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Citation for the published paper:

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Risk factors for depressive disorders in the Lundby cohort-a 50 year prospective clinical follow-up.
Journal of affective disorders, 2008, Issue: Aug 9

http://dx.doi.org/10.1016/j.jad.2008.07.002

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Risk factors for depressive disorders in the Lundby cohort- a 50 year prospective clinical follow-up

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Abstract *Background:* Depressive disorders are common and disabling. The Lundby Study is a prospective study of a community sample that started in 1947(N=2550). In 1957, 1013 newcomers were added. The latest field investigation was carried out in 1997. *Aim:* To identify risk factors for depressive disorders. *Method:* The Lundby database contains clinical assessments of the subjects made by psychiatrists. It also includes information about socio-demographic factors and episodes of somatic and mental disorders. Two different but partly overlapping cohorts from the same geographical area in 1947 (N=2470) and in 1957 (N=3310) were investigated. During follow-up 418 individuals experienced their first depressive disorder. For each cohort, possible risk factors were analysed by means of Cox regression analyses for the whole sample and for each sex separately. *Conclusion:* The personality trait nervous/tense and anxiety disorders were statistically significant risk factors for depression for both genders. For males, the diagnoses alcohol disorders and tiredness disorder were risk factors. The personality trait subvalidity (low grade of energy) and nervous symptoms as a child were also risk factors for males. For females personality traits such as being easily hurt, abnormal/antisocial and tired/distracted were associated with depressive disorders. *Clinical relevance:* Knowledge of risk factors may help to reduce incidence of depression.

Keywords Depressive disorder, community sample, prospective study, risk factors, the Lundby Study

Introduction

Depressive disorders are common and burdensome disorders in general populations (Michalak et al., 2002; Olsen et al., 2004). In general populations worldwide, depression has been found to be one of the most disabling diseases in the world (Murray and Lopez, 1996). Hence, it is important to identify risk factors to be able to implement preventive strategies against depressive disorders. However, prospective studies of first incidence depression that provide information about risk factors are infrequent. Risk factors can be of genetic, social and/or psychological nature.

Various depressive disorders aggregate in families (Chen et al., 2000; Angst, 2003). Genetic risk factors could be the same for different disorders, for instance the genetic risk factors for major depressive disorder and generalized anxiety disorder are strongly correlated (Kendler et al., 2007).

Also, several studies have found a higher risk for major depression in females compared with males (Anthony and Petronis, 1991; Blazer et al., 1994). Younger age has though been reported to be a risk factor for major depression in both sexes (Coryell et al., 1992).

Psychosocial risk factors such as poverty, isolation and experiencing little or no concern from friends (Bruce and Hoff, 1994; Lehtinen et al., 2005), negative life events and ongoing strains (de Graaf et al., 2002) have been pointed out as risk factors. For instance, in a review it was concluded that many studies have shown that depressed patients experience more life events prior to onset of depression than control samples from the general population (Paykel, 2003). However, part of the association between stressful life events and onset of depression may be non-causal, since individuals predisposed to major depression may have a tendency to select themselves into high-risk environments (Kendler et al., 1999). Evidence also suggests that psychosocial risk factors for depression sometimes could be buffered by personal and

environmental factors (Bruce, 2002). However, Angst did not find social variables to be predictive of onset of depression but that frequent “ups and downs” was the strongest independent risk factor for both bipolar and depressive disorders (Angst, 2003).

Personality and its interrelation with mental disorders have attracted substantial interest in psychiatry (Hirschfeld et al, 1989). The concept of vulnerability has been used to describe individuals with presumed higher risk for a depressive episode (Ormel et al., 2004). The Swedish psychiatrist Henrik Sjöbring developed a personality theory, in which he described four personality dimensions (Sjöbring, 1973). In the beginning of the Lundby Study in 1947, the subjects were rated according to the Sjöbring dimensions (Essen-Möller et al., 1956). The “validity” dimension of Sjöbring has been linked to subsequent mental illness (Nyström and Lindegård, 1975a). Subclinical symptoms of asthenia such as habitual fatigue and anxiousness (subvalidity according to Sjöbring) were prospectively reported to be overrepresented in patients with depression (Nyström and Lindegård, 1975b). Similarly, in a previous report from the Lundby Study it was found that predepressive personality features such as asthenia increased the risk for first incidence depression (Rorsman et al., 1993). Kendler reported that neuroticism is a significant risk factor for major depressive disorder (Kendler et al., 2004; Kendler et al, 2006). Findings from a study of subjects who completed the Temperament and Character Inventory (TCI) showed that high harm avoidance was a marker of emotional vulnerability to depression (Cloninger et al., 2006).

Prior history of other mental disorders such as anxiety disorders, substance abuse and conduct disorder has been found to increase the risk of depressive disorder (Hettema et al., 2003; Hettema et al., 2006; Coryell et al., 1992; Wittchen et al., 2001; Wittchen et al., 2003). Especially, problems with alcohol have proved to be an important risk factor for patients in primary care with depressive symptoms (Salokangas and Poutanen, 1998).

Risk factors may influence males and females differently. For instance, being single was

found to be a risk factor only for men in a study from Finland (Lindeman et al., 2000). It has also been suggested that for broadly defined depression, genetic influence in development of depression is stronger for women than for men (Bierut et al, 1999).

The aim of this study is to identify risk factors for first incidence of depressive disorder in the Lundby Study. As risk factors may be shared between males and females or sex specific, the analyses were stratified by gender. The focus will be on predepressive personality traits, including the Sjöbring dimensions, and previous mental disorders, including alcohol disorders, as well as changes in marital status.

Methods

Participants and procedure

The Lundby study is a longitudinal study that started in 1947 and has been going on for 50 years. Essen-Möller and his collaborators performed the first field investigation, a pioneer work and investigated 2550 subjects from two parishes in the south of Sweden (Essen-Möller et al., 1956), here referred to as the "Lundby district". The original aim in 1947 was to study the distribution of various personality traits, mental disorders and their interrelations in a geographically defined unselected population. Experienced psychiatrists did the fieldwork in the first as well as in all the following investigations. A follow-up in 1957 included the surviving part of the original cohort plus 1013 subjects who either were born or had moved into the area 1947-1957 (Hagnell, 1966). Between 1947 and 1957, 253 subjects of the original cohort had died while 228 newcomers in 1957 had been born. Consequently the age distributions were similar in 1947 and in 1957. After 1957 no new subjects have been added. Altogether 3563 subjects have been included in the Lundby Study.

The third field-investigation of the whole population was carried out in 1972 and the fourth in 1997, by when 1797 subjects were alive and 1766 had died. The attrition rate was 1-2 % in the follow-ups 1957 and 1972 (Rorsman et al., 1990) and 6 % in 1997 (Nettelbladt et al., 2005). In all follow-ups subjects who had moved away were traced and examined.

The sample consists of a homogenous population of ethnically Nordic people. During the study period the area has changed from rural to suburban and an occupational shift from farming to industry and service profession has taken place (Nettelbladt et al., 2005). From a socio-economic point of view the sample can be regarded as reasonably representative of the rural Swedish population in the forties and fifties. Thus, the majority of the subjects were classified as blue-collar workers and the divorces were few. During the study period many females have entered the labor market and earned their own living. The cohorts in the Lundby Study are assumed to have followed the same pattern of development as other rural populations in western society. Since no new participants have been added after 1957 the cohorts are ageing and the youngest participants were 40 years in 1997 when the latest field investigation took place.

All subjects were classified in 1997 according to their socio-economical level. The classification (SEI code, Statistics Sweden, 1984) is primarily based upon the occupation and contains three groups in its most aggregated form:

i) Blue-collar workers: unskilled and semiskilled and skilled workers.

ii) White-collar workers: assistant non- manual employees, intermediate non-manual employees and employed and self-employed professional higher civil servants and executives.

iii) Self-employed.

Since some items were added in 1957 different sets of items were scored in 1947 and in

1957. In order to study the influence of all items, we studied two partly overlapping cohorts, namely the 1947 cohort and the 1957 cohort. In the 1947 cohort, 80 subjects were excluded from the study. Thirty-seven of these subjects were excluded because of previous episodes of depression and three due to depression caused by substance abuse or a medical condition. Forty subjects were excluded because they had suffered from disorders, (25 with schizophrenia and 15 with dementia) that exclude the diagnosis of depression in the Lundby hierarchical diagnostic system. The 1947 cohort thus contained 2470 subjects.

The cohort from 1957 consisted of the original cohort minus 253 deceased subjects and the added new 1013 subjects. The 1957 cohort contained 3310 subjects. From these 3310 subjects 187 individuals were excluded from the 1957 cohort because of previous mental illness, leaving 3123 subjects. The 187 excluded cases consisted of 93 subjects with depression, 55 with dementia and 39 with schizophrenia. From the two overlapping cohorts 418 individuals, 261 females and 157 males with a first incidence depression with at least medium degree of impairment were identified. Of these 418 cases of first incidence depressive disorder, 304 belonged to the 1947 cohort and 358 cases belonged to the 1957 cohort, and 244 cases belonged to both. Characteristics of the subjects in the cohorts are shown in table 1.

Insert table 1 about here

In all field investigations face-to-face semi-structured interviews were carried out. Information was gathered about health problems and episodes of both mental and somatic disorders that had taken place since the previous field investigation. A variety of variables were recorded, among which were, socio-demographic variables including socioeconomic level, marital status, alcohol problems, drug abuse and prior psychiatric disorders. The semi-structured interview also contained several structured questions exploring personal disposition and the examiner was instructed to follow up hints at the time of the interview. Life events,

occupational problems and stress in the family were recorded; various mental complaints were noted and personality traits were assessed. Normal personality traits were evaluated according to the system of Sjöbring. Most interviews contained a free conversation part during which it was possible to observe the subjects′ behaviour and non-verbal communication during the examination (Hagnell, 1990). Information about the deceased was gathered from different sources of information, relatives, caregivers and various registers.

A free description of the content of the interview and the clinical assessments by the psychiatrist was made after the interview. The final diagnostic evaluations took place after collecting case-notes, data from key-informants and registers. Of special importance was the Patient Register (2004) containing information about all in-patient care 1972-1997, and a local outpatient care register covering the Lundby district (Dalby-Tierp Register, 2004). After gathering all available information about episodes of mental disorder as well as chronic diseases a best-estimate consensus diagnosis was reached.

Diagnostic Assessment

The Lundby Study started before the DSM system (American Psychiatric Association, 1994) was established and before structured diagnostic instruments were used as standard. Since the beginning the Lundby Study had applied a simplified diagnostic system adapted to fieldwork. The diagnostic criteria for depressive disorders have remained similar throughout the study, in 1947, 1957 and 1972 as well as in 1997 (Hagnell et al., 1982). The diagnosis of depression comprises two categories: “depression proper” and “depression plus”. Depression proper includes subjects with mainly melancholic, endogenous symptoms, such as lowered mood, guilt feelings, reduced activity, lack of initiative, better towards the evening, reduced self-

esteem, lowered enjoyment of life and feeling of low vitality, anxiety and fear. Sometimes retardation is present. Often the subject has sleep disturbances and wakes up during early morning or suffers from loss of appetite and weight, (Hagnell, 1966).

Depression plus refers to a diagnosis that is similar to a clear depression, but other symptoms may also be of clinical importance, such as obsessive-compulsive symptoms, anxiety symptoms and phobias, although the depressive symptomatology dominates. In this study depression proper and depression plus were combined and termed depression.

The depression diagnoses from the Lundby system are somewhat broader than major depressive disorder according to the DSM system.

The DSM-IV system (American Psychiatric Association, 1994) and ICD-10 (ICD-10, 1993) were applied together with the Lundby diagnostic system only in the last field investigation in 1997, thus assessments from 1972 and before are only using Lundby diagnoses. To achieve comparability the cases with the Lundby diagnosis depression (proper and plus) in earlier field-investigations were re-evaluated according to DSM-IV. Due to lack of information quite many diagnoses were labelled depression not otherwise specified, but probably many of them were in fact, major depressive disorder.

Further, cases in the period 1947-1972 with first episodes of other diagnostic categories: tiredness, anxiety, mixed neurosis (a group in which no neurotic symptom dominates) were re-evaluated in order to discover missed episodes of major depressive disorder (N=87). However, no missed diagnoses of depression were found among these cases.

Degree of impairment

An impairment rating according to Leighton et al. had been scored for every episode of mental disorders during 1947-1997 (Leighton, 1963). The degrees of impairment were: mild,

medium and severe. Medium degree of impairment was regarded as threshold for “caseness” in the present study. Subjects with a milder degree were not treated as cases in this analysis. Medium degree of impairment corresponds to a GAF-score between 60-51. Severe depression cases showed a total inability to work and function and depended usually on daily help.

Risk factors

The items studied are normal personality traits scored according to the Sjöbring personality theory (Sjöbring, 1973), other personality traits, subjective complaints, sociodemographic variables (like age, marital status, socioeconomic status) and previous episodes of mental disorders and alcoholism. The personality traits including the Sjöbring variables, subjective complaints and other variables were registered at the different investigations.

The Sjöbring variables are assumed to represent four independent dimensions of the personality. The underlying dimensions are assumed to be continuous and to show an approximately normal distribution. Sjöbring called these factors *validity* (the amount of energy), *solidity* (the degree of firmness versus flexibility in intellectual as well as in emotional life), *stability* (relates to a higher or lower degree of abstraction and precision in thought as well as motility connected with emotional engagement) and *capacity* (intellectual ability). The middle range of these variables is designated by the trait name with the prefix “medio”, values above the middle range are termed “super” and those below are termed “sub”. The subvalid subject is considered to be tense, fatigable, cautious, ambivalent and anxious, and the supervalid persistent, courageous and full of enterprise. The subsolid individual is described to be impulsive, changeable and suggestible, whereas the supersolid is objective, unchangeable, dependable and circumspect. The stability dimension is referring to the degree of capability of habituation of activities and experiences. The substable individual

is a warm, kind and sociable person, whereas the superstable individual is more directed to abstract ideas, is skilful and shows emotional distance towards other people.

The psychiatrists who conducted the fieldwork in 1947 were used to apply the Sjöbring personality theory in their daily clinical work, while the later fieldworkers had less practical experience with the Sjöbring system. Therefore we chose to use only the assessments performed in 1947.

The interviewing psychiatrist scored observed personality traits and the respondent scored subjective complaints according to structured questions. Some items assessed were based both on the psychiatric observation of the subjects' personality traits as well as the subjects' complaint about mental strain. From all of these items dichotomous risk factors were constructed. *Nervous/tense* comprises traits such as, being uncertain, anxious, insecure, strained and worrying. *Depressed mood* refers to traits such as melancholic, heavy, gloomy, sad, low-spirited or serious. *Abnormal/antisocial* refers to a severe deviance of the personality with for example psychopathic and aggressive traits. *Blunt/deteriorated* refers to blunt affects and/or signs of cognitive impairment. *Paranoid/schizotypal* traits refer to a being less accessible and chilly, giving poor contact and being suspicious, bizarre or paranoid.

Anxiety disorders, tiredness, child neurosis, separation and *alcohol disorders* were registered from the beginning of the Lundby Study in 1947. *Anxiety disorders* in Lundby correspond mainly to panic disorders and generalized anxiety disorder (Gräsbeck et al., 1993). *Tiredness disorder* refers to a diagnostic concept of mental fatigue, psychasthenia or neurasthenia and has no obvious relation with somatic diseases (Hagnell et al., 1994). *Child neurosis* refers to nervous symptoms before 15 years of age. In order to be counted as a case of *alcoholism* the following definition was used: (a) alcohol dependence with a persistent pattern of withdrawal symptoms, craving and tremor (DSM-IV 303.90); (b) alcohol abuse with a persistent pattern of heavy excessive drinking, frequent intoxications and a tolerance change (DSM-IV 305.00).

Separation was considered to be a possible risk factor in the present study. *Separation* refers to changes in the marital status, becoming single due to a divorce or death of a spouse. The changes in marital status were recorded at the different cross-sectional days July 1st in 1947 July 1st in 1957 and July 1st in 1972, in the different waves of investigation.

A few more variables were added in 1957. These were *affective lability, tired/distracted, sensitive/frail, easily hurt,* and *rigid/dry* personality (Hagnell et al., 1994). *Affective lability* means emotionally susceptible. *Tired/distracted* comprised feelings of fatigue, easily becoming tired and exhausted. *Sensitive/frail* refers to a frailty and brittleness in the personality. *Easily hurt* refers to feeling unjustly treated and having difficulties in forgetting being wronged. *Rigid/dry* refers to a person with limited flexibility. Table 2 shows the content of constructed risk factors. Table 3 and 4 present frequency statistics for subjects identified having different variables during time at risk.

Insert table 2, 3 and 4 about here

Statistical methods

Exploratory factor analyses of personality traits and subjective mental complaints were used in order to reduce the numbers of possible risk factors. Factor analysis (principal components with oblique rotation) was used as a first guideline to cluster subjective complaints and assessments of personality traits into groups of related items. A final solution was chosen after consensus in the research group. For each cluster a new risk factor was constructed indicating either absence or low severity in all the original items or high severity in at least one item. For each of the two overlapping cohorts Cox regression analyses with time to the following first depression incidence, as outcome were carried out; the time dependent risk factors are supposed to be constant between the field-investigations. First the influence of each risk

factor was assessed one by one in simple models for each sex separately and for the total sample, adjusting only for age, and for the total sample for sex. Second, to see whether the influence of the risk factors differed between the sexes, sex X risk factor interaction terms were included in simple models of the total sample.

Further, multivariate regression analyses were performed for the whole sample and for both sexes simultaneously, starting with models containing all possible risk factors. The least significant risk factor for both sexes was removed one by one. Thus the final models contain the same risk factors not necessarily statistical significant in both sexes. A similar backwards procedure was repeated in the whole sample. Results were considered statistically significant when $p < 0.05$(Clayton and Hill, 2004).

Results

The Lundby diagnosis of depression represents the DSM-IV diagnostic categories; major depressive disorder, depression NOS and adjustment disorder with depressed mood. Altogether 418 subjects, 261 females and 157 males were identified with the Lundby diagnosis of depression 304 cases in the 1947 cohort and 358 cases in the 1957 cohort. Of the 418 individuals, 253 (60.5%) had major depressive disorder according to DSM-IV, 112 (26.8%) had depression NOS and 53 (12.7%) had adjustment disorder with depressed mood.

Analyses 1947-1997

The influence of abnormal/antisocial traits on occurrence of depression differed significantly between the sexes ($p=0.040$); and there was an almost significant sex-difference for tiredness ($p=0.061$). Simple analyses (adjusting only for age, and in the total sample also for sex) were conducted for all risk factors for the whole sample and for each sex separately with the 1947-1997 file (N=2470). The results from the simple analyses are shown in table 5. For the total sample nervous/tense, anxiety disorders, alcohol disorders and the dimension subvalidity

appeared to be risk factors, whereas superstability was a protective factor. For males only nervous/tense, anxiety disorders, tiredness disorder, and subvalidity were significantly associated with risk, and superstability had a statistically significant protective effect. In the female subsample there was evidence of effects of nervous/tense and abnormal/antisocial personality traits.

Insert table 5 about here

Multivariate analyses 1947-1997

All independent variables were used in the multivariate models. The results are shown in table 5. Predictor variables with non-significant effects were omitted one by one in backwards stepwise multiple regression analyses for all subjects and for the genders separately. For the total sample, nervous/tense and the validity dimension, subvalidity was statistically significant risk factors and the superstability dimension was a protective factor. For males, child neurosis was a significant risk factor. Also, validity was a risk factor for males, with the dimension subvalidity showing the highest risk, while the dimension superstability was a protective factor for males. For females, abnormal/antisocial personality traits and nervous/tense were statistically significant risk factors in the multivariate analysis just like in the simple analyses.

Analyses 1957-1997

The influence of child neurosis on the occurrence of depression differed significantly between the sexes ($p= 0.04$) and there was an almost significant sex-difference for anxiety disorders ($p=0.059$) and for the trait, blunt/deteriorated ($p=0.063$). The results of the analyses from the 1957 cohort, presented in table 6 showed evidence of effects of the risk factors nervous/tense, anxiety disorders, tired/distracted and easily hurt in the total sample. Alcohol disorders and child neurosis only proved to be significant risk factors for males. The traits nervous/tense,

abnormal/antisocial, tired/distracted and getting easily hurt represented statistically significant risk factors for females in the separate analyses. Anxiety disorders were a significant risk factor for both sexes.

Insert table 6 about here

Multivariate analyses 1957-1997

Again all independent variables were used in the multiple models for the whole sample and for the genders separately. For the total sample anxiety disorders, alcohol disorders and the personality trait getting easily hurt appeared to be statistically significant risk factors. For males, anxiety disorders, child neurosis and alcohol disorder were significant risk factors, whereas for females the personal traits nervous/tense and abnormal/antisocial traits were significant risk factors.

Discussion

The Lundby diagnosis of depression is not totally congruent with major depressive disorder according to DSM-IV since a minority of cases identified in the Lundby Study were classified as having adjustment disorder with depressed mood. Probably due to lack of detailed information of some episodes of depression, quite many of them were labelled as DSM-IV depression NOS.

Similar to other studies more females than males were affected by depressive disorders in this study (Leon et al., 1993). Some risk factors influenced the sexes differently but statistically significant sex-differences were only obtained for child neurosis and abnormal/antisocial traits. Hence, the findings of different risk factors for the sexes must be interpreted with caution.

In essence, the results from the simple analyses for the whole sample showed that nervous/tense, anxiety disorders and alcohol disorders were statistically significant risk factors for both cohorts. For males other risk factors were tiredness, subvalidity (i.e. low grade of energy) and child neurosis, whereas for females there was evidence for effects of the personality traits abnormal/antisocial, tired/distracted and getting easily hurt. Superstability (i.e. being emotionally distant to other people, skilful, directed to abstract thinking) turned out as a protective factor for males both in the simple and in the multivariate analyses in the 1947 cohort.

The results from the multivariate analyses of the 1947 file showed that significant risk factors for men were nervous/tense, child neurosis and subvalidity and for females the personality traits nervous/tense and abnormal/antisocial traits. In the multivariate analyses of the 1957 file the significant risk factors for males were child neurosis, anxiety disorders and alcohol disorders, whereas the females had the same risk factors as in the 1947 file. Separation and age did not turn out as risk factors in the present study.

Not all differences in the analyses for the different cohorts are easily explained. However, the differences were small and can partly be caused by different sets of explanatory variables and random fluctuations. They could also be due to differences in diagnostic procedure or reflect increasing incidence of anxiety disorders and alcohol disorders, especially for men after 1957. Rorsman et al have previously reported from the Lundby Study an increase of anxiety for men in the period 1957-1972 compared with the period 1947-1957 (Rorsman et al., 1987). During this time period the closely knit ties in the rural society in Lundby area probably weakened with less social cohesion and maybe higher incidence of abuse of alcohol. High incidence of alcohol abuse and dependence especially in younger cohorts has also been reported from Germany (Perkonigg et al, 2006). On the whole, the most probable explanation for the differences in the multivariate analyses may be that the diagnostic skills in the study improved

after 1957 and that different sets of variables were used.

As expected, the results are congruent with the notion that depressive disorders probably are multifactorial, with a broad range of risk factors. Contrary to findings reviewed by Paykel, separation (referring to a change in marital status) did not appear as a risk factor for depressive disorder (Paykel, 2003). An explanation may be that a divorce or separation not always is a negative experience. In the same vein Angst et al reported that social variables like father's occupation, income, family status and educational level did not predict depressive disorders (Angst et al., 2003).

A personality profile of neuroticism has been shown to be associated with mood disorder (Nowakowska et al., 2005) and lifetime major depression (Kendler et al., 2006). The personality trait nervous/tense, which probably to a large extent overlaps with "neuroticism", was demonstrated to be a risk factor for both males and females in the regression analyses in the present study. Also the personality traits tired/distracted and easily hurt were statistically significant risk factors for women in the 1957 cohort. The risk factor easily hurt refers to items such as difficulties forgetting being wronged and feeling unjustly treated which may reflect, "decreased emotional strength", and which has been shown to increase the risk for depression (Hirschfeld et al., 1989).

Cloninger has systematized observations of the personality and developed the temperament and character inventory (TCI), (Cloninger et al., 1993). TCI harm avoidance quantifies differences in the extent to which a person is anxious, pessimistic and shy versus risk-taking, optimistic and out-going. Harm avoidance has been reported to be a marker of emotional vulnerability to depression (Cloninger et al., 2006). Higher harm avoidance personality has been reported for subjects with major depressive disorder than for healthy controls. Harm avoidance is related to the Sjöbring variable subvalidity. The personality dimension subvalidity (low grade of energy, often ambivalent, cautious, careful and fatigable) was a risk

factor in the multivariate model for the total sample and in the sex specific simple analyses for men. The finding of subvalidity as a risk factor for depressive disorders is consistent with earlier research and supports the view that evaluation of the personality is important in patients with mood disorders (Nyström and Lindegård, 1975b).

There has been a debate regarding the extent to which personality traits are risk factors for depression or whether depression itself causes development of certain personality traits. For instance, earlier research observed that personality disorders from clusters B and C are more often found in patients with early onset depression (Fava et al., 1996). Similarly, avoidant personality disorders were found to be common in depressed primary care patients (Ramklint and Ekselius, 2003). The findings presented here support the view that personality traits could be risk factors for onset of depressive disorder since in the present study the assessments of personality traits were performed before outcome. On the other hand superstability (i.e. being emotionally distant to other people, skilful, directed to abstract thinking) was a protective factor indicating that certain personality traits could be protective.

In prior research psychiatric disorders such as anxiety disorders and conduct disorder have been reported to be significant risk factors for major depressive disorder independent of the length of the intervening period between the onset of first disorder and major depressive disorder (Hettema et al., 2003). Consistent with this finding, major depressive disorder and generalized anxiety disorder appear to have strongly correlated genetic risk factors (Kendler et al, 2007). Also in the present study anxiety disorders was a risk factor for depressive disorders in several analyses especially for men, although the effects did not reach statistical significance for females in the 1947 file. This finding is in line with the finding from Hettema et al suggesting that males appear to be more vulnerable to the depressogenic effect of generalized anxiety disorders than females (Hettema et al, 2006). The diagnosis tiredness disorder was only a risk factor for males in the simple analysis of the 1947 cohort. This

finding is in accordance with the finding of asthenia as a prominent risk factor for males (Rorsman et al., 1993).

In our study another difference between the sexes was that males had child neurosis as a risk factor while the females did not. This finding is not congruent with the finding of Clark who reported that childhood psychological problems increased the risk for affective disorders in midlife for both sexes (Clark et al., 2007). However, the Lundby study was not originally designed for children and certainly there is lack of information in the database about psychological problems in childhood and adulthood.

As reviewed by Swendsen and Merikangas (2000) alcohol disorders have often been reported to be a risk factor for depressive disorders (Swendsen and Merikangas, 2000). However, their conclusion relied mostly on retrospective reports. In the present study alcohol disorders represented a risk factor for males.

It has been suggested this that the sexes could have different pathways to depressive disorder (Hill et al., 2004). However, a study in a primary care setting from Finland showed that the major risk factors were rather similar for the sexes (Salokangas and Poutanen, 1998). In our study females and males shared some risk factors but differed in others. In all, our findings may support the view that there is a link between some predepressive personality traits, prior non-affective psychiatric disorders and depressive disorders. Some risk factors may influence the sexes differently.

Conclusion

The personality trait nervous/tense appeared to be an important risk factor for both genders for depression according to the Lundby diagnosis of depression. Also prior anxiety disorders were a risk factor for both genders in most of the analyses. Alcohol disorder, subvalidity,

tiredness disorder and child neurosis were risk factors for males with the Lundby diagnosis of depression. For females the personality traits: being easily hurt, abnormal/antisocial and tired/distracted appeared to be risk factors. The genders shared some risk factors, but differed in some ways, maybe indicating different pathways to depression.

Limitations

The Lundby Study has a very long follow-up period with many inherent methodological problems such as changing diagnostic procedures, different teams of field-workers, few investigations during long time periods and a limited number of participants. The Lundby diagnosis of depression is not totally congruent with major depressive disorder making comparisons with other studies somewhat problematic. Another limitation is the use of a semi-structured interview with several questions aiming at exploring personality traits rather than applying an established personality inventory.

Acknowledgements

The study was supported by the Swedish Council for Planning and Coordination of research, The Swedish Council for Social research, The Swedish Research Council, The Swedish Medical Research Council, The Medical Faculty, Lund University, The Principal Government of Scania, The Söderström-Königska Foundation, The Bror Gadelius Foundation and The Ellen and Henrik Sjöbring Foundation, Department of Psychiatry, Lund University.

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Table 1. Socio-demographic information about the cohorts 1947 and 1957.

	COHORT 1947				COHORT 1957			
	MALE N=1275 (51.6%)		FEMALE N=1195 (48.4%)		MALE N=1619 (51.8%)		FEMALE N=1504 (48.2%)	
Age, years								
Mean (SD)	33.8	(21.8)	35.0	(22.9)	35.2	(20.8)	34.9	(21.3)
Range	1-87		1-92		1-90		1-96	
Marital status[1] **N (%)**								
Unmarried	661	(51.8)	556	(46.5)	744	(46.0)	652	(43.3)
Married	563	(44.2)	559	(46.8)	797	(49.2)	747	(49.7)
Divorced	10	(0.8)	7	(0.6)	28	(1.7)	16	(1.1)
Widow/widower	41	(3.2)	73	(6.1)	50	(3.1)	89	(5.9)
Socioeconomic status N (%)								
White collar	73	(7.5)	103	(11.2)	187	(14.0)	207	(16.6)
Blue collar	660	(67.8)	581	(63.1)	874	(65.5)	791	(63.4)
Self-employed[2]	241	(24.7)	236	(25.7)	273	(20.5)	250	(20.0)

[1]Not all subjects were classified.

[2]Many of the subjects were farmers and thus regarded as self-employed.

Table 2. The content of constructed risk factors.

Year of assessment	Risk factors	Original items scored by interviewer or self-reported (*)
1947, 1957, 1972	Down/semi-depressed	Heavy, gloomy, semi-depressed, down*
	Nervous/tense	Tense, restless, insecure, strained, vegetative, lachrymose Worried*, nervous*, susceptible to adversity*, cries easily*,difficulty to collect ones thoughts*
	Abnormal/antisocial	Indolent, hyperthymic, fanatic, suspicious, explosive, aggressive, emotionally labile
	Blunt/deteriorated	Torpid, blunt, empty, intellectually deteriorated, disturbed memory
	Paranoid/schizotypal	Unresponsive, reserved, paranoid, bizarre, schizoid
1947-1997	Anxiety disorders[1]	Generalized anxiety disorder, panic disorder
	Tiredness[1]	No obvious relation to somatic diseases
		Nervous fatigue, low threshold for fatigue*
	Alcohol disorders[1]	Alcohol abuse/dependence according to DSM–criteria
	Child neurosis	Nervous symptoms before 15 years
	Separation	Becoming single due to a divorce or death of a spouse
1957, 1972	Affective lability	Affective lability
	Tired/distracted	Tired, poorly concentrated
		Tires easily*
	Sensitive/frail	Sensitive, brittle, frail
	Easily hurt	Difficulty forgetting being wronged*,

[1] Anxiety disorders, Alcohol disorders and Tiredness disorder were assessed as continuous variables 1947-1997

Year of assessment	Risk factors	Original items scored by interviewer or self-reported (*)
		feels unjustly treated*
	Rigid/dry personality	Inflexible, difficulties in adjusting

[1]Anxiety disorders, Alcohol disorders and Tiredness disorder were assessed as continuous variables 1947-1997

Table 3. Risk factors in the 1947 cohort. Number of individuals observed with the risk factor during follow-up.

1947-1997		
VARIABLES		
Personality traits	**Male**	**Female**
Down/semi-depressed	49 (3.8%)	46 (3.8%)
Nervous/tense	436 (34.2%)	641 (53.6%)
Abnormal/antisocial	136 (10.7%)	63 (5.3%)
Blunt/deteriorated	151 (11.8%)	85 (7.1%)
Paranoid/schizotypal	170 (13.3%)	128 (10.7%)
CAPACITY[1]		
Medio	543 (51.8%)	568 (57.7%)
Sub	139 (13.2%)	137 (13.9%)
Super	367 (35.0%)	280 (28.4%)
VALIDITY[2]		
Medio	395 (38.7%)	351 (36.5%)
Sub	256 (25.1%)	319 (33.2%)
Super	369 (36.2%)	291 (30.2%)
STABILITY[2]		
Medio	287 (28.1%)	261 (27.1%)
Sub	268 (26.3%)	485 (50.5%)
Super	465 (45.6%)	215 (22.3%)
SOLIDITY[3]		
Medio	506 (49.8%)	510 (53.1%)
Sub	302 (29.7%)	342 (35.6%)
Super	208 (20.5%)	109 (11.3%)
Diagnoses		
Anxiety disorders	69 (5.4%)	117 (9.8%)
Tiredness disorder	22 (1.7%)	40 (3.3%)
Alcohol disorders	261 (20.4.1%)	19 (1.6%)
Other variables		
Child neurosis[4]	7 (2.4%)	5 (1.7%)
Separation[5]	155 (12 %)	202 (17%)

[1] 1049 male subjects and 985 female subjects were assessed.

[2] 1020 male subjects and 961 female subjects were assessed.
[3] 1016 male subjects and 961 female subjects were assessed.
[4] 293 male subjects (children) and 299 female subjects were assessed.
[5] 1275 males and 1195 females were assessed.

Percentages are given in the parentheses. Total numbers of subjects in 1947 N= 2470, males=1275 and females=1195. Separation means change from married to not married.

Table 4. Risk factors in the 1957 cohort. Number of individuals observed with the risk factor during follow-up.

1957-1997		
VARIABLES	Male	Female
Depressed	44 (2.7%)	22 (1.5%)
Nervous/tense	329 (20.3%)	497 (33.0%)
Abnormal/antisocial	106 (6.5%)	37 (2.5%)
Blunted/deteriorated	72 (4.4%)	26 (1.7%)
Paranoid/schizotypal[1]	105 (6.7%)	83 (5.5%)
Anxiety disorders	102 (6.3%)	160 (10.6%)
Tiredness disorder	30 (1.9%)	51 (3.4%)
Alcohol disorders	323 (19.9%)	23 (1.5%)
Child neurosis[2]	13 (3.9%)	11 (3.5%)
Separation[3]	148 (13.2%)	186 (12.3%)
Affective lability	106 (6.5%)	107 (7.1%)
Easy tired	272 (16.8%)	395 (26.2%)
Sensitive/frail	65 (4.0%)	175 (11.6%)
Easily hurt	93 (5.7%)	190 (12.6%)
Rigid/dry	57 (3.5%)	23 (1.5%)

[1] 1563 males and 1504 females were assessed.
[2] 331 male subjects (children aged less than 15 years), respectively 316 female subjects.
[3] 1121 male subjects and 1027 females were assessed.

Percentages are given in the parentheses. Total number of subjects in the 1957 file N= 3123, Males= 1619 and females= 1504.

Table 5. Simple Cox and multivariate stepwise multiple Cox regression models of risk factors for "Lundby depression" in the 1947 cohort. The outcome variable is the Lundby diagnosis of depression.

	MALE			FEMALE			ALL		
	HR	CI	P	HR	CI	P	HR	CI	P
Simple models									
Down/semi-depressed	1.77	0.56-5.61	.329	0.86	0.21-3.49	.834	1.25	0.51-3.03	.623
Nervous/tense	1.87	1.15-3.06	**.012**	2.04	1.48-2.82	**.000**	2.01	1.54-2.63	**.000**
Abnormal/antisocial	0.76	0.28-2.08	.598	2.66	1.30-5.42	**.007**	1.47	0.82-2.62	.198
Blunt/deteriorated	0.00	0.00-	.952	1.56	0.69-3.56	.287	0.74	0.33-1.67	.471
Paranoid/schizotypal	1.43	0.69-2.96	.332	1.22	0.62-2.41	.562	1.32	0.80-2.16	.276
Anxiety disorders	2.00	1.00-4.00	**.048**	1.47	0.93-2.30	.097	1.61	1.11-2.36	**.013**
Tiredness disorder	2.87	1.05-7.84	**.040**	0.66	0.21-2.07	.476	1.18	0.55-2.50	.670
Alcohol disorders	1.54	0.98-2.43	.063	2.13	0.67-6.74	.198	1.56	1.02-2.38	**.040**
Child neurosis	2.33	0.57-9.62	.241	0.00	0.01-	.943	1.04	0.25-4.19	.961
Separation	0.82	0.44-1.51	.517	0.63	0.20-2.04	.444	0.78	0.46-1.34	.378
Capacity	1		.674	1		.381	1		.335
Subcapacity	0.79	0.40-1.56	.498	1.02	0.65-1.59	.939	0.94	0.64-1.36	.732
Supercapacity	0.84	0.52-1.35	.469	0.77	0.52-1.13	.183	0.80	0.59-1.08	.139
Validity	1		**.046**			.025	1		**.002**
Subvalidity	1.72	1.02-2.90	**.041**	1.27	0.88-1.84	.194	1.41	1.04-1.9	**.025**
Supervalidity	0.93	0.58-1.64	.800	0.71	0.46-1.09	.117	0.78	0.56-1.10	.165
Solidity	1		.862	1		.516	1		.644
Subsolidity	1.12	0.68-1.84	.654	0.90	0.64-1.26	.542	0.97	0.52-1.26	.813
Supersolidity	0.99	0.52-1.77	.884	0.69	0.36-1.35	.281	0.81	0.52-1.26	.348
Stability	1		.115	1		.218	1		**.027**
Substability	0.82	0.44-1.51	.526	0.84	0.58-1.22	.365	0.83	0.46-0.88	.253
Superstability	0.59	0.36-0.98	**.039**	0.68	0.43-1.05	.082	0.63	0.46-0.88	**.007**
Multivariate models									
Age	1.0	0.98-1.01	.065	0.99	0.98-1.0	.019	0.99	0.98-1.00	.173
Nervous/ tense	2.39	1.39-4.13	**.002**	2.02	1.41-2.89	**.000**	2.09	1.55-2.82	**.000**
Validity	1		**.041**	1		.075	1		**.010**
Subvalidity	1.85	1.03-1.9	**.026**	1.23	0.85-1.78	.274	1.37	1.01-1.85	**.044**
Supervalidity	1.02	0.57-1.82	.941	0.73	0.47-1.14	.173	0.82	0.58-1.16	.256
Stability	1		.052	1		.243	1		**.031**
Substability	0.83	0.49-1.53	.545	0.97	0.67-1.42	.884	0.93	0.68-1.28	.658
Superstability	0.54	0.32-0.89	**.017**	0.70	0.45-1.09	.114	0.65	0.46-0.90	**.011**
Abnormal/antisocial*	0.46	0.11-1.01	.289	3.03	1.32-6.96	**.009**	---	---	---
Child neurosis**	10.33	1.29-82.73	**.028**	---	---	---	---	---	---

Age was included in all models. CI refers to 95% confidence intervals. P refers to p-value. HR refers to hazard rate ratio. Separation refers to a change in the marital status, becoming single due to death of a spouse or divorce.

* Abnormal/antisocial did not turn out as statistically significant risk factors in the final model for the whole sample.

** For females the table estimates could not be obtained because of small number of occurrences for the variable child neurosis in the separate analysis.

Table 6. Simple Cox and multivariate stepwise multiple Cox regression models of the"Lundby depression" in the Lundby material observed 1957-1997. Age is included in all models. The defined event tested is the Lundby diagnosis of depression.

	MALE			FEMALE			ALL		
	HR	CI	P	HR	CI	P	HR	CI	P
Simple models									
Down/semi-depressed	1.11	0.27-4.49	.886	1.14	0.28-4.59	.856	1.11	0.41-2.97	.839
Nervous/tense	1.46	0.90-2.38	.126	1.78	1.31-2.42	**.000**	1.69	1.30-2.19	**.000**
Abnormal/antisocial	0.99	0.43-2.24	.976	2.88	1.42-5.83	**.003**	1.58	0.92-2.71	.094
Blunt/deteriorated	0.30	0.04-2.17	.234	2.32	0.86-6.25	.097	0.99	0.41-2.40	.982
Paranoid/schizotypal	1.45	0.67-3.11	.343	1.08	0.51-2.30	.841	1.24	0.73-2.12	.438
Anxiety disorders	3.12	1.85-5.28	**.000**	1.64	1.11-2.42	**.012**	2.00	1.46-2.74	**.000**
Tiredness disorder	1.75	0.55-5.52	.340	0.84	0.35-2.05	.707	1.05	0.52-2.12	.889
Alcohol disorders	1.80	1.20-2.68	**.004**	1.12	0.28-4.52	.876	1.67	1.14-2.45	**.008**
Child neurosis	4.34	1.87-10.05	**.001**	0.43	0.06-3.12	.407	1.90	0.89-4.07	.095
Separation	0.81	0.29-2.24	.683	0.99	0.56-1.75	.966	0.96	0.58-1.57	.86
Affective lability	1.84	0.93-3.63	.079	1.19	0.66-2.14	.556	1.40	0.90-2.18	.137
Tired/distracted	1.58	0.91-2.72	.102	1.48	1.06-2.06	**.020**	1.51	1.14-2.01	**.004**
Sensitive/frail	0.31	0.04-2.23	.246	1.48	0.96-2.28	.072	1.29	0.85-1.95	.225
Easily hurt	1.75	0.81-3.76	.152	2.05	1.39-3.03	**.000**	2.00	1.41-2.81	**.000**
Rigid/dry	0.96	0.08-3.95	.951	0.55	0.08-3.95	.555	0.75	0.24-2.34	.618
Multivariate models									
Age	1.00	0.99-1.01	.474	1.00	0.99-1.01	.944	1.00	0.99-1.0	.521
Easily hurt*	---	---	---	---	---	---	1.73	1.64-4.92	**.002**
Abnormal/antisocial **	0.65	0.28-1.51	.313	2.90	1.43-5.88	**.003**	---	---	---
Anxiety disorders	2.84	1.64-4.92	**.000**	1.35	0.89-2.03	.157	1.79	1.30-2.48	**.000**
Alcohol disorders	1.81	1.20-2.72	**.004**	1.07	0.26-4.43	.922	1.61	1.10-2.35	**.014**
Child neurosis**	4.28	1.82-10.03	**.001**	0.33	0.04-2.46	.281	---	---	---
Nervous/tense**	1.15	0.69-1.91	.595	1.67	1.21-2.31	**.002**	---	---	---

CI refers to 95% confidence intervals. P refers to p-value. HR refers to hazard rate ratio. Separation refers to a change in the marital status, becoming single due to death of a spouse or divorce.

*The personality trait getting easily hurt did not turn out as a risk factor for males and females in the separate multivariate analyses.

**The personality traits abnormal/antisocial and nervous/tense did not turn out as risk factors in the model when the whole sample was analyzed. Also, child neurosis did not turn out as a risk factor when the whole sample was analyzed.