

**Dissertation**

**ASSOCIATION BETWEEN OVERWEIGHT, OBESITY AND  
MENTAL HEALTH**

submitted by

**Gregor Alexander RINDLER, MSc, BSc**

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**Univ.-Prof. Dr.phil. Wolfgang FREIDL**

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The following persons have contributed to either the thesis project or the publication resulting from this project:

Univ.-Prof. Dr. Wolfgang Freidl<sup>1</sup>

Univ.-Ass. Priv.-Doz. Dr. Erwin Stolz, MA<sup>1</sup>

Ao. Univ.-Prof.<sup>in</sup> Dr.<sup>in</sup> Anna Gries<sup>2</sup>

<sup>1</sup> Institute of Social Medicine and Epidemiology, Medical University of Graz

<sup>2</sup> Division of Physiology and Pathophysiology, Otto Loewi Research Center for Vascular Biology, Immunology, and Inflammation

### *Publication:*

Gregor Alexander Rindler, Anna Gries, Wolfgang Freidl, and Erwin Stolz contributed to the conception and design, the interpretation of the results, and the review of the drafts of the manuscript. Gregor Alexander Rindler (with input from Wolfgang Freidl) defined the hypotheses, statistically analysed the data, and drafted and revised the manuscript.

*Thesis:*

Gregor Alexander Rindler conceived and designed the thesis project (with input from Wolfgang Freidl and Erwin Stolz), defined the hypotheses, statistically analysed the data, interpreted the results, and wrote the thesis. All co-authors have agreed to the use of their data in this thesis.

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“Look mom, I did it!”

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## Abbreviations and Definitions

ACTH	Adrenocorticotrophic Hormone
ADHD	Attention Deficiency and Hyperactivity Disorder
AMYGD	Amygdala
BDNF	Brain Derived Neurotrophic Factor
BMI	Body Mass Index
CRH	Corticotropin Releasing Hormone
CSM	Complete State Model
DALY	Disability Adjusted Life Years
DHEA	Dehydroepiandrosterone
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (fourth axis)
EBC	European Brain Council
ECNP	European College of Neuropsychopharmacology
EU	European Union
FDA	Food and Drug Administration
GBD	Global Burden of Disease
GDP	Global Domestic Product
GHRELIN	Growth Hormone Release Inducing
GRRs	Generalized Resistance Resources
HPA	Hypothalamic-Pituitary-Adrenal Axis
HRQoL	Health-Related Quality of Life
HSD	Hydroxysteroid Dehydrogenase
IASO	International Association for the Study of Obesity
ICD-10	International Classification of Diseases (10th Version)
IOTF	International Obesity Task Force
LC	Locus Coeruleus
MAOIs	Monoamine Oxidase Inhibitors
NAC	Nucleus Accumbens
NPY	Neuropeptide Y
PET	Positron-Emission Tomography
PFC	Prefrontal Cortex
QoL	Quality of Life
SES	Socio Economic Status
SGAs	Second Generation Antipsychotics
SNRI	Serotonin Noradrenaline Reuptake Inhibitors
SNS	Sympathetic Nervous System
SOC	Sense of Coherence
SRH	Self-Rated Health
SSRIs	Selective Serotonin Reuptake Inhibitors
TCAs	Tricyclic Antidepressants
VTA	Ventral Tegmental Area
WHO	World Health Organization

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## Zusammenfassung

Sowohl Übergewicht als auch Adipositas sind häufig anzutreffende Erkrankungen und gelten daher als weit verbreitete Phänomene, die unter Gesundheitsexperten zunehmende Besorgnis hervorrufen. Bei Menschen mit psychischen Erkrankungen ist die Wahrscheinlichkeit größer, dass sie übergewichtig oder fettleibig sind. Adipositas steht in Zusammenhang mit einer Vielzahl medizinischer Begleiterkrankungen wie erhöhtem Blutdruck, Diabetes mellitus, Schlaganfall, koronarer Herzkrankheit oder Herzinsuffizienz, Gallensteinen, erhöhtem Schwangerschaftsrisiko, Osteoarthritis, Schlafapnoe -Syndrom, bestimmten Krebsarten und Fertilitätsstörungen. Adipositas ist die fünfthäufigste Todesursache weltweit und wird daher als globale Epidemie betrachtet, die nicht nur in den Industrieländern, sondern auch in den Entwicklungsländern eines der größten Gesundheitsprobleme darstellt. Sowohl Adipositas als auch psychische Erkrankungen weisen steigende Prävalenzraten auf und werden in vulnerablen Bevölkerungsgruppen mit zahlreichen medizinischen Komplikationen in Verbindung gebracht, wie in mehreren Studien gezeigt wurde. Vermutlich handelt es sich bei der Koexistenz dieser Erkrankungen um mehr als nur eine zufällige Überschneidung. Allerdings gibt es immer noch einen Mangel an Wissen über die zu Grunde liegenden Mechanismen zwischen Fettleibigkeit und psychischen Erkrankungen. Die mit Übergewicht und Adipositas verbundenen Komorbiditäten sind gut erforscht und wissenschaftlich belegt, während der Zusammenhang mit der psychischen Gesundheit noch unklar ist. Angesichts der Tatsache, dass nur wenige prospektive Studien den Zusammenhang zwischen psychischer Gesundheit und Übergewicht oder Adipositas unter Verwendung mehrerer Messpunkte untersucht haben, zielt diese Arbeit darauf ab, die Zusammenhänge zwischen psychischer Gesundheit und Übergewicht/Adipositas zu untersuchen und dazu beizutragen, einen besseren Einblick in die Art möglicher langfristiger Zusammenhänge zu gewinnen. Für diese Studie wurden zwei Datensätze verwendet, die im Rahmen einer retrospektiven Studie (Sekundärdatenanalyse) entsprechend der Forschungsfragen ausgewertet wurden. Der erste Schritt dieser Studie zielt darauf ab, die Korrelationen zwischen psychischen Gesundheitskonstrukten, einschließlich Depressionsstatus und Lebensqualität (QoL), und sowohl Übergewicht als auch Adipositas bei

15.461 österreichischen Personen im Alter von 15+ Jahren anhand von Querschnittsdaten aus der österreichischen Gesundheitsbefragung (ATHIS) zu untersuchen. In einem zweiten Ansatz werden die wechselseitigen Zusammenhänge zwischen Adipositas und psychischer Gesundheit anhand von Daten aus dem Survey of Health, Ageing and Retirement in Europe (SHARE) analysiert.

Mit Hilfe einer multiplen linearen Regressionsanalyse, die sich auf den Body Mass Index (BMI), den Depressionsstatus und die Lebensqualität konzentrierte, wurde ein cross-lagged Panel-Ansatz durchgeführt, der 16.184 erwachsene Europäer (50+) einschloss. Die Ergebnisse der Pearson-Korrelationsanalyse zeigen signifikante Korrelationen zwischen dem BMI und der körperlichen, sozialen, psychologischen, umweltbezogenen und allgemeinen Lebensqualität, wobei die Korrelation mit dem körperlichen Bereich unabhängig vom Geschlecht am stärksten war. Dementsprechend korrelieren höhere BMI-Werte signifikant mit einer niedrigeren Lebensqualität und höheren Werten für Depression, was auf einen Zusammenhang hindeutet. Die Ergebnisse zeigen signifikante verzögerte Effekte in eine Richtung hinsichtlich der Vorhersage des BMI für die Lebensqualität und den Depressionsstatus, während der Depressionsgrad und die Lebensqualität den BMI nicht klar vorhersagen. Übergewichtige, fettleibige und untergewichtige Personen weisen im Vergleich zu normalgewichtigen Personen über einen Zeitraum von 10 Jahren eine bedeutend niedrigere Lebensqualität sowie höhere Werte für Depression auf, wobei fettleibige Personen den stärksten Effekt zeigen. Die Ergebnisse bestätigen jedoch nicht, dass langfristig ein wechselseitiger Zusammenhang besteht.

Zusammenfassend lässt sich sagen, dass die Ergebnisse dieser Arbeit deutliche Hinweise auf langfristige Zusammenhänge liefern. Generell lassen sich über einen Zeitraum von 10 Jahren verzögerte, unidirektionale Zusammenhänge zwischen dem BMI und den psychischen Gesundheitsmerkmalen, wie Depression und Lebensqualität bestätigen. Allerdings lassen sich in dieser Untersuchung keine nennenswerten bidirektionalen Zusammenhänge auf lange Sicht nachweisen, die früheren Untersuchungen zu diesem Thema entsprechen. Diese Ergebnisse sind als schwacher Hinweis auf einen möglichen Zusammenhang zu werten, wenngleich dies kein Beweis für einen kausalen Zusammenhang ist. Insgesamt sollten diese Ergebnisse als Anstoß für weitere Forschungen zu diesem Thema gesehen werden. Ein Erkenntnisgewinn, nicht nur bei älteren Menschen, sondern auch im Hinblick auf die Erkennung früher pathologischer Entwicklungen bei Kindern und Jugendlichen, scheint für die Prävention von Krankheiten entscheidend zu sein.

## Abstract

Both overweight and obesity are medical conditions that are very common and considered widespread phenomena that lead to rising concerns among clinical populations. Individuals who have mental illnesses are more likely to be overweight or obese. Obesity is related to a wide array of medical comorbidities, including increased blood pressure levels, diabetes mellitus, stroke, coronary heart disease or congestive heart failure, gallstones, enhanced pregnancy risks, osteoarthritis, sleep apnoea syndrome, certain cancer types and fertility disorders. Obesity is the fifth leading cause of death worldwide and considered a global epidemic, demonstrating one of the major health-related issues not only in industrialised countries but also in developing countries. Both obesity and mental illness show increasing prevalence rates and are associated with numerous medical complications in vulnerable populations, as shown in several studies. Presumably, the coexistence of these conditions is more than just a random overlap, however, there is still a lack of knowledge in terms of linking mechanisms between obesity and mental illness. The comorbidities associated with overweight, and obesity have been well researched and scientifically proven, while their relationship to mental health is still deficient. Given the fact that only a few prospective studies have investigated the association between mental health and overweight or obesity using multiple points of measurement, this thesis aims to investigate the associations between mental health and overweight/obesity and to contribute a better insight into the nature of possible long-term associations.

Two datasets were used for this study, which were analysed in the context of a retrospective study (secondary data analysis) in accordance with the research questions. The first step of this study is aimed at investigating the correlations between mental health constructs, including depression status and quality of life (QoL), and both overweight and obesity among 15,461 Austrian individuals aged 15+ using cross-sectional data from the Austrian Health Interview Survey (ATHIS). In a second approach, this thesis further analyses reciprocal associations between obesity and mental health using data from the Survey of Health, Ageing and Retirement in Europe (SHARE). A cross-lagged panel approach was performed, including 16,184 adult Europeans (50+) using multiple linear regression analysis, focusing on the Body Mass Index (BMI), depression status, and QoL. According to Pearson's correlation analysis, the results indicate significant correlations between BMI and physical, social, psychological, environmental, and overall QoL, whereas the correlation with the physical domain was strongest, regardless of gender. Accordingly, higher BMI scores are correlated with significantly lower QoL scores and increased depression scores suggesting underlying linking

mechanisms. Findings yield significant cross-lagged effects in one direction regarding BMI predicting QoL and depression state, whereas depression state and QoL do not significantly predict BMI. Obese, overweight, and underweight individuals show significantly decreased levels of QoL as well as increased depression scores, compared to people of normal weight over a lag time of 10 years, where obese individuals indicate the strongest effect. However, results do not confirm reciprocal associations in the long term.

In conclusion, the results of this thesis suggest significant indications of long-term associations. Generally, cross-lagged, one-directional associations between BMI predicting mental health characteristics depression and QoL can be confirmed over a 10-year period. However, this examination does not verify any considerable bi-directional associations in the long-term corresponding to previous examinations on this topic. These findings should be taken as weak evidence of a possible relationship, although this is not proof of causality. Overall, these results should be seen as an impetus for further research on this topic. Gaining knowledge, not only among older populations, but also in terms of detecting early pathological developments among children and adolescents, seems to be crucial for preventing illness.

# 1. Introduction

Both overweight and obesity are medical conditions that are very common and considered widespread phenomena (McElroy et al. 2004; Pickering et al. 2007) leading to rising concerns among clinical professionals. Obesity portrays a public health issue with many long-term problems and increasing prevalence rates. Moreover, relapses during treatment are frequently observed and quite common. In fact, overweight and obesity are undoubtedly very serious epidemiological issues in Europe and worldwide and future predictions are rather worrying (Krzysztozek et al. 2019). Hence, the implementation of adequate interventions and the promotion of preventive strategies to establish causal evidence and in-depth knowledge are highly desirable (Flegal et al. 2012; Gutiérrez et al. 2012; Horwitz et al. 2008). Furthermore, personalised preventive measures are required in order to improve public health and avoid the development of overweight (Krzysztozek et al. 2019). Obesity is considered to be related to a wide array of medical comorbidities, including elevated blood pressure, diabetes mellitus, stroke, coronary heart disease or congestive heart failure as well as gallstones, increased risks during pregnancy, osteoarthritis, sleep apnoea syndrome, certain cancer types and fertility disorders (Chatterjee et al. 2020). As a result, the mortality of affected individuals is significantly increased (Wilborn et al. 2005). Nowadays, obesity is understood as a multifactorial disease comprising both genetic, environmental (Park 2009) and socioeconomic factors within an obesogenic environment (Xiao et al. 2020). Accordingly, obesity as well as being overweight are obviously among the most frequent risk factors for developing long-term morbidity. Over recent decades, however, sedentary lifestyles have increased, and calorie-rich foods have been consumed more frequently, leading to a substantial increase in body weight and BMI levels. This phenomenon applies not only to industrialised countries but also to developing countries (Popkin et al. 2006). The International Association for the Study of Obesity (IASO) emphasises that the prevalence of obesity has increased up to over 20% during the past years (International Association for the Study of Obesity 2006; Fry 2005). Moreover, the prevalence of overweight in Europe is often around 50% (Martinez et al. 1999), additionally, obesity ranks in the fifth position of the most frequent causes of death all over the world (Alwan et al. 2011; Safaei et al. 2021). Over 13% of deaths within the European region are caused by overweight or obesity (WHO Regional Office for Europe 2022). Thus, overweight and obesity are considered important public health issues. In addition to increased mortality rates and diminished QoL the related comorbidities have significant impacts on healthcare expenditures. Both direct costs resulting from treating overweight-related diseases and indirect costs from sick leave or premature death are remarkably high (Gorasso et al. 2021)

Obesity and overweight negatively affect psychosocial well-being and health-related QoL (Bull et al. 2020) Furthermore, mental disorders involving disruptions in mood, cognition, and behavior (American Psychiatric Association 2013) contribute to the overall burden of the condition.

According to the findings of the Global Burden of Disease Study (GBD 2010), mental disorders and disorders associated with substance use are identified as the fifth primary source of the burden assessed through disability-adjusted life years (DALYs) (Ferrari et al. 2014). Additionally, the Global Burden of Disease Study carried out in 2019 included 12 mental disorders from 204 countries and territories. Investigating prevalences and burden of mental disorders. Accordingly, findings yield that mental disorders are still among the major causes of burden worldwide without showing any signs of reduction in terms of DALYs in the long term from 1990 to 2019, showing increasing levels instead (GBD 2019 Mental Disorders Collaborators 2022). In the United States, the prevalence of mental disorders is characterised by high frequencies. According to estimates from 2012, approximately 43.7 million adult Americans displayed mental illnesses, which accounts for 18.6% of adults within the population of the United States (US) (Substance Abuse and Mental Health Services Administration 2012).

## **1.1 Economic burden of overweight and obesity**

According to the German Federal Statistical Office, around 5.500 treatments of inpatients in the year 1998 were due to obesity-related medical events. This resulted in 35,500 treatment days performed on inpatients, which amounts to the costs of 8.9 million euros (Federal Statistical Office Germany 2007). They are responsible for increasing health expenditure caused by chronic obesity associated diseases (Robert Koch-Institut 2014). In the UK, 61.3% of the population is estimated to be either overweight or obese. Related expenditure on the treatment of obesity-related diseases is approximately £5 billion per year, which is expected to double by 2050 (Department of Health 2013). In many Western countries, mental disorders are considered to be responsible for about 30-40% of chronically ill patients who are unable to work, which causes costs of about 3% of the gross domestic product (GDP) (WHO Regional Office for Europe 2015). According to a study by Okunogbe et al. examining economic trends of overweight and obesity, the economic burden of overweight is expected to globally rise to over 3% of the GDP by 2060 if this trend continues. Accordingly, total overweight-related health expenditures will increase fourfold in high-income countries by 2060 and 12 to 25 times in low-income countries (Okunogbe et al. 2022).

Addressing the economic burden of obesity-related impacts concerning healthcare expenditures, it is visible that up to 10.4 billion euros have been spent on various therapeutic medical interventions to treat comorbidities associated with obesity (Fry & Finley 2005). Consequently, obesity has tremendous economic effects in many European countries, which are associated with health expenditures ranging from 0.09% up to 0.61% of the GDP (Fry & Finley 2005). However, for estimating an overall view of healthcare expenditures it is important to take costs directly spent on sick leave and early retirement into account, alongside therapeutic regimens of obesity-associated comorbidities. Obesity-related health costs within the United States accounted for approximately 10% of the US. Health expenditures (Wolf & Colditz 1998; Thompson et al. 1998). Given that the prevalence rates of overweight and obesity in Europe are lower than in the United States, healthcare expenditures are also expected to be lower within most European countries. However, we must consider that there are no studies available that have been conducted across Europe including all European countries regarding health-economic matters in terms of burden of overweight and obesity (Müller-Riemenschneider et al. 2008).

In the United States, health expenditures due to overweight- or obesity-associated events are going to double each decade and will reach \$860.7 to 956.9 billion dollars until 2030. As a result, obesity- and overweight-related healthcare expenditures will account for 16 to 18% of the total costs with respect to health care (Zhao 2013).

Obesity and overweight are recognised major issues for both global and national public health, particularly confirmed by prevalence, incidence rates, and economic burden. In the year of 2014, almost 30% of the population were either overweight or obese, whereas 5 % of the global deaths were caused by obesity-related health issues. Accordingly, at this point, and in view of the rising incidence, approximately 50% of the adult population worldwide are predicted to be overweight by 2023 (Dobbs et al. 2014). In fact, obesity has a huge economic impact on communities, individuals, and nations (Birmingham et al. 1999; Levy et al. 1995). Besides obesity-related increased mortality, lost workdays or even permanent disability are more frequent among obese individuals. According to previous examinations, a gradient in terms of higher BMI scores and charges due to obesity are suggested (Andreyeva et al. 2004; Dee et al. 2014; Finkelstein et al. 2009; Specchia et al. 2015).

Required treatment can lead to far-reaching economic consequences posing a problem for healthcare systems. Within Europe, treatment costs for health issues associated with obesity account for around 7% of total health expenditure (Branca et al. 2007). This can be roughly compared with the costs for the therapy of neoplastic diseases (Krzysztozek et al. 2019).

## 1.2 Overweight and obesity

In the Western countries, the prevalence rates among children and adults have increased and are nowadays at a very high level (Mokdad et al. 1999; Seidell 1995; Kuczmarski et al. 1994). Additionally, obesity is considered a risk factor for developing several physical diseases such as cardiovascular events (Brancati et al. 1999) that are responsible for premature death (Pi-Sunyer 1993). Today, obesity is considered a global threat and does not only affect wealthy social classes, but also an increasing number of affected individuals can be found in developing countries (WHO 2000). In particular, abdominal obesity, measured by waist-to-hip ratio, is related to several medical conditions, including diabetes mellitus, type 2, stroke, and cardiovascular disease (Goodpaster et al. 2003; Suk et al. 2003).

Today, obesity is considered a dangerous and serious health-threatening problem in almost all of Europe. Within the last decades, the proportion of obese men has increased fourfold, while obesity in women has roughly doubled (Kontis et al. 2017). In epidemiological terms, obesity has long reached global epidemic proportions and is thus considered one of the main health-related issues in industrialised and developing countries (WHO 2000).

The degree of obesity is described differently in the different countries of the EU and varies within the European states. Furthermore, obesity contributes significantly to increased mortality rates around the world, and is therefore a much more frequent cause of death than, for example, undernourishment or malnutrition (WHO 2000).

More than 3.5 million people die every year because of being overweight or obese (Vandevijvere et al. 2015). More than one million of these deaths affect the European Union (EU) alone (Vandevijvere et al. 2015; Tsigos et al. 2008). Approximately 12 million people are affected by obesity or being overweight every year. A further complicating factor is that a large number of obesity-associated comorbidities occur, which can lead to further undesirable side effects that in turn have several health and psychosocial effects. Accordingly, more than 2.3 billion people over the age of 18 worldwide are considered overweight, of whom about 700 million are obese (Vandevijvere et al. 2015). In 2016, around 39% of adults worldwide suffered from overweight and its associated problems, while 11% of males and 15% of females aged 18 and above were affected by obesity. Within Europe, diagnosed cases of obesity range from 19% in Denmark to 31% in Malta (WHO 2017). The department of health in the United Kingdom forecasts a decimation of male life expectancy by 5 years in 2050 (WHO 2017).

According to the WHO, obesity is defined as abnormal or excessive accumulation of fatty tissue, which can lead to a significant deterioration in health (WHO 2000).

Following the definition of the WHO regarding the classification of weight status, overweight is defined by a body mass index (BMI), estimated by kilograms (Kg) and divided by square meters ( $m^2$ ), ranking between 25 and 29.9, whereas scores equal to, or above 30, indicate obesity (WHO 1995). Humans with a BMI of over 40  $kg/m^2$  show increased cancer mortality in 52% of men and 62% of women. For some specific types of cancer, the mortality rate is particularly high. The mortality rate increases by 525% in women with uterus cancer, and by up to 325% in men with liver cancer (Calle et al. 2003). Besides increasing mortality rates due to obesity, excessive body weight can also lead to other impairments and reduced QoL (Adams et al. 2006; Flegal et al. 2007; Renehan et al. 2008; Stevens et al. 2002; Roberts et al. 2003; Linde et al. 2004).

Only a few countries within the European Union (EU) have no food-related problems as the food supply situation is very good. The decline in food production in the EU is often a desirable effect to avoid excess food and to make production more environmentally friendly. This also involves market organisation, which opens up further opportunities to react more quickly in the event of naturally occurring problems such as poor harvests and to compensate for this by adapting production (Paszkowski 2013). According to the Food and Agriculture Organisation (FAO), a new form of malnutrition emerged in 2013 in 73 countries around the world, including 28 states within Europe that indicated overweight and obesity. As a result, 1 in 4 people in Europe would suffer from obesity, reflecting an increasing tendency (Krzysztozek et al. 2019). According to James (2008) and Branca et al. (2007), the prevalence of obesity in Europe is between 10 and 25% for men and between 10 and 30% for women, with only minor differences between countries (James 2008; Branca et al. 2007). In the year 2013, Europe accounted for about two-thirds of all countries that faced obesity (Pawlak 2012) in terms of European countries' share of nations around the world. Almost 60% of the adult population within the European region are affected by either overweight or obesity, whereas one in three children suffers from overweight (WHO 2021; WHO 2018). The EU and the European states are now regarded as states of prosperity and satisfaction. In some cases, however, this wealth can lead to health problems and economic losses. Consequences of social and economic changes, as well as urbanisation, modernisation, advanced globalisation, advances in the development of

services and technological developments and above all a changed socio-economic status (SES) (Krzysztozek et al. 2019).

With the increasing frequency of less affluent countries within the EU, such as Slovakia, Hungary, Poland and Bulgaria, the prevalence of obesity, especially among men, is also increasing significantly. In these nations, the nutritional level of the population has steadily improved. Compared to the years from 1990 to 1992, the food situation has improved considerably, especially in states such as Romania, Estonia, and Lithuania, although the situation in individual households is somewhat different. About 20 % of households in the newer countries of the EU show various problems in procuring adequate food for all family members.

By comparison, in the other EU countries this problem is only apparent in about 6 % (Pawlak 2012). The daily procurement of wholesome meals is often not possible, especially in countries such as Romania, Lithuania, Slovakia, Hungary, and Bulgaria (Pawlak 2012).

An excessive supply of energy (FAO 2013), which amounts to more than 142% of the normal calorie requirement that was observed in these countries between 2006 and 2008, promotes the development of overweight and obesity in this context (Krzysztozek et al. 2019). Berghöfer et al (2008) have already recognised that countries in central and Eastern Europe have significantly higher obesity rates than nations in Western Europe or northern Europe. This was primarily because of much greater difficulties in procuring sufficient food of high quality in order to be able to exist healthy. This was largely due to the economically unsound predicative situation in these countries (Berghöfer et al. 2008). According to a systematic review by Dinsa et al. (2012), it is postulated that in countries with low incomes, the prevalence of obesity is higher in higher socio-economic circumstances than in lower socio-economic groups. As a result, socio-economic inequalities in obesity appear to be more mixed in middle-income countries, especially among men (Dinsa et al. 2012). In Romania, however, obesity prevalence seems to be lower among males (Jarosz et al. 2008). People with low incomes often have limited opportunities to exercise in sports facilities or fitness centres. Additionally, the areas in which these people live contribute little to promoting physical activity (Jarosz et al. 2008). Low income therefore has a considerable effect on nutrition. A healthy and sensible diet, such as eating more fruits instead of sugary foods that also contain too much energy, is often quite costly in many EU countries.

In France, for example, a portion of fruit and vegetables costs about 5 times more than other foods with the same or similar energy content (WHO 2017). Most frequently, obesity actually occurs in highly developed states with high per capita incomes, including Ireland, the UK, Austria, and Luxembourg. These countries also have the highest surplus of energy consumed

via food, which is far higher than the daily amount needed. The supply of energy is up to 193% higher than the minimum quantity required. In addition, an above-average consumption of proteins and fats can be observed (Pawlak 2012).

According to the FAO, the minimum calorie requirement in the EU countries between 2006 and 2008 was between 1910 kcal per person in Malta and 2000 kcal in the Netherlands (Pawlak 2012). In 1961, the average energy intake within Europe was around 2,300 kcal per day. In 1998, it was already 2,800 kcal (WHO 2017) and from 2006 to 2008, the daily calorie intake in the EU countries was already 3,460 kcal per capita. This means that the daily calorie intake was about one fourth higher than the global average, and about two thirds higher than in the least developed countries (Pawlak 2012). From 2006 to 2008, daily protein consumption in the EU was almost one fourth, and fat consumption even 80% above the average, protein intake 20 times higher and 4 times higher fat intake than in economically less developed countries (Pawlak 2012). Moreover, extreme sugar consumption does not only lead to caries and dental problems, but it is also considered a risk factor for the development of diabetes, obesity, and increased triglyceride levels (Kowalowski et al. 2004).

According to the WHO (2003), increased sugar content in beverages contributes significantly to the development of overweight and is considered a risk factor (Myszkowska-Ryciak et al. 2010). This excessive energy consumption makes obesity a far-reaching health problem when it comes to nutritional issues and public health relevance in EU regions (Krzysztozek et al. 2019). With regard to possible differences between the sexes, changes primarily exist in highly developed countries with higher per capita incomes (Dinsa et al. 2012). In these countries, the obesity rate for women is lower than for men, whereas in other states, the number of obese women exceeds that of men. This suggests that obesity affects more women than men. However, this assumption cannot be confirmed unequivocally, as there are large discrepancies between the individual nations. The International Obesity Task Force (IOTF) states that in 14 out of 36 countries, obesity occurs more frequently among men than among women and overweight among men than among women in all 36 countries (Krzysztozek et al. 2019). The growing epidemic of obesity is substantially favored by various factors, all of which are associated with civilising progress.

These include, for example, reduced energy consumption in professional and domestic activities, sedentary activities, technological innovations, the use of cars for short distances, consumption of highly processed foods, and above all changes in eating habits.

First and foremost, the consumption of large meals that significantly exceed daily energy requirements, high-sugar foods, fast food, and animal fats (Knai et al. 2007). According to

some analyses, most obese people live in South and North America or in the Middle East. The main factors contributing to this high number of affected individuals are socio-economic nature and increased GDP per capita, indicating increased prosperity and growth, as well as increased individual SES. Thus, a clearly positive correlation between GDP per capita and the degree of obesity can be assumed. The GDP per capita was particularly examined and identified as the main factors that seems to be responsible for this association (Dinsa et al. 2012; Pisa & Pisa 2017; Egger et al. 2012; ALNohair 2014; Menifield et al. 2008). The currently largely reduced physical activities are mainly the result of the continuous technological development as well as the lifestyle, which predominantly includes sedentary behaviors (ALNohair 2014).

In addition, there are cultural and traditional restrictions in the lifestyle of women, for example, in South Africa or the Gulf states (al-Shammari & Khoja 1994). The adopted Western diet, i.e., the consumption of high calorie finished products and highly processed foods, strongly sweetened drinks (Cuevas et al. 2009) and the widespread use of corn syrup with a high fructose content (Bocarsly et al. 2010; Tappy et al. 2013) are mainly responsible for the increase in obesity. In Southeast Asia and the regions of the western Pacific, where a very low number of obesity can be observed, a particularly high growth rate can be noticed. During the "Green Revolution" (Gopalan 2013), eating habits in India changed dramatically as increasingly resorbable carbohydrates in the form of wheat starch became available and overall fat consumption rose (Cybulska & Szostak-Węgierek 2012). This led to an increase in the incidence of obesity. The same risk factors apply to the Asian population as apply to Caucasians. The distribution of these factors results essentially from the lifestyle patterns, in particular, eating habits, which partly differ within these countries playing an important role here (Cybulska & Szostak-Węgierek 2012). However, Japanese people consume many foods that prevent atherosclerotic processes in the blood vessels, which may also partly explain the longer life expectancy of the Japanese population (Cybulska & Szostak-Węgierek 2012).

Both overweight and obesity are recognised as being very serious epidemiological and global health problems that have far-reaching negative effects. This is true for Europe and for the world as a whole. As far as public health is concerned, preventive measures are becoming increasingly important, as personalised treatment strategies and global measures are needed to counteract this development (Krzysztozek et al. 2019).

### 1.3 Size and burden of mental disorders

Mental disorders include depression, panic disorders and schizophrenia as well as insomnia and addiction. These diseases are clearly distinguishable from the diseases known as neurological disorders. These include dementia, multiple sclerosis, and epilepsy. These two types of disorders are collectively classified as neuropsychiatric diseases, mental, neurological and substance abuse (MNS) (Collins et al. 2011) disorders or brain disorders. Indeed, mental disorders are very prevalent and pose a great burden. Accordingly, in 2019, 12% of the global population suffered from a mental disorder, which accounts for approximately 5% of the DALYs and about 16% of the years living with disabilities globally (Rehm & Shield 2019). Approximately 654 million cases of mental disorders were observed in 1990, whereas an increase of over 300 million (48%) cases by 2019 were observed within the Global Burden of Disease Study (GBD 2019 mental Disorders Collaboration 2022).

The complexity of the various diseases and the corresponding diagnoses with their coding in the respective diagnostic classification systems, including the International Classification of Diseases (ICD-10) (WHO 1993) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association 1994) was associated with the division into disciplines, that pursued different approaches and concepts.

This has impeded a thorough and inclusive evaluation of the magnitude and impact of diverse brain disorders. (Wittchen et al. 2011). Due to the fact that many brain diseases are associated with a certain stigmatisation and in part also marginalisation, this was often regarded as a hindrance when it came to generating a more far-reaching understanding and knowledge of the core issues of mental disorders (Saxena et al. 2007; Klin & Lemish 2008; Corrigan 2004). Both amateurs and professionally trained persons are largely unaware of the underlying mechanisms and interrelationships of brain disorders. In addition, the full extent of these diseases as well as the associated social burden that may result from them are not well investigated. Research endeavors on this topic are seriously hampered by a lack of awareness and knowledge, which leads to a considerable lack of research evidence in relation to causal research and treatment strategies. This also has a negative effect on the distribution of resources in mental healthcare management and thus on the treatment of mental health problems (Wittchen et al. 2011). In fact, there is a strong need for further investments in mental health care and a more balanced distribution of resources within European countries (Castelpietra et al. 2020).

Accordingly, there is increasing evidence that brain disorders are not only much more common than previously assumed, but that they also pose a much greater burden and threat to people than it was thought in earlier times. Brain diseases are considered one of the greatest health challenges of the 21st century (Collins et al. 2011; Murray & Lopez 1996; Prince et al. 2007; World Health Organization 2001; World Health Organization 2008, Wittchen & Jacobi 2005).

Several epidemiological studies on mental disorders around the world have shown that every year about one third of adults suffer from a mental disorder (Kessler & Üstün 2008). According to the Global Burden of Disease Study (GBD 2010) that covers all diseases and injury categories (Murray & Lopez 1996; World Health Organization 2002; World Health Organization 2008) associated with brain disorders, these medical conditions are among the proportionally most common and still on the rise. Collins et al (2011) postulate that an estimated 13% of all diseases affect brain impairments, exceeding cardiovascular and cancer rates (Collins et al. 2011). According to the later version of the Global Burden of Disease study from 2019, a considerable part of the burden of disease is caused by mental disorders (GBD 2019 Mental Disorders Collaborators 2022).

However, it should also be noted that such general assumptions within the European Union (EU) are of little significance and can therefore hardly be used, as it must be assumed that these assessments are highly influenced by the most densely populated countries with very different populations, health systems, mortality, and socioeconomic characteristics (Wittchen et al. 2011). Due to the lack of evidence and comprehensive data on the extent, burden and cost of neurological diseases and brain disorders in Europe, a Europe-wide interdisciplinary effort was initiated in 2003, coordinated by the European Brain Council (EBC) and the European College of Neuropsychopharmacology (ECNP). These efforts have involved different task forces and promising methodological approaches, such as the re-examination of epidemiological data sets derived from studies within the EU. By 2004, several publications had been produced in this way (Andlin-Sobocki et al. 2005; Wittchen et al. 2005).

The resulting findings proved the extent and burden of neurological (Olesen & Leonardi 2003; Berr et al. 2005; Campenhausen et al. 2005) and mental disorders (Wittchen & Jacobi 2005). These publications provided a comprehensive database on health, costs, and economic aspects for both pathologies. An estimated 27% of the adult population within the EU, aged 18 to 65, is affected by mental disorders each year. This means that in 2004, more than 82.7 million out of a total of 301.7 million people in the EU, within the 18 to 65 age range, were suffering from mental disorders. The most common impairments were anxiety disorders,

somatoform disorders, depression, and the use of various substances.

According to the 2005 report, mental disorders may have far-reaching psychosocial effects and lead to many impairments, not least due to low consultation rates. Only 26% of those affected seek professional help or consult a specialist. Those who were treated experienced a considerable delay from the onset of the first symptoms. Only a small number of people received the most emergency treatment. The main reason for these minimally adequate interventions and weak services was a lack of knowledge with regard to treatment methods, inadequate therapy, but also a lack of resources and low utilisation (Wittchen et al. 2011). Data sets on mental disorders and neurological diseases were used to estimate the costs incurred for treatment and to estimate the corresponding health and economic impacts. Both direct and indirect costs were calculated for countries of the EU (Andlin-Sobocki et al. 2005; Wittchen et al. 2005).

The result showed that mental disorders cause extremely high costs. Compared to health expenditure incurred due to somatic diseases, it was noticeable that indirect financial expenditure was disproportionately high compared to the direct expenditure in healthcare. Supported by some epidemiological studies, it could be assumed that the total financial burden of brain disorders within the EU in 2005 was about 386 billion euros, of which about 277 billion euros alone were spent on the treatment of mental disorders (Wittchen et al. 2011).

The disability-adjusted life years (DALY) lost due to either premature death or persistent disability, is a measure of the burden of disease. Mostly, disease-related stress, which occurs in the context of mental disorders and disorders of the brain, is responsible for the resulting disability. All these disorders have a negative effect on the functioning of the affected persons and not on mortality, as in the case of cancer or cardiovascular diseases (WHO 2008). Mental and other brain disorders account for a considerable proportion of the total burden of disease. For women about 1 out of 3, and for men about 1 out of 4 years of life are lost, due to premature death, is attributable to brain disorders (Wittchen et al. 2011). Depression (7.2 % of the general burden of disease within Europe), dementia, respectively Alzheimer's disease (3.7%), and alcohol consumption (3.4%) account for the largest share of the global burden of disease. Furthermore, there are clear gender-specific differences. Women are disproportionately affected by depression, which means that 1 year out of 10 years in health is lost due to impairments because of this disease. This corresponds to 10.3 % of all DALYs. As far as men are concerned, the consumption of alcohol is the greatest factor influencing the burden

of disease in Europe. It accounts for about 5.3% of the global burden of disease (Wittchen et al. 2011).

There are also some regional differences. The highest DALY rates among men are found in the Baltic countries of Eastern Europe, mainly due to the consumption of alcohol and related disorders. The frequency of DALYs in the rest of Europe seems to be similar for men. However, in Western Europe, in contrast to the rest of Europe, there are slight differences, with a lower frequency of depressions, higher rates of epilepsy, most often caused by alcohol, and lower incidence of dementia, such as Alzheimer's disease, mainly due to lower life expectancy (Zatonski et al. 2008). In Western Europe, there is also a greater proportion of burden of disease, primarily associated with drug-use disorders. As far as women are concerned, the DALY frequency seems to vary among different countries and regions within the EU. There is also less variability in life expectancy among women within the European states than for men (Zatonski et al. 2008). Nevertheless, the frequency of alcohol-associated disorders is also higher here, while dementia and Alzheimer's disease do not occur as often as in the rest of Europe (Wittchen et al. 2011). According to Wittchen et al. (2011), the three most frequently occurring mental disorders regardless of age groups are in the first-place anxiety disorders with 69.1 million, followed by unipolar depression with 30.3 million and in the third-place sleep disorders that affect about 29.1 million. The disability burden rate due to mental and neurological diseases is very high. Wittchen et al. (2011) claim that neuropsychiatric diseases are responsible for 30.1% of the total burden of disease in women, and about 23.4% of the burden of disease in men. As a result, mental disorders are much more prevalent in the EU than was initially assumed. In terms of DALY frequency, depressive disorders are by far the most profound and debilitating conditions in the EU (Wittchen et al. 2011).

The results of the analysis by Wittchen et al. (2011) clearly show that mental disorders and neurological diseases are considered the greatest challenge of the 21st century in the healthcare sector demonstrating a hugely demanding challenge. There are several groups of different disorders and various specific diagnoses that require different interventions in terms of prevention, therapy, or rehabilitation between different age groups. Due to a lack of effective treatment strategies, currently insufficient curability, and inadequate preventive measures in respect to mental disorders and other disorders of the brain, there is a strong need for joint action at all levels. This includes basic research, psychological treatment

strategies as well as public health research, including causal research and pharmacological approaches to therapy. In the same way, the provision of standards in mental healthcare needs to be reconsidered, because the social burden and impairments caused by brain disorders will continue to increase, also due to the limited life expectancy, there is an immediate demand for action and political prioritisation (Wittchen et al. 2011). There is a series of scientific evidence from longitudinal studies (de Graaf et al. 2011; Kessler et al. 2011; Beesdo et al. 2010; Beesdo et al. 2009) that clearly indicate that the vast majority of mental disorders begin in childhood or adolescence, which seldom spontaneously enter a remission phase during their further course. However, secondary symptoms and complaints occur quite often, at least temporarily. According to cross-sectional studies, these long-term patterns are referred to as multi-morbidities. These conditions are not only associated with various serious psychosocial dysfunctions and impairments, but also make a considerable contribution to the burden of disease caused by mental disorders. Such different developmental patterns and courses of different types of disorders could accordingly represent new approaches for interventions (Wittchen et al. 2011).

## **1.4 Scientific background**

The first reported results regarding associations between obesity and mental disease describing the increased risks of mentally ill individuals for developing obesity, were recognised in 1946 by Nicholson. Accordingly, emotional tensions as well as psychoneurosis aspects were suggested to interact with obesity (Nicholson 1946). Consecutively, a lot of investigations concerning this issue have been carried out in the past predominantly on the subject of bi-directional associations between obesity and mental health (Cameron et al. 2012). Following that, individuals who suffer from mental diseases display a 2 to 3-fold increased chance of suffering from obesity, whereas the risk of mental disorders in obese is expected to range from 30 up to 70% (De Hert et al. 2011). According to a recent study carried out by Leutner et al., obesity is identified as a significant risk factor for developing mental health issues within both young and old populations, while older patients showing more links between obesity and psychiatric disorders. Even though a vast majority of psychiatric diagnoses being observed in older people, a greater risk of mental disorders is observed in obese younger people earlier in life (Leutner et al. 2023). Furthermore, findings from Leutner et al. provide evidence for a significant link between obesity and mental health, while psychiatric illness usually manifested in a period of a few years (Leutner et al. 2023). Additionally, massive overweight is correlated with psychiatric illness and mental health (Holt

2019). Thus, obesity is expected to be related to various mental disorders such as anxiety, mood disorders, attention deficiency and hyperactivity disorder (ADHD), schizophrenia, binge eating disorder, trauma and personality disorders, including related events across the lifespan. Furthermore, obesity is often a result of adverse side effects of administered medication for the treatment of mental illness (Remington 2006). Particularly, antipsychotics to treat serious mental illness is recognized to induce metabolic dysregulation and drug-induced weight gain (Mazereel et al. 2020).

Mental disorders and obesity are common medical conditions showing high prevalence rates. Following some research findings, these two major public health issues seem to be associated with each other (Kivimäki et al. 2009), hinting at more than being just coincidental (Avila et al. 2015). Additionally, the underlying nature of the relationships between obesity and mental illnesses is still poorly understood. (Avila et al. 2015) and prospective evidence on the associations between depression and weight changes are inconsistent (Treviño-Alvarez et al. 2023). Possible associations between obesity, physical conditions, and compromised mental health have been focused on in several debates (De las Cuevas et al. 2011). Mental health disorders are prevalent and can impact health-related behavior, physical well-being, and social integration (Robert Koch-Institut 2013). Following the findings of a study on the associations between obesity and mental health, greater BMI levels may lead to bias and stigmatization, and thus leading to diminished mental health (Emmer et al. 2020).

Various studies have indicated that individuals afflicted with severe mental health conditions are categorised as "vulnerable individuals," placing them at an elevated risk for various medical incidents (Koran et al. 2002; Ceilley et al. 2006; Carney et al. 2006; Oud et al. 2009). Several studies suggest that people who experience severe psychiatric illnesses indicate an elevated risk of being obese (McElroy et al. 2004; Pickering et al. 2007; Zhang 2021). Consequently, those living with significant mental health issues are more prone to being overweight or obese compared to the general population (Mitchell et al. 2013). However, obesity seems to increase the likelihood of several mental disorders, including depression and anxiety, particularly in females. across all age groups (Leutner et al. 2023).

A study conducted in North America revealed that approximately 80% of 10,000 individuals diagnosed with schizophrenia, bipolar disorder, or depression were classified as either overweight or obese (Correll et al. 2010). The underlying cause behind this elevated prevalence of obesity among individuals living with severe mental illnesses has been the subject of extensive discussion. Various studies propose that complex interplays involving genetic factors, environmental influences, inherent disease traits, and the side effects of antipsychotic medications are accountable for weight gain (Holt & Peveler 2009, Lee et al.

2022). In contrast, other perspectives attribute the primary cause of weight increase to the adverse effects of antipsychotics (Strawn et al. 2023; Mazareel et al. 2020; Alvarez-Jimenez et al. 2008; McCloughen & Foster 2011; Allison et al. 1999; Foley & Morley 2011), which are often combined with antidepressants to enhance the effectiveness of depression treatment (Chen et al. 2011).

The general presumption is that weight gain associated with antipsychotic drugs might arise from various mechanisms, which include influencing hormone neurotransmission, such as serotonin, histamine, and epinephrine (Baptista 1999). Moreover, gaining weight also seems to be linked to the secretion of insulin by affecting  $\beta$ -cell function resulting in insulin resistance that has a diabetogenic effect that supports gaining body weight. Additionally, it is known that there are different polymorphisms explaining susceptibility of some patients to metabolic events caused by second generation antipsychotics (SGAs) (Grajales et al. 2019). The active components in antipsychotic medications impact neural pathways by modifying their activity. This, in turn, could lead to weight gain through the obstruction of specific receptors that affect the body's regulatory systems for appetite and weight (Stanton 1995). Both antidepressants (Solmi et al. 2020; Alonso-Pedrero 2019; Flava 2000; Serretti & Mandelli 2010; Montgomery et al. 1998; Uher et al. 2011) and antipsychotic drugs can elevate BMI levels, which might heighten the risk of cardiovascular issues, displaying a noticeable increase in both BMI scores and metabolic risk (Patel et al. 2022). Additionally, varying and sometimes unhealthy lifestyles like smoking and reduced physical activity further complicate efforts to determine causality (McCreadie et al. 1998; McCreadie et al. 2003). According to Keyes (2005), there are no examinations studying mental health that indicate a definition that is more than the absence of psychopathology (Keyes 2005). Nowadays, our concept of mental health is still more or less psychiatric. Thus, individuals can be diagnosed as either mentally ill, or mentally healthy, grounded on the presumption that measuring mental illness or health leads to a single bipolar aspect. Examinations that have been carried out on the issue of bi-directional relationships between obesity and mental impairments and mental health yielded significant associations between obesity and poor physical and mental health states, at least in older obese individuals (Levi et al. 2012; Friedmann et al. 2001). A meta-analysis of longitudinal studies suggests a bi-directional relationship between obesity and major depression in both males and females (Milaneschi et al. 2019). Furthermore, depression, mental health issues, and reduced QoL are frequently related to obesity (Luppino et al. 2010). Accordingly, this association seems to be more pronounced among individuals who face these demanding challenges also experience physical limitations. Another study by Stephenson et al. indicates that people living with obesity more frequently have lower QoL. Hence, a negative relationship between weight gain and QoL was

confirmed. However, significant results were only found in obese individuals, but not in overweight (Stephenson et al. 2021). This relationship between obesity and mental health seems to be even more significant later in life in comparison to earlier stages of life or middle-aged people (Kivimaki et al. 2009; Zabelina et al. 2009). With regard to interventions aimed at losing body weight, it can be stated that the loss of body weight appears to be associated with improved physical and mental health conditions. Nevertheless, most of the previous studies were not carried out on older adults. With respect to younger and middle-aged individuals, it could be shown that dietary as well as surgical interventions for losing body weight successfully led to a decrease of depression. Moreover, interventions regarding weight loss have also been shown to diminish the degree of stress (Elder et al. 2012) as well as improve QoL (Napoli et al. 2014; van Gemert et al. 2015). As a consequence, dietary and exercise interventions potentially improve mental health but there is still little evidence concerning older individuals. Investigations that have been conducted among older persons found merely improved health-related QoL, QoL and depression as well as perceived levels of stress (Napoli et al. 2014; Carson et al. 2014; Imayama et al. 2011; Pope et al. 2011; Rejeski et al. 2002). Additionally, a bi-directional link between the loss of body weight and mental health can be assumed. Interventions aimed at weight loss frequently result in improvements of QoL and depression, whereas mentally impaired people show less benefit regarding weight loss probably due to less adherence.

Depressive symptoms seem to be related to a decrease in body weight after receiving dietary and surgical interventions (Simon et al. 2010; Legenbauer et al. 2009; Faulconbridge et al. 2009). Even though many individuals who are not diagnosed with any kind of mental disorder, do not feel healthy. Approximately one-half of adults seek mental health treatment because of a mental health problem, despite missing diagnosable disorders (Regier et al. 1993). Positive and negative effects outline two factors that are related to each other (Bradburn 1969; Tellegen et al. 1999; Watson & Tellegen 1985).

The relationship between psychological distress and highly obese individuals has been the subject of controversy over the years. However, findings regarding its nature and direction are still unclear (McElroy et al. 2004; Atlantis & Baker 2008, Treviño-Alvarez et al. 2023), whereas there are some indications hinting to bi-directionality need to be confirmed (Leutner et al. 2023). Some results of studies report an increased risk for obese people to suffer from psychological distress (Roberts et al. 2003; Golden et al. 2008; Simon et al. 2006; Farmer et al. 2008). However, not all cohort examinations that have been carried out postulate these

findings (Istvan et al. 1992; Palinkas et al. 1996). Some studies conclude that obese individuals exhibit a reduced risk for developing psychological distress as well as in some cases a reduced probability of committing suicide (Crisp & McGuinness 1976; Magnusson et al. 2005; Mukamal et al. 2007; Lawlor et al. 2007; Davey Smith et al. 2008).

Several investigations conducted on this subject have reported that psychological distress is a predictor for obesity. Furthermore, some of these findings seem to be contradictory (Pine et al. 1997; Goodman & Whitaker 2002; Stunkard et al. 2003; DiPietro et al. 1992; Heo et al. 2006; Kivimäki et al. 2009a; Atlantis & Baker 2008). Moreover, a possible cause-effect association still needs to be verified (Angi & Chiarelli 2020)

According to a systematic review carried out by Luppino et al. (2010), a positive relationship between obesity and depression could be observed (Luppino et al. 2010). In addition, only 4 of the 15 selected studies were found to be of high quality by the authors. As a result, estimates of causal relationships may be inaccurate due to the presence of confounding factors, reporting bias or even reverse causality (Lawlor et al. 2011). Accordingly, Lawlor et al. published some interesting results in the *Journal of Internal Medicine* suggesting that there are two genetic variants which are shown to be significantly linked to obesity (Lawlor et al. 2011). A Mendelian randomization (MR), an epidemiological approach to examine causal effects between exposure and outcome while reducing the risk of confounders and reverse causation (Haycock et al. 2016) was used to get more insight into controversial results. A recently conducted meta-analysis (Hachula et al. 2023) stated that the results of four longitudinal meta-analyses show a bi-directional relationship between obesity and depression (Mannan et al. 2016, Luppino et al. 2010). Additionally, genetic variants thought to be related to obesity act as moderating variables in order to assess the causal impact on psychological disorders (Davey Smith & Ebrahim 2003; Lawlor et al. 2008).

Apart from that, germ line genotype is assigned during conception. Thus, the impact of psychological distress on obesity genotype in terms of a reverse causal relationship is impossible. Therefore, the Mendelian randomisation approach is a proper way to assess the association between obesity and psychological outcomes, which seem to be less susceptible for putative confounding factors and reverse causality in comparison to other usually applied multivariable analyses (Davey Smith & Ebrahim 2003; Lawlor et al. 2008; Davey Smith et al. 2008). According to the Mendelian randomisation, the obesity-related variability influenced by genetic factors is expected to be associated with respective outcomes. Additionally, genetic factors are not shown to be related to certain characteristics that act as confounding

aspects in observational examinations. Therefore, links between obesity-associated genotypes and psychological distress are highly unlikely to be influenced by any confounding variables (Davey Smith & Ebrahim 2003; Lawlor et al. 2008; Davey Smith et al. 2008). Moreover, contradictory results from previous studies investigating supposed bi-directional relationships can be explained by a variety of mechanisms. In this context, both social and biological mechanisms are described, which in some cases led in different directions. First, it should be considered that between psychological distress and disorders there is a link to eating disorders that can manifest itself either in the form of excessive or reduced consumption of food, which has an impact on body weight. In addition, obesity can lead to stigmatisation in many societies, with the result that affected individuals who are exposed to this may experience psychological distress (Andreyeva et al. 2008).

Furthermore, medications prescribed for the treatment of mental disorders such as depression, for example tricyclic antidepressants, very often lead to an increase in body weight, while other medications, such as selective serotonin reuptake inhibitors (SSRIs), can lead to weight loss. In some cases, long-term or short-term use of SSRIs may result in both weight loss and weight gain. However, the adverse event of gaining weight mostly emerges in later stages of the therapy (Strawn et al. 2023). Another important aspect in this context is that more severely obese individuals show increased insulin resistance (Grajales et al. 2019), higher concentrations of free fatty acids and tryptophan, which subsequently leads to increased serotonin concentration in the brain. This has an effect on the hypothalamic-pituitary-adrenal (HPA) stress axis of the body and thereby a reduction of psychological distress symptoms in highly obese people (Werdermann et al. 2021; Frayn & Kingman 1995; Bornstein et al. 2006; Lawlor et al. 2003; Lipsett et al. 1973).

Biasing due to various confounding factors such as socioeconomic status, behavioral aspects, including smoking, alcohol or physical activity and other lifestyle factors that were either inaccurately collected or not collected at all could be a cause of identified associations in several previous examinations (Schwartz et al. 2004; Devlin et al. 2000). Other reasons for the observed relationships could be reporting bias or reverse causality. This could mean that obese people feel they should report that they tend to be sadder because of their obesity (Lawlor et al. 2011). Socio-economic aspects are shown to affect mental health, while certain situations may affect people's resilience (Artiga & Hinton 2019; Mao & Agyapong 2021) and furthermore have an impact on gaining body weight (Lee et al. 2019).

Additionally, sociodemographic factors like age and educational status seems to affect body weight. People with lower education show a higher risk of being obese (Zhang 2021).

Kivimäki et al. (2009a) found evidence for the existence of a cumulative relationship between obesity and frequently occurring mental disturbances such as depression and anxiety in the Whitehall II cohort study of 4000 male and female office workers in London. This would suggest that individuals with frequent episodes of the respective mental impairments would be at higher risk for obesity than those who do not often indicate episodes of mental disorders.

In this context, a "dose-response effect" could be observed (Kivimäki et al. 2009a).

On the basis of the study, it could be shown that this effect was observed independently of a variety of mental health-associated factors (e.g., age, gender, ethnicity, marital status, socioeconomic status, and others) that might be associated with obesity on the one hand and frequent mental impairment on the other (Kivimäki et al. 2009a). Moreover, a temporal sequence from common mental disorders to overweight and obesity can be deduced (Kivimäki 2009a). Overweight and obesity develop over time. Thus, chronic, or recurrent mental disorders are shown to be much stronger predictors of obesity than transient mental impairment. However, as confirmed in many previous investigations, common mental disorders such as depression and anxiety disorders were often measured at only one time point (Kivimäki et al. 2009a). According to a study by Zhang, a positive bi-directional association between body weight and depression was identified showing a significant effect of depression on body weight in males and females. Vice versa, people with depression more often indicate overweight and obesity compared to those without experiencing depression, which is especially true for females (Zhang 2021).

Accordingly, there was a causal relationship in the other direction, that is, obesity was a risk factor for the development of mental disorders in the future. The results from these studies were contradictory (Atlantis & Baker 2008). According to some other studies, people with elevated BMI levels have a higher risk of developing depression or anxiety disorders (Roberts et al. 2003; Farmer et al. 2008; Golden et al. 2008, Holt 2019), whereas other investigations report no relationship between obesity and depression or anxiety (Istvan et al. 1992).

Furthermore, some examinations yield negative links, indicating that a higher level of obesity is associated with a decreased risk of mental health impairments and suicide in the future (Crisp & McGuinness 1976; Magnusson et al. 2006). As per Mannan et al. (2016), findings resulting from their meta-analysis and systematic review, suggest that depressed adolescents are at a 70% higher risk of being obese, whereas those adolescents who were

obese show a 40% increased risk of showing depression (Mannan et al. 2016).

According to these findings resulting from numerous different examinations, the measurements of subjective well-being and mental illnesses generate different correlating factors (Headey et al. 1993; Keyes & Ryff 2003). As a result, clinical professionals should take into account both mental health and mental illness (Keyes 2005). Health is considered a condition that is not just due to the absence of illness but is also positively affected (Ryff & Singer 1998; Siegerist 1941; World Health Organization 1948). The Problem is that there is no standardised instrument by which mental health can be measured or diagnosed. Thus, science defines mental health as the absence of psychopathology (Keyes 2005).

Over the past decades, many studies have been carried out and many results have been collected regarding the relationship between obesity and various psychiatric diseases, especially with the way individuals should be treated (Fitzgibbon et al. 1993; Lykouras & Michopoulos 2011; Lin et al. 2013). Despite all these studies, there is either no satisfactory data available on the strength and direction of the relationship between overweight and psychiatric disorders, or there is no corresponding scientific evidence. Due to the methodologically not uniform studies, there is a need for further research to generate more evidence in this area and thus better understand the relationship between obesity and overweight, especially for clinicians and scientists. In the broadest sense, it is a matter of formulating future research goals in order to identify possible neurobiological connections in these areas. However, obesity as a civilizational illness is substantially linked to a greater risk of developing depression and causing low QoL (Hachula et al. 2023)

Obviously, the early detection, as well as the treatment of frequent psychiatric diseases has an impact on the outcome of obese patients who become proactive for surgical treatment (Rajan & Menon 2017). The concurrent medical events associated with excessive body weight and obesity have undergone thorough examination and empirical validation within the domain of scientific inquiry, as attested by investigations conducted by Kearns et al. (2014) and Must et al. (1999). Conversely, the current corpus of scholarly research has not produced definitive evidence elucidating the exact nature of the connection between heightened body weight and mental health (Rajan & Menon 2017). Given the fact that only a few prospective studies have investigated the association between mental health and overweight or obesity using multiple points of measurement (Kivimäki et al. 2009a), this thesis aims to contribute to gaining a better insight into the nature of possible long-term and reciprocal associations and shed more light on cause-effect relationships.

This thesis is also meant to stimulate further discussion in the scientific community. Accordingly, the following hypotheses were formulated:

#### Hypothesis 1:

*Null hypothesis ( $H_0$ ): There is no significant association between overweight/obesity in Austrian female and male individuals aged 15 years and older and their depression status and quality of life (QoL).*

*Alternative hypothesis ( $H_1$ ): There is a significant positive association between overweight/obesity in Austrian female and male individuals aged 15 years and older and their depression score, and a significant negative association between overweight/obesity and their level of quality of life (QoL).*

#### Hypothesis 2:

*Null hypothesis ( $H_0$ ): European female and male adults aged 50 years and older who live with either overweight or obesity show no significant positive bi-directional association between their depression score and body mass index (BMI), and also no significant negative bi-directional association between their quality of life (QoL) levels and body mass index (BMI) over a 10-year follow-up period.*

*Alternative hypothesis ( $H_1$ ): European female and male adults aged 50 years and older who live with either overweight or obesity show a significant positive bi-directional association between their depression score and body mass index (BMI), and also a negative significant bi-directional association between their quality of life (QoL) levels and body mass index (BMI) over a 10-year follow-up period.*

## **2. Theoretical framework**

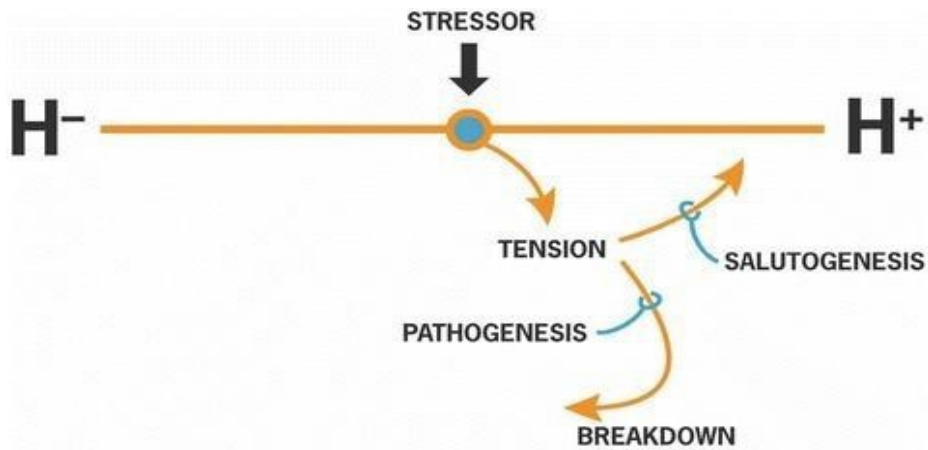
### **2.1 The Salutogenic Model-a concept of health**

Aaron Antonovsky, a medical sociologist, coined the model of salutogenesis, which has been introduced to the public as the salutogenic model of health (Antonovsky 1979; Antonovsky

1987; Lindström & Eriksson 2005). The theory of this concept mainly focuses on a person's ability to use his or her resources to create or maintain their own health, and does not take ill health or disease into account. The cornerstones of the salutogenic model, respectively the idea of salutogenesis, are the focus on problem solving, on the one hand, and the ability to use resources on the other hand (Lindström & Eriksson 2005).

Nowadays, the theory of salutogenesis is well established as a public health topic in health promotion. Today, more than 500 scientific articles can be obtained by the repositories of public health. However, a clear lack of evidence with respect to an extensive understanding in disciplines such as medicine, psychiatry, psychology, public health research, education, nursing, sociology, and social work can be constituted. Antonovsky postulated that health must be understood as a dynamic process in a continuum between disease or ill health and ease or total health. An individual's capacity to grasp the full size of the situation and the competence to use existing resources represents the so-called sense of coherence (SOC). This capability combines skills to comprehend the actual situation and find sense in pursuing a health promoting course. In this context, Antonovsky used the terms comprehensibility, meaningfulness, and manageability (Lindström & Eriksson 2005).

Antonovsky (1979) postulated that the concept of salutogenesis was considered an interdisciplinary method representing a question of coherence among various disciplines. Moreover, it should reveal how they are related to each other. It is all about the interaction between a person and his or her societal organisation comprising human resources and the circumstances of contextual life. The salutogenic concept as the basis of health is an approach that mainly focuses on coping mechanisms and should promote the movement towards a healthy state. That is the reason why people, who experience very demanding and stressful situations, still feel well. The concept is suitable to be applied to individuals, groups and at a communal level, in contrast to the pathogenic model which only focuses on deficits (Antonovsky 1979; Antonovsky 1987) (Figure 1).



**Figure 1:** The ease/dis-ease continuum (Antonovsky 1979; Antonovsky 1987). Graphic: Bengt Lindström, Monica Eriksson, Peter Wikström (Lindström & Eriksson, 2010). Reproduced without modifications from: Eriksson 2016, *The Sense of Coherence in the Salutogenic Model of Health (Chapter 11)* in: Mittelmark MB, Sagy S, Eriksson M, et al., 2017. *The Handbook of Salutogenesis* [Internet]. Cham (CH). Copyright 2017 by Springer. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. The reuse of this image complies with the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) Licence for open access publications, which permits any non-commercial use, distribution, and reproduction (<http://creativecommons.org/licenses/by-nc/2.5/>).

Hence, nobody can be defined as healthy or ill. Focused on the entire population, we all constantly are moving between the two poles of total wellness and total disease.

Even people who appear strong and healthy and are therefore supposed to be free of symptoms and functioning well, are at a certain risk of mortality. There may be times of depression, one could get flu or get malignant cells in their body that have not been detected yet. Available health services are providing health care primarily to those individuals at the disease pole of the continuum. However, the question for further research is, what are the key factors that individuals should be doing to achieve complete health (Sagy et al. 2015).

Antonovsky particularly analysed the different theories of stress and coping and discussed them in an extensive way. He did not accept the opinion of Lazarus & Folkman (1984) and their theories of life events and rejected the cognitive theory on stress and coping (Lazarus & Folkman 1984). The hypothesis of these theories was a life in homeostasis and balance. Disturbing factors are assumed to disrupt this balance of life and damage health according to a pathogenic perspective (Figure 2). Moreover, the theories on stress and coping are predominantly based on the theory of control. Salutogenesis stresses the ability of an individual to use internal and external generalised resistance resources (GRRs) in challenging stress situations. Antonovsky suggests that life is a chaos and defines it as the initial point of a changing mechanism. The way that we are able to handle this chaos seems to be crucial (Eriksson 2016). Accordingly, the salutogenic perspective of stress and coping is as described follows:

*“...life is inherently full of stressors, with life-situation stressor complexes by far deserving most of our attention if we wish to understand either health or disease. Focusing on health, I expressly rejected the implicit assumption that stressors are inherently pathogenic. Their health consequences can only be understood if we understand the coping process” (Antonovsky, 1992, p. 48).*

SALUTOGENIC ORIENTATION	PATHOGENIC ORIENTATION
Heterostasis	Homeostasis
<ol style="list-style-type: none"> <li>1. Health ease - dis/ease continuum</li> <li>2. The history of the person</li> <li>3. Salutary factors</li> <li>4. Stressors and tension might be pathogenic, neutral or salutary</li> <li>5. Active adaptation</li> <li>6. The "deviant" case</li> </ol>	<ol style="list-style-type: none"> <li>1. Healthy/sick dicotomy</li> <li>2. The person's disease/diagnosis</li> <li>3. Risk factors</li> <li>4. Stress is pathogenic</li> <li>5. The magic bullet</li> <li>6. Hypothesis confirmation</li> </ol>

**Figure 2:** The six main aspects of the salutogenic and pathogenic orientation, presented by Antonovsky in: *Unravelling the Mystery of Health* (Antonovsky 1987). Reproduced without modifications from: Hege Forbech Vinje, Eva Langeland, and Torill Bull, 2016. *Aaron Antonovsky's Development of Salutogenesis, 1979 to 1994 (Chapter 4)* in: Mittelmark MB, Sagy S, Eriksson M, et al., 2017. *The Handbook of Salutogenesis* [Internet]. Copyright 2017 by Springer. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. The reuse of this image complies with the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) License for open access publications, which permits any non-commercial use, distribution, and reproduction (<http://creativecommons.org/licenses/by-nc/2.5/>).

There are three possible ways of reaction with regard to stress situations. Firstly, one can stay neutral when facing a stressor. Secondly, holding the ability to handle stress and consecutively move to a healthy state in the continuum and thirdly, being not able to handle stress that may cause a breakdown or death (Antonovsky 1987). If certain events do not considerably worry us, such as daily hassles (Antonovsky 1987), it may be the case that we stay neutral to these events since health remains unaffected. However, if we cannot handle certain events by using internal or external resources, we would become ill. Using internal and external resources facilitates moving toward a healthy state (Eriksson 2016).

The SOC constitutes an individual's ability to react to challenging, stressful situations and does further reproduce people's point of view with respect to their lives. Overall, it means that a person tends to view life as structured, manageable, and meaningful or, with one word, coherent. It is an individual method of acting, thinking and being, with basic trust, which enables people to use their personal resources. Hence, the core elements of the SOC include *comprehensibility*, *manageability*, and *meaningfulness* (Antonovsky 1987). SOC originally defined by Antonovsky (1987):

*“a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that (1) the stimuli from one’s internal and external environments in the course of living are structured, predictable, and explicable; (2) the resources are available to one to meet the demands posed by these stimuli; and (3) these demands are challenges, worthy of investment and engagement.” (Antonovsky 1987, p.19).*

The development of a person’s SOC was believed to rise throughout life, but predominantly, SOC emerges when individuals manage to deal with life within the first decades of their life. The nature of salutogenesis is the active and flexible approach focusing on abilities of managing. In contrast to the conceptions of coping or resilience, the salutogenic theory is adaptable and considered universally applicable. The central point of interest, however, lies on problem solving (Lindström & Eriksson 2005).

*The Sense of Comprehensibility* means the ability of an individual to what extent the internal and/or external stimuli from the environment as consistent, structured, and well-organised information are recognised. If a person has a high comprehensibility score on SOC-scale, the person is expected to explicitly predict stimuli of the future. This is considered a cognitive part of the SOC (Antonovsky 1987).

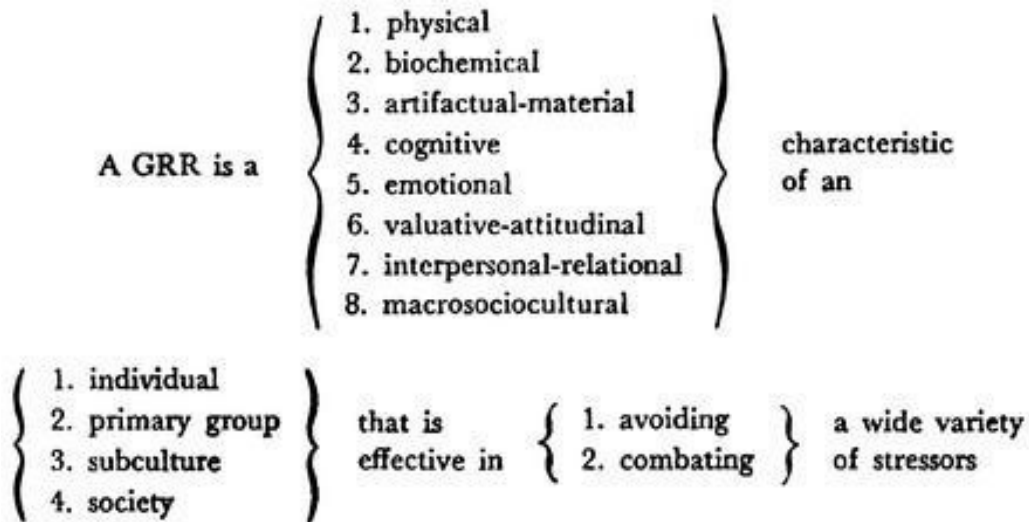
*The Sense of manageability* denotes the extent to which an individual recognises the own resources adequately to respond to the demands deriving from the stimuli. This is considered the instrumental, respectively behavioral part of the SOC (Antonovsky 1979; Antonovsky 1987).

*The Sense of meaningfulness* describes the extent to which an individual perceives that their own life is meaningful and makes sense in an emotional manner, and that difficulties of life are worth investing power in, to commit and engage and convert burdens into challenges. This is considered the motivational part of the SOC (Antonovsky 1979; Antonovsky 1987).

According to life event measuring instruments, a moderate correlation can be observed, showing that SOC is associated with an individual’s changed environment. Hence, a high level of SOC appears to be associated with a high level of QoL. Moreover, SOC seems to be related to individual behaviour and respective attitudes (Eriksson & Lindström 2005).

According to several longitudinal examinations, the results indicate a high predictability but do also state contradictory findings. In contrast to Antonovsky's assumption, SOC seems not to be as constant as postulated, except persons, who initially show high SOC levels. In fact, there are some variations in means showing small differences. Within a three-to-five-year perspective, no differentiation, or merely small differences are covered (Nilsson et al. 2003; Kivimäki et al. 2000; Virtanen & Koivisto 2001; Suominen et al. 2001; Kuuppelomaki & Utriainen 2003). A ten-year follow up examination, which was conducted among employees in Finland, reports equal findings (Kalimo et al. 2003). It can be assumed that SOC enhances over the lifetime and shows gender differences. Women generally demonstrate lower levels of SOC than men, even though the differences are quite small. They are more likely explained by societal circumstances than sexual biological inequalities (Eriksson & Lindström 2005).

Regarding the SOC, the major concept of the salutogenic model is the idea of resistance resources (Antonovsky 1979; Antonovsky 1987). Resistance resources include both, the generalised resources, which are at one's disposal to deal with various circumstances, and the specialised resources, which include certain resources important for particular circumstances. Thus, generalised resistance resources (GRRs) (Figure 3) are considered prerequisites for the creation of a high SOC. Lindström & Eriksson (2005) stated that these cornerstones show a different nature, including a genetic and constitutional, cultural and spiritual, psychosocial, as well as a material nature, oriented toward preventive health (Lindström & Eriksson 2005). These generalised resistance resources (GRR) persist at different levels of a group or family, an individual, society or subculture (Antonovsky 1979).



and thus preventing tension from being transformed into stress.

**Figure 3:** Definition of generalised resistance resources (GRRs). *Health, stress and coping* (Antonovsky, 1979, p. 103). Reproduced without modifications from: Hege Forbech Vinje, Eva Langeland, and Torill Bull, 2016. *Aaron Antonovsky's Development of Salutogenesis, 1979 to 1994 (Chapter 4)* in: Mittelmark MB, Sagy S, Eriksson M, et al., 2017. *The Handbook of Salutogenesis* [Internet]. Copyright 2017 by Springer. NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. The reuse of this image complies with the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) License, which permits any non-commercial use, distribution, and reproduction (<http://creativecommons.org/licenses/by-nc/2.5/>).

Research activities on the subject of GRRs and their role regarding the development of the SOC is insufficient. According to Antonovsky's early research (Antonovsky 1991), there are three key factors that seem particularly important in developing a strong SOC. These are a balance in regulating overload and underload, consistency, and furthermore, the possibility to participate in decision making processes, which affects individual situations. Considerations with regard to the question of which GRRs are involved in the formation of the SOC have increasingly moved into focus (Eriksson 2016). A study of Finns aged 65-69 (Read et al. 2005) concluded that family income, physical activity, marital status, income, cognitive ability, and educational attainment were identified as being particularly important resources to achieve high SOC levels. The results indicate that cognitive ability and physical activity appear to be related to SOC, and that SOC seems to be associated with positive mental and social health (Eriksson 2016).

In a Swedish qualitative study, caregivers for the elderly were investigated with regard to potential GRRs against stressors. A number of positive and negative experiences were identified such as taking care of a relative and the emerging resource "caregivinghood"

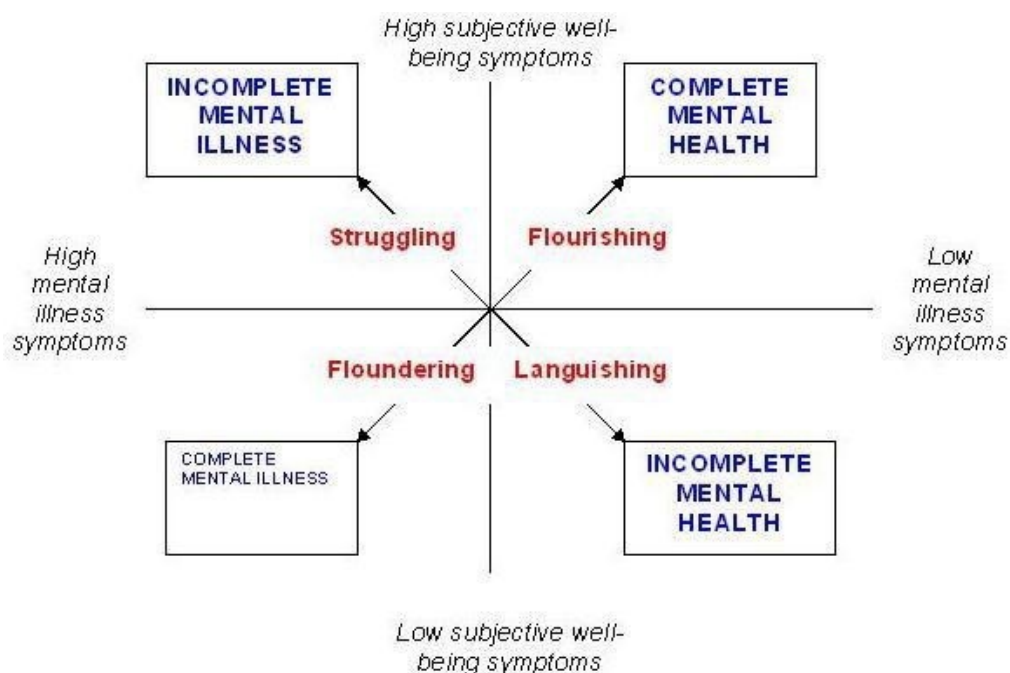
comparable to "parenthood" (Wennerberg et al. 2012). Based on an analysis of Antonovsky's research and additional research conducted by Griffiths et al., the following 15 GRR topics have been identified:

*"Structure in life, predictability in life, social support, coping strategies, life meaning, responsibility, comprehension, expression of confidence, challenges worth investing time and effort, health/illness, future orientation, past orientation, positive, solution focused outlook, emotional connection, and ensuring that you are justly treated." (Griffiths, Ryan and Foster 2011, p.170)*

## **2.2 The Complete State Model of mental health**

The complete state model of mental health was derived from Slade's model of mental health and well-being, considering Antonovsky's salutogenic theory. Accordingly, the complete state model (CSM) is also referred to as the dual-factor model of mental health (Suldo & Schaffer 2008) or the two-continua model of mental health (Westerhof & Keyes 2010). According to the CSM, mental well-being and mental illness are on a continuum where well-being and illness are defined as strongly or weakly present or absent (Keyes 2005).

The concept of the complete state model of mental health is based on two dimensions. Mental illness therefore always moves between present and absent. In addition, mental well-being moves along a continuum from low to strongly pronounced (Slade 2010). This concept of the complete state model of mental health can also be extended to the various topics of literature concerning recovery. Repeatedly, everything revolves around the question of how to achieve personal recovery despite continuing mental illness. Whatever the answer may be, it can only be fragmentary since the term recovery always has to do with illness. In contrast, access to mental health is possible for everyone. This enables a new framework concept for the understanding of recovery (Slade 2009).



**Figure 4:** Complete state model of mental health (Keyes & Lopez 2002). Reproduced without modifications from: Slade M., 2010. *Mental illness and well-being: The central importance of positive psychology and recovery approaches*. Copyright 2010 by Slade; licensee BioMed Central Ltd. The reuse of this image follows the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) License, which permits any non-commercial use, distribution, and reproduction <http://creativecommons.org/licenses/by-nc/2.5/>.

People who are currently in a recovery process are active in the effort to free themselves from floundering and languishing and to move towards struggling and flourishing. In the case of languishing, this can be done by developing a positive identity, while a distance away from floundering is encouraged by hopeful relationships. Struggling is initiated by the ability to self-manage one's own mental illness. Flourishing means that valuable social roles can be developed. This mental health framework concept is characterised by 13 operationalisable areas that include emotional, psychological, and social well-being (Keyes 2005; Keyes 2007). These 13 dimensions are considered empirically tested (Ryff & Keyes 1995; Keyes 1998). Positive psychology is particularly relevant for individual recovery. Factors to be considered include hope, empowerment, purpose, connection, spirituality, self-identity, stigma, and symptom management (Schrank & Slade 2007). Except for symptom management, these factors are almost completely excluded from the education programs of mental health professionals (Mental Health Commission 2001). Seligman's theory of *authentic happiness* provides the basis and framework for training health professionals (Seligman 2002; Jayawickreme et al. 2008). Consequently, there are different types of a good life:

### *1. The pleasant life*

Consists of as many positive emotions as possible and includes the learnable ability to maintain and intensify pleasures as long as possible.

### *2. The engaged life*

Consists of the knowledge about one's own character, strength, and the transformation of friendship, education, work, and love, in order to use them as often as possible.

### *3. The meaningful life*

Consists of the individual's ability to use one's own strengths of character, which serve to feel belonging to something that is above one's own person.

### *4. The achieving life*

The achieving life is a life in which it is primarily about achieving something for the sake of achieving (Seligman 2002; Jayawickreme et al. 2008).

This construct of good life points out that there are different types of good life, and in terms of health promotion towards well-being, it is necessary to consider accordingly between different approaches and procedures (Slade 2010).

## **2.3 The three components of mental health**

The World Health Organization (WHO) defines mental health as a “state of well-being in which every individual realizes his or her own potential, can cope with normal stresses of life, can work productively and fruitfully and is able to make a contribution to her or his community” (WHO 2004, p.12). According to this definition, mental health includes not only the absence of mental illness, but also the presence of positive functioning at individual and societal levels (Keyes 2002). In order to understand the state of mental health in its entirety, it is essential to consider the approaches of the hedonistic and eudaimonic traditions of well-being in addition to the concept of mental illness (Keyes et al. 2002, Lamers et al. 2015). The hedonistic concept of well-being implies feeling good in one's life and experiencing the majority of one's emotions as positive and pleasant, which also suggests a high level of satisfaction with one's life (Diener 1984, 2000; Keyes 2005; Keyes & Annas 2009; Petrillo et al. 2015). The eudaimonic concept of well-being involves recognising an individual's ability to identify human potential to function

well in life (Ryff 1989, Ryff & Keyes 1995). This concept encompasses psychological well-being, such as challenges one faces in daily life to become a better person (Ryff 1989), but also social well-being in the form of individual challenges one faces to become a better member of a society (Keyes 1998a; Keyes 1998b).

Hence, Keyes (2006, 2013) defines the three components of mental health as emotional well-being, psychological well-being, and social well-being. He describes emotional well-being as feelings of happiness, satisfaction and being interested in life. Furthermore, he defines psychological well-being in terms of being satisfied with one's own personality and managing the responsibilities of our daily life in a proper way. Moreover, he emphasises the importance of good relationships to others. Social well-being includes positive functioning and being able to contribute to society (social contribution) as well as feeling part of a community (social integration). Social well-being also comprises the belief that society becomes a better place for all humans (social actualisation) and the way our society works does make sense to them (social coherence) (Keyes 2006; Keyes 2013).

However, we have to keep in mind that such a strong focus as in the case of Keyes' three factors model of mental health, which in fact is strongly influenced by hedonistic and eudaimonic approaches that emphasise positive emotions and positive functioning (Deci & Ryan 2008), also leads to varying degrees of exclusion of different groups. People struggling against injustice or inequality, other minorities, and people with migration backgrounds as well as adolescents who are often afflicted with shyness anyway, could be affected (Galderisi et al. 2015).

## **2.4 Mental health and mental ill-health**

Mental health is a state in which individuals do not suffer from any kind of psychopathology or mental impairment and flourishing (Keyes 2002, Keyes 2003a, Keyes 2003b) increased levels of emotional, psychological, and social well-being (Keyes 2005). There are several reasons justifying the domination of the dichotomous and psychiatric idea of mental health. At the beginning of the National Institute of Mental Health, research in the field of psychopathology was much more advanced empirically than the theoretical literature concerning clinical and personality psychology and its conceptions of positive mental health (Jahoda 1958; Smith 1959). Sartorius points out that individuals who are free of major depression act more productively and function better in comparison to people diagnosed with depression (Sartorius 2001).


Another explanation for the dichotomous view of mental health is that mental illness is a serious and widespread public health issue. Moreover, mental disorders often recur during the lifespan and are expensive to manage. Mental disorders increase premature mortality rates, especially when being untreated (Garrison et al. 1989; Greenberg et al. 1993; Kessler et al., 1994; Keyes & Lopez, 2002; U.S. Public Health Service 1998; U.S. Public Health Service 1999).

Mental illness and its associated problems lead to deflection from the importance and meaning of mental health (Keyes 2005). Mental health has always been described as the absence of psychopathologies, such as depression or anxiety disorders. Despite the significant effects of mental illness on the individual functioning and society, it represents only part of the outcomes concerning lifetime-development (Westerhof & Keyes 2010). At the beginning of research studies conducted on the relationship between obesity and mental health issues, the findings were contradictory, partly due methodological variations (Friedman & Brownell 1995; Onyike et al. 2003). Most of the epidemiological examinations dealing with the relationship between overweight and depression were conducted as cross-sectional studies (Roberts et al. 2000; Friedman & Brownell 1995).

There is little knowledge as to whether being overweight increases the likelihood of depression occurring in later life (Roberts et al. 2000). Mental ill health, mental disabilities, as well as mental disease or mental health are terms used in order to combine varying aspects of mental distress. In the past, the different mental states were described as a continuum with various severity degrees, reaching from mental health to mental ill health starting with mental disturbance to mental illness and severe mental impairment.

Accordingly, early detection was considered to avoid mental illness and was the focus of treatment strategies at this early stage (Stefansson 2006). Nowadays, we look at mental ill health from several different perspectives. On the one hand, mental suffering means having numerous mental issues and disabilities, instead of being mentally healthy. On the other hand, one can say that an individual is suffering from mental illness in contrast to being in good mental health. The two concepts of mental disorder and mental health, as well as mentally ill and mentally healthy can be seen as different dimensions: namely a health dimension and a disease dimension.

		Disease dimension	
		Mentally healthy	Mentally sick
Health-dimension	Mental health	I	II
	Mental problems or disorders	III	IV

 Action by the community care/nursing/sick listing/disability pension

**Figure 5:** Matrix of the two dimensions to mental health-The health and the disease dimension. Reproduced without modifications from: Stefansson CG., 2006. Chapter 5.5: Major public health problems - mental ill-health. *Scandinavian journal of public health*, 2006; 34(Suppl 67): 87-103. The reuse of this image follows the terms of SAGE Publications, Copyright 2006. Permission has been granted for reusing the content of this article.

The *health dimension* stresses the individual knowledge of certain mental disturbances. The status of how a person feels basically depends on surrounding living conditions or the result from a person's individual way of living. Lifestyle factors are pivotal and mental disorders can affect the ability to compensate for varying states of stress (Stefansson 2006).

The *disease dimension* emphasises relevant biological factors dealing with the development of mental disturbances and diseases, especially concerning the biological system in the brain. Thus, a person cannot change their own condition. As a result, there is a need for treatment to restore health. Moreover, the focus lies on the pathogenic circumstances in which heredity constitutes a major part (Stefansson 2006) Depending on which kind of difficulties are addressed, and from whom, these different points of view are usually mixed.

In psychiatry, while the disease dimension serves as the guiding principle to be followed, it is essential to also consider patients' experiences and the biological aspects of the disease. According to figure 5, we presumably belong to the various fields of the matrix of the two dimensions of mental health, respectively mental ill health conditions. Being mentally healthy generally means not having any mental trouble (I). Under certain circumstances, such as stress situations, mental health problems increase and may be noticed as worrying (III). The matrix, shown in figure 5, is limited by the fact that it is not possible to read what is considered "normal" or "abnormal". Hence, there is no opportunity given by the matrix concerning the required individual treatment action. It seems to be crucial if people can live their life the way they want to, even with their manifestations of mental distress.

Nowadays, there is a growing interest in discussing the borderline of those who experience mental health issues but do not receive any required treatment, according to the matrix (Stefansson 2006).

### **2.4.1 The development of mental ill-health**

The mental state of an individual is affected by three circumstances. The first condition is a person's biological and physical state. The second condition includes the psychological skills, particularly the cognitive capability to understand and realise the world that surrounds us and the ability to handle the stresses of life for best possible survival. The third circumstance comprises an individual's social and material surroundings and the capability of inducing strain such as a stressed situation of living, relationship problems, a high workload, or an uncertain future. All these three factors together affect a person's life circumstances and are furthermore determined by genetic factors and situations during growing up. According to the psychosomatic overall view, there is scientific evidence indicating that most physical functions in health and sickness are affected by psychological functions and affect these functions themselves. Concerning the positive and negative environmental effects, these three circumstances are considered co-dependent factors that represent mental functions. Therapies and preventive interventions of mental ill health target bodily influences, which can be activated through medication, psychotherapy or efforts to modify environmental circumstances. In many cases, we can observe stability between these three circumstances and this balance enables us to manage daily life without any greater problems. However, when this balance is disturbed, mental health is threatened.

Malnutrition, alcohol, and narcotics and the abuse of other substances as well as lack of sleep can lead to disturbed bodily function. Most people experience burden from their environment as mentally troublesome. Thus, individual responses to varying stressors are reactions to stimuli, which may be harmful or threatening. The majority of people can cope with stressful situations without bothersome manifestations (Stefansson 2006). In some other cases, a number of problems emerge that affected individuals cannot manage. Obviously, some people are able to handle stressful situations, while others are not. Each individual has their own vulnerability and is therefore more or less able to deal with stress. The "stress-vulnerability" model (Zubin & Spring 1977) is frequently used to portray the development of mental health problems or illness (Brown & Harris 1978). According to this model, the main argument describes a state-and-trait interaction, which means that individuals who experience long-term

disposition (trait), referred to as vulnerability, are more likely to encounter stressful events that may cause stress (state) (Demke 2022). As per Goh & Agius, the stress-vulnerability model is considered a useful tool for managing and detecting relapses of mental illnesses (Goh & Agius 2010) and has proved to be a valuable model over decades that is even highly appreciated by proponents of alternative approaches in psychiatric care (Demke 2022). Hence, Zubin & Spring postulate that individuals possess an immanent genetic predisposition to develop a mental disease, they are “vulnerable”. However, this vulnerability alone is not sufficient for developing a mental illness, unless there is interaction with bio-psycho-social stressors, which subsequently may cause psychopathology (Zubin & Spring 1977). Thus, dysfunctional brain organisation and various psychosocial stressors such as life crisis, substance abuse, or even interpersonal stressors may result in mental illnesses, including psychosis, depression, and anxiety disorders, among others (Zubin & Spring 1977).

In fact, there are two developmental processes to mental ill health by which stress levels can increase. On the one hand, mental distress rises through manifestations of insomnia, tiredness or worry and may lead from field I to III in the matrix, as shown in figure 5. An individual or a group of persons that encounter stressful situations may experience serious mental health problems without significant manifestations leading to psychiatric diagnosis, for instance in crisis or even in situations of grief. Field IV represents states in which external burden increases to a diagnosable level where psychiatric diseases may be detected (Stefansson 2006).

Another way of developing a mental disease can be caused by stressors that affect an individual. Hence, experienced stress situations may lead a person quite rapidly from field I to field IV. It can be argued that there is a susceptibility of certain people, which may be genetically determined or possibly caused by other problematic circumstances or traumatic manifestations. It seems that today most people are switching between field I and field III concerning their mental health situation (Stefansson 2006).

## **2.5 The neurobiology of resilience and mental health**

Research dealing with mental health is largely determined by investigations of risks and vulnerabilities in relation to the emergence of mental ill health. In the present day, a shift in research interests is evident. This change has led to a shift in focus from solely investigating the mechanisms and vulnerabilities of mental ill health to exploring the factors that empower

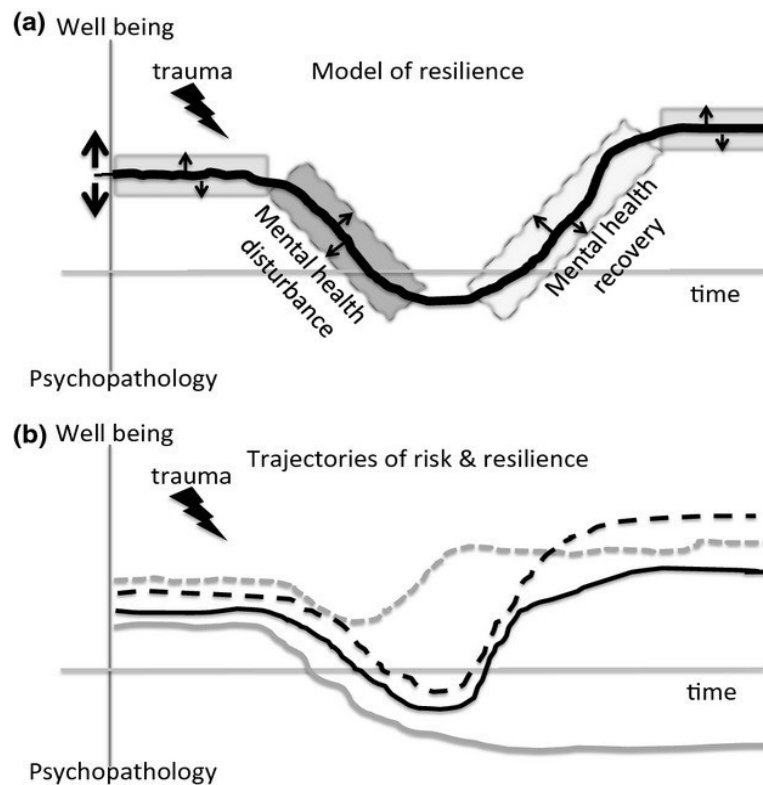
individuals to maintain good mental health or expedite their recovery when facing challenging circumstances. In this context, resilience is seen as a possibility to cope with serious adversities in the life course. If children experience severe traumatic experiences during childhood, this results in an increased risk later in life of developing a mental disorder as an adult. Epidemiological studies have clearly shown a causal relationship between childhood trauma and various mental disorders in adulthood (Kessler et al. 2010). However, some of the children who experienced a severe trauma remained healthy and did not develop any psychopathologies because they were able to successfully adapt to certain situations or recovered relatively quickly (Sapienza & Masten 2011). The mechanisms that alter and modulate a person's risks and resilience will be studied at different levels.

There are different levels ranging from more a general such as the environment in which a person lives, to more direct and more specific levels of social environment, such as peer group or neighbourhood, and more individual levels such as psychological abilities and the molecular and cellular biological foundations of an individual's neuronal circuits (Rutten et al. 2013). Studies on resilience have always used different definitions and measuring instruments, which leads to the fact that meta-analyses on resilience are not very practicable. An adequate and fast adaptability to various adverse circumstances during life is a generally accepted basis of resilience (Davydov et al. 2010). Following the statements from Davydov et al., the concept of resilience includes on the one hand the process of sustainability, which can alleviate disturbing influences on mental health, and on the other hand the process of rapid recovery after severe, experienced incisions in mental health (Davydov et al. 2010).

According to figure 6 (a), people change the level of their mental well-being over time and adapt their mental well-being before an experience (Figure 6). The speed and severity of each mental health disorder also changes depending on the response to exposure. Individuals also vary in terms of rapid mental health recovery and the resulting mental health level after experiential disorder and recovery (Rutten et al. 2013).

There are many different courses of risk and resilience towards the development of various psychopathologies as a reaction to profound, stressful situations or traumas. Some courses show an impairment of mental health after an exposure without subsequent restitution of mental health for a longer period. However, there is also the course, in which, after a reduction of mental well-being, the mental health level, which existed before the experience of these adverse circumstances, is quickly regained, which seems to even surpass the mental health levels before the exposure. This kind of reaction is called post-traumatic growth.

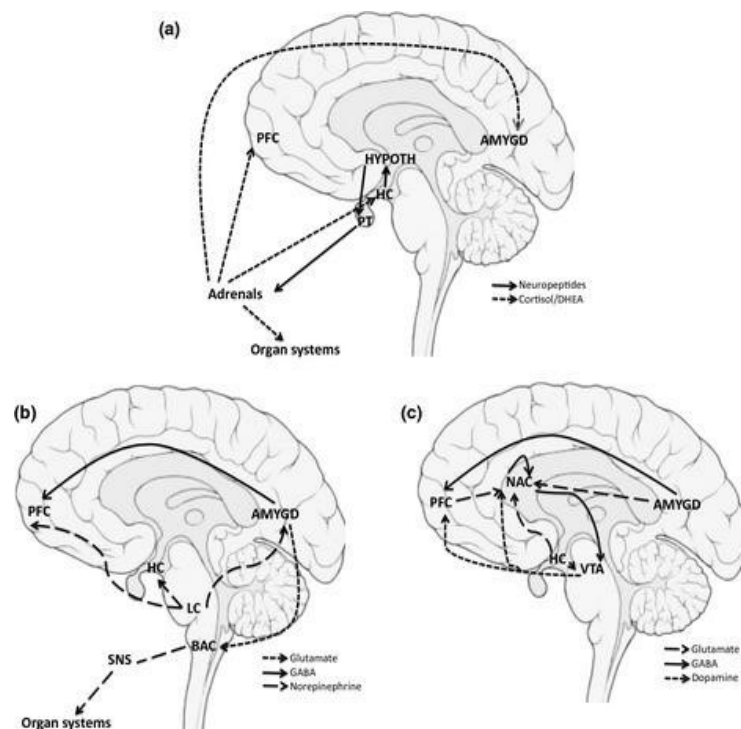
It is considered an adaptation by which an individual generates a better understanding of his own life. In doing so, a person learns to view his life from a different perspective and to develop methods to better respond to similar situations in the future (Zautra et al. 2010).



**Figure 6:** Model of resilience (a) and trajectories of risk and resilience (b) (Rutten et al. 2013). Reproduced without modifications from: Rutten et al. 2013, Resilience in mental health: Linking psychological and neurobiological perspectives. Copyright 2013 John Wiley & Sons A/S. The reuse of this image follows the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) License, which permits any non-commercial use, distribution and reproduction (<http://creativecommons.org/licenses/by-nc/2.5/>).

The basic mechanisms and determinants of various aspects of the concept of resilience are different. For example, determinants and mechanisms of a certain set value of mental health may differ from those occurring in mental health disorders, mental health recovery, or post-traumatic growth. A complex interplay of interactive factors ultimately determines the phenotype of resilience. Consequently, several factors related to aspects of resilience have at least a partly positive influence on various processes of resilience (Rutten et al. 2013). The neuronal circuits that mediate the response to stress as well as the experience of a certain reward seem to be of central importance and are involved in the neurobiological foundations

of resilience. A corresponding activation or elimination of an efficient stress response is regulated by a negative control loop system in the brain and other body regions. In order to be able to react adequately to stress situations, it is important for the maintenance of health and in particular mental health, to regain the previous health status as fast as possible, after serious adversities. A stress response that makes this possible is the prerequisite for sustainable health. The neuroendocrine stress axis that is referred to as the hypothalamic-pituitary-adrenal axis (HPA), as well as the sympathetic nervous system (SNS), the serotonergic and the dopaminergic neurotransmitter system play a central role in this context. These complex neuronal systems control the response to stress stimuli acting on the body (Figure 7).



**Figure 7:** Brain circuitries involved in the stress response and reward experience. Hypothalamus - pituitary-adrenal (HPA) axis (a), norepinephrine and sympathetic nervous system (SNS) (b), mesolimbic reward pathway (c) (Rutten et al. 2013). Reproduced without modifications from: Rutten et al. 2013, *Resilience in mental health: Linking psychological and neurobiological perspectives*. Copyright 2013 John Wiley & Sons A/S. The reuse of this image follows the terms of the Creative Commons Attribution-Noncommercial 2.5 (CC BY-NC 2.5) License, which permits any non-commercial use, distribution and reproduction (<http://creativecommons.org/licenses/by-nc/2.5/>).

Both psychological and physiological stressors lead to activation of the HPA axis. This leads to increased corticotropin releasing hormone (CRH) release from the hypothalamus and secretion of the adrenocorticotropic hormone (ACTH) of the anterior lobe of the pituitary gland. The ACTH, in turn, promotes the production of glucocorticoids from the adrenal cortex.

The glucocorticoids cause a negative feedback mechanism to the HPA activity through glucocorticoid receptor mediation in the hippocampus, whereby releasing activity is controlled. The stress hormone cortisol regulates the functions of the amygdala (AMYGD), the hippocampus and the prefrontal cortex (PFC). In contrast to the protective effect of short-term cortisol increases in the blood, long-term elevation of cortisol levels in the form of hypercortisolemia is regarded as harmful to health as it can impair neurogenesis.

The neuronal circuits, which mediate reward events, run through mesolimbic, dopaminergic projection paths of the ventral tegmental area (VTA) to the nucleus accumbens (NAC). The mesolimbic signal transduction comprises the NAC as an area of processing sensory bottom-up and top-down experiences due to dopaminergic signal transduction of cognitive adaptation. Thereby the dopamine transport to the VTA is regulated by the gabaergic feedback mechanism via the ventral pallidum. The activity of the mesocorticolimbic system is largely subject to reciprocal relationships between limbic and cortical structures. Besides cortisol, there is another steroid hormone of the adrenal cortex, synthesised under the influence of stress, which is called, dehydroepiandrosterone (DHEA). Like cortisol, DHEA is produced by the adrenal glands, practically simultaneously with the stress hormone.

DHEA has anti-glucocorticoid and anti-glutamatergic properties in the brain and leads to the inhibition of the HPA-axis. In addition to the activation of the HPA-axis, stress also stimulates an increased secretion of norepinephrine, which is synthesised from the locus coeruleus (LC) and reaches the neurons of the AMYGD, the PFC, and the hippocampus. As an additional consequence, the LC itself, along with AMYGD on the other side that promotes instinctive reactions over complex thinking, subsequently inhibits the PFC. Additionally, the AMYGD stimulates autonomous centers of the brainstem. In the context of the response to stress, the autonomous SNS produces epinephrine and norepinephrine. By stimulating the AMYGD, the hippocampus and the PFC, a mesolimbic reward cascade is then activated. Each of these three regions possesses glutamatergic projection pathways to the NAC. The extent of synaptic activity is mediated by dopaminergic signal transduction, which controls glutamate synthesis. During a reward experience, dopamine is released from the VTA. The gabaergic neurons of the NAC activate a negative feedback mechanism to the VTA, which regulates dopamine release and dopaminergic signal transmission to the PFC. The processing of VTA signals, learned behavior (hippocampus) and emotional behavior (amygdala) from the PFC is subject to the experienced feeling of reward. Furthermore, the brain derived neurotrophic factor (BDNF) is synthesised in the VTA and transported via dopaminergic afferents to the NAC.

BDNF is also related to inducing a stimulation of gabaergic neurons of the NAC, which in turn leads to an inhibition of the dopaminergic input from the VTA. Accordingly, this can result in a somewhat attenuated reaction to emotional stimuli, which under certain circumstances can produce feelings of anhedonia (Rutten et al. 2013).

## 2.6 The HPA-axis and obesity

Stress exposure triggers a series of complex physiological reactions that are mediated via the HPA-axis, the sympathetic nervous system, and the sympathetic-adrenal system (McEwen 2008). The human body adapts to such recurrent stress situations via the mechanism of homeostasis. Accordingly, the organism tries to react to them and to adjust the following behavioral mechanisms adequately in order to maintain a state of stability (Chrousos & Gold 1992). These long-term reactions to chronic stress do not pass by without a trace. Eventually, wear and tear will become observable, and this state is called allostatic load (McEwen 2008). As a reaction to various stressors, the parvocellular cells of the paraventricular nucleus (PVN) in the hypothalamus produce the CRH. Stressors can be hunger, fatigue, or psychological triggers. This activation leads to the release of the adrenocorticotrophic hormone of the anterior lobe of the pituitary gland, stimulating the adrenal cortex to produce glucocorticoids, mineralocorticoids, and adrenal steroids. The most important glucocorticoid is cortisol, which suppresses the immune system and causes glycogenolysis and insulin resistance (Balbo et al. 2010). Corticotropin releasing hormone (CRH) causes the activation of the sympathetic locus coeruleus-norepinephrine system, which leads to an increase in neuronal sensitivity to norepinephrine. Norepinephrine, in turn, stimulates hypothalamic CRH activity via reflective neuronal circuits (Chrousos & Gold 1992). It seems that the SNS is overactivated in obese individuals, especially in cases of stem obesity. This is partly illustrated by an increased neuronal discharge from sympathetic muscle activity (Smith & Minson 2012).

This overactivity of the SNS is probably triggered by an increased synthesis of adipokines, free fatty acids and leptin, predominantly abdominal fatty tissue, as adipokines can cross the blood-brain barrier.

A chronic overactivity of the SNS may lead to dysfunctions of various adrenergic signaling pathways and subsequently to the dysregulation of the HPA-axis, which promotes the development of obesity and overweight (Smith & Minson 2012).

The effects, which may vary in intensity, of the cortisol level on the body weight can emerge from certain circumstances in different disease patterns. On the one hand, Cushing's syndrome could be one related health issue that can be mentioned here. This syndrome is primarily characterised by hypercortisolism. This increased cortisol level can occur due to the intake of drugs with glucocorticoid as an active agent or can even be induced endogenously causing increased levels of the stress hormone cortisol. In addition, an increased ACTH, or CRH level can also lead to Cushing syndrome. Another disease that is associated with an increased cortisol level is called Addison's disease. In this case, a chronic insufficient adrenal gland leads to hypercortisolism, which is symptomatically often characterised by stem obesity or weight loss. In addition, an increased visceral fat deposition could be observed in primates after they had been exposed to physical or psychological stress over a longer period of time (Shively et al. 2009). In the presence of insulin, cortisol can also cause the accumulation of triglycerides in adipocytes. This, in turn, leads to increased gaining of stem fat tissue in the core area of the body (Björntorp 1997). Furthermore, long-term overactivity of the HPA-axis seems to promote the development of obesity, mainly due to increased food intake, triggered by factors such as artificial stress induction, administration of CRH from sheep and a reduced response to dexamethasone suppression, which leads to increased appetite, especially when very tasty foods are available (Cizza & Rother 2011).

According to functional MRI research, the brain's reward system is inhibited by the effects of stress, which may cause an increase in the demand for comfort foods (Duong et al. 2012). Strangely enough, stress, in its chronic form, may even be related to weight loss in a small subgroup of people. This may be caused by overactivity of beta-adrenergic lipolysis cascades, or different dietary patterns, respectively coping mechanisms (Pasquali 2012).

### **2.6.1 Dysregulation of the HPA-axis, inadequate sleep and obesity**

An altered and dysregulated HPA-axis in combination with obesity is frequently observed in individuals with chronic insomnia, depression, and sleep apnea syndrome (Balbo et al. 2010; Vgontzas et al. 2007; Kupfer et al. 1993). Individuals with depression often indicate elevated cortisol and ACTH levels. Consequently, the physiological inhibition of the HPA-axis is reduced due to the impaired sleep quality (Balbo et al. 2010). Even after three years, after the depressive disorder had subsided and cortisol levels had returned to normal levels, sleep changes could still be observed (Kupfer et al. 1993). In individuals suffering from insomnia increased levels of cortisol, ACTH and free cortisol were found in urine during a 24-hour

plasma examination (Balbo et al. 2010). Moreover, obese individuals show that ACTH and cortisol levels in the morning hours correlate positively with the frequency of sleep apnea events (de Jonge et al. 2012).

Whenever we start falling asleep, the cortisol level in the organism begins to be diminished leading to a reduction of the stress hormone level within about 1 to 2 hours (Balbo et al. 2010). This effect could be observed in individuals who were in a sleep-wake cycle of 3 hours as well as in sleep phases during the day. Similarly, studies have shown a reduction in cortisol levels in individuals who did not receive any temporal specifications and whose sleep was triggered somewhat later by the circadian cortisol system (Balbo et al. 2010). Nightly awakening phases increase the cortisol level at least for a short time, while awakening in the morning causes a more persistent increase of cortisol. The lowest cortisol and ACTH levels were detected after CRH occurred during the slow-wave sleep phase (Balbo et al. 2010).

Some studies indicate that people who suffer from poor sleep show an excessively strong reaction to dexamethasone or CRH (Hori et al. 2011). The lack of sleep in its acute form is considered a stressor that leads to an activation of the SNS with simultaneous reduction of the parasympathetic tonus. The same happens with increased epinephrine and norepinephrine levels in plasma (Lucassen et al. 2012). The mean 24-hour levels of ACTH are positively correlated with BMI. This may be related to increased hypothalamic activity or reduced negative feedback mechanism of cortisol (Vgontzas et al. 2007; Veldhuis et al. 2009). People with high BMI appear to react less strongly to cortisol suppression by administration of 4 mg dexamethasone (Rutters et al. 2010). According to Pasquali, women do respond by a weaker suppression of cortisol after administration of 1 mg dexamethasone than men. This suggests that the relationship between obesity and HPA inhibition appears to be both dose-dependent and gender-specific (Pasquali 2002). The stimulation of the HPA system by the administration of CRH (Vgontzas et al. 2007) from sheep, as well as ACTH (Mårin et al. 1992) or by mental stress testing (Mårin et al. 1992) higher cortisol levels were more frequently observed among obese individuals than among those with a slim appearance. Consequently, the HPA axis of obese individuals can be described as hyper-reactive to stress, and equally weakly responsive to negative feedback mechanisms. Under certain circumstances, due to efforts of the system to prevent a lowering of the free cortisol level, below a normal level (Lucassen & Cizza 2012).

## 2.6.2 Combating sleep deprivation and dysregulation of the HPA-axis as innovative approaches in obesity therapy

Since the activities of the HPA-axis and changes in normal sleep seem to play an important role in the development of body weight, these aspects must be considered in the fight against obesity and overweight.

According to a study conducted on obese African-American women, women with high self-awareness levels of stress increased weight loss under adequate stress management during a 12-week lifestyle-oriented program. Accordingly, the examination of the cortisol levels of saliva samples taken in the morning revealed a more pronounced reduction of cortisol in saliva in this group (Cox et al. 2013). Despite a weak statistical power of this study, these obtained results could be very useful indicating that the overall reduction of the stress level favors a reduction in body weight (Lucassen & Cizza 2012). Modern pharmacological interventions used in the treatment of obesity by influencing the HPA axis are primarily type 1 and 2, 11- beta hydroxysteroid dehydrogenase (11 $\beta$ -HSD) inhibitors that aim to alter the tissue-specific cortisol content without affecting the cortisol level of the body. According to some studies by which the 11 $\beta$ -HSD inhibitor carbenoxolone has been investigated, results are ambiguous suggesting that the 11 $\beta$ -HSD expression is sometimes reduced, while the synthesis remains unchanged in other cases (Sandeep et al. 2005; Pereira et al. 2012). According to an investigation carried out by Andrews et al., the administration of 300 mg carbenoxolone over 7 days was associated with decreased glycogenolysis and reduced cholesterol levels (Andrews et al. 2003). In the years 2008 – 2010, over 70 patents were filed for 11 $\beta$ -HSD<sub>1</sub> inhibitors (Carpino & Goodwin 2010).

Several research endeavors have been carried out in various preclinical studies to investigate other 11 $\beta$ -HSD inhibitors, mainly of type 1 (Pereira et al. 2012). People who suffer from being overweight show a changed HPA activity and disturbed sleep behavior in equal measure. Despite partly unchanged cortisol levels in the plasma, an overactivated HPA-axis showing consecutive simultaneous tissue-specific alterations in cortisol secretion is due to the increased 11 $\beta$ -HSDs expression. Insufficient or experimentally induced sleep deprivation may eventually lead to various physical changes that can possibly promote the development of obesity. A possible explanation for this effect could include an increased appetite resulting in a higher food consumption. In addition, sleep deprivation also seems to be related to certain disturbances or even interruptions of several cascades of the HPA axis. Currently, however, there is little evidence with regard to the associated HPA activity providing only sparse evidence of connections between 11 $\beta$ -HSDs, corticosteroid binding globulin (CBG) and sleep.

In turn, a dysregulated HPA-axis can lead to disturbed sleep behavior. In fact, however, there is no evidence that obesity could worsen sleep quality (Lucassen & Cizza 2012).

Since it can be assumed today that sleep and HPA activities are related to the development of obesity. Therefore, it seems crucial to focus on this field in order to be able to develop therapeutic measures targeting obesity. In particular, 11 $\beta$ -HSD inhibitors of type 1 that act tissue-specifically, are to be addressed. They are considered particularly promising in the fight against obesity as they selectively aim to influence the cortisol level in tissue without changing the circulating cortisol level. This is a decisive advantage of treatment, in order to prevent undesired drug effects.

Intense research is being conducted into new ways of being able to reduce general stress levels more strongly and to consider sleep hygiene aspects over a longer period of sleep. In conclusion, obesity, the HPA axis, and sleep are parts of a health-endangering system within which various interrelations exist. This concerns the immune system or the regulation of appetite. A successful fight against obesity is hardly possible without further research into the underlying mechanisms of this system (Lucassen & Cizza 2012).

## **2.7 Obesity and mental health**

Although mental health problems are among the most common reasons for health limitations and may have long-term effects, mental health needs have often been neglected (Kieling et al. 2011). According to the World Health Organization (WHO), mental health is a condition of well-being of an individual, in which a person is capable of realising own abilities, can cope with the stresses of everyday life, and is furthermore able to work in a productive and fruitful way, which contributes to the community (WHO 2001). Mental health does not only mean the absence of mental illness. As a result, the WHO published further reports on mental health prevention (WHO 2004) and mental health promotion (WHO 2005). Accordingly, there are three core elements of the WHO definition consisting of well-being, effective functioning of individuals and effective functioning for a community (WHO 2005).

While health expenditure on obesity has gradually become apparent (Kim & Popkin 2006; Kopelman 2000; Olhansky et al. 2005), the link between obesity and mental health in the population remains unclear. Examinations of the first generation studying this topic Friedman and Brownell (1995) criticised the large range of instruments used for psychopathology

measurement compared to a small number of studies using diagnostic measures of mental disorders (Friedman & Brownell 1995).

Depression is also considered a widespread disease and seems to be associated with a number of physical disorders. This applies in particular to diseases such as type 2 diabetes and cardiovascular diseases (Carney et al. 2002; Haupt & Newcomer 2002).

People suffering from cardiovascular disease have higher morbidity and mortality, if they also suffer from depression. However, the underlying mechanisms are still unknown (Carney & Freedland 2003; Glassman & Shapiro 1998).

Presently, little is known about the links between obesity and mental health. In the so-called "Jolly fat"-hypothesis a positive relationship between overweight, respectively obesity and a lower level of anxiety in men and women was postulated for the first time in the 1970s. In addition, a lower depression rate was observed among men (Crisp & McGuinness 1976). On the other hand, some studies have found an increased risk of depression in overweight people in the vast majority of cases (Goodman & Whitaker 2002; Roberts et al. 2000).

In fact, the adverse health effect of obesity as a cause of cardiovascular disease and premature death is evident (Li et al. 2006; Gu et al. 2006; Hu et al. 2005) indicating increased mortality rates within these populations (Dembling et al. 1999; Brown et al. 2000; Saha et al. 2007). Obesity is a disease that has long since reached pandemic proportions. It is noteworthy to mention that a growing prevalence can also be observed in the third world (Wolf et al. 2000). Since the beginning of the 21st century, obesity has been the disease with the highest prevalence and incidence within the United States of America (Buchwald et al. 2002).

Overweight and obesity in combination with sometimes severe forms of mental and psychiatric disorders are frequent reasons for consulting clinical institutions. In view of the current data situation, a relationship between obesity and mental disorders can be assumed today. Research mainly focuses on answering the question if there is a causal relationship between mental symptoms and somatic comorbidities such as obesity in psychiatric patients or whether obesity and some somatic disorders are predisposing for psychiatric disorders (De las Cuevas et al. 2011). Following the statements of De las Cuevas et al. (2011), this considered relationship is associated with certain demographic characteristics such as age, gender and other characteristics, including comorbidity and lifestyle factors of the populations. (De las Cuevas et al. 2011). McElroy et al. and Pickering et al. point out that people with severe psychiatric disorders are considerably more often obese than the average population (McElroy et al. 2004; Pickering et al. 2007).

Relevant research also exists on the risk of depression and various psychiatric pathologies among obese patients (Onyike et al. 2003; Roberts et al. 2000; Alciatia et al. 2007; Amann et al. 2009). Consequently, there is a weak correlation between obesity and depression in this context (De las Cuevas et al. 2011).

Several studies have also shown that childhood obesity is associated with an increased risk of developing various health problems. This applies to both childhood and later adulthood (Gidding 1995; Tremblay 2000; Eisenmann 2000). The manifestation of overweight and obesity in childhood is associated with a variety of health complications. Thus, neurological, pulmonary, gastrointestinal, or also diseases of the cardiovascular and endocrine system can be observed (Must & Strauss 1999; Deckelbaum & Williams 2001). Overweight and/or obesity can also have effects on individual self-confidence, body image and social mobility (Must & Strauss 1999; Ge et al. 2001). According to Stunkard and Wadden (1993), and the reports of the National Institutes of Health National Heart, Lung and Blood Institute (1998), it is well known that obese/overweight adults have an increased risk of developing mental disorders (Stunkard & Wadden 1993; National Institutes of Health National Heart, Lung and Blood Institute 1998). In accordance with the WHO, obesity in childhood is also considered a serious and highly serious health problem (WHO 1998).

### **2.7.1 Obesity and depression**

There is sufficient evidence that major depression increases the risk of premature death (Penninx et al. 2001; Zheng et al. 1997; Everson et al. 1998; Wassertheil-Smoller et al. 2004). Moreover, depression is also considered one of the most frequently diagnosed psychiatric disorders within industrialised countries (Simon et al. 2006; Australian Bureau of Statistics 1998; Hasin et al. 2005). Most recent studies suggest that obesity is clearly associated with a higher risk of developing depression implying for a reciprocal relationship between these two major public health concerns (Leutner et al. 2023; Holt 2019; Milaneschi et al. 2019; Hachula 2023). Accordingly, these results support prior statements derived from several investigations analysing the complex interrelationship between obesity and depression. However, evidence on possible long-term effects and statements on the underlying mechanisms are still rather scarce given its complexity (Rajan & Menon 2017). Most of the prior examinations focused on a cross-sectional approach that is not capable of investigating temporal effects (Brailean et al. 2020). Moreover, the robustness of these findings is still questionable in terms of different subgroups (Brailean et al. 2020; Badini et al. 2022; Kappelman et al. 2021).

The study of depressive impairments and symptom pictures, with regard to the development of obesity and various psychopathologies is particularly widespread (Atlantis & Baker 2008). Nowadays depression is considered a widespread mental health problem and therefore has a high public health relevance. In addition, depressive disorders are associated with numerous somatic disorders such as cardiovascular disease and type 2 diabetes (Carney et al. 2002; Haupt & Newcomer 2002). People suffering from cardiovascular problems also have increased mortality and morbidity if they also suffer from depression. However, the underlying mechanisms have not yet been clarified (Carney & Freedland 2003; Glassman & Shapiro 1998).

Epidemiological studies on the interacting mechanisms between mental health and high body weight that have been conducted predominantly use a cross-sectional design (Roberts et al. 2000; Friedman & Brownell 1996). Whether or not obesity increases, the risk of depression in later life remains unclear as there is little evidence in this respect. According to a one-year follow-up study, obesity is considered a predictive factor if other variable factors are controlled (Roberts et al. 2000).

Another observational study by Roberts et al. (2003), indicates an association between obesity and the increased risk of depression after a five-year follow-up. Conversely, depression did not increase the risk of obesity in the future (Roberts et al. 2003). Another study investigating the relationship between obesity and eight different aspects of mental health on persons aged 50 years of age or above showed that obese individuals have an increased risk of depression after 5 years (Roberts et al. 2003).

According to Noppa and Hällström (1981) who conducted a study in which they observed middle-aged women over a period of 6 years who initially suffered from severe depression, findings suggest that they were at higher risk of developing obesity (Noppa & Hällström 1981). Another study also found a positive correlation between abdominal obesity and depressive manifestations in middle-aged men (Ahlberg et al. 2002).

A dysregulated HPA axis of individuals with obesity who also show depressive symptoms, seems to be a conclusive explanation for a causal link (Stunkard et al. 2003; Bornstein et al. 2006; McElroy et al. 2004) of these two health issues. In addition, there is evidence for an attenuation of depressive symptoms after surgical weight reduction, which suggests that a reversibility of the effects of obesity can be observed (Dixon et al. 2003; Karlsson et al. 2003; Vage et al. 2003; Larsen et al. 2003; Rowston et al. 1992). There is also evidence of a so-called "dose-response effect", which means that the severity of obesity has an effect on the occurrence of depressive symptoms (Onyike et al. 2003).

To date, there have been a number of different reviews that have made various estimations regarding a possible link between obesity and depression (Stunkard et al. 2003; McElroy et al. 2004). The identification of causal factors in depressive disorders is considered particularly important with regard to the distribution of resources in order to better prevent the occurrence

of depressions in the future (Atlantis & Baker 2008).

Overall, after systematic review by Atlantis & Baker (2008), it can be assumed that there is a link between obesity and the incidence of depression. Some prospective studies show a certain consistency with at least a weak effect, but also with indications of some bias sources, as well as a limited generalisability of the results. The review of some American cross-sectional studies shows that there is a link between obesity prevalence and depressive symptomatology in the joint analysis of women and men. If, however, women and men are analysed separately, this relationship only becomes apparent in women, but not in men. Other cross-sectional studies, however, show no association in either women or men. Accordingly, real evidence for the existence of this connection is rather poor (Atlantis & Baker 2008).

Under certain conditions, obesity may promote the development of depression, especially if they suffer from various comorbidities. For example, the prevalence of depression is highest among people who suffer from eating disorders, such as binge eating, which result from randomised cross-sectional studies (John et al. 2006; Grucza et al. 2007). Similarly, some case-control studies show obese individuals seeking weight-reducing treatment (Tuthill et al. 2006; Pagoto et al. 2007) while others do not intend to undergo this therapy (Yanovski et al. 1993; Bulik 2002). According to a cross-sectional study, obesity increases the risk of depression in women and at the same time depressive disorders occur much more frequently among obese women than among obese men (Scott et al. 2008).

The frequency of depression is also clearly higher in people who experience bodily pain in the average population (Bair et al. 2003). Furthermore, various cross-sectional studies show a dose-response effect by which the severity of obesity affects the frequency of perceived bodily pain (Hitt et al. 2007).

It is assumed that depression might often be the result of previously perceived bodily pain, although cohort studies have not found a strong correlation between depression and the incidence of physically perceived pain (McBeth et al. 2001; Gupta et al. 2007). However, an association has been observed between obesity and the occurrence of bodily pain. According to this, the risk of obesity for the development of pain, especially in the knee joint, increases significantly (Peltonen et al. 2003; Jinks et al. 2006).

If people are treated surgically to achieve weight reduction, bodily pain is reduced (Peltonen et al. 2003), which strongly indicates a causal relationship. Therefore, it is likely that the effect of obesity on the development of depression, at least in some individuals, is also influenced by the sensation of bodily pain. Whether, or to what extent, depression is possibly associated with various disorders of eating habits and physical pain in obese individuals cannot be fully clarified due to lack of evidence (Atlantis & Baker 2008). Another point of the psychopathology of depression are psychosocial factors. In many cases there is an internalisation of classical negative stereotypes that are related to body weight (Puhl et al. 2007), a negative perception

of the body image (Cargill et al. 1999; Friedman et al. 2002) and a self-efficacy, especially related to low body weight (Linde et al. 2004). All these factors can further contribute to an increased risk for the development of depression among affected people. Psychosocial factors can increase the likelihood of depression in obese individuals under certain circumstances, regardless of whether the affected people are of normal weight or overweight. According to Atlantis and Ball and the results of their cross-sectional study, the perceived degree of overweight increases the likelihood of suffering a moderate or higher degree of psychological distress, even more than that caused by obesity per se. This applies to both women and men in a joint analysis (Atlantis & Ball 2007). Furthermore, the perception of social ideals in terms of body weight and body image that are strongly influenced by the media also play an important role in this context. The various media outlets mainly convey ideal images of people with slim bodies, but this is not considered representative for the general population (Greenberg et al. 2003). This effect often promotes the emergence of negative stereotypes about overweight people (Greenberg et al. 2003; Himes & Thompson 2007).

This contributes to the development of psychosocial factors (Lisa & Groesz 2002). Many of these factors seem to apply particularly strongly to women (Tuthill et al. 2006; Linde et al. 2004; Greenberg et al. 2003; Himes & Thompson 2007). This could also explain the 2 to 3 times higher prevalence of obese women attending treatment facilities compared to obese men (Tuthill et al. 2006; Pagoto et al. 2007; Friedman et al. 2002). In general, it can therefore be assumed that obese women are more strongly related to psychopathological factors than men. In addition, higher prevalence rates of depression can be observed in women (Scott et al. 2008). Eating disorders also occur significantly more often in obese women than in men (John et al. 2006). Furthermore, various biological factors also seem to play a role in the psychopathology of depression. Therefore, there is a relationship between these biological factors in obese people and the development of depression. As a reaction of the body, changes in hormone synthesis and its concentration can be observed through the neuroendocrine stress system of obese persons. This applies to both individuals with depressive symptoms (Ahlberg et al. 2002) and to those without depressive symptoms (Ljung et al. 2000). These modified hormone concentrations do also occur in obese individuals with binge eating disorder (Gluck et al. 2004) and in individuals with depression who are also experiencing bodily pain (Williams et al. 2006). Extensive discussions on this topic suggest that there might be an etiological similarity to the emergence of depression (Stunkard et al. 2003; Bornstein et al. 2006; McElroy et al. 2004).

However, the scientific evidence in this respect is not clear. Further epidemiological studies that provide more information on the biological aspects of obese people would even more strongly justify the investigation of further possible links between depression and obesity (Atlantis & Baker 2008). Obesity thus increases the risk of depression if the affected people also suffer from binge eating disorder and/or from bodily pain at the same time; possibly mediated by psychosocial factors. However, in order to confirm this, further cohort studies in different populations are needed to verify a causal relationship.

If it would be possible to prove the connection between accompanying eating disorders, pain, and the related psychopathological and/or biological aspects, it would represent a significant advance and approach for preventive measures to avoid the occurrence of depression. This would of course have far-reaching effects on the stresses and mortality rates associated with this disease, especially in the case of major depression (Penninx et al. 2001; Zheng et al. 1997; Everson et al. 1998; Wassertheil-Smoller et al. 2004).

Accordingly, systematic reviews are intended to aid in supporting current research on the topic and, above all, to examine existing findings with regard to possible uncertainties. In the future, it will primarily be prospective studies that will provide relevant information to determine psychopathological factors related to the occurrence of depression in obese individuals. The aim is to collect sufficient data to enable joint analyses to be carried out, including meta-analyses.

According to Atlantis & Baker (2008) a weak correlation between obesity and depression can be assumed. There are only a few high-quality cohort studies on this subject, even though cross-sectional studies have been conducted by now, the results of which are still too vague to draw conclusions in terms of significant causality. Further etiological studies are needed (Atlantis & Baker 2008).

## **2.7.2 Obesity and anxiety disorders**

About a quarter of the population is affected by an anxiety disorder during their lifetime. Anxiety disorders are among the most common psychiatric diseases in industrialised countries (Kessler & Wang 2008). These disorders are primarily characterised by psychological symptoms, including anxiety and fear. Furthermore, physical complaints such as heart palpitations, chronic fatigue or general tension can also be observed.

Frequently, anxiety disorders have a chronic course and show themselves in various forms that are associated with each other. In addition, there are also links to other psychiatric illnesses. It is well recognised that impairments due to various fears can lead to increased risks for worse health outcomes, chronic health problems and impaired QoL. Furthermore, fears also lead to an increase in mortality among those who are affected (Benninghoven et al. 2006; Weiser 2007; Roy-Byrne et al. 2008; Sareen et al. 2006).

Obesity can obviously be a predictor of several anxiety disorders. With regard to prevalence, obesity is considered a steadily increasing threat (Parikh et al. 2007). The main characteristic of obesity is an excessively high body weight, which makes it one of the main causes of the overall burden of disease worldwide (Ezzati et al. 2002). Obesity can lead to anxiety disorders by numerous mechanisms. For example, the affected individuals may perceive stigmatisation and discrimination based on overweight-related aspects as distress (Alloway & Bebbington 1987; Cairney et al. 2008). In addition, the impact of obesity on one's own health and QoL can also have a particular negative effect as a stressor (Sareen et al. 2006; Sareen et al. 2005; Vink et al. 2008). Any of these mechanisms could therefore lead to anxiety disorders. The current evidence on how obesity and anxiety disorders are linked is unclear. Even though there is no clear evidence providing a significant association, weak correlations or mixed forms that could be intrinsic and caused by the nature of obesity or anxiety disorders can be assumed (Garipey et al. 2010).

The interplay of obesity and anxiety disorders seems to be differently pronounced in subgroups within the population that differ in sociodemographic aspects, biological and behavioral characteristics. The frequent social discrimination of obese women (Puhl & Heuer 2009) suggests that the relationship between obesity and anxiety disorders is more prevalent among women than among men. A comprehensive search was able to identify seven relevant studies that examined the connection between obesity and individual psychological factors such as fears (Lykouras 2008; van Hout et al. 2004; van der Merwe 2007; Kyrou & Tsigos 2007; Fabricatore & Wadden 2004; Friedman & Brownell 1995; Stunkard & Wadden 1992).

In a majority of these studies, it was possible to identify a connection, which cannot be clearly limited to a specific psychopathological condition. However, some of these reviews differed in their methodology and deviated significantly from the usually applied approach of systematic reviews. There were also differences in the study population that was partly recruited in the clinical setting. As a consequence, some of the results could not be transferred to a general population (Garipey et al. 2010). Studies show that obese people are often confronted with

discrimination regarding their overweight. This discrimination actually happens in both private and public life (Puhl & Heuer 2009; Carr & Friedman 2005).

Obese people often receive less social support and have worse social networks (Carr & Friedman 2005). The socioeconomic status (SES) of obese people is also lower than that of the rest of the normal-weight population (Muennig 2008; Puhl & Brownell 2003; Maranto & Stenoien 2000). This lack of certain opportunities, combined with low availability of psychosocial resources, can lead to overweight people being at higher risk of psychological distress (Alloway & Bebbington 1987; Cairney et al. 2008), which in turn promotes the development of anxiety disorders. Overweight individuals also often have anti-fat prejudices against themselves (Puhl & Brownell 2003). Affected individuals feel under pressure to control their body weight, which is often perceived as particularly stressful, especially, if one has already made several failed attempts to lose weight. Constant occupying with eating and following diet plans and patterns is associated with the development of fears (Horner Jr & Utermohlen 1993). Obesity is considered a predictor of a wide variety of medical events (Jonsson et al. 2002; Osullivan 1982; Beuther & Sutherland 2007). Different types of adverse effects and impairments associated with obesity (Muennig et al. 2006; Ostbye et al. 2007) as well as weight-associated chronic events, may increase the risk of developing anxiety (Sareen et al. 2006; Sareen et al. 2005; Vink et al. 2008; Kroenke 2007).

A high calorie diet and a lack of exercise contribute to the development and maintenance of anxiety disorders (De Moor et al. 2008). Vice versa, however, it is also possible that anxiety can lead to an increase in bodyweight. It is assumed that a dysregulated HPA axis leads to a change in appetite, which in turn can cause an increase in weight in individuals who are frequently exposed to stress (Torres & Nowson 2007; Dallman et al. 2005). It is not only a matter of anxiety that increases appetite (Canetti et al. 2002), but also an increasing demand for sweet and fatty foods (Torres & Nowson 2007; Nieuwenhuizen & Rutters 2008; Adam & Epel 2007; Yannakoulia et al. 2008). Chronic medical events associated with anxiety such as bronchial asthma may have substantial health effects. This often leads to reduced physical activity, which in turn promotes the development of overweight (Garipey et al. 2010).

The association between obesity and anxiety disorders has also a genetic basis since both diseases are inherited to a certain extent (Walley et al. 2009; Hettema et al. 2001). Various environmental factors, such as certain chemicals that affect the endocrine system, can partly explain the link between obesity and anxiety disorders (Elobeid & Allison 2008). These substances affect hormonal homeostasis, which in turn affects the regulation of emotions and body weight (Torres & Nowson 2007; Dallman et al. 2005; Elobeid & Allison 2008).

Negative personal experiences during childhood, including child abuse, are considered individual factors that can contribute to the occurrence of various health issues and may further promote the development of excessive body weight (Rohde et al. 2008; Gustafson & Sarwer 2004). Similarly, these factors are considered to be predictors for anxiety disorders (Gibb et al. 2007).

Certain personality structures, such as hypersensitivity to personal criticism, neurotic tendencies, or avoidance behaviour, can provoke overweight and anxiety (Vink et al. 2008; Angst & Vollrath 1991; Spira et al. 2004). Avoiding behaviour is also associated with impaired eating behaviour (Martyn-Nemeth et al. 2009; Troop et al. 1994). In addition, many psychiatric diseases are associated with other diseases, while some of these pathologies lead to overweight and obesity, such as mood swings (Atlantis & Baker 2008; Petry et al. 2008), various eating disorders (Picot & Lilenfeld 2003; Javaras 2008) and personality disorders (Petry et al. 2008). If one considers the connection between fear and obesity, the definition of fear should always be present. In most cases, symptoms of anxiety occur when people are in particularly stressful situations. They only mutate into the pathological form of fear when the symptoms are strong enough to influence functioning abilities.

Anxiety disorders are context-dependent. Obsessive persons order their lives by avoiding situations that can cause anxiety. Accordingly, obese individuals make fundamentally different decisions than those who are of normal weight (Garipey et al. 2010). For example, obese people with lower SES report stigmatisation less frequently than those with higher SES (Carr et al. 2008). A causal connection between obesity and anxiety is not so easy to represent and presumably consists of different feedback mechanisms that include different psychosocial decisions of an individual (Garipey et al. 2010).

There are numerous approaches to carry out future research on the topic of causality between obesity and anxiety disorders. However, it seems particularly important to correctly assess the nature of these two pathological conditions. There are fundamental differences with regard to etiology, history, and degree of overweight (Friedman & Brownell 1995). The relationship between obesity and anxiety differs with respect to various determinants of obesity. However, the evidence on this issue is currently inconsistent and weak. Large-scale research and case-control studies would be useful to gain further insights into these relationships. Furthermore, methodological approaches should be reconsidered in the future. For example, analysed data should rather come from real measurements and not be generated based on self-declarations in order to avoid misinterpretations. The assessment of anxiety disorders

should happen within a short period of time, otherwise the danger of a recall bias would be too great. Ideally, the last 12 months should be assessed. Important parts are also the consideration of different confounding factors, such as health factors or overweight associated comorbidities, and integrate them into future examinations. High-quality longitudinal studies are also needed to generate further insights into the relationship between obesity and anxiety disorders (Garipey et al. 2010).

## **2.8 Eating behaviour and mental health**

In regard to eating behavior, many preventive interventions point out risk factors for both anorexia nervosa and bulimia nervosa, including compensatory eating behavior to lose weight. In fact, there is little interest in disturbed eating behavior related to weight gain (Unikel et al. 2006; Lora-Cortez & Saucedo-Molina 2006). External factors in the shape of the so-called “obesogenic environment” are considered causal factors and may contribute to the rising prevalence of obesity. The situation is aggravated by detrimental eating behavior and physical inactivity (Papas et al. 2007).

People suffering from emotional problems and inadequate coping mechanisms often control their emotional state by certain eating patterns and may possibly develop eating habits that can cause weight gain (Garipey et al. 2010; Pompa Guajardo & Montoya Flores 2011; Scott et al. 2008; Simon et al. 2006; Strine et al. 2008; Zysberg & Rubanov 2010; Anderson et al. 2006). In many cases, psychopathologies are both a cause and an effect of overweight and obesity and often show bi-directionality. Strine et al. (2008) postulate that the diagnosis of anxiety and depression during a lifetime was related to obesity in American adults (Strine et al. 2008). Therefore, anxiety can cause overeating, lead to weight gain, and reduce treatment adherence (Anderson et al. 2006; Zipper et al. 2001). People suffering from atypical depression indicating increased appetite and events of overeating are much more likely to be obese (American Psychiatric Association 2000). Accordingly, these eating habits may be in relation to the reward system of the brain and play a role in stress regulation mechanisms (Colantoni et al. 2002).

It is evident that pathological eating patterns are associated with an insufficient regulation of emotional conditions (Spoor et al. 2007; Van Strien et al. 2009; Whiteside et al. 2007). Moral de la Rubia and Meza Peña (2012) postulate in their study a relation between affective disorders, age, and overeating (Moral de la Rubia & Meza Peña 2012).

Lazarevich et al. (2013) analysed eating patterns among freshmen students in Mexico City suggesting that they are more likely indicating depressive episodes and higher levels of impulsiveness when presenting changed eating behaviour. Thus, the hypothesis that mental ill health is linked to certain eating patterns causing weight gain seems to be confirmed. Difficulties in regular eating are highly correlated with symptoms of depression (Lazarevich et al. 2013).

Even though there is clear evidence hinting to a possible relationship between mental health problems and eating behaviour, these eating habits do not meet the criteria for a particular eating disorder. Hence, there is no pathological basis in view of obesity prevention and therapy that could be considered. It is important to understand that essential interventions are pivotal for the management of obesity and overweight (Lazarevich et al. 2013).

Based on the association of disturbed eating habits and mental health problems combined with overweight and obesity, it is important to underline the psychological factors in preventive programs and treatment of obesity. Thus, evaluation of individual personality should be considered for all obese individuals within any interventional approach (Lazarevich et al. 2013). Healthy eating behaviour may be promoted and developed by various institutional services, including cultural activities, promotion of sports, nutritional programs and workshops or cognitive-behavioural therapy (Lazarevich et al. 2013).

### **2.8.1 Eating behaviour, stress, and the reward system**

By stimulating the HPA axis, the mesolimbic dopaminergic system is activated, which is directly related to the reward system. The experience of stress leads to an increased secretion of CRF, which connects to dopaminergic neurons of the VTA (Groesz et al. 2012; Sinha 2008). From there, several projection pathways exist to different areas of the brain, including the NAC, prefrontal regions, and limbic portions, all of which are part of the brain's reward system. This reward system plays a particularly important role in the abuse of various substances (Volkow et al. 2012; Clark 2013). Stress refers to various processes that include evaluation and assessment, perception, and response to various damaging events or stimuli (Fink 2010). The experience of stress can manifest itself in different ways. For example, stress can arise emotionally when one has lost a beloved person, or when one is facing interpersonal conflicts. Unemployment can also contribute to the perception of stress, however, there is also a physiological stress, which can be caused by starvation. Additionally, various illnesses or drug

withdrawal can favour the emergence of stress. The frequent and habitual use of various drugs with dependency potential can be a pharmacological stressor.

Acute stress situations lead to certain adaptations in the body. If, however, a chronic form occurs over a longer period, this leads to wear and tear, which is generally referred to as allostatic load. In this case, the regulation systems are permanently affected. The consequences include biological changes that impair mechanisms of adaptation. As a further consequence, this can lead to an increased susceptibility to diseases (McEwen 2004).

Slight stress due to challenges can have positive effects referred to as "eustress". It can have a motivating effect and contribute to achieving goals and maintaining homeostasis. These moderately pronounced stimuli can convey a feeling of controllability of the situation and fulfilability of tasks. This can often be perceived as positive and exciting by the persons concerned (Seyle 1976). The longer and more intense the stress experience, the lower the individual feeling of controllability and adaptability and the greater the stress reaction as well as the subsequent homeostatic dysregulation (McEwen 2004). The personal and individual perception of stress is based on specific factors that represent internal and external stimuli. Individual personality structures, emotional sensitivities and physiological aspects act as mediators and are responsible for the experience of distress (Yau & Potenza 2013). Stress has an effect on the homeostasis of the body. The organism reacts to the stressor in the form of a physiological response and aims to restore a state of balance. One aspect of this affected balance that can be disturbed by stressors is that of feeding behaviour. The physiology of eating behaviour has already been investigated many times. First and foremost, animal models were used, whereby the animals were supplied with standard laboratory food. However, the results of various experiments are inconsistent. Animals fed with monotonous food showed significant susceptibility to acute stress-associated hyper- and hypophagia (Levine & Morley 1981; Morley et al. 1983).

People show different reactions to food intake. Caloric intake increases by about 40% under the influence of stress, while there is also a corresponding decrease of approximately 40% in caloric intake. In addition, 20% of people under stress change their eating habits and calorie intake (Torres & Nowson 2007; Pasquali 2012; Block et al. 2009). These partly different results could depend on the different types of stressors, the different duration of the stress exposure and of course also the degree of saturation, respectively the feeling of hunger, which may have existed before the beginning of the examination. Moderately pronounced stimuli, for example, can trigger hyperphagia. However, a strong effect of stress can cause the opposite, namely hypophagia (Robbins & Fray 1980). Nevertheless, further individual factors must be

considered. However, the sometimes very complex results do not indicate which type of food was preferred here. In this context, it is particularly important to find out which foods are avoided, and which are consumed preferentially, in order to understand the mechanisms involved and to predict the impact of stress on health. For both animals and humans, a preference for very tasty and pleasurable foods can be observed when these individuals are exposed to stress situations. Therefore, there is a shift in the demand for food that arises independently of a caloric change in food intake. What is striking here is a significantly higher consumption of fat and sugar-rich foods in times of increased stress experience. Studies on rats show an increased intake of fat and/or sugary foods, such as lard or sugar. There was an increased intake of very tasty foods when they were under the influence of stress (Pecoraro et al. 2004; Dallman et al. 2003; La Fleur et al. 2005). Similar observations can also be made on human individuals. There is often a shift towards highly palatable foods, such as fast food, high calorie foods and various snacks (Zellner et al. 2006; Epel et al. 2001; Oliver et al. 2000).

To top it all off, this demand particularly for tasty foods also occurs especially when there is no feeling of hunger and thus no need for calories (Rutters et al. 2008). Furthermore, this effect could be particularly noticeable in overweight and obese people (Block et al. 2009; Jastreboff et al. 2013).

All these results suggest that the experience of stress can change the patterns of food intake and under certain circumstances favour hedonistic episodes of overeating. An intensification of this effect occurs particularly frequently in obese individuals. The underlying mechanisms of different eating behaviour patterns that can lead to the development of obesity are gradually being better understood (Yau & Potenza 2013). Drugs with addictive potential and food unfold their effects through the same mechanisms in the brain, whereby the dopaminergic and opioid systems are playing a central role (Volkow et al. 2012; Koob & Volkow 2010).

Drug abuse and the consumption of fatty food lead to changes in the activity of the noradrenergic system, CRH and glucocorticoids increasing the sensitivity of certain mechanisms of the reward system. This leads to an increase in the use of certain addictive substances and the consumption of particularly tasty foods (Sinha 2008).

Removal of the adrenal gland reduces dopamine release, especially in the NAC, both after drug administration and as a reaction to hypothalamic self-stimulation. In both cases, treatment with corticosterone can restore the original state (Barr et al. 2000). Even though the release of dopamine per se is in no way synonymous with seeking, it seems to be essentially linked to sensitisation to the reward system and control and conditioning. This assumption is in turn related to food and drugs. An increase in dopamine synthesis could often be observed as a

reaction to foods and various diets. These two aspects are central to food intake (Volkow et al. 2011). Repeated stimulation of the dopaminergic reward mechanism leads to subsequent neurobiological changes which may contribute to compulsive behaviour (Everitt et al. 2008). Furthermore, the administration of dopamine antagonists or even lesions within the dopaminergic system can lead to a weakened reaction to the food, and to a reduced activity of the reward system. According to research results, this applies to both sugar-rich, tasty foods and addictive drugs (Wise & Rompre 1989; Colantuoni et al. 2002; Avena & Hoebel 2003). Using positron emission tomography (PET) during acute stress situations show that the effect of stress and the release of cortisol lead to an increased synthesis of dopamine in the NAC (Wand et al. 2007).

The limbic system is involved in the mechanism of reward, the memory of emotional events and reward-based learning or nutrition (Berthoud 2012). In contrast, the PFC is at the more complex, cognitive, and controlling functions and is regulating impulse reactions, desires, and emotions (Berthoud 2012). During stress exposure, PFC activity is reduced, and the limbic structures are activated, leading to an automatic behavioural reaction aimed at survival. This also means paying attention to different cues regarding nutrition. Both chronic and acute stress lead to a decimation of synaptic connections within the amygdala and the anterior part of the gyrus cinguli. At the same time, synaptic connections with the hippocampus and certain prefrontal regions are reduced (Vyas et al. 2002). This mechanism constitutes the stress network in its chronic form that is focused on a limbic reaction. The experience of stress triggers a strong stimulus in the brain to consume food. At the same time, however, there is a weakened ability to inhibit this effect, which often leads to obesity. As a result, stress situations and negative sensations contribute to reduced emotional and behavioural control, which on the other hand can increase impulsive behaviour. These factors can promote the consumption of alcohol, substance abuse and eating (Sinha 2008). Because of the fact that both the consumption of food and the use of drugs with addictive potential are following the same mechanisms to unfold their corresponding effects, the discussion of one of these aspects can possibly explain the other.

As a consequence, rats treated with opioid injections into their NAC were shown to react with overeating (Kelley et al. 2000). Interestingly, patients who underwent surgical weight reduction treatment experienced a significant increase in alcohol consumption (King et al. 2012). The administration of the opioid antagonist naltrexone followed by very tasty food could not change the calorie intake in rats but showed a significant reduction of hyperphagia in hyperpalatable food (Apfelbaum & Mandenoff 1981).

Food is a convenient way to trigger a reward mechanism through very tasty and pleasurable meals, which, at least for a short time, can give a feeling of satisfaction and alleviate discomfort. An intensification of negative aspects, respectively the experience of distress, can lead to stress-related eating under certain circumstances in order to regulate the stress situation (Yau & Potenza 2013).

The drive to eat without actually needing calories is quite common but characterised by a high degree of individual variability. Weight-related changes in metabolism can affect the allostatic load. Several animal experiments have shown that obesity is often associated with a reduced signal transduction of fatty tissue. Another characterising factor is receptive resistance (Ikeda et al. 1986). If there is a reduced signal transmission from the fatty tissue, which is supposed to reduce the hedonistic content of food as negative feedback, the food intake can be prolonged and the interruption of the process of food intake can be impaired. Increased body weight and high-fat nutrition, as well as insulin resistance are associated with reduced glucocorticoid synthesis in stressful situations and altered catecholamine synthesis in peripheral and autonomic regions (Tyrka et al. 2012). These influences on negative feedback structures can explain the widespread dietary derailments (Figlewicz et al. 2004). People with a higher Body Mass Index (BMI) show a stronger correlation between prolonged stress and weight gain than those with a lower BMI who were exposed to the same stress level (Block et al. 2009). According to Laitinen et al., stress-related eating is clearly associated with obese women (Laitinen et al. 2002). In addition, overweight people in situations of stress tend to react more strongly to food cues. Slim people tend to feel a lower demand for food and energy without feeling hungry. This is true for both stressful situations and in non-tense conditions (Lemmens et al. 2011). Obviously, people with visceral obesity have a completely different situation. They tend to have an above-average demand for food, which corresponds to an increased energy intake. This effect usually happens in stressful situations without the feeling of hunger probably to compensate for the stress experience (Lemmens et al. 2011).

In fact, overweight people show increased activities in the structures of the reward centre of the brain in contrast to slim individuals. These are primarily regions of the insula, striatum and thalamus that are active during stress exposure or food cues (Jastreboff et al. 2013). Interestingly, there is a positive correlation between insulin resistance and the activation of brain regions of the reward system. This occurs as a reaction to food cues or situations of stress. However, this is only true for obese people and not for normal or slim people (Jastreboff et al. 2013). The activation of the reward system and the limbic system increases the demand

for hyper-palatable food. This is associated with an increase in cortisol levels, which in turn leads to reduced prefrontal activity. Consequently, the blood sugar level decreases. These mechanisms are influenced by BMI and are much more common in obese individuals (Page et al. 2011). High insulin concentrations and insulin resistance, which is quite commonly observed in obese people (Adam & Epel 2007), may affect the ability of insulin to reduce motivational mechanisms. This can cause an increased response to stress and food cues (Yau & Potenza 2013).

Chronic stress is often associated with certain symptoms, such as depression, apathy, alienation, anxiety, or anger (Cohen 2000). Certain meaningful or threatening stimuli can activate the emotional part of the nervous system resulting in an activation that provokes a behavioural reaction. Stress-induced elevations of the glucocorticoid system led to an amplification of emotions and motivations (Dallman 2010). Since the rewarding effect of hyper-palatable food is already proven, it is assumed that this kind of food is referred to as a so-called "comfort food" and could therefore be used as a form of self-medication to eliminate perceived stress episodes. In this context, people who were in a negative affective state were more likely to consume rewarding sugar-rich and fat-rich foods in the hedonistic sense than those who were in a more stable and happy state. The latter preferred less hyper-palatable food such as dried fruits (Garg et al. 2007).

Under laboratory conditions, it was shown that after exposure to threatening situations for the ego, a greater negative effect and even in some cases elevated cortisol concentration could be observed, which in turn, led to the consumption of high-fat and sugary foods (Rutters et al. 2009). Likewise, individuals under natural conditions with high cortisol levels were found to have a greater tendency to eat as a reaction to stress experiences in daily life (Newman et al. 2007).

### **2.8.2 Restrained eating**

The term restrained eating refers primarily to a deliberate, cognitively controlled effort to reduce food intake. In most of the cases, the goal is to reduce or maintain body weight. However, this renunciation of eating can in turn favour the consumption of food in stressful situations. Human beings who practice high restrained eating significantly increase their food intake, while individuals who do not follow the strategy of restrained eating reduce their food intake when they are in stressful situations (Wardle et al. 2000). This is fundamentally different from

emotional eating. Restrained eating means increased food intake under the influence of stress, while emotional eating is related to increased food intake after threatening states of the ego by a stressor (Wallis & Hetherington 2004). Restrained eating may possibly lead to an increased response to food and stress cues. Emotional eating improves negative and self-directed emotional states in the people concerned. Individuals who practice very pronounced restrained eating often differ only insignificantly in terms of energy intake from those who pursue a reduced form of restrained eating. There are also little differences in food intake between individuals observed under laboratory conditions (Stice et al. 2010) and in the natural environment (Stice et al. 2004). Restraint may be a consequence of failed attempts to limit food intake that is, under normal and stress-free conditions, eating less, with a tendency to supply too much energy during the experience of stressful situations (Yau & Potenza 2013). Some studies show that highly pronounced restraint is associated with elevated cortisol levels (Anderson et al. 2002; McLean et al. 2001). It can further be assumed that restraint is a central factor in the development of obesity. Moreover, affected individuals who engage in restrained eating often show a susceptibility to hyper-palatable food within their reward system.

Rats that were either repeatedly exposed to stress situations or fed limited amounts of food show no significant differences with the control groups in terms of total food intake, regardless of the type of food. The restriction alone led to a firm intake of food to compensate for the negative energy balance. However, when the reduced intake was associated with stress, the rats showed an increased preference for eating biscuits with the food. This suggests a form of hedonistic eating to reduce stress levels and not a diet to restore metabolic balance (Boggiano & Chandler 2008). A large-scale study on humans has shown that stress is apparently associated with an increased urge to eat. In this context, there is also a discussion of uninhibited eating or binge eating, which also implies the frequent consumption of hyper-palatable food such as hamburgers or chips. The experience of stressful situations is responsible for significantly more severe manifestations of restraint, referred to as rigid restraint (Groesz et al. 2012).

The flexible form of restraint is effective in dealing with body weight and avoiding uncontrolled handling of hyper-palatable food, while rigid restraint can create a preference for exactly these foods. Individuals who follow these rigid procedures seem to listen less to the physical signals that convey hunger or satiety. This leads in some cases to overeating (Heatherton et al. 1989). When people actively try to reduce their food intake or restrained eating, valuable cognitive resources can be lost, however, these are necessary for dealing with various stressors. This can result in impaired inhibitory control which can lead to increased susceptibility to overeating. Long-term loss of control over certain events in life can lead to inadequate attempts to bring

the handling of food under control. This often results in a conscious neglect of certain foods, which often turns into binge eating. In addition, a restricted food intake over a long period of time reinforces the rewarding effects of drugs with dependency potential (Carr 2002).

## **2.9 Drug-induced obesity**

The weight gain experienced during drug therapy with psychotropic medication poses a significant issue, potentially leading to severe consequences such as recurrent symptoms, comorbidity, and reduced patient compliance. These outcomes could be linked to the usage of the prescribed medications. In fact, prescribed drugs can lead to an increase in weight between 2 and 17 kg during the course of treatment (David et al. 1999; Masand 2000). Neuroleptics, mood stabilizer (Pijl & Meinders 1996; Nasrallah 2003; Corman et al. 1997), as well as certain antidepressants (Fava 2000) can cause weight gain. Particularly antipsychotics are responsible for gaining body weight (Mazereel et al. 2020). In contrast, there are only a few psychotropic substances that sometimes cause the opposite that is, a loss of body weight (Cantu & Korek 1988; Weisler et al. 1994; Chengappa et al. 2001).

### **2.9.1 Antipsychotics**

With the emergence of the newer antipsychotics of the second generation (SGAs) a significant association between drug intake and an increase in body weight was observed in the context of an antipsychotic therapy in long-term use. Almost every antipsychotic drug seems to be related to weight gain. Despite limited comparability of studies due to different study designs or recruitment procedures (Wellmer et al. 2009), a search in MEDLINE between 1966 and 2010 indicated that the most severe forms of weight gain were observed in patients who were treated with olanzapine, quetiapine, or clozapine. Treatment with risperidone leads to at least a moderate change in body weight in the form of about 1.0 kilograms (kg) weight gain per month. The antipsychotic zibrasidone, on the other hand, leads to only slight changes in body weight of about 0.8 kg per month. A brand-new investigation carried out by Zhao et al. suggests that weight gain during treatment with olanzapine and risperidone seems to be linked to a high level of the anorexigenic hormone leptin, which is considered a promotor of drug-induced obesity (Zhao et al. 2023).

According to a double-blind study, the treatment with aripiprazole leads to an increase in body weight of up to 0.9 kg within the first 3 weeks (McIntyre et al. 2010) and, according to the Food and Drug Administration (FDA), does not lead to any significant increase in weight during the

course of treatment, which suggests that any metabolic consequences should not be considered problematic (Bishara & Taylor 2009). In this context, a total of 19% of individuals treated with asenapine showed an increase in weight, whereas 31% of people under olanzapine treatment reacted with an enhanced body weight (McIntyre et al. 2009). The antipsychotic paliperidone that was approved in 2006, showed no significant side effects with regard to metabolic events such as weight gain, both in the long-term and short-term (Spina & Cavallaro 2007; Meltzer et al. 2008). Another study confirmed that olanzapine, asenapine, and risperidone were identified as major causes of gaining body weight after 3 to 12 weeks leading to gains of up to 7% (Barton et al. 2020).

The treatment with lurasidone over a short period does not induce relevant levels of weight gain and can be classified as harmless in terms of weight gain (Barton et al. 2020). A large - scale literature search showed that the neuroleptic active substance risperidone increased weight between 0.3 and 2.6 kg, whereas ziprasidone often causes significantly lower increases in body weight (Cohen et al. 2001; Russell & Mackell 2005; Ganguli et al. 2001; Barak 2002; Taylor & McAskill 2000; Vanina et al. 2002; Kinsbury et al. 2001; Keck et al. 2003; Cohen et al. 2003; Arato et al. 2002). The antipsychotic active agent olanzapine in the group of second-generation neuroleptics is today considered one of the main causes of weight gain within drug therapy (Barton et al. 2020).

The increase in body weight ranges from 4.2 to 7.4 kg and in some cases may even reach 12 kg. About 45 to 90% of the affected individuals show a significant increase in body weight (Frazier et al. 2001; Littrell et al. 2002; Soholm & Lublin 2003; Lieberman et al. 2003; Ratzoni et al. 2002; Gothelf et al. 2002). Quetiapine is another well recognised antipsychotic drug that is also known for its side effect of gaining body weight. In most of the cases, it causes weight gain ranging from 4.1 to 5.6 kg (Shaw et al. 2001; Brecher et al. 2000). Additionally, clozapine may cause weight gain ranging from 2.4 up to 31.3 kg. This often results in a body weight that is up to 10% higher than at the beginning of the treatment (Briffa & Meehan 1987; Hong et al. 2001; Masi et al. 2002; Allison et al. 1999; Lamberti et al. 1992). A short-term study confirmed a slight weight increase ranging from 0.5 up to 0.9 kg for the active ingredient aripiprazole compared to a placebo group (Potkin et al. 2003). It is recognized that even rather new active agents, including cariprazine and prexiprazole cause weight gain (Barton et al. 2020).

The most pronounced increase in body weight was observed among olanzapine, clozapine, quetiapine, and risperidone, while aripiprazole, paliperidone, ziprasidone, asenapine, and lurasidone were shown to affect body weight to a significant smaller extent (Nihalani et al. 2012).

## 2.9.2 Antidepressants

An increase in weight due to the intake of antidepressants is very common because antidepressants are also prescribed much more often than other weight-enhancing drugs, such as neuroleptics. Over a long period, weight gain as a side effect of antidepressants has been recognised within scientific community, as the increase in body weight was mainly known as a common side effect of atypical second-generation antipsychotics. Due to the fact that depression and anxiety disorders are diagnosed much more frequently than psychoses (Kaplan & Sadock 1998), a greater probability of an iatrogenic weight gain through these drugs can be assumed (Nihalani et al. 2012). It is suspected that both tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) may cause weight gain (Ghusn et al. 2022), which is expected to be higher than in patients receiving selective SSRIs (Fava 2000). The group of selective serotonin reuptake inhibitors (SSRIs) may also cause weight gain by inhibiting the thermogenic effect of brown adipose tissue. Thus, reduced peripheral serotonin activities may be used as an approach for obesity treatment (Suchacki et al. 2023).

The antidepressant mirtazapine ranks between tricyclics and SSRIs with respect to the side effect of weight gain, whereas mirtazapine is considered the drug showing the highest risk of weight gain. The newer bupropion is the only antidepressant that can even reduce body weight (Fava 2000). A possible weight gain of about 1 to 3 kg during antidepressant therapy at about 10 to 20% of the patients treated could possibly be a bigger problem than the approximately 2 to 10 kg increase in body weight at 1% of patients suffering from schizophrenia, within the population.

Despite the fact that antipsychotics are increasingly prescribed due to their approval for the treatment of bipolar disorders and major depressions, the number of antidepressants prescribed far exceeds the number of second-generation antipsychotics prescribed (Nihalani et al. 2012). The antidepressant imipramine is suspected to cause weight gain of about 3-4 kg (Fernstrom et al. 1986), while about 13.3 % of patients treated with imipramine increased their body weight by more than 10% compared to their initial weight. Patients treated with amitriptyline gained on average of about 2 kg in weight. A systematic review carried out by Sepúlveda-Lizcano and colleagues found that the TCAs, imipramine and amitriptyline, and the SSRIs like sertraline, fluoxetine or paroxetine among others, lead to a substantial weight gain (Sepúlveda-Lizcano et al 2023). In comparison, treatment with nortriptyline showed no evidence of an increase in body weight in adult patients over 60 years of age. If children suffering from attention deficit disorder are treated with this medication, there is also no significant increase in body weight (Frank et al. 1990; Prince et al. 2000).

According to some authors (Corman et al. 1997), MAOIs tend to induce less weight gain than TCAs. According to an examination (Corman et al. 1997), the MAO inhibitor phenelzine is responsible for the most cases of weight gain in treated patients. A weight increase by isocarboxazid or the transdermally administered selegiline, on the other hand, is rarely causally associated with gaining body weight. With regard to the clinical study situation, a slight increase in body weight due to MAOIs can be assumed. On closer examination of trazodone, for example, an increase in body weight of 0.5 to 1.1 kg could be observed in the course of treatment (Weisler et al. 1994; Paradis et al.1992). According to Patel et al., a positive correlation between the prescription of antidepressants, including SSRIs and antipsychotics and the increase of BMI levels can be observed within 12 months (Patel et al. 2022).

The most frequently prescribed SSRIs often show a small loss of body weight at the beginning of the therapy, while a significant overall increase in body weight could be observed during prolonged treatment, approximately after one year. Manifestations of weight changes during SSRI treatment may be caused by drug-related metabolic mechanisms (Aldrich et al. 2019). This effect could be confirmed by various clinical studies, whereas short-term, early clinical studies with SSRIs did not postulate this effect (Sussman et al. 2001). The data situation on SSRIs is contradictory with regard to a short-term appetite-suppressing effect of the antidepressant active substance fluoxetine, while the prolonged intake of the drug may lead to an increase in weight (Leinonen et al. 1999). The loss of body weight of about 0.35 kg was reported, while long-term intake resulted in an average weight gain of 2 to 2.5 kg (Michelson & Amsterdam 1999). The antidepressant citalopram may cause weight increases of 1 to 1.5 kg over a 1-year period (Bouwer & Harvey 1996; Abell et al. 1986). Two studies show that fluvoxamine (Fava 2000; Moon & Jesinger 1991) causes neither an increase nor a loss of body weight. Studies on sertraline showed a significant increase in body weight compared to control groups (Tohen et al. 2002). Following the suggestions made by Anagha et al., 49% of the patients indicated weight gain during SSRI treatment with escitalopram, sertraline or fluoxetine in the long term (Anagha et al. 2021). From the group of SSRIs, paroxetine is considered most likely to cause weight gain. According to the statements of Fava, paroxetine, compared to sertraline or fluoxetine, promotes a higher increase in body weight (Fava 2000). According to a cross-sectional study, weight gain of certain SSRIs is one of the common side-effects. However, studies focusing on adverse events of SSRIs are generally scarce (Anagha et al. 2021). The results of these studies indicate a less pronounced iatrogenic weight gain than with the intake of atypical second-generation antipsychotics (Nihalani et al. 2012). The intake of mirtazapine causes a significantly higher increase in body weight compared to the SSRIs paroxetine, citalopram, and fluoxetine (Harvey & Bouwer 2000; Ribeiro & Busnello 2001; Benkert & Szegedi 2000).

Mirtazapine seems to develop side effects similar to second-generation antipsychotics in terms of metabolic parameters and body weight (Nihalani et al. 2012).

However, some studies on a weight-independent effect of mirtazapine that directly increases the risk of dyslipidemia, irrespective of a healthy lifestyle and even in healthy people was identified (Lechner et al. 2023; Hennings et al. 2019).

A prospective, randomised, double-blind study of serotonin noradrenaline reuptake inhibitors (SNRI) in which individuals treated with duloxetine, escitalopram (SSRI) or a placebo showed an increase in body weight, especially when treated with escitalopram. While the average gain in body weight with duloxetine was about 0.61 kg, an increase in weight of 1.83 kg could be observed under escitalopram therapy. The frequency of a treatment-induced increase in body weight of 7% or more of the original weight was approximately the same for both active ingredients. Both duloxetine and escitalopram show significant responses compared to placebo (Nihalani et al. 2012). Mood stabilisers are used to treat bipolar disorders and schizo-affective disorders.

In fact, these kinds of drugs are also known to induce an increase in body weight. Mood stabilisers are similar to antipsychotics in terms of the side effect of weight gain that is often more pronounced than during antidepressant therapy (Nihalani et al. 2012). Especially the concomitant administration of mood stabilisers like valproic acid enhances the risk of gaining weight (Okura et al. 2023). Another study confirms that valproic acid is the most robust agent linked to increased appetite and weight gain (Buraniqi et al. 2022). Approximately 71% of people treated with divalproex, an anticonvulsant prescribed against manic episodes, develop a weight gain of 4 kg or even more (Corman et al. 1997). Other studies report weight gain of 0.9 to 14 kg after divalproex therapy (Chengappa et al. 2002; Biton et al. 2001) with an incidence of 8 to 59%. Another frequently used medication is lamotrigine. The administration of this antiepileptic drug indicates a relatively weight-independent efficacy profile. It has been reported that treatment with lamotrigine can lead to a weight loss of about 2 kg, while an increase in weight of only 0.6 kg was observed (Ginsberg et al. 2003). In contrast, treatment with carbamazepine indicates a change in body weight of up to 15 kg (Lampl et al. 1991; Luef et al. 2002). Moreover, it is also well known that using lithium for the treatment of bipolar disorder can also lead to weight gain.

According to a study, the intake of lithium can lead to a weight increase of 10 kg or more in 20% of treated patients. Another study observed weight increases of 6.3 kg (Baptista et al. 1995). However, Phelps et al. postulated that the administration of small doses of lithium was not linked to a higher body weight after six months showing that the increase in body weight was not higher than for lamotrigine (Phelps et al. 2021).

Zonisamide is an anticonvulsant active substance that can apparently lead to a reduction in body weight when being used off -label. In fact, the active ingredient has already been used for the treatment of some individuals to reduce weight.

The results of a study suggest a potentially effective applicability in obese patients suffering from binge eating disorder (McElroy et al. 2009). The therapy with zonisamide, in addition to individual cognitive behavioral therapy, can improve treatment strategies against binge eating by reducing body weight and reducing the occurrence of binge eating episodes. This effect was maintained for over 1 year after the completion of zonisamide therapy (Ricca et al. 2009). During this treatment, about 35% of the patients were able to reduce their body weight, especially those who were overweight, however, this weight-reducing effect was reversible (Wellmer et al. 2009).

The corresponding peripheral and central mechanisms underlying appetite behavior and nutrition are very complex regulatory systems. Various factors in the form of neuropeptides, neurotransmitters, and hormone-like peptides play an important role in the regulation of nutrition, metabolic cascades, and appetite (Harvey & Bouwer 2000). The endocrine and nervous systems are responsible for regulating the body weight by mechanisms controlling metabolism, appetite, and digestion (Parmar & Can 2023). Accordingly, weight gain caused by the intake of antidepressants is essentially achieved by activating a series of monoamine cascades. This mechanism includes dopaminergic, cholinergic, serotonergic, and adrenergic, respectively histamine receptor systems (Lee et al. 2016).

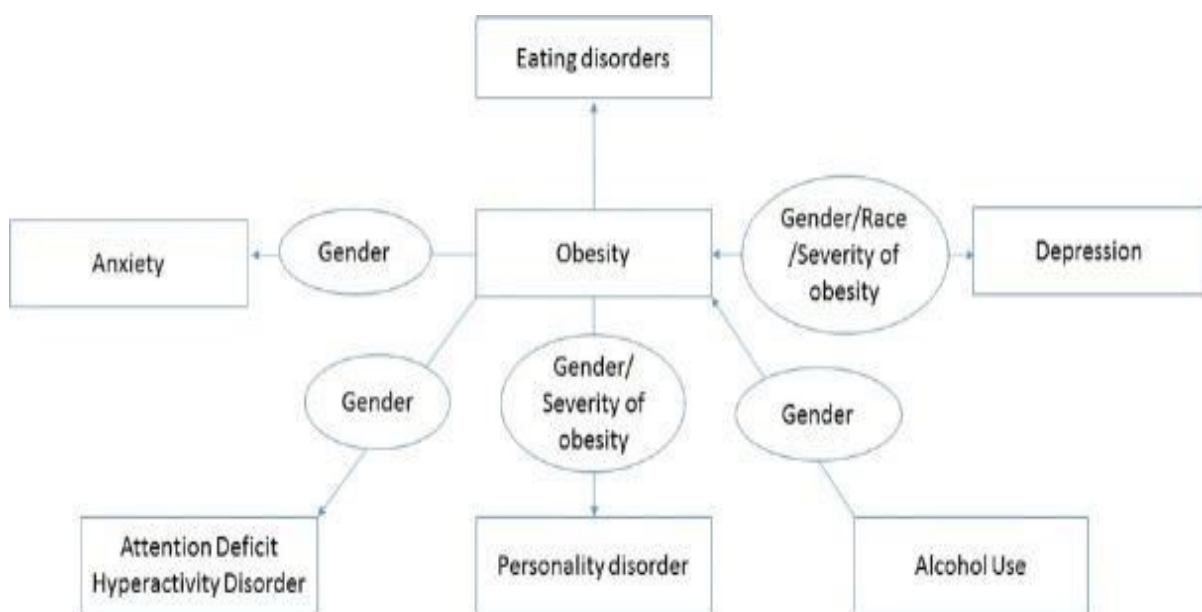
## **2.10 The Link between mental disorders and obesity**

It is clearly confirmed that there is a pathophysiological relationship between mental disorders, such as schizophrenia, and metabolic changes including obesity (Hansen et al. 2011; Venkatasubramanian et al. 2007; DE Hert et al. 2009; Agarwal & Venkatasubramanian 2013). Moreover, it is considered proven that psychiatric patients with a high body mass index (BMI) or obesity are at a higher risk when being treated with clozapine (Lamberti et al. 2006; Grover et al. 2011).

This triad of mental disorders, metabolic syndrome and obesity and the resulting associations open up new possibilities for understanding the pathogenetic basis in order to develop new therapeutic strategies (Rajan & Menon 2017) (Figure 8).

In this context, careful psychiatric evaluation appears to be particularly important in order to provide comprehensive care for patients suffering from obesity to establish a corresponding optimisation of therapeutic and functional outcomes. In addition, potential bi-directional

relationships should be considered and integrated in adequate therapeutic measures in the context of treating mental illnesses, possibly also reducing the disease burden through obesity. To the same extent, this could also be understood as a vice versa reaction in which the direction of the association changes. In the near future, it will be increasingly important to investigate these relationships between the severity of obesity in view of the different subgroups of depression and anxiety. Furthermore, scientists should also take a closer look at the methodology of the investigations and reconsider it if necessary. This applies in particular to the measurement of obesity, which should be carried out based on objective measuring instruments rather than self-reported information from patients. In addition, the results are distorted by possible confounding factors such as physical concomitant diseases. All these points should be considered when elucidating the underlying mechanisms between obesity and mental disorders (Rajan & Menon 2017).



**Figure 8:** Evidence-based model of associations between mental disorders and obesity (Rajan & Menon 2017). Reproduced without modifications from: Rajan & Menon 2017, *Psychiatric disorders and obesity: A review of association studies*. Copyright 2017 Journal of Postgraduate Medicine. The reuse of this image follows the terms of the Creative Commons Attribution-Noncommercial ShareAlike 3.0 License, which permits any use, copy and redistribution (<https://creativecommons.org/licenses/by-sa/3.0/>).

Mental illness and obesity seem to be clearly linked. There are clear indications of a strong and bi-directional relationship between obesity and depression. However, the reciprocal relationship between anxiety disorders and obesity proved to be rather weak and inconsistent. In terms of other psychiatric conditions, there was no clear significance in respect to reciprocal association with obesity. According to Rajan & Menon (2017), both men and women suffering from obesity are at increased risk of developing mental disorders, and vice versa. Nevertheless, a stronger correlation could be observed among women, which in turn suggests the possibility that gender of individuals seems to play a role. Based on these findings, a cost-

effectiveness analysis within the framework of a multidisciplinary approach appears to be sensible and necessary in the fight against obesity (Rajan & Menon 2017).

Today, obesity is considered a multifactorial disorder that combines both genetic and environmental factors (Park 2009). Mental illnesses fall broadly into the category of disorder, and are characterised primarily by mood swings, or disturbances of thought and behaviour (American Psychiatric Association 2013). In fact, mental disorders are also associated with a considerable burden of disease (Ferrari et al. 2014). Obesity and pathological mental impairments are considered chronic conditions, furthermore, there are indications of a relationship between these two pathological causes (Kivimäki et al. 2009; Kivimäki et al. 2009a). However, the links between obesity and mental illness are still unclear (Avila et al. 2015). Additionally, Avila et al. postulate that a bi-directional relationship between obesity and mental disorders appears to be affected by different aspects, including diet, exercise, and certain drugs, including antidepressants and antipsychotics amongst others. Moreover, some neurotransmitters like serotonin, norepinephrine, CRH, and neuropeptide Y (NPY) have an impact on this effect and can further contribute to the relationship between obesity and mental illness (Avila et al. 2015). During starvation, certain neurons that express NPY increase their activity, which results in stimulating the orexigenic effect of growth hormone release inducing (GHRELIN) accompanied by a decrease in insulin, which signals to enhance food consumption (Baldini & Phelan 2019).

Obesity and psychiatric disorders are often related. For example, mood disorders, anxiety disorders, personality disorders, binge eating, schizophrenia and various traumas or attention deficit and hyperactivity disorder (ADHD) are associated with obesity. In many cases, obesity also occurs because of taking medication prescribed for mental illnesses (Remington 2006). In fact, a bi-directional relationship between obesity and psychopathologies is confirmed. Mostly, mood disorders, personality disorders, anxiety disorders and schizophrenia are associated with obesity. Furthermore, a large number of different complex factors are involved in this interplay of obesity and mental illness. Therefore, in view of future political decisions, it seems particularly important to develop a better basic understanding in order to minimise the burden of mental illness on vulnerable individuals (Avila et al. 2015).

### **2.10.1 The reciprocity of obesity and depression**

Despite some research evidence on a biological relationship between obesity, overweight and depression, the results are unclear and deficient (Atlantis & Baker 2008; Stunkard et al. 2003; Bornstein et al. 2006; Bean et al. 2008). According to some investigations, obesity can be seen

as a kind of inflammatory process. Some of these inflammatory processes are suspected to be involved in the development of overweight (Emery et al. 2007; Shoelson et al. 2007), which may subsequently promote depression (Vacarino et al. 2007; Bremner et al. 2008; Milaneschi et al. 2009).

Inflammatory mechanisms play an important role in both obesity and depression. Various inflammatory processes could mediate the link between weight gain and depressive symptoms. Furthermore, the HPA axis seems to be involved in this mechanism. Overweight and obesity may produce a dysregulated HPA activity (Pasquali & Vicennati 2000; Walker 2001). Additionally, it is known that misdirected HPA activity is associated with the development of depression (Belanoff et al. 2001; Holsboer 2000).

Ultimately, obesity is involved in increasing the likelihood of developing diabetes mellitus and insulin resistance (Lee et al. 2008). This, in turn, can lead to various changes in the brain (Huber 2008), which increases the likelihood of depression developing (Ajilore et al. 2007). Suffering from being overweight and constantly being aware of that increases the psychological stress level (Atlantis & Ball 2007; Derenne & Beresin 2006). In both Europe and the United States, being slim corresponds to the ideal of beauty, which is determined by several socio-cultural factors, but also by what is socially accepted. Being overweight can undermine self-esteem and increase dissatisfaction with the own appearance. These factors are considered risk factors for the development of depression (Hoek et al. 2005).

A disturbed eating behaviour and eating disorders, including the experience of physical pain, can increase the risk for the development of depression (Beesdo et al. 2010; Gadalla & Piran 2008). According to Luppino et al (2010), the effect of obesity on the development of depression seems to be more pronounced among American studies. Thus, the underlying biological mechanisms of obesity and the occurrence of depression are most likely not to be culturally different, yet it is possible that socio-cultural mechanisms within a cultural domain will be different from another (Luppino et al. 2010).

One of the reasons why depressive symptoms increase the risk of body weight gain may also be due to neuroendocrine dysregulation. Björntorp (2001) claims that depression can trigger abdominal obesity by leading to long-term hyperstimulation of the HPA axis (Björntorp 2001). The stress hormone cortisol and insulin inhibit the activity of lipid activating enzymes. This mechanism is mediated by glucocorticoid receptors that primarily occur in visceral abdominal fatty tissue (Björntorp 1996).

Furthermore, another basic mechanism seems to be particularly important that is, the management of an unhealthy lifestyle. Especially, a lack of physical activity and the consumption of unhealthy food can be involved in the development of obesity. Finally, the previously discussed topic of antidepressants and their potential risk of weight gain is also worth mentioning (Stunkard et al. 2003), although most of the studies on this topic were community-based and many of the observed persons received no pharmacological treatment.

According to the findings from a systematic review and meta-analysis carried out by Luppino et al. in 2010, there was no difference between the results of studies using clinical diagnosis of depression and the results obtained based on information of symptoms of depression (Luppino et al. 2010). However, there were some limiting factors in this study. First, the investigation was limited to a computer-aided search for exclusively English literature. Second, unpublished studies were not included in the investigation. Under certain circumstances, one could have committed a publication bias with regard to the included works with baseline depression.

A further limitation of this study is that although the number of subjects involved seems appropriate, the number of articles ultimately used is relatively small (Luppino et al. 2010). Three of the articles could not be included in the study due to inadequate effect size.

Both Anderson et al. (2006) and Forman-Hoffman et al. (2007) expressed weight-related results as changes in weight (Forman-Hoffman et al. 2007; Anderson et al. 2006), while Franko et al. describe outcomes related to obesity as increases or decreases in depressive symptoms (Franko et al. 2005). Depression-related results are thus explained as functional weight loss or weight gain. Further epidemiological research on the connection between obesity and depression is necessary to understand basic processes of bi-directionality.

Luppino et al. (2010) state that a reciprocal relationship exists between obesity and depression (Luppino et al. 2010). In addition, obesity seems to develop particularly in the context of a long-term depressive disorder. This leads to the fact that during obtaining a professional treatment for depression, attention should also be paid to the monitoring of body weight. Furthermore, the current mood of the patients should be thoroughly observed in order to enable earlier detection of pathologies and to establish preventive strategies. This proves to be particularly important when it comes to initiating possible co-treatments for risk patients leading to improved conditions for both health problems (Luppino et al. 2010).

## **2.11 Quality of life and obesity**

Quality of life (QoL) has become increasingly important in both medicine and health sciences and is now a recognised concept that is targeted from many medical and health-related research activities (Fayers & Machin, 2016).

Over the past years, medicine has become aware of the relevance of psychosocial factors on the development and treatment of diseases. Both subjective perception and patient's mental status make an important contribution with regard to physiological events (Schipper et al. 1996).

According to Ware (1987), who was responsible for the development of the health-related QoL instrument (SF-36), health is basically understood as a concept based on dimensionality. This concept includes dimensions of physical health, mental health, functioning in daily life in terms of social and role-related activities, and subjectively perceived well-being. Consequently, health status can range from a negative condition in the context of illness to a more positive state of well-being (Ware 1987).

The term „quality of life“ and the somewhat more specific formulation health-related QoL (HRQoL) describe the different areas of health that account for different domains, including physical, psychological, and social aspects. These different aspects are influenced by personal experiences, expectations, beliefs, and perceptions (Testa & Simonson 1996). HRQoL mirrors individual reactions and evaluations of people to their health and disease (Fontaine & Bartlett 1998). The first approaches to measuring HRQoL started in the research fields of cancer, arthritis, and heart disease to assess QoL by medical professionals (Karnofsky & Burchenal 1949). Nowadays, measurements of QoL are mostly based on individual self-rated reports from patients. Different applications of these instruments are used by clinicians, researchers, administrators, policy makers and maintenance organisations.

Assessing QoL is a way to evaluate the efficacy of different treatment strategies that allows efficacy comparisons of different treatments. In addition, various effects of therapies on the state and functioning in daily life can be assessed. Furthermore, an impaired QoL can be treated and improved leading to symptom relief in the context of the underlying disease (Fontaine & Bartlett 1998).

Originally, primarily biomedical endpoints were prioritised in medicine and health sciences. Quality of life (QoL) was not defined as a primary outcome in the context of research intentions. However, in recent decades there has been an increased focus on patients' QoL. Consequently, assessment instruments have also been used more frequently (Staquet et al. 1996). In fact, there is a disagreement about the methodological and conceptual meaning of QoL and which measurements would be the most appropriate. Moreover, the concept of QoL is not clearly identified. Nevertheless, the World Health Organization (WHO) describes QoL as:

*“An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.”*  
(WHOQOL Group, 1995, p.1403-1409).

In addition to the QoL concept, there is another construct, that is, the HRQoL that refers to health aspects regarding QoL. Accordingly, health-related QoL (HRQoL) constitutes a foundation for the measurement of an assigned parameter during the life-course that impairs daily functioning, perceptions, and opportunities, which result from disease, injuries, or treatment and policy (Mayo 2015).

Considering the fact that obesity and overweight represent significant public health concerns with a diverse array of physical implications and potentially life-threatening conditions, the explicit impact on HRQoL is correspondingly alarming. People suffering from obesity are more often severely impaired in their capacity of managing physical activities in their daily life. Similarly, obesity seems to be related to substantial decreases in social functioning and mental health. However, those decrements appear to be slightly weaker than those observed in view of physical domains of functioning (Fontaine et al. 1996; Fine et al. 1999). Additionally, a dose-response-effect can be assumed in terms of BMI and the level of HRQoL impairment. As a result, individuals showing severe obesity indicate greater decreases in HRQoL than people of lower degrees of obesity. Therefore, the consequences on public health resulting from obesity by far exceed the medical implications. Decrements are also related to functioning and self-perceived well-being, which are sometimes of greater relevance for individuals than obesity-related physical comorbidities (Fontaine & Barofsky 2001).

Quality of life (QoL), in its complexity, is interpreted in various different ways and between a number of distinct disciplines. Today, many different assessment instruments are used to measure QoL. All of these measurements were developed on the basis of empirical considerations. Furthermore, there were no conceptual or definitional models on which these assessment procedures were based on. Accordingly, there is a lack of clarity in terms of a concept of what QoL means or measures. As a consequence, the validity of QoL research may be questionable (Fayers & Machin 2016). The multidimensional conception of QoL is often separated into three levels. In this hierarchy, global QoL is at the highest level and generic HRQoL is ranked second, followed by disease-specific QoL at the third position (Spilker 1996). Global QoL comprises general well-being (WB) as well as life satisfaction (LS) (Bowling 2005; Spilker 1996) on which we focus in this thesis, among other things. Several other aspects such as psychological, physical, social, or environmental evaluations of life (Bowling 2005) encompasses generic HRQoL including both positive and negative aspects (Bowling 2005; WHOQOL Group 1995). According to that, HRQoL represents a much larger concept than the current health condition of individuals (Sivertsen et al. 2015).

With regard to our main focus concerning putative links to overweight and according to the National Institute of Health, obesity is considered a complex and multifactorial disease in which numerous interactions between genetic, metabolic, social, behavioural, and cultural aspects

(National Institute of Health 2000) seem to play an important role in terms of its development. Kolotkin et al. (2008) postulated that obesity has a fundamental impact not only on an individual's health but also on psychosocial well-being, longevity and QoL.

Nowadays, there are many more ways to treat obesity and obesity-associated diseases and thus improve the QoL of affected people (Kolotkin et al. 2001).

Research approaches targeting QoL and its relationship to obesity have been carried out in the field of surgical treatment of severe obesity. Obviously, patients showed an increase in their QoL after surgical treatment, which subsequently led to further examination of this topic, as the patients concerned were well suited for further research projects.

According to numerous reports, improved functioning in psychosocial domains after surgical gastric bypass could be observed (Rand et al. 1982; Hocking et al. 1983; Solow 1977; Dano & Hahn-Pedersen 1977; Kalucy & Crisp 1974; Rae & Cleater 1993). Solow and colleagues (1974) postulated the liberation from feelings of hopelessness, failure and being trapped to be the most important psychological alteration in terms of improved functioning after surgical treatment (Solow et al. 1974).

In this context, patients who underwent gastric restriction surgery, which led to dramatic reductions in body weight, also experienced an increase in QoL (Stunkard et al. 1986; Harris & Green 1982; Hafner et al. 1991; Hawke et al. 1990; Gentry et al. 1984; Halmi et al. 1980; Sullivan et al. 1987; Weiner et al. 1999). Additionally, affected people reported improved sexual functioning in terms of increased sexual interest, enjoyment, and frequency (Harris & Green 1982; Hafner et al. 1991; Hawke et al. 1990). Moreover, increased physical and social activities could be observed (Harris & Green 1982; Hafner et al. 1991; Gentry et al. 1984) and people also reported an increase in self-confidence and self-concept (Harris & Green 1982; Hawke et al. 1990; Gentry et al. 1984). Some patients also showed a decrease in mirror avoiding, which is considered an indication of improved body image (Halmi et al. 1980).

## **2.12 Self-rated health and obesity**

Undoubtedly, obesity has an impact on physical health but may also be related to self-rated health (SRH) (Altman et al. 2016), and thus leading to social stigmatisation (Brewis 2014). Because of public health or medical statements regarding obesity highlighting negative health consequences (Brownell 2005), obese individuals may rate their health conditions more

negatively in comparison to normal weight people, despite similar health states (Altman et al. 2016).

According to a study which has been conducted by Keramat et al. (2021), findings suggest that obesity seems to be significantly related to poor general self-perceived health and mental health status (Keramat et al. 2021). Some examinations point out that obesity is at least weakly correlated with poor self-reported health conditions (Kepka et al. 2011). One attempt at explanation could be the fact that obese human beings are at a higher risk of showing certain comorbidities, which might let themselves perceive their general health conditions more negatively. Despite that obese individuals more often indicate hospital and health care admissions, which enable them to rate their health more rationally (Cullinan & Gillespie 2016). Another reason for negatively self-assessed health among obese might be the global stigmatisation related to overweight and obese, which in some cases, may lead to feelings of ill health and result in poor self-reported health states (Noh et al. 2017).

Addressing the relationship between obesity and SRH is a conception grounded on subjective perceptions and individual assessment of health (Bjorner & Kristensen 2012). Assessing self-rated health is a very common measurement in the field of health research (Brook et al. 1979). Accordingly, measuring SRH provides a valid and reliable indicator in terms of mental and physical functioning (Piko 2000; Krause & Jay 1994; Shields & Shooshtari 2001). Moreover, SRH seems to act as a predictor of claiming health care facilities and mortality (Idler & Benyamini 1997). Numerous investigations pointed out that overweight and obesity are considered risk factors regarding poor self-perceived health (Tremblay & Dahinten 2003; Vingilis et al. 2002; Manderbacka et al. 1999; Page et al. 2009; Freyer-Adam et al. 2011).

According to several international examinations, overweight and obesity in particular are significantly related to poor self-perceived health states. Consecutively, overweight as well as obese individuals more often report poor self-perceived health conditions than those of normal weight (Doll et al. 2000; Guallar-Castillon et al. 2002; Imai et al. 2008; Okosun et al. 2001; Pieniak et al. 2009; Wolk & Rössner 1996; Ferraro & Yu 1995; Molarius et al. 2007).

Some studies that examined the associations between BMI and self-perceived health in adults yield no significant relations to socioeconomic status (SES) or other social aspects determining health, which may be surprising and rather unexpected. Following these suggestions, SES and social health determinants do not seem to alternate the associations between BMI and self-perceived health status (Betha et al. 2012; Laaksonen et al. 2005; Mansson, Merlo 2001).

Altman et al. refers to this as „*subjective*“ component of self-rated health (Altmann et al. 2016). However, a study carried out by Diamantis et al. suggests that several socioeconomic

disadvantages, including low educational attainment, financial insecurity and unemployment seem to be positively associated with overweight and obesity (Diamantis et al. 2022).

The relationship between obesity and self-perceived health seems to be particularly strong with regard to young adults. In fact, there is a difference between younger and older adult individuals concerning self-assessing aspects, which can lead to distinct interpretations of subjective health.

While older people mostly focus on functional abilities, younger adult generations more often consider lifestyle factors and physical activities, diet, or obesity (Krause & Jay 1994). This is possibly due to the decreased occurrence of chronic medical conditions in comparison to older adults. Simultaneously, younger adults suffering from obesity tend to focus predominantly on their body weight when self-rating their health status. Apart from that, older persons often indicate an array of conditions that directly affect their QoL. Therefore, they tend to rather neglect their own body weight compared to younger adults (Altman et al. 2016).

Over time, obese individuals rate their own health more frequently negatively, which may be a result of increasing scientific interest over the last decades and corresponding statements regarding negative consequences associated with obesity (Saguy & Almeling 2008). Many of these messages and a considerable degree of stigmatisation appear to have a large impact on younger generations. According to Elder (1998), life course theory postulates that events occurring in early life have large impacts on adolescents and younger adults (Elder 1998). Furthermore, it has been claimed that adults of younger age were facing negative experiences regarding obesity in particular.

This generation of young adults was faced with messages concerning obesity associated with health risks at very vulnerable stages of their life (Reither, Hauser & Yang 2009). As a consequence, those people were more likely to suffer from obesity-associated discrimination and stigmatisation compared to older adults (Carr & Friedman 2005). Accordingly, the chance of integrating the current body weight into the assessment of their own health is increased and the results with respect to their health status are above expectations due to medical conditions. In fact, research findings concerning associations between obesity and cumulative health disadvantages yield significant decreases in SRH among adults aged 25 to 39 indicating high BMI levels at younger age that could not be explained by current health status (Zajacova & Burgard 2010). Altman et al. postulated that obesity is expected to be negatively related to the subjective component of SRH. Moreover, this association seems to be even stronger with respect to younger adults. Likewise, they assume that these connections are stronger for

recently born individuals as well. One possible explanation for this could be the focus of various media and public statements on obesity with regard to its early occurrence (Altman et al. 2016). On the other hand, associations could be even weaker due to progressing therapeutic possibilities and availability of treatments to manage obesity-related medical events (Altman et al. 2016).

According to Hardy et al. (2014), SRH comprises two separated aspects, called “*objective*” and “*subjective*” components of SRH. In their work, they suggest that the objective component contains physical functioning as an objective indicator of health, whereas the subjective part of SRH functions as a residual component (Hardy et al. 2014). It appears to play an important role whether “subjective” or “objective” components of SRH are predicted. As a consequence, the relationship between obesity and the objective component of SRH seems to be strongly negative and is also probably greater among older individuals (Altman et al. 2016). Additionally, findings with respect to differences between obese and non-obese people indicated that overall assessments of SRH seem to be more negative when being obese (Altman et al. 2016). Obviously, the relationship regarding subjective and objective components of SRH are quite different, depending on age and birth cohort leading to changes in persons’ conceptions of health, at least among adult citizens of the United States. Nevertheless, research regarding associations between obesity and SRH need to account for different possibilities of treatment strategies as well as educational opportunities available for individuals within the respective age group and birth cohort (Altman et al. 2016).

### **3. Material and methods**

Parts of this chapter are based on the following publication: Rindler et al. (2023).

#### **3.1 Data and research design**

Two datasets were used as the basis for this study that were analysed in the context of this retrospective study (secondary data analysis) according to the research questions. Hence, this study applied different methodological approaches adopting data from two surveys.

According to hypothesis 1, basic correlations between BMI and mental health characteristics, such as depression and general QoL (including four domains) were investigated using cross-sectional data from the Austrian Health Interview Survey (ATHIS) from 2019.

In a second step, longitudinal data from the Survey of Health Ageing and Retirement in Europe (SHARE) of waves 4 and 8 was analysed to examine potential bi-directional associations between BMI and mental health status of female and male individuals, aiming to answer the hypothesised research question, constituting the main objective of this thesis. This investigation applies a two-wave cross-lagged panel approach over a defined time lag of 10 years as a tool for elucidating potential long-term effects and cause-effect associations between body weight and mental health constructs that is depression and QoL in the context of a longitudinal analysis.

## **3.2 Data collection**

### **3.2.1 Austrian Health Interview Survey (ATHIS)**

The Austrian Health Interview Survey (ATHIS) was conducted among individuals aged 15+ throughout Austria from October 2018 to September 2019 by Statistik Austria (n = 15,461). Additionally, questions on the health status of persons under 18 years of age were answered by their parents if they lived in the same household assessing general health status and health well-being among others. A combination of Computer Assisted Personal Interviewing (CAPI), Paper and Pencil Interviewing (PAPI), as well as Computer Assisted Web Interviewing (CAWI) was applied. The Federal Ministry of Social Affairs, Health, Care and Consumer protection (BMSGPK) and the Federal Health Agency as well as Statistik Austria drafted an information letter including privacy information to make initial contact with the samplers in which aims and intentions of the survey as well as the characteristics to be collected were explained. The sample was drawn from the Central Civil Register (ZMR) in September 2018. In addition, it was necessary to divide the sample into two time points within one district, which was carried out in May 2019. Each individual was assigned a reference week for ensuring temporal equal distribution of the sample. Fieldwork started on October 1, 2018, and closed on September 29, 2019. Interviews were conducted mainly from October 2018 to March 2019 using face-to-face interviews and accounted for approximately 90% of the data. As of the end of March until the end of September, interviews were mainly web-based. This applies primarily to those areas that have not yet reached the required number of surveys (Statistik Austria 2020). The survey was mainly conducted using the CAPI method, which had the advantage that any input errors, corrections, and plausibility checks could be carried out immediately. Personal interviews were conducted by means of questionnaires, which were administered by the

surveyor. In addition, there were some questions in this questionnaire from areas that were answered without the guidance of a surveyor. The CAWI survey method was completed entirely independently by the respective respondents, and plausibility checks were also incorporated into this survey method. Information from third parties was not permitted during the interviews. However, there was an exception in the case of health impairments due to which the persons concerned were not able to answer questions themselves. In this case, an abbreviated questionnaire containing questions about the target person's state of health was answered by a fellow resident of the same household (Proxy-Questionnaire) (Statistik Austria 2020).

### **3.2.2 Survey of Health, Ageing and Retirement in Europe (SHARE)**

The primary questionnaire employed in the Survey of Health, Ageing and Retirement in Europe (SHARE) encompassed 20 modules addressing health, socioeconomic status, and social networks. Initiated in 2004, the SHARE project targeted individuals aged 50 and above, spanning 11 European countries. The wave 1 baseline study covered Scandinavia (Denmark, Sweden), central Europe (Austria, France, Germany, Switzerland, Belgium, the Netherlands), and Mediterranean countries, including Greece, Italy, and Spain. Israel was later incorporated into the survey by the end of 2004. The third regular panel, conducted during wave 4 in 2010, saw the inclusion of Estonia, Portugal, Slovenia, and Hungary, leading to a participant count of 58,000 for the study. The fieldwork for the eighth wave, initially planned for October 2019, was abridged in March 2020 due to the COVID-19 pandemic, resulting in a shorter questionnaire.

As a consequence, the countries represented in the study were Austria, Belgium, Bulgaria, Cyprus, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Israel, Italy, Luxembourg, Poland, Spain, Sweden, Lithuania, Latvia, Malta, Finland, Switzerland, Slovenia, Hungary, Netherlands, and Slovakia (SHARE 2022), constituting a total gross sample size of 46,733, with 19,915 participants completing main interviews in the fourth wave. Thus, the final net sample included 16,184 individuals who participated in both wave 4 and wave 8 for further analysis. The study's target population consisted of older individuals residing in the respective surveyed country at the time of the interviews. Those hospitalised, incarcerated, or abroad during the entire interview duration were excluded, along with individuals lacking sufficient language skills or moving to unknown addresses. All household members born in 1960 or earlier (wave 4) and 1969 or earlier (wave 8) were eligible for interviews (Börsch-Suppan

2022). Participation in the interviews was voluntary and confidential, and the data collected from these interviews was linked to a wave-specific identifying variable (ID) (SHARE 2022). Data collection was carried out using computer-assisted personalised interviews (CAPI) and in-person interviews. Additionally, self-administered paper and pencil questionnaires were employed in the data collection process (SHARE 2022). Interviewers used laptops equipped with the CAPI tool for face-to-face interviews, particularly necessary for conducting various physical assessments within the survey. SHARE employs an ex-ante harmonisation approach where a single standardised questionnaire is translated into different national languages. This translation is facilitated by an internet-based tool that automatically converts the questionnaire into the CAPI format (Börsch-Suppan 2022).

Due to a notable attrition rate over 10 years, including reasons such as participant deaths, relocations, unavailability, or refusals to participate, the final dataset comprised 16,184 individuals from the original 19,915 who participated in both wave 4 and wave 8. This subset provided complete data without any defined missing values, serving as the basis for subsequent analysis. The beginning of the COVID-19 pandemic in 2019/2020 may have contributed to participant withdrawals in the eighth wave, ultimately leading to the discontinuation of the study.

### **3.3 Ethical statement**

The study was conducted according to the guidelines of the Declaration of Helsinki and obtained approval from the Ethics Committee of the Medical University of Graz, Austria (Document Number 32-305 ex 19/20). Informed consent was obtained from all subjects involved in the study.

### **3.4 Measures**

#### **3.4.1 Central variables (ATHIS)**

The European Health Interview Survey (EHIS) served as the basis for the Austrian Health Interview Survey (ATHIS). The European Health Interview Survey covers modules on health determinants, health care and background characteristics. Written questionnaires including the Patient Health Questionnaire (PHQ-8) for the assessment of depression and the Abbreviated

World Health Organization Quality of Life Questionnaire (WHOQOL-BREF) were completed by respondents on the topics of health status, health behaviour and utilisation of health services. Two different approaches to measuring depression were applied. Self-reported depression was assessed by asking the question: "Have you had depression in the last 12 months?" (dichotomous), and the Patient Health Questionnaire (PHQ-8), a screening-tool for detecting depression by which current depressive symptoms and their severity within the last two weeks were assessed (Statistik Austria 2020). The PHQ-8 covers 8 items, each of which is scored 0 to 3 including: "Little interest or pleasure in doing things", "feeling down, depressed, or hopeless", "trouble falling or staying asleep, or sleeping too much", "feeling tired or having little energy", "poor appetite or overeating", "feeling bad about yourself -or that you are a failure or have let yourself or your family down", "trouble concentrating on things, such as reading the newspaper or watching television", "moving or speaking so slowly that other people could have noticed, or the opposite-being so fidgety or restless that you have been moving around a lot more than usual". Response categories in shape of a 4-point Likert scale were coded as 0 (Not at all), 1 (Several days), 2 (More than half the days) and 3 (Nearly every day) resulting in a total score ranging from 0 to 24. Severity of depression is defined by the scores 5 (mild), 10 (moderate), 15 (moderately severe) and 20 (severe)(Kroenke & Spitzer 2002). For measuring depression according to the PHQ-8 depression scale, all eight items were transformed into an overall sum score of depression in order to derive a severity scale.

Quality of life (QoL) was measured by the Abbreviated World Health Organization Quality of Life Questionnaire (WHOQOL-BREF). This multidimensional construct encompasses two questions concerning general QoL and general health as well as 24 questions regarding physical condition, mental well-being, social relations, and environment (Statistik Austria 2020). As a result, an overall QoL score can be derived yielding individual values that range from 0 to 100.

### **3.4.2 Central variables (SHARE)**

The process of identifying individuals with obesity or being overweight involves the utilisation of health-related data obtained from the survey's health module, denoted as "gv\_health." Essential measurements were extracted from participants' body weight and height, after which they were calculated using Quetelet's formula as originally introduced in 1832. The classification of participants' Body Mass Index (BMI) was carried out in accordance with the guidelines stipulated by the World Health Organization (WHO) in 1995. To assess the status

of depression among participants, the EURO-D scale, as developed by Prince et al. in 1999, was employed. This assessment instrument was specifically designed to evaluate depression later in life and has been used across various European countries.

It encompasses a comprehensive range of components, including depression, pessimism, guilt, sleep, interest, irritability, and more. The EURO-D scale is employed to assess depression levels on a scale that spans from 0 to 12. A score of 12 on this scale indicates a significant degree of depression, whereas a score of 0 signals the absence of depressive symptoms. Scores equal to or exceeding 4 are suggestive of the presence of depression, while scores below 4 imply the absence of depressive indicators, aligning with the criteria established by Prince et al. in their 1999 research.

For the assessment of the mental health dimension pertaining to QoL, the CASP-12 questionnaire was employed. This instrument is a modified version of the CASP-19 and encompasses a total of 12 items that are grouped into four sub-scales, namely control, autonomy, self-realisation, and pleasure. These items were presented in the form of inquiries, and participants' responses were recorded using a 4-point Likert scale.

As per Hyde et al., the CASP-19 scale is employed as a conceptual measure for assessing QoL among elderly individuals (Hyde et al. 2003). The items are formulated as questions and statements and offer the response choices "often," "sometimes," "rarely," and "never." The overall score, derived from the 12 items, ranges from a minimum of 12 to a maximum of 48, with higher scores signifying a higher QoL. Moreover, according to existing literature, a distinct threshold for categorising low and high levels of QoL has not been definitively established (Börsch-Suppan 2022). Nevertheless, von dem Kneseberg et al. (2005) indicated that the CASP-12 version can be categorised using a four-level approach to QoL. Scores between 39 and 41 represent a very high level, scores between 37 and 39 denote a high level, scores between 35 and 37 indicate a moderate level, and values below 35 are associated with a low level of QoL (von dem Knesebeck et al. 2005).

### **3.4.3 Control variables**

It is widely recognised that an individual's mental health status is influenced by the interplay of social and economic factors. Consequently, a range of both natural and human-induced challenges and circumstances possess the capacity to impact an individual's resilience and their ability to effectively navigate adversity. This assertion is substantiated by the research

findings of Mao and Agyapong (2021) and Artiga et al. (2019). Moreover, within the realm of weight gain, the role of social determinants has been brought into focus, as indicated in the study by Lee et al. (2019). To comprehensively investigate these dynamics, a thorough examination of potential influences stemming from a diverse set of control variables was undertaken. These variables include age, sex, living arrangements, and educational attainment, all of which bear the potential to act as confounding factors. This comprehensive inquiry was conducted through the application of multiple linear regression analysis.

### **3.5 Psychometric properties**

The internal consistency reliability of the mental health measures PHQ-8 and WHOQOL-BREF used in the ATHIS was calculated using Cronbach's alpha. The analysis involved data from a total of 15,461 respondents. The results indicate a strong internal consistency for the 8-item PHQ-8 depression scale ( $\alpha = 0.824$ ). Similarly, the 26-item WHOQOL-BREF shows high internal consistency with a Cronbach's alpha of 0.831 (Blanz 2015).

The reliability of mental health assessments within the SHARE study was assessed through the utilisation of Cronbach's alpha. The use of the EURO-D scale in both wave 4 and wave 8 yields Cronbach's alpha coefficients ranging from 0.62 to 0.78. These values indicate a moderate level of internal consistency across all European countries involved in the research (Castro-Costa et al. 2008). Furthermore, the abbreviated CASP-12 scale demonstrates satisfactory Cronbach's alpha values which range from 0.56 to 0.76 across various countries (von dem Knesebeck et al. 2005).

### **3.6 Preparation and data cleaning**

Body weight and size was collected by the European Health Determinants Module (EHDM) and Quetelet Index (BMI) (Quetelet 1832) was calculated: Body weight (Kg) divided by Body height (m)<sup>2</sup> and was then transformed into an ordinal variable of the four categories: “underweight” (BMI <18,5), “normal” (BMI 18 to <25), “overweight” (25 to <30), and “obesity” (BMI >30) according to WHO-classification (WHO 1995).

The initial stage involved matching the SHARE datasets that encompassed core variables from both wave 4 and wave 8, alongside sociodemographic factors. The identifier variable "mergeid" was utilised as a key variable for merging the data, previously organised in ascending order. This process yielded a dataset (n = 16,184) which was analysed in accordance with the research question. Given that certain cases offered data for wave 4 and not wave 8, all ensuing calculations, including relevant hypothesis tests, were exclusively focused on instances where complete data was accessible. Non-matched cases were omitted via a filter variable. For a clearer representation of the age distribution within the sample, the variable "age\_int" was transformed into a fresh variable called "age\_new," categorising ages into three groups: "50-59," "60-74," and "75+." Information concerning respondents' living situation, whether living alone or with a partner, was extracted through the "partner in household" ("partnerinhh") variable. This data was subsequently transformed into a binary variable labeled "partnerinhh\_recode," coded as "0" to denote living alone and "1" to signify living with a partner. This was done to integrate it into the multiple regression analysis.

Given the use of categorical predictors encompassing sex, educational level, and BMI categories, it became necessary to establish dummy variables to assess their effects on the corresponding outcome variables. Responses falling into categories such as "Refuse," "don't know," or those designated as "implausible or likely false" were recognised as missing data points. Consequently, these responses were assigned numeric codes, specifically "-3", "-2", or "-1", correspondingly. Subsequently, these coded values were excluded from the analytical procedure.

### **3.7 Statistical analysis**

In the present work, we used IBM SPSS Statistics Software v26 for running statistical procedures such as correlation- and multiple linear regression analyses. The level of significance (p-value) was defined at  $p < 0.05$  ( $\alpha = 5\%$ ) for both Pearson's correlation analysis and multiple linear regression modelling.

### 3.7.1 Austrian Health Interview Survey (ATHIS)

In order to test relationships between two interval-scaled characteristics, Pearson's correlation coefficient was calculated (Field 2013; Moosbrugger 2012). In order to do that, a total of six sub-hypotheses were established:

#### A) Depression

H0: There is no significant association between BMI and depression state.

H1: There is a significant association between BMI and depression state.

#### B) Overall QoL

H0: There is no significant association between BMI and overall QoL.

H1: There is a significant association between BMI and overall QoL.

#### C) Physical QoL

H0: There is no significant association between BMI and physical QoL.

H1: There is a significant association between BMI and physical QoL.

#### D) Psychological QoL

H0: There is no significant association between BMI and psychological QoL.

H1: There is a significant association between BMI and psychological QoL.

#### E) Social QoL

H0: There is no significant association between BMI and social QoL.

H1: There is a significant association between BMI and social QoL.

#### F) Environmental QoL

H0: There is no significant association between BMI and environmental QoL.

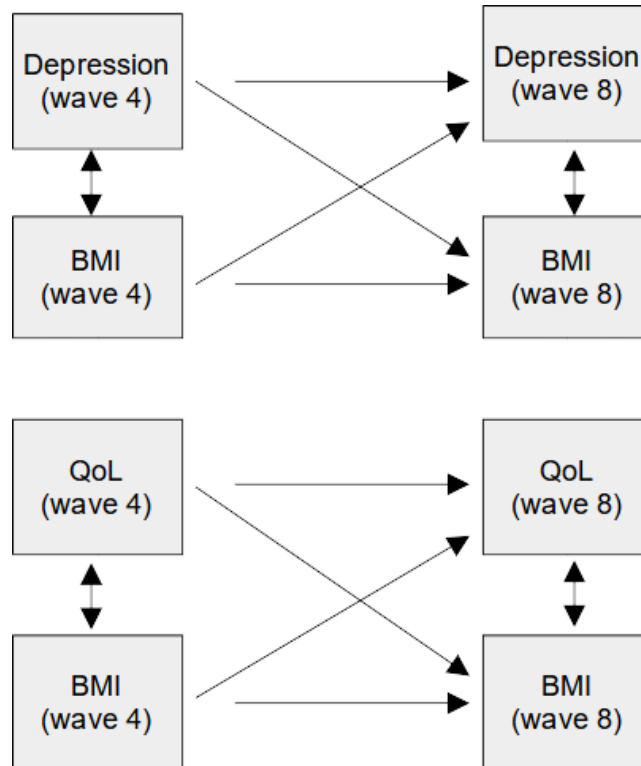
H1: There is a significant association between BMI and environmental QoL.

### **3.7.2 Survey of Health, Ageing and Retirement in Europe (SHARE)**

In line with our research question (hypothesis 2), we conducted multiple linear regression analyses to explore enduring impacts and associations between BMI and mental health indicators, such as depression and QoL.

To assess the link between predictive variables from wave 4 and outcome variables in wave 8, we employed a two-wave cross-lagged panel approach (Kuiper & Ryan 2018, Kearney 2017, and Kenny 2014) within the framework of a longitudinal analysis. Central variables, namely BMI, depression status, and QoL were measured at two distinct time points (waves 4 and 8). This setup led to six potential relationships (Kenny 2014), which were examined through multiple regression analysis to determine both stability (autoregressive) and cross-lagged effects. The analysis assumed that the constructs were synchronous at both time points. Synchronicity, stability, and cross-lagged associations of central variables between two waves generally yield two synchronous (cross-sectional), two stable (autoregressive), and two cross-lagged relationships (Kenny 2014).

To investigate the stability of the association between BMI values at two different points in time, BMI was utilised as a metric predictor. Consequently, autoregressive and cross-lagged effects between various measurements in waves 4 and 8 were simultaneously calculated to ascertain the degree of stability for each construct and the reciprocal relations over time (see Figure 9 and Table 1).



**Figure 9:** Overview of stability and cross-lagged pathways: Depression (EURO-D), QoL (CASP) and body mass index (BMI). Double-headed arrows represent synchronous (cross-sectional) paths; single-headed arrows demonstrate stability (horizontal) and cross-lagged (diagonal) associations. Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this image follows the terms of the Attribution International 4.0 License (CC BY 4.0), which permits any use, copy or redistribution of this illustration <https://creativecommons.org/licenses/by/4.0/>.

**Table 1:** Overview of models analysing stability and cross-lagged associations

Model	Stability path <sup>a</sup>		Cross-lagged path <sup>b</sup>	
1	CASP	CASP	underweight <sup>b</sup>	CASP
DV: CASP			overweight <sup>b</sup>	CASP
			obese <sup>b</sup>	CASP
2	EURO-D	EURO-D	underweight <sup>b</sup>	EURO-D
DV: EURO-D			overweight <sup>b</sup>	EURO-D
			obese <sup>b</sup>	EURO-D
3	BMI	BMI	CASP	BMI
DV: BMI			EURO-D	BMI

a) Autoregressive associations of constructs between wave 4 and wave 8. b) cross-lagged associations over a 10-year time lag. *BMI*= body mass index, *CASP* = QoL, *EURO-D*= depression. *DV*= dependent variable. **Source:** Reproduced without modifications from: Rindler G.A., Gries and Freidl (2023). Associations between overweight, obesity and mental health: A retrospective study among European

adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this table follows the terms of the Creative Attribution 4.0 International License (CC BY 4.0), which permits any use, copy or redistribution <https://creativecommons.org/licenses/by/4.0/>.

This research methodology formed the foundation for an inquiry into the impact of sociodemographic factors, including age, sex, living arrangements, and educational attainment (classified according to ISCED-97), on the distinct outcome variables. Furthermore, a multiple linear regression analysis was performed, incorporating sociodemographic variables as covariates and implementing requisite adjustments.

## **4. Results**

Parts of this chapter are based on the following publication: Rindler et al. (2023).

### **4.1 Descriptive statistics (ATHIS)**

A total of 15,461 people completed the questionnaires. In terms of sex distribution, women accounted for 53.7% and men for 46.3%.

Most participants were between 45 and 59 years of age (27%). 12.3% of the sample belonged to the age group 75+.

Most participants came from Styria and Upper Austria (18.5% each), followed by Lower Austria (15.3%) and Tyrol (12.3%) (Table 2).

**Table 2:** Distribution of demographic characteristics in ATHIS (n = 15,461)

<b>Federal States</b>	<b>n</b>	<b>%</b>
Burgenland	950	6.1
Lower Austria	2373	15.3
Vienna	1656	10.7
Carinthia	955	6.2
Styria	2867	18.5
Upper Austria	2860	18.5
Salzburg	947	6.1
Tirol	1896	12.3
Vorarlberg	957	6.2
<b>Sex</b>		
Male	7166	46.3
Female	8295	53.7
<b>Age</b>		
15-29	2773	17.9
30-44	3187	20.6
45-59	4172	27.0
60-74	3372	21.8
75+	1957	12.7

**BMI-categories:**

The average BMI index of the participants was 25.79 ( $SD = 4.8$ ). Based on the WHO (1995) categories (27), most participants had normal weight (46.0%), 35.1% were overweight, 16.4% obese and 2.5% underweight (see Table 9 in the Appendix and Table 3).

**Depression:**

Based on the established cut-offs of PHQ-8 scores, 19.4% of participants were assigned to the "depression" category. Severity of depression is shown in section of tables. The mean depression score was 3.38 ( $SD = 3.4$ ) (see Tables 10, 11 in the Appendix, and Table 3).

### Quality of Life:

According to the WHOQOL-BREF scores for the four domains of QoL – physical condition, mental well-being, social relations, and environment – as well as the overall QoL, mean values and standard deviations (SD) were calculated for each domain and overall QoL. This calculation was performed to provide an overview of the distribution among the sample population (Table 3).

**Table 3:** Descriptive statistics of relevant characteristics in ATHIS

Variables	n	Minimum	Maximum	Mean	SD
Physical QoL	15461	0	100	79.84	18.75
Psychological QoL	15461	0	100	80.27	14.78
Social QoL	15461	0	100	77.89	19.16
Envir. QoL	15461	0	100	81.75	12.94
Overall QoL	15461	0	100	77.81	20.01
BMI	15461	14	63	25.79	4.76
Depression	15461	0	24	2.64	3.38

## 4.2. Results of correlation analysis (ATHIS)

According to hypothesis 1, Pearson´s correlation test including male and female participants revealed significant results in terms of all six constellations. A positive correlation between BMI and depression score,  $r(15,461) = .036$ ,  $p < .001$  was observed. Higher scores of a person's BMI corresponded to higher depression scores. Although this correlation is significant, attention should be paid to the correlation index of 0.036, which demonstrates a very small effect. The significance of such a small effect is probably due to the large sample. Furthermore, a significant negative correlation between overall QoL and BMI,  $r(15,461) = -.155$ ,  $p < .001$  was observed. Individuals with high BMI scores show lower QoL scores. Considering each domain of QoL, the strongest correlation exists with the physical domain of QoL,  $r(15,461) = -.176$ ,  $p < .001$ . The correlations between BMI and psychological, social, and environmental domains of QoL were also significant. However, effects were smaller (Table 6). Both males

and females demonstrate negative correlations regarding overall QoL and BMI whereby women obviously show a stronger effect in comparison to men,  $r(7,166) = -.127, p < .001$ ;  $r(8,295) = -.184, p < .001$ . Depression appears to be weakly positively correlated with BMI scores in both women and men. Again, females indicate stronger correlation coefficients than male respondents,  $r(7,166) = .074, p < .001$ ;  $r(8,295) = .035, p = .03$ . Male and female individuals show clear negative effects with regard to the physical domain of QoL.

However, correlation coefficient in females demonstrate a stronger correlation between BMI and physical QoL,  $r(7,166) = -.222, p < .001$ ;  $r(8,295) = -.144, p < .001$  (Table 4).

**Table 4:** Pearson's correlation coefficients of BMI and depression/QoL (ATHIS)

Variable	n	Correlation coefficient <i>r</i>	<i>p</i>
Depression (PHQ-8)	15461	.039	< .001
Overall QoL	15461	-.155	< .001
Physical QoL	15461	-.176	< .001
Psychological QoL	15461	-.102	< .001
Social QoL	15461	-.070	< .001
Environmental QoL	15461	-.106	< .001
<b>Men</b>			
Depression (PHQ-8)	7166	.035	.003
Overall QoL	7166	-.127	< .001
Physical QoL	7166	-.144	< .001
Psychological QoL	7166	-.084	< .001
Social QoL	7166	-.042	< .000
Environmental QoL	7166	-.079	< .001
<b>Women</b>			
Depression (PHQ-8)	8295	.074	< .001
Overall QoL	8295	-.184	< .001
Physical QoL	8295	-.222	< .001
Psychological QoL	8295	-.144	< .001
Social QoL	8295	-.092	< .001
Environmental QoL	8295	-.141	< .001

### 4.3 Descriptive statistics (SHARE)

In the longitudinal analysis, a total of 16,184 individuals aged 50 years and above were included in the study, comprising 9,428 (58.3%) females and 6,756 (41.7%) males. The mean age of the participants was 63.63 years, with a standard deviation (SD) of 8.10. The age of the participants ranged from 50 to 92 years. The majority of study participants hailed from Estonia, constituting 13.1% of the sample, followed by individuals from the Czech Republic, accounting

for 10.1% of the total. Regarding living arrangements, a significant proportion of respondents reported living with their partners, representing 74.9% of the sample. Furthermore, 37.6% of the participants indicated having completed upper secondary education, categorised at level 3 (Table 5)

**Table 5:** Distribution of demographic characteristics in SHARE (n = 16,184)

<b>Country</b>	<b>n</b>	<b>%</b>
Austria	1216	7.5
Germany	552	3.4
Sweden	739	4.6
Netherlands	906	5.6
Spain	701	4.3
Italy	945	5.8
France	1588	9.8
Denmark	928	5.7
Switzerland	1581	9.8
Belgium	1153	7.1
Czech Republic	1632	10.1
Poland	480	3.0
Hungary	679	4.2
Slovenia	967	6.0
Estonia	2117	13.1
<b>Sex</b>		
Male	6756	41.7
Female	9428	58.3
<b>Age group</b>		
50-59	5631	34.8
60-74	8801	54.4
75+	1752	10.8
<b>Partner in household</b>		
Yes	12116	74.9
No	4068	25.1
<b>Level of Education*</b>		
ISCED-97 Code 1	2262	14.0
ISCED-97 Code 2	2906	18.0
ISCED-97 Code 3	6090	37.6
ISCED-97 Code 4	960	5.9
ISCED-97 Code 5	3837	22.9
ISCED-97 Code 6	129	0.8

\* **Code 1-6 of Education refers to the Level of 1-6 of Education:** Primary education/first stage of basic education (*ISCED-97 Code 1*), lower secondary education/second stage of basic education (*ISCED-97 Code 2*); upper secondary education (*ISCED-97 Code 3*), post-secondary, non-tertiary education (*ISCED-97 Code 4*), first stage of tertiary education (*ISCED-97 Code 5*), second stage of tertiary education (*ISCED-97 Code 6*). **Source:** Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this image follows the

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Within our study sample, the mean Body Mass Index (BMI) score stood at 27.0 kg/m<sup>2</sup> (SD = 4.7). The majority of participants were categorised as overweight (42.1%), followed by those with a normal weight (35.2%), and individuals falling into the obese category (21.8%). A relatively small minority (0.9%) were classified as underweight. In terms of depression scores assessed through the EURO-D scale, the mean score was 2.2 (SD = 2.1), predominantly indicating a minority of depression among the study population. Quality of life (QoL) was evaluated using the CASP-12 scale, which ranges from 0 to 12. Mean values and standard deviations were computed, revealing an average QoL score of 38.4 (SD = 5.9). For further details, please refer to Table 12 in the Appendix and Table 6.

**Table 6:** Descriptive statistics of relevant characteristics in SHARE

<b>Variables</b>	<b>Mean</b>	<b>SD</b>
BMI	26.97	4.664
CASP Index	38.39	5.908
Depression	2.23	2.079
Age	63.63	8.104

**Source:** Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this content follows the terms of the Attribution International 4.0 License (CC BY 4.0), which permits any use, copy or redistribution of this illustration <https://creativecommons.org/licenses/by/4.0/>.

#### 4.4 Results from multiple linear regression analysis (SHARE)

All three models exhibit good to excellent fit to the dataset. The initial model (referred to as model 1) displayed significance concerning the stability of QoL (CASP) scores and BMI categories in predicting QoL over time in the eighth wave ( $F(4,16179) = 1575.441, p < .001, R^2 = 28.0\%$ ). Thus, it appears that QoL scores in wave 4 have a notable predictive value for QoL scores in a subsequent time point in wave 8 ( $\beta = .515, p < .001$ ), signifying a robust mental health attribute that remains stable over approximately a decade. An examination of the impact of BMI categories on predicting QoL through cross-lagged analysis indicates that individuals categorised as overweight, obese, or underweight experience markedly reduced QoL levels in

contrast to those with a normal weight. Among these groups, the strongest effect is seen in obese individuals ( $\beta = -.084$ ,  $p < .001$ ).

In our second model (Model 2), we also obtained a significant outcome ( $F(4, 16179) = 820.656$ ,  $p < .001$ ,  $R^2 = 16.8\%$ ). This result underscores the confirmation of the long-term stability of depression scores ( $\beta = .403$ ,  $p < .001$ ). Further exploration of bidirectional relationships reveals that BMI categories, including underweight, overweight, and obesity, significantly serve as predictors of an individual's depression status over time, leading to elevated depression scores when compared to individuals with a normal weight. Once again, the most pronounced impact is observed among individuals classified as obese ( $\beta = .063$ ,  $p < .001$ ).

In the third model (Model 3), statistical significance is also observed ( $F(3, 16180) = 820.656$ ,  $p < .001$ ,  $R^2 = 61.2\%$ ). This finding underscores the presence of a robust and long-term relationship within the autoregressive pathway. Specifically, the BMI score recorded during wave 4 emerges as a potent predictor of BMI scores during wave 8, illustrating a substantial level of stability ( $\beta = .782$ ,  $p < .001$ ). Nevertheless, it is imperative to emphasise that neither the depressive state nor the QoL (Table 7) significantly forecast changes in BMI over the specified period (Rindler et al. 2023).

**Table 7:** Overview of stability and cross-lagged coefficients- unadjusted linear regression model ( $n = 16,184$ )

Variables	CASP (wave 8)		EURO-D (wave 8)		BMI (wave 8)	
	$\beta$	$p$	$\beta$	$p$	$\beta$	$p$
CASP Index	.515 <sup>b</sup>	<.001	-	-	.000 <sup>c</sup>	.950
EURO-D	-	-	.403 <sup>b</sup>	<.001	.006 <sup>c</sup>	.266
underweight <sup>a</sup>	-.026 <sup>c</sup>	<.001	.020 <sup>c</sup>	.005	-	-
overweight <sup>a</sup>	-.044 <sup>c</sup>	<.001	.026 <sup>c</sup>	.001	-	-
obese <sup>a</sup>	-.084 <sup>c</sup>	<.001	.063 <sup>c</sup>	<.001	-	-
BMI <sup>d</sup>	-	-	-	-	.782 <sup>b</sup>	<.001
Adjusted R <sup>2</sup>	28.0%		16.8%		61.2%	

a) Normal weight is a reference category. b) Stability (autoregressive) coefficients over 10-year time lag. c) Cross-lagged coefficients over 10-year time lag. d) metric scaled. -) not applicable. **Source:** Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this image follows the terms of the Attribution International 4.0 License (CC BY 4.0), which permits any use, copy or redistribution of this content <https://creativecommons.org/licenses/by/4.0/>.

#### **4.4.1 Results of multiple linear regression analysis- adjusted for sociodemographic confounders**

To examine the impact of sociodemographic factors on the designated outcomes, a second run of multiple regression analysis was conducted, accounting for the initial baseline characteristics, which encompassed sex, age, living situation, and educational attainment. Consequently, the cross-lagged associations between key variables and the stability correlations were reassessed. This reevaluation integrated the confounding predictors into the existing model framework, specifically Models 1 through 3, as outlined above.

The initial model, which investigated the interplay between BMI categories, and confounding elements on QoL, yields significant results ( $F(12,16171) = 647.113, p < .001, R^2 = 32.4\%$ ). The examination uncovers that respondents of advanced age show notably lower QoL, emerging as the most robust sociodemographic predictor within this model with regard to QoL prediction ( $\beta = -.166, p < .001$ ). Notably, this adjusted model does not present any conclusive evidence of sex significantly affecting QoL over time. However, the educational level of respondents appears to have a substantial impact on QoL. In particular, a higher level of education correlates with a heightened QoL over the long term, with the strongest educational predictor of QoL being educational level 5, associated with tertiary education ( $\beta = .118, p < .001$ ). Individuals living with partners demonstrate significantly greater QoL compared to those living alone ( $\beta = .032, p < .001$ ).

In the second model, which aimed to investigate the influence of confounding variables on depression scores, notable findings were obtained ( $F(12,16171) = 345.542, p < .001, R^2 = 20.3\%$ ). Similar to the initial model, the age of study participants emerges as a substantial factor in predicting depression scores over a roughly decade-long timeframe ( $\beta = .138, p < .001$ ). Furthermore, females exhibit significantly higher depression scores in comparison to males ( $\beta = .091, p < .001$ ). Educational attainment also demonstrates an association with depression scores. Specifically, individuals with higher educational levels exhibit markedly lower levels of depression over the course of a 10-year period in contrast to those with lower educational backgrounds. Once again, individuals with tertiary education, corresponding to educational level 5, display the most pronounced effect in terms of reduced depression scores ( $\beta = -.094, p < .001$ ). However, living with a partner does not yield a statistically significant impact on depression status when compared to individuals living without a partner.

The third model yielded statistically significant results ( $F(11, 16172) = 2421.248, p < .001, R^2 = 62.2\%$ ). Notably, advancing age among respondents is associated with a marked decrease in BMI scores ( $\beta = -.100, p < .001$ ), while sex demonstrates no statistically significant impact on BMI scores. In contrast to its effects on QoL and depression status, educational attainment at levels 5 and 6 (tertiary education) significantly contributes to the prediction of BMI ( $\beta = -.028, p < .001; \beta = -.013, p = .008$ ). This observation implies a negative correlation between tertiary education and BMI, suggesting that individuals with tertiary education tend to exhibit reduced BMI scores. It is noteworthy that the living arrangement, specifically "living with a partner," emerges as a significant predictor of lower BMI in comparison to individuals living alone, albeit the magnitude of this effect is relatively modest (Table 8) (Rindler et al. 2023).

**Table 8:** Overview of stability and cross-lagged coefficients- adjusted linear regression model ( $n = 16,184$ )

Variables	CASP Index (wave 8)		EURO-D (wave 8)		BMI (wave 8)	
	$\beta$	$p$	$\beta$	$p$	$\beta$	$p$
CASP Index	.487 <sup>c</sup>	<.001	-	-	-.001 <sup>f</sup>	.856
EURO-D	-	-	.378 <sup>e</sup>	<.001	.003 <sup>f</sup>	.567
<b>BMI Category</b>						
underweight <sup>d</sup>	-.025 <sup>f</sup>	<.001	.017 <sup>f</sup>	.014	-	-
overweight <sup>d</sup>	-.031 <sup>f</sup>	<.001	.025 <sup>f</sup>	.002	-	-
obese <sup>d</sup>	-.077 <sup>f</sup>	<.001	.060 <sup>f</sup>	<.001	-	-
BMI <sup>g</sup>	-	-	-	-	.779 <sup>e</sup>	<.001
Sex <sup>a</sup>	-.009	.168	.091	<.001	-.004	.414
Age	-.166	<.001	.138	<.001	-.100	<.001
<b>Education</b>						
ISCED-97 code 2 <sup>b</sup>	.025	.006	-.047	<.001	.002	.720
ISCED-97 code 3 <sup>b</sup>	.089	<.001	-.077	<.001	-.004	.588
ISCED-97 code 4 <sup>b</sup>	.052	<.001	-.050	<.001	.000	.997
ISCED-97 code 5 <sup>b</sup>	.118	<.001	-.094	<.001	-.028	<.001
ISCED-97 code 6 <sup>b</sup>	.014	.037	-.010	.153	-.013	.008
<b>Living Situation</b>						
Partner in household <sup>c</sup>	.032	<.001	.006	.434	-.010	.043
Adjusted R <sup>2</sup>	32.4%		20.3%		62.2%	

a) Female sex is a reference category. b) Primary educational level is a reference category. c) Living with a partner is a reference category. d) Normal weight is a reference category. e) Stability

(autoregressive) coefficients over 10-year time lag. f) Cross-lagged coefficients over 10-year time lag. g) Metric scaled. -) not applicable. **Source:** Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this image follows the terms of the Attribution International 4.0 License (CC BY 4.0), which permits any use, copy or redistribution of this illustration <https://creativecommons.org/licenses/by/4.0/>.

In summary, the stability of the central concepts in all three models shows considerable consistency over time. Remarkable effects in one direction are observed between BMI, which predicts quality of life status, and depression, but this is not true in the opposite direction. Consequently, individuals who are underweight, overweight or obese show lower QoL and higher depression scores compared to normal weight individuals. Among them, obese individuals show the strongest effect in predicting quality of life and depression over 10 years. Thus, the results do not confirm a bi-directional relationship. Therefore, depression status and QoL are not significant predictors of BMI. The relatively modest magnitude of the corresponding lagged effects is noteworthy.

Sociodemographic variables, specifically educational attainment and age among study participants, manifest a pronounced influence on longitudinal dynamics encompassing QoL, depression status, and BMI. Elevated levels of educational achievement are concomitant with a discernible reduction in BMI and a corresponding decrease in depression scores. Those individuals who have attained higher educational benchmarks tend to self-report a superior QoL compared to their counterparts with more limited educational backgrounds. In the context of sex, particularly with respect to the female category, it is worth noting an association with elevated depression scores; however, its impact on both QoL and BMI does not achieve statistical significance. Additionally, as the chronological age of participants advances, it surfaces as a robust predictor of declining QoL and heightened depression scores. Interestingly, a converse correlation becomes evident concerning BMI scores, intimating that the aging demographic tends to exhibit diminished BMI scores, consistent with our prior empirical investigation (Rindler et al. 2023).

## 5. Discussion

Given that both mental illness and overweight are public health issues of great importance, gaining more insight into the complexity of their relationship and examining the underlying nature of these two entities seem to be crucial in respect of disease prevention and developing innovative treatment strategies. Most of the studies that have been carried out in the past are based on a cross-sectional approach, while prospective studies using repeated measurements of both mental illness and overweight are scarce but highly required. Hence, there is a strong need to establish further in-depth research in order to elucidate possible bi-directional associations over time (Kivimäki et al. 2009a) and further investigations should consider all populations, including adolescent and teenagers using a longitudinal approach (Zhang 2021). This research was carried out aiming to contribute to gaining further knowledge on this issue using longitudinal data from an observational panel study. Therefore, it is intended to investigate long-term associations between increased body weight, i.e., obesity and overweight, represented by BMI, and mental health focusing on depression status and QoL.

This research delved into the proposition that there exists a noteworthy bi-directional correlation, spanning a decade, between depression scores and body mass index (BMI) among European adults aged 50 and above grappling with overweight or obesity. This supposition draws support from prior research findings (Hachula et al. 2023; McElroy et al.; Pickering et al. 2007; Avila et al. 2015; Zhang 2021; Milaneschi et al. 2019). To explore this relationship, longitudinal data from individuals aged 50 and older were employed.

The objective was to uncover potential associations working in both directions using a two-wave cross-lagged panel approach. To delve into the relationships between mental health indicators and overweight or obesity over a 10-year timeframe, the study employed multiple regression analysis with the aim of addressing the anticipated research query. The mental health aspects were assessed using established questionnaires with robust psychometric qualities, while BMI scores were computed to form the basis of our analysis. In relation to our primary research hypothesis, the outcomes of exploring potential relationships between BMI levels and variables related to mental health provide indications of minor yet significant effects when it comes to predicting both QoL and depression scores. This suggests that individuals living with underweight, overweight, or obesity tend to exhibit higher depression scores and lower QoL scores compared to those with normal weight. Notably, among these groups, individuals with obesity display the most pronounced impact on predicting both QoL and depression status. However, while the results are statistically significant, the magnitude of

these effects remain relatively small. Thus, interpreting these findings as suggesting substantial long-term associations should be done cautiously.

The premise of a one-directional connection (Leutner et al. 2023; De Hert et al. 2011; Mannan et al. 2016; Luppino et al. 2010; Kivimäki et al. 2009a) was built on the notion that males and females aged 50 and above, living with overweight or obesity, show a noteworthy positive relationship between their BMI, predicting depression scores, and a negative association between participants' BMI and levels of QoL over a decade. Consequently, a significant one-directional cross-lagged effect becomes apparent, where BMI scores are linked to predicting QoL and depression status. Individuals dealing with overweight and obesity tend to exhibit escalated depression scores and reduced QoL. Furthermore, the regression analysis underscores that neither depression nor QoL can predict BMI. Overall, the core findings of our investigation diverge from our initial hypothesis, which postulated a reciprocal link between overweight or obesity and mental health status (Rindler et al. 2023).

The findings resulting from our cross-sectional analysis of the Austrian Health Interview Survey pointed out significant results regarding associations between depression state and BMI score. According to hypothesis 1, we used the Austrian Health Interview Survey (ATHIS) dataset in a cross-sectional approach to examine whether there is a general association between BMI and two different aspects of mental health, including depression and QoL. Overall, results from Pearson's correlation analysis using calculated BMI scores of the ATHIS dataset proved significant with respect to both depression status and QoL.

Thus, both depression status and QoL levels seem to be correlated with BMI scores in the ATHIS dataset. More precisely, people's BMI scores are positively correlated with higher depression scores, according to the patient health questionnaire (PHQ-8), whereas females indicate stronger coefficients than men. With regard to the correlation between BMI and QoL, a significantly negative correlation can be observed in both men and women.

In accordance, people with higher BMI scores demonstrate significantly lower scores of QoL. Again, female individuals show stronger effects than males. The strongest correlation was found between BMI and the physical domain of QoL, regardless of gender. Even though findings resulting from the analysis using cross-sectional data reveal a significant positive correlation with respect to depression and BMI, some attention should be paid on very small correlation coefficients, especially in male individuals, which may only be significant due to the large sample size. In fact, there are also some indications of moderate effects regarding physical QoL and BMI in men and women. Both male and female individuals show significant negative correlations between those two characteristics.

Overall, findings demonstrate evidence for some significant indications of a relationship in terms of BMI scores predicting mental health, although these results can only be understood as rather small indications of hypothesised associations in the long term.

The findings of this study reveal significant indications that overweight and obese people are more likely to show increased depression scores and decreased QoL. This outcome aligns to some extent with the suggestions from a systematic review and meta-analysis carried out by Mannan et al., delving into reciprocal relations between obesity and depression (Mannan et al. 2016). The findings from Mannan et al.'s study propose a notable association between depression and obesity, irrespective of the causal direction. However, the degree of this relationship appears to be more pronounced when considering depression as a precursor to obesity rather than vice versa (Mannan et al. 2016). However, results from regression analysis do not agree with findings from Milaneschi et al. and Hachula et al. in terms of a bi-directional link between obesity and mental health (Milaneschi et al. 2019; Hachula et al. 2023).

However, the outcomes derived from the multiple regression analysis do not align with the viewpoints expressed by McElroy and Pickering, who proposed that individuals with mental health issues have an elevated susceptibility to developing overweight or obesity (McElroy et al. 2004; Pickering et al. 2007), which is due to the absence of any noteworthy relations between mental health disorders leading to overweight or obesity, specifically concerning depression status and QoL levels. However, results agree with the results from Leutner et al. who postulate that mental illness, including depression among obese individuals, usually occurs within a couple of years (Leutner et al. 2023). Moreover, results of this investigation reveals that an increased BMI predicts higher levels of depression, which corresponds to the suggestions made by Holt et al who stated that obesity is positively associated with depression (Holt 2019).

Nonetheless, our findings do exhibit certain similarities to the conclusions drawn by Luppino et al., who hypothesised that diminished QoL and depression often coincide with obesity and might be particularly prevalent among elderly individuals living with compromised physical conditions (Luppino et al. 2010). Our results suggest that older individuals dealing with obesity or being overweight tend to experience reduced QoL and heightened depression levels in comparison to those with a normal weight.

Furthermore, the outcomes of our multiple regression analysis are in line with the suggestions made by Avila et al., stating a substantial association between obesity and a decline in QoL.

Additionally, our results are partly in line with the suggestions made by Stephenson et al. who claims that obesity predicts low QoL showing an inverse association between weight gain and low QoL (Stephenson et al. 2021), which is also in line with findings by Bull et al. (Bull et al.

2020).). In alignment with this, mental health disorders such as depression appear to be significantly linked to obesity and could also lead to a notable decline in QoL. Notably, when these two conditions co-occur, the effects seem to be considerably magnified. Despite public awareness initiatives and corresponding endeavors, the escalating prevalence of both mental health disorders and obesity persists as a fundamental concern (Avila et al. 2015). Correll et al. suggest that the majority of mentally ill individuals suffer from obesity, respectively overweight, which suggests that there may be a link between mental illness and obesity (Correll et al. 2010). In line with this perspective, our findings concur with previous research (Correll et al. 2010) by recognising a substantial association between BMI and the state of depression, indicating that obesity contributes to higher depression scores. Nevertheless, the outcomes derived from our study also reveal that individuals classified as underweight demonstrate notably decreased QoL and increased depression scores, albeit with the smallest effect size observed in this context.

Some prior investigations also suggest that depression and decreased levels of QoL are frequently displayed to be associated with obesity (Luppino et al. 2010) among populations consisting of people of advanced age and accompanied physical impairments. In these cases, the co-occurrence of mental health problems and overweight, respectively obesity seems to be more likely and turned out to be stronger among individuals of higher age (Kivimäki et al. 2009; Zabelina et al. 2009), probably also due to several physical comorbidities and complaints. The findings of this thesis are partially consistent with suggestions by Levi et al. and Friedmann et al. who postulate that obesity and poor physical and mental health are associated with each other. In particular, this seems to be true for older individuals (Levi et al. 2012; Friedmann et al. 2001).

The core finding of this investigation is in line with the suggestions by De Hert and colleagues who postulate that people living with obesity are more likely to have a mental illness (De Hert et al. 2011). Besides, there are some similarities to findings from other studies indicating obesity to be positively linked to mental health issues like depression and QoL (Leutner et al. 2023; Holt 2019; Stephenson et al. 2021). However, this concordance, according to our result, may only apply to the constructs depression and QoL. Considering that the relationship between obesity and mental health seems to be more pronounced in older adults than in younger populations, our major finding that is, BMI is significantly associated with increased mental health issues, is consistent with the claims made by Kivimäki et al. 2009 and Zabelina et al. 2009 (Kivimäki et al. 2009; Zabelina et al. 2009)

Based on our findings, specific sociodemographic characteristics like age, educational level, and sex are linked to both mental health factors and BMI. Furthermore, living with a partner

seems to slightly enhance QoL and decrease BMI. Notably, being female is particularly indicative of higher depression scores. Our investigation also demonstrates that individuals of advanced age tend to display lower BMI scores (Rindler et al. 2023), which corresponds with the proposals from Wysokiński et al. who suggest that older individuals, even when in good health, often encounter weight loss possibly due to changed appetite, particularly among the very elderly referred to as "anorexia of aging" (Wysokiński et al. 2015). The negative association between older age and reduced BMI scores could be attributed to the inclusion of older participants in our sample. However, evidence for younger populations remains unclear. As noted in earlier research (Dent et al. 2018; Prell & Perner 2018), anorexia of aging and the related weight loss generally affect those above 65 years old who are hospitalised, in long-term care, or dealing with neurological or inflammatory conditions. This phenomenon is presumed to be age-related and linked to metabolic changes, decreased appetite, and frailty (Picca et al. 2022). Consequently, the decline in weight and body fat is seen as typical in late life (Hayes & Roberts 2006).

Numerous studies on depression risk establish that demographic factors such as being female (WHO 2008; Cole & Dendukuri 2003) and older age (Luppa et al. 2012; Iden et al. 2014) are acknowledged as predisposing factors for this mental health condition. Regarding sociodemographic aspects, our findings align with prior research outcomes (Artiga & Hinton 2019; Allen et al. 2014). Specifically, factors like age, sex, and education are associated with individuals' mental health (Mao & Agyapong 2021). Following the suggestions made by Zhang, certain sociodemographic factors like age and education affect body weight showing that people with lower education show a higher risk of being obese (Zhang 2021), which is in line with the findings of this study.

Consistent with earlier research (Mao & Agyapong 2021; WHO 2008; Cole & Dendukuri 2003), being female seems to be more closely associated with elevated depression scores compared to males, although participants' gender does not significantly impact QoL (Rindler et al. 2023). There is a strong need to carry out further research. In particular, examinations using longitudinal data are highly required in order to provide in-depth studies by which potential reciprocal associations as well as cumulative effects can be discussed in a broader sense. Moreover, generalisability of previous findings needs to be verified (Kivimäki et al. 2009a).

## 5.1 Limitations and strengths

Unlike the utilisation of randomised control trials (RCTs) to explore causal relationships within study groups, longitudinal studies employing observational data, like the Survey of Health, Ageing and Retirement in Europe (SHARE), present a chance to investigate prolonged and hypothesised bi-directional relations with a specific time delay. However, it is important to note that the outcomes of such studies cannot definitively establish absolute causation. However, this study offers a valuable longitudinal approach for investigating the associations between mental health and overweight across time. Although it claims a substantial sample size encompassing respondents from various parts of Europe, the study overlooks potential additional factors that could introduce bias. These factors include physical activity, dietary habits, physical health conditions, and the usage of psychotropic medication-all of which might have significantly contributed to the development of obesity and related metabolic consequences (Patel et al., 2022). It is worth noting that information regarding the use of psychotropic drugs by participants could potentially influence the results, in the light of earlier investigations (Solmi et al., 2020; Alonso-Pedrero, 2019; Fava, 2000; Serretti & Mandelli, 2010; Montgomery et al., 1998; Uher et al., 2011) that suggest certain antidepressants could potentially elevate the risk of weight gain, alongside antipsychotic drugs.

In line with insights from an earlier review led by Fava, it is suggested that older antidepressants like mirtazapine, categorised among tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs), could potentially lead to a more frequent increase in body weight (Ghusn et al. 2022) compared to the newer generation of selective serotonin reuptake inhibitors (SSRIs) (Fava 2000). Serotonin reuptake inhibitors may cause weight gain when used in the long term (Aldrich et al. 2019). This notion finds support in the viewpoints presented by Serretti & Mandelli among others who suggest, through their meta-analysis, that mirtazapine, among other antidepressants, is linked to weight gain (Serretti & Mandelli 2010; Montgomery et al. 1998; Uher et al. 2011). The side-effect of weight gain primarily occurs during antipsychotic treatment (Strawn et al. 2023; Mazareel et al. 2020). The weight gain triggered by these medications might, in certain cases, arise from intricate hormonal mechanisms. These mechanisms involve the antihistaminergic impact of certain antipsychotics and antidepressants on H1 histamine receptors, along with imbalances in hormones like ghrelin and leptin, which regulate appetite (Zhang et al. 2013; Himmerich et al. 2005; Pinar et al. 2008). However, it is important to acknowledge that the pathways through which antidepressants might contribute to weight gain remain unclear and not well comprehended (Himmerich et al. 2015). These findings imply that causal conclusions might not be warranted, with the potential for residual variables to potentially inflate this association (Gafoor et al. 2018).

According to Rogosa, utilising a two-wave cross-lagged approach to explore long-term effects does not provide substantial support for establishing causal links (Rogosa 1980), while Selig & Little argue that this panel design can offer deeper insights, enhance the comprehension of longitudinal relationships, and stimulate further investigations (Selig & Little 2012).

Another limitation of this study lies in the fact that the self-reporting of anthropometric measures, specifically body weight, introduces the risk of response bias. Furthermore, the study did not account for weight bias and the stigmatisation faced by individuals living with obesity, which can significantly impact their mental health and therefore the outcome of this thesis. People with obesity often face bias and ridicule due to their body weight, particularly through media channels, further reinforcing the societal notion that larger body sizes deviate from the norm and are socially unacceptable (Fruh et al. 2021; Jackson et al. 2014).

When interpreting the results, especially concerning the one-directional relationship between BMI and mental health indicators, it is crucial to consider that the participants were already aged 50 and above. The study lacks reliable data on the onset of obesity. Moreover, the classification into depressed/non-depressed categories did not incorporate the severity of depression that might arise from long-term obesity, potentially influencing the outcome of this study.

A notable strength of this study is its reliance on observational data acquired from an expansive panel survey. This method has the potential to significantly improve the formation of a sizable and relevant sample, inclusive of individuals in their respective home settings. Consequently, the analysis of longitudinal data emerges as a dependable approach for scrutinizing persistent cause-and-effect connections, along with reciprocal associations. Considering that data collection included individuals from a variety of backgrounds spanning 15 European countries, the sample is considered representative, thus yielding a pertinent dataset intended to generate results with wider applicability.

Therefore, this work is based on two methodological approaches which may be beneficial in comparison to examinations that solely focus on cross-sectional data. Due to that, this thesis allows to elucidate more profound, reciprocal associations and an in-depth analysis of longitudinal data on the foundation of a large sample size.

One limitation of this investigation is the fact that only respondents aged 50 or above were included in the longitudinal analysis. Mental health strains interacting with increasing body weight may also be interesting to investigate in younger populations including adolescents in order to determine long-term as well as cause-effect associations among younger individuals. Furthermore, it might also be valuable to identify cumulative effects by carrying out further

investigations to provide more empirical evidence on this major public health issue. In particular, when it comes to detecting emerging risks and serious development of illnesses. Moreover, a comprehensive analysis of psychometric properties was performed for both the Austrian Health Interview Survey (ATHIS) and the Survey of Health, Ageing and Retirement in Europe (SHARE) providing reliable measurements according to administered scales and questionnaires. However, potential measurement bias can never be ruled out completely, even if scales with high reliability and validity are used. Yet, this thesis project contributes to establishing knowledge based on well validated and reliable survey methods and psychometric properties.

Normally, Randomised Controlled Trials (RCTs) are used to investigate causal effects. However, when it comes to examining long-term effects as well as reciprocal associations, this type of research approach is not applicable (Kivimäki et al. 2009). In this case, data from observational studies are much more suitable to show long-term bi-directional associations, although complete causality cannot be proven in its entirety. Even if covariates are considered and adjusted as far as possible, and they can hardly have any more effect on the examined correlations, possible residual confounding factors can never be completely excluded in observational examinations (Kivimäki et al. 2009a). The same applies to the present work. As mentioned above, the chosen methodological approach that was applied during this thesis project does not allow for drawing any inferences hinting at causal associations in terms of central characteristics of mental health, including depression status and QoL, and obesity, respectively overweight, in affected people. Therefore, the results according to all models that have been used within the analysis are indications of potential, perhaps causal associations that need to be further investigated in the future by conducting appropriate research projects targeting this subject.

## **5.2 Outlook, implications for the future**

Considering the considerable importance of both mental health and obesity within the realm of public health, it becomes imperative to investigate the connections between them and probe into their fundamental mechanisms. Grasping the intricacies of these interplays holds significant value for disease prevention and the creation of inventive therapeutic approaches. Moreover, it is worth noting that mental health concerns have frequently been disregarded in prior times (Kieling et al. 2011).

The results of our study ought to stimulate more research in this field, particularly in delving deeper into how mental health issues and body weight reciprocally impact each other. This

becomes especially relevant when we focus on the older demographic, which frequently faces challenges related to excess weight and obesity. Consequently, it is imperative to include mental health considerations within treatment plans that encompass various facets, including the biological, psychological, and social aspects. Employing this comprehensive approach and integrating newly emerging empirical evidence into practical medical settings can significantly bolster our future approaches to addressing and preventing these issues. This study should also motivate researchers to conduct new and innovative investigations into the links between mental health and obesity. It is important to look at how common mental problems like depression and anxiety are connected to being overweight or obese. We should especially focus on the long-term effects in both directions and how they contribute to causing these problems. In fact, we still do not have clear evidence about the associations between mental health and obesity and previous studies have been inconclusive (McElroy et al. 2004). Since previous research predominantly concentrated on clarifying the relationship between mental health and obesity through short-term studies, there exists a significant need for research endeavours based on long-term data analysis. Specifically, there is a strong need for more comprehensive large-scale investigations to facilitate in-depth analyses of potential accumulative effects, contributing to a more comprehensive discussion. Furthermore, it is imperative to validate the applicability of earlier findings on a broader scale (Kivimäki et al. 2009).

In today's context, both mental health disorders and obesity rank among the greatest global challenges in public health. Delving into the subject and comprehending the fundamental essence of these complex interrelationships is of utmost importance and considerably sought after. This stems from the fact that the associations between obesity and mental health underscore the necessity of addressing physical and mental health concomitantly while addressing obesity. By tending to mental health concerns, individuals fighting obesity might enhance their ability to manage their weight and enhance their overall health and QoL. Consequently, the exploration and comprehension of the underlying complexities within these associations bear immense significance and are exceedingly demanded.

Due to the fact that this thesis is not able to prove, respectively profoundly explore causal effects regarding mental health status, including common psychopathological problems, such as depression, and anxiety disorders, more research activities and efforts are strongly recommended for the future to break new ground and establishing innovative paths of thinking targeting to disclose the undermining nature of the complex disease -inherent mechanisms. Research of the future should aim at analysing observational data derived

from an appropriate sample size, including people from all age groups, including both young and old participants. Results should be adopted and implemented in the respective settings facilitating the individual capacity to improve and optimise applied interventions and create personalised treatment strategies that focus on individual resources to prevent and overcome physical and mental health problems. In this regard, and according to prior research that have been carried out, interventional programs aiming at weight loss appear to be associated with significantly improved physical and mental health conditions. In addition, dietary and, in some cases, surgical interventions applied in younger and middle-aged individuals leading to weight loss, also induced a decrease of depression and reduced levels of perceived stress (Elder et al. 2012) and further increases QoL (Napoli et al. 2014; van Gemert et al. 2015). Thus, this is a proof of the positive effects of exercising and weight loss interventions. The implementation of weight loss programs and dietary patterns at early stages of pathological developments in affected populations is undoubtedly important but does only account for individuals who are already ill. In my opinion, putting effort into the prevention of illnesses is a key factor and a major field of research within the next decades in terms of early identification of imbalances that may possibly further develop to serious health problems and diseases. Besides, future research activities, weight loss programs and interventional regimens focusing on improving mental and physical health are particularly important for vulnerable individuals who are more frequently affected by mental strains and psychological problems than the general population. These people might be more susceptible for developing serious health problems resulting from excessive increase in body weight in the sense of a dose-response effect which has been postulated by Kivimäki et al. (Kivimäki et al. 2009a).

Accordingly, future monitoring activities among vulnerable populations, including regular monitoring of people with relevant psychopathological treatments or past events are highly desirable and should be carried out particularly thoroughly in order to avoid such developments. One substantial issue regarding the examination of interacting mechanisms and relationships between mental health, respectively mental illness and overweight is the fact that biasing in shape of several different confounding factors, such as socioeconomic status, behavioural risk factors, including lifestyle, physical activity or sedentary behaviour, and alcohol consumption, that were either not, or insufficiently collected (Schwartz et al. 2004; Devlin et al. 2000), may have an impact on the characteristics to be analysed. Hence, it further complicates causal research and could possibly identify biased relationships. In some cases, reporting bias or reverse causality are responsible for indicating relationships, where overweight people tend to claim being sadder because of their increased body weight (Lawlor et al. 2011).

Another important issue of our time is the experience of stress and stress-related problems which may contribute to obesity and weight gain in affected individuals by over activating the sympathetic nervous system (SNS) and its inherent stress-responding system (HPA-axis) (Smith & Minson 2012), particularly, when psychosocial stressors affect us over a long period of time and indicate that they become a chronic burden. Therefore, future investigations should also account for individual experiences with stressful situations, coping strategies and stress resilience, respectively individual ability to deal with psychological distress. As a result, these aspects may occasionally act as confounding factors, and could possibly influence the outcome of causal examinations on this subject. This is also true for people who regularly use psychotropic medication, such as antidepressants and antipsychotics, or even food supplements, which may also have an impact on mood and self-rated mental and physical health status.

### **5.3 Contribution to the field**

The objective of this work is to enhance awareness and encourage extended discourse on this matter. The exploration of longitudinal data employing a panel approach with multiple assessment points is imperative in order to illuminate the underlying dynamics between mental health and obesity. A substantial portion of earlier research focusing on the connection between obesity and mental health predominantly relies on cross-sectional data, aiming to elucidate synchronous effects within a specific population. However, this approach has led to results that are generally inconsistent in nature (Kivimäki et al. 2009).

In our investigation, we adopt a longitudinal framework, an approach that is relatively uncommon given the existing scientific evidence. This methodology enables us to determine long-term interactions that is infrequently studied. Given the prevalent occurrence of both obesity and mental health concerns among older individuals, emphasising a highly prevalent issue, our findings offer insightful observations about the relationships over an extended duration. These observations also hint at potential causal influences that warrant in-depth exploration in further research activities. Furthermore, a majority of previous studies have produced outcomes that lack the comprehensiveness required to draw generalisable conclusions encompassing diverse age groups. This limitation, in certain scenarios, could yield different results and may have a significant impact on the ultimate outcomes (Luppino et al. 2010).

Indeed, this study plays a pivotal role in enhancing our understanding of the prolonged impacts and interactions in the older population, which seems critical for exploring the trajectory of this

relationship. This foundation holds substantial potential for refining treatment approaches and preventive initiatives, as it enables the identification of potential risk elements. Notably, recognising that obesity could serve as a precursor for the development of depression, interventions targeting obesity might, in turn, foster depression prevention efforts and elevate overall QoL. Moreover, the outcomes of this thesis should constitute a fundamental cornerstone in clinical practice. This implies that medical practitioners and caregiving professionals should incorporate mood monitoring into their regimen when attending to overweight or obese patients, especially among the elderly with enduring obesity issues. This incorporation could significantly help in the formulation of treatment guidelines.

Furthermore, we aspire for this thesis's findings to heighten public awareness about the dual significance of addressing both obesity and mental health. This broader perspective aims to mitigate stigma and foster an environment where individuals affected by these concerns are encouraged to seek medical treatment. Moreover, this endeavor should additionally assist in the early identification of potential pathological developments and lead to enhanced interventions for individuals at higher risk.

Our aspiration is that this research serves as a catalyst for ongoing discussions and explorations aimed at revealing the underlying mechanisms of the relationship between mental health and obesity. Based on our results, we are confident in the need for further epidemiological inquiries to clarify the underlying complexity, with particular attention to potential moderating and confounding factors within the European population.

Lastly, we hope that our findings will contribute to the development of public health policies in accordance with the broader objectives of promoting well-being in the population.

## **5.4 Conclusions**

In this thesis, we have confirmed limited associations between BMI and depression, as well as links between BMI and various aspects of QoL using a cross-sectional approach. In summary, we can confirm that BMI predicts mental health aspects such as depression and QoL in a one- directional manner over a span of 10 years. However, our study does not establish significant bi-directional relationships over the long term, which is consistent with previous research on this subject (McElroy et al. 2004; Pickering et al. 2007; Avila et al. 2015; Mannan et al. 2016; Luppino et al. 2010). While our models indicate meaningful results in terms of explained variances, calculated beta coefficients turned out to be relatively small. It is worth noting that research into the relationship between mental health and body weight lacks consistency (McElroy et al. 2004) and remains ambiguous in the

scientific community (Kivimäki et al. 2009a). Additionally, our findings do not establish a definitive cause-effect relationship. Further analysis is needed to explore potential causal links in greater detail. Furthermore, there is a significant need to investigate the underlying long-term dynamics between these two public health concerns. Ultimately, these results should serve as impetus for more extensive research on this subject. Acquiring knowledge in this area is crucial, not only for older populations, but also for detecting early signs of health issues in younger populations, including children and adolescents, to effectively prevent illnesses.

## Bibliography

- Abell, C. A., Farquhar, D. L., Galloway, S. M., Steven, F., Philip, A. E., & Munro, J. F. (1986).** Placebo controlled double-blind trial of fluvoxamine maleate in the obese. *Journal of Psychosomatic Research*, 30, 143–146.
- Adam, T. C., & Epel, E. S. (2007).** Stress, eating and the reward system. *Physiology & Behavior*, 91, 449–458.
- Adams, K. F., Schatzkin, A., Harris, T. B., Kipnis, V., Mouw, T., Ballard-Barbash, R., et al. (2006).** Overweight, obesity and mortality in a large prospective cohort of persons 50 to 71 years old. *New England Journal of Medicine*, 355(8), 763–778.
- Agarwal, S. M., & Venkatasubramanian, G. (2013).** Metabolic syndrome in schizophrenia: Theoretical, clinical and translational perspectives. *Indian Journal of Psychological Medicine*, 35, 117–120.
- Ahlberg, A.-C., Ljung, T., Rosmond, R., McEwen, B., Holm, G., Akesson, H.-O., et al. (2002).** Depression and anxiety symptoms in relation to anthropometry and metabolism in men. *Psychiatry Research*, 112, 101–110.
- Ajilore, O., Haroon, E., Kumaran, S., Darwin, C., Binesh, N., Mintz, J., Miller, J., Thomas, M. A., & Kumar, A. (2007).** Measurement of brain metabolites in patients with type 2 diabetes and major depression using proton magnetic resonance spectroscopy. *Neuropsychopharmacology*, 32(6), 1241–1231.
- Alciati, A., D'Ambrosio, A., Foschi, D., Corsi, F., Mellado, C., & Angst, J. (2007).** Bipolar spectrum disorders in severely obese patients seeking surgical treatment. *Journal of Affective Disorders*, 101, 131–138.
- Aldrich, S. L., Poweleit, E. A., Prows, C. A., Martin, L. J., Strawn, J. R., & Ramsey, L. B. (2019).** Influence of CYP2C19 metabolizer status on escitalopram/citalopram tolerability and response in youth with anxiety and depressive disorders. *Frontiers in Pharmacology*, 10, 99.
- Allen, J., Balfour, R., Bell, R., & Marmot, M. (2014).** Social determinants of mental health. *International Review of Psychiatry*, 26, 392–407. doi:10.3109/09540261.2014.928274

**Allison, D., Mentore, J., Heo, M. L. P., Cappelleri, J. C., Infante, M. C., & Weiden, P. J. (1999).** Antipsychotic induced weight gain: A comprehensive research synthesis. *American Journal of Psychiatry, 156*, 1686–1696.

**Alloway, R., & Bebbington, P. (1987).** The buffer theory of social support —a review of the literature. *Psychological Medicine, 17*, 91–108.

**Al-Nohair, S. (2014).** Obesity in Gulf countries. *International Journal of Health Sciences (Qassim), 8*(1), 79–83.

**Alonso-Pedrero, L., Bes-Rastrollo, M., & Marti, A. (2019).** Effects of antidepressant and antipsychotic use on weight gain: A systematic review. *Obesity Reviews, 20*(12), 1680–1690. doi:10.1111/obr.12934

**Al-Shammari, S. A., Khoja, T. A., al-Maatouq, M. A., & al-Nuaim, L. A. (1994).** High prevalence of clinical obesity among Saudi females: A prospective, cross-sectional study in the Riyadh region. *Journal of Tropical Medicine & Hygiene, 97*(3), 183–188.

**Altman, C. E., et al. (2016).** What does self-rated health mean? Changes and variations in the association of obesity with objective and subjective components of self-rated health. *Journal of Health and Social Behavior, 57*(1), 39–58. doi:10.1177/0022146515626218.

**Alvarez-Jimenez, M., Gonzalez-Blanch, C., Crespo-Facorro, B., Hetrick, S., Rodriguez-Sanchez, J. M., Perez-Iglesias, R., & Vazquez-Barquero, J. L. (2008).** Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders: A systematic critical reappraisal. *CNS Drugs, 22*, 547–562.

**Alwan, A., Armstrong, T., Bettcher, D., et al. (2011).** Global status report on non-communicable diseases 2010. World Health Organization. Retrieved from [http://www.who.int/nmh/publications/ncd\\_report\\_full\\_en.pdf](http://www.who.int/nmh/publications/ncd_report_full_en.pdf).

**American Psychiatric Association. (2000).** *Diagnostic and Statistical Manual of Mental Disorders* (4th ed. Text Revision). Washington: American Psychiatric Press.

**American Psychiatric Association. (1994).** *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC.

**American Psychiatric Association. (2013).** *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington: American Psychiatric Publishing.

**Amann, B., Mergl, R., Torrent, C., Perugi, G., Padberg, F., El-Gjamal, N., et al. (2009).** Abnormal temperament in patients with morbid obesity seeking surgical treatment. *Journal of Affective Disorders, 118*, 155–160.

**Anagha, K., Shihabudheen, P., & Uvais, N. A. (2021).** Side effect profiles of selective serotonin reuptake inhibitors: A cross-sectional study in a naturalistic setting. *The Primary Care Companion for CNS Disorders, 23*(4), 20m02747. <https://doi.org/10.4088/PCC.20m02747>

**Anderson, S. E., Cohen, P., Naumova, E. N., & Must, A. (2006).** Association of depression and anxiety disorders with weight change in a prospective community-based study of children followed up into adulthood. *Archives of Pediatrics & Adolescent Medicine, 160*(3), 285–291.

- Anderson, D. A., Shapiro, J. R., Lundgren, J. D., Spataro, L. E., & Frye, C. A. (2002).** Self-reported dietary restraint is associated with elevated levels of salivary cortisol. *Appetite*, *38*(1), 13–17.
- Andlin-Sobocki, P., Olesen, J., Wittchen, H.-U., & Jönsson, B. (2005).** Cost of disorders of the brain in Europe. *European Journal of Neurology*, *12*, 1–27.
- Andreyeva, T., Puhl, R. M., & Brownell, K. D. (2008).** Changes in perceived weight discrimination among Americans, 1995–1996 through 2004–2006. *Obesity (Silver Spring)*, *16*, 1129–1134.
- Andreyeva, T., Sturm, R., & Ringel, J. S. (2004).** Moderate and severe obesity have large differences in health care costs. *Obesity Research*, *12*, 1936–1943. doi:10.1038/oby.2004.243
- Andrews, R. C., Roovackers, O., & Walker, B. R. (2003).** Effects of the 11 beta-hydroxysteroid dehydrogenase inhibitor carbenoxolone on insulin sensitivity in men with type 2 diabetes. *Journal of Clinical Endocrinology & Metabolism*, *88*, 285–291.
- Angi, A., & Chiarelli, F. (2020).** Obesity and diabetes: A sword of Damocles for future generations. *Biomedicines*, *8*, 478. <https://doi.org/10.3390/biomedicines8110478>
- Angst, J., Vollrath, M. (1991).** The natural history of anxiety disorders. *Acta Psychiatrica Scandinavica*, *84*, 446–452.
- Antonovsky, A. (1979).** Health, stress, and coping. San Francisco: Jossey-Bass.
- Antonovsky, A. (1987).** Unraveling the mystery of health: How people manage stress and stay well. San Francisco: Jossey-Bass.
- Antonovsky, A. (1992).** Can attitudes contribute to health? *Advances, The Journal of Mind-Body Health*, *8*(4), 33–49.
- Antonovsky, A. (1991).** The structural resources of salutogenic strengths. In C. L. Cooper & R. Payne (Eds.), *Personality and stress: Individual differences in the stress process*. New York: Wiley.
- Apfelbaum, M., & Mandenoff, A. (1981).** Naltrexone suppresses hyperphagia induced in the rat by a highly palatable diet. *Pharmacology Biochemistry and Behavior*, *15*(1), 89–91.
- Arato, M., O'Connor, R., & Meltzer, H. Y. (2002).** A 1 year double-blind, placebo-controlled trial of Ziprasidone 40, 80, and 160 mg/day in chronic schizophrenia: The Ziprasidone Extended use in Schizophrenia (ZUES) study. *International Clinical Psychopharmacology*, *17*, 207–215.
- Artiga, S., & Hinton, E. (2019).** Beyond health care: The role of social determinants in promoting health and health equity. *Health*, *20*, 1–13. Available online at: <https://files.kff.org/attachment/issue-brief-beyond-health-care>.
- Atlantis, E., & Baker, M. (2008).** Obesity effects on depression: Systematic review of epidemiological studies. *International Journal of Obesity (London)*, *32*(6), 881–891.
- Atlantis, E., & Ball, K. (2007).** Association between weight perception and psychological distress. *International Journal of Obesity (London)*, 1–7 (advance online publication).

**Australian Bureau of Statistics.** (1998). *4326.0—Mental Health and Wellbeing: Profile of Adults, Australia, 1997*. Canberra. Retrieved June 20, 2022, from <http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4326.01997?OpenDocument>

**Avena, N. M., & Hoebel, B. G.** (2003). A diet promoting sugar dependency causes behavioral cross-sensitization to a low dose of amphetamine. *Neuroscience*, *122*(1), 17–20.

**Avila, C., Holloway, A. C., Hahn, M. K., et al.** (2015). An overview of links between obesity and mental health. *Current Obesity Reports*, *4*(4), 303–310. <https://doi.org/10.1007/s13679-015-0164-9>

**Badini, I., Coleman, J. R. I., Hagenars, S. P., et al.** (2022). Depression with atypical neurovegetative symptoms shares genetic predisposition with immuno-metabolic traits and alcohol consumption. *Psychological Medicine*, *52*(4), 726–736. <https://doi.org/10.1017/S0033291720002342>

**Bair, M. J., Robinson, R. L., Katon, W., & Kroenke, K.** (2003). Depression and pain comorbidity: A literature review. *Archives of Internal Medicine*, *163*(21), 2433–2445.

**Balbo, M., Leproult, R., & van Cauter, E.** (2010). Impact of sleep and its disturbances on hypothalamo-pituitary-adrenal axis activity. *International Journal of Endocrinology*, *2010*, 759234.

**Baldini, G., & Phelan, K. D.** (2019). The melanocortin pathway and control of appetite—Progress and therapeutic implications. *Journal of Endocrinology*, *241*(1), R1–R33.

**Baptista, T., Tenaud, L., Contreras, Q., et al.** (1995). Lithium and body weight gain. *Pharmacopsychiatry*, *28*, 35–44.

**Baptista, T.** (1999). Body weight gain induced by antipsychotic drugs: Mechanisms and management. *Acta Psychiatrica Scandinavica*, *100*(1), 3–16.

**Barak, Y.** (2002). No weight gain among elderly schizophrenia patients after 1 year of risperidone treatment. *Journal of Clinical Psychiatry*, *63*, 117–119.

**Barr, A. M., & Brotto, L. A., Phillips, A. G.** (2000). Chronic corticosterone enhances the rewarding effect of hypothalamic self-stimulation in rats. *Brain Research*, *875*(1-2), 196–201.

**Barton, B. B., Segger, F., Fischer, K., Obermeier, M., & Musil, R.** (2020). Update on weight gain caused by antipsychotics: A systematic review and meta-analysis. *Expert Opinion on Drug Safety*, *19*(3), 295–314.

**Bean, M. K., Stewart, K., & Olbrisch, M. E.** (2008). Obesity in America: Implications for clinical and health psychologists. *Journal of Clinical Psychology in Medical Settings*, *15*(3), 214–224.

**Beesdo, K., Jacobi, F., Hoyer, J., Low, N. C., Hofler, M., & Wittchen, H. U.** (2009). Pain associated with specific anxiety and depressive disorders in a nationally representative population sample [published online April 10, 2009]. *Social Psychiatry and Psychiatric Epidemiology*.

**Beesdo, K., Pine, D. S., Lieb, R., & Wittchen, H. U.** (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of Generalized Anxiety Disorder. *Archives of General Psychiatry*, *67*(1), 47–57.

- Beesdo**, K., Höfler, M., Leibenluft, E., Lieb, R., Bauer, M., & Pfennig, A. (2009). Mood episodes and mood disorders: Patterns of incidence and conversion in the first three decades of life. *Bipolar Disorders*, *11*, 637-649.
- Belanoff**, J. K., Kalezan, M., Sund, B., Fleming Ficek, S. K., & Schatzberg, A. F. (2001). Cortisol activity and cognitive changes in psychotic major depression. *American Journal of Psychiatry*, *158*(10), 1612-1616.
- Berr**, C., Wancata, J., & Ritchie, K. (2005). Prevalence of dementia in the elderly in Europe. *European Neuropsychopharmacology*, *15*(4), 463-471.
- Benkert**, O., Szegedi, A., & Kohlen, R. (2000). Mirtazapine compared with paroxetine in major depression. *Journal of Clinical Psychiatry*, *61*, 656–663.
- Benninghoven**, D., Kaduk, A., Wiegand, U., Specht, T., Kunzendorf, S., & Jantschek, G. (2006). Influence of anxiety on the course of heart disease after acute myocardial infarction risk factor or protective function? *Psychotherapy and Psychosomatics*, *75*, 56–61.
- Berghöfer**, A., Pischon, T., Reinhold, T., Apovian, C. M., Sharma, A. M., & Willich, S. N. (2008). Obesity prevalence from a European perspective: A systematic review. *BMC Public Health*, *8*, 200.
- Berthoud**, H. R. (2012). The neurobiology of food intake in an obesogenic environment. *The Proceedings of the Nutrition Society*, *71*(4), 478–487.
- Bethea**, T. N., Lopez, R. P., Cozier, Y. C., White, L. F., & McClean, M. D. (2012). The relationship between rural status, individual characteristics, and self-rated health in the behavioral risk factor surveillance system. *Journal of Rural Health*, *28*, 327–338.
- Beuther**, D. A., & Sutherland, E. R. (2007). Overweight, obesity, and incident asthma: A meta-analysis of prospective epidemiologic studies. *American Journal of Respiratory and Critical Care Medicine*, *175*, 661–666.
- Birmingham**, C. L., Muller, J. L., Palepu, A., Spinelli, J. J., & Anis, A. H. (1999). The cost of obesity in Canada. *Canadian Medical Association Journal*, *160*, 483–488.
- Bishara**, D., & Taylor, D. (2009). Asenapine monotherapy in the acute treatment of both schizophrenia and bipolar I disorder. *Neuropsychiatric Disease and Treatment*, *5*, 483–490.
- Biton**, V., Mirza, W., & Montouris, G. (2001). Weight change associated with valproate and lamotrigine monotherapy in patients with epilepsy. *Neurology*, *56*, 172–177.
- Bjorner**, J. P., Kristensen, T. O., Orth-Gomér, K., Tibblin, G., Sullivan, M., & Westerholm, P. (2012). Self-rated health: A useful concept in research, prevention and clinical medicine. Uppsala, Sweden: Forskningsradnämnden, Ord & Form AB.
- Björntorp**, P. (1997). Hormonal control of regional fat distribution. *Human Reproduction*, *12*, 21–25.
- Björntorp**, P. (2001). Do stress reactions cause abdominal obesity and comorbidities? *Obesity Reviews*, *2*, 73–86.
- Björntorp**, P. (1996). The regulation of adipose tissue distribution in humans. *International Journal of Obesity and Related Metabolic Disorders*, *20*, 429–1302.

- Blanz, M.** (2015). *Forschungsmethoden und Statistik für die Soziale Arbeit: Grundlagen und Anwendungen*. Stuttgart: Kohlhammer.
- Block, J. P., He, Y., Zaslavsky, A. M., Ding, L., & Ayanian, J. Z.** (2009). Psychosocial stress and change in weight among US adults. *American Journal of Epidemiology*, *170*(2), 181–192.
- Börsch-Supan, A.** (2022). Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 1. Release version: 8.0.0. SHARE-ERIC. Data set. DOI: 10.6103/SHARE.w1.800
- Bocarsly, M. E., Powell, E. S., Avena, N. M., & Hoebel, B. G.** (2010). High-fructose corn syrup causes characteristics of obesity in rats: Increased body weight, body fat and triglyceride levels. *Pharmacology, Biochemistry, and Behavior*, *97*(1), 101–106.
- Boggiano, M. M., & Chandler, P. C.** (2006). Binge eating in rats produced by combining dieting with stress. *Current Protocols in Neuroscience*, Chapter 9, Unit9.23A.
- Bowling, A.** (2005). *Measuring Health* (3rd ed.). Maidenhead: Open University Press.
- Bornstein, S. R., Schuppenies, A., Wong, M. L., & Licinio, J.** (2006). Approaching the shared biology of obesity and depression: The stress axis as the locus of gene-environment interactions. *Molecular Psychiatry*, *11*, 892–902.
- Bouwer, C. D., & Harvey, B. H.** (1996). Phasic craving for carbohydrate observed with citalopram. *International Clinical Psychopharmacology*, *11*, 273–278.
- Brailean, A., Curtis, J., Davis, K., Dregan, A., & Hotopf, M.** (2020). Characteristics, comorbidities, and correlates of atypical depression: evidence from the UK Biobank Mental Health Survey. *Psychological medicine*, *50*(7), 1129-1138. <https://doi.org/10.1017/S0033291719001004>.
- Bradburn, N. M.** (1969). *The structure of psychological well-being*. Chicago: Aldine.
- Branca, F., Nikogosian, H., & Lobstein, T. (Eds.).** (2007). *The challenge of obesity in the WHO European region and the strategies for response: Summary*. Copenhagen: WHO Regional Office for Europe, 1–60.
- Brancati, F. L., Wang, N. Y., Mead, L. A., Liang, K. Y., & Klag, M. J.** (1999). Body weight patterns from 20 to 49 years of age and subsequent risk for diabetes mellitus. *Archives of Internal Medicine*, *159*, 957–963.
- Brecher, M., Rak, I. W., & Melvin, K.** (2000). The long-term effects of quetiapine monotherapy on weight in patients with schizophrenia. *International Journal of Psychiatry in Clinical Practice*, *4*, 287–291.
- Bremmer, M. A., Beekman, A. T., Deeg, D. J., Penninx, B. W., Dik, M. G., Hack, C. E., & Hoogendijk, W. J.** (2008). Inflammatory markers in late-life depression: Results from a population-based study. *Journal of Affective Disorders*, *106*(3), 249–255.
- Briffa, D., & Meehan, T.** (1987). Weight changes during clozapine treatment. *Australian and New Zealand Journal of Psychiatry*, *32*, 718–721.
- Brook, R. H., Ware, J. E. Jr., Davies-Avery, A., Stewart, A. L., Donald, C. A., Rogers, W. H., ... Johnston, S. A.** (1979). Overview of adult health measures fielded in RAND's health insurance study. *Medical Care*, *17*, 1–131.

- Brown, S., Inskip, H., & Barraclough, B. (2000).** Causes of the excess mortality of schizophrenia. *British Journal of Psychiatry*, *177*, 212–217.
- Brown, G. W., & Harris, T. O. (1978).** *Social origins of depression: A study of psychiatric disorder in women*. London: Tavistock.
- Buchwald, H., & Buchwald, J. N. (2002).** Evolution of operative procedures for the management of morbid obesity 1950-2000. *Obesity Surgery*, *12*, 705-717.
- Bulik, C. M., & Sullivan, P. F. (2002).** Medical and psychiatric morbidity in obese women with and without binge eating. *International Journal of Eating Disorders*, *32*, 72–78.
- Bull, F. C., Al-Ansari, S. S., Biddle, S., et al. (2020).** World Health Organization guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine*, *54*, 1451-1462.
- Buraniqi, E., Dabaja, H., & Wirrell, E. C. (2022).** Impact of antiseizure medications on appetite and weight in children. *Paediatric Drugs*, *24*(4), 335–363. <https://doi.org/10.1007/s40272-022-00505-2>
- Cairney, J., Corna, L. M., Veldhuizen, S., Kurdyak, P., & Streiner, D. L. (2008).** The social epidemiology of affective and anxiety disorders in later life in Canada. *Canadian Journal of Psychiatry*, *53*, 104–111.
- Calle, E. E., Rodriguez, C., Walker-Thurmond, K., & Thun, M. J. (2003).** Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *New England Journal of Medicine*, *348*(17), 1625–1638.
- Cameron, A. J., Magliano, D. J., Dunstan, D. W., et al. (2012).** A bi-directional relationship between obesity and health-related quality of life: Evidence from the longitudinal AusDiab study. *International Journal of Obesity*, *36*(2), 295–303.
- Campenhausen, S., Bornschein, B., Wick, R., Bötzel, K., Sampaio, C., Poewe, W., ... Dodel, R. (2005).** Prevalence and incidence of Parkinson's disease in Europe. *European Neuropsychopharmacology*, *15*(4), 473-490.
- Canetti, L., Bachar, E., & Berry, E. M. (2002).** Food and emotion. *Behavioural Processes*, *60*, 157–164.
- Cantu, T. G., & Korek, J. S. (1988).** Monoamine oxidase inhibitors and weight gain. *Drug Intelligence & Clinical Pharmacy*, *22*, 755–759.
- Cargill, B. R., Clark, M. M., Pera, V., Niaura, R. S., & Abrams, D. B. (1999).** Binge eating, body image, depression, and self-efficacy in an obese clinical population. *Obesity Research*, *7*, 379–386.
- Carney, C. P., & Jones, L. E. (2006).** Medical comorbidity in women and men with bipolar disorders: A population-based controlled study. *Psychosomatic Medicine*, *68*, 684-691. <http://dx.doi.org/10.1097/01.psy.0000237316.09601.88>
- Carney, R. M., Freedland, K. E., Miller, G. E., & Jaffe, A. S. (2002).** Depression as a risk factor for cardiac mortality and morbidity: A review of potential mechanisms. *Journal of Psychosomatic Research*, *53*, 897–902.

- Carney, R. M., & Freedland, K. E. (2003).** Depression, mortality, and medical morbidity in patients with coronary heart disease. *Biological Psychiatry, 54*, 241–247.
- Carpino, P. A., & Goodwin, B. (2010).** Diabetes area participation analysis: A review of companies and targets described in the 2008–2010 patent literature. *Expert Opinion on Therapeutic Patents, 20*, 1627–1651.
- Carr, D., & Friedman, M. A. (2005).** Is obesity stigmatizing? Body weight, perceived discrimination, and psychological well-being in the United States. *Journal of Health and Social Behavior, 46*, 244–259.
- Carr, D., Jaffe, K. J., & Friedman, M. A. (2008).** Perceived interpersonal mistreatment among obese Americans: Do race, class, and gender matter? *Obesity, 16*, S60–S68.
- Carr, K. D. (2002).** Augmentation of drug reward by chronic food restriction: Behavioral evidence and underlying mechanisms. *Physiology & Behavior, 76*(3), 353–364.
- Carson, T. L., Hidalgo, B., Ard, J. D., & Affuso, O. (2014).** Dietary interventions and quality of life: A systematic review of the literature. *Journal of Nutrition Education and Behavior, 46*(2), 90–101.
- Castelpietra, G., Nicotra, A., Pischiutta, L., Gutierrez-Colosía, M. R., Haro, J. M., & Salvador-Carulla, L. (2020).** The new Horizon Europe programme 2021–2028: Should the gap between the burden of mental disorders and the funding of mental health research be filled? *The European Journal of Psychiatry, 34*, 44-46.
- Castro-Costa, E., Dewey, M., Stewart, R., Banerjee, S., Huppert, F., Mendonca-Lima, C., ... Prince, M. (2008).** Ascertaining late life depressive symptoms in Europe: An evaluation of the survey version of the EURO-D scale in 10 nations. The SHARE project. *International Journal of Methods in Psychiatric Research, 17*(1), 12–29. DOI: 10.1002/mpr.236.
- Ceilley, J. W., Cruz, M., & Denko, T. (2006).** Active medical conditions among patients on an assertive community treatment team. *Community Mental Health Journal, 42*, 205-211. DOI: 10.1007/s10597-005-9019-2.
- Chatterjee, A., Gerdes, M. W., & Martinez, S. G. (2020).** Identification of risk factors associated with obesity and overweight—A machine learning overview. *Sensors, 20*(9), 2734. <https://doi.org/10.3390/s20092734>
- Chen, J., Gao, K., & Kemp, D. E. (2011).** Second-generation antipsychotics in major depressive disorder: Update and clinical perspective. *Current Opinion in Psychiatry, 24*(1), 10–17.
- Chengappa, K. N. R., Levine, J., Rathore, D., Parepally, H., & Atzert, R. (2001).** Long term effects of topiramate on bipolar mood instability, weight change and glycemic control: A case-series. *European Psychiatry, 16*, 186–190.
- Chengappa, K. N., Chalasani, L., Parepally, H., Houck, P., & Leuine, J. (2002).** Changes in body weight and body mass index among psychiatric patients receiving lithium, valproate, or topiramate: An open-label, non-randomized chart review. *Clinical Therapeutics, 24*, 1576–1584.
- Chrousos, G. P., & Gold, P. W. (1992).** The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *JAMA, 267*, 1244–1252.

- Cizza, G., & Rother, K. I.** (2011). Was Feuerbach right: Are we what we eat? *Journal of Clinical Investigation*, *121*, 2969–2971.
- Clark, A. M.** (2012). Reward processing: A global brain phenomenon? *Journal of Neurophysiology*, *109*(1), 1–4. <https://doi.org/10.1152/jn.00631.2011>
- Cohen, J. I.** (2000). Stress and mental health: A biobehavioral perspective. *Issues in Mental Health Nursing*, *21*(2), 185–202. <https://doi.org/10.1080/016128400248002>
- Cohen, S., Glazewski, R., Khan, S., & Khan, A.** (2001). Weight gain with risperidone among patients with mental retardation: Effect of calorie restriction. *Journal of Clinical Psychology*, *62*, 114–116.
- Cohen, S., Fitzgerald, B., & Okos, A.** (2003). Weight, lipids, glucose, and behavioral measures with ziprasidone treatment in a population with mental retardation. *Journal of Clinical Psychology*, *64*, 60–62.
- Colantuoni, C., Rada, P., McCarthy, J., Patten, C., Avena, N. M., Chadeayne, A., et al.** (2002). Evidence that intermittent, excessive sugar intake causes endogenous opioid dependence. *Obesity Research*, *10*(6), 478–488.
- Cole, M. G., & Dendukuri, N.** (2003). Risk factors for depression among elderly community subjects: A systematic review and meta-analysis. *American Journal of Psychiatry*, *160*, 1147–1156.
- Collins, P. Y., Patel, V., Joestl, S. S., et al.** (2011). Grand challenges in global mental health. *Nature*, *475*(7354), 27–30.
- Corman, C. L., Leung, N. M., & Guberman, A. H.** (1997). Weight gain in epileptic patients during treatment with valproic acid: A retrospective study. *Canadian Journal of Neurological Sciences*, *24*, 240–244.
- Correll, C. U., Druss, B. J., Lombardo, I., O’Gorman, C., Harnett, J. P., Sanders, K. N., Alvir, J. M., & Cuffel, B. J.** (2010). Findings of a US national cardiometabolic screening program among 10,084 psychiatric outpatients. *Psychiatric Services*, *61*, 892–898. doi: 10.1176/appi.ps.61.9.892.
- Cox, T. L., Krukowski, R., Love, S. J., et al.** (2012). Stress management-augmented behavioral weight loss intervention for African American women: A pilot, randomized controlled trial. *Health Education & Behavior*. doi: 10.1177/1090198112439411.
- Crisp, A. H., & McGuinness, B.** (1976). Jolly fat: Relation between obesity and psychoneurosis in the general population. *British Medical Journal*, *1*, 7–9.
- Corrigan, P.** (2004). How stigma interferes with mental health care. *American Psychologist*, *59*(7), 614–625.
- Cuevas, A., Alvarez, V., & Olivos, C.** (2009). The emerging obesity problem in Latin America. *Expert Review of Cardiovascular Therapy*, *7*(3), 281–288.
- Cullinan, J., & Gillespie, P.** (2016). Does overweight and obesity impact on self-rated health? Evidence using instrumental variables ordered probit models. *Health Economics*, *25*(10), 1341–1348. doi:10.1002/hec.3215.

**Cybulska, B., & Szostak-Węgierek, D. (2012).** Traditional Asian Diet. Why does it protect against myocardial infarction? *Problemy Higieny i Epidemiologii*, 93, 172–177. [Article in Polish]

**Dallman, M. F., Pecoraro, N., Akana, S. F., la Fleur, S. E., Gomez, F., Houshyar, H., et al. (2003).** Chronic stress and obesity: A new view of “comfort food.” *Proceedings of the National Academy of Sciences*, 100(20), 11696–11701.

**Dallman, M. F., Pecoraro, N. C., & la Fleur, S. E. (2005).** Chronic stress and comfort foods: Self-medication and abdominal obesity. *Brain, Behavior, and Immunity*, 19, 275–280.

**Dallman, M. F. (2010).** Stress-induced obesity and the emotional nervous system. *Trends in Endocrinology & Metabolism*, 21(3), 159–165.

**Dano, P., & Hahn-Pedersen, J. (1977).** Improvement in quality of life following jejunioileal bypass surgery for obesity. *Scandinavian Journal of Gastroenterology*, 12, 769–774.

**Davey Smith, G., & Ebrahim, S. (2003).** ‘Mendelian randomization’: Can genetic epidemiology contribute to understanding environmental determinants of disease? *International Journal of Epidemiology*, 32, 1–22.

**Davey Smith, G., Lawlor, D. A., Harbord, R., Timpson, N., Day, I., & Ebrahim, S. (2008).** Clustered environments and randomized genes: A fundamental distinction between conventional and genetic epidemiology. *PLoS Medicine*, 4, e352. <https://doi.org/10.1371/journal.pmed.0040352>

**David, B. A., Janet, L. M., & Moonseong, H. (1999).** Antipsychotic-induced weight gain: A comprehensive research synthesis. *American Journal of Psychiatry*, 156, 1686–1696.

**Davydov, D. M., Stewart, R., Ritchie, K., & Chaudieu, I. (2010).** Resilience and mental health. *Clinical Psychology Review*, 30, 479–495.

**de Graaf, R., Ten Have, M., van Gool, C., & van Dorsselaer, S. (2011).** Prevalence of mental disorders and trends from 1996 to 2009. Results from the Netherlands Mental Health Survey and Incidence Study-2. *Social Psychiatry and Psychiatric Epidemiology*. Advance online publication. <https://doi.org/10.1007/s00127-010-0334-8>

**Deckelbaum, R. J., & Williams, C. L. (2001).** Childhood obesity: The health issue. *Obesity Journal*, 9, 239S–243S.

**Dee, A., Kearns, K., O’Neill, C., Sharp, L., Staines, A., O’Dwyer, V., Fitzgerald, S., & Perry, I. J. (2014).** The direct and indirect costs of both overweight and obesity: A systematic review. *BMC Research Notes*, 7. <https://doi.org/10.1186/1756-0500-7-242>

**De Hert, M., Schreurs, V., Vancampfort, D., & VAN Winkel, R. (2009).** Metabolic syndrome in people with schizophrenia: A review. *World Psychiatry*, 8, 15–22.

**De Hert, M., Correll, C. U., Bobes, J., et al. (2011).** Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*, 10(1), 52–77.

**de Jonge, L., Zhao, X., Mattingly, M., et al. (2012).** Poor sleep quality and sleep apnea are associated with higher resting energy expenditure in obese individuals with short sleep duration. *Journal of Clinical Endocrinology & Metabolism*, 97, 2881–2889.

**De las Cuevas, C., Ramallo, Y., & Sanz, E. J. (2011).** Están relacionadas la obesidad y otras comorbilidades físicas con la enfermedad mental? [*Are obesity and other physical comorbidities related to mental illness?*] *Revista Psiquiatría y Salud Mental (Barcelona)*, *4*, 119-125.

**Dembling, B., Chen, D., & Vachon, L. (1999).** Life expectancy and causes of death in a population treated for serious mental illness. *Psychiatric Services*, *50*(8), 1036–1042.

**Demke, E. (2022).** The Vulnerability-Stress-Model-Holding Up the Construct of the Faulty Individual in the Light of Challenges to the Medical Model of Mental Distress. *Frontiers in Sociology*, *7*, 833987. <https://doi.org/10.3389/fsoc.2022.833987>

**De Moor, M. H. M., Boomsma, D. I., Stubbe, J. H., Willemsen, G., & de Geus, E. J. C. (2008).** Testing causality in the association between regular exercise and symptoms of anxiety and depression. *Archives of General Psychiatry*, *65*(7), 897–905.

**Dent, E., Hoogendijk, E. O., & Wright, O. R. L. (2018).** New insights into the anorexia of ageing. *Current Opinion in Clinical Nutrition & Metabolic Care*, *22*(1), 1. <https://doi.org/10.1097/MCO.0000000000000525>

**Department of Health. (2013).** Reducing Obesity and Improving Diet. Available online: <https://www.gov.uk/government/policies/reducing-obesity-and-improving-diet/> (accessed on 30 December 2013).

**Derenne, J. L., & Beresin, E. V. (2006).** Body image, media, and eating disorders. *Academic Psychiatry*, *30*(3), 257–261.

**Devlin, M. J., Yanovski, S. Z., & Wilson, G. T. (2000).** Obesity: What mental health professionals need to know. *American Journal of Psychiatry*, *157*(6), 854–866.

**Diamantis, D. V., Karatzi, K., Kantaras, P., Liatis, S., Iotova, V., Bazdraska, Y., Tankova, T., Cardon, G., Wikström, K., Rurik, I., et al. (2022).** Prevalence and socioeconomic correlates of adult obesity in Europe: The Feel4Diabetes Study. *International Journal of Environmental Research and Public Health*, *19*(19), 12572. <https://doi.org/10.3390/ijerph191912572>

**Di Chiara, G., & Imperato, A. (1988).** Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. *Proceedings of the National Academy of Sciences of the United States of America*, *85*(14), 5274–5278.

**Diener, E. (1984).** Subjective well-being. *Psychological Bulletin*, *95*, 542–575.

**Diener, E. (2000).** Subjective well-being: The science of happiness and a proposal for a national index. *American Psychologist*, *55*(1), 34–43. <https://doi.org/10.1037/0003-066X.55.1.34>

**Dinsa, G. D., Goryakin, Y., Fumagalli, E., & Suhrcke, M. (2012).** Obesity and socioeconomic status in developing countries: A systematic review. *Obesity Reviews*, *13*(11), 1067–1079.

**DiPietro, L., Anda, R. F., Williamson, D. F., & Stunkard, A. J. (1992).** Depressive symptoms and weight change in a national cohort of adults. *International Journal of Obesity and Related Metabolic Disorders*, *16*, 745–753.

**Dixon, J. B., Dixon, M. E., & O'Brien, P. E. (2003).** Depression in association with severe obesity: Changes with weight loss. *Archives of Internal Medicine*, *163*(17), 2058–2065.

- Dobbs**, R., Sawers, C., Thompson, F., Manyika, J., Woetzel, J. R., Child, P., McKenna, S., & Spatharou, A. (2014). Overcoming obesity: An initial economic analysis. *McKinsey Global Institute*. Jakarta, Indonesia.
- Doll**, H. A., Petersen, S. E., & Stewart-Brown, S. L. (2000). Obesity and physical and emotional well-being: Associations between body mass index, chronic illness, and the physical and mental components of the SF-36 questionnaire. *Obesity Research*, *8*, 160–170.
- Duong**, M., Cohen, J. I., & Convit, A. (2012). High cortisol levels are associated with low-quality food choice in type 2 diabetes. *Endocrine*, *41*, 76–81.
- Egger**, G., Swinburn, B., & Islam, F. M. (2012). Economic growth and obesity: An interesting relationship with worldwide implications. *Economics & Human Biology*, *10*(2), 147–153.
- Eisenmann**, J. C., Katzmarzyk, P. T., Arnall, D. A., Kanuha, V., Interpretor, C., & Malina, R. M. (2000). Growth and overweight of Navajo youth: Secular changes from 1955 to 1997. *International Journal of Obesity and Related Metabolic Disorders*, *24*, 211–218.
- Elder**, Glen H. (1998). The life course as developmental theory. *Child Development*, *69*(1), 1–12.
- Elder**, C. R., Gullion, C. M., Funk, K. L., Debar, L. L., Lindberg, N. M., & Stevens, V. J. (2012). Impact of sleep, screen time, depression, and stress on weight change in the intensive weight loss phase of the LIFE study. *International Journal of Obesity (London)*, *36*(1), 86–92.
- Elobeid**, M. A., & Allison, D. B. (2008). Putative environmental-endocrine disruptors and obesity: A review. *Current Opinion in Endocrinology, Diabetes, and Obesity*, *15*(5), 403–408.
- Emmer**, C., Bosnjak, M., & Mata, J. (2020). The association between weight stigma and mental health: A meta-analysis. *Obesity Reviews*, *21*, e12935. <https://doi.org/10.1111/obr.12935>
- Emery**, C. F., Fondow, M. D., Schneider, C. M., Christofi, F. L., Hunt, C., Busby, A. K., Needleman, B. J., Melvin, W. S., & Elsayed-Awad, H. M. (2007). Gastric bypass surgery is associated with reduced inflammation and less depression: A preliminary investigation. *Obesity Surgery*, *17*, 759–763.
- Epel**, E., Lapidus, R., McEwen, B., & Brownell, K. (2001). Stress may add bite to appetite in women: A laboratory study of stress-induced cortisol and eating behavior. *Psychoneuroendocrinology*, *26*(1), 37–49.
- Eriksson**, M. (2016). The Sense of Coherence in the Salutogenic Model of Health. In M. B. Mittelmark, S. Sagy, M. Eriksson, et al. (Eds.), *The Handbook of Salutogenesis* (Chapter 11). Cham, CH: Springer. doi: 10.1007/978-3-319-04600-6\_11.
- Eriksson**, M., & Lindström, B. (2005). Validity of Antonovsky's sense of coherence scale: A systematic review. *Journal of Epidemiology and Community Health*, *59*, 460–466.
- Everitt**, B. J., Belin, D., Economidou, D., Pelloux, Y., Dalley, J. W., & Robbins, T. W. (2008). Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences*, *363*(1507), 3125–3135.

- Everson**, S. A., Roberts, R. E., Goldberg, D. E., & Kaplan, G. A. (1998). Depressive symptoms and increased risk of stroke mortality over a 29-year period. *Archives of Internal Medicine*, *158*, 1133–1138.
- Ezzati**, M., Lopez, A. D., Rodgers, A., Vander Hoorn, S., & Murray, C. J. L. (2002). Selected major risk factors and global and regional burden of disease. *The Lancet*, *360*, 1347–1360.
- Fabricatore**, A. N., & Wadden, T. A. (2004). Psychological aspects of obesity. *Clinics in Dermatology*, *22*, 332–337.
- Farmer**, A., Korszun, A., Owen, M. J., Craddock, N., Jones, L., Jones, I., et al. (2008). Medical disorders in people with recurrent depression. *British Journal of Psychiatry*, *192*, 351–355.
- Fava**, M. (2000). Weight gain and antidepressants. *Journal of Clinical Psychiatry*, *61*, 37–41.
- Fayers**, P. M., & Machin, D. (2016). *Quality of life: The assessment, analysis and reporting of patient-reported outcomes* (3rd ed.). Hoboken, NJ: Wiley Blackwell.
- Federal Statistical Office**. (2007). *Federal Health Monitoring Information Services*. Federal Statistical Office Germany, Wiesbaden. Retrieved from <https://www.destatis.de>.
- Ferrari**, A. J., Norman, R. E., Freedman, G., et al. (2014). The burden attributable to mental and substance use disorders as risk factors for suicide: Findings from the Global Burden of Disease Study 2010. *PLoS One*, *9*(4), e91936.
- Ferraro**, K. F., & Yu, Y. (1995). Body weight and self-ratings of health. *Journal of Health and Social Behavior*, *36*, 274–284.
- Fernstrom**, M. H., Krowinski, R. L., & Kupfer, D. J. (1986). Chronic imipramine treatment and weight gain. *Psychological Research*, *17*, 269–273.
- Field**, A. (2013). *Discovering statistics using IBM SPSS Statistics*. London: SAGE.
- Figlewicz**, D. P., Sipols, A. J., Bennett, J., Evans, S. B., Kaiyala, K., & Benoit, S. C. (2004). Intraventricular insulin and leptin reverse place preference conditioned with high-fat diet in rats. *Behavioral Neuroscience*, *118*(3), 479–487.
- Fine**, J. T., Colditz, G. A., Coakley, E. H., et al. (1999). A prospective study of weight change and health-related quality of life in women. *JAMA*, *282*, 2136–2142.
- Fink**, G. (2010). Stress: Definition and history. In G. Fink (Ed.), *Stress Science: Neuroendocrinology* (pp. 3–9).
- Finkelstein**, E. A., Trogon, J. G., Cohen, J. W., & Dietz, W. (2009). Annual medical spending attributable to obesity: Payer- and service-specific estimates. *Health Affairs*, *28*, w822–w831. doi:10.1377/hlthaff.28.5.w822.
- Fitzgibbon**, M. L., Stolley, M. R., & Kirschenbaum, D. S. (1993). Obese people who seek treatment have different characteristics than those who do not seek treatment. *Health Psychology*, *12*, 342–345.
- Flegal**, K. M., Carroll, M. D., Kit, B. K., & Ogden, C. L. (2012). Prevalence of obesity and trends in the distribution of body mass index among U.S. adults. *JAMA*, *307*(5), 491–497.

- Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2007).** Cause-specific excess death associated with underweight, overweight and obesity. *JAMA*, *298*(17), 2028–2037.
- Foley, D., & Morley, K. I. (2011).** Systematic review of early cardio-metabolic outcomes of the first treated episode of psychosis. *Archives of General Psychiatry*, *68*, 609–616.  
doi:10.1001/archgenpsychiatry.2011.2
- Food and Agriculture Organization of the United Nations. (2013).** *The State of Food and Agriculture*. Rome: FAO. Retrieved from <http://www.fao.org/docrep/018/i3300e/i3300e00.htm> (accessed: 2022.06.26).
- Fontaine, K. R., & Bartlett, S. J. (1998).** Estimating health-related quality of life in obese individuals. *Disease Management & Health Outcomes*, *3*, 61–70.
- Fontaine, K. R., Cheskin, L. J., & Barofsky, I. (1996).** Health-related quality of life in obese persons seeking treatment. *Journal of Family Practice*, *43*, 265–270.
- Fontaine, K. R., & Barofsky, I. (2001).** Obesity and health-related quality of life. *Obesity Reviews*, *2*(3), 173-182. doi: 10.1046/j.1467-789x.2001.00032.x
- Forman-Hoffman, V. L., Yankey, J. W., Hillis, S. L., Wallace, R. B., & Wolinsky, F. D. (2007).** Weight and depressive symptoms in older adults: Direction of influence? *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *62*(1), S43-S51.
- Frank, E., Kupfer, D. J., Bulik, C. M., & Levenson, J. A. (1990).** Imipramine and weight gain during the treatment of recurrent depression. *Journal of Affective Disorders*, *20*, 165–172.
- Franko, D. L., Striegel-Moore, R. H., Thompson, D., Schreiber, G. B., & Daniels, S. R. (2005).** Does adolescent depression predict obesity in black and white young adult women? *Psychological Medicine*, *35*(10), 1505-1513.
- Frazier, J. A., Biederman, J., Tohen, M., Feldman, P. D., Jacobs, T. J., & Toma, V. (2001).** A prospective open-label treatment trial of olanzapine monotherapy in children and adolescents with bipolar disorder. *Journal of Child and Adolescent Psychopharmacology*, *11*, 239–250.
- Frayn, K. N., & Kingman, S. M. (1995).** Dietary sugars and lipid metabolism in humans. *The American Journal of Clinical Nutrition*, *62*, 250S–61S.
- Friedman, M. A., & Brownell, K. D. (1995).** Psychological correlates of obesity: Moving to the next research generation. *Psychological Bulletin*, *117*(1), 3–20.
- Friedman, K. E., Reichmann, S. K., Costanzo, P. R., & Musante, G. J. (2002).** Body image partially mediates the relationship between obesity and psychological distress. *Obesity Research*, *10*, 33–41.
- Friedmann, J. M., Elasy, T., & Jensen, G. L. (2001).** The relationship between body mass index and self-reported functional limitation among older adults: A gender difference. *Journal of the American Geriatrics Society*, *49*(4), 398–403.
- Fruh, S. M., Graves, R. J., Hauff, C., Williams, S. G., & Hall, H. R. (2021).** Weight bias and stigma: Impact on health. *Nursing Clinics of North America*, *56*(4), 479-493.
- Fry, J., & Finley, W. (2005).** The prevalence and costs of obesity in the EU. *Proceedings of the Nutrition Society*, *64*(3), 359–362.

**GBD 2019 Mental Disorders Collaborators.** (2022). Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. *The Lancet. Psychiatry*, 9(2), 137–150. [https://doi.org/10.1016/S2215-0366\(21\)00395-3](https://doi.org/10.1016/S2215-0366(21)00395-3)

**Gadalla, T., & Piran, N.** (2008). Psychiatric comorbidity in women with disordered eating behavior: A national study. *Women & Health*, 48(4), 467-484.

**Gafoor, R., Booth, H. P., & Gulliford, M. C.** (2018). Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: Population based cohort study. *BMJ*, 361, k1951. doi:10.1136/bmj.k1951

**Galderisi, S., Heinz, A., Kastrup, M., Beezhold, J., & Sartorius, N.** (2015). Toward a new definition of mental health. *World Psychiatry*, 14(2), 231-233. doi:10.1002/wps.20231

**Ganguli, R., Brar, J. S., & Ayrton, Z.** (2001). Weight gain over 4 months in schizophrenia patients: A comparison of olanzapine and risperidone. *Schizophrenia Research*, 49, 261–267.

**Garg, N., Wansink, B., & Inman, J. J.** (2007). The influence of incidental affect on consumers' food intake. *Journal of Marketing*, 71(1), 194–206.

**Gariepy, G., Nitka, D., & Schmitz, N.** (2010). The association between obesity and anxiety disorders in the population: A systematic review and meta-analysis. *International Journal of Obesity*, 34(3), 407-419.

**Garrison, C. Z., Schluchter, M. D., Schoenbach, V. J., & Kaplan, B. K.** (1989). Epidemiology of depressive symptoms in young adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, 28, 343–351.

**Ge, X., Elder, G. H., Regnerus, M., & Cox, C.** (2001). Pubertal transitions, perceptions of being overweight, and adolescents' psychological maladjustment: Gender and ethnic differences. *Social Psychology Quarterly*, 64, 363–375.

**Gentry, K., Halverson, J. D., & Heisler, S.** (1984). Psychologic assessment of morbidly obese patients undergoing gastric bypass: A comparison of preoperative and postoperative adjustments. *Surgery*, 95, 215–220.

**Ghusn, W., Bouchard, C., Frye, M. A., & Acosta, A.** (2022). Weight-centric treatment of depression and chronic pain. *Obesity Pillars (Online)*, 3, 100025. <https://doi.org/10.1016/j.obpill.2022.100025>

**Gibb, B. E., Chelminski, I., & Zimmerman, M.** (2007). Childhood emotional, physical, and sexual abuse, and diagnoses of depressive and anxiety disorders in adult psychiatric outpatients. *Depression and Anxiety*, 24, 256–263.

**Gidding, S. S., Bao, W., Srinivasan, S. R., & Berenson, G. S.** (1995). Effects of secular trends in obesity on coronary risk factors in children: The Bogalusa Heart Study. *Journal of Pediatrics*, 127, 868–874.

**Ginsberg, L., Calabrese, J., Bowden, C., et al.** (2003). Effects of lamotrigine and lithium on body weight in bipolar I disorder. Program and abstracts of the 43rd Annual New Clinical Drug Evaluation Unit (NCDEU) Meeting; May 28–June 1, 2003; Boca Raton, Florida. Poster Session II-16.

- Glassman, A. H., & Shapiro, P. A. (1998).** Depression and the course of coronary artery disease. *American Journal of Psychiatry, 155*, 4–11.
- Grajales, D., Ferreira, V., & Valverde, Á. M. (2019).** Second-Generation Antipsychotics and Dysregulation of Glucose Metabolism: Beyond Weight Gain. *Cells, 8*(11), 1336. <https://doi-10.10013b5hi048a.han.medunigraz.at/10.3390/cells8111336>
- Gluck, M. E., Geliebter, A., Hung, J., & Yahav, E. (2004).** Cortisol, hunger, and desire to binge eat following a cold stress test in obese women with binge eating disorder. *Psychosomatic Medicine, 66*, 876–881.
- Goh, C., & Agius, M. (2010).** The stress-vulnerability model: How does stress impact on mental illness at the level of the brain and what are the consequences? *Psychiatria Danubina, 22*(2), 198–202. PMID: 20562747.
- Golden, S. H., Lazo, M., Carnethon, M., Bertoni, A. G., Schreiner, P. J., Roux, A. V., et al. (2008).** Examining a bidirectional association between depressive symptoms and diabetes. *JAMA, 299*(23), 2751–2759.
- Goodman, E., & Whitaker, R. C. (2002).** A prospective study of the role of depression in the development and persistence of adolescent obesity. *Pediatrics, 110*(3), 497–504.
- Goodpaster, B. H., Krishnaswami, S., Resnick, H., Kelley, D. E., Haggerty, C., Harris, T. B., et al. (2003).** Association between regional adipose tissue distribution and type 2 diabetes and impaired glucose tolerance in elderly men and women. *Diabetes Care, 26*(2), 372–379.
- Gopalan, C. (2013).** The changing nutrition scenario. *Indian Journal of Medical Research, 138*, 392–397.
- Gorasso, V., Moyersoen, I., Heyden, V. der, De Ridder, K., Vandevijvere, S., Vansteelandt, S., et al. (2021).** Health care costs and lost productivity costs related to excess weight in Belgium [Internet]. Retrieved from <https://www.researchsquare.com/article/rs-860500/v1>
- Gothelf, B., Falk, B., & Singer, P. (2002).** Weight gain associated with increased food intake and low habitual activity levels in male adolescent schizophrenic inpatients treated with olanzapine. *American Journal of Psychiatry, 159*(6), 1055–1057.
- Greenberg, P. E., Stiglin, L. E., Finkelstein, S. N., & Berndt, E. R. (1993).** The economic burden of depression in 1990. *Journal of Clinical Psychiatry, 54*, 405–418.
- Greenberg, B. S., Eastin, M., Hofschire, L., Lachlan, K., & Brownell, K. D. (2003).** Portrayals of overweight and obese individuals on commercial television. *American Journal of Public Health, 93*, 1342–1348.
- Griffiths, C. A., Ryan, P., & Foster, J. H. (2011).** Thematic analysis of Antonovsky’s sense of coherence theory. *Scandinavian Journal of Psychology, 52*, 168–173.
- Groesz, L. M., McCoy, S., Carl, J., Saslow, L., Stewart, J., Adler, N., et al. (2012).** What is eating you? Stress and the drive to eat. *Appetite, 58*(2), 717–721.
- Grover, S., Nebhinani, N., Chakrabarti, S., Avasthi, A., & Kulhara, P. (2011).** Metabolic syndrome among patients receiving clozapine: A preliminary estimate. *Indian Journal of Pharmacology, 43*, 591–595.

- Grucza**, R. A., Przybeck, T. R., & Cloninger, C. R. (2007). Prevalence and correlates of binge eating disorder in a community sample. *Comprehensive Psychiatry*, *48*, 124–131.
- Gu**, D., He, J., Duan, X., Reynolds, K., Wu, X., Chen, J., et al. (2006). Body weight and mortality among men and women in China. *JAMA*, *295*(7), 776–783
- Guallar-Castillon**, P., Lopez Garcia, E., Lozano Palacios, L., Gutierrez-Fisac, J. L., Banegas Banegas, J. R., Lafuente Urdinguio, P. J., & Rodriguez Artalejo, F. (2002). The relationship of overweight and obesity with subjective health and use of health-care services among Spanish women. *International Journal of Obesity and Related Metabolic Disorders*, *26*, 247–252.
- Gupta**, A., Silman, A. J., Ray, D., Morriss, R., Dickens, C., MacFarlane, G. J., et al. (2007). The role of psychosocial factors in predicting the onset of chronic widespread pain: Results from a prospective population-based study. *Rheumatology (Oxford)*, *46*, 666–671.
- Gustafson**, T. B., & Sarwer, D. B. (2004). Childhood sexual abuse and obesity. *Obesity Reviews*, *5*, 129–135.
- Gutiérrez**, J. P., Rivera, D. J., Shamah, L. T., Villalpando, H. S., Franco, A., & Cuevas, N. L. (2012). Encuesta Nacional de Salud y Nutrición 2012. Datos Nacionales. México: Instituto Nacional de Salud Pública.
- Hachuła**, M., Kosowski, M., Zielańska, K., Basiak, M., & Okopień, B. (2023). The impact of various methods of obesity treatment on the quality of life and mental health: A narrative review. *International Journal of Environmental Research and Public Health*, *20*(3), 2122. <https://doi.org/10.3390/ijerph20032122>
- Hafner**, R. J., Watts, J. M., & Rogers, J. (1991). Quality of life after gastric bypass for morbid obesity. *International Journal of Obesity*, *15*, 555–560.
- Halmi**, K. A., Stunkard, A. J., & Mason, E. E. (1980). Emotional responses to weight reduction by three methods: Gastric bypass, jejunioileal bypass, and diet. *American Journal of Clinical Nutrition*, *33*, 446–451.
- Hansen**, T., Ingason, A., Djurovic, S., Melle, I., Fenger, M., Gustafsson, O., et al. (2011). At-risk variant in TCF7L2 for type II diabetes increases risk of schizophrenia. *Biological Psychiatry*, *70*, 59–63.
- Hardy**, M. A., Acciai, F., & Reyes, A. M. (2014). How health conditions translate into self-ratings: A comparative study of older adults across Europe. *Journal of Health and Social Behavior*, *55*(3), 320–341.
- Harris**, M. B., & Green, D. (1982). Psychosocial effects of gastric reduction surgery for obesity. *International Journal of Obesity*, *6*, 527–539.
- Harvey**, B. H., & Bouwer, C. D. (2000). Neuropharmacology of paradoxical weight gain with selective serotonin reuptake inhibitors. *Clinical Neuropharmacology*, *23*, 90–97.
- Hasin**, D. S., Goodwin, R. D., Stinson, F. S., & Grant, B. F. (2005). Epidemiology of major depressive disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Archives of General Psychiatry*, *62*, 1097–1106.
- Haupt**, D. W., & Newcomer, J. W. (2002). Abnormalities in glucose regulation associated with mental illness and treatment. *Journal of Psychosomatic Research*, *53*, 925–933.

- Hawke**, A., O'Brien, P., Watts, J., Hall, J., Dunstan, R. E., Walsh, J. F., Slavotinek, A. H., & Elmslie, R. G. (1990). Psychosocial and physical activity changes after gastric restrictive procedures for morbid obesity. *Australian and New Zealand Journal of Surgery*, *60*, 755–758.
- Haycock**, P. C., Burgess, S., Wade, K. H., Bowden, J., Relton, C., & Davey Smith, G. (2016). Best (but oft-forgotten) practices: The design, analysis, and interpretation of Mendelian randomization studies. *The American Journal of Clinical Nutrition*, *103*(4), 965–978. doi:10.3945/ajcn.115.118216
- Hays**, N. P., & Roberts, S. B. (2006). The anorexia of aging in humans. *Physiology & Behavior*, *88*(3), 257-266.
- Headey**, B. W., Kelley, J., & Wearing, A. J. (1993). Dimensions of mental health: Life satisfaction, positive affect, anxiety, and depression. *Social Indicators Research*, *29*, 63 – 82.
- Heatherton**, T. F., Polivy, J., & Herman, C. P. (1989). Restraint and internal responsiveness: Effects of placebo manipulations of hunger state on eating. *Journal of Abnormal Psychology*, *98*(1), 89–92.
- Hennings**, J. M., Heel, S., Lechner, K., Uhr, M., Dose, T., Schaaf, L., Holsboer, F., Lucae, S., Fulda, S., & Kloiber, S. (2019). Effect of mirtazapine on metabolism and energy substrate partitioning in healthy men. *JCI Insight*, *4*(1), e123786. doi:10.1172/jci.insight.123786
- Heo**, M., Pietrobelli, A., Fontaine, K. R., Sirey, J. A., & Faith, M. S. (2006). Depressive mood and obesity in US adults: Comparison and moderation by sex, age, and race. *International Journal of Obesity*, *30*, 513– 519.
- Herva**, A., Laitinen, J., Miettunen, J., Veijola, J., Karvonen, J. T., Laksy, K., et al. (2006). Obesity and depression: Results from the longitudinal Northern Finland 1966 Birth Cohort Study. *International Journal of Obesity*, *30*, 520–527.
- Hettema**, J. M., Neale, M. C., & Kendler, K. S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. *American Journal of Psychiatry*, *158*(10), 1568–1578.
- Hillman**, J. B., Dorn, L. D., & Huang, B. (2010). Association of anxiety and depressive symptoms and adiposity among adolescent females using Dual Energy X-ray Absorptiometry. *Clinical Pediatrics (Philadelphia)*, *49*(7), 671–677. doi:10.1177/0009922810363155.
- Himmerich**, H., Minkwitz, J., & Kirkby, K. C. (2015). Weight Gain and Metabolic Changes During Treatment with Antipsychotics and Antidepressants. *Endocrine, Metabolic & Immune Disorders Drug Targets*, *15*, 252-260. doi:10.2174/1871530315666150623092031.
- Himmerich**, H., Fulda, S., Künzel, H. E., Pfennig, A., Dzaja, A., Cummings, D. E., & Pollmächer, T. (2005). Ghrelin plasma levels during psychopharmacological treatment. *Neuropsychobiology*, *52*, 11-16.
- Himes**, S. M., & Thompson, J. K. (2007). Fat stigmatization in television shows and movies: A content analysis. *Obesity (Silver Spring)*, *15*, 712–718.
- Hitt**, H. C., McMillen, R. C., Thornton-Neaves, T., Koch, K., & Cosby, A. G. (2007). Comorbidity of obesity and pain in a general population: Results from the Southern Pain Prevalence Study. *The Journal of Pain*, *8*, 430–436.

- Hocking**, M. P., Duerson, M. C., O'Leary, J. P., & Woodward, E. R. (1983). Jejunoileal bypass for morbid obesity: Late follow-up in 100 cases. *New England Journal of Medicine*, 308, 995–999.
- Hoek**, H. W., van Harten, P. N., Hermans, K. M. K., Katzman, M. A., Matroos, G. E., & Susser, E. S. (2005). The incidence of anorexia nervosa on Curacao. *The American Journal of Psychiatry*, 162, 748–752.
- Holsboer**, F. (2000). The corticosteroid receptor hypothesis of depression. *Neuropsychopharmacology*, 23, 547–751.
- Holt**, R. I. G., & Peveler, R. C. (2009). Obesity, serious mental illness and antipsychotic drugs. *Diabetes, Obesity & Metabolism*, 11, 665–679.
- Holt**, R.I.G. (2019). The Management of Obesity in People with Severe Mental Illness: An Unresolved Conundrum. *Psychotherapy and Psychosomatics*, 88(6), 327–332.
- Hong**, C. J., Lin, C. H., & Yu, Y. W. (2001). Genetic variants of the serotonin system and weight change during clozapine treatment. *Pharmacogenetics*, 11, 265–268.
- Horwitz**, M., Tusie, M., Calzada, R., & Vázquez, V. (2008). La obesidad y el síndrome metabólico como problema de salud pública. Una reflexión. Primera parte. *Salud Mental*, 31(6), 489-496.
- Hori**, H., Teraishi, T., Sasayama, D., et al. (2011). Poor sleep is associated with exaggerated cortisol response to the combined dexamethasone/CRH test in a non-clinical population. *Journal of Psychiatric Research*, 45, 1257–1263.
- Horner Jr**, T. N., & Utermohlen, V. (1993). A multivariate analysis of psychological factors related to body mass index and eating preoccupation in female college students. *Journal of the American College of Nutrition*, 12, 459–465.
- Hu**, G., Tuomilehto, J., Silventoinen, K., Barengo, N. C., Peltonen, M., & Jousilahti, P. (2005). The effects of physical activity and body mass index on cardiovascular, cancer and all-cause mortality among 47 212 middle-aged Finnish men and women. *International Journal of Obesity*, 29, 894–902.
- Huber**, J. D. (2008). Diabetes, cognitive function, and the blood-brain barrier. *Current Pharmaceutical Design*, 14(16), 1594-1600.
- Hyde**, M., Wiggins, R. D., Higgs, P., & Blane, D. B. (2003). A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). *Aging & Mental Health*, 7(3), 186-194.
- Iden**, K.R., Engedal, K., Hjørleifsson, S., & Ruths, S. (2014). Prevalence of depression among recently admitted long-term care patients in Norwegian nursing homes: associations with diagnostic workup and use of antidepressants. *Dementia and Geriatric Cognitive Disorders*, 37, 154-162.
- Idler**, E.L., & Benyamini, Y. (1997). Self-rated health and mortality: A review of twenty-seven community studies. *Journal of Health and Social Behavior*, 38, 21-37.

- Ikedo**, H., West, D. B., Pustek, J. J., Figlewicz, D. P., Greenwood, M. R. C., Porte, D., Jr, et al. (1986). Intraventricular insulin reduces food intake and body weight of lean but not obese Zucker rats. *Appetite*, 7(4), 381–386.
- Imai**, K., Gregg, E. W., Chen, Y. J., Zhang, P., de Rekeneire, N., & Williamson, D. F. (2008). The association of BMI with functional status and self-rated health in U.S. adults. *Obesity*, 16, 402–408.
- Imayama**, I., Alfano, C. M., Kong, A., Foster-Schubert, K. E., Bain, C. E., Xiao, L., Duggan, C., Wang, C. Y., Campbell, K. L., Blackburn, G. L., & McTiernan, A. (2011). Dietary weight loss and exercise interventions effects on quality of life in overweight/obese postmenopausal women: A randomized controlled trial. *International Journal of Behavioral Nutrition and Physical Activity*, 8, 118.
- International Association for the Study of Obesity**. (2006, September 1). Global obesity prevalence in adults. Retrieved from <http://www.iaso.org>
- Istvan**, J., Zavela, K., & Weidner, G. (1992). Body weight and psychological distress in NHANES I. *International Journal of Obesity and Related Metabolic Disorders*, 16, 999–1003.
- Jackson**, S. E., Beeken, R. J., & Wardle, J. (2014). Perceived weight discrimination and changes in weight, waist circumference, and weight status. *Obesity*, 22(12), 2485–2488.
- Jahoda**, M. (1958). Current concepts of positive mental health. New York: Basic Books.
- James**, W. P. (2008). The epidemiology of obesity: The size of the problem. *Journal of Internal Medicine*, 263(4), 336–352.
- Jarosz**, M., & Rychlik, E. (2008). Overweight and obesity among adults in Poland, 1983–2005. *Advances in Medical Sciences*, 53(2), 158–166.
- Jastreboff**, A. M., Sinha, R., Lacadie, C., Small, D. M., Sherwin, R. S., & Potenza, M. N. (2013). Neural correlates of stress- and food-cue-induced food craving in obesity: Association with insulin levels. *Diabetes Care*. Advance online publication. <https://doi.org/10.2337/dc12-1939>
- Javaras**, K. (2008). Co-occurrence of binge eating disorder with psychiatric and medical disorders. *Journal of Clinical Psychiatry*, 69, 266–273.
- Jayawickreme**, J., Pawelski, J., & Seligman, M. (2008). Conference presentation: Subjective measures of well-being and the science of happiness: Historical origins and philosophical foundations. Birmingham, AL: Positive Psychology and Nussbaum's Capabilities Approach.
- Jinks**, C., Jordan, K., & Croft, P. (2006). Disabling knee pain—another consequence of obesity: Results from a prospective cohort study. *BMC Public Health*, 6, 258.
- John**, U., Meyer, C., Rumpf, H.-J., & Hapke, U. (2006). Psychiatric comorbidity including nicotine dependence among individuals with eating disorder criteria in an adult general population sample. *Psychiatry Research*, 141, 71–79.
- Jonsson**, S., Hedblad, B., Engstrom, G., Nilsson, P., Berglund, G., & Janzon, L. (2002). Influence of obesity on cardiovascular risk: Twenty-three-year follow-up of 22,025 men from an urban Swedish population. *International Journal of Obesity and Related Metabolic Disorders*, 26, 1046–1053.

**Kalimo, R., Pahkin, K., Mutanen, P., et al. (2003).** Staying well or burning out at work: Work characteristics and personal resources as long-term predictors. *Work and Stress*, 17, 109–122.

**Kalucy, R. S., & Crisp, A. H. (1974).** Some psychological and social implications of massive obesity. *Journal of Psychosomatic Research*, 8, 465–473.

**Kappelmann, N., Arloth, J., Georgakis, M. K., et al. (2021).** Dissecting the Association Between Inflammation, Metabolic Dysregulation, and Specific Depressive Symptoms: A Genetic Correlation and 2-Sample Mendelian Randomization Study. *JAMA Psychiatry*, 78(2), 161–170. <https://doi.org/10.1001/jamapsychiatry.2020.3436>

**Kaplan, H. I., & Sadock, B. J. (1998).** *Synopsis of psychiatry* (8th ed.). Williams & Wilkins.

**Karlsson, J., Taft, C., Sjostrom, L., Torgerson, J. S., & Sullivan, M. (2003).** Psychosocial functioning in the obese before and after weight reduction: Construct validity and responsiveness of the obesity-related Problems scale. *International Journal of Obesity and Related Metabolic Disorders*, 27, 617–630.

**Karnofsky, D. A., & Burchenal, J. H. (1949).** The clinical evaluation of chemotherapeutic agents in cancer. In C. M. Macleod (Ed.), *Evaluation of Chemotherapeutic Agents* (pp. 191–205). Columbia University Press.

**Kearney, M. W. (2017).** Cross-lagged panel analysis. In *The SAGE Encyclopedia of Communication Research Methods*. SAGE Publications, Inc. doi:10.4135/9781483381411.n117

**Kearns, K., Dee, A., Fitzgerald, A. P., Doherty, E., & Perry, I. J. (2014).** Chronic disease burden associated with overweight and obesity in Ireland: The effects of a small BMI reduction at population level. *BMC Public Health*, 14, 143.

**Keck, P., Versiani, M., & Potkin, S. (2003).** Ziprasidone in the treatment of acute bipolar mania: A three week placebo controlled, double blind randomized trial. *American Journal of Psychiatry*, 160, 741–748.

**Kelley, A. E., Bakshi, V. P., Fleming, S., & Holahan, M. R. (2000).** A pharmacological analysis of the substrates underlying conditioned feeding induced by repeated opioid stimulation of the nucleus accumbens. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, 23(4), 455–467. doi:10.1016/S0893-133X(00)00136-7

**Kenny, D. A. (2014).** Cross-lagged panel design. In *Wiley StatsRef: Statistics Reference Online*. John Wiley & Sons, Ltd. doi:10.1002/9781118445112.stat06464

**Kepka, D., Ayala, G. X., & Cherrington, A. (2007).** Do Latino immigrants link self-rated health with BMI and health behaviors? *American Journal of Health Behavior*, 31(5), 535–544. doi:10.5555/ajhb.2007.31.5.535

**Keramat, S. A., Alam, K., Ahinkorah, B. O., et al. (2021).** Obesity, disability and self-perceived health outcomes in Australian adults: A longitudinal analysis using 14 annual waves of the HILDA cohort. *ClinicoEconomics and Outcomes Research*, 13, 777–788. doi:10.2147/CEOR.S318094

**Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S., et al. (1994).** Lifetime and 12-month prevalence of DSM–III–R psychiatric disorders in the United States: Results from the National Comorbidity Survey. *Archives of General Psychiatry*, 51, 8–19.

**Kessler, R. C., Cox, B. J., Green, J. G., et al. (2011).** The effects of latent variables in the development of comorbidity among common mental disorders. *Depression and Anxiety, 28*(1), 29-39.

**Kessler, R. C., McLaughlin, K. A., Green, J. G., et al. (2010).** Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry, 197*, 378–385.

**Kessler, R. C., Üstün, T. B. (Eds.). (2008).** The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. New York: Cambridge University Press.

**Kessler, R. C., Wang, P. S. (2008).** The descriptive epidemiology of commonly occurring mental disorders in the United States. *Annual Review of Public Health, 29*, 115–129.

**Keyes, C. L. M. (2005).** Mental Illness and/or Mental Health? Investigating Axioms of the Complete State Model Of Health. *Journal of Consulting and Clinical Psychology, 73*(3), 539–548. doi:10.1037/0022-006X.73.3.539.

**Keyes, C. L. M. (2002).** The mental health continuum: From languishing to flourishing in life. *Journal of Health and Social Behavior, 43*, 207–222.

**Keyes, C. L. M. (2003a).** Complete mental health: An agenda for the 21st century. In C. L. M. Keyes & J. Haidt (Eds.), *Flourishing: Positive Psychology and the Life Well-Lived* (pp. 293–312). Washington, DC: American Psychological Association.

**Keyes, C. L. M. (2003b).** Promoting a life worth living: Human development from the vantage points of mental illness and mental health. In R. M. Lerner, F. Jacobs, & D. Wertlieb (Eds.), *Promoting Positive Child, Adolescent, and Family Development: A Handbook of Program and Policy Innovations* (Vol. 4, pp. 257–274). Thousand Oaks, CA: Sage.

**Keyes, C. L. M., Lopez, S. J. (2002).** Toward a science of mental health: Positive directions in diagnosis and interventions. In C. R. Snyder & S. J. Lopez (Eds.), *Handbook of Positive Psychology* (pp. 45–59). New York: Oxford University Press.

**Keyes, C. L. M., Shmotkin, D., & Ryff, C. D. (2002).** Optimizing well-being: The empirical encounter of two traditions. *Journal of Personality and Social Psychology, 82*(6), 1007–1022. <https://doi-10.1037/0022-3514.82.6.1007>.

**Keyes, C. L. M., & Ryff, C. D. (2003).** Somatization and mental health: A comparative study of the idiom of distress hypothesis. *Social Science and Medicine, 57*, 1833–1845.

**Keyes, C. L. M. (2007).** Promoting and Protecting Mental Health as Flourishing. A Complementary Strategy for Improving National Mental Health. *American Psychologist, 62*, 95–108. doi:10.1037/0003-066X.62.2.95.

**Keyes, C. L. M. (1998).** Social well-being. *Social Psychology Quarterly, 61*(2), 121–140. <https://doi-10.1037/0022-3514.61.2.121>.

**Keyes, C. L. M. (1998a).** Social well-being. *Social Psychology Quarterly, 61*(2), 121–140. <https://doi-10.1037/0022-3514.61.2.121>.

**Keyes, C. L. M. (1998b).** Social well-being. *Social Psychology Quarterly, 61*, 121–140.

**Keyes CL.** (2006). Mental health in adolescence: is America's youth flourishing? *American Journal of Orthopsychiatry*, 76, 395–402.

**Keyes, C. L. M., & Annas, J.** (2009). Feeling good and functioning well: Distinctive concepts in ancient philosophy and contemporary science. *The Journal of Positive Psychology*, 4(3), 197–201. <https://doi-org-10013b5o60008.han.medunigraz.at/10.1080/17439760902844228>.

**Keyes, Corey.** (2013). Mental Health as a Complete State: How the Salutogenic Perspective Completes the Picture. *Bridging Occupational, Organizational and Public Health: A Transdisciplinary Approach*, 179-192. 10.1007/978-94-007-5640-3-11.

**Kieling C, Baker-Henningham H, Belfer M, et al.** (2011). Child and adolescent mental health worldwide: evidence for action. *The Lancet*, 378, 1515–25.

**Kim, S., & Popkin, B. M.** (2006). Commentary: Understanding the epidemiology of overweight and obesity—a real global public health concern. *International Journal of Epidemiology*, 35, 60–67.

**King, W. C., Chen, J. Y., Mitchell, J. E., Kalarchian, M. A., Steffen, K. J., Engel, S. G., et al.** (2012). Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA : the Journal of the American Medical Association*, 307(23), 2516–25.

**Kinsbury, S. J., Fayek, M., & Trufasiu, D.** (2001). The apparent effects of ziprasidone on plasma lipids and glucose. *Journal of Clinical Psychol*, 62, 347–349.

**Kivimäki, M., Feldt, T., Vahtera, J., et al.** (2000). Sense of coherence and health: evidence from two cross-lagged longitudinal samples. *Social Science & Medicine*, 50, 583–97.

**Kivimaki, M., Batty, G. D., Singh-Manoux, A., Nabi, H., Sabia, S., Tabak, A. G., Akbaraly, T. N., Vahtera, J., Marmot, M. G., & Jokela, M.** (2009). Association between common mental disorder and obesity over the adult life course. *British Journal of Psychiatry*, 195(2), 149–155.

**Kivimäki, M., Lawlor, D. A., Singh-Manoux, A., et al.** (2009). Common mental disorder and obesity: Insight from 4 repeat measures over 19 years: prospective Whitehall II cohort study. *BMJ*, 339, b3765. doi: 10.1136/bmj.b3765.

**Klin, A., & Lemish, D.** (2008). Mental disorders stigma in the media: Review of studies on production, content, and influences. *Journal of Health Communication*, 13, 434-449.

**Knai, C., Suhrcke, M., & Lobstein, T.** (2007). Obesity in Eastern Europe: An overview of its health and economic implications. *Economics and Human Biology*, 5(3), 392–408.

**Kolotkin, R. L., Meter, K., & Williams, G. R.** (2001). Quality of life and obesity. *Obesity Reviews*, 2(4), 219-229. doi:10.1046/j.1467-789x.2001.00040.x

**Kontis, V., Bennett, J. E., Mathers, C. D., Li, G., Foreman, K., & Ezzati, M.** (2017). Future life expectancy in 35 industrialised countries: Projections with a Bayesian model ensemble. *The Lancet*, 389(10076), 1323–1335.

**Koob, G. F., & Volkow, N. D.** (2010). Neurocircuitry of addiction. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, 35(1), 217–238.

**Kopelman, P. G.** (2000). Obesity as a medical problem. *Nature*, 404, 635–643.

- Koran, L. M., Sheline, Y., Imai, K., Kelsey, T. G., Freedland, K. E., & Mathews, J. (2002).** Medical disorders among patients admitted to a public-sector psychiatric inpatient unit. *Psychiatric Services, 53*(12), 1623-1625. doi:10.1176/appi.ps.53.12.1623.
- Kowalowski, P., Kowalowska, M., Stanowska, K., & Burczyk, J. (2004).** [Natural sweeteners in terms of authorization for human consumption in Poland and EU countries.] *Post Fitoter, 1*, 4 –9.
- Krause, N. M., & Jay, G. M. (1994).** What do global self-rated health items measure? *Medical Care, 32*, 930–942.
- Kroenke, K. (2007).** Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Annals of Internal Medicine, 146*(4), 317–325.
- Kroenke, K., & Spitzer, R. L. (2002).** The PHQ-9: A new depression diagnostic and severity measure. *Psychiatric Annals, 32*, 509-521. [also includes validation data on PHQ-8]
- Krzysztozek, J., Laudańska-Krzemińska, I., & Bronikowski, M. (2019).** Assessment of epidemiological obesity among adults in EU countries. *Annals of Agricultural and Environmental Medicine, 26*(2), 341-349. <https://doi-org-10013b5te051d.han.medunigraz.at/10.26444/aaem/97226>
- Kuczmarski, R. J., Flegal, K. M., Campbell, S. M., & Johnson, C. L. (1994).** Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 –1991. *JAMA, 272*, 205–211.
- Kuiper, R. M., & Ryan, O. (2018-09-03).** Drawing Conclusions from Cross-Lagged Relationships: Reconsidering the Role of the Time-Intervall. *Structural Equation Modeling: A Multidisciplinary Journal, 25*(5), 809–823. doi:10.1080/10705511.2018.1431046.
- Kupfer, D. J., Ehlers, C. L., Frank, E., et al. (1993).** Electroencephalographic sleep studies in depressed patients during long-term recovery. *Psychiatry Research, 49*, 121–138.
- Kuuppelomaki, M., & Utriainen, P. (2003).** A 3-year follow-up study of health care students' sense of coherence and related smoking, drinking, and physical exercise factors. *International Journal of Nursing Studies, 40*, 383–388.
- Kyrou, I., & Tsigos, C. (2007).** Stress mechanisms and metabolic complications. *Hormone and Metabolic Research, 39*, 430–438.
- La Fleur, S. E., Houshyar, H., Roy, M., & Dallman, M. F. (2005).** Choice of lard, but not total lard calories, damps adrenocorticotropin responses to restraint. *Endocrinology, 146*(5), 2193–2199.
- Laitinen, J., Ek, E., & Sovio, U. (2002).** Stress-related eating and drinking behavior and body mass index and predictors of this behavior. *Preventive Medicine, 34*(1), 29–39. doi:10.1006/pmed.2001.0987. Epub 2001/12/26.
- Laaksonen, M., Sarlio-Lahteenkorva, S., Leino-Arjas, P., Martikainen, P., & Lahelma, E. (2005).** Body weight and health status: Importance of socioeconomic position and working conditions. *Obesity Research, 13*, 2169–2177.
- Lamberti, S., Terrance, B., & Schwarzkopf, S. (1992).** Weight gain among schizophrenic patients treated with clonazepam. *American Journal of Psychiatry, 149*, 689–690.

- Lamberti**, J. S., Olson, D., Crilly, J. F., Olivares, T., Williams, G. C., Tu, X., et al. (2006). Prevalence of the metabolic syndrome among patients receiving clozapine. *American Journal of Psychiatry*, *163*, 1273–1276.
- Lamers**, S. M. A., Westerhof, G. J., Glas, C. A. W., & Bohlmeijer, E. T. (2015). The bidirectional relation between positive mental health and psychopathology in a longitudinal representative panel study. *The Journal of Positive Psychology*, *10*(6), 553–560. doi:10.1080/17439760.2015.1015156.
- Lampl**, Y., Eshel, Y., & Rapaport, A. (1991). Weight gain, increased appetite, and excessive food intake induced by carbamazepine. *Clinical Neuropharmacology*, *14*, 251–255.
- Larsen**, J. K., Geenen, R., van Ramshorst, B., Brand, N., de Wit, P., Stroebe, W., et al. (2003). Psychosocial functioning before and after laparoscopic adjustable gastric banding: A cross-sectional study. *Obesity Surgery*, *13*, 629–636.
- Lawlor**, D. A., Harbord, R., Tybaerg-Hansen, A., et al. (2011). Using genetic loci to understand the relationship between adiposity and psychological distress: a Mendelian Randomization study in the Copenhagen General Population study of 53,221 adults. *Journal of Internal Medicine*, *269*, 525–537.
- Lawlor**, D. A., Hart, C. L., Hole, D. J., Gunnell, D., & Davey Smith, G. (2007). Body mass index in middle life and future risk of hospital admission for psychoses or depression: findings from the Renfrew/Paisley study. *Psychological Medicine*, *37*, 1151–1161.
- Lawlor**, D. A., Harbord, R. M., Sterne, J. A. C., Timpson, N. J., & Davey Smith, G. (2008). Mendelian randomization: using genes as instruments for making causal inferences in epidemiology. *Statistics in Medicine*, *27*, 1133–1163.
- Lawlor**, D. A., Davey Smith, G., & Ebrahim, S. (2003). Association of insulin resistance with depression: cross-sectional findings from the British women's heart and health study. *BMJ*, *327*, 1383–1384.
- Lazarevich**, I., Irigoyen-Camacho, M. E., Velazquez-Alva, M. d. C. (2013). Obesity, eating behaviour and mental health among university students in Mexico City. *Nutrición Hospitalaria*, *28*(Noviembre-Diciembre). Retrieved from <http://www.redalyc.org/articulo.oa?id=309230209017> ISSN 0212-1611
- Lechner**, K., Heel, S., Uhr, M., Dose, T., Holsboer, F., Lucae, S., Schaaf, L., Fulda, S., Kloiber, S., & Hennings, J. M. (2023). Weight-gain independent effect of mirtazapine on fasting plasma lipids in healthy men. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *396*(9), 1999–2008. <https://doi.org/10.1007/s00210-023-02448-y>
- Lee**, S. H., Paz-Filho, G., Mastronardi, C., Licinio, J., & Wong, M. L. (2016). Is increased antidepressant exposure a contributory factor to the obesity pandemic? *Translational Psychiatry*, *6*(3), e759. doi:10.1038/tp.2016.25
- Lee**, W. J., Lee, Y. C., Ser, K. H., Chen, J. C., & Chen, S. C. (2008). Improvement of insulin resistance after obesity surgery: A comparison of gastric banding and bypass procedures. *Obesity Surgery*, *18*(9), 1191–1195.
- Lee**, A., Cardel, M., & Donahoo, W. T. (2019). Social and environmental factors influencing obesity. In K. R. Feingold, B. Anawalt, M. R. Blackman, et al. (Eds.), *Endotext*. South Dartmouth (MA): MDText.com, Inc. Retrieved from <https://www.ncbi.nlm.nih.gov/books/NBK27897>

- Lee, K., Abraham, S., & Cleaver, R. (2022).** A systematic review of licensed weight-loss medications in treating antipsychotic-induced weight gain and obesity in schizophrenia and psychosis. *General Hospital Psychiatry, 78*, 58–67.
- Legenbauer, T., De Zwaan, M., Benecke, A., Muhlhans, B., Petrak, F., & Herpertz, S. (2009).** Depression and anxiety: Their predictive function for weight loss in obese individuals. *Obesity Facts, 2*(4), 227–234.
- Leinonen, E., Skarstein, J., & Behnke, K. (1999).** Efficacy and tolerability of mirtazapine versus citalopram: A double blind, randomized study in patients with major depressive disorder. Nordic antidepressant study group. *International Clinical Psychopharmacology, 14*, 329–337.
- Lemmens, S. G., Rutters, F., Born, J. M., & Westerterp-Plantenga, M. S. (2011).** Stress augments food 'wanting' and energy intake in visceral overweight subjects in the absence of hunger. *Physiology & Behavior, 103*(2), 157–163.
- Leutner, M., Dervic, E., Bellach, L., et al. (2023).** Obesity as pleiotropic risk state for metabolic and mental health throughout life. *Translational Psychiatry, 13*, 175.  
<https://doi.org/10.1038/s41398-023-02447-w>
- Levi, J., Segal, L. M., St. Laurent, R., Lang, A., & Rayburn, J. (2012).** *F as in Fat: How Obesity Threatens America's Future 2012*. Project Report. Princeton, NJ: Trust for America's Health / Robert Wood Johnson Foundation.
- Levy, E., Levy, P., Le Pen, C., & Basdevant, A. (1995).** The economic cost of obesity: The French situation. *International Journal of Obesity and Related Metabolic Disorders, 19*, 788–792.
- Li, T. Y., Rana, J. S., Manson, J. E., Willett, W. C., Stampfer, M. J., Colditz, G. A., et al. (2006).** Obesity as compared with physical activity in predicting risk of coronary heart disease in women. *Circulation, 113*, 499–506.
- Lieberman, J. A., Tolefaon, G., & Tohen, M. (2003).** Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first episode psychosis: A randomized double blind of Olanzapine versus Haloperidol. *American Journal of Psychiatry, 160*, 1396–1404.
- Lin, H. Y., Huang, C. K., Tai, C. M., Lin, H. Y., Kao, Y. H., Tsai, C. C., et al. (2013).** Psychiatric disorders of patients seeking obesity treatment. *BMC Psychiatry, 13*, 1.
- Linde, J. A., Jeffery, R. W., Levy, R. L., Sherwood, N. E., Utter, J., Pronk, N. P., et al. (2004).** Binge eating disorder, weight control self-efficacy, and depression in overweight men and women. *International Journal of Obesity and Related Metabolic Disorders, 28*(3), 418–425.
- Lindström, B., & Eriksson, M. (2005).** Professor Aaron Antonovsky (1923–1994): The father of the salutogenesis. *Journal of Epidemiology and Community Health, 59*, 511.
- Lindström, B., & Eriksson, M. (2005).** Salutogenesis. *Journal of Epidemiology and Community Health, 59*, 440–442. doi: 10.1136/jech.2005.034777.
- Lipsett, D., Madras, B. K., Wurtman, R. J., & Munro, H. N. (1973).** Serum tryptophan level after carbohydrate ingestion: selective decline in non-albumin-bound tryptophan coincident with reduction in serum free fatty acids. *Life Sciences II, 12*, 57–64.

- Lisa M. Groesz, MPLS, KM.** (2002). The effect of experimental presentation of thin media images on body satisfaction: a meta-analytic review. *International Journal of Eating Disorders*, *31*, 1–16.
- Littrell, K. H., Petty, R. G., & Hilligoss, N. M.** (2002). Weight loss associated with olanzapine treatment. *Journal of Clinical Psychopharmacology*, *22*, 436–437.
- Levine, A. S., & Morley, J. E.** (1981). Stress-induced eating in rats. *American Journal of Physiology- Regulatory, Integrative and Comparative Physiology*, *241*(1), R72–R76.
- Ljung, T., Holm, G., Friberg, P., Andersson, B., Bengtsson, B. A., Svensson, J., et al.** (2000). The activity of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system in relation to waist/hip circumference ratio in men. *Obesity Research*, *8*, 487–495.
- Lucassen, E. A., Rother, K. I., & Cizza, G.** (2012). Interacting epidemics? Sleep curtailment, insulin resistance and obesity. *Annals of the New York Academy of Sciences*, *1264*, 110–134. <https://doi.org/10.1111/j.1749-6632.2012.06538.x>
- Lucassen, E. A., & Cizza, G.** (2012). The Hypothalamic-Pituitary-Adrenal Axis, Obesity, and Chronic Stress Exposure: Sleep and the HPA Axis in Obesity. *Current Obesity Reports*, *1*(4), 208–215. <https://doi.org/10.1007/s13679-012-0028-5>
- Luef, G., Abraham, I., & Haslinger, M.** (2002). Polycystic ovaries, obesity and insulin resistance in women with epilepsy: A comparative study of Carbamazepine and valproic acid in 105 women. *Journal of Neurology*, *249*, 835–841.
- Luppa, M., Sikorski, C., Luck, T., Ehreke, A., Konnopka, A., Wiese, S., Weyerer, S., König, H.-H., & Riedel-Heller, S. G.** (2012). Age- and gender-specific prevalence of depression in latest-life - systematic review and meta-analysis. *Journal of Affective Disorders*, *136*, 212–221.
- Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. W., & Zitman, F. G.** (2010). Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Archives of General Psychiatry*, *67*(3), 220–229.
- Lykouras, L.** (2008). Psychological profile of obese patients. *Digestive Diseases*, *26*, 36–39.
- Lykouras, L., & Michopoulos, J.** (2011). Anxiety disorders and obesity. *Psychiatriki*, *22*, 307–313.
- Macmillan, R., Duke, N., Oakes, J. M., & Liao, W.** (2011). Trends in the association of obesity and self-reported overall health in 30 years of the integrated health interview series. *Obesity*, *19*(5), 1103–1105. <https://doi.org/10.1038/oby.2010.286>
- Magnusson, P. K., Rasmussen, F., Lawlor, D., Tynelius, P., & Gunnell, D.** (2005). Association of body mass index with suicide mortality: a prospective cohort study of more than one million men. *American Journal of Epidemiology*, *163*, 1–8.
- Magnusson, P. K., Rasmussen, F., Lawlor, D. A., Tynelius, P., & Gunnell, D.** (2006). Association of body mass index with suicide mortality: a prospective cohort study of more than one million men. *American Journal of Epidemiology*, *163*, 1-8.
- Manderbacka, K., Lundberg, O., & Martikainen, P.** (1999). Do risk factors and health behaviours contribute to self-ratings of health? *Social Science & Medicine*, *48*, 1713–1720.

**Mannan, M., Mamun, A., Doi, S., & Clavarino, A. (2016).** Prospective Associations between Depression and Obesity for Adolescent Males and Females: A Systematic Review and Meta-Analysis of Longitudinal Studies. *PLoS ONE*, *11*(6), e0157240. <https://doi.org/10.1371/journal.pone.0157240>

**Månsson, N. O., & Merlo, J. (2001).** The relation between self-rated health, socioeconomic status, body mass index and disability pension among middle-aged men. *European Journal of Epidemiology*, *17*, 65–69.

**Mao, W., & Agyapong, V. I. O. (2021).** The Role of Social Determinants in Mental Health and Resilience After Disasters: Implications for Public Health Policy and Practice. *Frontiers in Public Health*, *9*, 658528. <https://doi.org/10.3389/fpubh.2021.658528>

**Maranto, C. L., & Stenoien, A. F. (2000).** Weight discrimination: A multidisciplinary analysis. *Employee Responsibilities and Rights Journal*, *12*, 9–24.

**Mårin, P., Darin, N., Amemiya, T., et al. (1992).** Cortisol secretion in relation to body fat distribution in obese premenopausal women. *Metabolism*, *41*, 882–886.

**Martinez, J. A., Kearney, J. M., Kafatos, A., Paquet, S., & Martinez-Gonzalez, M. A. (1999).** Variables independently associated with self-reported obesity in the European Union. *Public Health Nutrition*, *2*(1A), 125–133.

**Martyn-Nemeth, P., Penckofer, S., Gulanick, M., Velsor-Friedrich, B., & Bryant, F. B. (2009).** The relationships among self-esteem, stress, coping, eating behavior, and depressive mood in adolescents. *Research in Nursing & Health*, *32*, 96–109.

**Masi, G., Mucci, M., & Millepiedi, S. (2002).** Clozapine in adolescent inpatients with acute mania. *Journal of Child and Adolescent Psychopharmacology*, *12*, 93–99.

**Masand, P. S. (2000).** Weight gain associated with psychotropic drugs. *Expert Opinion on Pharmacotherapy*, *1*, 377–383.

**Mayo, N. (Ed.). (2015).** *Dictionary of Quality of Life and Health Outcomes Measurement* (Version 1). Milwaukee, WI: International Society for Quality of Life Research.

**Mazereel, V., Detraux, J., Vancampfort, D., Van Winkel, R., & De Hert, M. (2020).** Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. *Frontiers in Endocrinology*, *11*, 573479.

**Menifield, C. E., Doty, N., & Fletcher, A. (2008).** Obesity in America. *ABNF Journal*, *19*(3), 83–88.

**McBeth, J., Macfarlane, G. J., Benjamin, S., & Silman, A. J. (2001).** Features of somatization predict the onset of chronic widespread pain: Results of a large population-based study. *Arthritis & Rheumatism*, *44*, 940–946.

**McCloughen, A., & Foster, K. (2011).** Weight gain associated with taking psychotropic medications: An integrative review. *International Journal of Mental Health Nursing*, *20*, 202–222.

**McCreadie, R., Macdonald, E., Blacklock, C., Tilak-Singh, D., Wiles, D., Halliday, J., & Paterson, J. (1998).** Dietary intake of schizophrenic patients in Nithsdale, Scotland: A case-control study. *British Medical Journal*, *317*, 784–785.

**McCreadie, R.** (2003). Diet, smoking and cardiovascular risk in people with schizophrenia. *British Journal of Psychiatry, 183*, 534–539.

**McElroy, S. L., Kotwal, R., Malhotra, S., Nelson, E. B., Keck, P. E., & Nemeroff, C. B.** (2004). Are mood disorders and obesity related? A review for the mental health professional. *Journal of Clinical Psychiatry, 65*, 634–651. In: De las Cuevas, C., Ramallo, Y., & Sanz, E. J. (2011). Are obesity and other physical comorbidities related to mental illness? *Revista de Psiquiatría y Salud Mental, 4*, 119–125.

**McElroy, S. L., Guerdjikova, A. I., Martens, B., Keck, P. E. Jr., Pope, H. G., & Hudson, J. I.** (2009). Role of antiepileptic drugs in the management of eating disorders. *CNS Drugs, 23*, 139–156.

**McEwen, B. S.** (2008). Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *European Journal of Pharmacology, 583*, 174–185.

**McEwen, B. S.** (2004). Protection and damage from acute and chronic stress: Allostasis and allostatic overload and relevance to the pathophysiology of psychiatric disorders. *Annals of the New York Academy of Sciences, 1032*(1), 1–7.

**McIntyre, R. S., Cohen, M., Zhao, J., Alphs, L., Macek, T. A., & Panagides, J.** (2010). Asenapine in the treatment of acute mania in bipolar I disorder: A randomized, double-blind, placebo-controlled trial. *Journal of Affective Disorders, 122*, 27–38.

**McIntyre, R. S., Cohen, M., Zhao, J., Alphs, L., Macek, T. A., & Panagides, J.** (2009). Asenapine versus olanzapine in acute mania: A double-blind extension study. *Bipolar Disorders, 11*, 815–826.

**McLean, J. A., Barr, S. I., & Prior, J. C.** (2001). Cognitive dietary restraint is associated with higher urinary cortisol excretion in healthy premenopausal women. *The American Journal of Clinical Nutrition, 73*(1), 7–12.

**Meltzer, H. Y., Bobo, W. V., Nuamah, I. F., Lane, R., Hough, D., Kramer, M., & Eerdeken, M.** (2008). Efficacy and tolerability of oral paliperidone extended-release tablets in the treatment of acute schizophrenia: Pooled data from three 6-week, placebo-controlled studies. *Journal of Clinical Psychopharmacology, 69*, 817–829.

**Mental Health Commission.** (2001). *Recovery Competencies*. Teaching Resource Kit. Wellington: Mental Health Commission.

**Michelson, D., & Amsterdam, J.** (1999). Changes in weight during a 1-year trial of fluoxetine. *American Journal of Psychiatry, 156*, 1170–1176.

**Milaneschi, Y., Simmons, W. K., van Rossum, E. F. C., et al.** (2019). Depression and obesity: evidence of shared biological mechanisms. *Molecular Psychiatry, 24*, 18–33.  
<https://doi.org/10.1038/s41380-018-0017-5>

**Milaneschi, Y., Corsi, A. M., Penninx, B. W., Bandinelli, S., Guralnik, J. M., & Ferrucci, L.** (2009). Interleukin-1 receptor antagonist and incident depressive symptoms over 6 years in older persons: The InCHIANTI Study. *Biological Psychiatry, 65*, 1197–1198.

- Mitchell**, A. J., Vancampfort, D., Sweers, K., van Winkel, R., Yu, W., & de Hert, M. (2013). Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—A systematic review and meta-analysis. *Schizophrenia Bulletin*, *39*, 306–318.
- Mokdad**, A. H., Serdula, M. K., Dietz, W. H., Bowman, B. A., Marks, J. S., & Koplan, J. P. (1999). The spread of the obesity epidemic in the United States, 1991–1998. *JAMA*, *282*, 1519–1522.
- Molarius**, A., Berglund, K., Eriksson, C., Lambe, M., Nordstrom, E., Eriksson, H. G., & Feldman, I. (2007). Socioeconomic conditions, lifestyle factors, and self-rated health among men and women in Sweden. *European Journal of Public Health*, *17*, 125–133.
- Montgomery**, S. A., Reimitz, P. E., & Zivkov, M. (1998). Mirtazapine versus amitriptyline in the long-term treatment of depression: A double-blind placebo-controlled study. *International Clinical Psychopharmacology*, *13*(2), 63-73. In: Blumenthal, S. R., Castro, V. M., Clements, C. C., Rosenfield, H. R., Murphy, S. N., Fava, M., ... & Perlis, R. H. (2014). An electronic health records study of long-term weight gain following antidepressant use. *JAMA Psychiatry*, *71*(8), 889-896.
- Moon**, C. A., & Jesinger, D. K. (1991/1994). The effects of psychomotor performance of fluvoxamine versus mianserin in depressed patients in general practice. *British Journal of Clinical Practice*, *45*, 259–262.
- Moosbrugger**, H., & Kelava, A. (Eds.). (2012). *Testtheorie und Fragebogenkonstruktion: Mit 66 Abbildungen und 41 Tabellen, 2., aktualisierte und überarbeitete Auflage*. Springer - Lehrbuch. Springer, Berlin Heidelberg.
- Moral de la Rubia**, J., & Meza Peña, C. (2012). Predicción de alteraciones de conducta alimentaria en mujeres mexicanas. *Salud Mental*, *35*(6), 491-7.
- Morley**, J. E., Levine, A. S., & Rowland, N. E. (1983). Stress induced eating. *Life Sciences*, *32*(19), 2169–2182.
- Müller-Riemenschneider**, F., Reinhold, T., Berghöfer, A., & Willich, S. N. (2008). Health-economic burden of obesity in Europe. *European Journal of Epidemiology*, *23*(8), 499-509. <https://doi.org/10.1007/s10654-008-9239-1>.
- Mukamal**, K. J., Kawachi, I., Miller, M., & Rimm, E. B. (2007). Body mass index and risk of suicide among men. *Archives of Internal Medicine*, *167*, 468–475.
- Muennig**, P. (2008). The body politic: The relationship between stigma and obesity-associated disease. *BMC Public Health*, *8*, 128.
- Muennig**, P., Lubetkin, E., Jia, H. M., & Franks, P. (2006). Gender and the burden of disease attributable to obesity. *American Journal of Public Health*, *96*(9), 1662–1668.
- Murray**, C. J., & Lopez, A. D. (1996). Evidence-based health policy — lessons from the Global Burden of Disease Study. *Science*, *274*(5288), 740-743.
- Must**, A., Spadano, J., Coakley, E. H., Field, A. E., Colditz, G., & Dietz, W. H. (1999). The disease burden associated with overweight and obesity. *JAMA*, *282*(16), 1523–1529.
- Must**, S., & Strauss, R. S. (1999). Risks and consequences of childhood and adolescent obesity. *International Journal of Obesity and Related Metabolic Disorders*, *23*(Suppl 2), S2-S11.

- Myszkowska-Ryciak, J., Harton, A., Gajewska, D., & Bawa, S. (2010).** [Sweeteners in obesity prevention and treatment]. *Kosmos – Problemy Nauk Biologicznych*, *59*, 365–374. [Polish]
- Nasrallah, H. (2003).** A review of the effect of atypical antipsychotics in weight. *Psychoneuroendocrinology*, *28*, 83–99.
- Napoli, N., Shah, K., Waters, D. L., Sinacore, D. R., Qualls, C., & Villareal, D. T. (2014).** Effect of weight loss, exercise, or both on cognition and quality of life in obese older adults. *American Journal of Clinical Nutrition*, *100*(1), 189–198.
- National Institute of Health. (2000).** *The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. Publication number 00–4084. National Institute of Health: October 2000.
- National Institutes of Health National Heart, Lung, and Blood Institute. (1998).** *Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults*.
- Newman, E., O'Connor, D. B., & Conner, M. (2007).** Daily hassles and eating behavior: The role of cortisol reactivity status. *Psychoneuroendocrinology*, *32*(2), 125–132.
- Nicholson, W. M. (1946).** Emotional factors in obesity. *American Journal of Medical Sciences*, *211*, 443–447.
- Nilsson, B., Holmgren, L., Stegmayr, B., et al. (2003).** Sense of coherence—stability over time and relation to health, disease, and psychosocial changes in a general population: a longitudinal study. *Scandinavian Journal of Public Health*, *31*, 297–304.
- Nieuwenhuizen, A. G., & Rutters, F. (2008).** The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. *Physiology & Behavior*, *94*, 169–177.
- Nihalani, N., Schwartz, T. L., Siddiqui, U. A., & Megna, J. L. (2012).** Obesity and psychotropics. *CNS Neuroscience & Therapeutics*, *18*(1), 57–63. doi:10.1111/j.1755-5949.2011.00232.x
- Noh, J.-W., Kim, J., Yang, Y., Park, J., Cheon, J., & Kwon, Y. D. (2017).** Body mass index and self-rated health in East Asian countries: Comparison among South Korea, China, Japan, and Taiwan. *PLoS One*, *12*(8), e0183881. doi:10.1371/journal.pone.0183881
- Noppa, H., & Hällström, T. (1981).** Weight gain in relation to socioeconomic factors, mental illness and personality traits: a prospective study of middle-aged women. *Journal of Psychosomatic Research*, *25*, 83–89.
- Okosun, I. S., Choi, S., Matamoros, T., & Dever, G. E. (2001).** Obesity is associated with reduced self-rated general health status: Evidence from a representative sample of white, black, and Hispanic Americans. *Preventive Medicine*, *32*, 429–436.
- Okunogbe, A., Nugent, R., Spencer, G., et al. (2022).** Economic impacts of overweight and obesity: Current and future estimates for 161 countries. *BMJ Global Health*, *7*, e009773.
- Okura, S., Deguchi, Y., Cho, T., Kageyama, Y., & Inoue, K. (2023).** Significant Weight Gain With the Administration of Lurasidone and Valproic Acid in Schizophrenia and Bipolar Disorder Patients. *Cureus*, *15*(11), e49005. <https://doi.org/10.7759/cureus.49005>
- Olesen, J., & Leonardi, J. M. (2003).** The burden of brain diseases in Europe. *European Journal of Neurology*, *10*, 471–477.

- Oliver, G., Wardle, J., & Gibson, E. L.** (2000). Stress and food choice: A laboratory study. *Psychosomatic Medicine*, *62*(6), 853–865.
- Olshansky, S. J., Passaro, D. J., Hershov, M. D., Layden, J., Carnes, B. A., Brody, J., et al.** (2005). A potential decline in life expectancy in the United States in the 21st century. *New England Journal of Medicine*, *352*, 1138–1144.
- Onyike, C. U., Crum, R. M., Lee, H. B., Lyketsos, C. G., & Eaton, W. W.** (2003). Is obesity associated with major depression? Results from the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*, *158*, 1139–1147.
- Ostbye, T., Dement, J. M., & Krause, K. M.** (2007). Obesity and workers' compensation: Results from the Duke Health and Safety Surveillance System. *Archives of Internal Medicine*, *167*, 766–773.
- O'Sullivan, J. B.** (1982). Body-weight and subsequent diabetes mellitus. *Journal of the American Medical Association*, *248*, 949–952.
- Oud, M. J., Meyboom-de Jong, B.** (2009). Somatic diseases in patients with schizophrenia in general practice: their prevalence and health care. *BMC Family Practice*, *10*, 32. <http://dx.doi.org/10.1186/1471-2296-10-32>.
- Page, K. A., Seo, D., Belfort-DeAguiar, R., Lacadie, C., Dzuira, J., Naik, S., et al.** (2011). Circulating glucose levels modulate neural control of desire for high-calorie foods in humans. *Journal of Clinical Investigation*, *121*(10), 4161–4169.
- Page, R. M., Simonek, J., Ihász, F., Iacob, H., Uvácsek, M., Kalabiska, I., et al.** (2009). Self-rated health, psychosocial functioning, and other dimensions of adolescent health in Central and Eastern European adolescents. *European Journal of Psychiatry*, *23*. doi:10.4321/S0213-61632009000200004.
- Pagoto, S., Bodenlos, J. S., Kantor, L., Gitkind, M., Curtin, C., & Ma, Y.** (2007). Association of major depression and binge eating disorder with weight loss in a clinical setting. *Obesity*, *15*, 2557–2559.
- Palinkas, L. A., Wingard, D. L., & Barrett-Connor, E.** (1996). Depressive symptoms in overweight and obese older adults: A test of the "jolly fat" hypothesis. *Journal of Psychosomatic Research*, *40*, 59–66.
- Papas, M., Alberg, A., Ewing, R., Helzlsouer, K., Gary, T., & Klassen, A.** (2007). The built environment and obesity. *Epidemiologic Reviews*, *29*(1), 129–143.
- Paradis, C. F., Stack, J. A., & George, C. J.** (1992). Nortriptyline and weight change in depressed patients over 60. *Journal of Clinical Psychiatry*, *12*, 246–250.
- Park, E.** (2009). Gender as a moderator in the association of body weight to smoking and mental health. *American Journal of Public Health*, *99*(1), 146–151.
- Parmar, R. M., Can, A. S.** (2023). Physiology, appetite, and weight regulation. In *StatPearls*. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK574539/>
- Pasquali, R.** (2012). The hypothalamic-pituitary-adrenal axis and sex hormones in chronic stress and obesity: pathophysiological and clinical aspects. *Annals of the New York Academy of Sciences*, *1264*, 20–35.

**Pasquali, R., Ambrosi, B., Armanini, D., et al. (2002).** Cortisol and ACTH response to oral dexamethasone in obesity and effects of sex, body fat distribution, and dexamethasone concentrations: a dose-response study. *Journal of Clinical Endocrinology & Metabolism*, *87*, 166–175.

**Pasquali, R., & Vicennati, V. (2000).** Activity of the hypothalamic-pituitary-adrenal axis in different obesity phenotypes. *International Journal of Obesity and Related Metabolic Disorders*, *24*(suppl 2), S47–S49.

**Patel, A., Shanthakumaran, Y., Rasheed, R., & Nazir, I. (2022).** Metabolic Effects of Antidepressants; Is It Time to Change the Conversation? *BJPsych Open*, *8*(S1), S66-S66. doi:10.1192/bjo.2022.231

**Pawlak, K. (2012).** Food security in EU countries. Economics and organization of food economy. *Scientific Journal of Warsaw University of Life Sciences*, *98*, 39–51.

**Pecoraro, N., Reyes, F., Gomez, F., Bhargava, A., & Dallman, M.F. (2004).** Chronic stress promotes palatable feeding, which reduces signs of stress: Feedforward and feedback effects of chronic stress. *Endocrinology*, *145*(8), 3754–3762.

**Peltonen, M., Lindroos, A.K., & Torgerson, J.S. (2003).** Musculoskeletal pain in the obese: A comparison with a general population and long-term changes after conventional and surgical obesity treatment. *Pain*, *104*, 549–557.

**Penninx, B.W., Beekman, A.T., Honig, A., Deeg, D.J., Schoevers, R.A., van Eijk, J.T., et al. (2001).** Depression and cardiac mortality: Results from a community-based longitudinal study. *Archives of General Psychiatry*, *58*(3), 221–227.

**Pereira, C.D., Azevedo, I., Monteiro, R., & Martins, M.J. (2012).** 11 $\beta$ -Hydroxysteroid dehydrogenase type 1: Relevance of its modulation in the pathophysiology of obesity, the metabolic syndrome and type 2 diabetes mellitus. *Diabetes, Obesity & Metabolism*. Advance online publication. doi:10.1111/j.1463-1326.2012.01582.x.

**Petrillo, G., Capone, V., Caso, D., & Keyes, C.L. (2015).** The Mental Health Continuum-Short Form (MHC-SF) as a measure of well-being in the Italian context. *Social Indicators Research*, *121*(1), 291–312.

**Petry, N.M., Barry, D., Pietrzak, R.H., & Wagner, J.A. (2008).** Overweight and obesity are associated with psychiatric disorders: Results from the national epidemiologic survey on alcohol and related conditions. *Psychosomatic Medicine*, *70*(3), 288–297.

**Phelps, J.R., Pipitone, O.R., Squires, K., & Bale, J.D. (2021).** Lamotrigine and lithium in primary care psychiatric consultation: Adoption and adverse effects. *Family Practice*, *38*(4), 381–386. <https://doi.org/10.1093/fampra/cmaa131>

**Picca, A., Calvani, R., Coelho-Júnior, H.J., Landi, F., & Marzetti, E. (2022).** Anorexia of aging: Metabolic changes and biomarker discovery. *Clinical Interventions in Aging*, *17*, 1761-1767. doi:10.2147/CIA.S325008

**Pickering, R.P., Grant, B.F., Chou, S.P., & Compton, W.M. (2007).** Are overweight, obesity, and extreme obesity associated with psychopathology? Results from the national epidemiologic survey on alcohol and related conditions. *Journal of Clinical Psychiatry*, *68*, 998–1009.

- Picot, A.K., & Lilenfeld, L.R.** (2003). The relationship among binge severity, personality psychopathology, and body mass index. *International Journal of Eating Disorders*, 34(1), 98–107.
- Pieniak, Z., Perez-Cueto, F., & Verbeke, W.** (2009). Association of overweight and obesity with interest in healthy eating, subjective health and perceived risk of chronic diseases in three European countries. *Appetite*, 53, 399–406.
- Pinar, M., Gulsun, M., Tasci, I., Erdil, A., Bolu, E., Acikel, C., & Doruk, A.** (2008). Maprotiline induced weight gain in depressive disorder: Changes in circulating ghrelin and adiponectin levels and insulin sensitivity. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 32, 135-139.
- Pijl, H., & Meinders, A.E.** (1996). Body weight changes as an adverse effect of drug treatment: Mechanisms and management. *Drug Safety*, 14(5), 329–342.
- Piko, B.** (2000). Health-related predictors of self-perceived health in a student population: The importance of physical activity. *Journal of Community Health*, 25(2), 125–137.
- Pine, D.S., Cohen, P., Brook, J., & Coplan, J.D.** (1997). Psychiatric symptoms in adolescence as predictors of obesity in early adulthood: A longitudinal study. *American Journal of Public Health*, 87(8), 1303–1310.
- Pisa, P.T., & Pisa, N.M.** (2017). Economic growth and obesity in South African adults: An ecological analysis between 1994 and 2014. *European Journal of Public Health*, 27(3), 404–409.
- Pi-Sunyer, F.X.** (1993). Medical hazards of obesity. *Annals of Internal Medicine*, 119(7\_Part\_2), 655–660.
- Pompa Guajardo, E., & Montoya Flores, B.I.** (2011). Evaluación de la manifestación de ansiedad y depresión en niños con sobrepeso y obesidad en un campo de verano. *Psicología y Salud*, 21(1), 119-124.
- Pope, L., Harvey-Berino, J., Savage, P., Bunn, J., Ludlow, M., & Oldridge, N., et al.** (2011). The impact of high-calorie-expenditure exercise on quality of life in older adults with coronary heart disease. *Journal of Aging and Physical Activity*, 19(2), 99–116.
- Popkin, B.M., Kim, S., Rusev, E.R., Du, S., & Zizza, C.** (2006). Measuring the full economic costs of diet, physical activity and obesity-related chronic diseases. *Obesity Reviews*, 7(3), 271–293.
- Potkin, S., Saha, A., & Kujawa, M.** (2003). Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. *Archives of General Psychiatry*, 60(7), 681–690.
- Prell, T., & Perner, C.** (2018). Disease-specific aspects of malnutrition in neurogeriatric patients. *Frontiers in Aging Neuroscience*, 10, 80. doi:10.3389/fnagi.2018.00080
- Prince, J.B., Wilens, T.E., & Biederman, J.** (2000). A controlled study of nortriptyline in children and adolescents with attention deficit hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, 10(3), 193–204.

- Prince, M.J.,** Reischies, F., Beekman, A.T.F., Fuhrer, R., Jonker, C., Kivela, S.L., ... Copeland, J.R. (1999). Development of the EURO-D scale – A European Union initiative to compare symptoms of depression in 14 European centres. *The British Journal of Psychiatry*, 174(4), 330-338.
- Prince, M.,** Patel, V., & Saxena, S. (2007). No health without mental health. *The Lancet*, 9590, 859-877.
- Puhl, R.M.,** Moss-Racusin, C.A., & Schwartz, M.B. (2007). Internalization of weight bias: Implications for binge eating and emotional well-being. *Obesity (Silver Spring)*, 15(1), 19–23.
- Puhl, R.M.,** & Heuer, C.A. (2009). The stigma of obesity: A review and update. *Obesity*, 17(5), 941–964.
- Puhl, R.M.,** & Brownell, K.D. (2003). Psychosocial origins of obesity stigma: Toward changing a powerful and pervasive bias. *Obesity Reviews*, 4(3), 213–227.
- Quetelet, A.** (1832). Recherches sur le poids de l'homme aux différents âges. *Nouveaux Memoires de l'Academie Royale des Sciences et Belles-Lettres de Bruxelles*, 1-83.
- Rae, A.J.,** & Cleator, I.G.M. (1993). Quality-of-life assessment of ileogastrostomy. *Obesity Surgery*, 3(4), 360–364.
- Rajan, T.M.,** & Menon, V. (2017). Psychiatric disorders and obesity: A review of association studies. *Journal of Postgraduate Medicine*, 63(3), 182–190. doi: 10.4103/jpgm.JPGM\_712\_16.
- Rand, C.S.W.,** Kuldau, J.M., & Robbins, L. (1982). Surgery for obesity and marriage quality. *JAMA*, 247(10), 1419–1422.
- Ratzoni, G.,** Gothelf, D., & Brand-Gothelf, A. (2002). Weight gain associated with olanzapine and risperidone in adolescent patients: Comparative prospective study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41(3), 337–343.
- Read, S.,** Aunola, K., Feldt, T., Leinonen, R., & Ruoppila, I. (2005). The relationship between Generalized Resistance Resources, Sense of Coherence, and health among Finnish people aged 65–69. *European Psychologist*, 10(3), 244–253.
- Regier, D.A.,** Narrow, W.E., Rae, D.S., Manderscheid, R.W., Locke, B.Z., & Goodwin, F.K. (1993). The de facto U.S. mental and addictive disorders service system: Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. *Archives of General Psychiatry*, 50, 85–94.
- Rehm, J.,** & Shield, K.D. (2019). Global Burden of Disease and the Impact of Mental and Addictive Disorders. *Current Psychiatry Reports*, 21(2), 10. <https://doi-org-10013b5hi03b9.han.medunigraz.at/10.1007/s11920-019-0997-0>
- Reither, E.N.,** Hauser, R.M., & Yang, Y. (2009). Do Birth Cohorts Matter? Age-Period-Cohort Analyses of the Obesity Epidemic in the United States. *Social Science & Medicine*, 69(10), 1439–1448.
- Rejeski, W.J.,** Focht, B.C., Messier, S.P., Morgan, T., Pahor, M., & Penninx, B. (2002). Obese, older adults with knee osteoarthritis: Weight loss, exercise, and quality of life. *Health Psychology*, 21(5), 419–426.

- Remington, G.** (2006). Schizophrenia, antipsychotics, and the metabolic syndrome: Is there a silver lining? *American Journal of Psychiatry*, *163*(7), 1132–1134.
- Renehan, A.G., Tyson, M., Egger, M., Heller, R.F., & Zwahlen, M.** (2008). Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. *The Lancet*, *371*(9612), 569–578.
- Ribeiro, L., Busnello, J.V., & Kauer-Sant'Anna, M.** (2001). Mirtazapine versus fluoxetine in the treatment of panic disorder. *Brazilian Journal of Medical and Biological Research*, *34*, 1303–1307.
- Ricca, V., Castellini, G., Lo Sauro, C., Rotella, C.M., & Faravelli, C.** (2009). Zonisamide combined with cognitive behavioral therapy in binge eating disorder: A one-year follow-up study. *Psychiatry (Edgmont)*, *6*, 23–28.
- Rindler, G.A., Gries, A., & Freidl, W.** (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, *11*. <https://doi.org/10.3389/fpubh.2023.1206283>
- Robbins, T.W., & Fray, P.J.** (1980). Stress-induced eating: Fact, fiction or misunderstanding? *Appetite*, *1*(2), 103–133.
- Robert Koch Institut.** (2013). Psychische Gesundheit. Retrieved from [http://www.rki.de/DE/Content/Gesundheitsmonitoring/Themen/Psychische\\_Gesundheit/Psychische\\_Gesundheit\\_node.html](http://www.rki.de/DE/Content/Gesundheitsmonitoring/Themen/Psychische_Gesundheit/Psychische_Gesundheit_node.html)
- Robert Koch Institut.** (2014). Übergewicht und Adipositas. Retrieved from [http://www.rki.de/DE/Content/Gesundheitsmonitoring/Themen/Uebergewicht\\_Adipositas/Uebergewicht\\_Adipositas\\_node.html](http://www.rki.de/DE/Content/Gesundheitsmonitoring/Themen/Uebergewicht_Adipositas/Uebergewicht_Adipositas_node.html)
- Roberts, R.E., Kaplan, G.A., Shema, S.J., & Strawbridge, W.J.** (2000). Are the obese at greater risk for depression? *American Journal of Epidemiology*, *152*, 163–170.
- Roberts, R.E., Deleger, S., Strawbridge, W.J., & Kaplan, G.A.** (2003). Prospective association between obesity and depression: Evidence from the Alameda County Study. *International Journal of Obesity and Related Metabolic Disorders*, *27*(4), 514–521.
- Rogosa, D.R.** (1980). A critique of cross-lagged correlation. *Psychological Bulletin*, *88*, 245–258. <http://psycnet.apa.org/doi/10.1037/0033-2909.88.2.245>
- Rohde, P., Ichikawa, L., Simon, G.E., Ludman, E.J., Linde, J.A., Jeffery, R.W., et al.** (2008). Associations of child sexual and physical abuse with obesity and depression in middle-aged women. *Child Abuse & Neglect*, *32*, 878–887.
- Rowston, W.M., McCluskey, S.E., Gazet, J.C., Lacey, J.H., Franks, G., & Lynch, D.** (1992). Eating behaviour, physical symptoms and psychological factors associated with weight reduction following the Scopinaro operation as modified by Gazet. *Obesity Surgery*, *2*, 355–360.
- Roy-Byrne, P.P., Davidson, K.W., Kessler, R.C., Asmundson, G.J.G., Goodwin, R.D., Kubzansky, L., et al.** (2008). Anxiety disorders and comorbid medical illness. *General Hospital Psychiatry*, *30*, 208–225.
- Russell, J.M., & Mackell, J.A.** (2005). Bodyweight gain associated with atypical antipsychotics: Epidemiology and therapeutic implications. *CNS Drugs*, *15*, 537–535.

- Rutters**, F., Nieuwenhuizen, A.G., Lemmens, S.G., et al. (2010). Hypothalamo-pituitary-adrenal (HPA) axis functioning in relation to body fat distribution. *Clinical Endocrinology*, *72*, 738–743.
- Rutters**, F., Nieuwenhuizen, A.G., Lemmens, S.G., Born, J.M., & Westerterp-Plantenga, M.S. (2009). Acute stress-related changes in eating in the absence of hunger. *Obesity*, *17*(1), 72–77. <https://doi.org/10.1038/oby.2008.514>
- Ryff**, C.D. (1989). Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *Journal of Personality and Social Psychology*, *57*, 1069–1081. <https://doi.org/10.1037/0022-3514.57.6.1069>
- Ryff**, C.D., & Singer, B. (1998). Human health: New directions for the next millennium. *Psychological Inquiry*, *9*, 69–85.
- Ryff**, C.D., & Keyes, C.L.M. (1995). The structure of psychological well-being revisited. *Journal of Personality and Social Psychology*, *69*, 719–727. <https://doi.org/10.1037/0022-3514.69.4.719>
- Safaei**, M., Sundararajan, E.A., Driss, M., Boulila, W., & Shapi'i, A. (2021). A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. *Computers in Biology and Medicine*, *136*, 104754. <https://doi.org/10.1016/j.combiomed.2021.104754>
- Saguy**, A.C., & Almeling, R. (2008). Fat in the fire? Science, the news media, and the “obesity epidemic. *Sociological Forum*, *23*(1), 53–83.
- Sagy**, S., Eriksson, M., & Braun-Lewensohn, O. (2015). The salutogenic paradigm. In S. Joseph (Ed.), *Positive Psychology in Practice: Promoting Human Flourishing in Work, Health, Education, and Everyday Life* (2nd ed., pp. 61–80). New York: Wiley.
- Sagy**, S., & Antonovsky, H. (1999). Factors related to the development of the sense of coherence (sense of coherence) in adolescents. A retrospective study. *Polish Psychological Bulletin*, *30*(4), 255–262.
- Saha**, S., Chant, D., & McGrath, J. (2007). A systematic review of mortality in schizophrenia. *Archives of General Psychiatry*, *64*(10), 1123–1131. <http://dx.doi.org/10.1001/archpsyc.64.10.1123>
- Sandeep**, T.C., Andrew, R., Homer, N.Z., et al. (2005). Increased in vivo regeneration of cortisol in adipose tissue in human obesity and effects of the 11beta-hydroxysteroid dehydrogenase type 1 inhibitor carbenoxolone. *Diabetes*, *54*, 872–879.
- Sapienza**, J.K., & Masten, A.S. (2011). Understanding and promoting resilience in children and youth. *Current Opinion in Psychiatry*, *24*, 267–273.
- Sareen**, J., Jacobi, F., Cox, B.J., Belik, S.-L., Clara, I., & Stein, M.B. (2006). Disability and poor quality of life associated with comorbid anxiety disorders and physical conditions. *Archives of Internal Medicine*, *166*, 2109–2116.
- Sareen**, J., Cox, B.J., Clara, I., & Asmundson, G.J.G. (2005). The relationship between anxiety disorders and physical disorders in the US national comorbidity survey. *Depression and Anxiety*, *21*, 193–202.
- Sartorius**, N. (2001). The economic and social burden of depression. *Journal of Clinical Psychiatry*, *62*, 8–11.

- Saxena, S., Thornicroft, G., Knapp, M., & Whiteford, H. (2007).** Global mental health 2 — resources for mental health: Scarcity, inequity, and inefficiency. *The Lancet*, *370*, 878–889.
- Schrank, B., & Slade, M. (2007).** Recovery in psychiatry. *Psychiatric Bulletin*, *31*, 321–325. doi: 10.1192/pb.bp.106.013425.
- Schwartz, T. L., Nihalani, N., Jindal, S., Virk, S., & Jones, N. (2004).** Psychiatric medication-induced obesity: A review. *Obesity Reviews*, *5*, 115–121.
- Selig, J., & Little, T. (2012).** Handbook of Developmental Research Methods: Autoregressive and cross-lagged panel analysis for longitudinal data, 16, 265-278.
- Selye, H. (1976).** *The Stress of Life*. McGraw-Hill.
- Shaw, J. A., Lewis, J. E., & Pascal, S. (2001). A study of quetiapine: Efficacy and tolerability in psychotic adolescents. *Journal of Child and Adolescent Psychopharmacology*, *11*, 415–424.
- Shields, M., & Shooshtari, S. (2001).** Determinants of self-perceived health. *Health Reports*, *13*, 35–52.
- Schipper, H., Clinch, J. J., & Olweny, C. L. M. (1996).** Quality of life studies: Definitions and conceptual issues. In B. Spilker (Ed.), *Quality of Life and Pharmacoeconomics in Clinical Trials* (pp. 11–23). Lippincott-Raven: Philadelphia.
- Scott, K. M., Bruffaerts, R., Simon, G. E., Alonso, J., Angermeyer, M., de Girolamo, G., Demyttenaere, K., Gasquet, I., Haro, J. M., Karam, E., Kessler, R. C., Levinson, D., Medina Mora, M. E., Oakley Browne, M. A., Ormel, J., Villa, J. P., Uda, H., & Von Korff, M. (2008).** Obesity and mental disorders in the general population: Results from the world mental health surveys. *International Journal of Obesity*, *32*(1), 192-200. doi: 10.1038/sj.ijo.0803701
- Sepúlveda-Lizcano, L., Arenas-Villamizar, V. V., Jaimes-Duarte, E. B., García-Pacheco, H., Paredes, C. S., Bermúdez, V., & Rivera-Porras, D. (2023).** Metabolic Adverse Effects of Psychotropic Drug Therapy: A Systematic Review. *European Journal of Investigation in Health, Psychology and Education*, *13*(8), 1505–1520. <https://doi.org/10.3390/ejihpe13080110>
- Serretti, A., & Mandelli, L. (2010).** Antidepressants and body weight: A comprehensive review and meta-analysis. *Journal of Clinical Psychiatry*, *71*(10), 1259-1272.
- Shively, C. A., Register, T. C., & Clarkson, T. B. (2009).** Social stress, visceral obesity, and coronary artery atherosclerosis: Product of a primate adaptation. *American Journal of Primatology*, *71*, 742–751.
- Seidell, J. C. (1995).** Obesity in Europe: Scaling an epidemic. *International Journal of Obesity and Related Metabolic Disorders*, *19*(Suppl 3), S1–S4.
- Seligman, M. (2002).** *Authentic happiness: Using the new positive psychology to realize your potential for lasting fulfillment*. New York: Free Press.
- Shoelson, S. E., Herrero, L., & Naaz, A. (2007).** Obesity, inflammation, and insulin resistance. *Gastroenterology*, *132*(6), 2169-2180
- Sigerist, H. E. (1941).** *Medicine and human welfare*. New Haven, CT: Yale University Press.

- Simon, G.**, Von Korff, M., Saunders, K., Miglioretti, D., Crane, P., Van Belle, G., & Kessler, R. (2006). Association between obesity and psychiatric disorders in the US adult population. *Archives of General Psychiatry*, *63*(7), 824-830.
- Simon, G. E.**, Rohde, P., Ludman, E. J., Jeffery, R. W., Linde, J. A., Operskalski, B. H., & Arterburn, D. (2010). Association between change in depression and change in weight among women enrolled in weight loss treatment. *General Hospital Psychiatry*, *32*(6), 583–589.
- Sinha, R.** (2008). Chronic stress, drug use, and vulnerability to addiction. *Annals of the New York Academy of Sciences*, *1141*(1), 105–130.
- Sivertsen, H.**, Bjørkløf, G. H., Engedal, K., Selbæk, G., & Helvik, A. -S. (2015). Depression and Quality of Life in Older Persons: A Review. *Dementia and Geriatric Cognitive Disorders*, *40*, 311–339. doi: 10.1159/000437299
- Slade, M.** (2010). Mental illness and well-being: The central importance of positive psychology and recovery approaches. *BMC Health Services Research*, *10*(1):26. DOI: 10.1186/1472-6963-10-26
- Slade, M.** (2009). *Personal recovery and mental illness: A guide for mental health professionals*. Cambridge: Cambridge University Press.
- Smith, M. B.** (1959). Research strategies toward a conception of positive mental health. *American Psychologist*, *14*, 673–681.
- Smith, M. M.**, & Minson, C. T. (2012). Obesity and adipokines: effects on sympathetic overactivity. *Journal of Physiology*, *590*, 1787–1801.
- Soholm, B.**, & Lublin, H. (2003). Long term effectiveness of Risperidone and Olanzapine in resistant or intolerant schizophrenic patients: A minor study. *Acta Psychiatrica Scandinavica*, *107*, 344–350.
- Solmi, M.**, Fornaro, M., Ostinelli, E. G., Zangani, C., Croatto, G., Monaco, F., Krinitski, D., Fusar-Poli, P., & Correll, C. U. (2020). Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: A large scale systematic meta-review of 78 adverse effects. *World Psychiatry*, *19*(2), 214-232. doi: 10.1002/wps.20765
- Solow, C.** (1977). Psychosocial aspects of intestinal bypass surgery for massive obesity: Current status. *American Journal of Clinical Nutrition*, *30*, 103–108.
- Solow, C.**, Silberfarb, P. M., & Swift, K. (1974). Psychosocial effects of intestinal bypass surgery for severe obesity. *New England Journal of Medicine*, *290*, 300–304.
- Specchia, M. L.**, Veneziano, M. A., Cadeddu, C., Ferriero, A. M., Mancuso, A., Ianuale, C., Parente, P., Capri, S., & Ricciardi, W. (2015). Economic impact of adult obesity on health systems: A systematic review. *European Journal of Public Health*, *25*, 255–262. doi: 10.1093/eurpub/cku170
- Spilker, B.** (1996). Introduction. In B. Spilker (Ed.), *Quality of Life and Pharmacoeconomics in Clinical Trials* (pp. 1-10). New York: Lippincott-Raven.
- Spina, E.**, & Cavallaro, R. (2007). The pharmacology and safety of paliperidone extended-release in the treatment of schizophrenia. *Expert Opinion on Drug Safety*, *6*, 651–662.

- Spira, A. P., Zvolensky, M. J., Eifert, G. H., & Feldner, M. T. (2004).** Avoidance-oriented coping as a predictor of panic-related distress: A test using biological challenge. *Journal of Anxiety Disorders, 18*, 309–323.
- Spoor, S., Bekker, M., van Strien, T., & van Heck, G. (2007).** Relation between negative affect, coping, and emotional eating. *Appetite, 48*(3), 368–376.
- Stanton, J. M. (1995).** Weight gain associated with neuroleptic medication: A review. *Schizophrenia Bulletin, 21*(3), 463–472.
- Statistik Austria. (2020).** Österreichische Gesundheitsbefragung 2019. Hauptergebnisse des Austrian Health Interview Survey (ATHIS) und methodische Dokumentation.
- Staquet, M., Berzon, R., Osoba, D., & Machin, D. (1996).** Guidelines for reporting results of quality of life assessments in clinical trials. *Quality of Life Research, 5*(5), 496–502. <https://doi-org-10013b5z20700.han.medunigraz.at/10.1007/BF00540022>
- Stefansson, C. G. (2006).** Chapter 5.5: Major public health problems – mental ill-health. *Scandinavian Journal of Public Health, 34*(Suppl 67), 87–103.
- Stephenson, J., Smith, C. M., Kearns, B., Haywood, A., & Bissell, P. (2021).** The association between obesity and quality of life: A retrospective analysis of a large-scale population-based cohort study. *BMC Public Health, 21*(1), 1990. doi: 10.1186/s12889-021-12009-8. <https://www-1ncbi-1nlm-1nih-1gov-10013b5hi04d1.han.medunigraz.at/pubmed/34732156>
- Stevens, J., Cai, J., Evenson, K. R., & Thomas, R. (2002).** Fitness and fatness as predictors of mortality from all causes and from cardiovascular disease in men and women in the Lipid Research Clinics Study. *American Journal of Epidemiology, 156*(9), 832–841.
- Strawn, J. R., Mills, J. A., Poweleit, E. A., Ramsey, L. B., & Croarkin, P. E. (2023).** Adverse effects of antidepressant medications and their management in children and adolescents. *Pharmacotherapy, 43*(7), 675–690. <https://doi.org/10.1002/phar.2767>
- Strine, T., Mokdad, A., Dube, S., Balluz, L., & González, O., Berry, J. (2008).** The association of depression and anxiety with unhealthy behaviours among community-dwelling US adults. *General Hospital Psychiatry, 30*(2), 127–137.
- Stice, E., Sysko, R., Roberto, C. A., & Allison, S. (2010).** Are dietary restraint scales valid measures of dietary restriction? Additional objective behavioral and biological data suggest not. *Appetite, 54*(2), 331–339.
- Stice, E., Fisher, M., & Lowe, M. R. (2004).** Are Dietary Restraint Scales Valid Measures of Acute Dietary Restriction? Unobtrusive Observational Data Suggest Not. *Psychological Assessment, 16*(1), 51–59.
- Stunkard, A. J., & Wadden, T. A. (1993).** *Obesity: Theory and Therapy* (2nd ed.). New York, NY: Raven Press.
- Stunkard, A. J., & Wadden, T. A. (1992).** Psychological aspects of severe obesity. *The American Journal of Clinical Nutrition, 55*(2 Suppl), 524S–532S.
- Stunkard, A. J., Faith, M. S., & Allison, K. C. (2003).** Depression and obesity. *Biological Psychiatry, 54*(3), 330–337. [https://doi.org/10.1016/S0006-3223\(03\)00608-5](https://doi.org/10.1016/S0006-3223(03)00608-5)

**Stunkard, A. J., Stinnett, J. L., & Smoller, J. W. (1986).** Psychological and social aspects of the surgical treatment of obesity. *The American Journal of Psychiatry*, *143*(3), 417–429.

**Substance Abuse and Mental Health Services Administration . (2013).** Results from the 2012 National Survey on Drug Use and Health: Mental Health Findings. NSDUH Series H-47, HHS Publication No. (SMA) 13-4805. Rockville: Substance Abuse and Mental Health Services Administration. Retrieved from <http://store.samhsa.gov/home>

**Suchacki, K. J., Ramage, L. E., Kwok, T. C., et al. (2023).** The serotonin transporter sustains human brown adipose tissue thermogenesis. *Nature Metabolism*, *5*, 1319–1336.  
<https://doi.org/10.1038/s42255-023-00839-2>

**Suk, S.-H., Sacco, R. L., Boden-Albala, B., Cheun, J. F., Elkind, M. S., & Paik, M. C. (2003).** Abdominal obesity and risk of ischemic stroke. *Stroke*, *34*(7), 1586–1592.

**Sullivan, M. B. E., Sullivan, L. G. M., & Kral, J. G. (1987).** Quality of life assessment in obesity: Physical, psychological, and social function. *Gastroenterology Clinics of North America*, *16*, 433–442.

**Suominen, S., Helenius, H., Blomberg, H., et al. (2001).** Sense of coherence as a predictor of subjective state of health: Results of 4 years of follow-up of adults. *Journal of Psychosomatic Research*, *50*, 77–86.

**Survey of Health, Ageing and Retirement in Europe (SHARE). (2022).** Retrieved March 14, 2022, from <http://www.share-project.org/data-documentation/waves-overview/wave-1.html>

**Sussman, N., Ginsberg, D. L., & Bikoff, J. (2001).** Effects of nefazodone on body weight: A pooled analysis of selective serotonin reuptake inhibitor- and imipramine-controlled trials. *Journal of Clinical Psychiatry*, *62*, 256–260.

**Tappy, L., Egli, L., Lecoultre, V., & Schneider, P. (2013).** Effects of fructose-containing caloric sweeteners on resting energy expenditure and energy efficiency: A review of human trials. *Nutrition & Metabolism*, *10*(1), 54.

**Taylor, D. M., & McAskill, R. (2000).** Atypical antipsychotics and weight gain—a systematic review. *Acta Psychiatrica Scandinavica*, *101*, 416–432.

**Tellegen, A., Watson, D., & Clark, L. A. (1999).** On the dimensional and hierarchical structure of affect. *Psychological Science*, *10*, 297–303.

**Testa, M. A., & Simonson, D. C. (1996).** Assessment of quality of life outcomes. *New England Journal of Medicine*, *334*, 833–840.

**Thompson, D., Edelsberg, J., Kinsey, K. L., & Oster, G. (1998).** Estimated economic costs of obesity to U.S. business. *American Journal of Health Promotion*, *13*(2), 120–127.

**Tohen, M., Baker, R. W., & Altshuler, L. L. (2002).** Olanzapine versus divalproex in the treatment of acute mania. *American Journal of Psychiatry*, *159*, 1011–1017.

**Torres, S. J., & Nowson, C. A. (2007).** Relationship between stress, eating behavior, and obesity. *Nutrition*, *23*, 887–894.

**Tremblay, S., Dahinten, S., & Kohen, D. (2003).** Factors related to adolescents' self-perceived health. *Health Reports, Statistics Canada*, *14*, 7–16.

- Tremblay, M. S., & Willms, J. D. (2000).** Secular trends in the body mass index of Canadian children. *Canadian Medical Association Journal*, *163*, 1429–1433.
- Treviño-Alvarez, A. M., Sánchez-Ruiz, J. A., Barrera, F. J., Rodríguez-Bautista, M., Romo-Nava, F., McElroy, S. L., & Cuéllar-Barboza, A. B. (2023).** Weight changes in adults with major depressive disorder: A systematic review and meta-analysis of prospective studies. *Journal of Affective Disorders*, *332*, 1–8.
- Troop, N. A., Holbrey, A., Trowler, R., & Treasure, J. L. (1994).** Ways of coping in women with eating disorders. *Journal of Nervous and Mental Disease*, *182*, 535–540.
- Tsigos, C., Hainer, V., Basdevant, A., Finer, N., Fried, M., Mathus-Vliegen, E., et al. (2008).** Obesity Management Task Force of the European Association for the Study of Obesity. Management of obesity in adults: European clinical practice guidelines. *Obesity Facts*, *1*(2), 106–116.
- Tuthill, A., Slawik, H., O'Rahilly, S., & Finer, N. (2006).** Psychiatric co-morbidities in patients attending specialist obesity services in the UK. *QJM*, *99*, 317–325.
- Tyrka, A. R., Walters, O. C., Price, L. H., Anderson, G. M., & Carpenter, L. L. (2012).** Altered response to neuroendocrine challenge linked to indices of the metabolic syndrome in healthy adults. *Hormone and Metabolic Research*, *44*(7), 543–549.
- Uher, R., Mors, O., Hauser, J., et al. (2011).** Changes in body weight during pharmacological treatment of depression. *International Journal of Neuropsychopharmacology*, *14*(3), 367-375.
- Unikel, C., Bojórquez, I., Villatoro, J., Fleiz-Bautista, C., & Medina-Mora, M. E. (2006).** Conductas alimentarias de riesgo en población estudiantil del Distrito Federal. Tendencias 1997-2003. *Revista de Investigación Clínica*, *58*(1), 15-27.
- U.S. Public Health Service. (1998).** *Suicide: A report of the Surgeon General*. Rockville, MD: Author.
- U.S. Public Health Service. (1999).** *Mental health: A report of the Surgeon General*. Rockville, MD: Author.
- Vaccarino, V., Johnson, B. D., Sheps, D. S., et al. (2007).** Depression, inflammation, and incident cardiovascular disease in women with suspected coronary ischemia: the National Heart, Lung, and Blood Institute-sponsored WISE study. *Journal of the American College of Cardiology*, *50*(21), 2044-2050.
- Vage, V., Solhaug, J. H., Viste, A., Bergsholm, P., & Wahl, A. K. (2003).** Anxiety, depression and health-related quality of life after jejunoileal bypass: a 25-year follow-up study of 20 female patients. *Obesity Surgery*, *13*, 706-713.
- Vandevijvere, S., Chow, C. C., Hall, K. D., Umali, E., & Swinburn, B. A. (2015).** Increased food energy supply as a major driver of the obesity epidemic: a global analysis. *Bulletin of the World Health Organization*, *93*(7), 446-456.
- van der Merwe, M. T. (2007).** Psychological correlates of obesity in women. *International Journal of Obesity*, *31*, S14-S18.

- van Gemert**, W. A., van der Palen, J., Monninkhof, E. M., et al. (2015). Quality of life after diet or exercise-induced weight loss in overweight to obese postmenopausal women: The SHAPE-2 randomised controlled trial. *PLoS One*, *10*(6), e0127520.
- van Hout**, G. C. M., van Oudheusden, I., & van Heck, G. L. (2004). Psychological profile of the morbidly obese. *Obesity Surgery*, *14*, 579-588.
- Vanina**, Y., Podolskaya, A., & Sedky, K. (2002). Body weight changes associated with psychopharmacology. *Psychiatric Services*, *53*, 842-847.
- Van Strien**, T., Herman, C. P., & Verheijden, M. W. (2009). Eating style, overeating, and overweight in a representative Dutch sample: Does external eating play a role? *Appetite*, *52*(2), 380-387.
- Veldhuis**, J. D., Roelfsema, F., Iranmanesh, A., et al. (2009). Basal, pulsatile, entropic (patterned), and spiky (staccato-like) properties of ACTH secretion: Impact of age, gender and body mass index. *Journal of Clinical Endocrinology & Metabolism*, *94*, 4045-4052.
- Venkatasubramanian**, G., Chittiprol, S., Neelakantachar, N., Naveen, M. N., Thirthall, J., Gangadhar, B. N., et al. (2007). Insulin and insulin-like growth factor-1 abnormalities in antipsychotic-naïve schizophrenia. *American Journal of Psychiatry*, *164*, 1557-1560.
- Vgontzas**, A. N., Pejovic, S., Zoumakis, E., et al. (2007). Hypothalamic-pituitary-adrenal axis activity in obese men with and without sleep apnea: Effects of continuous positive airway pressure therapy. *Journal of Clinical Endocrinology & Metabolism*, *92*, 4199-4207.
- Vingilis**, E. R., Wade, T. J., & Seeley, J. S. (2002). Predictors of adolescent self-rated health: Analysis of the national population health survey. *Canadian Journal of Public Health*, *93*, 193-197.
- Vinje**, H. F., Langeland, E., & Bull, T. (2016). Aaron Antonovsky's Development of Salutogenesis, 1979 to 1994. In M. B. Mittelmark, S. Sagy, M. Eriksson, et al. (Eds.), *The Handbook of Salutogenesis*. doi: 10.1007/978-3-319-04600-6\_4
- Vink**, D., Aartsen, M. J., & Schoevers, R. A. (2008). Risk factors for anxiety and depression in the elderly: A review. *Journal of Affective Disorders*, *106*, 29-44.
- Virtanen**, P., & Koivisto, A-M. (2001). Wellbeing of professionals at entry into the labour market: A follow-up survey of medicine and architecture students. *Journal of Epidemiology & Community Health*, *55*, 831-835.
- Volkow**, N. D., Wang, G. J., Fowler, J. S., Tomasi, D., & Baler, R. (2012). Food and drug reward: Overlapping circuits in human obesity and addiction. In C. S. Carter & J. W. Dalley (Eds.), *Brain Imaging in Behavioral Neuroscience* (pp. 1–24). Springer.
- Volkow**, N. D., Wang, G-J., & Baler, R. D. (2011). Reward, dopamine and the control of food intake: Implications for obesity. *Trends in Cognitive Sciences*, *15*(1), 37–46.
- von dem Knesebeck**, O., Hyde, M., Higgs, P., Kupfer, A., & Siegrist, J. (2005). Quality of life and well-being 2005, Health, Aging and Retirement in Europe. In A. Börsch-Supan (Ed.), Mannheim: Strauss, S. 199-203.

- Vyas, A., Mitra, R., Shankaranarayana Rao, B. S., & Chattarji, S. (2002).** Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. *The Journal of Neuroscience*, *22*(15), 6810–6818.
- Walker, B. R. (2001).** Activation of the hypothalamic-pituitary-adrenal axis in obesity: Cause or consequence? *Growth Hormone & IGF Research*, *11*(suppl A), S91-S95.
- Walley, A. J., Asher, J. E., & Froguel, P. (2009).** The genetic contribution to non-syndromic human obesity. *Nature Reviews Genetics*, *10*, 431–442.
- Wallis, D. J., & Hetherington, M. M. (2004).** Stress and eating: The effects of ego-threat and cognitive demand on food intake in restrained and emotional eaters. *Appetite*, *43*(1), 39–46. <https://doi.org/10.1016/j.appet.2004.03.003>
- Wand, G. S., Oswald, L. M., McCaul, M. E., Wong, D. F., Johnson, E., Zhou, Y., et al. (2007).** Association of amphetamine-induced striatal dopamine release and cortisol responses to psychological stress. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, *32*(11), 2310–2320. <https://doi.org/10.1038/sj.npp.1301359>
- Ware, J. E. (1987).** Standards for validating health measures: Definition and content. *Journal of Chronic Diseases*, *40*, 473–480.
- Wardle, J., Steptoe, A., Oliver, G., & Lipsey, Z. (2000).** Stress, dietary restraint and food intake. *Journal of Psychosomatic Research*, *48*(2), 195–202. [https://doi.org/10.1016/s0022-3999\(99\)00086-6](https://doi.org/10.1016/s0022-3999(99)00086-6)
- Wassertheil-Smoller, S., Shumaker, S., Ockene, J., Talavera, G. A., Greenland, P., Cochrane, B., et al. (2004).** Depression and cardiovascular sequelae in postmenopausal women. The Women's Health Initiative (WHI). *Archives of Internal Medicine*, *164*, 289–298.
- Watson, D., & Tellegen, A. (1985).** Toward a consensual structure of mood. *Psychological Bulletin*, *98*, 219–235.
- Weiner, R., Datz, M., Wagner, D., & Bockhorn, H. (1999).** Quality-of-life outcome after laparoscopic adjustable gastric banding for morbid obesity. *Obesity Surgery*, *9*(6), 539–545. <https://doi.org/10.1381/096089299765552639>
- Weiser, E. B. (2007).** The prevalence of anxiety disorders among adults with asthma: A meta-analytic review. *Journal of Clinical Psychology in Medical Settings*, *14*, 297–307.
- Weisler, R. H., Johnston, J. A., & Lineberry, C. G. (1994).** Comparison of bupropion and trazodone for the treatment of major depression. *Journal of Clinical Psychopharmacology*, *14*, 170–179.
- Wellmer, J., Wellmer, S., & Bauer, J. (2009).** The impact of zonisamide on weight. A clinical study in 103 patients with epilepsy. *Acta Neurologica Scandinavica*, *119*, 233–238.
- Wennerberg, M. M. T., Lundgren, S. M., & Danielson, E. (2012).** Using the salutogenic approach to unravel informal caregivers' resources to health: Theory and methodology. *Aging & Mental Health*, *16*(3), 391–402. <https://doi.org/10.1080/13607863.2011.615738>
- Werdermann, M., Berger, I., Scriba, L. D., Santambrogio, A., Schlinkert, P., Brendel, H., Morawietz, H., Schedl, A., Peitzsch, M., King, A. J. F., Andoniadou, C. L., Bornstein, S. R., &**

Steenblock, C. (2021). Insulin and obesity transform hypothalamic-pituitary-adrenal axis stemness and function in a hyperactive state. *Molecular Metabolism*, 43.

**Westerhof, G. J., & Keyes, C. L. M.** (2010). Positive aging: Introduction to the special issue. *Journal of Adult Development*, 17(2), 110. <https://doi.org/10.1007/s10804-009-9082-y>

**Whiteside, U., Chen, E., Neighborn, C., Hunter, D., Lo, T., & Larimer, M.** (2007). Difficulties regulating emotions: Do binge eaters have fewer strategies to modulate and tolerate negative affect? *Eating Behaviors*, 8(2), 162–169.

**The WHOQOL Group.** (1995). The World Health Organization Quality of Life Assessment (WHOQOL): Position paper from the World Health Organization. *Social Science & Medicine*, 41, 1401–1409.

**Wilborn, C., Beckham, J., Campbell, B., et al.** (2005). Obesity: Prevalence, theories, medical consequences, management, and research directions. *Journal of the International Society of Sports Nutrition*, 2, 4–31.

**Williams, L. J., Jacka, F. N., Pasco, J. A., Dodd, S., & Berk, M.** (2006). Depression and pain: An overview. *Acta Neuropsychiatrica*, 18, 79–87.

**Wise, R. A., & Rompre, P. P.** (1989). Brain dopamine and reward. *Annual Review of Psychology*, 40, 191–225.

**Wittchen, H. U., Jacobi, F., Rehmab, J., Gustavssonc, A., SvenssondB, M., Jönssone, B., Olesenf, J., Allgul anderg, C., Alonsoh, J., Faravellii, C., Fratiglionij, L., Jennumk, P., Liebl, R., Maerckerm, A., van Os, J., Preisi, M., Salvador-Carullap, L., Simonq, R., Steinhausenlrs, H.-C. et al.** (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European Neuropsychopharmacology*, 21(9), 655–679. <https://doi.org/10.1016/j.euroneuro.2011.07.018>

**Wittchen, H.-U., & Jacobi, F.** (2005). Size and burden of mental disorders in Europe — A critical review and appraisal of 27 studies. *European Neuropsychopharmacology*, 15(4), 357–376.

**Wittchen, H.-U., Jönsson, B., & Olesen, J.** (2005). Editorial: Towards a better understanding of the size and burden and cost of brain disorders in Europe. *European Neuropsychopharmacology*, 15(4), 355–356.

**Wolf, A. M., Falcone, A. R., Kortner, B., et al.** (2000). BAROS: An effective system to evaluate the results of patients after bariatric Surgery. *Obesity Surgery*, 10, 445–450.

**Wolf, A. M., & Colditz, G. A.** (1998). Current estimates of the economic cost of obesity in the United States. *Obesity Research*, 6(2), 97–106.

**Wolk, A., & Rössner, S.** (1996). Obesity and self-perceived health in Sweden. *International Journal of Obesity and Related Metabolic Disorders*, 20, 369–372.

**World Health Organization.** (1993). Tenth revision of the international classification of diseases, Chapter V (F): Mental and behavioral disorders: Clinical descriptions and diagnostic guidelines. Geneva: World Health Organization.

**World Health Organization.** (1995). Physical status: The use and interpretation of anthropometry. Report of a WHO Expert Committee. *WHO Technical Report Series*, 854. Geneva: World Health Organization.

**World Health Organization.** (1998). Report obesity: Preventing and managing the global epidemic. Geneva: World Health Organization. In: Roth, B., Munsch, S., Meyer, A., Winkler Metzke, C., Isler, E., Steinhausen, H. C., & Schneider, S. (2008). Die psychische Befindlichkeit übergewichtiger Kinder. *Zeitschrift für Kinder- und Jugendpsychiatrie und Psychotherapie*, 36(3), 163–176.

**World Health Organization.** (2004). Prevention of mental disorders: Effective interventions and policy options. Summary Report. A Report of the World Health Organization, Department of Mental Health and Substance Abuse in Collaboration with The Prevention Research Centre of the Universities of Nijmegen and Maastricht. Geneva: World Health Organization.

**World Health Organization.** (2008). The Global Burden of Disease: 2004 Update. Geneva: World Health Organization.

**World Health Organization.** (2005). Promoting mental health: Summary report. A Report of the World Health Organization, Department of Mental Health and Substance Abuse in collaboration with the Victorian Health Promotion Foundation and the University of Melbourne. Geneva: World Health Organization.

**World Health Organization.** (2021). Noncommunicable diseases: Risk factors. In: Global Health Observatory [website]. Geneva: World Health Organization. Retrieved from <https://www.who.int/data/gho/data/themes/topics/noncommunicable-diseases-risk-factors>.

**World Health Organization.** (2018). Childhood Obesity Surveillance Initiative (COSI) factsheet: Highlights 2015–17. Copenhagen: WHO Regional Office for Europe. Retrieved from <https://apps.who.int/iris/handle/10665/341189>.

**World Health Organization, WHO.** (2001). Mental health: Strengthening mental health promotion. Fact Sheet No. 220. Geneva, Switzerland. Retrieved June, 2022, from <http://www.who.int/mediacentre/factsheets/fs220/en/>.

**World Health Organization.** (1948). World Health Organization Constitution. In Basic Documents. Geneva, Switzerland: Author.

**World Health Organization.** (2008). The Global Burden of Disease: 2004 Update. Geneva, Switzerland: WHO.

**World Health Organization.** (2002). World Health Report 2002: Reducing risks, promoting healthy life. Geneva: WHO.

**World Health Organization.** (2000). Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. Geneva: WHO Technical Report Series 894. Retrieved from [http://libdoc.who.int/trs/WHO\\_TRS\\_894.pdf](http://libdoc.who.int/trs/WHO_TRS_894.pdf).

**World Health Organization.** (2004). Promoting mental health: Concepts, emerging evidence, practice: Summary report. Geneva: World Health Organization. Retrieved October 20, 2016, from [http://www.who.int/mental\\_health/evidence/en/promoting\\_mhh.pdf](http://www.who.int/mental_health/evidence/en/promoting_mhh.pdf).

**World Health Organization Regional Office for Europe.** (2015). Mental Health. Available at: <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/mental-health/mental-health>. Accessed on 23rd of March 2019.

**WHO Regional Office for Europe.** (2022). WHO European Regional Obesity Report 2022 [Internet]. Copenhagen: WHO Regional Office for Europe. Available from: <https://apps.who.int/iris/handle/10665/353747>.

**World Health Organization.** (2017). Geneva: The Organization. Retrieved from <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics>.

**Wysokiński, A., Sobów, T., Kłoszewska, I., & Kostka, T.** (2015). Mechanisms of the anorexia of aging—a review. *Age (Dordrecht)*, 37(4), 9821. <https://doi.org/10.1007/s11357-015-9821-x>

**Yannakouli, M., Panagiotakos, D. B., Pitsavos, C., Tsetsekou, E., Fappa, E., Papageorgiou, C., et al.** (2008). Eating habits in relations to anxiety symptoms among apparently healthy adults. A pattern analysis from the ATTICA Study. *Appetite*, 51, 519–525.

**Yanovski, S. Z., Nelson, J. E., Dubbert, B. K., & Spitzer, R. L.** (1993). Association of binge eating disorder and psychiatric comorbidity in obese subjects [Erratum appears in *Am J Psychiatry* 1993; 150: 1910]. *American Journal of Psychiatry*, 150, 1472–1479.

**Yau, Y. H., & Potenza, M. N.** (2013). Stress and eating behaviors. *Minerva Endocrinologica*, 38(3), 255–267.

**Zabelina, D. L., Erickson, A. L., Kolotkin, R. L., & Crosby, R. D.** (2009). The effect of age on weight-related quality of life in overweight and obese individuals. *Obesity (Silver Spring)*, 17(7), 1410–1413.

**Zhang, X., Zhang, M., Zhao, Z., Huang, Z., Deng, Q., Li, Y., Pan, A., Li, C., Chen, Z., Zhou, M., Yu, C., Stein, A., Jia, P., & Wang, L.** (2020). *Environmental Research Letters*, 15, 044009. <https://doi.org/10.1088/1748-9326/ab6614>

**Zajacova, A., & Burgard, S. A.** (2010). Body weight and health from early to mid-adulthood: A longitudinal analysis. *Journal of Health and Social Behavior*, 51(1), 92–107.

**Zatonski, W., Manczuk, M., Sulkowska, U., & HEM Project Team.** (2008). Closing the health gap in the European Union. Cancer Epidemiology and Prevention Division, the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland.

**Zautra, A. J., Hall, J. S., & Murray, K. E.** (2010). Resilience: A new definition of health for people and communities. New York: The Guilford Press.

**Zellner, D. A., Loaiza, S., Gonzalez, Z., Pita, J., Morales, J., Pecora, D., et al.** (2006). Food selection changes under stress. *Physiology & Behavior*, 87(4), 789–793.

**Zhang, Q., Deng, C., & Huang, X. F.** (2013). The role of ghrelin signaling in second-generation antipsychotic-induced weight gain. *Psychoneuroendocrinology*, 38, 2423–2438.

**Zhang, J.** (2021). The bidirectional relationship between body weight and depression across gender: A simultaneous equation approach. *International Journal of Environmental Research and Public Health*, 18(14), 7673. <https://doi.org/10.3390/ijerph18147673>

**Zhao, L.** (2013). The gut microbiota and obesity: From correlation to causality. *Nature Reviews Microbiology*, 11(9), 639–647.

**Zhao, S., et al. (2023).** Hyperleptinemia contributes to antipsychotic drug-associated obesity and metabolic disorders. *Science Translational Medicine*, 15, eade8460.  
<https://doi.org/10.1126/scitranslmed.ade8460>

**Zheng, D., Macera, C. A., Croft, J. B., Giles, W. H., Davis, D., & Scott, W. K. (1997).** Major depression and all-cause mortality among white adults in the United States. *Annals of Epidemiology*, 7(3), 213–218.

**Zipper, E., Vila, G., & Dabbas, M. (2001).** Obesity in children and adolescents, mental disorders and familial psychopathology. *Presse Médicale*, 30(3), 1489-1495.

**Zubin, J., & Spring, B. (1977).** Vulnerability: A new view of schizophrenia. *Journal of Abnormal Psychology*, 86, 103-126.

**Zysberg, L., & Rubanov, A. (2010).** Emotional intelligence and emotional eating patterns: A new insight into the antecedents of eating disorders? *Journal of Nutrition Education and Behavior*, 42(5), 345-348.

## Appendix

### Additional descriptive information

**Table 9:** Distribution of BMI categories in ATHIS

<b>BMI Category</b>	<b>n</b>	<b>%</b>
underweight	386	2.5
normal weight	7114	46.0
overweight	5427	35.1
obese	2534	16.4
Total	15461	100

**Table 10:** Depression severity according to the PHQ-8 depression scale (ATHIS)

<b>Depression Severity</b>	<b>n</b>	<b>%</b>
non-minimal	12462	80.6
mild	2204	14.3
moderate	569	3.7
moderately severe	179	1.2
severe	47	0.3
Total	15461	100

**Table 11:** Depression (yes/no) according to the PHQ-8 depression scale (ATHIS)

<b>Depression y/n</b>	<b>n</b>	<b>%</b>
no depression	12462	80.6
depression	2999	19.4
Total	15461	100

**Table 12:** Distribution of BMI categories in SHARE (wave 4)

<b>BMI Category</b>	<b>n</b>	<b>%</b>
underweight	145	0.9
Normal weight	5701	35.2
overweight	6815	42.1
obese	3523	21.8
Total	16184	100.0

**Source:** Reproduced without modifications from: Rindler G.A., Gries, A., Freidl, W. (2023). Associations between overweight, obesity and mental health: A retrospective study among European adults aged 50+. *Frontiers in Public Health*, Vol. 11, doi:10.3389/fpubh.2023.1206283. Copyright 2023 Frontiers in Public Health SA; Rindler, Gries and Freidl. The reuse of this content follows the terms of the Attribution International 4.0 License (CC BY 4.0), which permits any use, copy or redistribution of this illustration <https://creativecommons.org/licenses/by/4.0/>.