

# **Psychiatric symptoms and disorders in old age**

## **Prevalence, course and diagnostic thresholds**

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*The more we venture into the boundless sea,  
the more our professional instruments are likely to fail.*

Mario Maj, president of the World Psychiatric Association 2008-2011



## ABSTRACT

The aim of this thesis was to study the epidemiology of some psychiatric disorders, as well as their corresponding subthreshold symptoms, in order to explore the border between psychopathology and normality in the general population of older people.

Data came from population studies of older people in Gothenburg. Participants completed a semi-structured psychiatric interview and cognitive tests conducted by psychiatric research nurses. A key informant interview was also conducted. Psychiatric diagnoses were made using *DSM-IV* criteria. Dementia was an exclusion criterion for all studies.

*Study I* examined the one-year prevalence of psychotic symptoms (delusions and hallucinations) in 70-82-year olds. The one-year prevalence of psychotic symptoms, as determined by expert review of available information, was 1.0% with no age or sex differences. Subthreshold symptoms (paranoid ideation and illusions) had a similar prevalence. A lower prevalence than in most previous studies may reflect methodological differences, age differences or secular changes in the prevalence of these symptoms.

*Study II* and *Study III* examined the prevalence, correlates and course of specific phobia and subthreshold fears in 70-year olds followed-up at age 75 and 79 years. At age 70, specific phobia and subthreshold fears were present in 10% and 47%, respectively. Both were more common in women than in men. Specific phobia, but not subthreshold fears, was associated with other mental disorders. Specific phobia was associated with global functional impairment, but markedly less so than depression. The prevalence of specific phobia declined with age. Most individuals with specific phobia at age 70 did not have specific phobia during follow-up, but most had subthreshold fears, suggesting that these symptoms have a chronic course but with fluctuating severity and improvement with age.

*Study IV* examined the prevalence and course of depression in 70-year olds who were followed-up at age 75 and/or age 79. At baseline and follow-up, participants were placed in one of four categories of depression (no depression, subsyndromal depressive symptoms, minor depression and major depression). The majority of baseline cases of major and minor depression were chronic or recurrent. Subsyndromal depressive symptoms at age 70 differed from no depression with respect to mental health correlates and prognosis. About half of individuals with major depression at follow-up had minor or subsyndromal depressive symptoms at age 70. These symptomatic risk groups could be suitable targets for prevention of major depression in older people.

**Keywords:** epidemiologic studies, aged, population studies, longitudinal studies, psychosis, phobic disorders, phobias, depressive disorders, depressive symptoms

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## SAMMANFATTNING PÅ SVENSKA

Syftet med avhandlingen var att studera några olika psykiatriska diagnoser i ett befolkningsurval av äldre människor, och att också studera symtom på dessa tillstånd som inte var tillräckligt uttalade för att ge en diagnos. På detta vis skulle gränsen mellan sjuk och normalt studeras närmare.

Alla delarbeten baserades på befolkningsstudier av äldre i Göteborg. Alla deltagare genomgick en psykiatrisk intervju med en forskningsutbildad psykiatrijuksköterska. Anhörigintervju genomfördes också. Psykiatriska diagnoser ställdes enligt internationella diagnoskriterier. Deltagare med demens uteslöts ur alla delarbeten.

*Delarbete I* undersökte förekomsten av psykotiska symtom (vanföreställningar och hallucinationer) bland individer 70-82 år gamla. Bedömning av psykotiska symtom gjordes på basen av information från intervju med deltagare och anhörig. Psykotiska symtom förekom hos 1% av deltagarna. Inga ålders- eller könsskillnader i förekomst kunde påvisas. Psykosliknande symtom (paranoida tankar och illusioner) var ungefär lika vanliga. Förekomsten av psykotiska symtom var lägre än i tidigare studier, vilket kan förklaras av metodskillnader, åldersskillnader mellan deltagare i olika studier eller att förekomsten av dessa symtom minskat bland senare generationer av äldre.

*Delarbete II och III* undersökte förekomsten och förloppet av specifik fobi (överdriven rädsla för t ex djur, höjder, hissar och sprutor) och subkliniska rädslor bland 70-åringar (delarbete II) som sedan följdes upp vid 75 och 79 års ålder (delarbete III). Vid 70 års ålder var förekomsten av specifik fobi och subkliniska rädslor 10% respektive 47%. Båda var vanligare hos kvinnor än hos män. Specifik fobi var kopplat till andra psykiatriska diagnoser, men subkliniska rädslor var inte det. Specifik fobi hade ett visst samband med global funktionsnedsättning. Förekomsten av specifik fobi sjönk tydligt över tid. De flesta med specifik fobi vid 70 års ålder mötte ej diagnoskriterier under uppföljning, men de hade kvar subkliniska rädslor. Detta indikerar att fobier har ett kroniskt men fluktuerande förlopp, och att symtomen mildras med stigande ålder.

*Delarbete IV* undersökte förekomsten och förloppet av depression bland 70-åringar som följdes upp vid 75 och/eller 79 års ålder. Depression delades in i tre kategorier efter antal symptom (subsyndromala depressionssymptom, mild depression och egentlig depression). Av dem med egentlig eller mild depression vid 70 års ålder hade majoriteten något av dessa tillstånd även senare. Personer med subsyndromala depressionssymptom skiljde sig från dem utan depression vid 70 års ålder med avseende på en del indikatorer på psykisk ohälsa och risk för framtida depression. Fyra av tio individer med egentlig depression under uppföljningen hade mild depression vid 70 års ålder. Detta indikerar att interventioner i denna riskgrupp skulle kunna förebygga en betydande andel av alla egentliga depressioner hos äldre.





# LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. Sigström R, Skoog I, Sacuiu S, Karlsson B, Klenfeldt IF, Waern M, Gustafson D, Östling S. The prevalence of psychotic symptoms and paranoid ideation in non-demented population samples aged 70-82 years. *International Journal of Geriatric Psychiatry* 2009; 24: 1413-1419.
- II. Sigström R, Östling S, Karlsson B, Waern M, Gustafson D, Skoog I. A population-based study on phobic fears and DSM-IV specific phobia in 70-year olds. *Journal of Anxiety Disorders* 2011; 25: 148-153.
- III. Sigström R, Skoog I, Karlsson B, Nilsson J, Östling S. Nine-year follow-up of specific phobia in a population sample of older people. *Submitted manuscript*.
- IV. Sigström R, Skoog I, Östling S. The depressive spectrum in old age: a longitudinal population study. *In manuscript*.

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# ABBREVIATIONS

APA	American Psychiatric Association
AUDADIS	Alcohol Use Disorder and Associated Disabilities Interview Schedule
CAMDEX	Cambridge Examination for Mental Disorders of the Elderly
CIDI	Composite International Diagnostic Interview
CIE	Canberra Interview for the Elderly
CPRS	Comprehensive Psychopathological Rating Scale
DIS	Diagnostic Interview Schedule
DSM	Diagnostic and Statistical Manual of Mental Disorders
ESA-Q	Enquête sur la Santé des Aînés Questionnaire
GAF	Global Assessment of Functioning
GEE	Generalized estimating equations
GMS	Geriatric Mental State
ICD	International Statistical Classification of Diseases and Related Health Problems
MADRS	Montgomery-Åsberg Depression Rating Scale
MINI	Mini International Neuropsychiatric Interview
PSE	Present State Examination
RDC	Research Diagnostic Criteria
SCID	Structured Clinical Interview for DSM Disorders
SCL-90	Symptom checklist 90
VLOSP	Very late-onset schizophrenia-like psychosis
WHO	World Health Organization

# 1 INTRODUCTION

This thesis includes studies of three different types of psychiatric symptoms and disorders: psychotic symptoms, specific phobia and depression. Each of these will be given a separate introduction that should be possible to read separately. The first two sub-chapters of the introduction will review some general topics regarding the study of these symptoms and disorders in the general population of older people.

## 1.1 Psychiatric epidemiology in old age

Worldwide, increased life-span and lower birth rates will increase both the absolute number and the proportion of older people in the population (1, 2). Despite a rising prevalence of physical illness among older people (2), newer generations are more active and less dependent on others in their daily activities (3). Thus, older individuals may become more resilient to the effects of ageing. Together with the dissemination of concepts such as successful ageing (4), increased mental health literacy and reductions in stigma related to mental disorders<sup>1</sup> (5, 6), this may increase the demand for and interest in mental health among older people.

Epidemiological studies of the prevalence, incidence and course of mental disorders among older people can inform service planning and guide clinicians, not least in primary care. Considering the changes mentioned above, such studies are needed to be done repeatedly to discover secular trends. For example, the age-specific prevalence of dementia may be declining (7). This would not only have implications for service planning with respect to this disorder, but would also affect the epidemiology of other mental disorders.

Population studies of older people without marked cognitive impairment indicate that 12-17% meet the diagnostic criteria for a mental disorder at a given time (8, 9). Studies including individuals of all age groups find the prevalence of most mental disorders to decline with age (10, 11), despite that several established risk factors for mental disorders, such as cerebrovascular disease, functional disability and bereavement, become more prevalent with age (12, 13). This apparent paradox could have several explanations. First, it may to some extent be due to selective survival with respect to mental health. Persons with severe mental disorders have a 11-23 years reduction in life expectancy compared to the general population (14). Mortality is elevated also in less severe cases (15, 16). Second, it is suggested that there is a 'positivity effect' on emotional regulation with increasing

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<sup>1</sup> The terms 'mental disorder' and 'psychiatric disorder' will be used interchangeably.

age. Older people may be more likely to pay attention to positive *vs.* negative material, which may make them more resilient to external stressors (17). Third, an apparent decline may be due to methodological factors, some of which will be shortly reviewed.

### **Diagnostic criteria and methods**

As will later be discussed in depth, psychiatric symptoms not fulfilling standard diagnostic criteria for mental disorders may often be of clinical significance among older people (18, 19). With age, the manifestations of mental disorders may change so that they are not adequately captured by these criteria (19). Symptoms appearing in the course of physical illness and normal ageing are at risk of both over- and under-diagnosis with respect to psychiatric disorder (20). In the structured diagnostic interviews typically used in epidemiological studies, interviewers are not allowed to assist the respondent in the interpretation of questions. Older people are more likely to have complex health problems, making it more difficult for them to evaluate possible causes of their symptoms, and they may attribute symptoms of mental disorders to co-existing physical health problems (21). Lastly, the prevalence of for example dementia and psychotic symptoms may be underestimated if studies rely only on interviews with participants. Other important information sources are key informant interviews and medical records (22).

### **The importance of longitudinal studies**

Most studies finding an inverse association between increasing age and prevalence of mental disorders rely on cross-sectional data. In such studies, age differences may be reflections of birth cohort effects or that the difference between older participants and non-participants with respect to psychiatric morbidity is larger than in younger age groups (23). Furthermore, mental disorders are often episodic and previous mental health problems may be forgotten or not reported (24). Longitudinal studies may therefore give better estimates of the prevalence of a mental disorder over an extended period of time (25), and of how this prevalence changes with increasing age. Longitudinal studies of children, adolescents and young adults also indicate that already before the age of 30, a majority of individuals in the population may have had a mental disorder at some point in their life (26-28). This has implications for the interpretation of longitudinal studies with their baseline in old age. Incident mental disorders are unlikely to be truly of new-onset, and apparent risk factors for these incident disorders may reflect reverse causation.

## 1.2 Some general aspects of psychiatric research

It has been argued that epistemological questions are too rarely addressed in psychiatric research (29). They will be briefly addressed in this section. It also reviews some methodological issues, as well as historical aspects and critiques of the current system of psychiatric diagnosis. A comprehensive review and elaboration of a personal standpoint would be beyond the scope of this thesis.

### 1.2.1 The object of psychiatric research

#### Measurement versus evaluation

Psychiatry is a 'hybrid science' aiming at both explanation and interpretation. These aims have been in dialectic tension throughout its history (30, 31). Explanatory, quantitative research strives for objectivity by using methods of the natural sciences, and pays little attention to anecdote. However, such psychiatric research is dependent on interpretation of subjective experience, because psychiatric symptoms and signs aren't natural objects ('things') (32). They can therefore not be *measured* in the sense that blood levels of glucose or cardiac troponins are measured. From this should follow that every collection of data, in interviews or questionnaires, includes *evaluation*, some kind of judgment, on the side of the study participant as well as on the side of the interviewer (33-35). The study of psychiatric phenomena as they emerge from conversation and observation, psychopathology, is at the core of psychiatric practice and research, since it may be critical in defining the phenotype for a putative biological mechanism (36) and for which specific pharmacological treatments may be designed (37).

#### Different approaches to acquiring knowledge

The problem of objectifying and quantifying subjective experiences is a problem of *validity*, i.e. whether a scientific method captures something that is relevant to the matter in question and is in concordance with reality (38). A review of methods used in previous research on the subjects of this thesis suggests that assumptions about valid methods differ depending on the type of symptom that is studied.

The majority of studies aiming to report on the epidemiology of psychotic symptoms and disorders rely on information gathered and/or reviewed by clinical experts (See Table 1 and 2, page 17 & 18). Thus, detection and evaluation of psychotic symptoms is considered to require the psychopathological skill to evaluate a person's beliefs and perceptions.

The reason for this methodological assumption may be as follows. Loss of contact with reality, or 'lack of insight', is considered to be one important *quality* of

psychosis. Thus, individuals with psychotic symptoms may not evaluate their beliefs and experiences as psychiatric symptoms. A straightforward question about whether they 'have delusions or hallucinations' will obviously lead to 'false negative' cases<sup>2</sup> (39). This requires an indirect phrasing of questions regarding these symptoms, which will reduce their face validity, meaning that study participants will not, and shall not, understand the intention behind them. However, beliefs and experiences similar to psychotic symptoms (such as beliefs in telepathic communication) are not uncommon in the population (40, 41). A poor conception of what kind of experiences that are sought after, either by the interviewer or by the interviewed, results in a rate of 'false positive' cases that outnumbers the 'true positives' (39, 42-44). There may be support for that such psychosis-like experiences are on a continuum with clinical psychotic disorders, so that research into the first may help to explain the latter (40, 45-47). However, if there are important qualitative differences between these phenomena, the psychosis-like experiences may instead blur the picture in this pursuit (48, 49).

On the contrary, symptoms of depression and anxiety are often assumed to differ from normality rather in terms of *quantity* than in terms of *quality* (50); sadness, worry and fear are phenomena that many, if not everyone, have experienced, while thought broadcasting and commenting voices are not. Furthermore, for example phobias and depressive symptoms are considered to be in most cases recognized by individuals themselves as a deviation from other people's experiences or their own previous experiences; these symptoms are usually not accompanied by a 'lack of insight'. Peoples own evaluation of these symptoms, for example a 'yes' answer to the question 'Have you ever in your life had a period of time lasting several days or longer when most of the day you felt sad, empty or depressed?', may then justifiably be taken for granted. The assumed face validity of questions regarding symptoms of depression and anxiety may partly explain why many have been compelled to treat them from a psychometric perspective, i.e. as something measurable (51, 52).

Accepting this as a valid way to acquire knowledge about psychiatric symptoms has profound implications for psychiatric research. Data may be more justifiably collected by the use of self-report questionnaires or by interviewers without clinical experience. These data may then be processed by computerized algorithms to generate diagnoses of mental disorders. This reduces the costs of large-scale epidemiological studies and may standardize psychiatric diagnoses, thus making them more reliable, which is a major advantage for research purposes (35, 39).

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<sup>2</sup> This expression is put between quotation marks since the true/false statement is made with reference to a non-existent 'gold standard' for when the symptoms are present. However, the expression is useful for the purposes of this discussion.



However, even if such methods turn out to be highly reliable, they are not equivalents of measurement. *Qualitative* differences between positive answers could be important, but these are strictly not captured with these methods (53-55).

## 1.2.2 The scientific basis of psychiatric diagnosis

This section addresses on what grounds we can claim to know that someone has a psychiatric diagnosis.

The validity of diagnostic criteria for mental disorders is usually discussed with reference to the lack of a 'gold standard', i.e. what is considered to be the best available method of establishing whether a disease is actually present or not (29, 39, 56). In modern medicine, such a gold standard is usually something that can be measured with the methods of natural sciences. For example, the clinical evaluation of chest pain may be validated against the gold standard for establishing the presence of myocardial infarction (repeated measurement of cardiac troponins) (57). However, a gold standard need not necessarily be a laboratory test. There have been suggestions of a gold standard for determining the psychiatric diagnosis of a particular patient (39, 55). They acknowledge the expert judgment, as well as the expert's access to the best available information, including longitudinally collected data. At the group level, statistical methods of data reduction, such as latent class analysis, can be used to examine how a pre-specified diagnostic system fits with reality (58, 59).

Our acknowledgement of some method as an acceptable gold standard, and thus our acknowledgment of a phenomenon as being a mental disorder, is obviously determined by our implicit or explicit definition of the concept of 'mental disorder'. This is the *point of view* from where we make such evaluations (56), which can be illustrated by a quote from Kendler (60), p. 1116:

The fact that humans are vulnerable to substantial dysfunctions of their mind/brain systems, which lack localizing neurologic signs and cause much suffering and disability, is a robust fact about our world. It will be here in a hundred or a thousand years, or would arise if we played the tape of time over and over again starting with the rise of our species.

This statement invokes Wakefield's definition of a mental disorder as a 'harmful dysfunction', perhaps the most elaborate and influential contemporary attempt in providing such a definition (56, 61, 62). Whether some phenomenon is caused by dysfunction in the mind/brain is an empirical question. Even if there are gaps in the sum of our current knowledge regarding such dysfunctions, we may have good reason to believe that they exist. Whether something is harmful (causing suffering and disability) is a normative question, but most would agree that there are

expressions of our mind/brain systems, dysfunctional or not, that are harmful. Kendler seems to argue that because of this we have very good reason to believe that there exists *something* that lives up to this definition. However, marking the boundaries of the concept of mental disorder is difficult. Before discussing this further, it is in order to briefly review some historical aspects of the system of psychiatric diagnosis applied in the current thesis and in the vast majority of psychiatric research.

### **Historical aspects of current psychiatric diagnosis**

In 1952, the American Psychiatric Association published its first edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*. It was needed in the light of a dramatic change in the scope of psychiatry during the World War II. American military psychiatrists found that only about 10% of their patients could be reasonably assigned any diagnosis covered in the old classification system used in psychiatric hospitals. This system did not include 'minor personality disturbances', stress reactions or psychosomatic problems (63, 64). In its first two editions (64, 65), many of *DSM's* diagnoses were quite vaguely described, exhibiting the strong influence of psychoanalysis on its authors; the particular diagnosis was less interesting than to understand how the symptoms could be related to the biography and psychic structure of a particular patient (66).

In the United States, the oppositional stronghold was the Department of Psychiatry at Washington University in St Louis, which came to lead what was later called the 'neo-Kraepelinian revolution' in psychiatry (30, 63, 67). The term acknowledges Kraepelin's descriptive approach to psychiatric diagnosis: groups of patients can be delineated based on careful observation and description of their *clinical picture*.<sup>3</sup> This includes the symptoms, signs and course of the illness, and factors such as family history and precipitating events. It is assumed that psychiatric disorders are idiopathic (of unknown etiology) and that their causes can only be known by first describing diagnoses which may then be examined empirically in a *validation process* (68, 69), including: (i) clinical description (ii) laboratory studies (of various biological correlates of a diagnosis) (iii) delineation from other mental disorders as well as from individuals without any mental disorder (iv) follow-up studies, which establish the predictive validity of a diagnosis and (v) family studies (or other genetically informed studies). This is a 'medical model' of mental disorders; they are assumed to be diseases of the brain and their etiology should be sought with modern biomedical methods (36, 70).

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<sup>3</sup> This approach was not invented by Kraepelin, but his famous textbook of clinical psychiatry made it widely spread.

Scholars from Washington University published their first diagnostic criteria for mental disorders in 1972<sup>4</sup> (68). These evolved into the Research Diagnostic Criteria (*RDC*) published in 1978 (71). Diagnoses were generally completely descriptive, formulated as a combination of certain operational diagnostic criteria, a 'checklist'. An important aim was to improve reliability, i.e. precision, of diagnoses in order to improve communication between psychiatrists and to foster empirical research on etiology and treatment. This approach was timely since the reliability of psychiatric diagnoses was considered to be in deep crisis (72, 73). Criteria-based diagnoses achieved their route into mainstream psychiatry with the third edition of the *DSM* in 1980 (74). Using the terminology of Kuhn (75), it seems justified to say that this established a new paradigm in psychiatric research. The following editions of the *DSM*, as well as its international counterpart *ICD-10*, may be considered revisions within this paradigm. However, since 1980, research in epidemiology, clinical psychiatry and neuroscience has accumulated immensely, and some argue that a new revolution is needed to accommodate this research (66, 76-80). Two issues with the current system is its distinction between many different categories of mental disorder and how its criteria categorically distinguish disorders from normality.

### **The border between different disorders**

While the Washington University criteria and the *RDC* listed 14 and 25 psychiatric diagnoses, respectively, the *DSM-III* and the following editions listed a far higher number.<sup>5</sup> One critical point is the utility of distinguishing between many different disorders. Population studies, which typically cover only a minority of all diagnoses (usually about 20 or less), have found that applying current diagnostic criteria without clinical distinction between 'main' and 'secondary' disorders results in that 40-45% of all individuals with psychiatric disorders have more than one diagnosis and that this group accounts for a large majority of all diagnoses in the population (58, 81). Multiple diagnoses may reflect a complex clinical picture in which specification of several different disorders is not clinically meaningful, resulting in patients receiving a 'not otherwise specified' diagnosis (80). Alternatively, one primary diagnosis, for example bipolar disorder, may cast its shadow over a number of secondary diagnoses, which may be uncovered only with a structured diagnostic interview typically used in epidemiological studies (58), but which may be of importance in clinical management (82). This makes the system complicated to use, especially in settings outside specialized mental health care. Furthermore, comorbidity may indicate shared etiology, and thus may be only an artifact. Thus, it is not clear whether the current system does what it aims

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<sup>4</sup> These are often referred to as the 'Feighner criteria', after the first author of this seminal paper.

<sup>5</sup> The exact number of disorders is probably no less than 150.

to do, i.e. to make distinctions that are clinically useful and that may help to uncover the etiology of mental disorders (50, 83, 84).

Heterogeneity of disorders thus exists within many patients, but patients within the same diagnostic category may also be highly heterogeneous. A prominent example is the current diagnosis of major depression, which will be further discussed from this perspective in Section 1.5.1.

### **The border between disorder and normality**

The current diagnostic system in psychiatry treats mental disorders as categories that are distinct from 'normality'. One criticism of this concerns what may be called some of its unintended consequences; how it may be used in the 'real world' and how it shapes our understanding of human suffering and individual peculiarities. This approach to diagnosis, at least if injudiciously used, may lead to that symptoms that are clinically significant, but are not best described as mental disorders (such as grief or reactions to other life events) are 'medicalized' (56, 85, 86).

Assuming that diagnoses are made with clinical judgment, another problem is that their diagnostic criteria are arbitrary.<sup>6</sup> Many psychiatric disorders, such as depressive and anxiety disorders, may be best understood as being on a continuum with normal mood swings, common fears, transient worries or compulsive behaviour (50, 76, 87). A categorical, criteria-based approach to diagnosis is not compatible with this continuum of duration, severity and impairment and has been an argument for adopting a more dimensional one (50, 88).

A somewhat *ad hoc* solution to this problem is the creation of the concept of subthreshold disorders, defined as clinically significant symptoms of a disorder that do not fulfill all its diagnostic criteria (54, 89). For example, subthreshold depression, i.e. depression that is not symptomatic or durable enough to fulfill the diagnostic criteria for major depression, is often impairing and associated with adverse outcomes (15, 18). Yet, this 'subthreshold' concept only concerns the threshold of a diagnosis from the aspects of symptoms and duration. The same problem of continuum holds for clinical significance. It has been argued that it may be wrong to speak of *one* threshold of clinical significance. There may be one threshold for when a condition deserves clinical attention and one threshold for, for example, pharmacological treatment is warranted (90). The current system gives little guidance in this respect.

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<sup>6</sup> A major depressive episode requires the presence of five out of nine possible symptoms for at least 14 days, but what about eight symptoms for 13 days or four severely disabling symptoms for 15 days?

**Validity in an epidemiological context**

It cannot be assumed that all, or even most, people with mental health problems seek treatment and are correctly diagnosed by the health care system. Therefore, estimates of the prevalence and prognosis of psychiatric diagnoses through surveys of representative population samples may be needed uncover the true burden of mental disorders on the population (35).

Another argument for applying psychiatry's diagnostic criteria to the general population is that this may challenge the general conception of a particular mental disorder. Clinical experience and epidemiological data on mental disorders are sometimes remarkably different, which may be due to a number of biases creating what has been called the 'clinician's illusion' (91, 92). Among other things, this illusion may result in that some 'minor' mental health problems are overlooked. In patients with severe mental disorders, a flying phobia may not be considered a clinical issue, while it may be in an otherwise mentally healthy person who, instead of seeking treatment, copes by declining a job promotion that would have necessitated flying. The clinician's illusion may also create incorrect perceptions of for example the prognosis of mental disorders, since this will be poorer for patients than in the community. Since epidemiological studies don't include only individuals who, for one reason or the other, become patients, it is argued that epidemiological studies contribute to assess the validity of diagnostic criteria for mental disorders (93).

This argument can be examined by from a clinical perspective by viewing the instruments used in epidemiological research as diagnostic tests. The validity of such tests is often expressed in terms of sensitivity and specificity, i.e. their ability to rule in or rule out presence of a disease. Since diagnostic tests are not always right, their validity is also determined by context. The pre-test probability of a positive test result influences what conclusions that can be drawn from a positive test result (94, 95).<sup>7</sup> The pre-test probability of a person to have specific phobia or major depression is higher in specialized mental health care than in a randomly selected sample of the general population. Thus, the validity of diagnostic interviews may be lower in the general population. Some have argued that the largest problem may be low specificity, so that epidemiological studies overestimate the psychiatric morbidity in the population (39, 54, 96). However, others seem to come to the opposite conclusion. For example, the concept of subthreshold disorders, built largely upon results of studies conducted in primary care or general population settings, indicates that many believe that diagnostic criteria also have low sensitivity in such settings, i.e. that what has been

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<sup>7</sup> To take an extreme example: a urinary pregnancy test has excellent sensitivity and specificity, but a positive result is not valid if applied to a specimen from a man, since we have reason to believe that the pre-test probability of pregnancy in such persons is zero.

constructed from the clinician's point of view does not capture all phenomena in the population that would qualify for being a mental disorder.

These different conclusions may reflect disagreement on what should be the aim of psychiatry; should it confine itself to some kind of core of psychiatric patients, a context in which the pre-test probability of success for its instruments may be fairly high, or should it also use these instruments to define mental health problems in the wider community, a context where failure may be more likely? Answers to this question may come easier with future developments in psychiatric diagnostics, but they are also dependent on our implicit or explicit definitions of the concept of mental disorder, as well as on our ethical and political views (54, 97).

## 1.3 Psychotic symptoms in old age

### 1.3.1 Phenomenology of psychosis

An in-depth discussion of descriptive psychopathology of psychosis would be beyond the scope of this text. For a comprehensive review, see (98). The *Glossary of technical terms* in the *DSM-IV* (99) quoted a broad definition of psychosis: 'a loss of ego boundaries or a gross impairment in reality testing' but acknowledged that this didn't more precisely describe the phenomenon. In the *DSM-5 Glossary of technical terms* the term psychosis is no longer defined, but the term 'psychotic features' refers to 'delusions, hallucinations or formal thought disorder'. Formal thought disorder is thus considered to be at the core of psychosis, manifesting itself mainly in the speech of the patient, for example as loosening of associations, incoherence or poverty of speech. It is a phenomenon of substantial heterogeneity, and also rather a sign than a symptom (100). It was not studied in the present thesis. In any case, if psychotic symptoms are delusions and hallucinations, this leaves us with the question of the definition of these phenomena.

#### Delusions

According to the *Glossary of technical terms* in the *DSM-5* (101), a delusion is 'a false belief based on incorrect inference about external reality that is firmly sustained despite what almost everyone else believes and despite what constitutes incontrovertible and obvious proof of evidence to the contrary'. Furthermore, the belief should not be accepted in the individual's culture or subculture. This definition originates from Karl Jaspers, who suggested that delusions are different from normal beliefs in that they are (i) held with a special form of certainty, (ii) incorrigible and (iii) impossible (or at least false) (102).

However, it has been pointed out that several aspects of this definition are not coherent with how the term delusion is used in clinical practice (103): What clinical judgment says is a delusion is sometimes not falsifiable (for example

religious delusions), or may be very difficult to falsify (for example claims of being followed by an intelligence agency).

Furthermore, the term 'incorrect inference' suggests that the deluded is characterized by impaired logical reasoning, which has little empirical support (104). Indeed, some research indicates that when logic and common sense are in conflict, individuals with delusions are more likely to follow logic than non-deluded control persons (105). This is coherent with the idea that delusions arise not from an impaired ability of logical reasoning, but rather from an impaired ability to use common sense (105, 106).

Another definition of a delusion is purported by Cutting ((98), p. 59): 'the deluded is he or she who claims to know some matter in a certain way ... that is inappropriate to the matter in question.' The deluded for example make claims about facts in the external world (i. e. being followed by an intelligence agency) with a conviction that people usually only feel justified to have about their inner experiences (i. e. having pain) (103).

According to the *Glossary of technical terms* in the *DSM-5*, *paranoid ideation* is understood as ideas of being persecuted, harassed or unfairly treated that do not reach delusional proportions (101).

### **Hallucinations**

Hallucinations may seem somewhat simpler to define than delusions. The *Glossary of technical terms* defines a hallucination as 'a sensory perception that has the compelling sense of reality of a true perception but that occurs without external stimulation of the relevant sensory organ'.

According to this definition of a hallucination, it is perfectly possible that the individual realizes that the perception is not real. Such a realization, which may accompany for example the normal phenomena of sleep-related hallucinations and hallucinations of a deceased spouse (107, 108), is not compatible with the broad definition of psychosis described above ('a loss of ego boundaries or gross impairment in reality-testing'). Another example, relevant in old age, is the Charles Bonnet syndrome, which originally denoted visual, complex hallucinations in an older, cognitively intact person, who recognizes the phenomena as unreal (109). This may occur in for example eye disease (such as macular degeneration) or in lesions of the visual cortex.

Somewhat paradoxically, hallucinations may thus not always be psychotic in a broader sense, and should not always be considered a clinical psychiatric problem. This highlights the need of a qualitative judgment of these symptoms in psychiatry (49), especially if the terms of psychiatry are applied to a population sample, as in epidemiology.

Hallucinations are also qualitatively distinguished from *illusions*, which is a misconception or misinterpretation of an actual external stimulation.

### 1.3.2 Evolution of the concept of late-life psychosis

Kraepelin made the highly influential clinical distinction between the manic depressive insanity and dementia praecox (110). For him, a clinically important difference between them was the prognosis; the periodic nature of manic depressive insanity versus the chronic, deteriorating nature of dementia praecox (110, 111). This 'Kraepelinian dichotomy' has been clinically useful but already Kraepelin himself partly came to refute it ((112), p. 527). It is questioned by for example substantial overlap in the genetic risk for these disorders (113, 114).

Dementia praecox, now named schizophrenia, is already by its name a condition with an age of onset fairly early in life. However, it was early acknowledged that schizophrenia may have a 'late' onset (after the age of 40) (110, 115). During the 20<sup>th</sup> century, European psychiatrists used terms such as senile schizophrenia (116) or late paraphrenia (117) to label late-onset psychosis (118). However, as late as in 1980, the American *DSM-III* (74) excluded the possibility of a schizophrenia diagnosis if the age at onset was 45 years or older and the clinician was left with diagnoses such as paranoia or atypical psychosis.

Thus, the nosological status of schizophrenia-like disorders with late onset has been controversial. In 2000, an international consensus statement (119) distinguished between early onset schizophrenia (age of onset  $\leq 40$  years), late onset schizophrenia (age of onset 41-60 years) and very late-onset schizophrenia-like psychosis (VLOSP, age of onset  $> 60$  years). It was suggested that symptomatology differs little with age at onset, although formal thought disorder and blunted affect was stated to be rarely seen in very late-onset cases.

In addition to dementia praecox and manic depressive insanity, Kraepelin put the category of 'paranoia', a category for the 'partially insane' (120), which may be considered an equivalent the current concept of delusional disorder (121).

### 1.3.3 Nosology of late-life psychosis

Psychotic symptoms in late life may be primary (within the clinical picture of a 'functional' psychiatric disorder) or secondary (within the clinical picture of dementia, delirium or other neurologic or physical disorders) (122). Furthermore, in line with the Kraepelinian dichotomy, functional psychoses are commonly separated into affective (manic or depressive episodes) and non-affective (schizophrenia spectrum disorders).

Two studies of older patients presenting with new-onset psychotic symptoms in psychiatric settings find dementia and mood disorder to be the final clinical



diagnosis in about one third of cases each (123, 124). One of these studies found delirium, other medical causes and toxic effects of medication to account for the absolute majority of the rest of the cases, with non-affective psychotic disorder being rare (123). In the other, about 20% of psychotic symptoms had a final diagnosis of non-affective psychosis (124). These studies may suffer from selection bias in that individuals with non-affective psychosis may be less likely to reach contact with health care services than individuals whose symptoms are due to dementia or physical disorders.

### **Non-affective psychosis**

A diagnosis of *schizophrenia* according to the *DSM-5* (101) requires presence of two of five main symptoms (delusions, hallucinations, formal thought disorder, disorganized or abnormal motor behaviour and negative symptoms) of which one must be among the first three. One study found more similarities than differences between early- and late-onset schizophrenia when comparing them to healthy controls, notably also similar rates of negative symptoms (125). Early-onset cases had worse quality of life and everyday functioning, more 'general' psychopathology and more cognitive deficits. A study comparing individuals with VLOSP with age-matched individuals with early-onset schizophrenia found similar rates of family history of schizophrenia in both groups, but individuals with VLOSP were more likely to have been married and had longer education (126).

In *delusional disorder*, the main symptom is one or more delusions. Hallucinations should not be prominent and should be related to the theme of the delusion. Delusions may be of different types such as persecutory type, erotomania and morbid jealousy (101). There is little behavioural disturbance and the level of functioning may be substantially higher than in schizophrenia (127, 128). Delusional disorder is assumed to be rare in psychiatric settings and there has been debate on whether it's just an early manifestation of paranoid schizophrenia (127, 129). A 10-year follow-up study of first episode psychosis showed that 60% of individuals initially diagnosed with delusional disorder were later diagnosed with schizophrenia and only 1.5% of all individuals with first-onset psychosis received a 'life-time best estimate' diagnosis of delusional disorder (130). A prospective clinical study of delusional disorder, starting instead at a mean of six years after the first encounter with mental health services, found conversion to other diagnoses in only 20% of patients over 10 years (128). Thus, delusional disorder seems to be an unstable diagnosis in young patients with first onset psychosis, but, in concordance with accumulated clinical experience (129), a stable condition in middle age, once it has been present for several years.

### **Affective psychosis**

Psychotic symptoms, most often mood-congruent delusions, have been reported to be present in 5-45% of major depressive episodes in in- or outpatient settings (131-133), and may be more common among older patients (134). Psychotic symptoms are also reported to be present in 35-60% of manic episodes (135).

### **'Secondary' psychotic symptoms**

Psychotic symptoms are reported to be present in 15-45% of individuals with dementia (136, 137) and about 40% of individuals with delirium (138). The phenomenology of psychotic symptoms in delirium differs from that in primary psychotic disorders; hallucinations are rather visual than auditory (138), Schneiderian first-rank symptoms (such as thought broadcasting and thought echo) are very rare and delusional content may be absurd and dream-like, often concerning the immediate environment and dangers within it (139). Psychotic symptoms due to a general medical condition is strongly related to increasing age (140).

## **1.3.4 Epidemiology of late life psychosis**

### **Methodological aspects**

Individuals with psychotic symptoms may be reluctant to reveal these because of previous negative experiences from doing so (141). This phenomenon may be of greater methodological importance for delusional disorder and isolated psychotic symptoms than for schizophrenia, since schizophrenia may be more likely to reveal itself by behavioural disturbances (hallucinatory behaviour, language and motor disturbance) or signs of global functional impairment (101).

Individuals with psychosis may be more reluctant than others to participate in epidemiological studies (142). Since the phenomenon studied is fairly rare, a selection bias involving a small number of individual non-participants can have a high relative impact on prevalence estimates (143).

Some studies rely solely on information drawn from hospital records or registers, which avoids non-detection and non-participation. This instead introduces the bias of only capturing cases that have been identified by health care services. This bias may be significant, even for schizophrenia. A longitudinal study following 96% of a birth cohort with repeated examinations from age 3 to 38 years identified a 2% cumulative incidence of schizophrenia when counting cases confirmed by pharmacological treatment or hospital records (144). An additional 1.7% of this cohort formally met the diagnostic criteria for schizophrenia but had not (yet) been diagnosed by health care services.

Another difficulty is the assessment of the quality of psychotic symptoms, as discussed in Section 1.2.1. Furthermore, if the aims are to examine psychotic

symptoms that could benefit from treatment in a psychiatric setting and to study correlates of such symptoms, a problem of special importance among older people is to ascertain the etiology of the symptoms, i. e. whether they appear in the context of dementia, delirium, a general medical condition, ongoing medication or substance abuse.

Considering all these factors, epidemiological studies of psychosis should utilize several sources of information, such as key informants or medical records (22). They should also include some expert judgment of the quality and etiology of these symptoms, at least if the aim is to examine those symptoms that could be a psychiatric problem.

### **Prevalence**

The prevalence of psychotic *symptoms* in older people has been estimated to be between 1% and 13.4%. References are displayed in Table 1 (page 17). The median prevalence of the included studies is 3.6%.

Non-affective psychotic *disorders* are present in less than 1% of older adults in the majority of studies (see Table 2, page 18). In most studies, the majority of cases are of schizophrenia. Two studies reporting the current prevalence of delusional disorder in older adults find it to be very rare, 0.04% (141) and 0.03% (145). Others find a life time prevalence of 0.46% (140) or find it to be more common than schizophrenia (2.0%) (146). The very low prevalence of delusional disorder reported by some studies may be underestimations related to methodological factors mentioned above.

### **Age of onset**

Schizophrenia has its peak incidence in adolescence and early adulthood (147, 148). Delusional disorder has a later age of onset (mean age 40-50 years) (128, 149, 150). Of all older persons with a psychotic disorder, about 60% had an onset before age 40 (145).

### **Relationship to ageing and dementia**

Since psychotic *disorders* most often have an onset before age 40 and the mortality rate in the most common psychotic disorder, schizophrenia, is 2-3 times higher than in the general population (151), it might be expected that the point prevalence of psychotic disorders declines with age. Only one of the reviewed prevalence studies examined this and found schizophrenia to be less common with increasing age among older adults (145). Because of its rarity, age trends in the prevalence of delusional disorder are difficult to examine.

In contrast, at least two studies find that psychotic *symptoms* become more common with increasing age among older people without dementia (152, 153). A possible explanation could be that new-onset psychotic symptoms are prodromal

symptoms of dementia, which is related to increasing age (154). However, while several population studies, with a follow-up of between three and ten years, have reported an elevated relative risk for incident dementia among older individuals with prevalent (22, 155) or first-onset (156) psychotic symptoms and late-onset delusional disorder (157), the absolute risk for this was less than 50% in all studies and considerably lower (15%, 22%) in two of them (155, 157). These findings corroborate an early clinical study of late-life psychosis which found that only a minority of these patients developed dementia within two years (117).

### **Risk factors**

The life time risk for the most common psychotic disorder, schizophrenia, is higher in men than in women (147, 148), but no studies reporting the prevalence of psychotic disorders in old age (see Table 2) found a higher prevalence in men. Women have been reported to have a later age at onset for schizophrenia (158). One recent study (145) found the prevalence of schizophrenia in older adults to be two times higher in women than in men. This may reflect a higher likelihood of survival up to old age in women with schizophrenia or a higher incidence among women in old age.

Based on clinical experience, cross-sectional population studies and case-control studies, it is generally believed that sensory impairment (visual or hearing), social isolation and premorbid paranoid personality traits are risk factors for psychotic symptoms in old age (22, 159, 160). Furthermore, there are reported associations between psychotic symptoms and structural brain pathology (119, 160), for example basal ganglia calcification (161).

One systematic review of risk factors for late-onset psychosis has been published (162). It included only studies with a longitudinal design. Temporal antecedence is of course *one* prerequisite for causal relationship between a possible risk factor and a disease (163). However, the review included eleven studies that were very heterogeneous with respect to important factors such as study design, definition of psychosis, baseline age of the samples and length of follow-up. In this review, visual impairment, a history of psychotic symptoms, cognitive dysfunction, poor physical health and negative life events emerged as risk factors. Increasing age and female gender were not risk factors for psychotic symptoms and results on social isolation were ambiguous.

Table 1. Prevalence estimates of psychotic symptoms in older individuals without dementia.

Study (Reference)	Year	Country	Instrument	N	Age	Prevalence (%)
Durham study (164)	1972	USA	Mini-Mult, 'persecutory ideation'	781	≥65	2
Göteborg H85 (22)	1986	Sweden	Expert judgment based on CPRS, informant interview, medical records	347	85	10.1
Kungsholmen Study (159)	1987	Sweden	CPRS, informant interview, medical records	~1000*	≥75	2.6
Canberra Study (165)	1990	Australia	CIE, informant interview	~900	≥70	4.2
MRC CFAS (155)	1991	Great Britain	GMS, close informant	11916*	≥65	13.4
Islington Study (166)	N R	Great Britain	GMS, Expert judgment	656	≥65	2.4
EURODEP (153)	N R	Western Europe	GMS, CPRS, Expert judgment	8762	≥65	2.6
Cache County Study (167)	1995	USA	Neuropsychiatric inventory (informant interview)	~4700*	≥65	2.6 (delusions), 0.4 (hallucinations)
Brooklyn study (168)	1996	USA	Symptom checklist 90	1027	≥55	3
Göteborg H95 (169)	1997	Sweden	Expert judgment based on CPRS, informant interview	163	95	7.4
Göteborg H70 (present study) (170)	2000	Sweden	Expert judgment based on CPRS, informant interview	894	70-82	1.0
Sao Paulo Study (171)	2002	Brazil	CAMDEX	1125	≥60	9.1

The prevalence period is current to one-year for all studies. Gender-specific prevalence was not possible to extract from most studies and was omitted in this table. *N* denotes total number of study participants and is approximate for studies where an exact *N* could not be determined. Year denotes year in which study was initiated. \*Two-phase survey. N R= not reported.

Table 2. Studies reporting prevalence estimates of psychotic disorders according to DSM-criteria in old age.

Study (Reference)	Year	Diagnostic instrument	Diagnostic criteria	Age	N	Prevalence (%)		
						Women	Men	Total
Gothenburg H85 (146)	1986	CPRS/Expert judgment	DSM-III-R schizophrenia, delusional disorder, psychotic NOS	85	494	4.6	4.9	4.7
MRC ALPHA (141)	1989	GMS/Expert judgment	DSM-III-R schizophrenia, delusional disorder, psychotic NOS	≥65	5222	N.R.	N.R.	0.16
NCS-R (42)	2002	CIDI screen, SCID	DSM-IV non-affective psychosis	≥60	N.R.	N.R.	N.R.	0.2
PIF Study* (140)	2002	CIDI screen, SCID, medical records, expert judgment	DSM-IV non-affective psychosis	≥65	N.R.	2.67	1.71	2.32*
ESPRIT (9)**	2000	MINI, Expert judgment	DSM-IV affective and non-affective psychosis	≥65	1873	1.5	1.9	1.7
Amsterdam Study (145)†	2008	MINI-plus, Expert judgment	DSM-IV schizophrenia spectrum	≥60	185/26351†	0.90	0.44	0.71

All prevalence estimates are current to one-year except \* which is life-time prevalence estimate. Dementia was an exclusion criterion for psychotic disorder in all studies except\*. Prevalence figures includes whole population including individuals with dementia except \*\* which excluded individuals with moderate-severe dementia from the study sample. Year denotes year in which study was initiated. † Case-register study of patients (numerator) in a catchment area population (denominator).

## 1.4 Specific phobia in old age

According to several large epidemiological studies (see for example (58, 172)), specific phobia is the most common anxiety disorder or even the most common of all mental disorders in the population. It is a disorder of fear, which is probably the most studied of all emotions (173) and it is highly responsive to treatment (174). However, help-seeking behaviour is low (175) and descriptions of clinical populations are rare, at least in the psychiatric literature. This has been called ‘the paradox of phobias’ (176).

It seems fair to say that specific phobia in itself has received relatively little attention in the literature. As of June 15<sup>th</sup>, 2015, a PubMed search of the term ‘major depression’ OR ‘major depressive disorder’ returns 38 842 matches, a search for the term ‘social phobia’ OR ‘social anxiety disorder’ returns 4543 matches and a search for the term ‘simple phobia OR specific phobia’ returns 826 matches.<sup>8</sup> Specific phobia in older people has been the focus of a scant literature (177-181). Since it is the topic of two of the studies in this thesis, it will be reviewed in somewhat more length than the others.

### 1.4.1 Phenomenology and definitions

Fear is an emotion provoked by stimuli recognized by the organism as a threat to physical or psychological integrity (182). The ancient Greek word for fear, phobos (derived from the mythological personification of fear) has given name to the term phobia, which denotes a special type of fear (183). The *Glossary of technical terms* in the *DSM-5* defines a phobia as ‘a persistent fear of a specific object, activity or situation (the phobic stimulus) out of proportion to the actual danger ... that results in a compelling desire to avoid it. If it cannot be avoided, the phobic stimulus is endured with marked distress’ (101). The fear arises at every encounter with the phobic stimulus, or things that are reminiscent of it. Many will experience fear at the encounter with a black mamba, but someone with a severe snake phobia may be horrified by the tiniest grass snake, seeing a picture of a snake, or even signs of curvy road ahead. This also illustrates what may be meant by ‘out of proportion’.

#### **Fear and anxiety**

Fear can be distinguished from anxiety, although they are highly correlated. While anxiety is a state of preparation for future, possible negative events, fear is a response to a perceived present or imminent danger. Anxiety is largely characterized by subjective distress such as tension or nervousness, while fear is

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<sup>8</sup> If this search term is extended with the names of several of the most common specific phobias, the number of hits increases to a little more than 1000.

characterized by objective physiological arousal such as tachycardia, paleness or blushing (184). A twin study found that fear-related and anxiety-related disorders load on different genetic factors (185).

In current classification systems, specific phobias denote phobias of circumscribed objects or situations such as animals, heights, enclosed spaces and blood. However, the concept of specific phobias is a recent one and historical and theoretical perspectives will be discussed for phobias in general.

### **1.4.2 History**

Hippocrates described patients suffering from unreasonable fears of social situations, heights and even the sound of flutes, which he saw as a form of melancholy. The term phobia was first used in a medical setting by Roman encyclopaedist Celsus referring to rabies, in which there is an intense fear of drinking or being in water (hydrophobia) secondary to swallowing difficulties (186). This was its only medical use until the late 18<sup>th</sup> century, which reflects that for a long time, at least in European history, minor mental symptoms such as phobias were not considered within the realm of medicine. The unreasonable fears are however subjects in literature and philosophy, for example in the works of English philosopher John Locke (1632-1704) (187).

In 1798, American physician Benjamin Rush suggested that, as an extension to previous systematic classifications of diseases of the time, hydrophobia should be classified as a sub-species to the genus of phobias (188). He defined a phobia as ‘a fear of an imaginary evil, or an undue fear of a real one’ and listed 18 different phobias, partly ironizing over various human characteristics, but also giving vivid descriptions of phobias of thunder, water, blood and rats.

In the 19<sup>th</sup> century, most psychiatrists, practicing in asylums with severely ill patients, did not consider phobias as clinical syndromes in their own right (189). Phobias were viewed as a manifestation of broader categories such as ‘mania without delirium’, ‘partial insanity’ or ‘lucid insanity’, reflecting that in contrast to asylum patients, these persons had no intellectual deficit or had not lost their contact with reality. Except for fear in itself, authors recognize symptoms such as dizziness, associated with height phobia and agoraphobia, which also led some to conclude that such symptoms were not mental, but caused by for example inner ear disease (189). They describe the early onset of the symptoms, the chronic, but fluctuating course, and that these patients rarely needed hospital admissions (186).

In 1871, Westphal described a condition he termed agoraphobia, fear of the marketplace (190). Three men had sought help in his Berlinese community practice for a disabling fear of crossing squares or walking empty streets at night, a fear that they considered completely irrational. He especially noted the



circumscription of this symptom, i. e. that it was not accompanied by other psychopathology. A further discussion about agoraphobia will follow in section 1.4.4.

At the end of the 19<sup>th</sup> century, the diagnosis of neurasthenia was popular among physicians and included a variety of symptoms including fatigue and various psychosomatic symptoms. Freud, in 1895, was one of the first to demarcate anxiety symptoms from this broader category with his concept of the anxiety neurosis (191, 192). Although most psychiatrists did not share Freud's view on the etiology of anxiety, he contributed to the acknowledgement of anxiety as a distinct type of mental disorder (189). Freud argued that pathological phobias, as opposed to normal fears, are a part of the anxiety neurosis, which most often has its etiology in various forms of restrictions on the libido and that many phobias arise from a displacement of fear from its actual stimulus, which is usually found in the sexual history of the patient (193, 194). In the two first editions of the *DSM* (64, 65), no distinctions are made between different types of phobias and the Freudian view of their etiology, the displacement of fear, is central in the description of the diagnosis of phobic neurosis.

### **1.4.3 Current classification and diagnosis of phobias**

#### **Diagnostic categories**

In 1970, Marks (183) suggested a classification based on the type of phobic stimulus: social phobia (now referred to as social anxiety disorder), agoraphobia, animal phobias and mixed specific phobias. This classification was incorporated into the third edition of the *DSM* in 1980 (74), although animal and mixed specific phobias were both included in the diagnosis of simple phobia.

#### **Specific phobia in the DSM-IV and DSM-5**

In the *DSM-IV* (99), simple phobia was renamed specific phobia. The core symptom is a marked and persistent fear towards a specific object or situation that is not better explained by another mental disorder. Five sub-types are introduced, based on the type of phobic stimulus: animals, the natural environment, specific situations, blood-injection injury and 'other' (which may include phobia of for example vomiting or specific illnesses such as cancer). The person should recognize the fear as excessive or unreasonable, and should avoid the phobic stimulus or endure it with intense anxiety. The symptoms should interfere significantly with normal routine, occupational or academic functioning, social activities or relationships, or there should be marked distress about having the phobia. The diagnosis and sub-typing is highly similar in *ICD-10* (195), although it also allows for a diagnosis of phobic anxiety disorder, unspecified.

According to the *DSM-5* (101), the judgment of whether the fear is excessive or unreasonable is made by the clinician and not by the patient. Judging by some published background work for the *DSM-5*, this change was partly due to the idea that older people were prone to not consider their fears excessive (196). Indeed, it may affect the prevalence estimate of specific phobia in older people: In a recent population study, about 57% of older people who otherwise met diagnostic criteria for *DSM-IV* specific phobia did not think their phobia was excessive (178). A study on social anxiety disorder in older people gave similar findings (197). Interestingly, a study of psychiatric outpatients and bariatric surgery candidates found that almost none of the participants were excluded from a diagnosis of specific phobia or social anxiety disorder because they did not think their fear was excessive (198). The authors of this study also suggested that the 'excessiveness' criterion could be omitted, not because it excludes clinically relevant cases from a diagnosis, but because it was redundant. These remarkably different findings may partly be due to that the utility and validity of diagnostic criteria are dependent on the context in which they are used, as is discussed in Section 1.2.2.

### **Reliability of diagnostic criteria for specific phobia**

Specific phobia has not been included in the published *field trials* of the *DSM-IV* or *DSM-5* diagnostic criteria, which compare their inter-rater reliability in clinical settings (199). There are some reliability studies of interview instruments generating a *DSM-IV* diagnosis of specific phobia. One study (200) of a semi-structured interview instrument used in the setting of a specialized anxiety clinic, found excellent inter-rater reliability for specific phobia as a principal diagnosis, but it declined to being only 'good' when also including cases where it was an additional diagnosis. The majority of disagreements between raters concerned whether the condition was clinically significant or not, a more difficult question for additional diagnoses than for principal diagnoses. A reliability study of the frequently used lay-interviewer instrument *CIDI* showed excellent test-retest reliability (between two separate interviews with different interviewers) for *DSM-IV* specific phobia (201).

A clinical reappraisal study, comparing the *CIDI* to the more comprehensive, clinician-administered *SCID*, found only fair agreement between the two interviews, and the agreement for specific phobia was the lowest of all mental disorders (202). A study of another layperson-administered interview (*AUDADIS-IV*) found fair test-retest reliability for *DSM-IV* specific phobia (203). This was similar to other anxiety disorders, but considerably lower than for alcohol dependence and major depression. A study examining reliability of individual items of the *CIDI* diagnosis of specific phobia in a population sample found excellent agreement on the item pertaining to persistent fear symptoms, but only fair agreement on the item pertaining to interference with daily life/distress (204).

To sum up, most inter-rater disagreements on a diagnosis of specific phobia seem to arise with respect to the clinical significance of the symptoms.

#### 1.4.4 Subtypes of specific phobia

There are hundreds of named phobias (205), so they need to be sorted into larger groups (183). Currently, this is done on the basis of the type of phobic stimulus, as described above. Some characteristics of the different subtypes will be briefly reviewed below.

##### Clinical features

*Age of onset* differs between different phobia subtypes. Animal and blood-injection-injury phobia most often begin in the first decade of life, phobia of specific situations usually begins in late adolescence and the natural environment type most often begins somewhere in-between (206-208). The *bodily symptoms* of blood-injection-injury phobia typically involve fainting, as opposed to the physiological arousal accompanying animal phobias in particular (183, 196). Height phobia is usually accompanied by vertigo and has been conceptualized as visual height intolerance (209, 210). On a height, the distance increases to visual cues that help to retain postural control, which produces vertigo and disorientation. This, in turn, produces a compensatory postural sway of the lower limbs.<sup>9</sup> In some individuals, this physiological mechanism becomes a thrill, but in visual height intolerant individuals with high sensitivity to bodily symptoms such as vertigo, it may result in agonizing fear of falling (211). The *focus of fear* of different subtypes is in alignment with these clinical features. In individuals with blood-injection-injury phobia, the fear most often focuses on the risk of fainting. The focus of fear in animal phobia is often disgust and revulsion, whereas in the natural environment and situational subtypes, it is most often the danger of the situation itself (196, 208).

##### Neuroimaging

Experimental neuroimaging studies (212, 213) of specific phobia have almost exclusively been carried out in the animal and blood-injection-injury sub-types, especially spider phobia (most likely for practical reasons). Studies have most often been conducted without a control group or with a non-phobic control group. Upon confrontation with an image of the feared stimulus, those with spider phobia show hyperactivation of the amygdala, the insula, the anterior cingulate cortex and in the thalamus. Studies comparing animal and blood-injection-injury

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<sup>9</sup> The brave subjects participating in the study by Brandt et al. (209), who were put at the outer edge of a 20 meter high building, found it more discomforting to stand up than to lie down, which cannot be explained by the extra one and a half meters of height added by this position.

phobia reveal that they have somewhat different functional neural correlates (214, 215), which may support current distinction between them and casts some doubt over the suitability of spider phobia as a 'disease model' for other phobias and other anxiety disorders.

### **Specific vs. clustering phobias**

Marks (216) observed that animal phobias were most often specific to a particular animal so that someone with a severe spider phobia does not necessarily have a phobia of snakes. In contrast, he found other phobias to rarely occur in isolation; a fear of leaving home alone is most often accompanied by fears of for example enclosed spaces and public transportation (the agoraphobic syndrome, discussed below). To some extent, later studies challenge this notion. Epidemiological studies find that some fears within the agoraphobic syndrome, such as fear of flying and enclosed spaces, may often occur as specific phobias (207). Furthermore, even individuals with specific phobia of animals or the natural environment have a higher number of fears than those who have subthreshold fears but not specific phobia (207, 217). In one clinical study, one third of patients with specific phobia had multiple fears that met its diagnostic criteria (218) and in another, two thirds had additional subthreshold fears (208). The disposition for developing specific phobia seems to come both from a common underlying general fear factor and factors related to a specific subtype of phobia (217, 219, 220).

### **The special case of agoraphobia**

Agoraphobia is not a specific phobia, but rather a cluster of phobias that are connected to being in situations where it may be difficult to escape or get help, such as using public transportation, being in open or enclosed spaces or leaving home alone (101). Such fears may have internal cues. One of Westphal's patients spoke of *Angst vor der Angst* (fear of the fear) (190). Freud suggested that agoraphobia was the consequence of what is now considered a typical *panic attack*, a sudden onset of fear and panic not preceded by confrontation with a phobic stimulus (192). In 1967, it was discovered that panic attacks could be induced by lactate infusion in persons with a history of such spontaneous attacks, but not in normal control persons (221). Around this time, recurrent panic attacks were also successfully treated with the tricyclic antidepressant imipramine (222). In 1980, the *DSM-III* (74) introduced the new condition panic disorder and agoraphobia was considered a secondary phenomenon in most cases. The diagnosis was largely constructed on the ground of pharmacological and physiological research into this 'endogenous anxiety' (191).

However, one longitudinal population study found that while panic disorder increased the risk for later agoraphobia, agoraphobia also increased the risk for later panic disorder (223). Another longitudinal study, of older people, found

agoraphobia to have a high 4-year cumulative incidence (11%) but almost no case of new-onset agoraphobia was associated with panic attacks (224). In contrast, a small clinical reappraisal study of cases of agoraphobia without panic attacks, collected in an epidemiological study, found that almost all of the cases were better labelled specific or social phobia or did not have a clinical phobia diagnosis at all (225). There is a continuing debate on if, and how, agoraphobia and specific phobias of the situational subtype can be distinguished from each other (226).

### **Specific fears in older people**

Since so little research has been carried out on fears and phobias in old age, it may be that there are fears and phobias specific to older people which are not recognized. Indeed, in the development of a fear questionnaire for older people, it was found that the fears most commonly endorsed were related to ageing, for example fear of mental decline, illnesses and being a burden (227). No studies have been found that used this questionnaire, so little is known about if these fears have the characteristics of phobia (i.e. out of proportion to actual threats), or whether they are best viewed as something else.

A fear that seems to typically have its onset in old age and which may have the characteristics of a phobia is fear of falling (space phobia, ptophobia) (228, 229), which is common, especially after fractures, and may reduce mobility (230, 231).

## **1.4.5 Theories of the etiology of specific fears and phobias**

The etiology of fears and phobias has mainly been addressed from three theoretical perspectives: psychoanalysis, behaviourism and evolutionary theory. All are subject to a rich literature. This short summary is not written with the intention to do them complete justice.

### **Psychoanalysis**

A famous case of phobia was presented by Freud in 1909 (232). Briefly, a five year old boy acquired a phobia of horses after witnessing a dramatic accident involving a horse. Mostly based on information from the boy's father, Freud made the interpretation that this fear was a manifestation of an Oedipal conflict; the boy experienced fear of retribution from his father because of his sexual desire for his mother, and fear of losing his mother as a sexual object. This fear was displaced from its original stimulus; horses were merely *symbols* of this original stimulus, in accordance with Freud's view of the anxiety neurosis (discussed in Section 1.4.2).

While psychoanalytic interpretations of phobias are prevalent, the existence of Oedipal conflicts and their relevance to the development of phobias has not been supported by empirical and quantitative research, but rather by theoretical discussions and case studies (233). A more detailed discussion of this literature was considered to be beyond the scope of this thesis. It should only be

acknowledged, that Freud himself did not aim to explain all phobias in the way outlined above. He argued that evolution could easily explain common phobias, such as that of snakes (see below), while other phobias, for example phobia of urination in the presence of others (paruresis) or phobias of dirt were obviously related to the sexual life of the patient (193, 194).

### **The associative (learning) theory**

Proponents of behaviourism argue that the frightening horse accident in itself is a perfectly sufficient explanation of the phobia described by Freud (234, 235). Locke encapsulates their *associative theory* (also called learning or conditioning theory) of the etiology of phobias:

The only thing we naturally are afraid of is pain, or loss of pleasure. And because these are not annexed to any shape, colour, or size of visible objects, we are frighted with none of them, till either we have felt pain from them, or have notions put into us that they will do us harm (187).

The foundation of empirical support for this theory is what has been learned from experiments with *fear conditioning*. Exposure to some stimulus (the conditioned stimulus) in association with trauma (the unconditioned stimulus) is followed by a 'defense reaction' to the conditioned stimulus even in the absence of trauma (235-237). According to this theory, such learning to fear may also occur through other pathways, such as witnessing trauma, role-modelling and information about dangers (236, 238). These pathways may also have synergistic effects (239).

Some problems with the associative theory may be mentioned here. First, its experimental model of fear conditioning may not be a valid model of 'real world' phobias; conditioned fears may for example not show the same life-long persistence as phobias (240). The 'defense reaction', found also in primitive mammals and even invertebrates, may not correspond to the human emotion of fear (173). The theory may be too simple given the complexities of the human central nervous system. Second, it is contradicted by the observation that phobias towards some stimuli, such as snakes, to which dangerous exposure is unlikely in many societies, are very common, while phobias towards stimuli such as motor vehicles and electricity, to which dangerous exposure is likely, are rare.

### **The non-associative (evolutionary) theory**

French philosopher André-Francois Deslandes (1689-1757) may introduce the notion that some persons are born with certain fears, which invokes a *non-associative theory* of fear acquisition:

Nobody has yet been able to explain these strong aversions which one brings with one at birth and which it is so difficult to be rid of

later in life. It seems to me that they might be due to a sixth sense which nature accorded to certain humans; but an impractical sense and one which causes difficulties (cited in (186)).

Despite that phobias may cause difficulties, the ability to fear dangerous things without learning may have improved fitness in animals and humans (241). There is no second try after a bite from a black mamba or a fall off a high cliff. It is thus argued that genetic factors may play an important role in the etiology of certain common, evolutionary relevant fears, such as fear of heights, snakes and deep water (242, 243). According to this theory, the fact that not everyone has a severe snake phobia should be partly explained by the opposite of fear conditioning: repeated controlled exposure to a phobic stimulus (and possibly the other pathways referred to above) results in *habituation* (242, 243).

While there is an abundance of hypotheses of how evolution may explain different phobias (244), such hypotheses may be difficult to falsify since we know little about the death rate and risk factors for snake bite in our prehistory (245). However, indirect support for this theory may be given. First, twin studies show moderate heritability of several common phobias, although this partly reflects heritability of a general 'phobia proneness' (219, 220). Second, many people with phobias cannot recall a triggering event, as associative theories postulate (246, 247). This argument has been criticized for relying too much on retrospective information and that such events may be forgotten (246). However, a prospective study found that adolescents with height phobia experienced significantly less childhood fall traumas than those without height phobia. Those with a lot of childhood fall traumas were less likely to be height phobic in adolescence than others (248). Data from the same study showed a similar lack of association between adverse experiences with water in childhood and later water phobia (249).

These findings may speak against fear conditioning as etiologically relevant for these phobias, but fits with the hypothesis that they are innate. Also, different ages of onset of animal and situational phobias may be explained by that natural selection has made humans start to fear things at a time in life when they are most likely to experience dangerous exposure.<sup>10</sup> Longitudinal twin studies of fears and phobias have given some indirect support for this hypothesis (250, 251).

Lastly, the theory of *preparedness* takes both learning and evolution into account (240). It hypothesizes that a fear response must be learned, but is much more easily learned for certain, evolutionary relevant stimuli. This thus offers a mix of the associative and non-associative theories, but is distinct from both (182).

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<sup>10</sup> Compared to adolescents, small children are more likely to be exposed to dangerous animals than to life-threatening aggression from peers (the evolutionary advantage of social phobia may be hypothesized to be that shyness reduces the risk of such violent conflicts).

## **1.4.6 Epidemiology of specific phobia**

### **Prevalence of specific fears and specific phobia**

The prevalence of specific fears has been estimated to be between 11% and 74%. References are displayed in Table 3 (page 34), in which the median prevalence is 49.5%. Despite a large variation in prevalence estimates between studies, it is noteworthy that studies reporting both the prevalence of all fears and specific phobia (178, 207, 217, 252) are relatively consistent in their estimation of the proportion among those with phobic fears who have specific phobia (17-23%).

The point to one-year prevalence estimates of specific phobia in adults from different countries vary between 1% and 20%, but most studies report a figure of 5-10% (58, 207, 217, 253-259). Cultural factors could influence this variation (260), but most of it is likely due to methodological factors (180). Given the high prevalence of phobic fears, and given that many cases of specific phobia are mild (58), many individuals in population studies could be around the threshold for a diagnosis, and a small shift in the diagnostic threshold can give a major shift in prevalence. Prevalence estimates of specific phobia in older adults are displayed in Table 4 (page 35). Estimates vary between 2% and 11% (median one-year prevalence=4.9%).

Some prospective studies have reported on the cumulative prevalence of specific phobia over an extended time period. In a sample examined four times between from ages 18-32, 18% had specific phobia at some point (25) and in a sample examined seven times between age 20 and 50 years, 26.9% had specific phobia at some point (261).

The most common types of specific fears in the population are those of animals and the natural environment, but fears of specific situations are relatively more likely to be associated with a diagnosis of specific phobia (207, 217, 258). Few studies have been able to closer study individual subtypes of specific phobia. This is due to the construction of interview instruments used in epidemiological studies. In individuals with multiple fears or multiple fear types (which is common), the 'main' phobia cannot be ascertained. One study reported the prevalence of several subtypes and found animal phobia to have a prevalence of about 4%, while the others had a prevalence of 2% or less (256). Another study reported the prevalence of blood-injection-injury phobia to be 3.5% (262).

### **Age and age of onset**

Cross-sectional epidemiological studies find that specific phobia is less common in older than in younger people (10, 258). Interestingly, in studies reporting both cross-sectional prevalence and life-time prevalence, both are lower at older ages (10, 258, 263). This may represent cohort effects, but is more likely due to recall



failure, meaning that older people have more difficulties to recall previously having specific phobia (25). Experimental studies suggest that older people are less prone to fear conditioning than younger persons (264) and have a decreased reactivity to negatively valenced stimuli in general (264, 265). This may be due to either neurodegeneration or improved emotional regulation with increasing age (266). The autonomic response to panic-inducing stimuli may be diminished in older people (267). This response may be diminished also for phobic stimuli, which would prevent a fear from reaching the diagnostic threshold for specific phobia.

Clinical (206) and population (263) studies relying on retrospective information find that specific fears most often have its onset in the first decade of life, although there may be a significant delay from symptom onset to the time at which they become severe enough to merit a diagnosis (268). In a prospective study of children and adolescents with data collection between age 11 and 19 years, almost all cases of phobia (including agoraphobia and social phobia) had their onset before age 14 (27). A late age of onset of specific phobia seems to be rare; phobic disorders arising in old age seem most often to be agoraphobic (179, 224). Two studies reporting the incidence of specific phobia in older people have been found. One study reported the three-year incidence of specific phobia in adults  $\geq 60$  years to be 1.35% (269). The other reported a one-year incidence of 1.1% in adults  $\geq 65$  years (270). The likelihood of recall failure makes it disputable whether incident cases are new-onset, or merely represent worsening of a life-long fear that may have met diagnostic criteria also earlier in life.

### **The course of specific phobia**

The *DSM-5* describes specific phobia as a chronic disorder; once persistent into adulthood, it rarely remits (101). Clinical studies of the long-term prognosis of specific phobia are rare, but support this assumption. One follow-up of successfully treated patients found that 75% of patients experienced clinically significant symptoms during a period of 10-16 years after treatment (271). A naturalistic study of psychiatric outpatients with specific phobia as a comorbid disorder found 80% to meet diagnostic criteria also five years after a baseline examination (218).

Prospective, longitudinal population studies of the prognosis of specific phobia according to *DSM* criteria stand in sharp contrast to these figures. The studies and their rates of persistence are found in Table 5 (page 36). As can be seen, all studies find only a minority (15-40%) to have an unremitting course. Age of the sample and length of follow-up seems to make little difference. Two studies report also partial remission. The *ESA* study of older people found that a total of 47.8% of individuals with specific phobia had at least some symptoms of the disorder at follow-up, while the corresponding figure for the Dresden Predictor Study of

young women was 81.3%. This may suggest that the prognosis is better in old than in young people, but differences may also be explained by different definitions of remission and by that the Dresden Predictor Study included only women. These figures also indicate that reporting of subthreshold specific fears may give a better description of the course.

#### **1.4.7 Sociodemographic correlates**

Weak associations are reported between specific phobia and lower income (258) and not being married (in older adults) (177). The most prominent and consistent sociodemographic correlate of specific phobia is female gender. As can be seen in Table 3 and Table 4, and as has been examined more in detail (254, 257), specific phobia and specific fears in general are consistently and considerably more prevalent among women than among men. This gender difference is more marked than for social fears (272). A longitudinal study of older people reported a five times higher incidence of specific phobia in women than in men (270). One longitudinal population study of phobic fears in adolescents indicated that girls were more likely to have a stable course of phobic fears than boys (273), but no studies have been found that examine gender influences on the prognosis of phobic fears and specific phobia among adults.

These marked gender differences may have explanations at both the biological, psychological and social level (272). Some suggested mechanisms are difficult to disentangle, such as the hormonal changes and social consequences of puberty (274). Society's expectation of men is to be independent and to master situations they are confronted with, while women may rather be expected to be dependent and in need for protection (275). This may cause a lower rate of controlled exposure to phobic stimuli in girls so that their childhood fears are more often persistent into adulthood (254).

Additionally, gender differences in fears and phobias may in part be due to methodological error. Men may be less likely to admit having a phobia because of it being in conflict with the male gender role. One experimental study found that men were more likely to disclose a fear when they were led to believe that their truthfulness could be revealed by measurement of their heart rate at confrontation with a phobic stimulus (276). Such an effect was not observed among women. Still, gender differences in fears persisted at a smaller magnitude even under this experimental condition.

#### **1.4.8 Association with other mental disorders**

Specific phobia is most strongly associated with other anxiety disorders, particularly panic disorder with agoraphobia and social anxiety disorder, but is also associated with mood- and substance disorders (177, 207, 217, 258). Some

studies, however, indicate that specific phobia is more often occurring as a 'pure' disorder (without comorbidities) than do other anxiety disorders (277).

In younger populations, specific phobia and other anxiety disorders have been associated with later development of depression (278, 279). However, some studies found no association between specific phobia and later depression after adjustment for comorbid other anxiety disorders (280, 281). One study found no longitudinal association between specific phobia and 'first onset' depression in an older population (269), but anxiety may be more related to recurrent than to late-onset depression in older adults (282). There is a broader discussion of whether anxiety disorders in effect of their consequences, such as demoralization and avoidance behaviour, may be causal factors in the development of depression, or whether their association is due to shared etiological factors (283).

#### **1.4.9 Possible effects on general health**

One population study found no obvious effect of a diagnosis of specific phobia on all-cause mortality (284). However, several population based studies have found phobias, as assessed by a self-report symptom scale, to be prospectively related to cardiovascular disease, especially fatal myocardial infarction and sudden cardiac death (285-287). This symptom scale mostly measures fear of specific situations, including agoraphobic fears, so it is not known whether this association exists also for other subtypes of phobia. With the same measurement, phobias have also been prospectively associated with incident type 2 diabetes (288). The mechanisms behind these associations are not clear but may include autonomic dysregulation (289) and a more unhealthy lifestyle (290) not accounted for by measured confounding and mediating variables.

#### **1.4.10 Help-seeking behaviour, impairment and quality of life**

The functional impairment due to specific phobia is dependent on the consequences of the avoidance behaviour. Not being able to go by airplane or use elevators may obviously impose restraints. Those with blood-injection-injury phobia may avoid seeking health care and may have trouble during pregnancy (291) or in managing diabetes (262). Bird phobia may keep persons from sitting outside in a restaurant and insect phobia may keep them from leaving home when such creatures are abundant outside (218).

Population studies have found that only a minority of persons with specific phobia seek treatment for this disorder (175, 292). In the *WHO* World Mental Health Survey, rates of help-seeking and disability in specific phobia were the lowest among all mental disorders assessed (292). About 13% of individuals with specific phobia in high income countries had been treated for this disorder in the last year and 18% of individuals with specific phobia themselves rated this condition as

severely disabling. The figures may be compared to those for major depression in the same study, where 29% were treated and 65% were severely disabled. However, given the high prevalence of specific phobia, a relatively small proportion of severely disabled becomes high in absolute numbers.

In a study of specific phobia in psychiatric outpatients, of whom all had other affective or anxiety disorders, having specific phobia was not related to functional impairment and only 17% of patients with specific phobia had received a treatment deemed appropriate for this disorder (218). Another study found that only 30% of patients presenting in a psychiatric outpatient clinic and diagnosed with specific phobia indicated this as one of their reasons for seeking treatment (293).

Studies on help-seeking and functional impairment in specific phobia among older people are scant. In one population study, only 8% of those diagnosed with specific phobia had used health services for this condition in the last year (8). No clinical study of older patients with specific phobia has been found. One study did a clinical interview with individuals with phobic disorder diagnosed in a population study (179). None of these individuals received any treatment for this condition.

Qualitative studies of the experiences of individuals with specific phobia (294, 295) suggest a sort of inverted stigma related to the disorder, such that it is trivialized (contested as an illness) and considered childish and ridiculous. Fear of not being taken seriously emerged as an important reason for not seeking treatment in primary care.

Some other suggested explanation to the low help-seeking behaviour and treatment rates may be mentioned although they are only speculations or based on anecdotal evidence. First, many cases of specific phobia are mild and may not require treatment if the feared stimulus can relatively easily be avoided or endured with support of other people. Second, the early onset of the symptoms may result in that they are not perceived by the individual as a deviation from 'pre-morbid' functioning or behaviour (296). Individuals may see their avoidance behaviour as a way of coping with 'how they are' (293). Third, the standard therapy of specific phobia, exposure therapy, may seem to some persons too large a challenge in relation to the perceived benefit (297). Fourth, a minority of those with height phobia reported to cope with it by intentionally seeking exposure to heights (210), suggesting the possibility of self-treatment as another explanation to low help-seeking behaviour.

### **1.4.11 Treatment**

The first line treatment of specific phobia is various forms of exposure therapy, also called desensitization therapy and behavioural therapy, which has been found to have excellent short term results (174). In uncomplicated cases, a single session of exposure therapy may result in major improvements (298). Only one controlled treatment study of specific phobia in older adults (which was not able to recruit any participant above age 68 years) has been found (181) and it showed an effect of a 10-session exposure therapy intervention.

The long-term effects of exposure therapy are less impressive, with major proportions of patients experiencing 'return of fear' (271, 299). Little solid research exist into how this therapy can more successfully extinct fear (300). Recent experimental developments include the concurrent administration of 'cognition enhancing' substances (301) to facilitate fear extinction (302), as well as behavioural disruption of fear memory reconsolidation (303). Both these developments aim to perform extinction therapy when a fear memory is labile (under reconsolidation), in which case the fear may be permanently attenuated.

Table 3. Studies reporting the prevalence of specific fears and specific phobia in adults

Study (Reference)	Year	Country	Instrument	Diagnostic criteria	Age	N	Prevalence period	Prevalence of specific fears including specific phobia (%)			Prevalence of specific phobia (%)	
								Women	Men	Total	Total	In those with fear
Calgary Study (304)	?	Canada	PSE	-	18-65	449*	-	73.8	-	73.8	-	-
NCS (217)	1991	USA	CIDI	DSM-III-R	15-54	1461	Life-time	NR	NR	49.5	11.3	22.7
NEMESIS (207)	1996	Netherlands	CIDI	DSM-IV	18-65	7076	Life-time	NR	NR	41.2	9.6	23.3
Gothenburg (145) (current study)	2000	Sweden	CPRS	DSM-IV	70	558	Last month	71.0	37.9	57.7	10.0	17.4
ESA study (178)	2004	Canada	ESA-Q	DSM-IV	≥65	2784	Last year	NR	NR	10.7	2.0	18.3

\*Included women only.

Table 4. Studies reporting prevalence of Specific phobia in older adults

Study (reference)	Year	Country	Instrument	Diagnostic criteria	Age	N	Prevalence period	Women	Men	Total
Guy's/Age Concern Survey (305)	1986	Great Britain	Own	Own	≥65	890	Current	3.0	0.6	2.1
Iceland Study (306)	1986	Iceland	DIS	DSM-III	55-57	862	Life-time	10.2	7.5	8.8
Amsterdam study (307)*	1992	Netherlands	DIS	DSM-III	55-85	3056	Six-month	4.4	1.6	3.1
Brooklyn study (308)*	1996	USA	Own	Own	≥55	1074	Current	N.R.	N.R.	8.9
NCS-R (10)	2002	USA	CIDI	DSM-IV	≥65	1461	Life-time/One-year	9.1/6.8	3.6/1.9	6.8/4.7
NESARC (177)	2001	USA	AUDADIS-IV	DSM-IV	≥65	8205	Life-time/One-month	N.R.	N.R.	6.1/4.5
ESPRIT (9)*	2000	France	MINI	DSM-IV	≥65	1873	Life-time/One-month	22.4/12.9	10.9/6.2	17.6/10.1*
Gothenburg (145) (current study)	2000	Sweden	CPRS	DSM-IV	70	558	One month	13.8	4.5	10.0
New Zealand Survey (11)	2003	New Zealand	CIDI	DSM-IV	≥65	N.R.	One-year	N.R.	N.R.	3.2
ESA study (178)	2004	Canada	ESA-Q	DSM-IV	≥65	2784	One-year	N.R.	N.R.	2.0
Sivas Study (309)	2003	Turkey	SCID-I	DSM-IV	≥65	462	Life-time/one-month	17.7/17.7	4.9/4.9	11.5/11.5

\*Study did not distinguish between different phobic disorders \*\*Study did not distinguish between agoraphobia and specific phobia. N.R. = not reported

*Table 5. Rates of persistence of specific phobia in prospective population studies*

Study (Reference)	Follow-up (months)	Country	Instrument	Criteria	Age	N*	Persistence (%)
NEMESIS (207)	12 and 36	Netherlands	CIDI	DSM-IV	18-65	>400	'About 15%'**
NESARC (310)	36	USA	AUDADIS-IV	DSM-IV	≥55	600	24.2
ESA (311)	12	Canada	ESA-Q	DSM-IV	≥65	46	23.9***
Dresden Predictor Sutdy (312)†	17	Germany	ADIS-IV	DSM-IV	18-25	137	39.4%****

Persistence: the rate of individuals diagnosed with specific phobia at a baseline examination who met diagnostic criteria at a follow-up examination. \*N denotes number of individuals with specific phobia at the baseline of each study who could be followed-up. \*\*Proportion of individuals with 'life-time specific phobia' who had specific phobia at both follow-up examinations. Number inaccurately reported in the study. \*\*\*A further 23.9% were in partial remission. \*\*\*\*A further 41.9% were in partial remission. †Study includes women only.



## 1.5 The depressive spectrum in older people

In 1886, Danish neurologist Lange gave a clinician's report on depression in a community setting:

The disease that in my announcement of this speech I have described as periodical depression is of such common occurrence that in my private practice, with which I have been occupied for a number of years, there is no other form of illness which by far occurs as frequently (313), p. 116.

This statement is reinforced by the *WHO* Global Burden of Disease Study for the year 2010, which ranked unipolar depressive disorders as a leading contributor to years lived with disability worldwide, second only to lower back pain (314). Depression is thus considered to be of major clinical and public health significance. It is covered by a vast literature (see Section 1.4). At a closer look, it is also a heterogeneous concept and its epidemiology is complex. The present is not an exhaustive review of depression in older people, but focuses on some general perspectives on classification and epidemiology as well as on previous research of particular relevance to the topic of Study IV.

### 1.5.1 The diagnosis of major depression

A diagnosis of major depressive disorder according to the *DSM-5* requires the presence of at least five symptoms from nine 'domains'<sup>11</sup> listed in Table 7 (page 53), one of which should be the core symptoms (depressed mood and diminished interest) (101). The *ICD-10* diagnosis of depression (195) adds reduced energy as a core symptom and grades the condition into mild, moderate or severe, partly based on number of symptoms. According to both classification systems, the duration should be at least two weeks but the *DSM-5* more explicitly requires clinical significance, defined as some form of functional impairment.

The current diagnosis of major depression is coherent with a widely spread unifying theory of depression, according to which this syndrome is the expression of a final common neurobiological pathway for several conditions with different etiology (315). This contrasts with previous approaches to classification of depression, for example psychotic/endogenous *vs.* neurotic/reactive (316, 317).

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<sup>11</sup> It is not nine different symptoms. For example, appetite disturbance/weight change includes both decreased and increased appetite. It also includes weight loss and weight gain, which are signs rather than symptoms. They can appear in the absence of the corresponding appetite disturbance. This domain thus includes four different symptoms and signs.

The nine depressive symptom domains listed by the *DSM* are highly conserved from the list proposed in 1972 by Feighner et al. (68), arrived at not so much on the basis of empirical study as on the basis of consensus among senior clinicians at Washington University, St. Louis, United States (30, 318, 319). Already from this list, it is clear that major depression is a highly heterogeneous condition, allowing two persons with almost non-overlapping symptomatology to have the same diagnosis (320).<sup>12</sup> This heterogeneity puts the clinician to the test and may partly explain why primary care physicians fail to identify about 50% of older patients who have depression according to a structured or semi-structured diagnostic interview (321).

Some research that has addressed the validity and utility of the current symptomatic diagnostic criteria for major depression may be mentioned. One study suggested that they could be simplified, since some symptoms (such as suicidal ideation) seemed to be redundant, meaning that individuals with these symptoms would almost always qualify for a diagnosis even without counting them (319). Another study suggested that some symptoms (those typically considered as melancholic) seemed to be more strongly correlated to severity of major depression and that these should be given more weight in the diagnostic criteria (322). One study showed differences in the association between individual symptoms and sociodemographic and clinical variables, in support of heterogeneity of the condition (318). Finally, one study found 1030 different symptom combinations among 3703 patients (323). Almost half of these combinations were unique to one patient.

### **1.5.2 Subthreshold depression and the depressive spectrum**

From a theoretical point of view, depression may be best understood as a spectrum, or continuum, with no clear demarcation from 'normal' mood fluctuations (50). It shares this characteristic with other common medical conditions such as hypertension or type 2 diabetes (90), for which the threshold for diagnosis may change as a consequence of new research or changes in expert opinion. In addition to the heterogeneity of major depression in itself, it is therefore also debated whether the requirements of five symptoms for 14 days actually captures such a threshold, or cut-off, for clinically relevant depression (38, 87). The cut-off of five symptoms for 14 days was never anything else than arbitrary (30).

As discussed in Section 1.2.2, the *DSM* system was developed for use in specialized mental health care. In such a setting, where depressive episodes often feature

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<sup>12</sup> One patient may have loss of interest, reduced sleep, loss of energy, psychomotor retardation and weight loss, while another may instead have depressed mood, increased sleep, increased appetite, concentration difficulties and psychomotor agitation.

suicide attempts or marked weight loss, most patients will be well beyond the diagnostic threshold both with respect to clinical significance and number of symptoms. However, in primary care or the general population, the question of clinical significance may be raised more often (87, 89). It has been suggested that the current 'checklist' diagnosis of major depression may result in over-diagnosis in these contexts (86, 324). This criticism unites scholars aiming to define depression as a disease of the brain (325, 326) with scholars arguing that sadness need not be a pathological condition (56, 324). This is thus a debate on diagnostic validity. However, suggested markers of clinical significance, such as functional impairment, help-seeking, level of distress and recurrence, all have inherent problems (326). Studies using recurrence as a marker of a 'real' depressive disease (324) may be misleading if the follow-up time is too short (327). It has also been argued that an explicit requirement of clinical significance is redundant, because depressive symptoms, at least those that qualify for a diagnosis major depression, can be thought to be intrinsically distressing, irrespective of functioning in everyday life (328).

In parallel to the debate of over-diagnosis of major depression, there seems to be agreement on that depression not fulfilling diagnostic criteria for major depression may have clinical significance, especially in older people (18), which suggests that these diagnostic criteria miss clinically significant depression so that depression is under-diagnosed. Such depression may be called minor, subsyndromal, subthreshold (89) or clinically relevant non-major depression (329). In the present text, 'subthreshold depression' will be used to denote this category. Minor depression will be used only when referring to the diagnosis introduced in text revision of *DSM-IV* as a diagnosis for further study (330). This research diagnosis differs from major depression only in that two, instead of five, depressive symptoms are needed to be present. Other suggested definitions of subthreshold depression require the presence of three symptoms (329, 331). In epidemiological studies, subthreshold depression has also been defined on the basis of scores on a symptom scale (332, 333). Other forms of non-major depression include recurrent brief depression and persistent depressive disorder (dysthymia), which differ from major depression also in duration (101). These states will not be reviewed here.

To further confuse the terminology, the concept of subsyndromal depression, discussed in Section 1.5.6, may also refer to depressive symptoms that do not fulfil the criteria for *any* specified depressive disorder mentioned above.

Thus, depressive episodes may vary with respect to type of symptoms, number of symptoms, symptom severity, duration, and functional impairment. There are several suggested categorical entities of subthreshold depression and all these conditions may fall under the label of the *depressive spectrum* (also called continuum) (331, 334). This concept can be used to capture how manifestations of

depression differ *between* individuals at a given time and to describe how manifestations of depression differ *within* the same individual followed over time.

### 1.5.3 The prevalence of depression

A meta-analysis of cross-sectional population studies of major depression in older people estimated the 'current' prevalence to 3.3% (335). Among studies of 'current' subthreshold depression in older people, systematic reviews and meta-analyses suggest a median prevalence of 10-20% (18, 335, 336), making it several times more common than major depression. Most studies of subthreshold depression do not formally apply the diagnostic criterion for clinical significance, but at least one study in a younger population indicated that this may reduce the prevalence (337).

Given that major depression is an episodic condition, the life-time prevalence may be substantially higher than the 'current prevalence'. Studies relying on retrospective recall of previous episodes of major depression find a life-time prevalence of 9-27% in older people (9, 263, 338). However, this is likely to be an underestimation since individuals may forget or not fully recall all the information about a previous episode that is necessary to establish a diagnosis (24). A direct comparison of retrospectively and prospectively collected data on the prevalence of major depression between ages 18-32 years found that the cumulative prevalence was just below 20% in the retrospective studies, but about 40% in the longitudinal study (25). A study of individuals followed from 20-50 years found a cumulative prevalence of 32.5% for major depression (261). A study of individuals followed from 70-85 years using several sources of information, but that could not in all cases ascertain a diagnosis of major depression, found a life-time prevalence of 35.6% (339). Since none of these prospective studies has covered the whole life-span, so that they either cannot ascertain previous episodes or do not cover all the time at risk, extrapolation of these data may suggest that most people will have a major depressive episode in their life (340).

### 1.5.4 Epidemiological studies of subthreshold depression

In a landmark paper from the The Medical Outcomes Study, conducted in the United States in 1986, it was found that patients with subthreshold depression had worse functioning and well-being than non-depressed patients with chronic physical illnesses (341). It has since then been found in several studies of older people (333, 342-344) that clinically significant depression exists beyond major depression, irrespective of whether participants were recruited from a primary care setting or from the general population. Subthreshold depression and major depression have a similar association with mortality (15). Subthreshold depression has further been associated with suicide (345) and stroke (346) in old age.

### **1.5.5 Prospective studies of the course of subthreshold depression**

The prognosis of depression in community samples of older people has been extensively studied (310, 311, 347). However, only few studies both have a follow-up of more than three years and apply diagnostic criteria to ascertain depression (as opposed to a cut-off on a symptom severity scale) (348, 349). Overall, the prognosis of depression in older people in community and primary care settings is considered to be poor; a chronic or recurrent course is found in about half of the cases (347).

Population studies find subthreshold depression to be the strongest and most important predictor for future major depression in older people (350-354). This could be due to that subthreshold depression in many cases is a snapshot of the course of a long-term depressive illness. In line with this hypothesis of a depressive spectrum, major depression in old age may develop over several years (355).

### **1.5.6 Subsyndromal depressive symptoms**

This condition was originally defined as the presence of at least two depressive symptoms at the 'disorder level' of severity, which not meet diagnostic criteria for major or minor depression (356). This definition precludes the presence of sad mood and diminished interest, since this would give a diagnosis of minor depression. One presentation could be the combination of fatigue and sleep disturbance. Other definitions have been suggested, such as having several symptoms below the threshold for what diagnostic criteria define as a symptom (i. e. sadness less than 'all or most of the time' or a minor sleep disturbance) (357). In any case, having this condition is unlikely to be enough to become a case of subthreshold depression according to most definitions. However, in line with the hypothesis of a depressive spectrum, older primary care patients with subsyndromal depression have been shown to differ from those with no depression with respect to functional impairment, mental health correlates and risk of developing major depression (357, 358). The authors of a qualitative study concluded that these symptoms may also be related to the process of ageing rather than being a manifestation of depression (359).

### **1.5.7 Subthreshold depression as a target for intervention**

According to models based on epidemiological data, even in the unlikely scenario of optimal treatment coverage of major depression, 40% of its burden on the population will not be averted with current evidence-based treatments (360). For this reason, preventive strategies may be needed to reduce the burden of depression on the individual and on society (361).

One preventive strategy is to target symptomatic risk groups, i.e. individuals who already have some symptoms of a disorder (subthreshold depression in this case). However, even a highly effective intervention in such risk groups may be of little public health significance if most new episodes of major depression occur in individuals without preceding subthreshold depression. In this case, preventive interventions targeting the whole population may be better. Thus, to evaluate subthreshold depression as a target for preventive interventions, not only the relative risk for major depression is of interest, but also the absolute proportion of all future cases with major depression that can be found in this group (362). Previous research specifically addressing this question has only been carried out in one population study of older people (354, 363) but supports the notion of preventive measures targeting symptomatic risk groups. Some randomized clinical trials of psychosocial interventions demonstrated the efficacy of such interventions at the individual level (364, 365), but further epidemiological studies are needed to assess their potential public health benefits (361).

## 2 AIM

The overall aim of this thesis was to study the prevalence and course of different psychiatric symptoms and disorders in older people with special reference to diagnostic thresholds, course and qualitative evaluation of symptoms.

### **Study I**

The aim of this study was to examine the prevalence of psychotic symptoms, paranoid ideation and illusions in a population sample of 70-year old men and 70-82 year old women without dementia.

### **Study II**

The aim of this study was to explore the epidemiology of specific phobia and subthreshold phobic fears in a population sample of 70-year old women and men without dementia.

### **Study III**

The aim of this study was to examine the course of specific phobia and subthreshold phobic fears in a population sample of 70-year old individuals without dementia who were followed-up at age 75 and 79 years.

### **Study IV**

The aim of this study was to explore the epidemiology of the depressive spectrum from a longitudinal perspective in population sample of 70-year old men and women without dementia who were followed for five to nine years.

## 3 METHODS

### 3.1 Samples

Study I-IV all include samples derived from the Prospective Population Study of Women (PPSW) and from the H70 Birth Cohort Study in Gothenburg, Sweden (366-369). The PPSW is a longitudinal study of women born in 1908, 1914, 1918, 1922 and 1930. It started in 1968, with follow-ups in 1974, 1980, 1992, 2000, 2005 and 2009. The H70 studies have repeatedly studied new cohorts of 70-year-olds since 1971. In 2000, PPSW and H70 merged to become one study, with the recruitment of a new 70-year-old cohort born in 1930. Studies I-IV are based on data collected in 2000-2001 and forward. The sample is systematically selected from the Swedish Population Register based on birth date, and includes both persons living in private households and in institutions.

Participants were initially contacted by mail, followed by a telephone call. The study was conducted at geriatric and psychogeriatric outpatient clinics. Those who declined to visit the clinic were offered home visits, including those who in-between study follow-ups had moved from Gothenburg to other places in Sweden.

#### 3.1.1 Study I

The study used data collected in 2000-2001. In total, 1481 individuals born in 1918, 1922 and 1930 and living in Sweden on 1 September 2000 according to the Swedish population register were selected.<sup>13</sup> Thirty-six died before they could be examined, six could not speak Swedish and 20 had emigrated outside Sweden, leaving an effective sample of 1419. Among these, 967 individuals (171 women born in 1918, 216 women born in 1922 and 351 women and 229 men born in 1930) accepted to participate in the psychiatric examination (response rate 68.1%).

Among men, non-participants were more likely than participants to have been discharged from hospital with a main psychiatric diagnosis (13.6% vs. 6.1%,  $p<0.05$ ) or stroke (13.6% vs. 3.5%,  $p<0.001$ ) according to the Swedish Hospital Discharge Register. They were also more likely to die before January 2005 (16.4% vs. 6.1%,  $p<0.001$ ). Among women, no differences were observed regarding psychiatric hospitalization or stroke but non-participants were less likely to survive January 2005 (14.4% vs. 9.8%,  $p<0.05$ ). In the present study, all individuals with a diagnosis of dementia were excluded from analysis ( $N=73$ ), resulting in an effective sample of 894 individuals, of whom 564 were aged 70 years (229 men and

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<sup>13</sup> Women born in 1908 and 1914 were not included in Study I because of low sample size ( $N=52$ ).



351 women), 194 were aged 78 years and 136 were 82 years. A key informant interview could be conducted in 665 (74.4%) of these individuals.

### 3.1.2 Study II, III and IV

A flow-chart of these studies is provided in Figure 1, page 47.

#### Baseline sample

Study II, III and IV include men and women born in 1930 who participated in a baseline examination at age 70 years. In 2000, 896 individuals born on pre-specified dates in 1930 and living in Sweden on September 1 according to the Swedish Population Register were selected to a cohort of 70-year olds. Of these, five persons could not be found, 13 died before they could be examined, 18 could not speak Swedish and 15 had emigrated outside Sweden, leaving an effective sample of 845 individuals. Among them, 579 (350 women and 229 men) accepted participation in a psychiatric examination (response rate 68.5 %). The response-rate was higher in women than in men (72.2% vs. 63.6%,  $p=0.008$ ). Non-participants were more likely to die before age 75 both among men (18.3% vs. 6.1%,  $p<0.001$ ) and among women (6.7% vs. 2.0%,  $p=0.01$ ). Among men, non-participants tended to be more likely to have received in-patient care in the year preceding the interview (30.5% vs. 22.7%,  $p=0.10$ ) and to have a main or additional psychiatric diagnosis in the Swedish Hospital Discharge Register (23.7% vs. 16.2%,  $p=0.080$ ). Female non-participants and participants did not differ with respect to these factors (29.0 vs. 28.2%,  $p=0.78$  and 25.1% vs. 25.0%,  $p=0.97$ ).

Individuals diagnosed with dementia at age 70 years ( $N=16$ ) were excluded from the present study, leaving 563 participants for the baseline examination.

#### Study II

Among the 563 participants without dementia, 5 had missing data on items used to diagnose specific phobia and 558 participants could be included in Study II.

#### Study III

Follow-up examinations were performed in 2005-2006 (at age 75 years) and 2009-2010 (at age 79 years). Of the 558 individuals participating in Study II, 90 died before the follow-up examination at age 79 years. The mortality rate was higher among men than among women (22.3% vs. 12.0%,  $p=0.001$ ). Of the 468 surviving individuals, 327 (69.9%) participated at follow-up examinations at both age 75 and 79 years. Among survivors, there was a tendency for a lower participation rate among men compared to women (65.5% vs. 72.4%,  $p=0.11$ ). After age 79, non-participants had a higher 3-year mortality rate among men (23.3% vs. 10.5%,  $p=0.024$ ), but not among women (6.6% vs. 3.7%,  $p=0.42$ ). Individuals with incident dementia ( $N=21$ ) or missing data on fear items ( $N=3$ ) were excluded

from analysis, leaving 303 persons (197 women and 106 men) for inclusion in Study III.

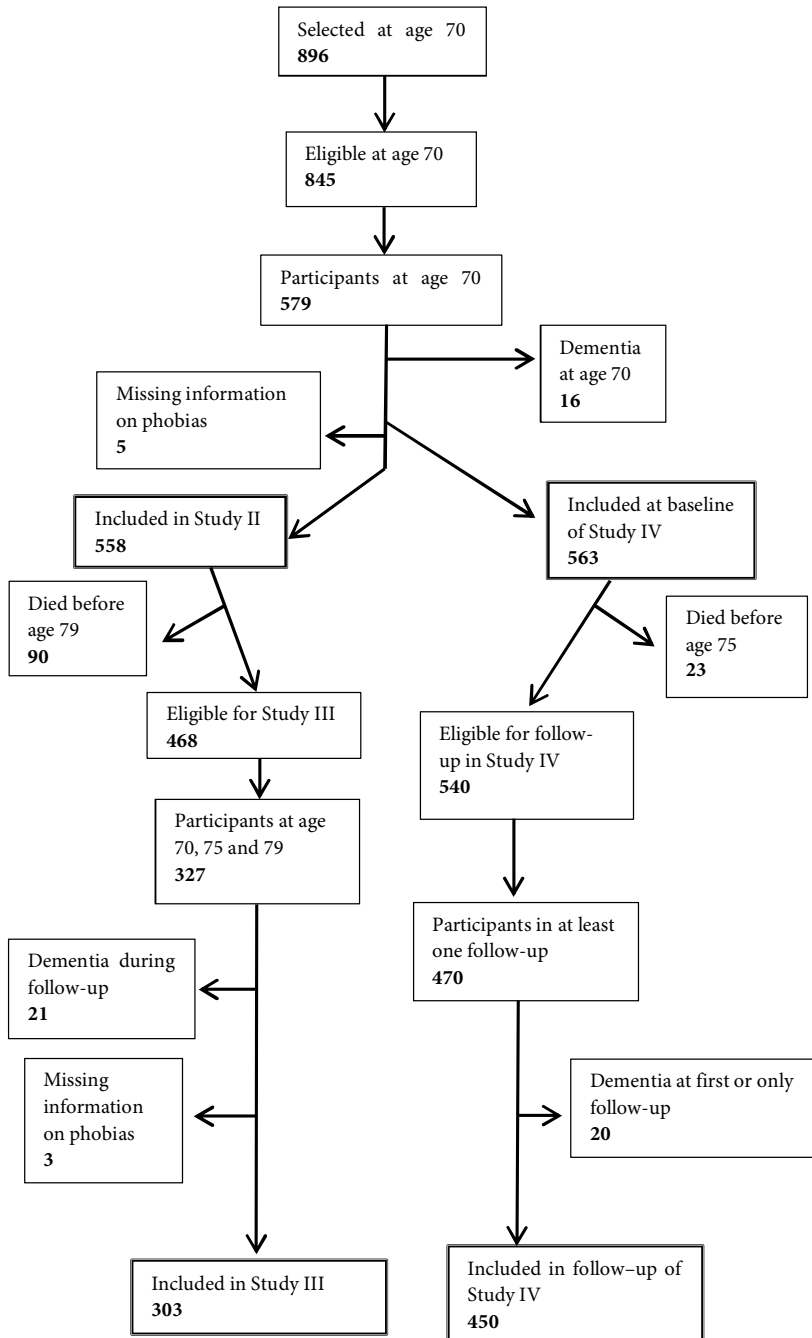
#### **Study IV**

At baseline, the study included the whole sample of 563 70-year-old participants as described above. Follow-up examinations were performed at age 75 and 79 years. Baseline participants refusing participation at age 75 were invited again at age 79 years.

Among baseline participants, 23 (12.6%) died before the first follow-up at age 75 years, leaving 540 individuals eligible for follow-up. Of these, 470 (87.0%) participated in at least one follow-up examination at age 75 or 79 years. The follow-up participation rate did not differ between men and women (86.5% vs. 87.3%,  $p=0.79$ ). Information on mortality was obtained from the Swedish Population Register up to March, 2013. Between age 75 and this date, individuals who did not participate at follow-up tended to have a higher mortality among men (19.4% vs. 11.0%,  $p=0.11$ ) and among women (24.6% vs. 10.0%,  $p=0.002$ ).

Twenty individuals received a diagnosis of dementia at follow-up examinations and were excluded, leaving 450 individuals for inclusion in Study IV. Of these, 307 (68.2%) were followed-up at both age 75 and 79 years, 113 (25.1%) at age 75 years only and 30 (6.7%) at age 79 years only, giving a mean follow-up time of 8.0 years and a mean number of follow-ups of 1.7.

Figure 1. Description of the sample of Studies II, III and IV



## 3.2 Assessments and diagnostic procedures

### 3.2.1 Psychiatric interview

A psychiatric interview was completed by all participants at all time-points. It was performed by psychiatric research nurses who were continuously supervised by a psychiatrist. Interviewers assessed symptoms during the past month and signs during the interview. The interview was mainly based on the Swedish version of the Comprehensive Psychopathological Rating Scale (*CPRS*) (370), but also included some questions from the Mini International Neuropsychiatric Interview (*MINI*) (371) and the Yale-Brown Obsessive Compulsive Scale (*Y-BOCS*) (372).

The *CPRS* has a semi-structured design, allowing for clarifying questions. The instrument may be used by any health professional with experience in psychiatric interviewing. It was originally constructed to be sensitive to change with the goal to use it in the evaluation of treatments. Every item is rated on a scale from 0-6.<sup>14</sup> Ratings 2-6 indicate clear presence of symptoms, which does not necessarily signal abnormality. Ratings 4-5 indicate a symptom or sign that is always or almost always pathological and a rating of 6 indicates a very severe symptom or sign. The interviewer is guided by short descriptions of symptoms and signs covered by each item as well as descriptions of what features of these that corresponds to a specific rating. The Swedish and English versions of *CPRS* were made simultaneously to reach as high agreement between them as possible.

The *CPRS* has been shown to have good inter-reliability in older psychiatric inpatients (373). Inter-rater-reliability in the present study is further reported in paragraph 3.2.4 and 3.2.5. *MINI-D* was used only to diagnose social anxiety disorder and panic attacks. The interview did not include all questions necessary to diagnose panic disorder, agoraphobia and post-traumatic stress disorder. The *Y-BOCS* was part of the diagnosis of obsessive-compulsive disorder. Global functional impairment due to mental health problems was assessed by the interviewer using the *DSM-IV* Global Assessment of Functioning scale (*GAF*) (99).

The assessment of cognitive function included items from the Alzheimer's Disease Assessment Scale-Cognitive (*ADAS-Cog*) (374), including tests of short-term memory, aphasia, apraxia, agnosia, orientation and abstract thinking (comprehension of proverbs). Global cognitive function was also assessed with the Mini-Mental State Examination (375). Based on all gathered information and observations, interviewers also made a global rating of participants' long- and short term memory.

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<sup>14</sup> In the original version, the rating was 0-3 but recommended the use of half-steps. More recent versions include these in the scale, extending the rating to 0-6, translating 1 to 2, 2 to 4 and 3 to 6.

### 3.2.2 Key informant interview

After completion of the psychiatric examination, participants were asked for permission to contact a key informant. Semi-structured key informant interviews were conducted by telephone and included questions about behaviour and intellectual function (personality, memory, orientation, language, activities of daily living and psychiatric symptoms), as well as questions about the participant's medical history and environmental exposures.

### 3.2.3 Assessment of psychotic symptoms

The *CPRS* includes 11 items for assessing psychotic symptoms during the past month and one item for signs observed during the interview (Table 6, page 50). The key informant interview included questions about suspiciousness, delusions, hallucinations and paranoid personality traits. Answers to questions on these items were rated on the basis of how often such symptoms appeared. Key informants were also asked about symptom onset, course, duration, insight and likely causes (for example delirium or ongoing medication). In both interviews, interviewers were encouraged to make side notes concerning the symptoms.

The psychiatric interview recorded symptoms during the preceding month and information from the key-informant interview was based on symptoms present any time during an individual's 70th, 78th or 82nd year. Thus, the prevalence period for Study I was one year.

Presence of psychotic symptoms, i.e. delusions and hallucinations, was determined as follows: First, all individuals with any positive rating on items pertaining to possible psychosis in the *CPRS* and the key informant interview (Table 6) were selected. Second, side-notes from interviewers were collected and reviewed by the author of this thesis and an experienced geriatric psychiatrist. Based on this information, psychotic symptoms were judged to be present or absent according to the definitions of delusions and hallucinations in the *DSM-IV Glossary of Technical Terms* (99). Delusions were classified as persecutory or other. Hallucinations were classified as auditory, visual or other.

Transient hallucinatory experiences (such as hearing or seeing one's deceased spouse), sleep-related hallucinations or misinterpretation of perceptions were classified as illusions based on notes from the psychiatric examination and the key informant interview. Beliefs involving persecution, harassment or unfair treatment that did not reach delusional proportions were classified as paranoid ideation.

If one information source indicated paranoid ideation and the other indicated persecutory delusions, the individual was classified as having persecutory delusions in the final classification. Side notes from the interviewers and information from the key informant interviews were used to aid identification of

any of the following etiological factors: ongoing medication, substance abuse, an acute medical condition, an episode of delirium or terminal illness. These cases were not included when the prevalence was calculated.

*Table 6. Items used to assess psychotic symptoms*

<i>CPRS items</i>	<i>Key informant interview items</i>
Ideas of grandeur	Accusing others
Ideas of persecution	Suspiciousness
Morbid jealousy	Paranoid personality traits
Delusional mood	Delusions
Feeling controlled	Hallucinations
Disrupted thoughts	Auditory
Other delusions	Visual
Commenting voices	Tactile
Other auditory hallucinations	Olfactory
Visual hallucinations	Gustatory
Other hallucinations	
Hallucinatory behaviour	

CPRS items are rated from 0-6.

Key informant interview items are rated 'never, very occasionally, in periods, happened before but not now, sometimes, often, always, don't know'

### 3.2.4 Assessment of specific fears and diagnosis of specific phobia

During the psychiatric examination, participants were asked if there were any situations or objects for which they perceived irrational dread or anxiety, and were given a list of examples. Responses were rated by the interviewer from 0 ('no fear') to 6 ('incapacitating fear'). Ratings 2-3 (vague discomfort mastered without help or by simple precautions) were labelled 'mild-moderate fears' and ratings 4 (certain situations consistently provoke marked discomfort and are avoided) to 6 (incapacitating fear which severely restricts activities) were labelled 'fears with prominent anxiety'.<sup>15</sup> Interviewers were instructed to rate social and agoraphobic fears elsewhere. Inter-rater reliability was assessed among individuals who had dual ratings by psychiatric research nurses and psychiatrists. Inter-rater agreement for the rating of a fear as not present, mild-moderate or with prominent anxiety was good, with Cohen's  $\kappa=0.85$  (142 comparisons).

Social or other consequences of fears were rated as none, some (such as being unable to use an elevator or travel by airplane) or severe (incapacitating). The inter-rater reliability for this item among individuals with any specific fear was  $\kappa=0.75$  (35 comparisons).

A diagnosis of specific phobia according to the *DSM-IV* (330) was made when the fear was associated with prominent anxiety and avoidance behaviour (rating 4-6) and had at least some social or other consequences. Fears with a rating of 2-3 and/or without social or other consequences were labelled subthreshold fears. The category 'any specific fear' includes both those with specific phobia and those with subthreshold fears.

Figure 2. Classification of fears

		Fear intensity	
		Mild-moderate	Prominent anxiety
Social or other consequences	No	Subthreshold fear	Subthreshold fear
	Yes	Subthreshold fear	Specific phobia

<sup>15</sup> The terminology unfortunately differs somewhat between the manuscripts of Study II and Study III. The terminology here follows that of Study III. In Study II, fears were labelled 'phobic fears', subthreshold fears were labelled 'non-diagnostic fears', 'any specific fear' was labelled Fear and fears with prominent anxiety were labelled 'strong fears.'

Fears were categorized into five sub-types as described in the *DSM-IV*: animals, natural environment, specific situations, blood-injection-injury and 'other'. The inter-rater reliabilities for these categorizations were  $\kappa=0.89$  for animals (59 comparisons),  $\kappa=0.93$  for natural environment (60 comparisons),  $\kappa=1.00$  (59 comparisons) for blood-injection-injury,  $\kappa=0.92$  (62 comparisons) for specific situations and  $\kappa=0.73$  (60 comparisons) for other types of fear. Finally, individuals were asked for the age at onset of their fear.

The construction of the interview generated some loss of information. First, in participants with multiple sub-types of fear, it was not ascertained which of these that met the diagnostic criteria for specific phobia. Therefore, the prevalence of specific phobia subtypes cannot be reported. Second, age of onset could only be determined for the fear that had the earliest age at onset.

### **3.2.5 Assessment and diagnosis of depression**

Diagnoses of depression were made with items from the *CPRS* (Table 7). First, symptoms from each of the nine symptom domains listed in the *DSM-IV* were defined as present or absent using expert opinion-based cut-offs for relevant items. Then, algorithms were used to define three different depressive spectrum categories: Major depression, minor depression and subsyndromal depressive symptoms. Major depression and minor depression according to proposed research criteria were diagnosed according to the text revision of the *DSM-IV* (330). Subsyndromal depressive symptoms was defined according to Judd et al (356). Depressive disorder denotes individuals with either major or minor depression.<sup>16</sup> If there was missing data on any symptom or sign used to diagnose depression, the symptom was treated as not present. At age 70, presence of the symptom(s) with missing data could potentially have shifted two participants into a worse depressive spectrum category. At ages 75 and 79, this could have occurred in 16 and two participants, respectively.

Depression severity was assessed with the Montgomery-Åsberg Depression Rating Scale (*MADRS*) (376), a sub-scale of the *CPRS*.

Dual ratings by psychiatric research nurses and psychiatrists were conducted in 50 individuals to assess inter-rater reliability for the items used to diagnose depression, which varied between  $\kappa=0.62$  and  $\kappa=1.00$ .

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<sup>16</sup> In Studies II and III, depression means major or minor depression.



Table 7. Definition of depressive symptoms and depressive disorders

	Symptom domain	CPRS Items (Required rating)
1.	Depressed mood	Sadness (2-6), <i>Apparent sadness</i> (4-6)
2.	Diminished interest	Inability to feel (2-6)
3.	Appetite disturbance/Weight change	Decreased appetite (2-6), Increased appetite* (4-6)
4.	Sleep disturbance	Reduced sleep (3-6), Increased sleep (4-6)
5.	Psychomotor disturbance	<i>Agitation</i> (3-6), <i>slowness of movement</i> (3-6), <i>reduced speech</i> (2-6)
6.	Fatigue/energy loss	Fatiguability (3-6), lassitude (3-6)
7.	Worthlessness/guilt	Pessimistic thoughts (3-6)
8.	Inability to think	Concentration difficulties (4-6), indecision (3-6), <i>distractability</i> (4-6), <i>inability to think or concentrate*</i> (4-6)
9.	Thoughts of death or suicidal ideation	Suicidal thoughts (2-6)

Items written in *italics* are observed, others are reported

\*Item is not originally part of CPRS

Major depression: At least five of symptoms 1-9, of which at least one must be 1 or 2

Minor depression: At least two of symptoms 1-9, of which at least one must be 1 or 2

Depressive disorder: Major or minor depressive disorder

Subsyndromal depressive symptoms: At least two of symptoms 3-9, but neither symptom 1 nor 2.

### 3.2.6 Diagnosis of other anxiety disorders

Social anxiety disorder, panic attacks, obsessive compulsive disorder (*OCD*) and generalized anxiety disorder (*GAD*) were diagnosed according to the *DSM-IV-TR* (330). Items from the *CPRS*, the *MINI* and the *Y-BOCS* were combined to follow diagnostic criteria as closely as possible. These diagnostic procedures have been described in detail elsewhere (197, 377, 378). In Study II, other anxiety disorders denote social anxiety disorder, *OCD* and panic attacks. *GAD* was added in Study III.

### 3.2.7 Diagnosis of dementia

A diagnosis of dementia was made according to the *DSM-III-R* (379) and was an exclusion criterion for all the studies presented in this thesis. The diagnosis was made by consensus between psychiatrists on the basis of information from the psychiatric examination and the key informant interview (380).

### 3.2.8 Other variables

The following other variables were used in Study IV: the psychiatric interview included an open question about past year's mental health problems and treatment. Answers were rated by the interviewer. In the present study, ratings were divided into 'no problem disclosed', 'problems but no treatment', and 'treatment received'. The interview also included a question about previous episodes of depression, rated by the interviewer as 'yes' or 'no'. Information on previous inpatient care with a psychiatric discharge diagnosis (main or additional) was retrieved from the Swedish Hospital Discharge Register (381). Life-time history of suicidal feelings and suicide attempts were assessed according to Paykel et al. (382). Self-reported psychotropic drug use at the time of examination was categorized according to the Anatomic Therapeutic Chemical Classification System (383).

## 3.3 Statistical analysis

Data analyses were made in SPSS versions 15 to 22 (IBM corp., Armonk, NY, USA). In all studies, differences in proportions were tested with a Pearson Chi-square test or a Fisher's exact test, unless not otherwise indicated. All tests were two-tailed and results were considered significant when  $p < 0.05$ , or the 95% confidence interval did not include 1.

### Study II

Binary logistic regression analyses were used to estimate strength of associations, which were expressed as odds ratios. In an attempt to sort out the association between specific phobia in itself and *GAF* score, we first used the Mann-Whitney U-test to test if specific phobia was associated with a lower *GAF* score in those with or without other mental disorders. However, when the *GAF* score is treated as a continuous variable, statistically significant, but clinically less significant, differences may emerge. To achieve a more meaningful description of *GAF*-scores, it was further divided into four classes ( $\leq 60$ , 61-70, 71-80 and 81-100, lower is worse). Diagnoses were then hierarchically ordered into four mutually exclusive groups: (i) those with no diagnosis, (ii) those with 'pure' specific phobia, (iii) those with any other anxiety disorder, without depression and with or without specific phobia and (iv) those with depression, irrespective of comorbidity. The proportional odds model, a form of ordinal logistic regression analysis (384), was used to measure the strength of the association between mental disorders on *GAF* score. This analysis gives a summarizing odds ratio for a shift in the distribution between the classes of the *GAF* scale, when comparing each diagnostic category with those with no diagnosis.

**Study III**

Binary logistic regression analyses with repeated measurements (generalized estimating equations, *GEE*), with a robust estimator of the covariance matrix, were used to analyze the effect of ageing on the prevalence of specific phobia and fears. *GEE* takes the statistical dependence of data from repeated measurements of the same individual into account (385). Ageing from age 70 to age 79 was operationalized as a continuous variable from 0-9. *GEE* was also used to analyze the effects of factors that could possibly predict persistence of specific fears at follow-up among those with such fears at age 70.

**Study IV**

The depressive spectrum was entered as an ordinal scale variable, assuming that its categories can be ordered and that the difference is the same between each step on the scale. The Mantel-Haenszel Chi-square test (386) was used to test for trends in the distribution of categorical variables across the depressive spectrum. Differences between depressive spectrum categories in continuous variables were tested with a Kruskal-Wallis one-way ANOVA (Analysis of variance) (386). The effect of age on the prevalence of depressive spectrum categories was examined with logistic regression models for repeated measurements using *GEE* as described above, but age was instead treated as a factor (age 70=0, age 75=1, age 79=2).

In longitudinal analyses, we assigned one outcome to each participant. Individuals with two follow-up assessments were assigned their worst depressive spectrum category during follow-up. Prospective course denotes for example the proportion of those with minor depression at baseline who have major depression at follow-up. Retrospective course denotes for example the proportion of those with major depression at follow-up who had no depression at baseline. Strength of associations were expressed as odds ratios, derived firstly from the proportional odds model, which gave a summarizing odds ratio for a shift in the distribution on the dependent variable (0=no depression, 1=subsyndromal depressive symptoms, 2=minor depression, 3=major depression) when comparing each depressive spectrum category with the category 'no depression'. This analysis utilizes all the information in the dependent variable, but the resulting odds ratio is somewhat difficult to interpret. It further assumes that the difference is the same between each step on the dependent variable (the proportional odds assumption). This analysis was complemented by binary logistic regressions, which give a more straightforward result and helps to evaluate whether the proportional odds assumption is justified. Different estimates in ordinal and binary analyses may indicate violation of the proportional odds assumption.

These analyses were used to assess strength of associations between depressive spectrum categories both prospectively and retrospectively. Because of a low

number of individuals with major depression at age 70, major and minor depression at age 70 were combined into one group in the retrospective analysis.

### **3.3.1 Ethical considerations**

All participants provided written and informed consent for the studies. For those who could not do this because of cognitive impairment, this was done by their next of kin. The population studies as a whole were approved by the Regional Ethical Review Board in Gothenburg. The present studies only utilized data collected under this ethical permission.

## 4 RESULTS

### 4.1 Results of Study I

#### Prevalence of psychotic symptoms

Table 8 presents the prevalence of various ratings of items possibly assessing psychotic symptoms. In total, 177 (19.8%) of the participants had some rating that could indicate psychotic symptoms and the records of their psychiatric and key informant interviews were further reviewed.

*Table 8. Prevalence of interviewer ratings possibly indicating psychotic symptoms*

	Psychiatric interview (N=894) N (%)	Key informant interview (N=665) N (%)	Both sources (N=894) N (%)
Any CPRS item rated above 0	119 (13.3)		
Rating 1	76 (8.5)		
Rating 2-3	54 (6.0)		
Rating 4-6	10 (1.1)		
Any positive rating from key informant interview		69 (10.4)	
Rating: rarely-occasionally		51 (7.7)	
Rating: sometimes-always		22 (2.5)	
Any possible psychotic symptom			177 (19.8)
Rating 4-6 or sometimes- always			30 (3.4)

% don't add up because one individual may have more than one positive rating

The prevalence of psychotic symptoms in relation to age and sex is presented in Table 9. In total, the prevalence was 1.0% (95% CI 0.5-1.9%). No significant age or gender differences were observed for psychotic symptoms, but among women, paranoid symptoms (persecutory delusions and paranoid ideation) were more common among 70-year olds than 78-82 year-olds.

The exact reason for not classifying experiences as psychotic was not formally stated in all reviewed cases, but most often it was due to unconvincing or vague information, or, based on the key informant interview, because the symptom did not occur within the prevalence period.

Of the nine individuals with psychotic symptoms, five were detected based on the psychiatric interview and four based on the key informant interview (Table 10). There was no case where psychotic symptoms were identified according to both sources.

*Table 9. One-year prevalence of psychotic symptoms in relation to age and sex*

	Women age 70 years (N=340)	Men age 70 years (N=224)	Women and men, age 70 years (N=564)	Women 78-82 years (N=330)
	N (%)	N (%)	N (%)	N (%)
Psychotic symptoms				
Any	3 (0.9)	2 (0.9)	5 (0.9)	4 (1.2)
Hallucinations	0 (0.0)	1 (0.4)	1 (0.2)	3 (0.9)
Delusions	3 (0.9)	1 (0.4)	4 (0.7)	1 (0.3)
Other symptoms				
Paranoid ideation	6 (1.8)	2 (0.9)	8 (1.4)	1 (0.3)
Illusions	4 (1.2)	2 (0.9)	7 (1.2)	6 (1.8)
Paranoid symptoms	9 (2.6)	3 (1.3)	12 (2.1)	2 (0.6)*

Paranoid symptoms: Persecutory delusions or paranoid ideation.

\*p<0.05 compared to 70-year old women (Fisher's exact test).

Reprinted from Sigström et al. *Int J Geriatr Psychiatry* 2009; 24: 1413–1419.

*Table 10. Prevalence of psychotic symptoms according to source of information*

	Psychiatric interview (N=894)	Key informant interview (N=665)	Total (N=894)
	N (%)	N (%)	N (%)
Any psychotic symptom	5 (0.6)	4 (0.6)	9 (1.0)
Any hallucination	2 (0.2)	1 (0.1)	3 (0.3)
Visual	0 (0.0)	0 (0.0)	0 (0.0)
Auditive	1 (0.1)	1 (0.1)	2 (0.2)
Other	1 (0.1)	0 (0.0)	1 (0.1)
Any delusion	3 (0.3)	2 (0.3)	5 (0.6)
Persecutory	3 (0.3)	2 (0.3)	5 (0.6)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Other symptoms			
Paranoid ideation	4 (0.4)	5 (0.6)	9 (1.0)
Illusions	11 (1.2)	2 (0.2)	12 (1.3)*
Paranoid symptoms	7 (0.8)	7 (1.1)	14 (1.6)

\*In one case, illusions were reported from both sources.

Paranoid symptoms: Persecutory delusions or paranoid ideation.

Reprinted from Sigström et al. *Int J Geriatr Psychiatry* 2009; 24: 1413–1419.

### Three examples of psychotic symptoms

One man claimed with conviction that somebody else had divorced him from his wife and complained of persistent harassment from previous workplaces and authorities. He was judged to have persecutory delusions. He refused a key informant interview.

A woman who had symptoms of anxiety and depression and, according to the key informant, 'self-medicated' with considerable amounts of alcohol, complained of distressing choirs and 'church music' at home. These hallucinations were judged to likely be due to substance abuse and were excluded from the prevalence estimate.

One woman lived in a nursing home and had a long history of psychiatric disorder, according to the key informant. It was not considered appropriate to address psychotic symptoms during the interview. According to the key informant, she persistently claimed to be haunted by the evil spirit of a deceased relative. She used to waive her handbag in the air, possibly to chase the spirit away. She was judged to have persecutory delusions but there was not considered to be enough detailed information to judge presence of hallucinations.

## 4.2 Results of Study II

### Prevalence of fears and specific phobia

The majority of participants (57.7%) had any specific fear (Table 11). The prevalence of *DSM-IV* specific phobia was 10.0% (95% CI 7.8-12.8%). Both conditions were more common in women than in men. Fear of animals and the natural environment were most common.

Table 11. Prevalence of phobic fears and specific phobia in 70-year-olds

	Men (N=224)	Women (N=334)	Total (N=558)	% in those with Any specific fear
	N (%)	N (%)	N (%)	
Any specific fear	85 (37.9)	237 (71.0)***	322 (57.7)	-
Mild-moderate fear	72 (32.1)	187 (56.0)***	259 (46.4)	80.4
Mild-moderate fear with consequence	6 (2.7)	19 (5.7)	25 (4.5)	7.8
Fear with prominent anxiety	13 (5.8)	50 (15.0)***	63 (11.3)	19.6
<i>DSM-IV</i> specific phobia	10 (4.5)	46 (13.8)***	56 (10.0)	17.4
Type of fear				
Animals	47 (21.0)	177 (52.9)***	224 (40.1)	69.6
Natural environment	45 (20.1)	164 (49.1)***	209 (37.5)	64.9
Specific situations	31 (13.8)	92 (27.5)***	123 (22.0)	38.2
Blood-injection injury	7 (3.1)	37 (11.1)**	44 (7.9)	13.7
Other	7 (3.1)	27 (8.1)*	34 (6.1)	10.6

Fisher's exact test \* $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  compared to men.

Reprinted from Sigström et al. *Journal of Anxiety Disorders* 25 (2011) 148–153.

**Relation between specific phobia, subthreshold fears and other mental disorders**

When compared to individuals with no specific fears, those with specific phobia were more likely to have other anxiety disorders, especially obsessive compulsive disorder and social phobia (Table 12). In total, 35.7% of those with specific phobia had a comorbid disorder. However, having subthreshold fears was not associated to any mental disorder.

Among those with any specific fear, having a higher number of types of fear was associated to having specific phobia and other anxiety disorders, but not to depression (Table 13).

*Table 12. Association between other mental disorders and subthreshold fear and specific phobia*

	No fear (N=236)		Subthreshold fear (N=266)		Specific phobia (N=56)	
	N (%)	OR	N (%)	OR (95% CI)	N (%)	OR (95% CI)
OCD (N=18)	4 (1.7)	1.0	4 (1.5)	0.7 (0.2-2.9)	10 (17.9)	8.7 (2.4-30.8)
Panic attacks (N=9)	0 (0.0)	N. E. †	4 (1.5)	N. E.	5 (8.9)	N. E.
Social phobia (N=10)	3 (1.3)	1.0	3 (1.1)	0.8 (0.1-4.1)	4 (7.1)	7.1 (1.3-39.2)
Depression (N=48)	14 (5.9)	1.0	22 (8.3)	1.2 (0.6-2.5)	12 (21.4)	3.1 (1.3-7.4)
≥ 1 other diagnosis (N=66)	20 (8.5)	1.0	26 (9.8)	1.0 (0.5-1.9)	20 (35.7)	4.5 (2.1-9.5)
≥ 2 other diagnoses (N=13)	1 (0.4)	1.0	4 (1.5)	2.1 (0.2-18.6)	8 (14.3)	38.9 (4.2-359.0)

% are of columns. OR (Odds ratio): The odds for comorbid mental disorders among those with subthreshold fears or those with specific phobia, compared to those with no fear. Logistic regression analyses, adjusted for gender. N. E.: Not estimable.

Reprinted from Sigström et al. Journal of Anxiety Disorders 25 (2011) 148–153.

*Table 13. Number of types of fear in relation to specific phobia and other mental disorders*

	Number of types of fear					OR	95% CI
	One N (%)	Two N (%)	Three N (%)	Four N (%)	Five N (%)		
All with Fear (N=322)	124 (38.5)	110 (34.2)	65 (20.2)	20 (6.2)	3 (0.7)		
Specific phobia (N=56)	13 (23.2)	15 (26.8)	17 (30.4)	9 (16.1)	2 (3.6)	1.9	1.4-2.6
'Pure' specific phobia (N=36)	10 (27.8)	9 (25.0)	11 (30.6)	5 (13.9)	1 (2.8)	1.6	1.1-2.2
Comorbid specific phobia (N=20)	3 (15.0)	6 (30.0)	6 (30.0)	4 (20.0)	1 (5.0)	2.1	1.4-3.2
Any other anxiety disorder (N=21)	3 (14.3)	8 (38.1)	4 (19.0)	5 (23.8)	1 (4.8)	2.0	1.3-3.1
Depression without anxiety disorder (N=34)	13 (38.2)	9 (26.5)	6 (17.6)	4 (11.8)	2 (5.9)	1.3	0.9-1.9

% are of rows. OR: The odds ratio for having the condition per every additional number of fear types. Logistic regression adjusted for gender.

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Table 14 shows the relation between mental disorders and the five subtypes of fear. Fear of specific situations was strongly related to all anxiety disorders. Also the ‘other’ fear type was strongly related to all anxiety disorders, and more so to other anxiety disorders than to specific phobia.

*Table 14. Association between types of specific fears and mental disorders*

	Type of fear				
	Animals	Natural environment	Specific situations	Blood-injection-injury	Other
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Specific phobia	1.1 (0.6-2.2)	1.5 (0.8-2.9)	4.1 (2.2-7.5)	1.2 (0.5-2.7)	3.0 (1.4-6.4)
OCD	1.0 (0.3-3.2)	3.1 (0.7-14.4)	4.3 (1.3-14.0)	1.0 (0.2-4.5)	7.2 (2.3-22.6)
Social phobia	0.5 (0.1-2.3)	0.6 (0.1-3.0)	10.1 (1.2-84.7)	N.E.	6.6 (1.4-31.2)
Panic attacks	0.7 (0.2-3.1)	1.0 (0.2-4.0)	5.9 (1.2-28.9)	N.E.	11.8 (3.0-46.7)
Depression	0.7 (0.3-1.5)	1.3 (0.6-2.7)	1.9 (1.0-4.0)	1.0 (0.4-2.9)	1.9 (0.7-5.1)

Those with specific phobia are excluded from the other disorders in these analyses.

OR: Odds for disorder in those with fear type compared to odds for disorder in those without the fear type. Logistic regression, adjusted for sex.

N. E.: Not estimable because of cells with zero.

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### **Global functioning in specific phobia compared to other mental disorders**

In analyses of global functioning, individuals with specific phobia were separated into those having comorbid mental disorders and those having ‘pure’ specific phobia. Those with ‘pure’ specific phobia had a lower GAF score than individuals with no diagnosis (median 85 vs. median 95,  $p < 0.01$ ), but specific phobia did not influence GAF score in individuals with other mental disorders (median 65 vs. 70,  $p = 0.72$ ). However, comorbidity influenced GAF score in those with specific phobia (median 65 vs. 85,  $p < 0.001$ ).

Table 15 presents an ordinal regression analysis of GAF score in relation to specific phobia and other disorders. Having ‘pure’ specific phobia was associated with lower global functioning, compared to having no diagnosis, but the association was weaker than for other anxiety disorders and for depression.

*Table 15. Specific phobia and other mental disorders in relation to functional impairment*

	GAF score				OR	95% CI
	≤60 N (%)	61-70 N (%)	71-80 N (%)	81 – 100 N (%)		
No diagnosis (N=455)*	14 (3.1)	25 (5.5)	59 (13.0)	357 (78.5)	1.0	
'Pure' specific phobia (N=36)	0 (0.0)	4 (11.1)	13 (36.1)	19 (52.8)	2.5	1.3–5.0
Other anxiety disorder, without depression (N=18)	3 (16.7)	2 (11.1)	4 (22.2)	9 (50.0)	4.0	1.6–9.7
Depression (N=48)	23 (47.9)	9 (18.8)	11 (22.9)	5 (10.4)	26.4	14.1–49.5

% are of rows. Lower GAF score indicates worse functioning.

\*GAF score was missing for one person in this group.

'Pure' specific phobia: Specific phobia without other mental disorder.

OR (Odds ratio): The odds for belonging to a lower class on the GAF scale compared to the odds in those with no diagnosis. Ordinal regression analysis, adjusted for sex.

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### 4.3 Results of Study III

Of 468 surviving and eligible participants of Study II, 303 (197 women and 106 men) participated at follow-up at both age 75 and 79 years. They did not differ from surviving non-participants (N=165) in the prevalence of specific phobia (9.9% vs 10.9%,  $p=0.73$ ) or any specific fear (59.1% vs 61.2%,  $p=0.65$ ) at age 70. Among men, prevalence of specific phobia at age 70 was higher among non-participants at follow-up (8.8% vs. 1.9%,  $p=0.06$ ), but not among women (12.4% vs. 14.2%,  $p=0.67$ ).

From age 70 to age 79, there was a decline in the prevalence of specific phobia (OR per year 0.90, 95% CI 0.85 – 0.96,  $p<0.001$ ) and any specific fears (OR per year 0.92, 95% CI 0.89 – 0.94,  $p<0.001$ ). The prevalence of fears with prominent anxiety declined with age (OR per year 0.91, 95% CI 0.86 – 0.96,  $p=0.001$ ), but not the prevalence of fears that gave social or other consequences (OR per year 0.99, 95% CI 0.95 – 1.03,  $p=0.63$ ).

The course of specific phobia is described in Table 17. A total of 44 participants met diagnostic criteria for specific phobia at least once during the study. Of these, 31.8% (4.6% of the total sample) met diagnostic criteria at least at two out of three examinations. Among individuals with specific phobia at age 70, 40.0% met diagnostic criteria at least once during follow-up and 93.3% had any specific fear at least once during follow-up. The cumulative 9-year incidence of SP during follow-up was 7.4% (N=11) in those with subthreshold fear and 2.4% (N=3) in those with no specific fears (OR 3.2, 95% CI 0.9-11.8).

Table 16. Prevalence of specific phobia and any specific fears in a population examined at age 70, 75 and 79 years (N=303)

	Specific phobia		Any specific fears	
	N	%	N	%
Age 70	30	9.9	179	59.1
Age 75	21	6.9	133	43.9
Age 79	12	4.0	120	39.6
With condition at				
Three examinations	5	1.7	72	23.8
Two examinations	9	3.0	71	23.4
One examination	30	9.9	74	24.4
Any examination	44	14.5	217	71.6

Table 17. Course of specific phobia over nine years

Course in individuals with specific phobia at any time during the study (N=44)						
	At 3 examinations		At 2 examinations		At 1 examination	
	N	%	N	%	N	%
Any specific fears	29	65.9	12	27.3	3	6.8
Specific phobia	5	11.4	9	20.5	30	68.2
Subthreshold fears	-	-	16	36.4	19	43.2
No specific fears	-	-	3	6.8	12	27.3
Condition at follow-up in individuals with specific phobia at age 70 (N=30)						
	At both follow-ups		At 1 follow-up only		At any follow-up	
	N	%	N	%	N	%
Any specific fears	21	70.0	7	23.3	28	93.3
Specific phobia	5	16.7	7	23.3	12	40.0
Subthreshold fears	10	33.3	12	40.0	23	76.7
No specific fears	2	6.7	7	23.3	9	30.0

## 4.4 Results of Study IV

### Prevalence of depressive spectrum categories

As can be seen in Table 18, major depression (MD), minor depression (MIND) and subsyndromal depressive symptoms (SSD) were more prevalent at age 75 and 79 years than at age 70 years. Table 19 shows the prevalence of each depressive spectrum category for the whole study period. About half of this population sample (55.3%) were in some depressive spectrum category (MD, MIND or SSD) at least once and about one fourth (23.6%) were in any of these categories twice.

Table 18. Cross-sectional prevalence of depressive spectrum categories

	Age 70 (N=563)		Age 75 (N=420)		Age 79 (N=337)	
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
Major depression	20	3.6 (2.3-5.4)	22	5.2 (3.5-7.8)	18	5.3 (3.4-8.3)
Minor depression	56	9.9 (7.7-12.7)	64	15.2 (12.1-19.0)	49	14.5 (11.2-18.7)
SSD	46	8.2 (6.2-10.7)	74	17.6 (14.3-21.6)	64	19.0 (15.2-23.5)
Depressive spectrum	122	21.7 (18.5-25.3)	160	38.1 (33.6-42.8)	131	38.9 (33.8-44.2)
No depression	441	78.3 (74.7-81.5)	260	61.9 (57.2-66.4)	206	61.1 (55.8-66.2)

SSD: Subsyndromal depressive symptoms. Depressive spectrum: major or minor depression or SSD.

Table 19. Longitudinal prevalence of depressive spectrum categories among those included at follow-up (N=450)

	Proportion in category at least once		Proportion in category at least twice	
	N	% (95% CI)	N	% (95% CI)
Major depression	42	9.3 (7.0-12.4)	7	1.6 (0.8-3.2)
Minor depression	124	27.6 (23.6-31.9)	26	5.8 (4.0-8.3)
SSD	139	30.9 (26.8-35.3)	33	7.3 (5.3-10.1)
Depressive spectrum	249	55.3 (50.7-59.9)	106	23.6 (19.9-27.7)
No depression	400	88.9 (85.6-91.5)	267	66.0 (54.7-63.8)

% add up to more than 100 because one person can have more than one condition.

SSD: Subsyndromal depressive symptoms. Depressive spectrum: major or minor depression or SSD.

### Prospective course of baseline depressive spectrum categories

Around 70% of those with MD or MIND at baseline had any of these conditions (depressive disorder) also during follow-up (Table 20). One third of those with MIND developed MD. Their odds for this outcome were 13 times higher than for those with no depression at follow-up (Table 21). About half of those with SSD at age 70 had SSD also at follow-up and 36% had depressive disorder (MD or MIND) at follow-up. Their odds for this outcome were about twice as high as the odds for those with no depression.

### Retrospective course of follow-up depressive spectrum categories

As can be seen in Table 22, 36.1% of individuals with major depression at follow-up had no depression at age 70 and 55.6% had depressive disorder. The corresponding figures for minor depression were 69.7% and 19.1%. Table 23 presents the retrospective association between depressive spectrum categories. MD at follow-up was strongly associated with having a more severe depressive condition at age 70, as well as with having had depressive disorder. This association was also present for MIND, but less pronounced. SSD at follow-up had no relation to having had depressive disorder at age 70.

*Table 20. Prospective course of depressive spectrum categories over five to nine years of follow-up*

Baseline category	In same category at follow-up N (%)	Depressive disorder at follow-up N (%)	Major depression at follow-up N (%)
Depressive disorder (N=54)	37 (68.5)	37 (68.5)	20 (37.0)
Major depression (N=12)	6 (50.0)	9 (75.0)	6 (50.0)
Minor depression (N=42)	14 (33.3)	28 (66.7)	14 (33.3)
SSD (N=36)	17 (47.2)	13 (36.1)	3 (8.3)
No depression (N=360)	201 (55.8)	75 (20.8)	13 (3.6)

Depressive disorder: Major or minor depression. SSD: Subsyndromal depressive symptoms.

*Table 21. The association between baseline depressive spectrum category and depression at follow-up*

Baseline depressive spectrum category	Ordinal outcome OR (95% CI)	Binary outcome	
		Depressive disorder OR (95% CI)	Major depression OR (95% CI)
Major depression	18.0 (5.7-57.1)	11.4 (3.0-43.2)	26.7 (7.6-94.1)
Minor depression	7.9 (4.1-15.3)	7.6 (3.8-15.2)	13.3 (5.7-31.1)
SSD	3.1 (1.7-5.6)	2.1 (1.0-4.4)	2.4 (0.7-9.0)
No depression	1.0	1.0	1.0

Ordinal OR:s estimated with ordinal regression analysis, refers to the odds of being in a worse depressive spectrum category at follow-up, as compared to individuals with no depression at baseline

Binary OR:s estimated with logistic regression analysis, with individuals with no depression as the reference group

*Table 22. Retrospective course of follow-up depressive spectrum categories*

Follow-up category	In same category at baseline N (%)	Depressive disorder at baseline N (%)	No depression at baseline N (%)
Depressive disorder (N=125)	37 (29.6)	37 (29.6)	75 (60.0)
Major depression (N=36)	6 (16.7)	20 (55.6)	13 (36.1)
Minor depression (N=89)	14 (15.7)	17 (19.1)	62 (69.7)
SSD (N=106)	17 (16.0)	5 (4.7)	84 (79.2)
No depression (N=219)	201 (91.8)	12 (5.5)	201 (91.8)

*Table 23. Strength of retrospective consistency between follow-up and baseline depressive spectrum category*

Follow-up depressive spectrum category	Ordinal analysis	Depressive disorder
	OR (95% CI)	OR (95% CI)
Major depression	24.5 (13.3-55.5)	21.6 (9.0-51.9)
Minor depression	4.9 (2.5-9.5)	4.1 (1.9-8.9)
SSD	2.7 (1.4-5.2)	0.85 (0.3-2.5)
No depression	1.0	1.0

Ordinal OR:s estimated with ordinal regression analysis, refers to the odds of being in a worse depressive spectrum category at baseline, as compared to individuals with no depression at follow-up

Binary OR:s estimated with logistic regression analysis, with individuals with no depression as the reference group

## 5 DISCUSSION

### 5.1 Strengths and limitations of the studies

#### Strengths

The systematic sampling of participants from the population register made the sample representative of the background population. Use of national population registers also made it possible to perform a relatively comprehensive drop-out analysis. Comprehensive psychiatric assessments of all participants by clinically experienced interviewers using a semi-structured instrument is relatively unusual in epidemiological studies, but may provide data of higher quality than fully structured interviews (35). Furthermore, the follow-up time was long and the rate of follow-up participation was fairly high.

#### Limitations

First, participants had lower rates of mortality and previous psychiatric inpatient care than non-participants. This likely caused some underestimation of psychiatric morbidity. Second, sample sizes were rather small in light of the population-based design, which reduced the statistical power in analyses, especially those involving subgroups with few individual cases. This may have generated several false negative results. Many results are also imprecise and should therefore be interpreted with caution. Although the follow-up time was long, the interval between follow-ups was also relatively long, resulting in rather crude estimates of the course of mental disorders. Further strengths and limitations more specific to each study will be addressed below.

### 5.2 Discussion of Study I

The main finding was that the prevalence of psychotic symptoms was quite low (1%) compared to the estimates given by comparable studies (2.0-13.4%), referred to in Table 1 (page 17).

#### Strengths and limitations

The low prevalence of psychotic symptoms found in this population study could be due to methodological factors, as is discussed in Sections 1.2.1 and 1.3.4.

The strengths of the study include the key informant interview, from which about half of the psychotic symptoms in this study were detected. Furthermore, it also in some cases gave information indicating that symptoms detected during the interview were attributable to for example excess alcohol consumption.

Some limitations should be mentioned. First, individuals with psychotic symptoms may be especially reluctant to participate in population studies, resulting in underestimation of the prevalence. However, this is unlikely to explain the difference between the present study and other studies, which should also suffer from this bias. Second, because of the low number of individuals with psychotic symptoms, it was not possible to examine associations to clinical and sociodemographic variables. Third, reluctance to reveal, and failure to detect, psychotic symptoms may also have contributed to underestimation. This bias should be counteracted using a semi-structured interview that enabled clarifying questions. Furthermore, even if the key informant interview also counteracted this bias, it was not conducted in about 25% of the sample, among which individuals with undetected psychotic symptoms may have been over-represented. Fourth, a major proportion of possible psychotic symptoms were not classified as such because descriptions were unconvincing or not detailed enough. While this probably eliminated 'false positive' symptoms, it may also have resulted in an unknown number of 'false negative' symptoms.

### **Comparison to other studies**

The low prevalence of psychotic symptoms may partly be due to exclusion of symptoms from the prevalence estimate if they were related to substance misuse or a general medical condition, such as delirium. This was not done in some other studies reporting a high prevalence (155, 171). Furthermore, our sample was considerably younger than in other previous studies using the same methods as the present study (22, 169). This means that fewer individuals in the present study would have psychotic symptoms in a prodromal stage of dementia or due to cerebrovascular lesions, both of which are associated to increasing age (154, 387).

Since the present study was also conducted at a later date than many of the previous studies (Table 1), the lower prevalence may also partly be due to a birth cohort effect. Secular changes in determinants of health (388) may have resulted in a lower prevalence of subtle degenerative or vascular brain pathology, which could reduce the prevalence of psychotic symptoms in later born cohorts. This hypothesis can be tested by future studies that can compare different birth cohorts examined at the same age and with the same methods.

## **5.3 Discussion of Studies II and III**

The main findings were that specific phobia was common, especially among women, and could be contrasted to subthreshold fears on the basis of its association to comorbid mental disorders and to two types of fear, the situational and 'other' subtype. The prevalence declined with age and over long term follow-

up, it seemed that most cases of specific phobia were exacerbations of chronic subthreshold fears.

### **Strengths and limitations**

The semi-structured interview, with an open question on phobias, may capture a larger proportion of all phobias than the structured interviews used by most other studies, which only address a limited number of phobias.

Some limitations should be mentioned. First, due to a relatively small sample and the female preponderance among those with specific phobia, the number of men with specific phobia was low and therefore sensitive to drop-out. Second, although our instrument had good inter-rater reliability, the age-related decline in the prevalence of specific phobia could have been influenced by how individuals change their report of its symptoms and their consequences, for example by attributing them to age-related constraints (196). Third, the construction of the interview generated some loss of information. In those with multiple subtypes of fear, type of fear was not documented in relation to age at onset, strength and consequences of fear, so we could not report the prevalence of individual subtypes of specific phobia.

### **The prevalence of specific phobia**

The results of Study II and III indicate that as many as 14% of septuagenarians have specific phobia at some time during the 8<sup>th</sup> decade of life. As may be seen in Table 4 (page 35) and in a recent meta-analysis in which the study was included (335), the herein reported prevalence of specific phobia is high compared to previous studies in older people. A possible explanation is the use of a semi-structured interview, as mentioned above. The prevalence of specific phobia among individuals reporting a fear in the present study was similar to other studies (Table 3, page 34), which may support this explanation of a higher prevalence. No other study has used the same instrument, which makes comparison difficult.

We found that 14% of the population had specific phobia at some point during the nine-year study period. This is similar to the 18% cumulative prevalence in a sample examined four times between ages 18 and 32 years (25) and the 26.9% cumulative prevalence in a sample examined seven times between ages 20 and 50 years (261). However, our nine-year prevalence figure is considerably higher than some recent retrospective estimates of life-time prevalence of SP in older people (6.1-7.5%) (177, 263). Retrospective estimates may not be reliable and failure to recall previous episodes of a disorder may be of special importance in older populations, and for relatively mild conditions, such as specific phobia.



### **Functional impairment**

In the present study, 'pure' specific phobia was related to a somewhat lower global functioning but specific phobia did not influence global functioning in those with comorbid mental disorders. About half of those with 'pure' specific phobia had a GAF-score above 80, which may be interpreted as no relevant global functional impairment. It is possible that our requirement of 'some' social or other consequences of the phobia is too unspecific as a marker for capturing clinical significance. Previous studies have also found a major proportion of those with specific phobia to have a mild disorder (58, 292). This means that many cases will be around the threshold for a diagnosis, and a somewhat lower threshold, as may have been the case in the present study, can give a marked increase in the prevalence of the condition.

A limitation of the present study is that functional impairment was only assessed with the *GAF* scale which, although useful and widely used in psychiatric practice, has been criticized for its tendency to lead the rater to assess symptom severity rather than functional impairment in cases where these may differ (389). The symptoms of specific phobia manifest themselves mostly upon confrontation with the phobic stimulus, and not during the interview, which may lead to that the *GAF* scale does not capture the functional impairment caused by to this disorder.

### **The components of the diagnosis**

In the present study, specific phobia was assessed with two items, one that rated the intensity of the fear in itself, including avoidance behaviour, and one that rated the consequences of the phobia (i.e. functional impairment). The inter-rater reliability was lowest for the item pertaining to social or other consequences of the phobia, which is in agreement with previous inter-rater studies of specific phobia (200, 204). Furthermore, fear intensity and avoidance behaviour, rather than social consequences, seemed to be limiting step for receiving a diagnosis. Almost all fears with prominent anxiety had social or other consequences, but a significant proportion of fears with social or other consequences were without prominent anxiety. The decline in prevalence observed at age 75 and 79 years was fully accounted for by a reduction in the prevalence of fears with prominent anxiety, while the prevalence of fears causing some social or other consequences remained stable. Again, this may point to that our operationalization of clinical significance was unspecific (over-inclusive).

### **The course of specific phobia**

As reviewed in the introduction (Table 5, page 36), population studies challenge the conception of specific phobia as a chronic disorder. Also in this study, specific phobia had a good prognosis in at least 60% of cases at age 70, meaning that they did not meet diagnostic criteria at a five or nine-year follow-up. Less than half of all those diagnosed with specific phobia at some point during the study met the

diagnostic criteria more than once. However, a majority had subthreshold fears at the other examinations, suggesting that these symptoms have a chronic, but fluctuating course.

### **Psychopathological correlates**

The results regarding the relation between specific phobia and fear subtypes and between specific phobia and other mental disorders were in line with studies of younger samples (207, 217, 258). Specific phobia was related to having more subtypes of fear, compared to those with subthreshold fears. Interestingly, the same was found also for other anxiety disorders.

Although the majority of those with specific phobia at age 70 did not have another mental disorder, specific phobia was related to all of the studied disorders, especially other anxiety disorders. Those with subthreshold fears did not have higher rates of any mental disorder compared to those without fears.

Fear of animals and the natural environment were the most common fears, but were not related to a diagnosis of specific phobia or other mental disorders. Instead, fear of specific situations had the strongest relationship with specific phobia. The strength and consequences of a life-long fear of specific situations may increase in old age due to poorer physical health, which may influence perceived control in specific situations (390).

One other study of older people has examined the factors discussed above. It also showed a strong relationship between specific phobia and other anxiety disorders (178). It is otherwise in disagreement with the present study: it found that fear of specific situations was more common than fear of animals and the natural environment, it found no relation between any fear subtype and a diagnosis of specific phobia and it found that most with specific phobia had only one fear.

### **The age-related decline of specific fears and phobias**

The prevalence of both specific phobia and any specific fear declined with time, which confirms findings from cross-sectional studies (10, 258). This decline has been hypothesized to be due to either neurodegeneration or improved emotional regulation with increasing age (264), but we were not able to test any of these hypotheses in the present study.

## **5.4 Discussion of Study IV**

The main findings were that a majority of individuals in the sample were in some degree of depression at least once during the study period, that the prognosis of major and minor depression (MD and MIND) was relatively similar and that only

a minority of those with major depression at follow-up had no symptoms of depression at baseline.

### **Strengths and limitations**

An important strength is that all participants were evaluated for all depressive symptoms. This is not possible in studies using a two-phase design<sup>17</sup> (348, 391) or in studies that assess depressive symptomatology only in participants who endorsed a life-time history of sad mood or diminished interest (349, 351).

The long time interval between follow-ups means that there is a high probability of 'interval' depressive episodes that began and ended in-between examinations. This may have caused underestimation of the number of depressive episodes during follow-up and thus underestimation of the cumulative incidence of depression as well as the number of individuals with a recurrent course. Furthermore, those with no depression at baseline were by far the largest group at risk for MD at follow-up. Interval episodes in even a small proportion of this group could markedly increase the proportion of individuals with MD at follow-up who had no depression at baseline. In such a scenario, MD, MIND and subsyndromal depressive symptoms (SSD) would have less importance as predictors of major depression than our study indicates. However, interval episodes are more likely to be either self-limiting or responsive to treatment than those captured by our examinations.

### **Support for the depressive spectrum hypothesis**

About 70% of those with MD and MIND at baseline were in any of these categories during follow-up, but there was substantial exchange between MD and MIND. Given the long follow-up time, this fluctuation may be better understood as a long-term depressive illness rather than a major depressive episode with prodromal or residual symptoms (392). The prospective course of MD and MIND differed clearly from that in SSD, but the course of SSD also differed from that in those with no depression. SSD was stable in about 50% of baseline cases and only 17% had no depression at follow-up. The risk for future depressive disorder was moderately higher than in individuals with no depression, but it was also markedly lower than in studies of SSD in primary care settings (353, 358). This indicates when the criteria of SSD are applied in the general population, it may to some extent be an expression of an ageing process or of physical illness rather than a state of depression (359). In support of this, we found SSD to be the depressive spectrum category that increased most with age, especially among men.

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<sup>17</sup> Two phase design: the full sample is only screened for mental health problems. Typically, only screen positive and a subsample of screen negative go through a more comprehensive examination (if they don't drop out and are still alive at this second assessment).

When followed back to age 70, a minority of those with MD during follow-up, but a majority of those with MIND and SSD were non-depressed. Many MD episodes could thus be prevented by efficacious interventions in symptomatic risk groups.

Overall, the depressive spectrum seemed to be a meaningful concept at the group level. With respect to clinical and public health significance, there seemed to be a threshold between MIND and SSD.

## 6 CONCLUSIONS

The prevalence of psychotic symptoms in this study was lower than in previous studies, which may be due to that the sample was younger than in some previous studies, or due to birth cohort effects.

Specific phobia was common and associated with global functional impairment, but markedly less so than for example depression. Inclusion of subthreshold symptoms produced a more fine-grained picture of the prevalence and course of specific phobia. Long-term prospective data showed that fears in older people with specific phobia are chronic. However, chronicity at the disorder level seems to occur only in a minority. Most cases rather seem to be exacerbations of a chronic subthreshold fear.

Major and minor depression became more prevalent with age and the course was chronic or recurrent in the majority of cases. Only a minority of individuals with major depression at follow-up had no depression five to nine years earlier. Successful interventions in symptomatic risk groups could have substantial impact on the prevalence of major depression in old age. Subsyndromal depressive symptoms seemed to be a theoretically meaningful extension of the depressive spectrum in old age, although it generally seemed to be of less clinical significance than minor depression.

## 7 FUTURE PERSPECTIVES

The study of psychotic symptoms in population studies of older people is hampered by several methodological problems. There is a need of good quality data that may come at the price of low statistical power, because of the high costs of more rigorous studies. Pooling of several such smaller studies, as has been done previously (153), is an obvious option also in future research.

With respect to specific phobia, further research should expand the sparse knowledge of the most likely very different and unobvious ways in which specific phobia manifests itself in older people and contributes to functional impairment. Studies examining this topic will help to answer questions regarding the unmet need for treatment. Clinical studies of specific phobia in older adults do not exist but would likely not be able to recruit a representative sample of potential patients in the community. Clinical reappraisal or qualitative studies of cases of specific phobia diagnosed in population studies could cast more light on this seemingly highly prevalent disorder.

Regarding depression, the heterogeneity of symptoms within this condition could be an object of more epidemiological research among older people. Examination of the correlates of individual depressive symptoms and their frequency in major depression and subthreshold depression compared to non-depressed persons may aid in refining and simplifying diagnostic criteria, which may be one strategy for improving detection and treatment rates. Studies of individual symptoms may also be of help in improving the ability to predict an unfavorable course of subthreshold depression, which would make interventions more feasible.



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