study series if (a) their ZSDS score was below the cut-off point after filling in the missing items with the mean value of the same sex (adding 29 people to the non-depressed group) or (b) they were clinically examined and interviewed due to clinical interests (3 non-depressed and 5 depressed people). (There were 82 people who had many somatic and/or psychosomatic symptoms or reported previous depression, and they were examined because of clinical interests, though they had missing values in ZSDS or scored under the cut-off point in ZSDS and did not belong to the random sample.)

Altogether 290 people were found to suffer from depression in clinical interviews and examinations, 6% of them scoring less than 40 raw points in ZSDS. 214 people (71 men and 143 women) were found to suffer from dysthymic disorder, 48 from major depression, 26 from atypical depression and 2 from cyclothymic disorder. A control group was made up of the non-depressed population, i.e. the people considered not to suffer
from depression in clinical interviews and the people scoring less than 40 raw ZSDS sum points, but who were not examined or interviewed (N=982; 417 men and 565 women). This study population (N=1272) will be called the first cohort.

4.1.2 Second cross-sectional study

Five years later, in 1989–1990, a second cross-sectional study was performed on a series consisting of the total population born in 1923 or earlier (aged ≥65 yrs) and living in Ähtäri on 1 Jan 1989 (N=1225, 480 men and 745 women) (Table 9). Postal questionnaires, interviews and clinical examinations were used to collect the data. Postal questionnaires were sent to the participants two weeks prior to the examinations, which were carried out between 2 October 1989 and 31 May 1990. Most of the interviews and examinations were performed at Ähtärinjärvi health centre. Some people were examined at home or in the long-term institutions where they lived. The postal questionnaires were inspected by a research assistant or a nurse and uncompleted questions were filled in at the beginning of the interview.

The interviews and examinations were performed by three general practitioners skilled in diagnosing depression in the elderly, and 94% of those alive at the time were reached. Possible dementia was assessed in a clinical examination using the scale described by Wilson and Brass (1973), medical files and clinical evaluation. Those found to be suffering from moderate or severe dementia were excluded from the study series, because their interview would not have been reliable. The statistical analyses were thus performed on an eventual population of 1022 people, comprising 396 men and 626 women (88% of those alive).

Table 9. Formation of the study population in the second cross-sectional study.

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original study population (aged 65 years and over and living in Ähtäri on 1 Jan 1989)</td>
<td>1225</td>
</tr>
<tr>
<td>Those who died before the clinical examinations</td>
<td>–67</td>
</tr>
<tr>
<td>Those who had moved or could not be traced</td>
<td>–5</td>
</tr>
<tr>
<td>Those who refused to participate</td>
<td>–67</td>
</tr>
<tr>
<td>Population participating in the study</td>
<td>=1086</td>
</tr>
<tr>
<td>Those who had moderate or severe dementia</td>
<td>–62</td>
</tr>
<tr>
<td>Those who could not be interviewed because of severe cancer or debility</td>
<td>–2</td>
</tr>
<tr>
<td>Study population in the mortality study</td>
<td>=1022</td>
</tr>
</tbody>
</table>

Altogether 169 people were diagnosed as suffering from depression: 115 from dysthymic disorder (35 men and 80 women), 29 from major depression, 20 from atypical depression and 5 from cyclothymic disorder. The control group (non-depressed) consisted of all people who had not been found to suffer from depression during the interviews (N=853; 339 men and 514 women). This population (N=1022) will be called the second cohort.
4.1.3 Longitudinal study

The population covered in the longitudinal study was derived from these two cross-sectional studies. There were 897 people in the above study populations who participated in both studies. Because the aim was to describe the mortality of subjects with a long-standing or recurrent course of depression and those who had recovered, three groups were formed out of the non-demented subjects alive in both 1984–85 and 1989–90: 1. those depressed in both assessments (N=78), 2. those depressed in 1984–85, but non-depressed in 1989–90 (N=101), and 3. those non-depressed in both assessments (N=634). People not depressed in the first study but depressed in the second study were not included, because the outcome of their depression is unknown. Two articles have been published earlier concerning these people (Kivelä et al. 1996a, b).

4.2 Measurement of factors used in the analyses

4.2.1 Sociodemographic factors

Sociodemographic factors were measured using the postal questionnaires. They contained a question of gender and social security number, from which age was counted. In the analyses, age on 1 Jan 1984 (in the first cross-sectional study) and age on 1 Jan 1989 (in the second cross-sectional study) were used.

Educational level was measured in the questionnaire by asking about basic education. For the analyses, the educational level was dichotomized into those who had completed only part of elementary school or nothing (less than compulsory education in the beginning of this century) and to those who had completed at least elementary school (compulsory education or more).

Marital status was measured in the questionnaire by giving a choice between five alternatives: unmarried, married and living together, married but living separately, widowed and divorced. The alternatives were reduced to two in the analyses: married versus the others.

Other sociodemographic factors, such as previous occupation were also measured by the questionnaire, but they are not described here because they have not been used in the analyses.

4.2.2 Health habits

Smoking was measured in the postal questionnaire by inquiring about the present smoking status (yes/no).
4.2.3 Physical health

In the first cohort, physical health was measured in the postal questionnaires by two variables: (a) the presence of a chronic illness or impairment affecting daily activities, (b) the number of medicines used. The latter alternative was dichotomized in the analyses into those who reported the use of two or fewer medicines and those who used more than two medicines.

In the second cohort, the assessments of the participants’ physical health were made by general practitioners using a five-point scale: excellent - good - average - poor - very poor. The assessments were based on the clinical interviews and examinations and the medical records of Ähtärinjärvi Health Centre and Ähtäri District Hospital. In the analyses, physical health was dichotomized by combining good and excellent as good physical health and average, poor and very poor as poor health. Most of the people had good health, and it was practical to dichotomize the elderly into those who had good or excellent health and those who had some problems with their physical health (average, poor and very poor health). Only when studying depressive symptoms predicting mortality was physical health dichotomized so that average health was included in good health, because there were not many persons with excellent and good health among the depressed group.

Another measure of physical health was also used in the second cohort, namely the presence of chronic disease (heart disease, cancer, pulmonary disease, diabetes, cerebrovascular diseases). The variable was used as a dichotomous variable: physical health was good if the participant had no chronic diseases.

4.2.4 Functional abilities

In the first cohort, the sum score representing functional abilities included such items as the abilities to negotiate stairs, dress, bath or have sauna, wash oneself and do toiletting, which were inquired in the postal alternatives. The answers on all functions had four possibilities: managing tasks (a) independently, (b) needing auxiliary means, (c) needing the help of another person, (d) unable to do it at all. People were divided in the analyses into those independent in all of these functions and those needing help/aid in one or more of these functions.

In the second cohort, functional ability was measured in more detail because the variables in the first study did not discriminate the population very well. Functional abilities were measured with a scale used in the international comparative study on the health care of the elderly in 12 countries coordinated by the WHO Regional Office for Europe in 1979 (e.g. Heikkinen et al. 1981, Lammi et al. 1989). It consists of variables representing the abilities to move outdoors, walk between rooms, walk at least 400 metres, negotiate stairs, carry heavy things, do toiletting, wash and bath oneself, dress, go to bed, eat, cut one’s toe nails, do light housework and do heavy housework. People were divided in the analyses into those independent in all of these functions and those needing help/aid in one or more of these functions.
4.2.5 Depressive symptoms

Depressive symptoms were measured with ZSDS (Zung 1965), which was included in the postal questionnaire and with HDRS (Hamilton 1960) in interviews by physicians. The ZSDS questionnaires were checked by a nurse before the interviews and clinical examinations, and the omitted items were completed by interviewing in the second cross-sectional study. Depressive symptoms predicting mortality were studied in the second cohort, because all participants in the second cross-sectional study were interviewed by general practitioners, whereas a two-phased methodology was used in the first cross-sectional study.

Firstly, to analyse the individual symptoms predicting mortality, the mean of each item in both ZSDS and HDRS was compared between the survivors and the deceased during the six-year follow-up. Secondly, multivariate analyses were performed and the depressive symptoms were dichotomized for them. ZSDS measures the frequency of depressive symptoms, and the symptoms were dichotomized as follows: having a symptom never, seldom or occasionally was considered as not having the symptom. If the participant reported having a symptom for a good part of the time, most of the time or always, she/he was considered to have that symptom. Weight loss was an exception. This item was considered positive if the participant reported having experienced any weight loss. HDRS measures the intensity of symptoms, and they were dichotomized in the analyses based on their mean values (i.e. weight loss: 1= not at all, 2= weight loss according to the patient’s reply; suicidal thoughts: 1= not at all, 2= thoughts of death/suicide or suicidal behavior; gastrointestinal symptoms: 1= not at all/ or no pleasure of eating, 2= must be asked to eat, uses laxatives or other gastrointestinal drugs).

4.2.6 Depression

In the first cross-sectional study a two-phased method was used to detect depression, first by screening with the Zung Self-Rating Depression Scale (ZSDS) (Zung 1965) and after that by interviewing and examining those who scored 40 raw sum points or more in ZSDS and a random sample of those scoring less than 40 points. Depression was determined according to the DSM-III criteria (APA 1980) after detailed semistructured interviews. The participants were interviewed by two general practitioners trained in diagnosing depression in the elderly. If necessary for diagnosing or excluding depression, the participant was interviewed and examined twice or even three times at intervals of about one week.

In the second cross-sectional study, all participants were interviewed, and depression was determined according to the DSM-III criteria (APA 1980) after semistructured interviews similar to those in the first study. The interviews were performed by three general practitioners skilled in diagnosing depression in the elderly.

The role of depression as a predictor of mortality wasanalysed with the Cox proportional hazards model, taking into account age, sex, marital status, educational level, smoking and variables representing functional abilities and physical health (in the first cohort: 1. the occurrence of a chronic illness or impairment affecting daily activities and
2. the number of medicines; in the second cohort: general practitioner’s assessment of the participant’s physical health). All populations were analysed by a model, where age and sex were forced and the other variables introduced into the model as potential predictors together with depression following a stepwise procedure. Some other models were also performed in the whole population. All populations included the non-depressed subjects and that part of the depressed population which was the target of the study, e.g. major depressives, those suffering from dysthymic disorder, those suffering from long-standing or relapsing disorder, and those recovered from depression. The two last mentioned groups were also analysed together, using depression as a three-level variable (1. level = no depression, 2. level = recovered from depression, 3. level = depressed in both studies).

4.3 Follow-up periods

The individual follow-up periods of the subjects in the first cross-sectional study started from the date when the postal questionnaire was returned, and mortality was assessed till 30 June 1990, i.e. for a period approximately six years. The mortality of those suffering from dysthymic disorder was also assessed for a longer follow-up period, till 31 Dec 1995 (about 11.5 years).

The follow-up of the people in the second cross-sectional study started from the date of the interview and the examination and lasted till December, 31, 1995 (approximately six years).

The dates and causes of death were derived from Central Statistics Finland.

4.4 Statistical analyses

Cross-tabulation was used to analyse the background data, and the significances were tested by either the Kruskal-Wallis test or the Chi-square test. The survival analysis was based on a technique where the time to death was the dependent variable. The Kaplan-Meier survival curves were used to represent the survival distributions, which were then tested using the Mantel-Cox (log-rank) statistics (Dixon 1985, Matthews & Farewell 1988). The Cox proportional hazards model was used to analyse the simultaneous relationships between mortality and possible variables. In the computer program, the result is a set of estimated regression coefficients, which represents the relative effect of each covariate on the survivor function (Dixon 1985). With the Cox model and binary covariates, the conversion factor (exp(coeff)) can be interpreted as the relative risk (RR) (Matthews & Farewell 1988), and its estimation can be complemented with the 95% confidence intervals (95%CI). These two parameters are given in the tables showing the results of the Cox models. The statistical analyses were carried out using the BMDP Statistical Software (Dixon 1985).
5 Results

5.1 Background data

5.1.1 Participants

The depressed and non-depressed men (or women) in the first cohort did not differ from
each other in marital status, educational level and living conditions (Table 10). Overall
educational level was low. Mean age was somewhat higher among the depressed women
than the non-depressed ones (p=0.015). The majority of depressed people were suffering
from dysthymic disorder. The other diagnoses were major depression, atypical depression
and cyclothymic depression. No people suffering from bipolar disorder at the moment of
examinations were found.

In the second cohort, there were more differences between the depressed and non-
depressed people (Table 10). Marital status did not differ significantly between these
groups, though there were more widows and widowers among the depressed. The
depressed men were older (p=0.004) and had a lower educational level (p=0.002) than the
non-depressed ones, but the depressed women did not differ significantly from their non-
depressed counterparts. The distribution of the subtypes of depression was similar to that
in the first cross-sectional study.

5.1.2 Non-participants

Some data concerning the non-participants in the first cross-sectional study have been
analysed earlier (Pahkala 1990, Kivelä et al. 1988). Generally the people who were not
contacted, were older and a greater proportion of them were not married, were in long-
term care and had poor physical health.

In the second cross-sectional study, the non-participants consisted of two groups: 1)
those who did not want to participate or had moved away (N=71) and 2) those who could
not be interviewed reliably because of possible dementia or another illness (N=64) (Table
11). Of those who did not want to participate, 85% (N=60) simply refused to participate.
<table>
<thead>
<tr>
<th>Variable</th>
<th>1. cross-sectional study</th>
<th>2. cross-sectional study</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Depressed (N=290)</td>
<td>Non-depressed (N=982)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Men (N=101)</td>
<td>Women (N=189)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Women (N=160)</td>
<td>Women (N=803)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Men (N=57)</td>
<td>Women (N=112)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Women (N=514)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>70.4 (7.4)</td>
<td>69.6 (6.8)</td>
<td>76.2 (6.1)**</td>
<td>75.6 (6.8)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td>73.8 (5.9)</td>
<td>74.3 (6.1)</td>
</tr>
<tr>
<td>–unmarried (%)</td>
<td>11</td>
<td>9</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>–married (%)</td>
<td>64</td>
<td>36</td>
<td>42</td>
<td>61</td>
</tr>
<tr>
<td>–widowed (%)</td>
<td>23</td>
<td>53</td>
<td>44</td>
<td>25</td>
</tr>
<tr>
<td>–divorced (%)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Type of residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–living alone (%)</td>
<td>14</td>
<td>32</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>–living with someone else (%)</td>
<td>82</td>
<td>62</td>
<td>83</td>
<td>63</td>
</tr>
<tr>
<td>–in long-term care (%)</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Proportion (%) of those who had</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than compulsory education</td>
<td>35</td>
<td>28</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Proportion (%) of those suffering</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>from</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–major depression</td>
<td>14</td>
<td>18</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>–dysthymic disorder</td>
<td>70</td>
<td>76</td>
<td>61</td>
<td>71</td>
</tr>
<tr>
<td>–atypical depression</td>
<td>14</td>
<td>6</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>–cyclothymic disorder</td>
<td>2</td>
<td>–</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01; ***p<0.001, ref. group is the corresponding group of non-depressed people.
Four percent (N=3) refused to participate due to a poor physical status and 4% (N=3) said their relatives did not want them to participate. Seven percent had moved away (N=4) or could not be traced (N=1). Most of those who did not want to participate in the second cohort had not been participating the first cross-sectional study, either, in 1984–1985 (77%, N=53). Some information of non-participants was collected from medical registers and the personnel of Ähtärinjärvi Health Centre and Ähtäri District Hospital (table 11). Generally, it can be concluded that those who did not participate in the study were older and in a poorer physical condition than the participants.

**Table 11. Comparison of participants to non-participants in the second cross-sectional study.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Those who participated</th>
<th>Those who did not participate or were excluded from the study material</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=1022)</td>
<td>Men (N=396) Women (N=626)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–74</td>
<td>546 (53%) 221 (56%) 325 (52%)</td>
<td>63 (47%) 25 (53%) 38 (43%)</td>
</tr>
<tr>
<td>75–84</td>
<td>410 (40%) 153 (39%) 257 (41%)</td>
<td>54 (48%) 17 (36%) 37 (42%)</td>
</tr>
<tr>
<td>85–</td>
<td>66 (7%) 22 (5%) 44 (7%)</td>
<td>25(13%) 5 (11%) 13 (15%)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>unmarried</td>
<td>112 (11%) 41 (10%) 71 (11%)</td>
<td>23 (17%) 5 (11%) 18 (20%)</td>
</tr>
<tr>
<td>married</td>
<td>498 (49%) 281 (71%) 217 (35%)</td>
<td>44 (36%) 25 (53%) 19 (22%)</td>
</tr>
<tr>
<td>widowed</td>
<td>390 (38%) 67 (17%) 323 (52%)</td>
<td>57 (42%) 9 (19%) 48 (55%)</td>
</tr>
<tr>
<td>divorced</td>
<td>22 (2%) 7 (2%) 15 (2%)</td>
<td>11 (8%) 8 (17%) 3 (3%)</td>
</tr>
<tr>
<td><strong>Capacity to move</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>independently without aids</td>
<td>827 (81%) 336 (85%) 491 (78%)</td>
<td>58 (57%) 23 (59%) 35 (56%)</td>
</tr>
<tr>
<td>needs an aid or help from another person</td>
<td>195 (19%) 60 (15%) 135(22%)</td>
<td>44 (43%) 16 (41%) 28 (44%)</td>
</tr>
</tbody>
</table>

*0.05*p<0.01; **0.01*p<0.001; ***p<0.001, ref. group is the corresponding group of those who participated

### 5.2 Cumulative survival

#### 5.2.1 Total depressed population

**5.2.1.1 First cohort**

Cumulative survival decreased steadily during the follow-up in both the non-depressed and depressed men, but the decrease was more evident in depressed men (p=0.024) (Fig. 1). 34% of depressed men and 23% of non-depressed men had died during the six years.
When the differences between the Kaplan-Meier survival curves of men were tested year by year, there was no difference after a follow-up of one year or two years. After a three-year follow-up, however, the difference tended to be significant (p=0.055), and after four (p=0.028) or five years (p=0.029) the differences were significant.

Among women, 25% of the depressed and 19% of the non-depressed subjects had died by the end of the follow-up period. The cumulative survival of the depressed women was lower than that of the non-depressed ones (p=0.035).

![Kaplan-Meier survival estimates for non-depressed and depressed in both sexes in the first cohort.](image)

When the Kaplan-Meier survival curves were tested year by year, the difference between the survival curves was not significant after a one-year or two-year follow-up. After a three-year follow-up, however, the difference tended to be significant (p=0.069), and after a four-year (p=0.032) and five-year (p=0.008) follow-up the survival curves differed significantly.

The difference in cumulative survival between all depressed and non-depressed people was not significant in the younger age group (60–69 years), but in the older age group (≥70 years) the depressed people had lower survival rate than the non-depressed ones (p=0.037). When these two age groups were divided according to sex, no significant differences were found between the survival curves, but in the group of older men (≥70 years) the depressed tended to show significantly poorer survival than the non-depressed men (p=0.070).
5.2.1.2 Second cohort

Forty-six per cent of the depressed subjects had died during the follow-up versus 26% of the non-depressed people. The difference between the survival curves was significant ($p<0.001$). Among men, 49% of the depressed had died during the follow-up, the corresponding figure being 32% for the non-depressed. The survival curves differed significantly from each other ($p=0.004$) (Fig. 2). Among women, 44% of the depressed subjects and 23% of the non-depressed subjects had died, the difference between the survival curves being significant ($p<0.001$) (Fig. 2).

When mortality was analysed at one-year intervals from one to six years of follow-up, the difference between the survival curves was statistically significant after only one-year follow-up among both men ($p=0.017$) and women ($p <0.001$).

![Kaplan-Meier survival estimates for non-depressed and depressed in both sexes in the second cohort.](image)

5.2.2 Population with major depression

Cumulative survival was poorer for the men suffering from major depression than for the non-depressed men ($p=0.019$) (Fig. 3) in the second cohort. Sixty percent of the men suffering from major depression had died during the follow-up, the corresponding figure for the non-depressed men being 32%. Among the women, 47% of those depressed and 23% of those non-depressed had died, and the difference between the survival curves was significant ($p=0.007$) (Fig. 3).
5.2.3 Population with dysthymic disorder

5.2.3.1 First cohort

Thirty-four percent of the dysthymic men had died by the end of the six-year follow-up period, the corresponding figure for the non-depressed men being 23%. The Kaplan-Meier survival curves tended to differ significantly (p=0.055). When the follow-up time was continued till the end of the year 1995, 62% of the dysthymic men and 50% of the non-depressed men had died, and the difference between the survival curves was significant (p=0.019) (Fig. 1, III).

Altogether 22% of the women suffering from dysthymic disorder and 19% of the non-depressed women had died by the end of the six-year follow-up. The difference between the Kaplan-Meier survival curves did not reach statistical significance. But as noticed among men, when the follow-up period was longer, the survival curves differed significantly between the dysthymic and non-depressed women (p=0.002). At the end of the year 1995, 52% of the dysthymic women and 39% of the non-depressed women had died (Fig. 1, III).
5.2.3.2 Second cohort

Forty-four percent of the men suffering from dysthymic disorder had died by the end of the follow-up of about six years, compared to only 32% of the non-depressed men, their survival curves differing significantly from each other (p=0.026) (Fig. 2, III). Of the women suffering from dysthymic disorder, 41% had died, whereas the mortality rate of the non-depressed women was 23%. The difference between survival curves was significant (p<0.001) (Fig. 2, III).

5.2.4 Population with long-lasting or recurrent depression

According to Kaplan-Meier survival analysis, 48% of the people who were depressed in both cross-sectional studies had died during the six-year follow-up, while only 26% had died among those who were non-depressed in both studies (p<0.001).

5.2.5 Population recovered from depression

Of the people who were depressed in the first cross-sectional study, but not depressed in the follow-up study, 31% had died. Their survival rate did not differ from that of those non-depressed in both studies (26%).

5.2.6 Non-participants

In the first cohort, the mortality rate was higher among the non-participants than the participants (Fig. 4). Forty percent of both the men and women who did not participate in the study had died during the six-year follow-up, whereas 20% of the female (p <0.001) and 25% of the male participants (p<0.001) had died.

In the second cohort the survival of the non-participants was also poorer than that of the participants (Fig. 5). Among the non-participants, 51% of both sex had died, whereas 26% of the female (p<0.001) and 35% of the male participants (p=0.008) had died.
Fig. 4. Kaplan-Meier survival estimates for participants and non-participants in both sexes in the first cohort.

Fig. 5. Kaplan-Meier survival estimates for participants and non-participants in both sexes in the second cohort.
5.3 Depression as a predictor of mortality

5.3.1 Total depressed population

5.3.1.1 First cohort

In this group, the basic model showed the following covariates to be predictors of mortality: high age, high number of medicines, lowered functional abilities, smoking, male sex and a chronic illness or an impairment (Table 12). This model was also applied separately to men and women. The predictors of mortality in the male model were high age and a high number of medicines. High age, a high number of medicines, lowered functional abilities and smoking emerged as predictors in the female model.

Table 12. Predictors of mortality according to the Cox models (RR = relative risk and 95% CI = 95% confidence interval) in the first and second cross-sectional studies in the population consisting of non-depressed and depressed people.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>1. cross-sectional study</th>
<th>2. cross-sectional study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.4</td>
<td>1.07–1.77</td>
</tr>
<tr>
<td>High age*</td>
<td>1.1</td>
<td>1.07–1.11</td>
</tr>
<tr>
<td>High number of medicines used</td>
<td>1.6</td>
<td>1.26–2.15</td>
</tr>
<tr>
<td>Occurrence of chronic somatic disease</td>
<td>1.4</td>
<td>0.97–2.16</td>
</tr>
<tr>
<td>Poor or average physical health</td>
<td>–</td>
<td>1.8</td>
</tr>
<tr>
<td>Lowered functional ability**</td>
<td>1.4</td>
<td>1.10–1.90</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.6</td>
<td>1.12–2.26</td>
</tr>
<tr>
<td>Widowed, divorced or unmarried marital status</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Low educational level</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Depression</td>
<td>–</td>
<td>1.3</td>
</tr>
</tbody>
</table>

*RR = variable was not included in the final model. *RR is a relative risk of one year. – = variable was not usable in this cross-sectional study. **Lowered functional ability = Non-independence in at least one of the measured functions: (1st cross-sectional study) eat, dress, negotiate stairs, bath or have sauna, wash oneself and do toileting; (2nd cross-sectional study) in addition to the aforementioned functions, move outdoors, walk between rooms, walk at least 400 metres, carry heavy things, go to bed, cut one’s toe nails, do light and heavy housework.

The models were also applied to the different sex and age groups by using variables similar to those used in the second phase, excluding sex. In the younger male age group (60–69yrs), a high number of medicines (RR 3.31, 95 % CI 1.59–5.91) and a low educational level (RR 2.0, 95 % CI 1.04–3.95) were associated with higher mortality. Among the older men (≥70 yrs), high age (RR 1.1, 95 % CI 1.05–1.12) and lowered functional abilities (RR 1.6, 95 % CI 1.01–1.28) were predictors of mortality. Among the younger women (60 – 69 years), a high number of medicines (RR 3.82, 95 % CI 1.00–1.28), smoking (RR 6.0, 95 % CI 2.19–16.50) and high age (RR 1.1, 95 % CI 1.80–8.16)
and among the older women (≥70 yrs), high age (RR 1.1, 95 % CI 1.08–1.15), lowered functional abilities (RR 1.6, 95 % CI 1.09–2.38) and the presence of a chronic somatic illness (RR 2.2, 95 % CI 1.12–4.21) were associated with higher mortality.

A model without variables representing physical health and functional abilities was also constructed including only age, sex, marital status, educational level, smoking and the presence of depression (Table 2, I). A higher risk of mortality was associated with smoking, high age, male sex and the occurrence of depression. When the variable representing sex was excluded and similar models were fitted separately for men and women, higher age was the only predictor of mortality in men. In women, higher age and smoking emerged as predictors.

5.3.1.2 Second cohort

The following factors were associated with higher mortality: male sex, high age, depression, smoking, poor physical health and lowered functional abilities (Table 12).

5.3.2 Population with major depression

High age, male sex, smoking, poor physical health, lowered functional abilities and the presence of major depression were related to higher mortality (Table 13).

Table 13. Predictors of mortality according to the Cox models (RR = relative risk and 95% CI = 95% confidence interval) in the second cross-sectional study in the population consisting of non-depressed and major depressed people.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.7</td>
<td>1.30–2.21</td>
</tr>
<tr>
<td>High age</td>
<td>1.1</td>
<td>1.07–1.12</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.5</td>
<td>0.98–2.34</td>
</tr>
<tr>
<td>Moderate or poor physical health</td>
<td>1.7</td>
<td>1.31–2.31</td>
</tr>
<tr>
<td>Lowered functional abilities</td>
<td>1.7</td>
<td>1.26–2.40</td>
</tr>
<tr>
<td>Major depression</td>
<td>2.0</td>
<td>1.17–3.41</td>
</tr>
<tr>
<td>Widow, divorced or unmarried marital status</td>
<td>dł</td>
<td></td>
</tr>
<tr>
<td>Low educational level</td>
<td>dł</td>
<td></td>
</tr>
</tbody>
</table>

(dl = not a significant predictor (variable did not emerge in the final model)}
5.3.3 Population with dysthymic disorder

5.3.3.1 First cohort

The factors predicting mortality in the first cohort were identical during both the shorter (6 yrs) and the longer (11.5 yrs) follow-up period (Table 14). They were male sex, high age, smoking, low educational level, the use of more than two medicines and lowered functional abilities. The occurrence of dysthymic disorder did not emerge in the model.

Table 14. Predictors of mortality according to the Cox models (RR = relative risk and 95% CI = 95% confidence interval) in the first and second cross-sectional studies in the population consisting of non-depressed subjects and ones suffering from dysthymic disorder.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>1. cross-sectional study</th>
<th>2. cross-sectional study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Follow-up of 6 yrs</td>
<td>Follow-up of 11.5 yrs</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.4(1.10–1.87)</td>
<td>1.5(1.22–1.76)</td>
</tr>
<tr>
<td>High age*</td>
<td>1.1(1.08–1.12)</td>
<td>1.1(1.08–1.11)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.5(1.07–2.23)</td>
<td>1.4(1.10–1.84)</td>
</tr>
<tr>
<td>Number of medicines used &gt;2</td>
<td>2.0(1.50–2.55)</td>
<td>1.6(1.34–1.92)</td>
</tr>
<tr>
<td>Impairment affecting daily activities</td>
<td>✎</td>
<td>✎</td>
</tr>
<tr>
<td>Moderate or poor physical health</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lowered functional abilities</td>
<td>1.4(1.07–1.92)</td>
<td>1.5(1.26–1.90)</td>
</tr>
<tr>
<td>Dysthymic disorder</td>
<td>✎</td>
<td>✎</td>
</tr>
<tr>
<td>Widowed, divorced or unmarried marital status</td>
<td>✎</td>
<td>✎</td>
</tr>
<tr>
<td>Low level of education</td>
<td>1.3(0.99–1.67)</td>
<td>1.3(1.07–1.55)</td>
</tr>
</tbody>
</table>

* = not a significant predictor (the variable did not emerge in the final model), –= variable not included in the modelling, * = RR is the relative risk of one year.

5.3.3.2 Second cohort

The factors predicting higher mortality were male sex, high age, smoking, poor physical health and lowered functional abilities (table 14). It appeared in the stepwise modeling that dysthymic disorder was associated with poor physical health and lowered functional abilities. When these variables (poor physical health, lowered functional abilities) emerged in the model, the power of the dysthymic disorder variable to predict death disappeared.
Long-standing depression predicted mortality even when the other factors were controlled. Among those having recovered from depression, the history of depression did not predict mortality when the other factors were controlled (table 15). The results were also similar when depression was not a three-level variable, but two separate models for these groups of depressed people were constructed.

Table 15. Predictors of mortality according to the Cox model (RR=relative risk; 95% CI=confidence interval) in the population consisting of the non-depressed, the recovered and those suffering from long-standing depression (forced model).

<table>
<thead>
<tr>
<th>variable</th>
<th>RR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>high age (continuous variable)</td>
<td>1.1</td>
<td>1.07–1.12</td>
</tr>
<tr>
<td>male sex</td>
<td>1.4</td>
<td>1.04–1.80</td>
</tr>
<tr>
<td>smoking</td>
<td>1.7</td>
<td>1.11–2.70</td>
</tr>
<tr>
<td>lowered functional abilities*</td>
<td>1.7</td>
<td>1.21–2.39</td>
</tr>
<tr>
<td>poor physical health**</td>
<td>1.8</td>
<td>1.38–2.42</td>
</tr>
<tr>
<td>depression***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>recovered from depression</td>
<td>1.3</td>
<td>0.85–1.87</td>
</tr>
<tr>
<td>long-standing/recurrent depression</td>
<td>1.5</td>
<td>1.06–2.20</td>
</tr>
</tbody>
</table>

* reference group consists of subjects independent in view of functional abilities. ** reference group consists of subjects in good physical health according to the attending general practitioner. *** reference group consists of subjects non-depressed in both studies.

5.4 Causes of death

The causes of death did not differ between the depressed and non-depressed men or women in the first cohort and in the second cohort (Table 16). One depressed man had committed suicide in the first cohort. In the second cohort, two people determined as non-depressed at the beginning of the study had committed suicide during the follow-up.

There were no differences in the causes of death either between those suffering from major depression and non-depressed people or between dysthymic and non-depressed people. Cardio- and cerebrovascular causes tended to be more common among the dysthymic than the non-depressed people (66% versus 52%) in the second cohort, but there was no statistical difference (Table 2, III).
Table 16. Distribution of depressed and non-depressed people who died during the follow-up periods in the first and second cross-sectional studies by causes of death.

<table>
<thead>
<tr>
<th>Cause of death (ICD code)</th>
<th>First cross-sectional study</th>
<th>Second cross-sectional study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Depressed people N (%)</td>
<td>Non-depressed people N (%)</td>
</tr>
<tr>
<td>Neoplasms (140–239)</td>
<td>12 (15%)</td>
<td>40 (20%)</td>
</tr>
<tr>
<td>Mental disorders (290–315)</td>
<td>3 (4%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Cardio- and cerebrovascular diseases (390–448)</td>
<td>41 (50%)</td>
<td>109 (56%)</td>
</tr>
<tr>
<td>Pulmonary diseases (480–519)</td>
<td>17 (21%)</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>Gastrointestinal diseases (530–577)</td>
<td>2 (2%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Injuries and poisonings (800–999) and E-codes</td>
<td>1 (1%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Other diseases, symptoms and unspecified cases</td>
<td>6 (7%)</td>
<td>9 (5%)</td>
</tr>
</tbody>
</table>

5.5 Depressive symptoms predicting mortality in the depressed elderly

5.5.1 Self-assessed depressive symptoms

Baseline dissatisfaction, frequent feelings of emptiness and weight loss reported on ZSDS were more frequent among the deceased than the survivors (Table 2, V). None of the depressive symptoms on ZSDS were significantly more frequent or more severe among the survivors compared to the deceased. When the aforementioned symptoms (dissatisfaction, emptiness and weight loss) were included in a multivariate model (Cox model) as possible predictors of mortality, high age, poor physical health, weight loss and dissatisfaction emerged as factors predicting mortality during the six-year follow-up (Table 3, V).

To gain more understanding about the specific symptoms predicting mortality, the value of each item of ZSDS was compared between the deceased subjects and the survivors even in the non-depressed population. Weight loss and emptiness did not differ between the survivors and the deceased, but dissatisfaction was more common among the non-depressed people who died during the follow-up compared to the survivors (p=0.001).

Later on, it was analysed whether weight loss was more common among the depressed people with chronic diseases than among those without such diseases. The mean value of the item representing weight loss on ZSDS did not differ significantly between the people with and without a chronic disease (malignant neoplasm, diabetes, cardiovascular disease or chronic pulmonary disease).
5.5.2 Interview-based depressive symptoms

Weight loss, suicidal thoughts and gastrointestinal symptoms (anorexia and constipation) were more marked among the depressed people who died during the follow-up of six years than among those who remained alive (Table 2, V). None of the depressive symptoms on HDRS were significantly more frequent or more severe among the survivors compared to the deceased. In a multivariate analysis (Cox model) of the HDRS items, high age, poor physical health, gastrointestinal symptoms (anorexia and constipation) and weight loss emerged as predictors of mortality (Table 4, V).

The HDRS symptoms were also studied among the non-depressed people. When the mean values of the items were compared between the deceased and the survivors, suicidal thoughts and weight loss did not differ between these two groups, but gastrointestinal symptoms did. The latter symptoms were more marked among the non-depressed deceased than among the survivors.

Later on, the differences in the intensity of weight loss and gastrointestinal symptoms were analysed between the depressed people with a chronic disease (malignant neoplasm, diabetes, cardiovascular disease or chronic pulmonary disease) and those without such disease. The mean value of the item representing weight loss did not significantly differ between these two groups. The mean value of the item representing gastrointestinal symptoms was higher among those having cardiovascular diseases, especially myocardial infarction (p=0.025).
6 Discussion

6.1 Study population

The study material was collected in Ähtäri, a semi-rural municipality in western Central Finland. The study population consisted of all the elderly people in the community. Those in the wards of the local health centre and nursing home and the district hospital of Ähtäri were also included in the study population. The people in long-term care constituted less than ten per cent of the study population. In view of the high participation rates, it can be concluded that the study population is a representative sample of the Finnish elderly people in the 1980s living in rural area and small towns.

Only 14% of the population were non-participants in the first study, the corresponding figure being 9% in the second study after the exclusion of those who had died between the time when the study population was drawn from the register and the examinations were done. The survival of the dropouts was poorer than that of the participants. Due to the high participation percentage, this did not have a remarkable effect to the results.

6.2 Methods

6.2.1 Postal questionnaires, interviews and examinations

Postal questionnaire is a frequently used and practical method to collect information in community-based studies. Most of the questions in the postal questionnaires in the Ähtäri study were drawn from earlier questionnaires used in Finnish geriatric studies. At the beginning of the project, the workers of Ähtäri Health Centre were trained to assist the clients in filling in the questionnaires, if necessary.

How reliable are the replies to a postal questionnaire, especially when the older population is concerned? It has been previously shown that, as far as the basic functional abilities are concerned, the level of agreement between questionnaire-based and provider ratings is surprisingly high, whereas in more complex self-care activities agreement decreases (Kivelä 1984).
The reliability of the answers, especially to a postal questionnaire, can be questioned when dealing with an old population having memory problems. In the first cohort, the persons in long-term institutional care and some persons using home nursing or home help services were interviewed to see, if they were able to answer the questions. Probably those suffering from severe dementia and even some of those suffering from moderate dementia were excluded, because most of these persons were long-term patients either in institutional care or in home care, and the interviewers could not get reliable answers. In the second cohort, those having moderate or severe dementia were excluded from the study population, because they could not be reliably interviewed. Those having mild dementia were included in the study population in the second cross-sectional study. Depression and depressive symptoms have been shown to increase mortality among people with mild dementia (Janzig et al. 1999).

6.2.2 Measurement of factors and their use

Sociodemographic factors. Marital status and educational level were requested in the postal questionnaire using structured questions. Marital status was used in the analysis as a dichotomized variable: the married versus the others (single, widowed and divorced). The married were selected as a reference group because they have the lowest mortality when mortality differentials by marital status are observed in different cultures (Hu & Goldman 1990). The difference in mortality by marital status decreases with age (Martelin 1996). Educational level was low in the study population, which is usual in this generation of rural population, and there was not much difference in this variable between the participants.

Health habits. Only smoking was used as a marker of poor health habits predicting mortality. The use of alcohol was also asked about in the questionnaires, but the consumption of alcohol is so low in the old population of the studied generation outside big cities that it could not be taken as an adjusted factor. Smoking was asked about with a very simple question: whether the subject smoked or not. Nothing was asked about past smoking or about the number of cigarettes smoked per day. This formulation of the question proved to be satisfactory, however, because smoking correlated with the risk of death in the present study.

Physical health. In the first cross-sectional study, the postal questionnaire contained many questions concerning physical health, e.g. the use of medicines, the occurrence of a chronic illness or an impairment affecting daily activities, somatic and psychosomatic symptoms, self-reported diseases and self-assessed health. Diseases were asked about with an open-ended question and were reported unreliably. Because self-reported health is directly associated with depression, the use of medicines was selected to describe health together with the occurrence of a chronic illness or an impairment affecting daily activities. The latter was not very good variable due to its frequency distribution; most of the participants reported having such an impairment.

In the second cross-sectional study a more objective measure of physical health was used: the attending general practitioner rated the participant’s physical health based on the examination and medical files. Physical health was rated on a five-point scale (excellent –
good – moderate – poor – very poor). In the analyses concerning the whole study population, the scale was simplified and dichotomized using good/moderate as the cut-off point, because about 60% of the subjects among both sexes had good or very good physical health. It was practical to dichotomize the elderly into those who had good health and to those who had some kind of problems with their physical health (average, poor and very poor health) when the majority had good health. When this dichotomy was used, poor health correlated with mortality. This supports the view that this measure of physical health can be relied on. The other measure of physical health, i.e. the occurrence of chronic physical disease, was not an equally good measure of physical illness as the aforementioned variable.

**Functional abilities.** In the first cross-sectional study, only the basic abilities (ability to eat, dress, bath or have sauna, wash oneself, do toileting and negotiate stairs) were measured. In the second cross-sectional study, questions concerning functional abilities were added because those in the first study did not discriminate the home-dwelling population very well. In addition to the variables in the first study, functional ability was measured by variables representing the abilities to move outdoors, walk between rooms, walk at least 400 metres, carry heavy things, do toileting, go to bed, cut one's toe nails, do light housework and do heavy housework. In both studies, it was practical to divide the population in the analyses into those independent in all of these functions and those needing help or an aid in even one of these functions. This division separates those who are really independent in daily life.

Functional abilities was selected as one of the possible predictors of death, although there is a connection between functional abilities and depression. Lowered functional abilities predict depression (Kivelä *et al.* 1996a), but depression also predicts impaired functional capacity (Wells *et al.* 1989, Kivelä & Pahkala 2001).

**Depression.** The measurement of depression was done carefully. In the first cross-sectional study, one researcher (KP) did almost all the examinations as well as the one-year follow-up examinations. He was familiar with the literature concerning geriatric depression and discussed the diagnostics of depression with many psychiatrists and psychogeriatricians. He also contacted the psychiatrists who had translated DSM-III into Finnish. Another general practitioner from the local health centre was also worked as a researcher in this project. She, too, was familiar with geriatric depression. They recorded the interviews and discussed all the problematic cases at the beginning of the study. If needed, the diagnosis was confirmed by a re-interview within two weeks. About two thirds of the depressed subjects were getting antidepressants. Though the criteria of depression are quite explicit, there may be some minor differences in the diagnostic practices in different disciplines. As an example, there were slight differences when the diagnoses made by psychiatrists and geriatricians were compared, e.g. the agreement between psychiatrists and geriatricians only just reached the level of significance in the diagnosis of depression (Ryan *et al.* 1995).

In the second cross-sectional study, the same researcher who had initiated the examinations in the first study examined all those who had been diagnosed as depressed in the first study. The rest of the study population were interviewed by two experienced general practitioners who had familiarized themselves with the diagnosis of depression in
the elderly. There was no statistical difference in the prevalence of depression among either men or women between these two researchers (Pahkala et al. 1995), which shows the marked consistency in the diagnostics.

Mortality data. Mortality statistics in Finland can be considered perfect as far as the times of death and the reporting of deaths are concerned. Those who had moved away from Ähtäri after the examinations could also be included in the mortality analysis with the exception of those few who had moved abroad. The mortality follow-up is practically complete. As far as the causes of death are concerned, the statistics are not so reliable. Autopsies are made less often on older than younger people.

6.2.3 Statistical methods

Kaplan-Meier survival analysis and Cox proportional hazard models are modern statistical methods and frequently used in mortality analysis. The analysis of survival data is based on a technique where the time to death is the dependent variable. That makes it possible to use all the available information about the participants as long as they have been followed, which is very useful whenever there are incomplete and censored observations (Dixon 1985).

6.2.4 Results

The results of this study showed a poorer survival among the community-living depressed elderly people. The adjusted (by age, sex, socioeconomic status, smoking, physical health, functional ability) mortality rate was higher among the depressed elderly in the second cross-sectional study, but not in the first study. This is due to differences in these studies, mortality rates, methodology, age composition, and intervention during the first cross-sectional study. As a matter of fact, the inconsistency seen here reflects the variability of the previously published results concerning the mortality of the depressed elderly. Methodological differences, populations from different settings, different follow-up times and measures of depression contribute to the inconsistency of the results. One published study examined the associations between depressive symptoms and mortality risk in many ways and found that it was affected by baseline physical health, the duration of follow-up and the measurement of depression (Fredman et al. 1999).

An important finding in the present study was that the survival of those who recovered from depression during the five-year interval did not differ from that of the non-depressed ones. However, the mortality rate of those depressed at both measures at a five-year interval was higher than that of non-depressed ones.
6.2.5 Cumulative survival of the older population


In both main subgroups of depression, i.e. major depression and dysthymic disorder, the depressed people also had poorer survival than the non-depressed ones. Proportional mortality was highest among those suffering from major depression. The results concerning those suffering from major depression confirm the results of the previous studies (Rabins et al. 1985, Murphy et al. 1988, Bruce & Leaf, 1989, Koenig et al. 1989, Burvill et al. 1991, Parmalee et al. 1992, Brodaty et al. 1993, Rovner, 1993, Zubenko et al. 1997, Ganzini et al. 1997, Penninx et al. 1999). The main focus in the previous studies has usually been on people suffering from major depression. Not much interest has been targeted to those suffering from dysthymic disorder. According to our results, however, their crude mortality seems to be higher than that of non-depressed persons. In the study by Penninx and colleagues (1999), minor depression was studied separately and unadjusted mortality was higher when compared to those having no depression, similarly to our study.

6.2.6 Depression as a predictor of mortality

Many findings, including those from this study, support the view that the mortality rate of depressed people is increased. There are several possible explanations for these findings. Depressed people as a group have certain characteristics which may predispose them to premature death. Low social class and low educational level are related to an increased risk of death (Valkonen et al. 1993, Martelin 1994, 1996) and also to an increased risk of depression (Lehtinen & Joukamaa 1994). Marriage protects people not only from death, but also from depression (Lehtinen & Joukamaa 1994), when compared to the other classes of marital status. Poor health habits, at least smoking and a abundant consumption of alcohol, are factors predisposing to premature death, and they are also associated with depression. Naturally, poor health, diseases and poor functional abilities, mostly due to poor health, are major factors predisposing to excess death and also to depression.

In a review of mortality studies among the depressed in all-aged populations, Wulsin and colleagues (1999) suggested that the most important factors related to both depression and mortality are chronic physical illnesses, smoking, abuse of alcohol and suicides and related accidents. However, it depends on the study population whether all these factors should be controlled. Lesperance and Frasure-Smith (1999) remark that suicides are very rare in community populations and that there is hence no need to control them. Controlling smoking and alcohol abuse is also a complex task. The question also remains
as to whether physical illness could ever be controlled well enough (O’Brien & Ames, 1994). It is not easy to measure physical health objectively, and only apparent illnesses can be controlled at the moment of the study.

6.2.6.1 Results in two cohorts

The results concerning the adjusted mortality of depressed people differed between the first and second cross-sectional studies. In the first cross-sectional study, depression did not emerge in the final Cox model as an independent predictor of death. Instead of that, the predictors of death were male sex, high age, high number of medicines used, lowered functional abilities and smoking. In the second cross-sectional study, depression was incorporated into the final Cox model together with male sex, high age, smoking, poor physical health and lowered functional abilities.

When comparing these results with previous community studies that have used DSM-III or similar criteria, the results differ from those obtained by Fredman and colleagues (1989), who failed to find any association between depression and mortality in a population aged 60 years or over. The explanation could be the small number of deaths and the short follow-up time (2 years) in the aforementioned study. In an Australian study among people 70 years or over, the higher mortality of the depressed elderly during the five-year follow-up was explained by the relationship between physical illness and depression (Jorm et al. 1991a), which is similar to our results in the first cross-sectional study. Jorm and colleagues used in their study self-rated physical health, which is a subjective measure associated with depression. In the present study, too, the measure of physical health was probably more subjective in the first cohort than in the second one.

Two community studies using similar criteria have given results similar to those obtained in our second cross-sectional study, namely that depressed persons had higher adjusted mortality. Bruce and Leaf (1989) and Penninx and colleagues (1999) reported this in a population aged 55 or over. The first of these studies had a follow-up of 15 months and the latter 4 years. In both of these studies, higher mortality was found especially among those having major depression. In the present study, too, the role of major depression in predicting mortality was crucial.

In the study by Penninx and colleagues, the relation of minor depression to mortality was also studied. The mortality of women with minor depression did not increase when sociodemographics and physical health were controlled. Our results among people with dysthymic disorder were parallel. But the behavior of men with minor depression differed from that seen in our study. In the study of Penninx et al. (1999) an increased risk of mortality persisted even after adjustments. We did not see such gender differences.

The differences in the results between the two cohorts in the present study may be caused by methodological differences in these two cross-sectional studies, different measures used and the intervention (community-based therapy) at the time of the first cross-sectional study. The higher mortality in the second, older cohort makes it easier for differences to be revealed.
When mortality is studied, the two-phased methodology in the first cross-sectional study causes some inaccuracy at the beginning of the follow-up of mortality. Among those with higher ZSDS scores, many were excluded from the study population because they could not be interviewed due to poor physical health or they died before they had been interviewed. The interval between the postal questionnaires and the interviews was approximately six months. However, among those with ZSDS below the cut-off point, no such clean-up could be done and the follow-up of mortality began immediately after the returned postal questionnaire was received. In the second cross-sectional study such inaccuracy was not possible, because all the participants were examined two weeks after the filling in of the postal questionnaires. This explanation is supported by the Kaplan-Meier survival analysis, where follow-up began from the first year, and the data were analysed once a year. In that analysis, the difference between survival curves in the first cohort was not evident until after three years of follow-up, whereas in the second cohort it was evident immediately after one year of follow-up.

Another explanation for the differences in the results between the first and second cross-sectional studies could be the intervention, individual treatment and the provided community-based therapy in Ähtäri during and after the first cross-sectional study (Pahkala 1990). Information and education concerning normal aging, geriatric depression, etc. was provided. Social and health care workers also got more education concerning these matters. The aim was to enhance communication between the generations and to emphasize the continuing need for social support and networks when aging. The positive effects of this intervention could include a decrease in the prevalence of depression and therefore also a decrease in excess mortality due to depression. As a matter of fact, the prevalence of depression in the second cross-sectional study was lower than in the first one (Pahkala et al. 1995), but it is hard to say how much of this decrease is due to intervention, because of the differences between the studies. It has been shown previously that active intervention and treatment of depression decrease mortality (e.g. Avery & Winokur 1976, Weeke et al. 1987, Muller-Oerlinghausen et al. 1992). The second cross-sectional study had a more naturalistic character, leaving the treatment of depression to the patients and their doctors.

Some measures were also different in these two studies. Depression was measured with a two-phased method in the first cross-sectional study, whereas in the second study all the participants were interviewed clinically. The variables used to describe physical health were different in these two cross-sectional studies and they were used in the mortality analyses. The measures in the second cross-sectional study were more objective than in the first, which may have affected the results.

6.2.6.2 Results in depression subgroups

There were differences between those suffering from major depression and those suffering from dysthymic disorder. In the second cross-sectional study, the independent effect of depression as a predictor of mortality was due to those suffering from major
depression. When only those suffering from dysthymic disorder were included in the depressed group, depression did not emerge in the final Cox model as a factor predicting mortality.

There has been a lot of discussion about whether the various types of depression are distinct entities or whether they form a continuum of depressive disorder (Pichot 1986). The results of this study suggest that, as far as major depression and dysthymic disorder are concerned, they might have differences in pathophysiology, and the possibility that they might be different clinical entities cannot be excluded. Though the etiology of these disorders is multifactorial, different factors may be more marked in their etiology. Later in the analyses of Ähtäri study, relapses of depression were related to major depression and psychomotor retardation, not to stressful life events or the deterioration of one’s health, suggesting that biochemical factors may have a marked role in the etiology of major depression (Kivelä et al. 2000). Beekman and colleagues (1995) also found that major depression was much less strongly related to physical health than minor depression. Instead, it was closely related to long-standing vulnerability factors, such as the family and personal histories of depression. (Beekman 1996).

The notable result was that there was a difference in mortality between those suffering from long-standing depression and those cured from depression. The mortality of those who were depressed only in the first cross-sectional study, but not in the second, did not differ from that of non-depressed people. It has been previously shown in younger populations that depressed people having adequate treatment have lower mortality than those having inadequate treatment or no treatment at all (e.g. Avery & Winokur 1976, Weeke et al. 1987, Muller-Oerlinghausen et al. 1992).

Further results from the Ähtäri study support these mortality results. Especially those suffering from major depression had a relapsing course of depression (Kivelä et al. 2000). The results of the present study show that mortality increased especially among those suffering from major depression and those having a long-standing/relapsing course of depression. Recurrence and cyclicity are characteristic of depression. Among adult populations or general practice attenders, only 20–25% of those having depression did not have any new episode of depression during a ten-year follow-up (Angst 1992, van Weel-Baumgarten et al. 1998). The length of follow-up did not play any specific role in the association between depression and mortality in the previous studies supporting the view that, for many people, depression is a chronic or recurrent disease that increases the risk of death not only in the short term but also over a long follow-up. This supports the view that, for many people, depression is a chronic or recurrent disease increasing the risk of death not only within a short interval but also in the long run.

Future research should focus on factors that maintain depression, precipitate to relapses and promote recurrence. These factors should then be actively intervened in.
6.2.6.3 Increased mortality in depression

How does depression increase mortality in certain groups? The confounding factors explained partly the increased mortality, but other explanations are also needed. Depression itself may increase mortality directly (by suicides) and indirectly. The neurobiology and physiology of depression may predispose depressed people to certain diseases. It is also possible that diseases cause depression and increase the risk of death.

Suicide can be thought to directly emanate from depression. It did not explain the excess mortality in the present study. Depression and mortality may be associated indirectly with a relationship mediated by, for example, poor self-care and deficient health behavior. Depressive people have been shown to have poorer compliance with treatment compared to non-depressed people (e.g. coronary artery disease patients, Carney et al. 1995a). They also refuse active treatment more often than non-depressed people (Lee & Ganzini 1992), even when resuscitation is concerned (Ganzini et al. 1995, Hooper et al. 1996). Indirect factors are difficult to measure and could partly explain the increased mortality among depressed elderly people.

Biological changes associated with depression may predispose to diseases leading to death. Sympathoadrenal hyperactivity, diminished heart rate variability, ventricular instability and myocardial ischemia in reaction to mental stress, and alterations in platelet receptors and/or reactivity are important pathophysiological alterations in depression that contribute to an increased vulnerability to cardiovascular diseases among depressed patients (Musselmann et al. 1998). The physical consequences of hypercortisolism include e.g. reduced bone mineral density and redistribution of body fat, which increase the risk of coronary artery disease (Dinan 1999, Mayo-Smith et al. 1989, Michelson et al. 1996). The autonomic dysfunction demonstrated by reduced heart rate variability lowers the threshold for ventricular fibrillation, increasing the possibility of sudden cardiac death (Carney et al. 1995b, Roose et al. 1991). Depression after myocardial infarction has been found to predict death (Frasure-Smith et al. 1993, 1995).

There are also findings suggesting that depressed elderly people would be more vulnerable to immune-mediated diseases, such as cancer, infections and autoimmune diseases (Herbert & Cohen 1983).

It is possible that certain somatic diseases cause depression via biological alterations, and these somatic diseases are later causes of death. Examples are silent cerebral infarction (SCI), which have been found to associate with late-onset senile major depression (Fujikawa et al. 1993). The excess prevalence of depression in stroke patients has also been demonstrated (Starkstein & Robinson 1989).

In any case, the causes of death did not differ significantly between the depressed and non-depressed people in the present study, which means that special disease groups do not explain the excess mortality found. Consequently, in this study, the path(s) from depression to mortality remain at a hypothetical level. Further studies are needed to examine the possible pathways between depression and mortality.
6.2.7 Depressive symptoms predicting mortality

There were very few individual depressive symptoms associated with mortality. Only weight loss was a predictor of mortality among the depressed people, dissatisfaction and gastrointestinal symptoms being more general markers of death. Although the study population was of a moderate size, a larger study population would have allowed the recognition of possible smaller differences.

The significance of weight loss as a depressive symptom specifically predicting mortality is controversial. It is very difficult to interpret the origin of symptoms which are somatic by nature. The two entities, depression and physical illness, may be inextricable from each other and may even cause the somatic symptoms by enhancing each other’s effects. In any case, weight loss is a remarkable symptom of depression, being included in the criteria of classification of diseases. Clinical experiences also emphasize its value as a prognostic mark. It has been proposed that although there is no completely satisfactory way to determine whether a symptom such as fatigue or weight loss is due to depression or to a medical illness, it is generally in the patient’s best interests to attribute the symptoms to depression if there is reasonable doubt (Reifler 1994).

6.3 Strengths and limitations of the study

The main strength of this study is that it is a population-based study. The participation rate in both studies was high, and the number of people lost to follow-up was thus low. The strengths also include the perfect mortality statistics and the use of identity numbers in Finland, which enable a reliable follow-up. The evaluation of physical health, especially in the second cross-sectional study, was based on an interview by the attending general practitioner using several complementary sources, i.e. the clinical examinations and the medical records of Ähtärinjärvi Health Centre and Ähtäri District Hospital, not only self-report as in many other studies.

The facts that screening of depression was used in the first cross-sectional study and that not every participant was examined and interviewed cause some inaccuracy in the measures of physical health. In measuring depression, this is a usual and acceptable epidemiologic strategy. The diagnosis of depression was clinically relevant from the viewpoint of a general practitioner in every diagnosed case. No inter-rater reliability was counted here, but consistency in the diagnostics of depression was assured in many ways. Because the study population was drawn from one semirural municipality in Finland and though the Finnish population is quite homogenous, any generalization of the results has to be made cautiously, especially to the elderly living in bigger towns in Finland.
7 Conclusions

The following conclusions based on this epidemiological research data on a community population aged 60 years or over can be drawn:

1. The survival of the depressed elderly is poorer when compared to the non-depressed elderly.
2. Major depression increases the risk of death even when the other mortality-increasing factors (age, sex, marital status, education, smoking, physical health, functional abilities) have been taken into account. The poorer survival of those suffering from dysthymic disorder is explained by the other mortality-increasing factors, especially poor physical health and lowered functional abilities.
3. Those suffering from long-standing/recurrent depression (depressed in two examinations at a five-year interval) have increased mortality, whereas the mortality of those who have recovered from depression does not differ from the mortality of the non-depressed ones.
4. Only a few individual symptoms of depression are related to an increased risk of death. Of the symptoms of depression, weight loss among elderly depressed people is related to an increased death rate. Two other depressive symptoms, gastrointestinal symptoms and dissatisfaction, are more general markers of death also predicting mortality among the non-depressed elderly.
5. There were no significant differences in the causes of death between depressed and non-depressed people.
8 References


Minor and major depression and the risk of death in older people. Arch Gen Psych 56: 889–895.


