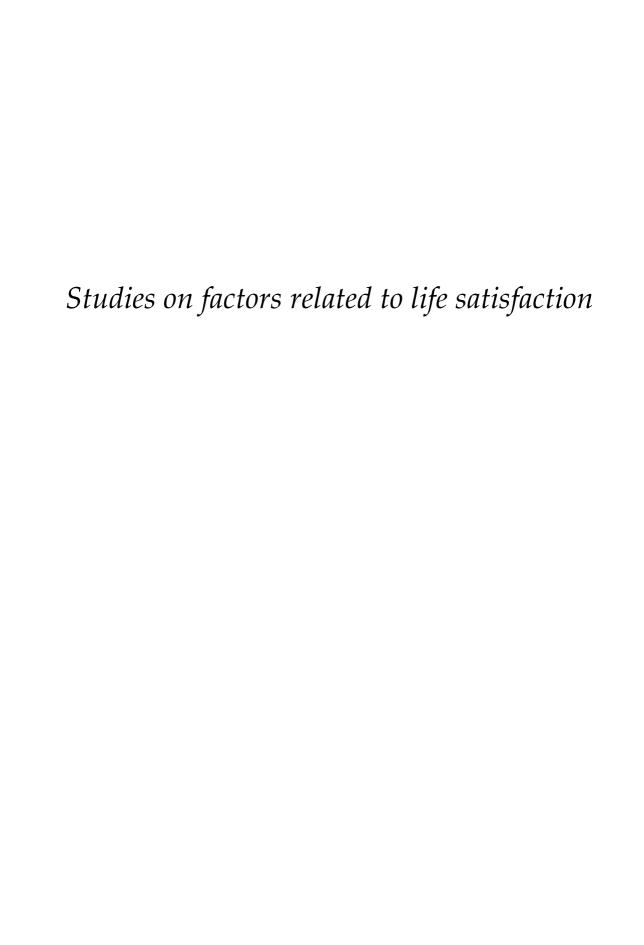Teemu Rissanen

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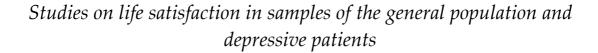
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Studies on factors related to life satisfaction

TEEMU RISSANEN

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V

ABSTRACT

Mental health is interconnected with somatic health and affects biological processes. Mental disorders are the leading cause of years lost with disability worldwide. The identification of early indicators of poor mental health may enable early intervention and health monitoring and promotion. One of the early indicators could be self-reported life satisfaction. This is a key indicator of subjective well-being, which is one of the main dimensions of mental health.

The present studies aimed at increasing knowledge of life satisfaction by exploring its less studied areas, such as its role in recovery from and its predictive value for major depressive disorder. In a population-based sample, its relationship with childhood adversities and various psychological comorbidities, as well as certain biological correlates, was also investigated, both cross-sectionally and retrospectively.

The data for these substudies (I–IV) were obtained from health questionnaires and structured diagnostic interviews in a natural 6-year follow-up study of depressive patients (N = 121) and in a 7-year follow-up of a general population sample (N = 333), both belonging to the Kuopio Depression Study. Among the population-based sample, a selected subsample of the participants was invited for clinical evaluation and laboratory analyses (e.g. inflammatory-based biomarkers). Life satisfaction was measured with four items: interest in life, happiness, loneliness, and general ease of living.

Depressive symptoms and hopelessness were the strongest correlates of life dissatisfaction after 6 years among the depressive patients. Higher baseline interpersonal sensitivity as well as poor self-rated health and wealth, regardless of the assessment time point, were also associated with it. In the general population sample, a broad spectrum of poor mental health indicators was associated with concurrent life dissatisfaction, depression being the strongest one. Long-term life dissatisfaction predicted the onset of major depressive disorder in a 7-year follow-up, being associated with several adversities in terms of health, health behavior, and social factors. One possible pathway from life dissatisfaction to somatic morbidity was suggested via a decreased anti-inflammatory buffer capacity.

TIIVISTELMÄ

Mielenterveys on ihmisen terveyden, hyvinvoinnin ja toimintakyvyn perusta. Se liittyy erottamattomasti yksilön somaattiseen terveyteen. Mielenterveyden häiriöistä kärsivillä on lyhyempi elinajanodote yleisväestöön verrattuna. Mielenterveyden heikkenemisestä kertovia osoittimia tarvitaan terveyden edistämiseksi sekä sairastavuuden vähentämiseksi. Itsearvioitu elämäntyytyväisyys voisi olla yksi sopiva osoitin, sillä elämäntyytyväisyys on hyvinvoinnin ja mielenterveyden tärkeä osatekijä.

Tämän neljästä osajulkaisusta koostuvan tutkimuksen tarkoituksena oli selvittää itsearvioidun elämäntyytyväisyyden taustatekijöitä, kykyä ennustaa masennusta ja siitä toipumista. Väestöpohjaisessa tutkimuksessa selvitettiin lapsuudenaikaisten vastoinkäymisten, psyykkisten kuormitustekijöiden sekä somaattisten ja biologisten tekijöiden yhteyksiä elämäntyytyväisyyteen. Analyysit tehtiin sekä poikkileikkausasetelmassa että seuranta-asetelmassa.

Tutkimusaineiston muodosti Kuopion Depressioprojektiin kuuden vuoden ajan osallistuneet potilaat (N=121) sekä pohjoissavolaisen väestöotoksen osajoukko (N=333), jolle tehtiin kolme kyselytutkimusta vuosina 1998, 1999 ja 2001 ja kliiniset tutkimukset vuonna 2005. (sisältäen mm. inflammatoristen biomarkkereiden analyysit). Elämäntyytyväisyyttä mitattiin neljällä kysymyksellä elämän mielenkiintoisuudesta, onnellisuudesta ja helppoudesta sekä koetusta yksinäisyydestä.

Masennussairaudesta toipuvilla potilailla elämäntyytymättömyys oli kuuden vuoden seurantatutkimuksessa yhteydessä kliiniseen oireiluun, erityisesti masennusoireisiin ja toivottomuuteen. Lisäksi lähtötilanteen suurempi interpersoonallinen herkkyys sekä seuranta-ajankohdasta riippumatta itsearvioitu huono terveydentila sekä vaikeampi taloudellinen tilanne olivat yhteydessä elämäntyytymättömyyteen. Väestöotoksessa tyytymättömyys elämään oli yhteydessä useaan mielenterveyshäiriöiden osatekijään, vahvimmin masennukseen. Pitkäaikainen tyytymättömyys elämään ennusti vakavan masennustilan diagnoosin saamista henkilöillä, jotka olivat olleet aiemmin terveitä. Pitkäaikainen elämäntyytymättömyys oli myös tilastollisesti merkitsevästi yhteydessä huonompaan terveydentilaan sekä huonon terveyskäyttäytymiseen, epäsuotuisiin sosiaalisiin tekijöihin ja sosiaalisen tuen puutteeseen. Elämäntyytyväisyys sen sijaan liittyi vahvasti itsearvioituun hyvinvointiin, somaattiseen terveyteen sekä psykiatriseen sairastavuuteen. Pitkäaikaisesti elämäänsä tyytymättömillä henkilöillä oli havaittavissa viitteitä elimistön vähentyneestä anti-inflammatorisesta puskurikapasiteetista.

Acknowledgements

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List of the original publications

This dissertation is based on the following original publications, which are referred to in the text by the Roman numerals **I–IV**.

I   Koivumaa-Honkanen H, Rissanen T, Hintikka J, Honkalampi K, Haatainen K, Saharinen T, Viinamäki H. Factors associated with life satisfaction in a 6-year follow-up of depressive out-patients. Soc Psychiatry Psychiatr Epidemiol 2011;46:595-605.

II   Rissanen T, Viinamäki H, Lehto SM, Hintikka J, Honkalampi K, Saharinen T, Koivumaa-Honkanen H. The role of mental health, personality disorders and childhood adversities in relation to life satisfaction in a sample of general population. Nord J Psychiatry 2013;67:109-15.

III   Rissanen T, Viinamäki H, Honkalampi K, Lehto SM, Hintikka J, Saharinen T, Koivumaa-Honkanen H. Long-term life dissatisfaction and subsequent major depressive disorder and poor mental health. BMC Psychiatry 2011;11:140.

IV   Rissanen T, Lehto SM, Hintikka J, Honkalampi K, Saharinen T, Viinamäki H, Koivumaa-Honkanen H. Biological and other health related correlates of long-term life dissatisfaction burden. BMC Psychiatry 2013;13:202.

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Contents

Abbreviations

ANOVA	Analysis of variance
BDI	Beck Depression Inventory
BMI	Body Mass Index
CNS	Central Nervous System
DES	Dissociative Experiences Scale
DSM-III-R	Diagnostic and Statistical Manual for Mental Disorders, 3rd edition, revised
DSM-IV	Diagnostic and Statistical Manual for Mental Disorders, 4th edition
DSM-5	Diagnostic and Statistical Manual for Mental Disorders, 5th edition
GAF	Global Assessment of Functioning Scale
GHQ	General Health Questionnaire
HDRS	Hamilton Depression Rating Scale
HS	Beck Hopelessness Scale
hsCRP	High-sensitivity C-reactive Protein
ICD-10	International Classification of Diseases and Related Health Problems 10th, revised version
IL-6	Interleukin-6
KUDEP	Kuopio Depression Study
KUH	Kuopio University Hospital
LS	Allardt's four-item scale on life satisfaction
MAC-Q	Memory Complaint Questionnaire
MADRS	Montgomery-Åsberg Depression Rating Scale
MDD	Major Depressive Disorder
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
NIM	Not Included in the Model due to nonsignificant association in the bivariate model

ns	Non-significant
NSAID	Non-Steroidal Anti-inflammatory Drug
OR	Odds ratio
SCID-I	Structured Clinical Interview for DSM-III-R, axis I disorders
SCID-II	Structured Clinical Interview for DSM-III-R, axis II disorders
SCL	Symptom Check List
SD	Standard deviation
SDQ	Somatoform Dissociation Questionnaire
SOFAS	Social and Occupational Functioning Assessment Scale
SPSS	Statistical Package for Social Sciences
SWB	Subjective well-being
TAS	Toronto Alexithymia Scale
TNF-α	Tumor Necrosis Factor alpha
WHO	World Health Organization

1 Introduction

The search for happiness in life has encouraged individuals (McMahon, 2008), as well as motivating vast works in art, such as Bronzino's (1564) *Allegory of Happiness* (Smith, 1984), in religion, such as St. Augustine's *Confessions* (397–398), and in science, such as Aristotle's *Nicomachean Ethics* (350 BC) and Epicurus' *Principle Doctrines* (341–270 BC). Scientifically, well-being research was for long mostly concentrated on correlates and predictors of life satisfaction (Bortner & Hultsch, 1970; Diener & Diener, 1995). Only much later has its possible health effects gained attention (Danner et al., 2001; Darling et al., 2012; Koivumaa-Honkanen, 1996–2012). Nowadays, mortality and morbidity, as well as individual, societal, and financial costs due to mental health problems have increased for several reasons (Murray et al., 2012). Thus, knowledge of the health effects of subjective well-being (SWB) has made it a more relevant research focus in health sciences.

Mental health has been conceptualized as a renewable resource, closely interwoven with physical health. One of its main dimensions is SWB, which has two key indicators, i.e. life satisfaction and happiness (Headey et al., 1993; Horley, 1984, Vaillant, 2003). Life satisfaction, measured with a short four-item life satisfaction scale (LS) modified by Allardt (1973), has been noted as a health predictor associating, for instance, with psychiatric morbidity and total mortality (Koivumaa-Honkanen, 1998; Koivumaa-Honkanen et al., 2000 & 2004a & b; Härkönen, 2012) among the general population. Among psychiatric and somatic patients, life satisfaction (LS) has been found to be a valid tool in measuring treatment efficiency (Koivumaa-Honkanen et al., 1999), also reflecting the recovery process among patients with depression (Koivumaa-Honkanen et al., 2001a & 2008) and surgical treatment (Sinikallio et al., 2009 & 2011). Nowadays, the role of individuals in maintaining and promoting health has strengthened (Pietilä, 2010). Subjectively assessed life satisfaction could be an important measure in health promotion and in illness prevention (Koivumaa-Honkanen, 1998; Koivumaa-Honkanen et al., 2002 & 2004b). It has been also associated with a reduced need for health care and thus also with reduced health expenditures (Kim et al., 2014).

Thus, in health promotion and the prevention of poor mental health, positive mental health and the availability of mental resources should be focused on (Vaillant, 2003). This may enable the adequate coping and adaptation of individuals and reduced societal costs of poor mental health (Michaud et al., 2001; Luppa et al., 2007; WHO, 2010). Positive and negative emotions are known to also affect performance in cognitive tasks (Ashby et al., 1999; Anderson et al., 2006; Osaka et al. 2013; Sakaki et al., 2014a & b). In addition, SWB has been reported to be one of the most important goals of psychiatric outpatients during the recovery process (Jormfelt, 2010; Zimmerman et al., 2006). The reduction of adverse mental symptoms was not enough for these patients, as they wanted to return to their former selves.

In order to promote health and facilitate the recovery process of patients, research on life satisfaction and its health effects is needed. Its clinical aspects as well as its biological correlates – concurrent or longitudinal – should be investigated. The studies of this thesis aimed at assessing the determinants and predictors of both concurrent and long-term life satisfaction using both general population and patient samples.

2   Concepts of well-being

Researchers have offered multiple meanings for what constitutes a good life (Hill, 1993; Ryff et al., 2004). Empirical research on well-being was launched in the 1960s via an interest in researching the quality of life in America (Campbell et al., 1976). Subsequently, research on SWB has proliferated (Diener et al., 1999) and diverged into two distinct but related constructs of Aristotelian **eudaimonic** and Epicurean **hedonic** well-being (Keyes et al., 2002; Dodge et al., 2012; Ryff et al., 2004). The eudaimonic tradition highlights positive psychological functioning and human development (i.e. purpose in life, personal growth). The hedonic tradition deals with cognitive assessment of life satisfaction and constructs of happiness due to positive affect and low negative affect.

SWB has been seen as a fascinating but elusive concept (McDowell & Newell, 1987). The literature is concerned with how and why people experience their lives in the ways they do, including both cognitive judgments and affective reactions (Abbey & Andrews, 1984). The definition of life satisfaction basically relies on the standards of a respondent to determine what comprises his or her experience of a good life, e.g. Freud's concept of communal life as the ability to work and power to love (Freud, 1930). However, the way in which satisfaction with specific domains of one's life is assessed tends to depend on the culture and the way one's life is structured (Diener, 1984). Thus, the various concepts of SWB should not be regarded as rigid. Changing social circumstances tend to bring changes in the definitions of some of these concepts. Due to the rich diversity of the conceptual variety of SWB and life satisfaction, these measures can and have been approached from various points of views.

2.1   MENTAL HEALTH

Mental health is also a somewhat vague concept. The term has been used since the 11th century, including two components: state of mind and competence (Stones et al., 2011). In the 19th century, mental health was viewed as related to morality, varying between moral insanity and good character (Vaillant, 2003). The boundary between mental health and mental illness is not clear (Patil & Giordano, 2010; Bingham & Banner, 2014). Mental health has been considered as a continuum consisting of complete and incomplete mental health (Keyes, 2002). Definitions and diagnostic assessments of mental illnesses via psychiatric diagnoses have been seen to reflect the societal stand between the individual and society (Winnicott, 1963). Mental health research has traditionally had a strongly disorder-based orientation. It has mainly focused on negative affective states rather than on positive mental health states, which could have limited and biased the theories of mental health (Gillham & Seligman, 1999; Katschnig, 2006). Classically, mental illness has been defined based on the presence or absence of selected symptoms (ICD-10; DSM-5).

As early as in 1948, the World Health Organization (WHO, 1947) introduced the pioneering definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." In 2011, WHO defined mental health as a state of well-being in which an individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community. According to a statement of the Academy of Finland (1976), the concept of mental health has been regarded as a developmental process

providing an individual or group with the necessary resources to achieve the demands of life without the simultaneous appearance of negatively experienced moods of longer duration.

Mental health has also been seen as an umbrella term behind the terminology of well-being, including emotional, psychological, and social well-being (Keyes, 2002). George Vaillant (2003) viewed mental health from the concepts of positive psychology, healthy adult development (maturity), emotional and social intelligence, SWB (happiness and life satisfaction), and as in successful adaptation (resilience) and hence homeostasis in life events. The *complete mental health model* according to Gilmour (2014) combines the subjective assessment of mental health with the presence or absence of mental illness, which is then classified into six groups.

2.2 SUBJECTIVE WELL-BEING

Following World War II, the mid-1940s can be conceptualized as the beginning of the formative period in the development of **subjective well-being** (SWB) indicators (Horley, 1984). In practice, a major influence on well-being research came from gerontologists, quality of life researchers, and sociologists, who initiated surveys to determine how socio-demographic factors such as income and marriage influence SWB (Andrews & Withey, 1976; Campbell et al., 1976; Diener et al., 2003). The increase in life expectancy due to improved health care as well as due to the multidisciplinary prevention of adversities in health and life has assumedly also contributed to the growth in research into subjective well-being.

SWB has been seen as a broad category of phenomena that includes people's emotional responses, domain satisfactions, and global judgments of life satisfaction (Diener et al., 1999). According to Horley (1984), SWB can be viewed through its indicators, i.e. life satisfaction, happiness, and morale. Vaillant (2003) later regarded only the first two as the key indicators of SWB. In general, SWB is broadly referred to as a balance between dynamic positive and negative affect, also including a more stable cognitive evaluation of life satisfaction (Andrews & Withey, 1976; Diener, 1984; Keyes et al., 2002; Metler & Busseri, 2015; Veenhoven, 1984). Studies have documented that a lack of ill-being (e.g. depressive symptoms) is no guarantee of possessing high levels of well-being (Keys et al., 2002).

2.2.1 Happiness

Historically, Aristotle (350 BC) related subjective assessment of **happiness** to the property of virtue. He defined happiness as the *summum bonum*, the supreme good, being the ultimate motivation for human action (Aristoteles, 1989). According to Saint Augustine, happiness is the result of acquired wisdom, which all human beings desire (Augustinus, 1947). McDowell & Newell (1987) stated that happiness can be viewed as transient, short-term feelings of well-being in response to day-to-day events. Thus, it would be a reflection of pleasant and unpleasant affects in one's immediate experience. However, it has not only been seen as a consequence of life circumstance, but also as a propensity (Stones et al., 2011).

2.2.2 Life satisfaction

Life satisfaction has been conceptualized as a cognitive assessment of life as a whole based on the fit between personal goals and achievements (Andrews & Withey, 1976; Campbell et al., 1976; McDowell & Newell, 1987; Pavot et al., 1991; Pavot & Diener, 1993).

It has also been referred to as a component and a crucial indicator of SWB (Horley, 1984; Vaillant, 2003) and quality of life (Moons et al., 2006). According to Diener (1984), the way in which life satisfaction and positive affect relate to one another is an empirical question, not one of definition.

2.2.3 Quality of life and welfare

Quality of life has been defined as a key outcome measure in psychiatric research, relating to both the adequacy of material circumstances and people's feelings about these circumstances (McDowell and Newell, 1987). Albrecht and Devlieger (1999) stated that quality of life is more than just objective measures. It is proposed to be dependent upon finding a balance between body, mind, and spirit in the self, establishing and maintaining a harmonious set of relationships within the person's social context and external environment (Moons et al., 2006).

Relating to this, the concept of perceived **welfare** is similar to the concepts of mental health and happiness. It can be further defined according to either needs or resources. According to Allardt (1973), welfare is perceived as a multidimensional phenomenon composed of several dimensions of values, including *having*, *loving*, and *being*, which are based on the *needs* of individuals. Needs can be divided into three groups, including material needs, social needs, and needs related to self-fulfillment (Allardt, 1975). Welfare would be experienced when one's needs are being met. Thus, the aspect of resources claims that experience of welfare arises from an individual's feeling of being able to control his or her central resources.

2.2.4 Other concepts of well-being

Morale is said to refer an individual's mental orientation as the level of individual psychological well-being based on such factors as a sense of purpose and confidence in the future. According Horley (1984), the concepts of morale, happiness, and satisfaction have something in common, but they do point to discrete terms. **Morality** is also a different concept, being defined as "population conformity to ideals" (Cattell & Gorsuch, 1965). Societally, positive SWB has been associated with the character of a good society and a good life in it (Diener et al., 2003). Likewise, the morale of an individual has been considered to relate to morale in the organization (Cattell & Gorsuch, 1965).

3 Measures of subjective well-being and life satisfaction

Through history, there has been much discussion about whether well-being constitutes an objective dimension, subjective dimension, or both (Andrews & Withey, 1976). Objective dimensions refer to observable life conditions or physical functioning that can be operationalized by tests. On the other hand, subjective dimensions refer to the respondent's perception. The development of well-being measures has progressed from early social surveys looking for external indicators of well-being (Andrews and Withey, 1976; Campbell, 1976) to the measurement of subjective well-being and its dimensions.

   Self-reported measures of well-being have been shown to correlate moderately with each other and have adequate temporal reliability, factor invariance, internal consistency, and sensitivity to change (Atkinson, 1982; Diener, 1984). However, critical concerns over the use of SWB indicators and their interpretation have been presented in relation to their conceptual clarity and consistency. Various single and multi-item approaches have been applied to define SWB, how a person senses and assesses it, which factors have an influence on it, and how well-being should be measured. Regardless of the variety, no specific measurement has been chosen as the golden standard for life satisfaction or SWB.

   A classic one-item scale to measure global well-being was developed by Andrews and Withey (1976), including a single question: "How do you feel about your life as a whole?" Fordyce (1988) created a similar scale concerning happiness and the proportion of time the respondent feels happy or unhappy (Diener, 1984). It mainly reflected emotional well-being instead of a cognitive judgment of life as a whole. The *Cantril Ladder of Life* (LOL) assesses respondents' life satisfaction with three separate one-item self-reports indicating life satisfaction in the past, present, and future. Ratings are based to a 10-point scale ranging from "best possible life" to "worst possible life", thus providing a global rating of life satisfaction (Cantril, 1965).

   Despite the obvious advantages of brevity, single-item scales have been criticized. According to Diener (1984), life satisfaction may be indirectly influenced by affect, but it is not itself a direct measure of emotion, like happiness. The specific wording of the scale may pose difficulties in comparing single-item measures with each other. Scores for single-item scales scores are often skewed, with most responses falling in the "happy categories" (Andrews & Withey, 1976). These short scales may also be more sensitive than multi-item scales to contextual effects from the preceding questions in a survey (McDowell, 2010), exposing them to less reliability over time than multi-item scales. Despite these arguments, single-item life satisfaction measures have been defended as performing very similarly compared to the frequently used multi-item *Satisfaction with Life Scale (*SWLS*)* (Cheung & Lucas, 2014).

   In the 1960s, emotional well-being was seen as a cluster of symptoms reflecting the presence or absence of positive feelings about life. According to the suggestion of Bradburns (1969), happiness was viewed as a global judgment people make by comparing their negative affect with their positive affect. This resulted in the *Affect Balance Scale* (ABS). Bradburn concluded that positive and negative affects are independent. Thus, the enhancement of well-being requires both a reduction in negative affect and an increase in positive affect. Bradburn's statements sparked a controversy in the field of well-being and were not unquestionably replicated later, but the independence of positive and negative affect have subsequently been accepted (e.g. Diener & Emmons, 1984).

The 5-item World Health Organization Well-Being Index (WHO-5) is a popular and widely used questionnaire assessing subjective psychological well-being (Topp et al., 2015). Global life satisfaction can be assessed by asking about well-being without identifying any causal factors or any concrete circumstances leading to life satisfaction. According to this, the subjective judgment of life satisfaction seems not to be based on feelings but more on the attitude to one's life. A few national-level studies have introduced their own measures of life satisfaction, such as Allardt (1973; a 4-itemed *Life Satisfaction scale (*LS*)*, Scandinavian countries), Andrews & Withey (1976; 1-itemed *"How do you feel about your life as a whole?"* USA), Atkinson (1982; Canada) and Campbell et al. (1976; 1-item *Overall life satisfaction,* USA; 2004, Britain and USA), and Headey (1981; a 5-item *Satisfaction with Life Scale* & 1-temed *Fordyce 0-10 Happy Scale,* Australia), some to be mentioned.

Multi-item tools measuring life satisfaction and subjective well-being represent the domain-specific evaluation of multiple facets of life experiences. This is seen in measures of social indicators of the quality of life (Andrews & Withey, 1976) and in the multi-item *Affectometer 2* (40-item), which was developed in 1983 from the *Affectometer 1* (96-item) to include various aspects of positive well-being (Kammann & Flett, 1983; Tennant et al., 2007). This approach to measuring global life satisfaction is problematic, since the sum score is a sum of domain-specific satisfactions rather than an indicator of life as a whole. As Veenhoven (1984) stated, "…arbitrary definitions of life satisfaction may reflect the investigator's idea on what life ought to be rather than how people actually appreciate their life." The variety of multi-item well-being scales may also cause difficulties in comparing the findings across samples when using different age groups and scales. Furthermore, some multi-item scales have been designed, for example, as geriatric measurement tools and are not recommended for younger or middle-aged respondents (Diener, 1984).

The five-item SWLS (Diener et al., 1985) was designed for general survey research and originally comprised 48-items to reflect life satisfaction and well-being (Pavot & Diener, 1993), but due to a reduction in the number items, it was explicitly designed to measure cognitive judgments of life satisfaction rather than affect. The *Life Satisfaction Index A* (LSI-A; 20-items) and *Life Satisfaction Index B* (LSI-B; 12 items) (Neugarten et al., 1961) conceptualize life satisfaction as a person's evaluation of his or her current life with reference to him- or herself, others, the context, and the time dimension.

4 Life satisfaction

4.1 DETERMINANTS OF LIFE SATISFACTION

Previous research on SWB has extensively investigated the concepts, relationships, and correlates of well-being, life satisfaction, and happiness, mostly with cross-sectional study designs. Well-being research has later been extended and has also used longitudinal designs. The complex relationship of SWB and somatic health has become evident.

4.1.1 Sociodemographic factors

Research on well-being and standard demographic or social variables (e.g. age, gender, race, education, income, marital status) has shown only modest relationships with most self-assessments of life quality (Abbey & Andrews, 1984). Findings of **gender** differences in global happiness or satisfaction have been discordant (Andrews & Withey, 1976; Campbell et al., 1976, Diener, 1984). Along with this, the effect of parenthood, i.e. having **children**, on subjective well-being has been observed to be heterogeneous (Galatzer-Levy et al., 2011). According to Campbell (1976), older people tend to report greater satisfaction in most life domains, except health. In a study of SWB among primary health care patients, an older age, higher educational level, and a lack of depressive or affective symptoms were associated with increased happiness (Ozcakir et al., 2014). Among an elderly study population in Finland, mid-life satisfaction and retirement were followed by life satisfaction in later life (Härkönen, 2012). On the other hand, the intensity of negative emotions associated with an individual's memory of an event in a certain moment of time has been noted to fade to a greater extent over time than positive emotions (Muir et al., 2014; Szpunar et al., 2012). Positive emotions appear to have a greater effect on the aging brain than on the young CNS (Mather, 2012). Diener (1984) proposed that young people might appear to experience higher levels of joy, whereas older people tend to judge their lives in more positive ways. However, according to the 15-year follow-up data of the Finnish Twin Cohort Study, there was no marked difference in mean life satisfaction scores between age or gender groups (Koivumaa-Honkanen et al., 2005). The effect of **age** or gender on life satisfaction and happiness has been more elusive (Mehlsen et al., 2003) than subjectively assessed **income** and **economic status**, which have been more consistent correlates of life satisfaction among both population-based (Diener, 1984; Marum et al., 2014; Kapteyn et al., 2013) and psychiatric patient samples (Koivumaa-Honkanen et al., 1996 & 1999). Nevertheless, subjective life satisfaction does not equate with objective life status (Lingjiang et al., 2010). The effect of income on SWB is not unequivocal. A high income appears to improve the evaluation of life, but not emotional well-being (Kahneman & Deaton, 2010). According to a general social survey study in the United States, the increased wealth of an adult cohort did not improve well-being (Easterlin, 2001). On the contrary, materialism was found to correlate significantly and negatively with well-being in a meta-analysis studying the relationships between individuals' materialistic orientation and well-being (Dittmar et al., 2014). Likewise, increasing wealth and material prosperity among Western countries during past decades has not increased the national life satisfaction (Blanchflower & Oswald, 2004). However, **employment** has been noted as an important contributor to well-being, also facilitating access to social

networks (Huppert & Whittington, 2003). Life dissatisfaction has additonally been associated with increased costs due to absence from the workplace (Wright et al., 2002).

4.1.2 Social support

People with greater well-being appear to invest more in prosocial behavior, which in turn promotes positive well-being (Thoits & Hewitt, 2002). Life satisfaction has been strongly correlated with **personal relationships** and **social support** among general (Lacruz et al., 2011; Stansfeld et al., 2013; Strine et al., 2009) and patient populations (Koivumaa-Honkanen et al., 1996 & 1999). The same applies to **social situations** such as living with a partner (Koivumaa-Honkanen et al., 1996 & 2000; Kroenke, 2008; Hammaström et al., 2011). **Marital status**, its quality and its changes have been associated with quality of life (Lucas et al., 2003; Sung & Yeh, 2007; Trivedi et al., 2006) and life satisfaction (Evans & Kelley, 2004; Kinnunen & Pulkkinen, 2003).

4.1.3 Childhood adversities

In retrospective general population studies, the association of **childhood hardship** and a later poor health status in adulthood, including depression, anxiety disorders, psychological distress, and early disability retirement, has previously been reported (Brown & Harris, 1993; Coyle et al., 2014; Harkonmäki et al., 2007; Iversen et al., 2007; Kessler et al., 1997; Lacey et al., 2014; Molnar et al., 2001). Indeed, the most powerful childhood predictor of adult life satisfaction has suggested to be the child's emotional health (Layard et al., 2014). Retrospectively, the quality of **paternal care** and adult quality of life (Rikhye et al., 2008), as well as childhood **physical abuse** and adult life dissatisfaction, have also been linked (White et al., 2007). Childhood experiences, such as **parental problem drinking** and **family disharmony**, have predisposed to significant mental health consequences among children, which have persisted far into adulthood (Balsa et al., 2009; Braithwaite & Devine, 1993). The more difficult and chronically adverse these childhood experiences are, the more profound effects these experiences may have on the developing personality (Korkeila et al., 2004; Winnicott, 1956 & 1963). Nevertheless, research concerning the impact of family history and traumatic childhood experiences on life satisfaction is scarce, particularly in the general population.

4.1.4 Personality features

Personality refers to individual differences in characteristic patterns of thinking, feeling, and behaving (APA, 2015). **Personality disorders** are characterized by impaired interpersonal functioning. The DSM-5 defines personality disorder as "an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment" (APA, 2013). **Personality traits** are defined as "enduring patterns of perceiving, relating to, and thinking about the environment and oneself that are exhibited in a wide range of social and personal contexts" (APA, 1994). To cope with life adversities, well-functioning mental defenses and coping mechanisms are needed (Elliot et al., 2011; Vaillant, 2012).

   Interest has grown in studying the relationships between personality and SWB (Appelberg et al., 1991; Anusic et al., 2014; Sheldon et al., 2015; Tanksale, 2015). Personality features and life circumstances can markedly influence the levels of SWB (DeNeve & Cooper, 1998; Diener et al., 2003). **Optimism,** being linked with SWB, is also linked with better physical health (Carver et al., 2010). **Sense of coherence,** i.e. the ability to cope with

stress in a meaningful and understandable way (Antonovsky, 1987), has a strong correlation with life satisfaction (Sagy et al., 1990; Suominen, 1993).

The personality trait **alexithymia**, an inability to recognize and verbalize emotions (Sifneos, 1972), has been associated with life dissatisfaction in population-based studies (Honkalampi et al., 2000 & 2004; Mattila, 2009; Shibata et al., 2014), as well as in samples of primary health care patients (Mattila et al., 2007), depressive outpatients (Honkalampi et al., 1999), and college students (Le et al., 2002). Alexithymia has also been characterized as a poverty of imagination or of a fantasy world (Haviland & Reise, 1996), having associations with several psychiatric (Taylor, 2000) and physical illnesses (Lumley et al., 1996).

Even though it has been suggested that personality plays an important role in the construct of global SWB and life satisfaction of an individual, the role of personality disorder in life satisfaction is a less studied area. After all, life satisfaction is an indicator of good mental health, which includes good personality qualities or capacities such as better than average functioning, abilities to use one's positive qualities, resources and coping mechanisms, resilience, personal maturity, emotional and social intelligence, as well as factors such as the capacity for love and hope (Vaillant, 2003; 2012).

4.1.5 Health behavior

Health behavior has been demonstrated to associate with life satisfaction. In Finland, this inverse relationship has been shown with heavy drinking of alcohol and current **smoking** among a general population sample (Koivumaa-Honkanen et al., 2001b), whereas a moderate alcohol intake has been suggested to be linked with better self-reported health (Poikolainen et al., 1996). Among a Finnish patient population, the relationship between life dissatisfaction and both **alcohol consumption** and smoking was dose dependent (Koivumaa-Honkanen et al., 1996). Elsewhere, smoking (Yawson et al., 2013; Bogdanovica et al., 2011) and **physical inactivity** have also been related to life dissatisfaction (Grant N et al., 2009; Department of Health, UK, 2004; Strine et al., 2008a&b). **Health stress** and stressful life changes, in addition to **poor quality of sleep**, were linked with lower life satisfaction among midlife Caucasian women (Darling et al., 2012). **Dietary intake** may also have the potential to influence well-being (Rooney et al., 2013). **Nutritional habits**, i.e. consuming a diet rich in fruits and vegetables, have been linked with well-being (i.e. flourishing) among a sample of university students (Conner et al., 2014). In longitudinal settings, adverse alcohol consumption and life dissatisfaction have predicted each other with a dose-response pattern (Koivumaa-Honkanen et al., 2012). Poor sleep predicted life dissatisfaction in the Finnish Twin Cohort Study (Paunio et al., 2009). Quitting of smoking has improved quality of life and well-being (Piper et al., 2012). Longitudinal studies are still needed to enrich knowledge in this field.

4.1.6 Mental health

Globally, mental health disorders are the leading cause of the disease burden (WHO, 2010), with a 38% increase between 1990 and 2010 (Whiteford et al., 2013). Nowadays, over 38% of the European Union population has claimed to suffer from a mental disorder (27% in 2005) (Wittchen et al., 2011). The increase in psychiatric morbidity, especially among young people, has mainly taken place due to an increase in mood disorders and alcohol-related disorders. Indeed, major depressive disorder (MDD) has accounted for 8.2% of global years lived with disability (YLDs), also being a leading cause of disability adjusted life years (DALYs) (Ferrari et al., 2013) and an increasing economic burden worldwide

(Michaud et al., 2001; Üstûn et al., 2004, Luppa et al., 2007). It is also a contributor to the burden allocated to suicide and ischemic heart disease (Ferrari et al., 2013).

Life dissatisfaction is strongly associated with poor mental health. Psychiatric inpatients have lower life satisfaction than any other inpatient group (Koivumaa-Honkanen, 1998). The internalized stigma of the illness in psychiatric outpatients has also been negatively related with SWB (Pérez-Garin et al., 2015). In general, psychiatric comorbidities and the duration of a disorder have an inverse relationship with life satisfaction (Meyer et al., 2004). Life dissatisfaction was strongly associated with hopelessness in a population-based sample (Haatainen et al., 2004), but especially with mood disorders in both patient (Koivumaa-Honkanen et al., 2001b & 2008) and general population samples (Headey et al., 1991; Strine et al., 2009). In the recovery from mental illness, especially from depression, the aspects of positive psychology, e.g. life satisfaction and happiness, could have a major role (Schrank et al., 2014).

4.1.7 Depression

Depression is a common mental disorder worldwide, characterized by sadness, feelings of guilt or low self-worth, loss of interest or pleasure, feelings of tiredness, disturbed sleep or appetite, and poor concentration (Appendix I). These severe and persistent symptoms in major depressive disorder (MDD) can lead to impairments of important social roles and increased mortality (Angst et al., 2013; Kessler et al., 2003; WHO, 2012). Difficulties in recognition and the high rate of inadequate treatment of depressive disorders are a serious problem (WHO, 2012). Nevertheless, it has been estimated that over 16% of the population could be affected by MDD at some point during the life time of an individual (Kessler et al., 2005).

In psychiatric patients, depression and poor self-rated health have been shown to be strongly correlated to life dissatisfaction (Koivumaa-Honkanen et al., 1996). Patients with depression have reported that their primary aim is to attain changes that indicate good mental health, not only a reduction in adverse mental symptoms (Zimmerman et al., 2008). Thus, life satisfaction is an important goal for the treatment outcome (Jormfeldt, 2010; Ravindran et al., 2002; Rutz, 2006; Zimmerman et al., 2006 & 2008). The recovery process can also be measured by it (Koivumaa-Honkanen et al., 2008). Eventually, depressive patients along with psychiatric treatment can reach the level of life satisfaction of the general population (Koivumaa-Honkanen, 1998; Koivumaa-Honkanen et al., 2008), but this may take time (Koivumaa-Honkanen et al., 2008). A rapid recovery from depression and short treatment period did not guarantee either a sustained absence of symptoms or life satisfaction in a 6-year follow-up.

In general population studies, a strong association has also been found between depressive symptoms, low self-rated health, and life dissatisfaction (Härkönen, 2012; Strine et al., 2009; Sabatini, 2014). Allardt's Life satisfaction scale (LS) was able to identify individuals with a high risk of having or developing depressive symptoms among those categorized as healthy in a large sample of the general population (Koivumaa-Honkanen et al., 2004a).

4.1.8 Somatic health and biological factors

Life satisfaction is closely linked with **health status, limitations**, and **disability** (Diener, 1984; Härkönen 2012; Bellis et al, 2012; Strine et al., 2008). A better physical status (i.e. cardiopulmonary endurance, muscular strength, muscular endurance, flexibility, and explosive muscular strength) was significantly associated with life satisfaction in a large sample of Korean workers (Yoo et al., 2015). In elderly women, life dissatisfaction has been

related to osteoporosis and longitudinally with bone loss (Rauma et al, 2014), but also to **obesity** and physical inactivity, both of which may also serve as mediators in pathogenesis of somatic diseases (Strine et al., 2008). The association between life satisfaction and chronic pain was observed to be strongly negative in a large Australian survey (McNamee & Mendolia, 2014). Life dissatisfaction (LS) also negatively affects recovery from lumbar spinal stenosis surgery (Pakarinen et al., 2014). More generally, SWB may be linked with variety of health risks, either independently or mediated by social and health behavior, or through unmeasured latent factors such as hostility and coping strategies. In addition, it can affect psychological and behavioral responses to disease symptoms and the use of health care (Kirana et al., 2009).

Thus, life satisfaction is considered to have a major role in the pathogenesis of psychological and also somatic morbidity processes. However, research on the mechanisms and pathways underlying this relationship is needed, including the link between inflammatory factors, life satisfaction, and its associates (Steptoe et al., 2012). As early as in the 1980s, Diener (1984) suggested that hormonal and other biological events could mediate mood and SWB at some level.

According to the literature, **biological** processes are linked with affects (Dockray & Steptoe, 2010) and SWB (Jacobs et al., 2007). The brain is a plastic and dynamic organ and its functions are linked with emotions, as well as with SWB (Kong et al., 2014). Cytokines, chemokines, and damage-associated soluble mediators of systemic inflammation have access to the CNS via blood flow, and thus may break the balance in brain homeostasis. This, in turn, may result in cognitive and behavioral manifestations, which may even become permanent (Sankowski et al., 2015). The relationship between **psychosocial stress**, depression, and **inflammation** has been shown to be involved at both systemic and CNS levels (Berk et al, 2013). Among aging women, higher levels of eudaimonic well-being, including self-development, personal growth, and purposeful engagement, were related to lower levels of daily salivary cortisol, pro-inflammatory cytokine IL-6, cardiovascular risk, and a longer duration of REM sleep (Ryff et al., 2004). In an English longitudinal study on ageing, well-being was noted to relate to a low level of the inflammatory marker hs-CRP in women and to low **central adiposity** in men (Steptoe et al., 2012).

A variety of previously mentioned risk factors of depression are associated with inflammation, such as cardiovascular disorder (CVD) (Maes et al., 2011) and poor health behavior, including poor sleep (Friedman, 2011; Motivala et al., 2005; Rohleder et al., 2012), diet and thus obesity (Berk et al, 2013). **Stressful life changes**, **health stress**, a high **body mass index** (BMI) and poor sleep have also been related to lower life satisfaction (Darling et al., 2012). Life dissatisfaction has also been shown to be associated with **coronary heart disease** (Boehm et al., 2011), which additionally has an inflammatory pathogenesis (Kaptoge et al., 2013; Jung et al., 2012). More generally, the activation of inflammatory and cell-mediated immune pathways has been found across major psychiatric disorders (Berk et al., 2014).

Altogether, evaluation of the inflammatory state with regard to SWB and self-reported life satisfaction is one step further in understanding the pathogenesis of somatic morbidity. In general, due to the lack of an integrated model for conceptualizing modifiable risk factors for poor health, including psychiatric disorders, the primary prevention strategies are not coherent and the focus is on the treatment of established disorders.

4.2   DISTRIBUTION OF LIFE SATISFACTION

Globally, human beings appear to be quite satisfied with their lives (mean 6.6, scale 0 to 10), but regional differences exist (http://www.oecdbetterlifeindex.org/topics/life-satisfaction/). Across OECD countries, 76% of people reported having more positive experiences in an average day than negative experiences. It has been assumed that economic conditions, cultural factors, and other contextual characteristics play a role in the differences in country-specific levels of SWB (Diener et al., 2003; Kim et al., 2012; Margolis & Mysrkylä, 2013). Since higher SWB is also linked with many desirable consequences at the national level, national data on SWB would provide valuable information to policymakers on the effectiveness of their policies in improving overall societal well-being (Diener et al., 2015).

The mean life expectancy is considerably higher in developed than developing countries, which challenges the comparison of their national level of well-being and age. According to data from the World Values Survey (Margolis & Myrskylä, 2013), the least developed regions have both higher income inequalities and lower average levels of SWB compared to Western Europe and Anglophone countries. However, the differences between nations in SWB are predicted not only by economic development, but also by factors such as environmental health, social capital, equality, and freedom in nations (Diener & Tay, 2015; Jorm & Ryan, 2014).

4.3   STABILITY OF LIFE SATISFACTION

SWB has been reported to have both stable and changing components. Variation in the individual level of SWB and life satisfaction has been under research (Cummins, 2015; Fujita et al., 2005, Lykken & Tellgren, 1996). In individuals with stable life satisfaction, this level may be higher than among those with less stable life satisfaction. One's hedonic level of happiness is affected by life circumstances and changes in life. On the other hand, genetic factors also play a role in SWB (De Neve et al., 2012; Franz at al., 2011; Koskenvuo et al., 2000, Stubbe et al., 2005).

Long-term SWB is likely to have considerable stability (Atkinson, 1982; Costa et al., 1987; Lu, 1999; Pavot et al., 1993). This stability has led to study of the interaction between internal factors (personality traits) and external circumstances. In parallel to previous studies on SWB, life satisfaction could be affected by momentary judgments, as well as personality characteristics (Schimmack et al., 2002). In the large Finnish Twin Cohort, the 4-item life satisfaction scores (LS, range: 4–20) had moderate stability in a follow-up of 15 years. Only 5.9% of the study subjects changed from being satisfied to dissatisfied, or vice versa (Koivumaa-Honkanen et al., 2005). The chronically dissatisfied subjects were susceptible to disadvantages and comorbidities, but they were easily identified with the LS score.

The life satisfaction (LS) of psychiatric in-patients is lower than in any other patient group (Koivumaa-Honkanen, 1998). Among depressive outpatients (Koivumaa-Honkanen et al., 2001a), the mean level of LS of the patients remained lower than in a general population sample during a one-year follow-up. However, it improved later along with psychiatric treatment, concurrently with recovery, and reached the levels of life satisfaction in the general population in a 6-year follow-up (Koivumaa-Honkanen et al., 2008).

4.4   LIFE SATISFACTION AS A PREDICTOR OF HEALTH

SWB has been associated with good long-term health outcomes (Danner et al., 2001). In follow-ups of 15–20 years, self-reported life dissatisfaction (LS) has predicted various adverse mental outcomes in the general population, such as morbidity (Koivumaa-Honkanen, 1998), premature work disability both due to somatic and psychiatric causes (Koivumaa-Honkanen et al., 2004b), and mortality (Koivumaa-Honkanen et al., 2000), including suicides (Koivumaa-Honkanen et al., 2001b) and fatal unintentional injuries (Koivumaa-Honkanen et al., 2002). Longitudinally, life dissatisfaction has been related to several forms of adverse alcohol use (Koivumaa-Honkanen et al., 2000; 2001b; 2004b; 2012), unfavorable self-rated health, and poor social support (Koivumaa-Honkanen et al., 2000). Recently, life dissatisfaction was also shown to predict bone loss in a 10-year follow-up of aging women (Rauma et al., 2014). Among the seriously mentally ill, SWB and hope in human life have been found to be related (Werner et al., 2012). Hope has been considered as a healing force also promoting well-being in other patient groups (Spiegel et al., 1989; Penson et al., 2007).

5 Aims of studies I–IV

I To investigate differences in life satisfaction and its concurrent correlates at baseline and at the final 6-year follow-up in depressive outpatients.
To determine which baseline factors are associated with subsequent life satisfaction at the end of the follow-up in depressive patients.

II To examine the sociodemographic and mental health indicators of life dissatisfaction in a general population sample with a broad range of factors, including less studied areas such as personality disorders and childhood adversities.

III To assess how the long-term life dissatisfaction burden is longitudinally associated with subsequent poor mental health, including major depressive disorder, in a general population sample.

IV To explore biological (incl. inflammation markers) and other health-related correlates of the long-term life dissatisfaction burden in a general population sample.

6 Subjects and methods

Study I included a sample of depressed patients (Viinamäki et al., 2002) recruited in the Kuopio Depression Study (KUDEP) at the beginning of 1996 and followed up until 2004 with several data collections (cf. later). It had both a cross-sectional and a longitudinal design. Studies II–IV were conducted on a sample of the general population derived from a follow-up study performed in Kuopio between 1998 and 2005. Study II was based on a cross-sectional setting in 2005. The naturalistic follow-ups of studies III–IV were performed in 1998–2005. Background characteristics of the samples are presented in Table 1.

Table 1. Background characteristics of the samples (Studies I–IV).

	Study I$_{1998}$	Study II$_{2005}$	Study III$_{2005}$	Study IV$_{2005}$
N	121	328	330	305
Gender, female (%)	62.0	57.9	57.0	57.4
Age, mean (SD)	44.8 (9.2)	55.7 (9.6)	55.8 (9.5)	56.2 (9.5)
Living alone (%)	29.8	14.9	14.8	14.4

6.1 PATIENTS WITH DEPRESSIVE DISORDER (Study I)

The Kuopio Depression Study (KUDEP) involved 203 consecutive outpatients (84 men, 119 women) from the eastern part of Finland who were referred to the psychiatric clinic of Kuopio University Hospital (KUH), which provides psychiatric services for a population of 200 000. The baseline sample was collected between 1996 and 1998. The patients were included in the study principally if their psychiatrist subsequently suspected or diagnosed depression (Viinamäki et al., 2000). Thus, patients were referred to the outpatient unit from another department of the same hospital (53%) or the occupational health service (14%), by general practitioners in public health centers (14%) or private physicians (9%), or they came to the outpatient unit without referral (10%). The inclusion criteria were that the patient suffered from at least one specific mood disorder (F31.3-5; F32, F33, F34, and F41.2) according to the ICD-10 diagnostic classification (WHO, 1992). Exclusion criteria were severe somatic disease such as central nervous system (CNS) disease, recent myocardial infarction, or sequelae of stroke. Those with alcohol or drug dependency, with a marked deficiency in cognitive capacity, or with other serious mental disorders, such as schizophrenia or other psychosis, were excluded from the study population, but patients with major depressive disorder (MDD) with psychotic symptoms were included. The existence of other somatic diseases was not regarded as a criterion for exclusion if the patient was well looked after by the doctor responsible for treatment and if the treatment balance had been achieved as far as possible (Viinamäki et al., 2000). At baseline, ten patients refused to participate in the study and five patients (3%) were excluded because of central nervous system diseases (e.g. Alzheimer's disease). No information on these patients was collected. Thus, the baseline sample consisted of 185 subjects who provided written informed consent.

The baseline questionnaire included questions on sociodemographic background, health behavior, quality of familial and social life, and family history, as well as self-assessed psychometric scales. Participation in this naturalistic follow-up did not affect the standard psychiatric treatment of the study subjects. Treatment methods such as drug treatment, individual psychotherapy, and family therapy were used in a combination that the attending psychiatrist working with a multiprofessional team assessed as the best for each individual patient (Koivumaa-Honkanen et al., 2008). The Ethics Committee of KUH and the University of Kuopio approved the study protocol.

To add diagnostic reliability at baseline (1996) and during the follow-up (2004), the Structured Clinical Interview for DSM-III-R (SCID-I) was conducted (Viinamäki et al., 2006). It was also confirmed during the SCID interview that no organic factor or somatic disease had initiated and maintained the depressive syndrome. At baseline, all 185 patients were diagnosed to have depression according to the ICD-10. According to the SCID-I for DSM-III-R, 135 (73%) of the study subjects had MDD, 25 (14%) another type of depression, mainly dysthymia or adjustment disorder, and 19 (10%) had depressive symptoms but did not meet the criteria for diagnosis according to DSM-III-R in SCID.

Data collection took place at baseline (T1, N = 185) and on follow-up after 0.5 years (T2, N = 148, i.e. 80%), 1 year (T3, N = 161, i.e. 87%), 2 years (T4, N = 148, i.e. 80%), and 6 years (T5, N = 121, i.e. 65%). The final dropout rate was 35% (64). Out of the final study sample (N = 121) who attended the whole 6-year follow-up, 72% (87) suffered from major depressive disorder (MDD), one subject (1%) had bipolar disorder with depressive episodes, and 12% (33) had dysthymia or another diagnosis indicating depressiveness at baseline. Their mean age was 44.8 years (SD 9.2; range 22–63) at the baseline. After 6 years of follow-up (T5), 16% of the study subjects had major depressive disorder (MDD), while 84% had no diagnosis indicating current depression (Figure 1).

Figure 1. The design and flow chart of the depressive outpatients during the naturalistic 6-year follow-up according to the diagnosis (Study I).

6.2   GENERAL POPULATION-BASED SAMPLE (Studies II–IV)

Studies II–IV were based on the longitudinal KUDEP among a sample of the general population. The study population (N = 3004) living in North Savo, aged 25–64 years, was randomly selected from the National Population Register. At baseline, a study questionnaire that included questions on sociodemographic variables and health behavior, as well as self-assessed psychometric scales, was mailed in 1998 (T1) with a response rate of 68% (N = 2050). Two subsequent similar health questionnaires were mailed in 1999 (T2) (N = 1722) and 2001 (T3) (N = 1593). A total of 1347 (45%) study subjects responded to all the three data collections. In 2005 (T4) (i.e. seven years after the baseline), a sub-sample (n = 427) of the subjects was invited for clinical evaluation, including a similar questionnaire. The study protocol was approved by the Research Ethics Committee of KUH and the University of Kuopio. All subjects provided written informed consent before entering the study.

The inclusion criteria for the 2005 sub-sample were based on the presence or absence of previously self-reported adverse mental symptoms during 1998–2001. The following cut-offs (based on the distribution of the sample) were used: **BDI-21** score > 9 (Beck et al., 1961; Beck et al., 1988), **TAS-20** score > 57 (Honkalampi et al., 2010 & 2011) or **LS-4** score > 11 (Koivumaa-Honkanen, 1998; Koivumaa-Honkanen et al., 2000). Half (N = 209) of the final study subjects fulfilled at least one of these adverse mental symptom criteria in all previous three data collection years (1998, 1999, and 2001) and formed the symptomatic group. The second half (N = 218) of the final sample comprised subjects who were asymptomatic with respect to any of these adverse symptoms during the follow-up in 1998, 1999, and 2001, but who had the same age and gender distribution compared to the symptomatic group. Finally, the participation rate in the clinical evaluation in 2005 was 78% (total N = 333) (Figure 2). This sub-sample included symptomatic [N = 164; age (mean 49.1, SD 9.1); female 58.5%] and asymptomatic subjects [N = 169; age (mean 49.3, SD 9.9); female 56.2%].

6.2.1   Study population in study II
The number of the study subjects was 333 in 2005 (cf. 6.2.). After excluding five cases with inadequate data on self-reports of life satisfaction in 2005, the final sub-sample in study II comprised 328 subjects [symptomatic 49.7% (163)] with a mean age of 56.4 years (SD 9.6) for men (N = 138; 42%) and 55.4 years (SD 9.5) for women (N = 190; 58%) (p = ns).

6.2.2   Study population in study III
The number of the study subjects was 333 in 2005 (cf. 6.2.). While assessing the long-term life satisfaction burden, three cases with inadequate data on self-reports of life satisfaction at any of the follow-up points (1998, 1999, and 2001) were excluded, and the sub-sample in study III thus comprised 330 subjects [symptomatic 48,8% (161)] with a mean age of 56.4 years (SD 9.6) for men (N = 142; 43%) and 55.4 years (SD 9.5) for women (N = 188; 57%) (p = ns).

6.2.3   Study population in study IV
The number of the study subjects was 333 at 2005 (c.f. 6.2.). After excluding 28 cases with inadequate data on laboratory measurements or any self-reports of life satisfaction in 1998, 1999, 2001, and 2005, the final sub-sample in study IV comprised 305 subjects [symptomatic 48.9% (149)] with a mean age 56.7 years (SD 9.7) for men (N = 130; 42.6%) and 55.9 years (SD 9.3) for women (N = 175; 57.4%) (p = ns).

Figure 2. The design and flow chart of the general population-based sample (Studies II–IV).

6.2.4   Study population in study II

The number of the study subjects was 333 in 2005 (cf. 6.2.). After excluding five cases with inadequate data on self-reports of life satisfaction in 2005, the final sub-sample in study II comprised 328 subjects [symptomatic 49.7% (163)] with a mean age of 56.4 years (SD 9.6) for men (N = 138; 42%) and 55.4 years (SD 9.5) for women (N = 190; 58%) (p = ns).

6.2.5   Study population in study III

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6.2.6   Study population in study IV

The number of the study subjects was 333 at 2005 (c.f. 6.2.). After excluding 28 cases with inadequate data on laboratory measurements or any self-reports of life satisfaction in 1998, 1999, 2001, and 2005, the final sub-sample in study IV comprised 305 subjects [symptomatic 48.9% (149)] with a mean age 56.7 years (SD 9.7) for men (N = 130; 42.6%) and 55.9 years (SD 9.3) for women (N = 175; 57.4%) (p = ns).

6.3   LIFE SATISFACTION SCALE (LS-4)

Life satisfaction was assessed (**studies I, II, III, IV**) with the 4-item life satisfaction scale [(**LS-4,** range 4-20), Allardt, 1973] (Table 2). The development of LS-4 was based on a quality of life questionnaire developed by the Survey Research Center of the University of Michigan (Andrews & Withey, 1976; Campbell et al., 1976). It was modified by the Finnish sociologist Erik Allardt for a comparative Scandinavian survey (Allardt, 1973). In general, the life satisfaction scale is easily administered and has been well accepted in both population-based samples (Allardt, 1973; Koivumaa-Honkanen et al., 1998; 2000; 2001; 2002; 2004; 2005; 2012) and in patient studies (Koivumaa-Honkanen et al., 1996; 1999; 2001; 2008). All the items had a significant positive correlation with the other items and the life satisfaction score (Koivumaa-Honkanen, 1998). The correlation was irrespective of sex, health status, or age group.

   The four-item life satisfaction scale includes both the subject's global cognitive (life satisfaction) and affective (happiness) assessment of life as a whole. The study subjects were asked to rate their general interest and happiness in life, ease of living, and self-perceived feelings of loneliness as follows:

Do you feel that your **life at present** is (score points in the parentheses)

1. very **interesting (1)**, fairly interesting (2), cannot say (3), fairly boring (dull) (4) or very boring (dull) (5)?
2. very **happy (1)**, fairly happy (2), cannot say (3), fairly sad (unhappy) (4) or very sad (unhappy) (5)?
3. very **easy (1)**, fairly easy (2), cannot say (3), fairly hard (severe) (4) or very hard (severe) (5)?
4. Do you feel that at the present moment you are very **lonely (5)**, fairly lonely (4), cannot say (3) or not at all lonely (1)?

The range of the total score is 4–20. A higher value for the total score represents higher life dissatisfaction. If a response was missing for at least three items, the total score was regarded as "missing data". Missing data for one or two items was scored each as a three (Koskenvuo et al., 1979).

In the **substudies** of **I–II**, the life satisfaction score was dichotomized (Koivumaa-Honkanen 1996): 4–11 = satisfied and 12–20 = dissatisfied.

In longitudinal **study III,** long-term life satisfaction (LS-4) was assessed based on item scores in 1998, 1999, and 2001. The range of the long-term life satisfaction burden score was 12–60. It was mainly treated as a continuous score, but a 3-category variable (tertiles) was also formed: the satisfied (range 12–21; N = 116; 35.2%), the intermediate (range 22–33; N = 107; 32.4%), and the dissatisfied group (range 34–60; N = 107; 32.4%).

In longitudinal **study IV,** life satisfaction (LS-4) and the long-term life satisfaction burden were calculated, but the latter included scores from 1998, 1999, 2001, and 2005 (range: 16–80). The long-term life satisfaction burden score was mostly treated as a continuous score, but a dichotomous categorization was also made based on the median score: the satisfied (range 16–33; N = 159; 52.1%) and the dissatisfied group (range 34–80; N = 146; 47.9%). The mean LS scores (95% confidence intervals) in the long-term satisfied group during the follow-up were as follows: 1998, 6.96 (6.77–7.16); 1999, 6.85 (6.61–7.09); 2001, 6.69 (6.48–6.91); and 2005, 6.45 (6.24–6.67). The respective figures for the long-term dissatisfied group were: 1998, 12.68 (12.16–13.21); 1999, 12.43 (11.87–12.99); 2001, 12.16 (11.64–12.68), and 2005, 11.14 (10.58–11.71).

Subsequently, to assess individual changes in the life dissatisfaction level during the follow-up period, the previously used cut-off point of 11/12 for the life satisfaction score was applied to categorize the subjects into the satisfied (LS: 4–11) and the dissatisfied (LS: 12–20) at baseline in 1998 and at the end of the study in 2005. After this, three different subgroups were formed according to the change in individual life satisfaction:

Group A "Stable Satisfied": LS score 1998 ≤ 11 and LS score 2005 ≤ 11; N_A = 197
Group B "Increasing Dissatisfaction": LS score 1998 ≤ 11 and LS score 2005 ≥ 12; N_B = 14
Group C "Stable Dissatisfied": LS score 1998 ≥ 12 and LS score 2005 ≥ 12; N_C = 51

Table 2. Characteristics of the life satisfaction assessments (Studies I–IV).

Study	Sample	Design$_{year}$	Life Satisfaction (LS)	LS grouping variable	N_{final}
I	Patients	Cross-sectional$_{1998\&2004}$ Follow-up$_{1998-2004}$	Dichotomized + Continuous	Satisfied (LS=4-11) Dissatisfied (LS=12-20)	121
II	Genpop	Cross-sectional$_{2005}$	Dichotomized	Satisfied (LS=4-11) Dissatisfied (LS=12-20)	328
III	Genpop	Follow-up$_{1998-2001}$	LT LS Burden(LS$_{1998}$+LS$_{1999}$+LS$_{2001}$) continuous + trichotomized (tertiles)	LT satisfied (LS$_{burd}$=12-21) LT intermediate (LS$_{burd}$=22-33) LT dissatisfied (LS$_{burd}$=34-60)	330
IV	Genpop	Follow-up$_{1998-2005}$	LT LS Burden (LS$_{1998}$+LS$_{1999}$+LS$_{2001}$+LS$_{2005}$) continuous + dichotomized (median)	LT satisfied (LS$_{burd}$=16-33) LT dissatisfied (LS$_{burd}$=34-80)	305

Patients = depressive outpatients
Genpop = general population-based
LT = Long term

6.4   OTHER VARIABLES AND MEASUREMENTS

All of the items concerning sociodemography, health behavior, and psychometric scales, as well as biological parameters in the study questionnaires I–IV are described below. However, not all the items were used in each of the studies I–IV. The exact methods and design for each study are described in detail in the original publications (Table 3).

6.4.1   Sociodemographic and health behavioral background

The baseline questionnaire of the patient **study I** included questions on **sociodemographic background** and **health behavior** to record the following variables: age, gender, marital status, having children, work status, subjective ability to work, subjective wealth, subjective health, vocational education, use of alcohol, and smoking. The subjects were additionally asked to retrospectively assess their family history with respect to happiness in the childhood home and family violence (Table 3).

In the population-based data (**studies II–IV,** Table 3), the health questionnaires for each follow-up point in 1998, 1999, 2001, and 2005 included questions on the following **socio-demographic** factors: age, gender, marital status, children, area of residence, education, employment status, subjective economic status, subjective working ability, and subjectively assessed social support. **Health behavior** questions asked about current smoking, alcohol consumption, and the quality of sleep. The health questionnaires also included self-assessments of the presence of previous physician-given diagnoses of coronary heart disease, hypertension, cancer, and rheumatoid arthritis. The presence of metabolic syndrome, which is a cluster of risk factors that include abdominal obesity, hyperglycemia, hypertension, low HDL, and high triglycerides, was diagnosed according to the modified National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) criteria. Additionally, information on the usage of oral corticosteroids, statins and nonsteroidal anti-inflammatory drugs (NSAID) was obtained from the questionnaire, as well as the register of the nationwide Social Insurance Institute.

Among the population-based sample, self-reported data on previous physician-diagnosed MDD in 1999 (**study III**) were obtained from the health questionnaire. In 2005 (**studies II–III**), the diagnoses of MDD were assessed by means of the Structured Clinical Interview for DSM-IV (SCID-I) [Spitzer et al., 1990; First et al., 2002]. Additionally, diagnoses of personality disorder (**study II**) were assessed by a trained nurse using the SCID-II for DSM-IV (Zimmerman, 1994)]. The numbers of subjects with each type of personality disorder were the following (one subject can have several disorders): 1) **Cluster A**: paranoid personality 5, schitzotypal personality 4, and schizoid personality 5 cases; 2) **Cluster B**: histrionic (hysterical) personality 3, narcissistic personality 5, antisocial personality 2, and borderline personality 8 cases; 3) **Cluster C**: avoidant personality 7, dependent personality 5, and obsessive-compulsive personality 5 cases; 4) other personality types: passive-aggressive (negativistic) personality 5 and depressive personality 6 cases. The personality disorders were analyzed as a whole due to the small sample sizes in the subgroups. Additionally, the body mass index [kg/m^2] was calculated from height and body weight measured in light clothing without shoes (Table 3).

6.4.2   Childhood parenthood circumstances (study II)

In 1999, the health questionnaire included retrospective questions on the **childhood environment**. The parental relationship, happiness of the childhood home, parenting style, corporal punishment, domestic violence against oneself (sexual and/or physical),

and alcohol consumption in the childhood home (mother and/or father) were asked about (Table 3).

Table 3. Variables (Studies I–IV).

Variable	Item	Study
Age	Continuous	I, II, III, IV
Gender	Male / female	I, II, III, IV
Marital status*	Cohabiting / non-cohabiting	I, II, III, IV
Children	≥1 / 0	I, II, III, IV
Employment status	Employed / unemployed	I, II
Area of residence	Urban / rural	II
Subjective ability to work	Able to work / unable to work	I, II, III
Subjective economic status**	Good (/fairly) / poor (/fairly)	I, II, III
Subjective health	Good (/fairly) / poor (/fairly)	I, II
Vocational education	University, college / vocational school, none	I, II
Alcohol consumption	≤Once a month / 2–3 times a month / weekly	I, II, III, IV
Smoking	Non-smoker / current smoker	I, II, III, IV
Subjective social support	Good, normal / poor	IV
Subjective quality of sleep	Good, normal / poor	IV
Coronary heart disease	No / yes	IV
Hypertension	No / yes	IV
Cancer	No / yes	IV
Rheumatoid arthritis	No / yes	IV
Metabolic syndrome (MetS)[A]	No / yes	IV
Major Depressive Disorder (MDD)	No / yes	II, III
Personality Disorder	No / yes	II
Use of oral corticosteroids	No / yes	IV
Use of NSAIDs	No / yes	IV
Use of statins	No / yes	IV
CH parental relationship	Good (/fairly) / poor (/fairly)	II
Happiness of the CH	Good / poor	I, II
CH Parenting style	Gentle / strict	II
CH Corporal punishment	No / yes	II
CH Domestic violence (sexual and / or physical)***	No / yes	I, II
CH Alcohol consumption in the CH home (mother and / or father)	No / yes	II
Body Mass Index	BMI, [kg/m^2]	Continuous

CH = Childhood Home
*Married or living with a partner / unmarried, separated or divorced, widowed, other
***Domestic violence against oneself
[A]The presence of metabolic syndrome (NCEP ATP III) based on the presence of three or more of the following (values as mg/dl are given in parentheses): fasting plasma glucose levels ≥5.6 mmol/l (≥100mg/dl), serum triglycerides ≥1.7 mmol/l (≥150mg/dl), serum high-density lipoprotein cholesterol (HDL-C) <1.0 mmol/l (<40 mg/dl) in men and <1.3 mmol/l (<50 mg/dl) in women, systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg, or waist girth >102 cm for men and >88 cm for women

6.4.3 Laboratory measurements (study IV)

In 2005, the **laboratory measurements** took place in the accredited KUH medical laboratory. The levels of **IL-6** [pg/ml], **TNF-α** [pg/ml], **high-sensitivity C-reactive protein** (**hsCRP**) [mg/l], **adiponectin** [μg/ml] and **resistin** [ng/ml] were analyzed (Table 4).

Table 4. Clinical assessments in 2005 (Study IV).

Serum adiponectin	s-Adipo [μg/ml]	Continuous
Serum resistin	s-Resist [ng/ml]	Continuous
High-sensitivity C-reactive protein	hs-CRP [mg/l]	Continuous
Tumor necrosis factor alpha	TNF-α [pg/ml]	Continuous
Interleukin 6	IL6 [pg/ml]	Continuous

In 2005, the **laboratory measurements** took place in the accredited KUH medical laboratory. Venous blood samples were drawn after a 12-h overnight fast. The samples were frozen after the blood draw, and stored at -80 °C until run. The levels of **IL-6** (pg/ml) and **TNF-α** (pg/ml) were analyzed by multiplexing with Bio-Plex Human Cytokine Panel 1, utilizing a Bio-Plex instrument based on Luminex xMAP technology (Bio-Rad Laboratories Inc., Hercules, California, USA). **High-sensitivity C-reactive protein** (**hsCRP**) was determined by an immunoturbidimetric method (Konelab CRP, code 981699; Thermo Electron Co., Finland). The samples were analyzed using a Konelab 60i clinical chemistry analyzer (Thermo Electron). **Adiponectin** and **resistin** were quantified with a human serum adipokine (Panel A) LincoPlex kit (Millipore, MA, USA) using a Bio-Plex Suspension Array System (Bio-Rad Laboratories Pty Ltd, Hercules, CA, USA). The assay conditions were controlled, standardized, and pre-optimized to ensure optimal repeatability and reproducibility of the assays. Furthermore, the kit instructions and instrument manuals were carefully followed. The assayed kits were from the same lot, which allows better control of inter-assay variability. The samples were measured as a batch at the end of the study. The analysis process has been reported more precisely in previous studies (Lehto et al., 2010 & 2012; Honkalampi et al., 2011).

6.4.4 Psychometric scales (studies I–IV)

Health questionnaires included Finnish versions of the several psychometric scales measuring various perspectives of mental health (incl. SWB, symptoms, functioning, personality features) (Table 5). Depressive symptoms were rated using the self-administered Beck Depression Inventory (**BDI**) and the Hamilton Depression Rating Scale (**HDRS**), which have been recommended for use as screening tools in the Finnish guidelines. Life satisfaction was assessed with the self-reported life satisfaction scale (**LS**). Hopelessness was assessed using the Beck Hopelessness Scale (**HS**). Alexithymic symptoms were screened using the validated Toronto Alexithymia Scale (**TAS**). General psychopathology was assessed with the validated Symptom Check List (**SCL**), which is a self-report inventory. It is composed of 90 questions that yield nine subscale scores: somatization (12 items), obsessive-compulsive (10 items), interpersonal sensitivity (9 items), depression (13 items), anxiety (10 items), hostility (6 items), phobic anxiety (7 items), psychoticism (10 items), and paranoid ideation (6 items). The SCL also includes seven items primarily on sleep and eating disturbances. The SCL Global Index of distress, the Global Severity Index (GSI), is the mean value of all items. The validated self-reported General Health Questionnaire (**GHQ**) was used to assess mental distress. Subjective self-evaluation of memory function was assessed using the Memory Complaint Questionnaire (**MAC-Q**). The self-reported Dissociative Experiences Scale (**DES**) was used to assess psychological dissociation. Additionally, the Somatoform Dissociation Questionnaire (**SDQ**) was assessed for the purpose of evaluating the severity of somatoform dissociation. Scales on functional ability included the Global Assessment of Functioning (**GAF**) and the validated Social and Occupational Functioning Assessment Scale (**SOFAS**). The objective

scales were carried out by a trained research nurse, but **GAF** was assessed at baseline by the physician referring the patients to the study and later by a trained nurse. In all scales other than those measuring functional ability (SOFAS and GAF), higher scores indicate more severe symptoms and thus higher psychopathology. **SOFAS** measures the individual's level of functioning but does not consider the severity of symptoms. In GAF and SOFAS, a total score exceeding 70 indicates adequate functioning with at most only minor deficiencies.

Table 5. Psychometric scales.

Variable	Name	Assessment method	Items	Range	Reference	Study
Depressive Symptoms	Beck Depression Inventory (**BDI**)	Self-report	21	0–63	Beck et al., 1961 Viinamäki et al., 2004	I, III
Depressive Symptoms	Hamilton Depression Rating Scale (**HDRS**)	Objective	17	0–52	Hamilton, 1960; Viinamäki et al., 2005	I, III
Life satisfaction	Life Satisfaction Scale (**LS**)	Self-report	4	4–20	Koivumaa-Honkanen et al., 2008	I, II, III, IV
Hopelessness	Hopelessness Scale (**HS**)	Self-report	20	0–20	Beck et al., 1974 Haatainen, 2004	I, II, III
Alexithymia	Toronto Alexithymia Scale (**TAS**)	Self-report	20	20–100	Bagby et al., 1994 a&b; Joukamaa et al., 2001	I, II, III
General Psychopathology	Symptom Check List (**SCL**)**	Self-report	90	0–360*	Derogatis et al., 1973; Holi et al., 1998	I
Mental Distress	General Health Questionnaire (**GHQ**)	Self-report	12	0–36	Goldberg, 1972 Holi et al., 2003	II, III
Memory Function	Memory Complaint Questionnaire (**MAC-Q**)	Self-report	6	7–35	Crook et al., 1992 Antikainen et al., 2001	II
Psychological Dissociation	Dissociative Experiences Scale (**DES**)	Self-report	28	0–100	Bernstein & Putman, 1986 Maaranen, 2008	II, III
Somatoform Dissociation	Somatoform Dissociation Questionnaire (**SDQ**)	Self-report	20	20–100	Nijenhuis et al., 1996; Maaranen, 2008	II
Functional Ability	Global Assessment of Functioning (**GAF**)	Objective		1–100	Spitzer et al., 1966; Viinamäki et al., 1998	I
Level of Functioning	Social and Occupational Functioning Assessment Scale (**SOFAS**)	Objective		0–100	APA, 1994 Jääskeläinen & Miettunen, 2011	I

*General Severity Index is a total score of SCL-90 divided by responded questions (max 90): a mean value of all items (range 1–5)
**SCL-90 is composed of 90 questions that yield nine subscale scores: somatization (12 items), obsessive-compulsive (10 items), interpersonal sensitivity (9 items), depression (13 items), anxiety (10 items), hostility (6 items), phobic anxiety (7 items), psychotism (10 items), and paranoid ideation (6 items). It includes seven additional items primarily on sleep and eating disturbances

6.5 STATISTICAL METHODS

The majority of the data analyses were carried out with the statistical software package SPSS (versions 13.0–17.0). However, indirect mediation effects (II) between a poor parental relationship in the childhood home and current life dissatisfaction due to current MDD, hopelessness, and mental distress were investigated using the equations by MacKinnon and Dwyer (1993) based on Baron and Kenny's four steps in establishing mediation (1986).

The differences between the study groups were examined with the Pearson chi-squared test for categorical variables and the *t*-test or ANOVA for continuous variables. In the case of continuous variables not following a normal distribution, the non-parametric Mann-Whitney *U*-test or Kruskal-Wallis was used. Logistic regression was used as a multivariate method.

In **study I**, the statistical significance of changes during the follow-up was tested using repeated measures ANOVA e.g. general linear model. The improvement effect was defined as the effect size (Cohen´s *d*), i.e., the standardized difference (divided by the pooled standard deviation) between two means.

In **study II**, three sets of multiple age- and gender-adjusted logistic models (method: forward LR) were used. **Model 1** dealt with socio-demography, **model 2** with childhood factors, and **model 3** with clinical factors. The significant factors from models 1–3 were included in the **final model** (method: forward LR).

In **study III**, logistic regression (method:enter) was used to prospectively examine how the life dissatisfaction burden in 1998–2001 was related to a subsequent diagnosis of MDD in 2005, and to retrospectively examine how MDD in 2005 was related to the previous long-term life satisfaction burden. In the logistic models, the LS burden was mostly treated as a continuous score, but as an outcome variable the dissatisfied group was compared with the satisfied group (LS 34-60 vs. LS 12-21). The **final** logistic regression model was adjusted for possible confounders with and without including MDD in the model.

In **study IV**, both Pearson and Spearman correlations were used to study associations between continuous variables. A logarithmic transformation for the continuous life dissatisfaction burden score (logLSburd) was carried out due to its non-normal distribution. Linear regression was used as a multivariate method with logLSburd as a dependent variable. Based on the bivariate analyses, the significant correlates were gathered into two age- and gender-adjusted multivariate models (method: enter). **Model 1** dealt with sociodemographic factors and health behavior, **model 2** with biological and health-related factors. The **final model** included all the significant correlates from models 1 and 2. Additional analyses were performed to observe the stability of life satisfaction between groups A–C, and to assess the association between a cancer diagnosis (no/yes) (Izadi et al., 2012) and inflammatory markers.

7 Results

7.1 LIFE SATISFACTION AMONG DEPRESSIVE OUTPATIENTS (Study I)

7.1.1 Baseline life satisfaction and concurrent assessments
Among depressive outpatients (N = 121), those who belonged to the satisfied group (N = 28; 23%; LS 4–11) were statistically significantly older, more often married/cohabiting, were more often parents, assessed their partnership more positively, and more often reported happiness in their childhood home compared to those who belonged to the dissatisfied group (N = 93; 77%; LS 12–20). The satisfied assessed their wealth and their clinical symptoms scales more positively than the dissatisfied. The functional ability assessed with SOFAS by the research nurse was also significantly better among the satisfied.

7.1.2 Life satisfaction in a 6-year follow-up
The general linear model indicated that an improvement in life satisfaction and recovery from depression took place during the 6-year follow-up without significant gender differences (Table 6). Improvement effects were high for both life satisfaction (LS) and depression (BDI). At baseline, 37.0%/26.7% (men/women) belonged to the group with at most only slight depression (BDI 0–16) and 26.1%/21.3% belonged to the satisfied group (LS 4–11), while at the end of the study, these figures were 84.8%/81.3% and 80.4%/76.0%, respectively.

Table 6. Means (95% CI) of life satisfaction and improvement effect according to sex during the 6-year follow-up among the study sample of patients with depression at baseline (Study I).

	Imp. Effect*		Baseline		6 months		12 months		24 months		6 years	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
LS												
Men	1.24	0.21-3.10	13.8	12.8-14.7	11.4	10.3-12.5	10.7	9.55-11.9	10.7	9.55-11.9	9.28	8.19-10.4
Women	1.32	0.64-2.18	13.8	13.1-14.6	11.0	10.1-11.9	10.9	9.95-11.8	10.1	9.19-11.0	9.37	8.52-10.2
BDI												
Men	1.12	-1.47-3.69	19.3	16.6-21.9	12.7	9.86-15.5	10.7	9.55-11.9	10.8	8.37-13.2	9.31	6.66-12.0
Women	1.25	-0.62-3.25	20.7	18.8-22.6	12.8	10.8-14.9	10.9	9.93-11.8	10.6	8.28-13.0	9.98	7.95-12.0

LS = Life satisfaction scale
* Imp. effect = Improvement effects [mean (baseline) – mean (6 years)] / pooled SD
Table 6 from original article I.

7.1.3 Baseline and 6-year non-clinical factors

In separate age- and gender-adjusted logistic models, good self-rated wealth ($OR_{baseline}$ = 3.76; 95% CI 1.25–11.3; OR_{6year} = 7.83; 2.96–20.76) and good self-rated health ($OR_{baseline}$ = 3.94; 1.08–13.4; OR_{6year} = 10.85; 3.82–30.83), regardless of the assessment time point, as well as concurrently being loved by someone (OR_{6year} = 3.18; 1.26–8.04) were associated with life satisfaction on 6-year follow-up of depressive outpatients, while the other non-clinical variables were not. When all the variables were included with age and gender in the multivariate regression model (method: forward), concurrent good **self-rated health** (OR_{6year} = 8.33; 2.86–24.26) and **good self-rated wealth** (OR_{6year} = 4.43; 1.57–12.50) were significantly associated with life satisfaction on 6-year follow-up.

7.1.4 Baseline and 6-year clinical factors

When all the baseline clinical variables were analyzed separately as continuous variables in age- and gender-adjusted logistic models, only a lower functional ability measured with the SOFAS ($OR_{baseline}$ = 0.95; 0.90–1.00), a higher SCL interpersonal sensitivity ($OR_{baseline}$ = 2.20; 1.20–4.02), and psychotism ($OR_{baseline}$ = 2.17; 1.02–4.63) were associated with life dissatisfaction on 6-year follow-up among depressive outpatients. When these three variables were included with age and gender in the model (method: forward), only SCL **higher baseline interpersonal sensitivity** ($OR_{baseline}$=2.22; 1.21-4.06) was significantly associated with life dissatisfaction.

On 6-year follow-up, all the concurrent clinical variables were separately associated with the LS status in an age- and gender-adjusted logistic model (others $p < 0.001$, SCL hostility $p = 0.003$), except for the eating problems subscale of the SCL. When the BDI (statistically the most significant depression score) and SOFAS (statistically the most significant scale for functional ability) were analyzed together with the HS, SCL, and TAS 6-year scores (method: forward), only higher **BDI** (OR_{6year} = 1.15; 1.05–1.26) and **HS** scores (OR_{6year} = 1.19; 1.03–1.39) remained significantly associated with concurrent life dissatisfaction. When all significant SCL subscales on 6-year follow-up were simultaneously included in the age- and gender-adjusted model (method: forward), only higher SCL depression (OR_{6year} = 19.41; 5.35–70.42) was significantly associated with concurrent dissatisfaction.

7.2 LIFE SATISFACTION AMONG THE GENERAL POPULATION-BASED SAMPLE (Studies II–IV)

7.2.1 Socio-demographic and health behavior factors in concurrent and long-term life satisfaction (studies II–IV)

The general population based sample (N = 328, **study II**) was divided into the satisfied (LS = 4–11) (N = 256, 78%) and the dissatisfied (LS = 12–20) (N = 72, 22%) according to the self-reported life satisfaction sum score in 2005. Living alone, a reduced working ability and poor economic status were significantly associated with belonging to the dissatisfied group, while gender, having children, education, and area of residence did not associate with current life satisfaction. In a multivariate logistic regression model, a reduced working ability (OR 0.9; 0.9–1.0) and a poor economic status (OR 5.7; 2.8–11.6) significantly increased the likelihood of belonging to the dissatisfied group.

According to the long-term life satisfaction burden (**study III**, N = 330) based on the assessments in 1998, 1999, and 2001, subjects with long-term life satisfaction (N = 116)

were, in general, better off than those with long-term dissatisfaction (N = 107) with respect to subsequent socio-demographic and clinical factors. Long-term dissatisfaction associated with living alone, having no children, a reduced working ability and a poor economic status. Health behavior parameters were significantly worse for the long-term life dissatisfied in terms of current smoking and more frequent alcohol consumption. In a multivariate logistic regression model, a reduced working ability (OR 3.68; 1.56–8.68), poor economic status (OR 6.29; 1.78–22.2), and current smoking (OR 5.73; 1.95–16.8) significantly increased the likelihood of belonging to the long-term dissatisfied group.

According to the 7-year long-term life dissatisfaction burden (**study IV**, N = 305) based on the assessments in 1998, 1999, 2001, and 2005, respondents in the long-term dissatisfied group (N = 146) more often reported living alone, more often had poor social support and poor sleep, and were more often current smokers compared to the long-term satisfied (N = 159). No significant differences were found in gender or alcohol consumption with respect to the long-term life dissatisfaction burden.

According to both bivariate and multivariate linear regression analysis (**study IV,** Table 7), poor sleep, living alone, current smoking, and especially poor current social support were significantly associated with the 7-year long-term life dissatisfaction (logLSburden). Subsequently, 197/305 of the study participants remained constantly satisfied and 51/305 constantly dissatisfied in the follow-up. Only 14 satisfied cases out of 305 became dissatisfied and 43 dissatisfied cases out of 305 became satisfied by the end of the follow-up. The result from the comparison between group A vs. group C was similar to the original comparison of the long-term dissatisfied with the long-term satisfied. Likewise, comparing all the same biomarkers between group A vs. group B (N = 14), no significant differences were detected, but the group sizes were small.

Table 7. Socio-demographic factors and health behavior as correlates of long-term life dissatisfaction burden[1] in linear regression models (Study IV).

Variables	Bivariate model[2] B (95% CI)	p-value[2]	Multivariate model 1[3] B (95% CI)	p-value[3]
Age	-0.002 (-0.004–0.000)	0.014	-0.001 (-0.002 – 0.001)	ns
Gender (male)	0.018 (-0.016–0.051)	ns	0.022 (-0.007 – 0.051)	ns
Marital status (living alone)	0.077 (0.031–0.124)	0.001	0.055 (0.014–0.096)	0.009
Social support (poor)	0.179 (0.133–0.225)	<0.001	0.144 (0.099–0.188)	<0.001
Sleep (poor)	0.081 (0.049–0.114)	<0.001	0.051 (0.021–0.080)	0.001
Smoking (yes)	0.111 (0.070–0.152)	<0.001	0.098 (0.060–0.136)	<0.001
Alcohol consumption ≥2/week	0.022 (-0.021–0.065)	ns	Nim	Nim

[1]Long-term life dissatisfaction burden score (logLSburden): sum of life satisfaction scores in 1998, 1999, 2001, and 2005 with logarithmic transformation
[2]Bivariate linear regression analysis separately for each variable
[3]Multiple adjusted linear regression model 1 (method: enter) included the following factors: age (continuous), gender (0 = female, 1 = male), marital status (0 = married/living in a partnership, 1 = living alone), social support (0 = good/normal, 1 = poor), sleep (0 = good, 1 = poor), and smoking (0 = no, 1 = yes)
Nim = not included in the model due to nonsignificant association in the bivariate model
Table 7 from the original article IV.

7.2.2 Childhood experiences (study II)

Altogether, 22% (N = 72) of the study sample (N = 328) was classified as being dissatisfied and 35% of these reported having an unhappy childhood home, whereas only 16% of the satisfied assessed their childhood home atmosphere as unhappy. In general, retrospectively assessed adverse childhood factors, such as a poor relationship between the parents or their alcohol use, domestic unhappiness or violence, associated significantly with subsequent life dissatisfaction. According to a multiple adjusted logistic regression model that included retrospectively assessed childhood adversities, a poor parental relationship (OR 3.4; 1.8-6.1) was significantly associated with subsequent life dissatisfaction, whereas the retrospective assessments of alcohol consumption, domestic violence, and domestic unhappiness in the childhood home lost their significance during the multiple adjusted model.

7.2.3 Mental health indicators of concurrent and long-term life dissatisfaction in 2005 (studies II–III)

The indicators of poor mental health were widely associated with the life dissatisfaction group. A diagnosis of MDD (**study II**, N = 93) assessed by using SCID-I in 2005 was obtained for 28.4% of the study subjects. The corresponding figure for personality disorders was 14.9% (N = 49) assessed by using SCID-II in 2005. Both of the diagnoses, as well as all psychometric scales scores (TAS, HS, SDQ, MACQ, GHQ, and DES) in 2005, were significantly associated with concurrent life dissatisfaction in a cross-sectional design. Finally, when all the above-mentioned significant correlates of life dissatisfaction were simultaneously included into the same final multivariate logistic regression model, the diagnosis of MDD (OR 2.5; 1.2-5.8), hopelessness (OR 1.4; 1.2-1.5), and mental distress (OR 1.2; 1.1-1.3) remained the most powerful and significant correlates for belonging to the group of life dissatisfaction. Statistically significant portions of indirect mediation effects were found between a poor parental relationship in childhood and life dissatisfaction due to current MDD (46.4%, Z = 4.22, p < 0.001), hopelessness (45.1%, Z = 3.19, p = 0.001) and mental distress (60.4%, Z = 4.00, p < 0.001).

According to the 3-year long-term life satisfaction burden (**study III**, N = 330), subjects with long-term life satisfaction (N = 116) were better off than those with long-term life dissatisfaction (N = 107) with respect to the health status and clinical factors in general. Previous long-term life dissatisfaction associated with poorer subsequent mental health in 2005. This was the case with all of the psychometric scales (TAS, HS, GHQ, DES, LS) of the study, including both self-reported (BDI) and objectively assessed depression (HDRS) in 2005, as well as with a subsequent MDD diagnosis in 2005. Out of those with long-term life dissatisfaction, 55% (N = 59) had MDD in 2005, whereas among those with long-term life satisfaction, the respective figure was 5% (N = 6).

Those with MDD in 2005 had a strongly increased likelihood for having previously belonged to the long-term life dissatisfied group (LS burden scores 34–60 vs. 12–21) compared to those without MDD, even after adjustment for several concurrent socio-demographic and life style factors (Table 8). In this model, a reduced ability to work, a poor economic situation and current smoking in 2005 were also significantly associated with the previous long-term life dissatisfaction burden (model 1). When all the psychometric scales in 2005 were assessed in another model (model 2), those with low life satisfaction and hopelessness had a significantly increased risk of having belonged to the previous long-term life dissatisfaction group.

Table 8. The adjusted risks (OR 95% CI) of having belonged to the 3-year long-term dissatisfied group (LS burden scores: 34–60 vs. 12–21) (Study III).

Retrospective model 1: Incl. major depressive disorder, health behavior and socio-demographic variables in 2005	Age- and gender-adjusted separate OR (95% CI)	Multiple adjusted OR (95% CI) [1]
Age	0.97 (0.94-1.00)*	0.97 (0.93-1.02)
Gender (male)	0.89 (0.52-1.53)	0.92 (0.43-1.95)
Children (none)	2.75 (1.35-5.58)**	2.08 (0.68-6.38)
Marital Status (non-cohabiting)	3.00 (1.35-6.65)**	2.04 (0.59-7.11)
Reduced work ability	8.43 (4.18-17.0)***	3.68 (1.56-8.68)**
Poor economic status	14.7 (5.00-43.1)***	6.29 (1.78-22.2)**
Current Smoking	7.24 (3.03-17.3)***	5.73 (1.95-16.8)**
Alcohol consumption ≥2/week	2.20 (1.01-4.78)*	2.49 (0.90-6.96)
Major Depressive Disorder	22.2 (8.89-55.5)***	11.0 (3.97-30.4)***
Retrospective model 2: Clinical variables in 2005	**Age- and gender-adjusted separate OR (95% CI)**	**Multiple adjusted OR (95% CI) [2]**
Current LS	2.51 (1.94-3.26)***	2.16 (1.58-2.96)***
Current HS	1.81 (1.49-2.20)***	1.41 (1.09-1.84)*
Current HDRS	1.34 (1.23-1.47)***	1.02 (0.88-1.18)
Current TAS	1.13 (1.09-1.17)***	1.02 (0.95-1.09)
Current DES	1.17 (1.09-1.26)***	1.06 (0.96-1.17)
Current GHQ	1.46 (1.3-1.6)***	1.05 (0.89-1.25)

$*p < 0.05$; $**p < 0.01$; $***p < 0.001$
[1]Multiple adjusted logistic model 1 (method:enter) including: age (continuous), gender (0=female; 1=male), children (0=yes; 1=no), marital status (0=cohabiting; 1=non-cohabiting), subjectively assessed reduced work ability (0=no; 1=yes), subjectively assessed poor economic status (0=no; 1=yes), current smoking (0=no; 1=yes), alcohol consumption (0=<2/week; 1=≥2/week), current MDD (0=no; 1=yes)
[2]Multiple adjusted logistic model 2 (method:enter) including: LS, HS, HDRS, TAS, DES, and GHQ as continuous scales
Table 8 from the original article III.

According to the retrospective final logistic model including all the above-described significant variables from models 1–2, MDD in 2005 (OR = 7.79; 2.00–30.4), or life dissatisfaction in 2005 (continuous score: OR = 2.12; 1.59–2.84) remained the only significant factors associating with the previous long-term life dissatisfaction burden. After excluding those who already had MDD in 1999 from the final model hopelessness (OR = 1.35; 1.03–1.75) and life dissatisfaction (OR = 2.30; 1.67–3.17) in 2005 were significantly and MDD marginally significantly (OR = 4.67; 0.97–22.4, p = 0.05) associated with the previous LS burden.

In a prospective logistic final model (Table 9) adjusted for work ability, economic status, smoking, hopelessness, and the LS score in 2005, the 3-year long-term life dissatisfaction burden as a continuous score predicted strongly the subsequent MDD diagnosis in 2005. In this model with the long-term life dissatisfaction burden, the significant concurrent correlates of the MDD diagnosis were hopelessness, smoking, and a reduced ability to work. When those with MDD in 1999 were excluded, the continuous 3-year long-term life dissatisfaction burden still similarly predicted MDD in 2005, while smoking and a reduced work ability were its significant concurrent correlates. When the 3-category LS burden

score was used instead of a continuous score in the same models, the long-term dissatisfied group (scores 34–60) had a 5-fold increased OR (5.11) (95% CI 1.72–15.2; p = 0.003) of having MDD in 2005. After excluding those with MDD in 1999, the OR of having MDD diagnosis in 2005 was 3.52 (1.10–11.3: p = 0.034).

Table 9. The prospective final multivariate logistic model[1] to assess the correlates of current MDD (Study III).

Variable	Adjusted OR (95% CI) All subjects	Adjusted OR (95% CI) Subjects without MDD in 1999
LS burden	1.07 (1.03-1.12); p < 0.001	1.06 (1.01-1.11); p = 0.013
Current LS	1.04 (0.92-1.17); p = 0.582	1.09 (0.95-1.26), p = 0.234
Current HS	1.11 (1.02-1.21); p = 0.020	1.10 (1.00-1.22); p = 0.063
Current smoking	2.19 (1.08-4.45); p = 0.031	2.45 (1.10-5.46); p = 0.028
Poor economic status	1.93 (0.89-4.18); p = 0.094	2.37 (0.98-5.72); p = 0.055
Reduced work ability	2.37 (1.19-4.73); p = 0.014	2.32 (1.07-5.00); p = 0.032

[1] Model included (method enter): LS burden (continuous scale), LS score in 2005 (continuous), HS score in 2005 (continuous), current smoking (0=no; 1=yes), subjectively assessed poor economic status (0=no; 1=yes), subjectively assessed reduced work ability (0=no; 1=yes)

7.2.4 Somatic health, comorbidity and long-term life dissatisfaction (Study IV)

Among the group with the 7-year long-term dissatisfaction, metabolic syndrome was more prevalent compared to the group with 7-year long-term life satisfaction. Despite this, the use of statins was less frequent among the long-term dissatisfied. No significant differences were found in the use of NSAIDs or oral corticosteroids, in gender, alcohol consumption, or the prevalence of coronary heart disease, rheumatoid arthritis, or cancer with respect to the long-term life dissatisfaction burden.

The anti-inflammatory cytokine adiponectin was significantly lower among the long-term dissatisfied (p = 0.014) compared to the long-term satisfied. The levels of proinflammatory markers TNF-α, IL-6, resistin and hs-CRP were also higher in the long-term satisfied, but statistical significance was not reached.

In further analyses, no significant association was found between the use of statins (yes vs. no) and the inflammatory markers. The same pattern was seen when those categorized as stable dissatisfied were compared with those with stable satisfaction. Additionally, no significant association was found between a cancer diagnosis (yes vs. no) and the inflammatory markers.

According to both bivariate and multivariate linear regression analysis (model 1, Table 7) of sociodemographic and health behavior factors, poor sleep, living alone, current smoking, and especially poor current social support were significantly associated with long-term life dissatisfaction (logLSburden).

According to both bivariate and multivariate linear regression analysis (model 2, Table 10) of biological factors and medication, metabolic syndrome, the use of statins, and low serum levels of adiponectin were significantly associated with the logarithmic transformation of long-term life dissatisfaction (logLSburden). On the other hand, age, gender, alcohol consumption, coronary heart disease, rheumatoid arthritis, the use of oral corticosteroids or NSAIDs, body mass index, and the serum proinflammatory markers resistin, hs-CRP, TNF-α, and IL-6 were not significantly related to logLSburden.

Table 10. Biological factors and medication in respect to 7-year continuous long-term life dissatisfaction burden[1] in linear regression models (Study IV).

Variables	Bivariate model[2] B (95% CI)	p-value[2]	Multivariate model 2[3] B (95% CI)	p-value[3]
Age	-0.002 (-0.004 – 0.000)	0.014	-0.001 (-0.003 – 0.001)	ns
Metabolic syndrome (yes)	0.038 (0.004 – 0.073)	0.030	0.046 (0.010 – 0.081)	0.012
Use of statins (yes)	-0.062 (-0.100 – -0.023)	0.002	-0.064 (-0.106 – -0.023)	0.002
Adiponectin, [µg/ml]	-0.001 (-0.002 – 0.000)	0.016	-0.001 (-0.002 – 0.000)	0.023

[1]Long-term life dissatisfaction burden score: sum of life satisfaction scores in 1998, 1999, 2001, and 2005 with logarithmic transformation
[2] Bivariate linear regression analysis separately for each variable
[3]Multiple adjusted linear model 2 (method: enter) included the following factors: age (continuous), gender (0 = female, 1 = male), metabolic syndrome (0 = no, 1 = yes), use of statins (0 = no, 1 = yes), and serum adiponectin level (continuous)
Non-significant (p>0.05), not included in the multivariate model: gender (male/female); hypertension (yes/no); coronary heart disease (yes/no); rheumatoid arthritis (yes/no); use of oral corticosteroids (yes/no); use of NSAIDs (yes/no); BMI (continuous); resistin (continuous); hs-CRP (continuous); TNF-α (continuous); IL6 (continuous)

When correlations between continuous variables were tested, age (Pearson 0.141, $p = 0.014$; Spearman 0.156, $p = 0.006$) and adiponectin (Pearson 0.139, $p = 0.016$; Spearman 0.133, $p = 0.021$) were significantly correlated with logLSburd.
In the final linear regression model (Table 11), including all the above-mentioned significant variables from multivariate models 1 (Table 7) and 2 (Table 10), poor social support, marital status (i.e. living alone), smoking, poor sleep, use of statins and adiponectin were independently associated with a higher life dissatisfaction burden score (logLSburden), whereas the association of metabolic syndrome was marginally nonsignificant.

Table 11. The association between the long-term life dissatisfaction burden[1] and its significant correlates in the final multivariate linear regression model (Study IV).

Variables	Final model[2] B (95% CI)	p-value
Marital status	0.049 (0.008 – 0.090)	0.019
Sleep (poor)	0.052 (0.022 – 0.081)	0.001
Social support (poor)	0.138 (0.094 – 0.183)	<0.001
Smoking (yes)	0.087 (0.049 – 0.124)	<0.001
Adiponectin, [µg/ml]	-0.001 (-0.002 – 0.000)	0.039
Metabolic syndrome (yes)	0.029 (-0.001 – 0.059)	ns (0.055)
Use of statins (yes)	-0.052 (-0-086 – -0.019)	0.002

[1]Long-term life dissatisfaction burden score: sum of life satisfaction scores in 1998, 1999, 2001, and 2005 with logarithmic transformation
[2]The final linear regression model (method: enter) included all the significant factors from models 1 and 2: marital status (0 = married/living in a partnership, 1 = living alone), sleep (0 = good, 1 = poor), social support (0 = good, 1 = poor), smoking (0 = no, 1 = yes), serum adiponectin level (continuous), metabolic syndrome (0 = no, 1 = yes), and use of statins (0 = no, 1 = yes)
Table 11 from the original article IV.

8 Discussion

8.1 DISCUSSION OF THE RESULTS

Life dissatisfaction was shown to indicate a risk of accumulating health risks. It was associated with several disadvantages with respect to sociodemographic, social, economic, and health-related factors, including an impression of poor somatic health care among the dissatisfied. The importance of life dissatisfaction as a long-term health risk was seen in all the assessed mental heath indicators, even if being most strongly evident with respect to depression and hopelessness. Interpersonal sensitivity was one of the strong predictors of life dissatisfaction, and prolonged life dissatisfaction strongly predicted MDD as a new diagnosis in a 7-year follow-up. Long-term life dissatisfaction appears to represent a form of psychological stress, which may stimulate pathophysiological processes and modulate inflammatory processes. However, this was seen in our studies only in a reduction in the anti-inflammatory marker adiponectin. Nevertheless, the main clinical importance of our results is that it is possible to intervene early in the process leading to psychiatric morbidity. The easily applied 4-item life satisfaction scale could be a valid tool in health promotion, screening poor mental health in the general population and monitoring recovery in patient populations.

8.1.1 Correlates of life satisfaction during recovery from depression

Childhood experiences of family disharmony have predisposed to significant mental health consequences, which have persisted far into adulthood (Balsa et al., 2009; Braithwaite & Devine, 1993). In **study I**, the subjects who were satisfied among the depressive outpatients retrospectively assessed their childhood home as happy significantly more often than those who were dissatisfied with their life. Likewise, marital status and its quality, as well as being a parent, were associated with life satisfaction at baseline. Nevertheless, after the participants had mainly recovered, only concurrently being loved by someone was an important correlate of life satisfaction, not the childhood or marital assessments. The satisfied could have had a better social functional capacity from the very beginning, to have and to hold and enrich their social relationships, even during and after recovery from depression. Along with this, the individual level of functioning measured with the SOFAS was also significantly associated with life satisfaction both baseline and after 6 years of follow-up. However, being loved by someone was more important for life satisfaction than having someone to love, which amplifies the view that depression is demanding for those close to the patients. Thus, the value of social relationships for depressive patients should be appreciated and supported from the very beginning of psychiatric treatment.

While depression and hopelessness were the most potent correlates of life dissatisfaction, general psychopathology in all its aspects as well as a lower alexithymia score and higher functional ability were also significantly associated with the satisfied. Baseline lower interpersonal sensitivity was the strongest clinical factor and, as in a cross-sectional setting (Koivumaa-Honkanen et al., 1996), good self-rated health and wealth were the strongest non-clinical factors associated with the subsequent life satisfaction status on 6-year follow-up. Interpersonal sensitivity deals with personal inadequacy, inferiority in comparison to others, self-deprecation, uneasiness, and discomfort during

interpersonal interactions. Depressive patients in whom these features are prominent should be considered as a high-risk group for subsequent life dissatisfaction and thus, due to strong intercorrelation, also for non-recovery from depression.

Previously, depressive patients have been shown to be able to reach the level of life satisfaction of the general population (Koivumaa-Honkanen, 1998; Koivumaa-Honkanen et al., 2008). In the present study I, gender differences in improvement were also investigated, but not found. It should be noted that after most of the participants had recovered, their health behavior had also improved. However, due to the small sample size, the possibility of type II errors is increased and may have affected the results of some of the studied associations.

8.1.2 Socio-demographic and health behavior factors in life dissatisfaction

Previously, correlates of life dissatisfaction have included poor health behavior (Koivumaa-Honkanen, 1998), a poor social (Koivumaa-Honkanen et al., 2002) and economic situation (Diener, 1984; Marum et al., 2013; Kapteyn et al., 2013), a poor ability to work (Koivumaa-Honkanen et al., 2004a), and depressive symptoms (Koivumaa-Honkanen et al., 2004b). Poor social support in 2005 was the strongest correlate of the previous 7-year long-term life dissatisfaction burden (**study IV**), which is consistent with former research (Lacruz et al., 2011; Castillo-Carniglia et al., 2012). The study verified that longitudinally, long-term life dissatisfaction is also significantly related to the subsequent social and economic status, health behavior, as well as various clinical adverse outcomes. Subjects with a poor economic status, reduced working ability, smoking, and MDD in 2005 all had an independently increased probability of having previously belonged for several years to the long-term life dissatisfaction group. Thus, monitoring SWB and life satisfaction in the general population should be a task of health care, but also of other sectors of society (Honkanen et al., 2011) in order to facilitate mental health promotion and early prevention of disorders.

8.1.3 Childhood adversities and life dissatisfaction

Childhood adversities have adverse consequences in adulthood. The retrospectively assessed overall quality of paternal care and current level of depressive symptoms have been independent correlates of the adult quality of life (Rikhye et al., 2008). In our **study II**, the quality of the parental relationship in the childhood home was the most significant childhood factor associated with life dissatisfaction. Approximately a half of its effect was independent of current depression and other adverse mental symptoms. However, retrospectively reported childhood adversities were not significantly associated with life satisfaction in adulthood among the general population sample when indicators of concurrent mental health were included in the same model. This parallels the findings with depressive outpatients after psychiatric treatment (study I). Further research is needed to examine these relationships in more detail.

8.1.4 Mental health indicators and life dissatisfaction

In **studies II–III**, a consistent association was shown between life dissatisfaction and concurrent poor mental health, also including an objectively assessed psychiatric diagnosis. Major depression, overall distress, and hopelessness were the main correlates of life dissatisfaction in a sample of the general population. Previously, a strong association has been observed between life dissatisfaction and depressive symptoms in both general population samples (Korkeila et al., 1998; Koivumaa-Honkanen et al., 2004a; Strine et al., 2008) and in patient samples (study I; Koivumaa-Honkanen et al., 1996). In addition, an

inverse association between positive well-being and depressive symptoms has been found in a cohort study (Wood & Josep, 2010). Here, study III demonstrated that the long-term life dissatisfaction burden was also strongly and independently related to a subsequent MDD diagnosis, along with other indicators of poor mental health, in a seven-year follow-up among those who had not previously reported having MDD. Multiple adjustments did not change the association. MDD is a severe mental disorder with a strong impact on the quality of life and is also a correlate as well as a predictor of working disability (Michaud et al., 2001) and functional impairment (Murray & Lopez, 1997). Thus, the outcomes of **study III** continue to highlight both the possibilities and importance of early screening. Long-term life dissatisfaction is detrimental to subsequent mental health and an antecedent to MDD.

Our **studies II–III** further underlined the importance of monitoring SWB by also demonstrating the strong association of life dissatisfaction with symptoms of hopelessness (Haatainen et al., 2004) and general mental distress in a sample of the general population. Depression, hopelessness, and life dissatisfaction are indicators of poor mental health. As comorbidity is almost the rule in mental disorders, including at the symptom level, these symptoms appear to go hand in hand.

Personality dispositions can markedly influence the levels of SWB (Diener et al., 2003). In **study II**, even though personality disorder and childhood adversities were significant correlates of life dissatisfaction, adverse concurrent mental symptoms, i.e. general distress, hopelessness, and MDD, were the strongest correlates of being dissatisfied after multiple adjustments. The diagnosis of personality disorder did not independently correlate with life dissatisfaction after multiple adjustments, including MDD, hopelessness, and general mental distress, which also were partial mediators between a poor parental relationship during childhood and adult life dissatisfaction. Fortunately, the main factors underlying life dissatisfaction appear not to be objective and unchangeable, but closely related to concurrent mental health and well-being and disposed to intervention, treatment, and change

8.1.5 Somatic health indicators and life dissatisfaction

Study IV investigated the significant independent correlates of the 7-year long-term dissatisfaction burden from a set of several biomarkers. To the best of our knowledge, this was the first study on a general population sample to present lowered serum adiponectin levels in individuals experiencing long-term life dissatisfaction. This was also true after using the life dissatisfaction burden as a continuous score in a multivariate linear regression model including significant sociodemographic and health-related factors such as BMI, metabolic syndrome, and the use of statins. Previously, a low adiponectin level has been associated with MDD (Shelton et al., 2015; Lehto et al., 2010) and panic disorder (Unsal et al., 2012). In study IV, poor sleep was also an independent correlate of life dissatisfaction in the model including adiponectin, but it has additionally been reported to have predictive ability in relation to inflammation processes (Friedman, 2011; Motivala et al., 2005; Rohleder et al., 2012). On the other hand, positive affect may have distinctive biological correlates that can benefit health (Steptoe et al., 2009). Chronic psychological stress, in general, has been linked with inflammation (Cohen et al., 2012), for instance through elevated levels of IL-6 and hs-CRP (Ranjit et al., 2007; Rohleder et al., 2012). This was not verified in our data with statistical significance, but our findings suggest that the long-term life dissatisfaction burden presents a form of psychological stress, which may stimulate pathophysiological processes and modulate inflammation processes by reducing the levels of the anti-inflammatory marker adiponectin. According to Vaillant (2003), the

mental health status also reflects an individual's social competence and coping style, which, in addition to subjective adaptation skills, resilience, and plasticity, have biological manifestations and alterations. However, more research is needed with larger general population samples and with longitudinal and more detailed data, which would allow further study of the mechanisms underlying these associations.

The health status is strongly associated with life satisfaction (Bellis et al., 2012). A recent study found a strong relationship, both longitudinally and cross-sectionally, between health-related quality of life and life satisfaction among the same general population sample (Saharinen et al., 2014) as used in studies II–IV. The long-term life dissatisfaction burden could also compromise somatic health in various ways. In study IV, poor sleep was an independent correlate of life dissatisfaction in the model including adiponectin. Previously, the weight status has been suggested to have an effect on SWB (Robertson et al., 2015). In our study IV, we could not verify this, since BMI lost its significance in the regression analysis.

As a consequence of adverse health behavior, smoking appears to increase low-grade inflammation, e.g. IL-6 levels (Helmersson et al., 2005), but it has also been noted to be independently associated with life dissatisfaction (study III; Bogdanovica et al., 2011; Grant N et al., 2009; Yawson et al., 2013). Previously, a decreasing level of health care has been reported in relation to an increasing severity of mental disorders (Laursen & Nordentoft, 2006). In a study among cardiovascular risk factors, health behaviors and socioeconomic factors of coronary angiography patients, subjects with a history of physical inactivity, cardiovascular symptoms, obesity, diabetes, and hypercholesterolemia were more likely to be dissatisfied with their lives (Baumann et al., 2015). In our study, the use of statins was significantly less frequent among individuals with long-term life dissatisfaction, even though they had a higher prevalence of metabolic syndrome. This might suggest poor somatic health care among the dissatisfied. However, causality in our findings could not be verified.

The psychosocial factors linked with life dissatisfaction, such as a low socioeconomic status, poor health behavior, adverse childhood experiences, low social support, negative affect (depression) and a lack of positive affect (positive, happiness and joy), and hopelessness, resemble those previously found with cardiovascular disease (von Känel, 2012; Kaplan & Keil, 1993). Indeed, life satisfaction has been significantly linked with a decreased risk of coronary heart disease (Boehm et al., 2011), which is in line with the present study.

In general, life satisfaction and SWB can be approached from different angles, such as with biological, psychological, and sociological methodologies, without invalidation of the different theories. On the contrary, they may even enrich the different theories, or serve as one of the connecting factors between them (Diener, 1984). Thus, due to the lack of previous studies, interest in the biological aspects of life satisfaction and in its relationships with health behavior and somatic health (e.g. metabolic syndrome, cardiovascular risk factors) increases knowledge and the possibilities to prevent adverse somatic consequences among those with low SWB.

8.2 METHODOLOGICAL CONSIDERATIONS OF THE STUDY

The results of the present thesis are based on the clinical substudies I–IV. The size of the patient sample (**study I**) during the 6-year follow-up study was sufficient compared with earlier investigations focusing on similar questions (Jormfeldt, 2010, Ravindran et al., 2002, Sung et al., 2007), even though a larger sample size would have been beneficial. The final

study sample (N = 121) did not differ significantly from the drop-outs (N = 64) with respect to age, gender, education, financial situation, work status, subjective health, subjective work ability, the use of alcohol, the delay in receiving psychiatric treatment, several psychometric scale sum scores, or the proportion of those suffering from major depression (Koivumaa-Honkanen et al, 2008). Nevertheless, a greater proportion of the dropouts were single and current smokers compared to the study final sample. However, there were a limited number of patients with different types of depressive disorder, according to which it was not possible to conduct separate statistical analyses. In **study I**, the factors associated with life satisfaction at baseline and the effect of baseline life satisfaction on subsequent mental health were examined. The cross-sectional information enabled us to control for confounding factors at baseline and on 6-year follow-up. The follow-up period was long enough to study the process of recovery from depression (Posternak et al., 2006; Romera et al., 2013).

The data obtained from self-reported questionnaires could be seen as having somewhat limited validity due to their subjective character. However, subjective assessments (Koivumaa-Honkanen et al., 2000) as well as personality features (Terracciano et al., 2008) have provided valuable clues to the long-term trajectory of a subject, even though the associations may have been attenuated or mediated by confounding factors (Bernheim et al., 2007; Everson-Rose et al., 2004). In general, subjective health assessments have been found to be valid health status indicator in the working-age population (Miilunpalo et al., 1997). The longitudinal approach provides knowledge on the course of the recovery process among depressive outpatients (Koivumaa-Honkanen et al., 1996 & 2008). In spite of the limitations presented above, the results of study I can be considered to be representative of the depressive outpatient sample.

The original general population-based sample in **studies II–IV** was randomly selected from the National Population Register from those living in the Kuopio area in 1998. The sample sizes of studies II–IV were sufficient with respect to the previous literature (Chiang et al., 2012; Joung et al., 2014). The 7-year follow-up time can also be considered as a sufficient period for the development of most health disorders. The age difference of the study participants may have exposed them to some recall bias. However, the actual range in age within the study sample (e.g. in study II) was less marked (Age$_{2005}$: mean = 55.8; SD 9.6).

The Structured Diagnostic Interview for concurrent DSM was used to ensure the validity of the diagnostic profile of depressive patients. SCID has been found to be a reliable tool for the diagnostic process *(*Zanarini et al., 2000, Lobbestael J et al., 2011). The interviewer had passed a clinical training course and achieved a good total kappa against an experienced trainer in SCID diagnoses.

The strength of **study II** was its community sample and wide study orientation, including important factors concerning socio-demographics and objective life status, childhood adversities, and health behavior, as well as several indicators of mental health. Most of all, it included objectively assessed psychiatric diagnoses of MDD and personality disorders. Furthermore, separate analyses were conducted in order to investigate mediation effects for the relationship between life satisfaction and a poor parental relationship in the childhood home. However, some covariates were based on retrospective self-reports**.** The intensity of negative emotions associated with event memories has been presented to fade to a greater extent over time than positive emotions (Muir et al., 2014; Szpunar et al., 2012), even establishing neurobiological changes in emotion processing and emotional memory (Addis et al., 2010). Thus, subjective factors, such as current life satisfaction, may play a role in how childhood factors can be remembered and interpreted later in life, not the objective number of adversities.

Retrospective questions on childhood adversities may also be somewhat biased due to the age difference in the study population. Nevertheless, retrospective reports in adulthood concerning serious adverse childhood experiences can be regarded as sufficiently valid to warrant their use (Hardt & Rutter, 2004).

One limitation is that alcohol consumption was measured with frequency only, not quantitatively or qualitatively. Its dichotomous categorization may lead to some further loss of information. However, alcohol use appears not to be linearly associated with life satisfaction, and this complex association has been addressed in more detail elsewhere (Koivumaa-Honkanen et al., 2012).

The main strength of **study III** was its longitudinal setting, which was used both prospectively and retrospectively in order to investigate the association between the life dissatisfaction burden and subsequent MDD. Concurrent life satisfaction in 2005 and previous MDD was also taken into account in the analyses. No previous studies have utilized such a design. Moreover, the use of multiple psychometric scales indicating poor mental health and diagnostic interviews added to the reliability and importance of the findings. However, MDD in 1999 was based on a self-reported diagnosis, i.e. not on the SCID, as in 2005.

The design of **study IV** was unique in terms of previous research. A strength was its community sample and the availability of several important health-related measures (O´Connor et al., 2009), including biological markers, for assessing the factors related to the long-term life dissatisfaction burden. The multivariate analyses including the body mass index, and the use of statins helped to control for potential bias. The life satisfaction burden was used as a continuous variable in addition to dichotomous categorization. Due to the non-normal distribution of continuous life dissatisfaction burden (skewness 0.701), logarithmic transformation was carried out, resulting in a logarithmic life dissatisfaction burden score, i.e. logLSburd (skewness 0.175), which was suitable for the linear regression analyses. The correlation between continuous variables was tested. Information on the cumulative burden of dissatisfaction was obtained, while also measuring aspects of positive mental health. Due to the somewhat small sample size and considerable long-term stability of life satisfaction, the changes in life satisfaction over time were only investigated to a limited extent (stable satisfied – changing life satisfaction – stable dissatisfied) with respect to the identified correlates. A more detailed disease history and longitudinal data on health-related factors of the participants would have been beneficial and should be covered in future research. All in all, despite the limitations presented above, the results of studies II–IV can be considered to be representative of the general population.

9 Conclusion

Study I: Among a sample of depressive outpatients, mental health was strongly related to life satisfaction throughout the follow-up, while most of the non-clinical factors were not. Relieving depression and interpersonal sensitivity and endorsing social networks should be focused on in psychiatric treatment in order to improve life satisfaction among depressive patients.

Study II: Mental health was closely interwoven with life satisfaction in a general population-based sample. Although personality disorder and childhood adversities were significant correlates of life dissatisfaction, adverse concurrent mental symptoms and MDD were the strongest correlates. The main factors underlying life dissatisfaction are not unchangeable, but are closely related to mental health and well-being and responsive to intervention, treatment, and change.

Study III: Among a general population sample, the long-term life satisfaction burden was significantly related to major depressive disorder and other indicators of poor mental health in both cross-sectional and longitudinal settings.

Study IV: Among a general population sample, social and health behavioral factors, along with stress and inflammation, played a role in life dissatisfaction, but further research is needed to verify the biological associations found in this study. Several correlates of long-term life dissatisfaction resembled common risk factors for somatic diseases, supporting the close relationships between subjective well-being and somatic morbidity.

Long-term life dissatisfaction is deleterious to mental health and an antecedent to MDD. These studies highlighted both the possibilities and importance of early screening for poor mental health. Early intervention is possible due to its adverse outcomes, i.e. increased psychiatric and somatic morbidity and mortality. The value of social relationships among depressive patients, as well as among the general population, in the prevention of poor mental health should be acknowledged, appreciated, and supported.

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Appendices

Appendix I. International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) WHO Version for 2015.

Mood (affective) disorders (F31-39)

This block contains disorders in which the fundamental disturbance is a change in affect or mood to depression (with or without associated anxiety) or to elation. The mood change is usually accompanied by a change in the overall level of activity; most of the other symptoms are either secondary to, or easily understood in the context of, the change in mood and activity. Most of these disorders tend to be recurrent and the onset of individual episodes can often be related to stressful events or situations.

F31 Bipolar affective disorder

A disorder characterized by two or more episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (hypomania or mania) and on others of a lowering of mood and decreased energy and activity (depression). Repeated episodes of hypomania or mania only are classified as bipolar.

F31.3 Bipolar affective disorder, current episode mild or moderate depression

The patient is currently depressed, as in a depressive episode of either mild or moderate severity (F32.0 or F32.1), and has had at least one authenticated hypomanic, manic, or mixed affective episode in the past.

F31.4 Bipolar affective disorder, current episode severe depression without psychotic symptoms

The patient is currently depressed, as in severe depressive episode without psychotic symptoms (F32.2), and has had at least one authenticated hypomanic, manic, or mixed affective episode in the past.

F31.5 Bipolar affective disorder, current episode severe depression with psychotic symptoms

The patient is currently depressed, as in severe depressive episode with psychotic symptoms (F32.3), and has had at least one authenticated hypomanic, manic, or mixed affective episode in the past.

F32 Depressive episode

In typical mild, moderate, or severe depressive episodes, the patient suffers from lowering of mood, reduction of energy, and decrease in activity. The capacity for enjoyment, interest, and concentration is reduced, and marked tiredness after even minimum effort is common. Sleep is usually disturbed and appetite diminished. Self-esteem and self-confidence are almost always reduced and, even in the mild form, some ideas of guilt or worthlessness are often present. The lowered mood varies little from day to day, is unresponsive to circumstances and may be accompanied by so-called "somatic" symptoms, such as loss of interest and pleasurable feelings, waking in the morning several hours before the usual time, depression worst in the morning, marked psychomotor retardation, agitation, loss of appetite, weight loss, and loss of libido. Depending upon the number and severity of the symptoms, a depressive episode may be specified as mild, moderate or severe.

F32.0 Mild depressive episode

Two or three of the above symptoms are usually present. The patient is usually distressed by these but will probably be able to continue with most activities.

F32.1 Moderate depressive episode

Four or more of the above symptoms are usually present and the patient is likely to have great difficulty in continuing with ordinary activities.

F32.2 Severe depressive episode without psychotic symptoms

An episode of depression in which several of the above symptoms are marked and distressing, typically loss of self-esteem and ideas of worthlessness or guilt. Suicidal thoughts and acts are common and a number of "somatic" symptoms are usually present.

F32.3 Severe depressive episode with psychotic symptoms

An episode of depression as described in F32.2, but with the presence of hallucinations, delusions, psychomotor retardation, or stupor so severe that ordinary social activities are impossible; there may be danger to life from suicide, dehydration, or starvation. The hallucinations and delusions may or may not be mood-congruent.

F32.8 Other depressive episodes

F32.9 Depressive episode, unspecified

F33 Recurrent depressive disorder

A disorder characterized by repeated episodes of depression as described for depressive episode (F32.-), without any history of independent episodes of mood elevation and increased energy (mania). There may, however, be brief episodes of mild mood elevation and overactivity (hypomania) immediately after a depressive episode, sometimes precipitated by antidepressant treatment. The more severe forms of recurrent depressive disorder (F33.2 and F33.3) have much in common with earlier concepts such as manic-depressive depression, melancholia, vital depression and endogenous depression. The first episode may occur at any age from childhood to old age, the onset may be either acute or insidious, and the duration varies from a few weeks to many months. The risk that a patient with recurrent depressive disorder will have an episode of mania never disappears completely, however many depressive episodes have been experienced. If such an episode does occur, the diagnosis should be changed to bipolar affective disorder (F31.-).

F33.0 Recurrent depressive disorder, current episode mild

A disorder characterized by repeated episodes of depression, the current episode being mild, as in F32.0, and without any history of mania.

F33.1 Recurrent depressive disorder, current episode moderate

A disorder characterized by repeated episodes of depression, the current episode being of moderate severity, as in F32.1, and without any history of mania.

F33.2 Recurrent depressive disorder, current episode severe without psychotic symptoms

A disorder characterized by repeated episodes of depression, the current episode being severe without psychotic symptoms, as in F32.2, and without any history of mania.

F33.3 Recurrent depressive disorder, current episode severe with psychotic symptoms

A disorder characterized by repeated episodes of depression, the current episode being severe with psychotic symptoms, as in F32.3, and without any history of mania.

F33.4 Recurrent depressive disorder, currently in remission

The patient has had two or more depressive episodes as described in F33.0-F33.3, in the past, but has been free from depressive symptoms for several months.

F33.8 Other recurrent depressive disorders

F33.9 Recurrent depressive disorder, unspecified

F34 Persistent mood (affective) disorders

Persistent and usually fluctuating disorders of mood in which the majority of the individual episodes are not sufficiently severe to warrant being described as hypomanic or mild depressive episodes. Because they last for many years, and sometimes for the greater part of the patient's adult life, they involve considerable distress and disability. In some instances, recurrent or single manic or depressive episodes may become superimposed on a persistent affective disorder.

F34.0 Cyclothymia

A persistent instability of mood involving numerous periods of depression and mild elation, none of which is sufficiently severe or prolonged to justify a diagnosis of bipolar affective disorder (F31.-) or recurrent depressive disorder (F33.-). This disorder is frequently found in the relatives of patients with bipolar affective disorder. Some patients with cyclothymia eventually develop bipolar affective disorder.

F34.1 Dysthymia

A chronic depression of mood, lasting least several years, which is not sufficiently severe, or in which individual episodes are not sufficiently prolonged, to justify a diagnosis of severe, moderate, or mild recurrent depressive disorder (F33.-).

F34.8 Other persistent mood (affective) disorders

F34.9 Persistent mood (affective) disorder, unspecified

F41.2 Mixed anxiety and depressive disorder

This category should be used when symptoms of anxiety and depression are both present, but neither is clearly predominant, and neither type of symptom is present to the extent that justifies a diagnosis if considered separately. When both anxiety and depressive symptoms are present and severe enough to justify individual diagnoses, both diagnoses should be recorded and this category should not be used.

TEEMU RISSANEN
Studies on life satisfaction in samples of the general population and depressive patients

The identification of early indicators of poor mental health may enable health monitoring and promotion as well as early intervention of adverse health processes. The present studies investigated the role of life satisfaction in prediction of and in recovery from depression. Additionally, the relationship of life satisfaction with childhood adversities and indicators of certain psychological or biological factors was investigated. Life satisfaction was measured with happiness, loneliness and interest in life as well as with general ease of living.

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