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Prediction of depressive disorders based on psychosocial parameters in a naturalistic cohort recruited in an outpatient setting

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vorgelegt von Lisa Monika Pfeiffer

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Erstes Gutachten: Prof. Dr. Peter Falkai

Zweites Gutachten: Prof. Dr. Antonius Schneider

Drittes Gutachten: Dr. Dominic Landgraf

Viertes Gutachten: Priv. Doz. Dr. Daniela Eser-Valeri

Dekan: Prof. Dr. med. Thomas Gudermann

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Abstract

It is generally known that the prevalence of depression rises dramatically when there are severe crises in the population. Since the COVID-19 pandemic, the number of new major depressive episodes has risen by around 27.6% worldwide. These alarming figures show that the prediction of depression is essential for the population worldwide. It is important to keep an eye on depression at an early stage, even after the rise of the pandemic and to make further efforts to ensure that depression can be recognized and treated at an early stage. Psychosocial parameters are of central importance in the diagnosis of depression, as they enable a comprehensive understanding of the factors influencing the development and severity of depression. They help to identify risk factors such as unemployment, social isolation and experiences of discrimination, which may increase the risk of depression. They may also enable individualized diagnosis and treatment that is tailored to the specific psychosocial challenges of patients. By taking these parameters into account, preventive measures and targeted interventions can be developed to improve treatment outcomes and increase the quality of life of those affected. Therefore, this study focusses on the prediction of depressive disorders using psychosocial parameters. The care of depression in multimorbid patients should be significantly improved in general practitioner (GP) care and depression should be detected as early as possible so that chronicity can be minimized. Psychosocial parameters should be considered in GP practice so that preventive action can be taken against the onset of depressive symptoms. To this end, the following parameters will be focused on in the GP setting: Age, gender, level of education, financial problems, previous mental illness in the family, discrimination, physical activity, loneliness and well-being. The logistic regression analyses showed significant correlations between the psychosocial variables (unemployment, population, discrimination at school, family history of illness, loneliness and social support) and the probability of depressive illness (SKID II) in the outpatient setting. Using a machine learning approach, a model was created to better classify the depressed patients from the mentally unimpaired patients. We found that loneliness, social well-being, number of inhabitants, physical activity and unemployment play a substantial role in improving the diagnosis of depression. Future studies should have a focus on psychosocial parameters in outpatients with depression. Since our study sample was small, results should be confirmed in independent cohorts.

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IV List of abbreviations

AUC Area under curve

BDI-II Beck-Depression-Inventory

ELSA The Brazilian Longitudinal Study of Adult Health

GP general practitioner

ICD-10 International Statistical Classification of Deseases and related health problems

KNN K-Nearest Neighbors Imputation

Imbfgs Limited-memory Broyden-Fletcher-Goldfarb-Shanno Algorithm

LSNS6 Lubben Social Network Scale

MADRS Montgomery-Asberg Depression Rating Scale

ML Machine learning

PHQ Patient Health Questionnaire

ROC Receiver Operating Characteristic

SCID-5-CV Structured Clinical Interview for DSM-5 Disorders - Clinical Version

SMOTE Synthetic Minority Over-sampling Technique

UCLA University of California, Los Angeles

WHO World health organization

WHO-5 5-Item-Well-beeing-Index

1. Theoretical background

1.1 Depression

Depression is a serious illness that significantly impairs quality of life and is associated with high health and social burdens. According to the World Health Organization (WHO), more than 300 million people worldwide suffer from a depressive disorder, which accounts for around 4.4% of the world's population (WHO, 2017). The most common mental illness in Germany, right after anxiety disorder at 15.4%, is affective disorders at 9.8%, of which unipolar depression alone accounts for 8.2% (Jacobi et al., 2016). Millions of people across Europe are affected by depression, and the data for Germany reflects this worrying trend. There has also been a significant increase in cases of depression in this country, which underlines the need for targeted measures and support (WHO, 2017). The latest findings show that the data for depressive disorders has risen by 16.4%. Worldwide, a high burden of disease has been detected (GBD, 2024). This underlines the urgency of investing heavily in prevention and treatment

1.1.1 Prevalence and diagnosis of depression

In the following, the prevalence in relation to the effects of the psychological and social parameters will be taken across Europe and then specifically in Germany. In order to be able to compare the prevalence to the European area, depressive symptoms were surveyed using the Patient Health Questionnaire 8 (PHQ8) with 254.510 participants from Germany and 24 EU member states. This study showed a prevalence of 9.2% in Germany, which is higher than the European average of 6.6%. This affects 10.8% of women and 7.6% of men. The EU average was 7.9% for women and 5.2% for men, which was significantly lower than in Germany. Looking specifically at the severity of depression, the prevalence of a mild depressive episode in Germany is 6.3% and the European average is 4.1% (Hapke, Cohrdes, & Nübel, 2019). In Germany, there is a population-representative health survey for adults, Gesundheit in Deutschland aktuell, which is linked to the Robert Koch Institute. Since 2014/2015, the main focus has been on self-assessment of general health, health complaints and the resulting restrictions in everyday life, as well as mental health. In particular, people who had their place of residence in Germany were surveyed. Between 2008 and 2011, the Patient Health Questionnaire 9 (PHQ9) was used to measure depressive symptoms in 7.988 German adults aged 18 to 79. In this study, 8.1% of adults (10.2% of women and 6.1% of men) had experienced depressive symptoms (Busch et al. 2013). The older population (aged 65 and over) had a lower level of depressive symptoms (6.7%) in contrast to the younger population (aged 15-29) with 11.5%. Compared to the European average, older people in Germany are affected at 9.1% and younger people at 5.2% (Hapke, Cohrdes, & Nübel, 2019). Alarming figures were published by the WHO in 2015. It is estimated that 322 million people worldwide are affected by depression. This corresponds to 4.4% of the world's population and has increased by 18% in the last ten years (WHO, 2017). In the study by Jacobi and colleagues (2016), 23.602 people aged 18 and over with permanent residence in Germany were surveyed between November 2014 and July 2015. For this purpose, depressive symptoms were calculated using the PHQ8 within the last two weeks. The lifetime prevalence of depressive symptoms in this study was 11.6% overall (15.6% for women and 8.6% for men). An earlier study by Busch et al. (2013) already showed an accumulation of depression in the 18 to 29 age group, with a prevalence of 11.8% among women. The research group of Strine et al. (2006) came to the same conclusion, showing that the probability of having depressive symptoms is lower in adults aged 55 than in 18 to 24-year-olds. A subsequent study (Heidemann, 2021) collected further data from the general population between April 2019 and September 2020. These were based on a random sample and due to the COVID-19 pandemic, were mainly recruited via landline and mobile phone numbers. The PHQ8 was also used again to survey depressive symptoms. A total of 22,708 people between the ages of 18 and 99 took part in the survey (11.959 women, 10.687 men and 60 participants with a different gender identity or no gender identity). Within the last two weeks, 8.3% of participants reported depressive symptoms (8.8% women and 7.5% men).

1.1.2 Diagnostics of depression

Affective disorders can occur in both unipolar and bipolar forms, but this paper only refers to unipolar depression. In the *International Statistical Classification of Diseases and related health problems* (ICD-10), depression is subdivided into a mild (F32.0), moderate (F32.1) and severe (F32.2) episode (WHO, 2019). The latter can be present with or without psychotic symptoms. In all episodes, those affected suffer from the following three main symptoms: a depressed mood, a loss of interest/joylessness and a reduction in drive. There are also accompanying symptoms such as concentration and attention difficulties. There may be an increase in pronounced tiredness and early waking with difficulty falling asleep and sleeping through

the night. The symptoms can also affect eating behavior with a reduced appetite. The ability to feel pleasure may be diminished, a reduced sense of self-worth and difficulties with self-confidence may occur. Feelings of guilt or thoughts about one's own worthlessness can permeate everyday life. In addition to hopelessness, suicidal thoughts or actions can also occur. The depressed mood is either present with a morning low or constantly. The effects can also influence the loss of libido. Other somatic symptoms may also be present, as well as marked psychomotor inhibition or agitation. Depending on the predominant symptoms, a mild, moderate or severe episode can be diagnosed. In order to be diagnosed, the main symptoms must have been present for at least 14 days without interruption. A repeated depressive episode is coded as a recurrent depressive disorder. There are also several other diagnoses that involve a persistent and usually fluctuating mood disorder, such as persistent affective disorder with cyclothymia (F34.0) or dysthymia (F34.1) (WHO, 2019).

In order to fully understand the diagnostic process of unipolar depression, the symptoms, the course over time and the differential diagnosis of other disorders must be recorded. It is also necessary to determine whether comorbidities such as metabolic syndrome and suicidal tendencies are present (WHO, 2019). In addition to ICD diagnostics, the S3 guidelines (AWMF, 2022) recommend diagnostics based on the bio-psycho-social model according to the IDF criteria (International Classification of Functioning, Disability and Health) with a psychosocial history and the recording of limitations in quality of life, functioning and participation of associated components of a diagnostic process. This approach is primarily intended to reduce over- and under-diagnosis and the resulting incorrect, under- or over-therapy. The diagnostic interview is the gold standard of diagnostics. The following psychometric tests are recommended as self-assessment scales: PHQ9, Beck Depression Inventory (BDI-II), Hospital Anxiety and Depression Scale (HADS), Questionnaire for the Diagnosis of Depression (FDD-DSM.IV) and the General Depression Scale (CES-D). The following four questionnaires were recommended as external assessment scales: Hamilton Depression Rating Scale (HDRS₁₇, HDRS₂₁ & HDRS₂₄), Bech-Rafaelsen Melancholia Scale (BRMS), Montgomery-Asberg Depression Rating Scale (MADRS) and the *Inventory of Depressive Symptoms* (IDS-C).

With regard to differential diagnosis, the following diagnoses must be ruled out in advance: bipolar disorders and cyclothymia, adjustment disorders, grief reactions and organic affective disorders (neurological focal symptoms, pronounced cognitive impairment psychotic

symptoms, known severe chronic or acute somatic comorbidities, etc.). Multifactorial explanatory concepts are convinced that an interaction between biological and psychosocial factors can be assumed. Several risk factors for the occurrence of a depressive disorder have been identified. On the one hand, biological factors can have an influence on depression. A family history of depressive disorders or first-degree relatives may have a genetic vulnerability (Köhler et al., 2018). Another aspect is socio-demographic factors, which are discussed in particular in this study. These include gender, older age, belonging to an ethnic minority and low socio-economic status. Other psychological factors and psychosocial risk factors such as loneliness, widowhood, social isolation, current stressful life events or chronic stress can be risk factors for the development of depression (Köhler et al., 2018). In addition, lifestyle changes such as diet, smoking or lack of exercise can increase the risk of developing depression (Berger et al., 2019). Engel (1977) developed the biopsychosocial model as an explanation for the development and course of depression, which emphasizes that biological, psychological and social factors play a reciprocal role.

1.2 Psychosocial impairments

The following section provides an overview of psychosocial factors and their role in depressive disorders. These influence not only the risk of developing depression, but also the course and treatment of the illness. The bio-psycho-social model (Engel, 1977) already shows us the interaction that both psychological and social components are closely linked. Psychosocial factors include, for example, family and interpersonal relationships, life events, occupational and financial stressors, as well as social support and integration. There is no single definition for psychosocial components (Engel 1977). The following section focuses specifically on social determination and its aspects and then describes loneliness and well-being in detail.

1.2.1 Social determinants

Social determination has focused on how living and working conditions can influence people's health status (Marmot, 2005). Social determinants are considered to be the driving cause of many global health inequalities, such as lower life expectancy, higher infant mortality rates and a higher disease burden in disadvantaged population groups. Social determination was based on the concept of *social gradient*. This indicates that people with lower social status face greater health risks and have a shorter life expectancy compared to those with higher status, and that the impact of social position can build up over time (Marmot & Bell, 2016).

Differences in social determinants are viewed as a consequence of unequal resource distribution and can be mitigated through targeted social and economic policies and program development (Marmot et al., 2008). In terms of mental health, the social gradient affects both the risk of disorders and access to services. In a review of social determination, Allen and colleagues (2014) used a model that incorporated: a life-course perspective, spanning from prenatal stages to old age; community-level contextual factors, such as environmental conditions and healthcare systems; and country-level factors, including political and economic conditions, cultural norms, and specific policies. Overall, they found that mental disorders disproportionately impact poor and disadvantaged populations. They also acknowledged that cumulative stress and physical health may act as mechanisms through which the effects of social determinants intensify over the course of a lifetime (Allen et al., 2014). Other research shows how cumulative aspects can influence health over several generations (Braveman, Egerter & Williams, 2011). With the development of social determinants, a distinction between upstream and downstream determinants has arisen. Braveman and colleagues (2011) highlight those downstream social determinants, such as economic opportunities, serve as underlying causes that typically influence health through upstream social determinants, such as living conditions. They broadened the concept of social determinants to encompass all non-medical factors affecting health. This includes not only fixed individual characteristics like gender and race/ethnicity but also more flexible factors such as educational attainment, occupational status, and social support. Fisher and Baum (2010) discuss the impact of chronic stress on mental health and explore how low socioeconomic status affects mental health for individuals at the lower end of the social gradient. This includes the stress of managing daily challenges, fear of uncertain and unpredictable living conditions, and a perceived lack of control.

In the 1970s, it was first established that there is a gender-specific difference in depression (Bebbington (1996); Piccinelli & Wilkinson (2000), Kühner (2003)). In some cases, it was found that almost twice as many adult women as adult men suffer from depression (Weissman and Klerman (1977). The study by Frank, Carpenter & Kupfer (1988) examined gender differences in a cohort of 230 patients with recurrent depression. The subjects came by self-referral, physician referral or a broad-based public information campaign. Both male and female patients had comparable clinical characteristics and baseline severity. However, gender differences were found in specific depressive symptoms and response to treatment, particularly in the use of self-report instruments. Female patients showed increased levels of

appetite and weight gain, increased somatization, and increased expressions of anger and hostility. In contrast, male patients responded more quickly to treatment. Despite the large number of studies that found that there are differences in relation to gender, critical opinions on the study situation are also expressed. Hammarström et al. (2009) aimed to critically evaluate medical publications on depression about gender-specific factors and their explanatory models. It was specifically pointed out that a closer look at and a better understanding of gender differences in depression are of great importance. In particular, it was criticized that many medical articles often relied on stereotypical or generalized assumptions about gender. The complex interactions between biological, social and psychological factors were not sufficiently taken into account. As a result, important nuances in the diagnosis and treatment of depression may have been overlooked. The study by Salk, Hyde & Abramson (2017) examined gender-specific differences in depression using a meta-analysis. In particular, the influence of gender on diagnosis and symptoms was examined. Women were diagnosed with depression more frequently than men and differences were found in the specific symptoms. Sadness and feelings of hopelessness were reported equally frequently in both genders. Women tended to show a higher burden of sleep disturbances, weight loss and weight gain, excessive fatigue and increased feelings of guilt. Men, on the other hand, showed abnormalities such as irritability, aggression or risky behavior, especially at the behavioral level. The results of the study are primarily aimed at focusing not only on the prevalence of depression, but also on the type and intensity of the symptoms. While extensive studies have already shed light on the genderspecific difference, the effects in the context of primary care are less well understood.

Concerning the size of the place of residence, the lowest prevalence of depressive symptoms was found in small towns compared to people living in large cities, medium-sized towns and rural areas (Busch et al. 2013). Robinson and his research team (2017) also confirmed in relation to urbanicity that a lower prevalence of disorders is shown in rural areas compared to city dwellers. The prevalence of depressive symptoms varied between federal states (e.g. Berlin: 14.6%, Thuringia: 7.4%). Among men, the lowest prevalence was found in Bavaria (5.7%). The gender differences are particularly striking in Bavaria (11.2% to 5.7%) and Brandenburg (14.6% to 7.5%). There were probably several reasons for the increase from 8.1% in 2014 to 10.1% in 2017. One of the causes may be the temporal trend, as well as the different questionnaire selection of the PHQ; further research on this is necessary (Bretschneider, Kuhnert & Hapke, 2017).

When looking at the educational status, it is also clear to see that a lower prevalence was shown in the upper education group than in the middle or lower education group. When age, gender and level of education are combined, it was found that one in five women in the lower education group aged between 18 and 29 had depressive symptoms (22.4%). For men in the lower education group, the highest prevalence was found between the ages of 30 and 44 (17.8%) (Strine et al., 2006).

Here too, the frequency of depressive symptoms decreased with increasing education. Women in the lower education group were three times as likely to be affected by depressive symptoms, men four times as often. Overall, depressive symptoms were found to be lower with increasing age and higher education (Heidemann, 2021).

In addition, a correlation was found between socioeconomic status and the prevalence of depressive symptoms. People with a low socioeconomic status showed a threefold higher prevalence than people with a low socioeconomic status (Busch et al. 2013).

The assessment of factors such as prevalence, age, gender, level of education and socio-economic status is crucial to obtain a comprehensive picture of depression. Concerning to the factors mentioned, the studies show an influence on the severity of depressive symptoms. To specifically examine the various factors, several aspects are usually examined simultaneously in studies, which sometimes makes the individual presentation difficult. In view of the psychosocial aspects as described: Age, gender, level of education, place of residence, it is important to keep the living and working circumstances in mind as well. As determinants, these can have a significant influence on people's health outcomes and are therefore now explained in more detail.

In recent years, it has been shown that social determinants have an impact on mental health in certain population groups. For example, unemployment, precarious employment and working conditions have been associated with increased psychological distress (Hans & Lee, 2015; Reibling et al., 2017). More specifically, employment status has even been found to impact mental health. Affleck, Carmichael, and Whitley (2018) demonstrated that unemployment has a more significant impact on men mental health compared to women. Research from Sweden has shown that individuals with lower incomes commonly experience poor mental health (Amroussia, Gustafsson & Mosquera, 2017). Family relationships also have an impact on mental health, both negative and positive. More specifically, reduced depressive symptoms were linked to living with family, positive family relationships, and strong family

bonds (Han & Lee, 2015; Brydsten, Hammarström & San, 2018). Health data also showed a strong connection with support from others, feelings of community belonging, and confidence in others (Brydsten, Hammarström & San, 2018; Han & Lee, 2015; Salami et al, 2017; Pflum et al, 2015). Other protective factors against mental health disorders are the impact of perceived emotional support and the size of the friend and family network (Smyth et al., 2015).

Concerning society, the focus was increasingly placed on safety in the neighborhood. Based on personal perceptions and experiences, neighborhood safety has been examined and found to be an important predictor of mental health (Chen et al., 2017; Stansfeld et al., 2017). A study in China showed that a lower level of depression is associated with satisfaction in the living environment and safety in the neighborhood. The study by (Fu, 2018) can substantiate this aspect with the result that a higher level of depression stands out in neighborhood conflicts. The psychosocial aspects play an important role in the analysis of social determination. These factors not only shape individual experiences and perspectives, but also significantly influence social positioning and access to resources within a society. By understanding the interactions between psychosocial variables and social determinants, deeper insights can be gained into how structural inequalities emerge and persist. This makes it clear that a holistic view of these aspects is essential in order to develop effective strategies for prevention and health promotion. However, the reverse approach must also be kept in mind. Mental illness can have an impact on social factors such as homelessness, dropping out of school and unstable marriages (Corrigan et al., 2012; Ljungqvist et al., 2016; Hjorth et al., 2016).

1.2.2 Loneliness

If the variable of loneliness is now examined, this must be specified in the context of depression. This plays an important role in the development of effective prevention and treatment approaches. For this reason, the focus is now specifically on loneliness and several research findings have already been presented and reviewed for the GP setting. It should be noted that research interest in loneliness has increased, especially during the COVID-19 pandemic (Entringer, 2022), so the current studies are often related to COVID-19. However, this paper does not specifically address the pandemic period, but the latest figures should illustrate that loneliness is an important parameter. Loneliness, or subjective social isolation, is defined as an aversive experience that occurs when a person's network of social relationships is perceived as quantitatively or qualitatively desolate. This means that a person can be lonely

both when they have fewer social relationships than they would like (quantitatively) and when their social relationships are not as deep and fulfilling as they would like (qualitatively). Loneliness can occur when a person realizes that their social environment is insufficient and their need for attachment is unmet. A defining characteristic here can be the lack of controllability or changeability, as well as the fact that it is not observable from the outside. Objective social isolation can be distinguished, as this refers to the objective absence of a caregiver. It is important to distinguish between the two terms, as objective isolation is not a sufficient condition for loneliness. For example, a high number of social contacts does not protect against the feeling of being alone. A person can very well be alone and not feel lonely, but it also means that a person can be in a relationship but feel lonely in it. A further conceptual distinction must be made with the word being alone. In most cases, the state of being alone is consciously chosen and is an objective state. For example, you can do something on your own and enjoy the time. Objective isolation is only as bad as it is voluntarily chosen (Krieger & Seewer, 2022). Various researchers (Knight et al., 1988; McWhirter, 1990; Brewer & Gardner, 1996) have undertaken different categorizations over time to better represent loneliness. The following categorization is now presented: Emotional loneliness describes the lack of a close, intimate bond, such as in a romantic relationship. Social loneliness, on the other hand, describes the lack of friendships and other personal relationships. Collective loneliness refers to the feeling of not being part of a larger community or society as a whole. Although this distinction is useful in theory, in practice it is often difficult to separate these different aspects (Hawkley, Browne & Cacioppo, 2005). As loneliness is not a formal diagnosis in a medical context, there are no standardized diagnostic criteria that clearly define loneliness. In addition, there is a lack of standardized and systematically collected epidemiological data to specifically describe it. This severely limits comparability between the various studies. There is no clearly defined, generally valid threshold that determines when a person is considered lonely (Krieger & Seewer, 2022). In the SOEP (Socio-Economic Panel) and the SOEP-CoV (Socio-Economic Panel Corona Special Survey) study, loneliness was measured using the SOEP-UCLA loneliness scale (Hawkley et al., 2016). The Socio-Economic Panel is a long-term study of a representative nature that is conducted in Germany and includes both households and individuals. The questionnaire contains three questions, which together should reflect the respondents' current feelings of loneliness. These questions are as follows: "To what extent do you feel that you lack the company of others?", "How often do you feel excluded?" and "How often do you experience social

isolation?". Respondents were asked to answer these three questions on a five-point response scale from "1 = Never" to "5 = Very often". The answers to all three questions were averaged to produce a loneliness index for each person for the following analyses, with possible values ranging from 1 to 5 and higher values indicating greater loneliness. Individuals who scored a mean of at least three on the loneliness scale were conspicuous. This means that, on average, they felt lonely at least occasionally.

In 2013, the proportion of people in Germany who were at least occasionally affected by loneliness was 14.4%, while in 2017 it was 14.2% (Entringer, 2022). This prevalence rate makes it clear that loneliness is a widespread phenomenon and not just an isolated occurrence. In fact, a considerable number of people in Germany are affected by loneliness. According to the study results, 40.1% of the German population experienced loneliness at least occasionally during the period under review (Entringer, 2022). This proportion is alarmingly high and is likely to be due to social isolation caused by restrictions on interpersonal contact. However, it should be noted that most studies on loneliness during the COVID-19 pandemic are based on cross-sectional data, which means that a direct comparison with values from previous years is not possible. In addition, loneliness during the second lockdown has hardly changed compared to the first lockdown. At 42.3%, it remained at a consistently high level, even though contact restrictions were still in place. However, it is unclear whether this longlasting loneliness has become chronic over the course of the COVID-19 pandemic or whether it is a temporary state of loneliness that decreases as contact restrictions are eased. This cannot be assessed based on the available data. It is therefore important to closely monitor loneliness in the German population in the coming years. This is the only way to identify at an early stage whether the figures are falling significantly. Before the outbreak of the COVID-19 pandemic, older people over the age of 75 had the highest prevalence of loneliness (16.6%), followed by people aged 30 to 45 (15.3%) and people under the age of 30 (14.5%). People aged 45 to 60 (13.1%) and 60 to 75 (12.7%) were the least affected by loneliness (Entringer, 2022). The prevalence of loneliness by gender showed no significant differences between 2013 and 2017. Women tended to be slightly lonelier than men, with prevalences of 15.7% and 12.5% respectively. A similar pattern emerged in relation to education level and income. People with low education or income were lonelier than those with medium or high education or income. Before the pandemic, 22.1% of those with low education were lonely, compared to 14.1% of those with medium education and only 10.0% of those with high education (Entringer, 2022). The post-pandemic results further confirm that those with a low level of education are at increased risk (Kirkland et al., 2023).

Entringer (2022) was also able to find significant results with regard to migration background: People with a direct migration background were more likely to be affected by loneliness before the pandemic than those without a migration background, with prevalences of 21.8% and 12.6% respectively. People in employment had a lower prevalence of loneliness than those not in employment, with prevalence rates of 11.1% [10.4% - 11.9%] and 18.9% [17.7% - 20.1%] respectively. Household structure was also an important factor: single parents had the highest prevalence of loneliness (22.7%), followed by people living alone (18.5%) and couples with children (12.8%). The prevalence of loneliness also differed depending on the type of employment. Full-time employees were less lonely than non-full-time employees (10.0% vs. 16.8%). Shift work was also associated with a lower prevalence of loneliness (11.5% vs. 15.1%). Place of residence and previous depression diagnosis were other important factors. People with a previous diagnosis of depression had an increased risk of being lonely (33.7%). The trend across different population groups has been mixed during the COVID-19 pandemic. Some groups, such as women, younger people and couples with children, became new risk groups. On the other hand, pre-pandemic risk factors such as education level, income and employment no longer played a significant role in the prevalence of loneliness during the pandemic (Entringer, 2022). The effects of the COVID-19 pandemic will not be discussed further in this report. The prevalence of loneliness in Germany is comparable to that in other European countries. For example, in Spain in 2011, 11.5% of the population reported being lonely regularly (Yang & Victor, 2011), while in the UK in 2018, around 16% of people were affected by loneliness at least occasionally (Pyle & Evans, 2018). In Greece, loneliness even affected around 21% of the population in 2016 (Baarck et al., 2021). Studies show that loneliness is associated with a major health risk. Chronic loneliness can promote both mental and physical illnesses. People with a chronic illness have a lower level of life satisfaction and a lower sense of well-being. In addition, the risk of developing an anxiety disorder or depression increases (Domènech-Abella et al, 2019). The study by Domènech-Abella et al. (2019) also provided important insights into the complex relationships between mental health problems, loneliness and social networks in old age. They emphasized the importance of social relationships and the role of loneliness as a risk factor for mental health problems in older people.

1.2.3 Well-being

The last psychosocial parameter to be examined in this study is well-being. When researching this topic, it is noticeable that it has mainly been studied in relation to older people and that there is little research on younger people. In the Irish Longitudinal Study on Ageing (TILDA), older people were defined as those who had reached an advanced stage of life, typically retirement age or beyond. In this longitudinal study, researchers focused specifically on health, well-being and other aspects of ageing in people in Ireland. The research group (Hom et al., 2020) analyzed a large number of studies using a meta-analysis to determine whether there was a consistent relationship between sleep problems and loneliness. Sleep problems were defined as problems such as insomnia, restless sleep, too little sleep or other sleep disorders. It was shown that sleep problems and loneliness are significantly linked. People with sleep problems have an increased risk of feeling lonely and vice versa. A systematic review and meta-analysis (Valtorta et al., 2016) also found that there is a link between loneliness, social isolation and the risk of coronary heart disease and stroke. People who feel lonely or socially isolated have an increased risk of developing cardiovascular disease compared to people with strong social ties and a sense of belonging. A considerable number of studies have found statistically significant associations between depressive symptoms and loneliness. Two research teams identified a small but significant association (Hsueh et al., 2019; Lim & Kua, 2011). Other studies found a moderate effect size (Conde-Sala et al., 2019; Green et al., 1992; Sjöberg et al., 2013), while a single study found a significant effect size (de la Torre-Luque et al., 2019). In order to shed more light on the aspect of well-being, the study by Henkel and colleagues (2003) is included, as they provided essential study results. The results of the study suggest that the use of the WHO-5 as a diagnostic tool improves the ability of GPs to recognize depressive symptoms. The questionnaire could serve as a checklist for GPs to clarify the diagnosis of depression as quickly as possible. The WHO (1998) already recommends integrating this step as a standard part of the general practitioner's consultation and having it available in the waiting room as standard.

1.3 Psychosocial impairments in primary care

As primary care providers for patients with a depressive disorder, GPs are crucial in setting the course for guideline-based intervention. Depression is one of the most commonly diagnosed mental disorders in patients who consult a general practitioner. Studies estimate

that up to 20% of patients attending primary care outpatients have clinically significant depression (Burnham et al., 1989; Coulehan et al. 1990; Gerber et al., 1992). Then, as now, most patients with depression are first treated in primary care and not in the psychiatric sector (Manderscheid et al., 1993 and Regier et al., 1993).

1.3.1 Influence of psychosocial factors on depression care

In the current global scientific debate on medical care, the importance of psychosocial factors for the health and well-being of the population is increasingly emphasized. These factors, which include both socio-demographic and clinical variables, are of crucial relevance to the structure and effectiveness of the healthcare system. A recent empirical study addresses this issue by examining the relationship between psychosocial parameters and the implementation of preventive mental health interventions in primary care practices. For the study by Müller et al, (2024), comprehensive data were collected from a total of 126,306 patients (57.6% women and 42.2% men) in primary care in Michigan. The sample included a variety of individuals of different ages (16-104 years), gender, ethnicity, and clinical characteristics. The retrospective cohort sample was collected from 18 primary care clinics within the health system. Subjects were interviewed using the PHQ4, PHQ9 and the GAD7. Sociodemographic data were collected uniformly during the first encounter with patients. Results showed that certain demographic characteristics, such as younger age and female gender, were associated with higher rates of mental health screening in primary care. Clinical characteristics, such as the presence of certain chronic conditions or the number of physician visits, were also significant. The descriptive analyses revealed a significant association between clinic size and location and the prevalence of mental health screening, which was confirmed in both regression models. It was surprising to find that smaller clinics and clinics in areas with a shortage of mental health providers had significantly higher rates of mental health screening (Müller et al., 2024). No gender-specific differences were found in the assessment of health status by doctors. However, women usually rate their state of health worse than men. They mainly report pain or problems during sexual intercourse (Krönke & Spitzer, 1998). Men, on the other hand, rate their lack of appetite, overeating and a feeling of failure or guilt more frequently as problematic (Williams et al., 1995). The 2003 study by Hildebrandt, Stage and Kragh-Sørensen examined gender differences in the severity and symptoms of depressive disorders in general practices in Denmark. The authors analyzed data from 230 patients who had to have met the criteria for recurrent depression according to the ICD-10 criteria. They found that male and female patients had similar clinical characteristics and severity. However, there were genderspecific differences in symptoms. Women were more likely to show symptoms such as increased appetite, weight gain, somatization and expressions of anger and hostility. In contrast, male patients responded more quickly to treatment. In the study by Bertakis et al. (2001), it was observed that women had a higher prevalence of depressive symptoms, which they selfreported using the BDI. Women with elevated BDI scores indicating severe depression were more likely to be diagnosed by their GP than men with comparable BDI scores (N=508). Recruitment took place as follows, prior to the first GP appointment, study participants were interviewed to collect socio-demographic data and to assess their self-reported depressive symptoms and general health. In the study described, the following hypothesis was put forward: female patients are more likely to be diagnosed as depressed by their GPs, which is associated with a higher clinical prevalence of depression. In addition, it was suggested that the increased use of healthcare services by female patients contributes to the higher proportion of women diagnosed with depression. This is because increased contact with female patients enables doctors to identify their depression more accurately. Subsequently, Poutanen and colleagues (2009) also addressed the question of whether there may be gender-specific differences in the diagnosis of depression. In the Finnish sample, however, it was shown that men exhibited more severe depressive symptoms than women. In general, empirical evidence has shown that the low treatment rate among men is not due to a better state of health, but to the discrepancy between the perception of need and help-seeking behavior. This is mostly due to outdated traditional social norms of masculinity (Möller-Leimkühler, 2002). Other aspects of social determination have not yet been studied more specifically in the GP and outpatient setting in Germany.

1.3.2 Empirical studies on depression treatment in primary care

There are already studies in Germany that have looked at depressive symptoms in primary care. The *Depression 2000* study (Winter et al., 2000) was one of the first nationwide epidemiological cross-sectional studies in primary care to provide data on the prevalence of depressive illnesses on a specific reference date. Complete data were collected from a total of 14,758 patients aged 16-65 years in 412 GP practices and compared with GPs' statements.

On that day, every patient was requested to fill out a standardized survey that gathered details about their biosocial background, the purpose of their doctor's visit, the impact of their symptoms on daily life, any prior treatments or assistance sought, signs of depression, and the progression of their condition. Depressive symptoms were evaluated using the Depression Screening Questionnaire (DSQ) (Wittchen & Perkonigg, 1997), a well-established tool known for its high diagnostic sensitivity and specificity in diagnosing depression based on DSM-IV and ICD-10 criteria. After the patient questionnaires were completed, the physicians performed a separate clinical evaluation using a standardized assessment tool to determine the diagnostic status, severity of the condition, ongoing and past treatments, and other therapeutic measures. According to the completed patient questionnaires in the study, the prevalence of depressive disorders (according to ICD-10 criteria) in GP practices is 10.9%. However, one disadvantage of the study is that it does not allow any conclusions to be drawn about the connection between depression and physical illness. Beesdo-Baum and colleagues (2017) recruited 3499 completed patient questionnaires in the form of an epidemiological study. This questionnaire recorded the reason for the consultation, biosocial characteristics, health conditions, depressive and other psychological complaints, treatments and current quality of life. The participating patients were on average 53.8 years old (range: 18-95 years) and 60.4% were female. After the consultation, the practitioner completed a questionnaire on physical and mental health conditions, diagnoses and treatments. A total of 3367 patients and doctors' questionnaires were included in the data analysis. Depressive symptoms were also measured in this study using the DSQ. On the cut-off date of the study, the prevalence of depression according to the DSQ (ICD-10 criteria) was 14.3% and 10.7% according to the medical diagnosis. Half of the patients identified by the DSQ were also diagnosed with depression by their doctor. The DSQ shows that people over the age of 65 were less likely to be affected. The practitioners mainly diagnosed women aged 40 and over with full-blown depression. In comparison, only a few physician variables were associated with a match between the study diagnoses of the DSQ and the physician's assessment. Doctors with an additional qualification in psychotherapy recognized the conspicuous DSQ cases significantly better (65.3 %) than doctors without this additional qualification (47.0 %) (Beesdo-Baum et al., 2017). Another study (Jacobi et al., 2002) in the past deals with reported depressive disorder in the GP setting measured on one day. A total of 20,421 patients were also surveyed with the DSQ in several GP practices in Germany. The information provided by the patients was compared with the information on the doctors' assessment forms. The results confirmed that here too, 11.3% of patients fulfilled the ICD-10 criteria for a depressive disorder. On the reference date, 4.2% of primary care patients met the criteria for major depression according to DSM-IV. The probability of meeting these criteria was higher in women than in men. The analyses of potential predictors showed that people over 40 years of age were more frequently affected than people under 40 years of age. On a positive note, the detection rate of general practitioners was 59%, which is slightly higher than in the comparative studies. This may have been mainly due to the fact that 13.6% of doctors had additional qualifications in psychotherapy. In addition, 59% stated that they had completed at least three further training courses on depression in the last two years. The doctors' self-assessment revealed that 66.6% rated their ability to recognize and diagnose depression as "good". In addition, being unemployed, retired and being a housewife were predictors of an increased likelihood of a major depression diagnosis compared to being employed. The number of days of incapacity for work could not be identified as a predictor here. When diagnosed using the DSM-V criteria, 74.8% of depressed patients were correctly identified by the family doctor, but when diagnosed using ICD-10, only 17.2% of patients were identified as depressed. 11.7% of subjects who did not meet DSM or ICD criteria on the patient questionnaires were diagnosed with depression by the practitioner. This showed that the specificity of the doctors' judgments is significantly lower than the sensitivity. The sensitivity of physicians' diagnoses of depression may be promising, but this is obviously accompanied by a high rate of false positive diagnoses. This suggests that the increased attention paid to depressive syndromes in general practice over the last decade has contributed to improved detection. Nevertheless, the high rate of false positive diagnoses remains problematic (Jacobi et al., 2002). Kendrick (2000) showed that initiatives to improve primary care physicians' adherence to depression guidelines have not resulted in significant advances in diagnostic accuracy or patient outcomes. In addition, two thirds of adults with depression continue to be underserved and the choice of treatment in primary care is limited (Thornicroft et al, 2017).

1.3.3 The role of the General practitioner in the treatment of depression

Various aspects were examined in relation to depression and its diagnosis by the GP. One aspect of this was that active feedback from the GP to the patient could minimize the severity

of depression, but the study situation on this is very ambiguous (Löwe et al., 2024). A notable feature of the German healthcare system is that the doctors involved had an exceptionally heavy workload, managing an average of 62 patients each day. In total, 8% of the doctors were pursuing additional training in psychotherapy, and another 8% were in the process of obtaining such qualifications. Only 24% of doctors reported finding the treatment of depressed patients rewarding, while 54% indicated they felt inadequate in managing patients with depression. Overall, 90% of doctors reported that patients with depression require significantly more time compared to those with other medical conditions. Given this, it was surprising that few doctors (7.5%) reported referring depressed patients to mental health specialists whenever possible (Wittchen & Pittrow, 2002). The fact that GPs are one of the first and therefore essential points of contact for patients has been explained above. However, the shortage of doctors in Germany must also be taken into account. The Robert Bosch Stiftung (2021) assumes that around 11,000 GP positions will be vacant in Germany in 2023. This would mean that 40% of rural districts are undersupplied. Here, too, solutions are desperately being sought and general health centers could provide relief, even a solution to the problem (Robert Bosch Stiftung, 2021). Fewer and fewer newly licensed GPs are willing to set up in rural areas in particular. Existing practices are finding it difficult to find successors, meaning that more and more practices are having to close, especially in rural areas. There are many reasons for this, such as the poor local infrastructure. Despite various concepts (remuneration supplements, turnover guarantees), it is difficult to minimize the prevailing shortage of doctors (Kassenärztliche Bundesvereinigung, 2024).

2. Research questions and hypotheses

There are gaps in previous research with regard to the consideration of psychosocial parameters in the diagnosis of depressive patients, particularly in naturalistic cohorts of GPs. The prediction of depressive symptoms, their course and the associated psychiatric risks have not been investigated in previous studies. These gaps are to be closed and therefore the following hypotheses derived from the literature are put forward for this study:

1. The influence of demographic variables and living environment

H1a: There is a significant difference in the occurrence of depressive symptoms between the ages and genders of patients in GP care.

H1b: The current relationship status, especially living with a partner, has a significant influence on the occurrence of depressive symptoms in patients in GP care.

H1c: The occupational situation has a significant influence on the occurrence of depressive symptoms in patients in primary care.

H1d: The number of inhabitants of the place of residence has a significant influence on the occurrence of depressive symptoms in patients in general practitioner care.

2. The influence of psychosocial stressors

H2a: Discrimination at school has a significant influence on the occurrence of depressive symptoms in patients in primary care.

H2b: Discrimination in the workplace has a significant influence on the occurrence of depressive symptoms in patients in primary care.

H2c: There is a significant influence between a patient's financial problems and the likelihood of developing a depressive disorder in the GP practice.

H2d: There is a significant association between the presence of mental and depressive disorders in the family and the likelihood that a patient will develop a depressive disorder in the GP practice.

H2e: There is a significant association between a patient's low physical activity and the likelihood of developing a depressive disorder in GP practice.

H2f: There is a significant influence between a patient's high level of loneliness and the likelihood of developing a depressive disorder in GP practice.

H2g: There is a significant relationship between a patient's lower general well-being and the likelihood of developing a depressive disorder in GP practice.

3. Methods

In the following, the study design and the recruitment setting are presented and an overview of the samples is given. The questionnaires used are then presented and the test quality is described. Finally, the statistical analysis follows and explains the statistical procedure with the data set.

3.1 Study design

The Graduate College POKAL (Predictors and Clinical Outcomes of Depressive Disorders in Primary Care) has the main goal of significantly improving the care of depression in primary care patients. Through the collaboration of various specialist disciplines and leading scientists, new starting points for better primary care are to be developed. In particular, new diagnostic and therapeutic options are to be developed. The main aim is to fundamentally improve the productive interaction between doctors, practice teams and patients. There are nine projects in total, with the following three focal points: 1. the challenge of diagnostics, 2. the challenge of treatment and 3. the challenge of implementation. The present work is thematically located in point 1 of the diagnostic challenge and includes the "Prediction models for depression using psychological markers". The aim here is to significantly improve markerbased prediction models for patients with unipolar depression for general practitioner assessment and diagnosis. The topic of the dissertation presented here is derived from the overarching theme described above: "Prediction of depression using psychosocial parameters in a naturalistic cohort recruited in GP practices". The data was collected and analyzed at the Psychiatric Clinic of the LMU University Hospital in Munich under the direction of Prof. Dr. Peter Falkai. In addition, GP practices in and around Munich were recruited. Funding and support were provided by the German Research Foundation (DFG-GrK 2621). The ethics application for the outpatient cohort was approved by the Ethics Committee of LMU University Hospital in October 2022. This study is a Cross-sectional study that compares depressed subjects (diseased cases) with non-depressed subjects (controls) with regard to demographic and psychosocial factors.

3.2 Sample and recruitment procedure

In order to generate a representative outpatient sample, recruitment was carried out in three cooperating GP practices, in the psychiatric outpatient clinic of the LMU University Hospital and from the general population. The inclusion criterion for the outpatient cohort was the age of 18 and not older than 70. In addition, no illness from the schizophrenic spectrum or bipolar disorder was allowed to be present. Acute suicidal tendencies, a current addiction, cognitive impairments and pregnancy were also not permitted. The German language had to be understood in order to be able to sign the written declaration of consent. The consent form was obtained from licensed physicians and psychotherapists. The subjects were informed that all questions should be answered as truthfully as possible. Patients were excluded if they developed an exclusion criterion during the course of the study. Study participants could withdraw their consent at any time and without giving reasons. The inclusion and exclusion criteria were discussed in consultation with the treating GPs and information was obtained from the treating psychiatrists at the clinic. The general population was selected and included through direct contact (flyers, direct approach). In order to make the sample as large as possible, the inclusion and exclusion criteria were set to ensure broad participation. Recruitment took place on site in the GP practices, usually between 07:00 and 12:00 am. At the same time, flyers and information material were distributed in other GP practices, which then referred patients to us. The psychiatric outpatient clinic is located in the same building as the study office, so an appointment was made with these patients in the same building. The general population was also examined in the psychiatric clinic of the LMU University Hospital. In order to be able to address as many population groups as possible, recruitment took place not only in the center of Munich, but also in outlying areas and outside of Munich. The recruitment process was continuously monitored so that under-representative groups could be specifically included if necessary. This measure made it possible to obtain a cohort that reflects the demographic diversity of the general population. Subjects were offered a 25€ Rewe voucher as subject allowance. Each subject who came to the LMU University Hospital to participate had

the opportunity to be connected to the outpatient clinic immediately in case of acute symptoms. General practitioners in and around Munich were contacted by e-mail to see if they were interested in participating in the study. The GP practices were able to contact the study team by e-mail or telephone. The GP practices received an expense allowance of 500€ per month for the additional organizational work. The recruitment period was from the beginning of October 2022 to the end of June 2024.

The patient data was collected using external and self-rating scales and questionnaires. In order to ensure comparability of the data, a questionnaire package was compiled for the subjects (see Appendix). Both mentally conspicuous and mentally inconspicuous subjects were included in the recruitment. Due to the different recruitment locations, it was not possible to determine a specific sequence of examinations. The study complied with the requirements of the DSGVO and all subjects were pseudonymized. The patient data was processed in the Centraxx database (Kairos GmbH 2009-2021 Version: 3.18.3.22). In this study, the regulations of medical confidentiality and data protection are observed. All collected personal data and findings will be pseudonymized and the personal data will be replaced by a number code. All pseudonymized study documents will be kept under lock and key at the Clinic for Psychiatry and Psychotherapy for 15 years after completion or discontinuation of the study. The pseudonymized electronic data will be stored on a password-protected clinic drive for this period and deleted at the end of this period (Eder & Pfeiffer et. al 2023). The course of the inclusion date was as follows: Subjects were informed again regarding the informed consent form and included after the study background, procedure and risks were explained. The interviews were conducted and analyzed by trained personnel. The questionnaire package of self-ratings, which was affixed with a prepaid return envelope, was handed out on site after the interviews. The reason for this was that answering the questionnaire would take around 45 minutes and time should be set aside for this at home.

At the end of June 2024 after recruitment, the data were completely digitized and cleaned in Centraxx (Kairos GmbH, 2009-2021, version: 3.18.3.22). To achieve the statistical objectives, a sample size of 450 subjects (alpha = .05, power = .85) was required. The primary outcome of the study is the prediction of the development of depressive disorders. Specifically, the study aims to determine how accurately psychosocial parameters can be used in the GP setting to predict depression. The psychosocial parameters are to be used to reliably predict the development of new depression.

3.3 Measuring instrument

As depressive symptoms do not only occur with depression, but can also occur as concomitant or secondary symptoms, a number of interviews were used. The following two external rating questionnaires were selected on the basis of existing experience in order to specify the depressive symptoms:

Structured Clinical Interview for DSM-5 Disorders - Clinical Version (SCID-5-CV). The interview is conducted using a structured, fixed manual and asks for psychiatric diagnoses according to the DSM-5. This should serve to validate the diagnosis of depression (First et al., 2016).

The Montgomery Asberg Depression Rating Scale (MADRS) is a questionnaire for external assessment of the severity of depressive symptoms and is administered as an interview. The assessment period refers to the past week and the questionnaire consists of ten questions. The questions are rated on a seven-point scale from zero to six. After adding up all the questions, the total score can be between zero and 60. The following symptoms are assessed: visible sadness, reported sadness, inner tension, insomnia, loss of appetite, difficulty concentrating, inactivity, numbness, pessimistic thoughts and suicidal thoughts. The score range is divided into four categories: 0-6 (no depression), 7-19 (mild depression), 20-34 (moderate depression) and 35 (severe depression (Snaith et al., 1986).

The other self-rating questionnaires were specifically selected for the psychosocial variables in order to cover as many areas of the respondents' lives as possible:

Collection of socio-demographic information based on the basic phenotyping of the biobank (BBM) taken from the inpatient setting. This comprises standardized questions on the occupational situation, living situation and other psychosocial stress factors that are collected as part of the biobank of the Psychiatric Clinic of the LMU University Hospital. The questionnaire was expanded to include additional contextual factors on the experience of the occupational situation and family stress factors. Survey of psychiatric history (if available) and family history of psychiatric and somatic illnesses. This questionnaire mainly collected anamnestic data on the psychiatric history and illnesses in the family context.

The *Patient Health Questionnaire 9* (PHQ-9) as a depression module is a self-assessment instrument that asks about the presence and frequency of nine depressive symptoms

within the last two weeks in accordance with the diagnostic criteria for major depression according to DSM-IV. These include the following aspects: reduced interest or pleasure, depressed mood, sleep disturbances, tiredness or loss of energy, appetite disturbance, feelings of worthlessness or guilt, concentration disturbance, psychomotor slowness or restlessness, suicidal thoughts. Depending on the stated frequency of the symptoms, each item is assigned 0 (not at all), 1 (on individual days), 2 (on more than half of the days) or 3 (almost every day) points. The scale sum value then corresponds to the sum of the point values of all nine items and varies between zero and 27 points. A score of ten or more points is defined as the presence of depressive symptoms (Kroenke, Spitzer & Williams, 2001).

The University of California, Los Angeles (*UCLA*) *Loneliness Scale* was designed to measure loneliness, but without specifying the concept of loneliness. The three questions can be answered on a Likert scale of 0 (not at all), 1 (rarely), 2 (often) and 3 (very often). Research into the three-point scale has shown good internal, convergent and discriminant validity (Russell, 1996).

The Lubben Social Network Scale (LSNS6) examines social isolation in older adults living in the community. The questionnaire consists of six questions, with six different response options. These are aimed at how many people there is contact with: 0 (9 or more), 1 (5 to 8), 2 (3 or 4), 3 (2), 4 (1) and 5 (none). Three of the questions asked about contact with family members and relatives and the other three about contact with friends and neighbors. There is a high degree of internal consistency, high correlations with criterion variables and good convergent validity (Lubben et al., 2006).

The 5-Item Well-Being Index (WHO-5) measures subjective psychological well-being over the past two weeks. The Well-Being Index consists of five questions, with six different response options 0 (all the time), 1 (most of the time), 2 (about more than half the time), 3 (slightly less than half the time), 4 (now and then) and 5 (at no time). There is a high level of clinical validity and the questionnaire has already been used successfully in a large number of study areas (Topp et al., 2015). In addition, the WHO-5 showed good sensitivity and specificity in predicting major depression in adults (Henkel et al., 2004)

The questionnaire on contextual factors associated with depression from *The Brazilian Longitudinal Study of Adult Health* (ELSA) was derived from the ELSA dataset and consists of a total of 26 questions. The main objectives of the ELSA study in Brazil are to investigate the incidence and progression of diabetes, cardiovascular diseases, their biological, behavioral,

environmental, organizational, psychological and social factors. The questionnaire was administered to 15,105 civil servants in Brazil and the age range was between 35 and 74 years. The collection of data on reproductive patterns, marriages, family composition and care grouping, and work-family interactions allows the role of these often less studied variables to be examined. The ELSA study provides a basic understanding of the causation and progression of psychosocial and pathophysiological disease through the variables surveyed. Among the sociocultural and psychological factors, stress at work, ethnicity and discrimination, the interface between work and family, neighborhood characteristics, social class, social capital and social networks are queried as social risk factors (Aquino et al., 2012).

3.4 Statistical analysis

The dataset was first preprocessed (Pyle 1999): strings had to be given numerical values in order to be able to feed them into the models. For example, no into a zero and a yes into a one. Further, one-hot encoding was applied to categorical variables such as occupation, marital status and current occupational situation. For each category a new column was created and whether one category was present or not the row value was one or zero (Harris & Harris, 2015). Row values with more than 50% missing values were dropped. Columns with low variance below a threshold of 0.01 are also excluded. Since the missing data is classified as MAR (Missing at Random) and not MCAR (Missing Completely at Random), KNN (K-Nearest Neighbors Imputation) imputation is used. In this method, missing values are estimated based on the similarity of the data points by using the values from nearest neighbor data sets (Little & Rubin, 1987). Descriptive statistics were calculated to obtain a comprehensive overview of the recruited outpatient cohort. The dataset included ordinal questions (e.g. age, neighborhood conditions) and binary items (e.g. gender, marital status) as well as continuous data, including scores from the MADRS, WHO5, and PHQ9 scales. For the latter the mean and standard deviation were reported. In order to better characterize the cohort and highlight potential differences between groups, a comparative analysis was conducted between depressed and non-depressed participants. Depending on the distribution of the data, a T-test, the chi-square test or the Mann-Whitney U test were calculated.

For Analysis was used: python version 3.9.18 with Pandas version: 1.5.2; NumPy version: 1.24.3, scipy version 1.9.3 for general calculations, statsmodels version 0.13.5 for logistic

regression, imblearn version 0.11.0 for borderline smote, matplotlib version: 3.6.2 and scikit-learn version 1.2.2 for Machine learning (ML) Modell.

3.4.1 Logistic Regression

Logistic regression is a statistical technique used to model the relationship between a binary dependent variable and one or more independent variables. Originally introduced by David Cox (1958), logistic regression allows the probability of a particular outcome to be calculated using the logistic function. This function transforms the linear combination of predictors into a probability that lies between zero and one, which is particularly useful for dichotomous outcomes such as yes/no or sick/healthy (Cox, 1958). In the calculations the dependent variable is depression (SKID II), and the independent variables are age, gender, number of inhabitants, relationship status, occupational situation, number of inhabitants, discrimination, financial problems, presence of mental and depressive disorders in the family, physical activity, loneliness and well-being. The calculations were carried out on 372 non-depressed patients and 72 depressed patients. The effect size was calculated for each independent variable of the logistic regression with the OR, which represents the ratio of the odds of the event occurring with a change in the independent variable. Statistical significance of the results was assessed using p-values. A p-value less than 0.05 was considered statistically significant. Within the Machine Learning Pipeline Logistic Regression was used as a prediction model, which will be described in further detail in 3.4.2.

After that we performed classical frequentist logistic regression twice on the whole dataset. First, we perform logistic regression with a hypothesis-based approach based on the hypotheses derived from a literature search. Second, we also used the factors found by the machine learning pipeline to compare the performances. Gender and age at study inclusion were considered as covariates and added in both models.

3.4.2 Machine Learning Pipeline

Machine learning is a broad and dynamic field that involves the development of algorithms capable of learning from and making predictions or decisions based on data. Contrary to classical hypothesis-led study design and building, where models are typically constructed around pre-existing theories or assumptions, ML is inherently data-driven. In ML, patterns, relationships, and insights are derived directly from the data itself, without requiring predefined rules

or hypotheses (Bishop, 2006). One of the foundational techniques within machine learning is regression analysis. Regression models are integral to ML because they provide a straightforward yet powerful method for understanding the relationships between variables and making predictions. In essence, regression models are designed to predict an outcome based on one or more input features. They work by estimating the coefficients of the input features that minimize the difference between the predicted and actual values. They are widely used not only for their simplicity and interpretability but also as building blocks for more complex machine learning models (Hastie et al., 2009). Moreover, they provide valuable insights into the nature of data and the relationships between variables, which can inform the design and improvement of more sophisticated algorithms. By learning from data, regression models can adapt to new information, making them a key tool in the broader context of machine learning (Breiman, 2001). The hyperparameters were optimized by grid search. Hyperparameters are parameters whose values must be set before training the model and which influence the learning behavior of the model. Grid Search systematically searches through a defined grid of hyperparameters to identify the best combination. The goal is to find the combination that achieves the best performance of the model based on a specific metric. Grid search is widely used in machine learning practice especially in combination with methods such as cross-validation to validate model performance and minimize the risk of overfitting (Bergstra & Bengio, 2012).

Following hyperparameters were optimised: *C, Limited-memory Broyden-Fletcher-Gold-farb-Shanno Algorithm* (Imbfgs) and the alpha value of the Lasso regression which was performed in order to conduct a feature selection. The regularization strength *C* of the logistic regression was optimized and set to one (Byrd et al., 1995). Detemined by grid search Imbfgs was chosen as the optimization algorithm, a standard solver that is well suited for small data sets and is characterized by a good convergence speed. In addition to the model configuration, as feature selection procedure Least Absolute Shrinkage and Selection Operator (Lasso) regression was integrated to select the most relevant features for the model. Within this procedure, another hyperparameter, the alpha value, was set to 0.05. This value indicates that a regularized model is used for feature selection, where alpha determines the regularization strength for the feature selection model. Lasso regression reduces the number of features by setting less important features to zero, which reduces the complexity of the model (Tibshirani, 1996).

Data was split into training (80% of participants) and testing subsets (20% of participants) with randomly and stratified selected – were Bordeline SMOTE was conducted with the Training set. SMOTE (Synthetic Minority Over-sampling Technique) generates synthetic examples specifically near the borderline between classes, which helps improve model performance on minority classes without oversampling indiscriminately. A distinction is then made between training data and test data. In the training data set, SMOTE (Synthetic Minority Over-sampling Technique) is used to artificially create new data points for the less represented classes, thereby improving the classification of these classes (Chawla et al., 2002). More specifically, the Borderline-SMOTE (Synthetic Minority Over-sampling Technique) as an extension of the classical SMOTE technique. Borderline SMOTE aims to improve the quality of the synthetic examples by focusing on the examples that are on the edge of the decision boundary. These examples are more critical as they often represent the most difficult cases that are the most challenging for the model to learn. The method generates synthetic data points that shift the decision boundary and thus improve the performance of the classifier on the boundary cases (Han, Wang & Mao, 2005). This technique identifies borderline cases in our cohort that are close to the cut-offs for depression and generates synthetic data sets to better represent less represented classes (Little & Rubin, 1987). The test set, however, was left unaltered to ensure an unbiased evaluation of model performance on real-world data.

The nested cross-validation framework consisted of two levels: an inner and an outer cross-validation loop, both utilizing five folds. Nested cross-validation is an extended method of cross-validation that is used in particular when hyperparameter optimization is involved. The method addresses the problem of *double dipping*, where the data is used both to select the best hyperparameters and to evaluate the model (Varma & Simon, 2006). In nested cross-validation, the data is split into multiple folds. In each round, one-fold is used as a test set, while the remaining folds are used for training and hyperparameter optimization. This method involves two levels of cross-validation:

- Outer loop: The data set is split into training and test sets, with the test set being used for the final evaluation of the model.
- Inner loop: A further cross-validation is performed within the training sets of the outer loop to find the best hyperparameters.

This nested structure helps Nested Cross-Validation to avoid overfitting and provide a more realistic estimate of model performance on new, unknown data. Separating the optimization from the evaluation in two nested loops ensures a bias-free estimation of model performance.

After completing the nested cross-validation, the final model performance was determined by the results from the last iteration of the outer cross-validation loop. Various metrics are used to evaluate model performance. A key metric for this work is the F1 score. The F1 score is a metric for evaluating the accuracy of a classification model. It is the harmonic mean of precision and recall and is used in particular when a balance between these two metrics is desired (Sokolova & Lapalme, 2009). To better evaluate the diagnostic accuracy of the test under investigation, the specificity and sensitivity are considered. The sensitivity of a test indicates the proportion of people correctly diagnosed as sick among all those actually sick in the sample examined. A test procedure with high sensitivity can rule out a disease with a high degree of certainty. Specificity describes the proportion of people correctly diagnosed as healthy among all those in the sample who are not ill. A test with high specificity is particularly good at confirming an illness with a high degree of certainty (Altmann & Bland, 1994). To evaluate a binary classifier, the accuracy is determined based on the proportion of correctly classified cases in a data set. Both the correctly classified cases, true positives and true negatives, are considered in relation to the total number of cases. To determine how well a model performs in identifying the respective classes, the positive predictive values and the negative predictive values are included. This provides information on the overall accuracy of a classifier (Bishop, 2006). Additionally, the permutation importance was calculated in order to determine features with the highest predictive performance of the model. A higher value means that permuting this feature strongly degrades the model performance, indicating a greater importance of the feature (Breiman, 2001). The permutation importances were calculated using the scikit-learn inspection module. In the code, the permutation importances are averaged over several repetitions (n_repeats = 30) to reduce random fluctuations (Breiman, 2001). In addition, a Receiver Operating Characteristic (ROC) curve was created for all the regression models (Zwei & Campbell, 1993). Figure 1 illustrates the process of ML.

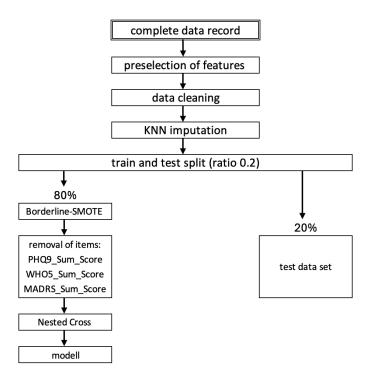


Fig.: 2 Machine learning process

4. Results

This section begins by describing the descriptive results of the sample in more detail. The relationship between psychosocial parameters and depression in the outpatient sector is then discussed. The number of patients who were not recruited from the GP environment was not specifically recorded during recruitment. The number of responses (N) varies, as not all respondents answered every question in full. This was considered in the calculation and is shown accordingly in the results.

4.1 Descriptive statistics

The present sample with a total of 454 test persons consisted of 60% female and 40% male study participants. The average age at study inclusion was 41.2 years (SD = 14.28), with an age range of 18 - 70 years. Most participants were between 29 and 54 years old (25%-75% interquartile range). 93.9% of the participants had been born in Germany. When asked whether they themselves, their parents or grandparents had grown up in another country, 15.8% answered yes. When asked about the language, 95.7% stated that their mother tongue was German. On average, participants currently lived in a larger city or metropolitan region

(Tab.: 1). The place where they had grown up was on average in a smaller medium-sized town (Tab.: 2).

Variable	non-depressed (%)	depressed (%)
until 5.000 (village/country town)	2	3
until 20.000 (small town)	23	13
until 50.000 (small medium-sized town)	16	11
until 100.000 (large medium-sized town)	9	1
until 500.000 (large city)	5	0
above 500.00 (large city)	45	60

Tab.: 1 What is the size of your current place of residence (inhabitants)?

^{*}Non-depresses N=372, depressed N=63

Variable	non-depressed (%)	depressed (%)
until 5.000 (village/country town)	20	26
until 20.000 (small town)	34	40
until 50.000 (small medium-sized town)	13	11
until 100.000 (large medium-sized town)	6	3
until 500.000 (large city)	5	0
above 500.00 (large city)	23	19

Tab.: 2 What is the population of the town/city in which you (mainly) grew up?

Regarding their current marital status, the respondents stated the following cohabitation: 22.3% single, 15.5% living in a couple, 27.0% married (including registered civil partnership), 2.0% unmarried, separated, 5.9% divorced. With regard to their occupational situation, 32.9% worked full-time, 18.7% part-time, 46.6% were in other categories (housewife/house-husband, maternity or parental leave, in retraining, pupil, student, in vocational training/ap-prenticeship/dual studies, pensioner, semi-retirement, early retiree, permanently unable to work, marginally employed/mini-job, occasionally employed, federal voluntary service/voluntary social year or other) and 1.8% stated that they were currently unemployed. The calculations were carried out including unemployment, since the other variables were not significant. Looking at family life, 20.3% stated that their parents had separated. In 56.5% of cases, a family history of mental illness is already known (anxiety disorders, depression, obsessive-com-

^{*}Non-depressed N=373, depressed N=72

pulsive disorder, alcohol or drug addiction, medication dependence, schizophrenia or psychosis, manic-depressive illness and autism). If the level of education of this sample was examined more closely, most of the test persons had a school-leaving certificate with a vocational baccalaureate. With the 25%-75% interquartile range, most of the qualifications ranged from intermediate school leaving certificate to A-levels. Overall, 84.5% were employed during the survey and worked an average of 29.5 hours per week. The average weekly working hours are 27 hours per week (SD = 15.37) and the average monthly net income is itemized in Tab.: 3.

Variable	non-depressed (%)	depressed (%)
missing	3	0
less than 500€	2	4
500 - 1.000€	5	8
1.000 - 1.500€	5	8
1.500 - 2.000€	8	17
2.000 - 2.500€	9	22
2.500 - 3.000€	12	11
3.000 - 3.500€	10	3
3.500 - 4.000€	7	7
4.000 - 5.000€	11	6
5.000 - 6.000€	8	4
6.000 - 7.000€	7	7
7.000 - 8.000€	3	3
8.000 - 9.000€	2	0
9.000 - 10.000€	2	0
10.000 - 12.000€	2	0
above 12.000€	2	0

Tab.: 3 What is the approximate average net monthly household income?

^{*}Non-depressed N=372, depressed N=72

Tab.: 4 showed the group comparison between the entire sample, the non-depressed subjects and the depressed subjects in tabular form in order to provide a better overview of the cohort presented. The p-values were corrected using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995).

Variable	total	•	non-depre	essed	depresse	ed	p-value
	N=454		N=372	N=372		2	
	SD	M	SD	M	SD	M	
age	14,3	41,2	14,6	41	11,9	39	0,29
discrimination (school)	0,98	2,39	0,91	2,28	0,91	1,99	0,01
discrimination (work)	1,05	2,32	0,93	2,24	0,99	2,01	0,08
LSNR 6	6,34	17,42	5,21	18,24	5,27	13,14	0,01
Loneliness-Scale	2,1	2,79	1,53	2,37	2,21	4,57	0,01
MADRS	8,86	7,74	5,33	4,79	7,94	22,78	0,01
PHQ9	5,57	6,62	3,2	4,98	5,58	13,53	0,01
WHO5	5,93	16,4	4,43	14,95	4,35	22,51	0,01
sports activity	0,47	0,68	0,42	0,77	0,5	0,51	0,01
people in the neighbourhood are trustworthy	0,89	1,04	0,81	1,14	0,95	1,44	0,04
people in the neighbourhood help each other	1,10	1,36	0,91	1,31	1,10	1,88	0,01
people generally don't get along in the neighbourhood	1,01	3	0,88	2,98	0,94	2,72	0,05
	total (%)		non-depre	essed (%)	depresse	ed (%)	
parents separated	27		19		28		0,22
marital status (unmarried)	22		19		39		0,01
marital status (married)	27		30		11		0,01
Currently in psychiatric treatment	20		69		29		0,01
previous mental illnesses	57		56		78		0,01
unemployment	11		1		10		0,01
sex (woman/men)	60 / 40		59 / 41		46 / 26		0,71

Tab.: 4 socio demographic Data

4. 2 Relationship between psychosocial parameters and depression in the outpatient setting Based on the SKID interview, 16.2% of participants currently had a diagnosed depressive disorder. In the second external rating, the MADRS, the average score was 7.7 (SD = 8.8). Most participants had a score between one and 11 (25% - 75% interquartile range). The PHQ9 total score had an average value of 6.4 (SD = 5.57) with a range of three to 26 points for the participants. Currently, 19.5% of the study participants were undergoing psychiatric treatment. The average age at first psychiatric complaints was 22.8 years (SD = 14.28) and the age at first seeking help was 29.4 years (SD = 13.37). The average number of (partial) inpatient psychiatric treatments was 1.7 treatments (SD = 2.66). Experiences of discrimination in the workplace (SD = 1.05) and at school (SD = 0.98) were measured below. The values ranged from zero to three and in both categories the average value was 2.2. The spread of responses was similar in both areas, which indicated a certain diversity in the experiences of the test subjects.

Regarding other questionnaires, the following results were obtained: for social networks (LSNS6), the average score was 17.5 (SD = 6.34), with a range of zero to 30 and a median score

^{*}M = mean; SD = standard deviation. The N can vary for the values, because the participants have left out questions.

of 18. The feeling of loneliness (*UCLA Loneliness Scale*) had an average score of 2.8, (SD = 2.10) with a range of zero to nine. Here, 50% of the participants had values between one and four and the standard deviation is 2.1. The average well-being score of the WHO-5 was 16.4 (SD = 5.93).

In the present data set, classic logistic regressions produced the following results for the variables: A more intense feeling of loneliness ("Lonliness_overall") is strongly positively associated with the prediction of the positive class (coefficient = .89). "Loneliness_overall" had the highest permutation Importance (Importance = .09) of the variables, which showed that loneliness was the most important feature in the model which was determined by the ML Pipeline. A more intense feeling of LSNS6 score (which measures social networks and social support) was negatively associated with the diagnosis of depression (coefficient = -.61). The LSNS6 score also had a significant permutation Importance (Importance = .04). The number of inhabitants (coefficient = -.48), which possibly indicated the size of the place of residence, had a negative coefficient. The number of inhabitants had a moderate importance (Importance = .02). Unemployment was positively associated with the prediction of positive class (coefficient = .35). Unemployment had the lowest permutation Importance among the listed characteristics (Importance = .01). Regular physical activity also had an influence on the model, but less strongly than the other characteristics (coefficient: - .25). Physical activity had a low permutation importance (Importance = .01).

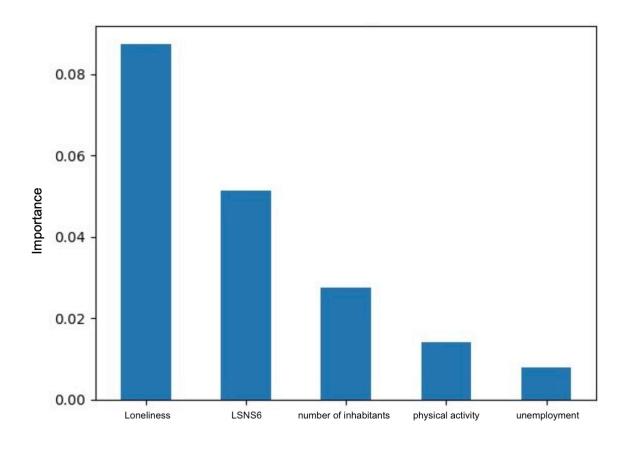


Fig. 2.: Permutation Importance

To better illustrate the logistic regression models in training, the specificity and sensitivity were described with the help of the model's confusion matrix:

	predicted not depressed	predicted depressed
actually not depressed	234	63
actually depressed	34	49

^{*} Loneliness measured with the: UCLA Loneliness Scale and physical activity was measured using the question: "Do you engage in physical activity at least once a week?"

4.2.1 Training Data

The model achieved an overall accuracy of .74 for the socio-demographic data during training. The sensitivity for depressive cases was .59 and the specificity was.59. For the non-depressed cases, the sensitivity and specificity were .79. Depressive cases had an accuracy of .58. This resulted in an F1-score of .50 for depressive cases and the AUC value was .75. For the PHQ9, the model achieved an overall accuracy of .83. The sensitivity was .78 and the specificity was .59. The PHQ9 model using the PHQ9 Sum Score shows a high performance with an area under curve (AUC) score of .89 and an overall accuracy of .83. The depressive cases achieved a precision of .58 and a sensitivity of .78, which represented an improvement in sensitivity compared to the logistic regression model. The F1 score for the depressed cases achieved an F1 score of .66. For the WHO5 model, the sensitivity was .72 and the specificity was .59. The WHO5 model, which only uses the WHO5 Sum Score, achieved an AUC score of .87 and an overall accuracy of .77. The non-depressive cases also performed better in this model, with a precision of .91 and a sensitivity of .78, which indicated a high specificity in the prediction of non-depressive cases. The depressive cases achieved a precision of .48 and a sensitivity of .72, resulting in an F1 score of .57 for the depressive cases.

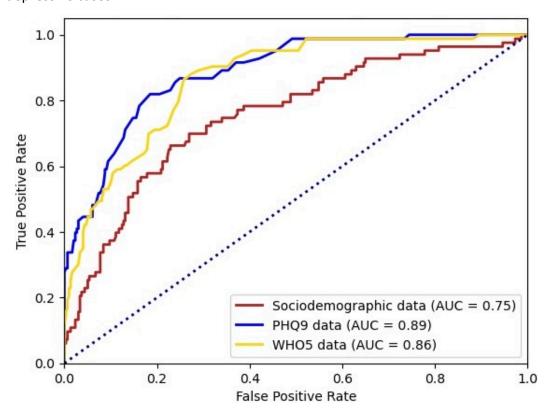


Fig. 3.: Receiver Operating Characteristic – Training Data – where additional borderline cases were introduced due to using borderline SMOTE - Logistic Regression

4.2.2 Test Data

The model achieved an overall accuracy of .85 for the socio-demographic data in the test. The sensitivity was .57 and the specificity was .57. The non-depressive cases performs better than the depressive cases with a precision of .92 and a sensitivity of .91. The latter achieved a precision of .53 and a sensitivity of .57. This led to an F1 score of .55 for the depressed cases. For the PHQ9 model in the test, the model achieved an overall accuracy of .84. The sensitivity for depressive cases was .86, and the specificity was .84. The PHQ9 model, as measured by the PHQ9_Sum_Score, performed strongly with an AUC of .90 and an overall accuracy of .84. For the depressed cases achieved an accuracy of .50 and a sensitivity of .86. The F1 value of the depressed cases was .63. In the test, the WHO5 model showed an overall accuracy of .80. For depressive cases, a sensitivity of .79 and a specificity of .80 were measured. With the WHO5_Sum_Score, the WHO5 model achieved an AUC value of .87 and an overall accuracy of .80. The precision is .95, and the sensitivity is .80. Depressive cases achieved a precision of .42 and a sensitivity of .79, resulting in an F1 score of .55 for the depressed cases.

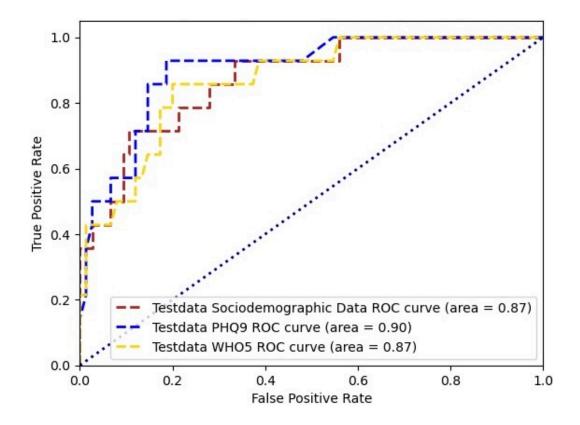


Fig. 4.: Receiver Operating Characteristic – Test Data – Logistic Regression

4.2.3 Logistic regression

Two logistic regression models were calculated. Model one was developed and calculated on a hypothesis-driven basis. A logistic regression analysis for the hypothesis-driven model revealed a statistically significant result, χ^2 (22, N = 444) = 139.44, p < .001, and explained 35.42% (Pseudo R²) of the variance. Model two, on the other hand, is based on the factors identified in the machine learning pipeline and was calculated considering the entire data set (N=444; *Pseudo R².: 0.29; p* < 0.001). In Tab.: 5 the results of the hypothesis-based, classical regression are presented and in comparison, to this, Tab.: 6 shows a regression that was carried out with the entire data set and then compared with the variables of the ML model.

dependent va	ii iabie. uepi e	ssion with the	וו עואכ:			
				95	% CI	
b	SE	z	р	lower value	upper value	OR
- 2.1606	0.185	-11.661	0.001	-2.524	-1.797	0.099
- 0.0608	- 0.378	0.161	0.706	- 0.377	0.255	0.711
0.0146	0.153	0.095	0.924	- 0.286	0.315	1.056
0.2851	0.192	1.484	0.138	- 0.091	0.662	1.100
0.1044	0.157	0.663	0.507	- 0.204	0.413	1.094
0.5066	0.196	2.586	0.010	0.123	0.891	1.642
- 0.7293	0.298	-2.448	0.014	- 1.313	- 0.145	0.423
0.0207	0.246	0.084	0.933	-0.461	0.502	0.977
0.3752	0.168	2.237	0.025	0.046	0.704	0.785
0.4516	0.172	2.623	0.009	0.114	0.789	1.391
-0.1990	0.166	-1.198	0.231	-0.524	0.126	1.370
	b - 2.1606 - 0.0608 0.0146 0.2851 0.1044 0.5066 - 0.7293 0.0207 0.3752 0.4516	b SE - 2.1606 0.185 - 0.0608 - 0.378 0.0146 0.153 0.2851 0.192 0.1044 0.157 0.5066 0.196 - 0.7293 0.298 0.0207 0.246 0.3752 0.168 0.4516 0.172	b SE z - 2.1606 0.185 -11.661 - 0.0608 - 0.378 0.161 0.0146 0.153 0.095 0.2851 0.192 1.484 0.1044 0.157 0.663 0.5066 0.196 2.586 - 0.7293 0.298 -2.448 0.0207 0.246 0.084 0.3752 0.168 2.237 0.4516 0.172 2.623	-2.1606 0.185 -11.661 0.001 -0.0608 -0.378 0.161 0.706 0.0146 0.153 0.095 0.924 0.2851 0.192 1.484 0.138 0.1044 0.157 0.663 0.507 0.5066 0.196 2.586 0.010 -0.7293 0.298 -2.448 0.014 0.0207 0.246 0.084 0.933 0.3752 0.168 2.237 0.025 0.4516 0.172 2.623 0.009	b SE z p lower value - 2.1606 0.185 -11.661 0.001 -2.524 - 0.0608 - 0.378 0.161 0.706 - 0.377 0.0146 0.153 0.095 0.924 - 0.286 0.2851 0.192 1.484 0.138 - 0.091 0.1044 0.157 0.663 0.507 - 0.204 0.5066 0.196 2.586 0.010 0.123 - 0.7293 0.298 -2.448 0.014 - 1.313 0.0207 0.246 0.084 0.933 -0.461 0.3752 0.168 2.237 0.025 0.046 0.4516 0.172 2.623 0.009 0.114	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

3.903

-2.914

0.001

0.004

0.379

-0.947

1.142

-0.185

1.929

0.550

dependent variable: depression with the SKID II

Tab.: 5 classical hypothesis-based regression

0.7603

-0.5663

0.195

0.194

loneliness

well-beeing

95% CI									
independent variable:	b	SE	z	р	lower value	upper value	OR		
constant	- 2.1747	0.186	- 11.711	0.001	- 2.539	-1.811	0.114		
age	- 0.3106	0.176	- 1.761	0.078	- 0.656	0.035	0.742		
gender	0.1173	0.160	0.735	0.462	- 0.196	0.430	1.123		
loneliness	0.8865	0.171	5.180	0.000	0.551	1.222	2.425		
well-beeing	- 0.5886	0.175	- 3.364	0.001	- 0.932	- 0.246	0.558		
number of inhabitants	- 0.3354	0.165	- 2.037	0.042	- 0.658	- 0.013	0.716		
unemployement	0.4736	0.183	2.594	0.009	0.116	0.831	1.604		
physical activity	- 0.1224	0.151	- 0.811	0.417	- 0.418	0.173	0.882		

Tab.: 6 classical regression with the ML parameters

An ROC curve (area = .83) was calculated in order to have a comparison metric (Fig.: 5). In addition to the modeling, a multiple linear regression was performed using the machine

learning model. Age and gender were included in the model as additional covariances. Finally, the ROC curve (Fig.: 6) for the hypotheses put forward was presented graphically, showing an area under the curve (AUC) of .88, which confirmed the high performance of the model in distinguishing between depressed and non-depressed cases in GP practice.

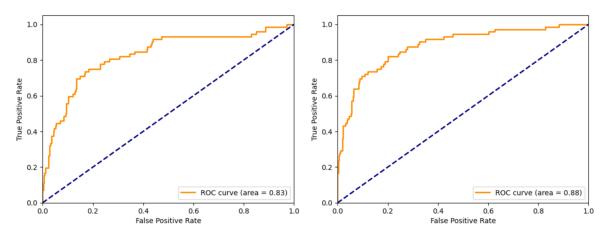


Fig. 5.: Shows the Receiver Operating Characteristic of the factors found trough the ML pipeline within the Logistic Regression Model

Fig. 6.: Depicts the Receiver Operating Characteristic of predefined hypotheses that were found trough a literature search

5. Discussion

In this chapter, the results of the study presented are interpreted and discussed. The results are then compared with the current state of research. Finally, the strengths and limitations of the present work for research are drawn.

5.1 Summary of the results in the context of the hypotheses

The sample consisted of predominantly German participants who were on average 41 years old and most of whom lived in a larger city or metropolitan area. The proportion of women (60%) must be considered when interpreting the data. The majority of the participants had a higher level of education (vocational baccalaureate or higher), which may indicate a higher social and economic status. In addition, the test subjects had a high average net income of 2.500 - 3.000€. Since most of the participants were employed and work an average of 29.5 hours per week, this could indicate a stable economic situation for the test subjects. At the same time, however, there was a small group that was unemployed, which can be seen as a risk factor for psychological stress and depression. The high proportion of married people or people living in couple relationships (around 42.5% in total) indicate a stable social support

system, which could have a positive effect on well-being. However, the proportion of participants whose parents had separated (20.3%) and the high number of known mental illnesses in the family (59.5%) could indicate increased mental stress within this recruited cohort. The high prevalence of an urban lifestyle and an economically stable situation suggests that both protective and stressful factors were captured by the socio-demographic data in this population. These factors could influence the risk of mental illness, which should be considered in future studies or interventions. The SKID interview showed that 16,2% of subjects currently suffered from a depressive disorder, which means that the majority did not show any noticeable symptoms in this interview. The MADRS score (7.7) indicated low to moderate depressive symptoms, whereby the high standard deviation (8.8) indicates a considerable variance in the severity of symptoms among the participants. The PHQ-9 values (6.4) also showed a moderate depressive burden in the sample. A significant proportion of the study participants were currently undergoing psychiatric treatment, which indicates an existing burden. The average age at the onset of first symptoms and at first seeking help shows a time delay, which indicates a delay in seeking help of around seven years. Although the mean value for first psychiatric help is 29.17, the large standard deviation indicates that some participants had many treatments, while others had few or no treatments. The average number of (partial) inpatient psychiatric was 1.7 treatments, which specifically means that 50% of the participants have had between zero and two treatments in their lifetime. In terms of experienced discrimination, it was shown that most respondents had a moderate to high experience of discrimination in the workplace (SD = 1.05). The LSNDR6 indicates a moderate social network in the sample population (M =17.42; SD = 6.34). In the UCLA Loneliness Scale (M = 2.8), the standard deviation of 2.1 indicates that the respondents' answers are widely dispersed. This suggests that there are participants with both a very low and a very high loneliness score. With its mean value, the WHO-5 indicated a medium level of well-being (M = 16,4; SD = 5.93). This means that most participants experience a balanced sense of well-being, with no extremes such as zero or 30. As 25% of participants scored 21 or above, this indicates that a quarter of participants had a fairly high sense of well-being.

With regard to the machine learning process, the following results were shown in the **training dataset**: the identification of 234 *true negatives* means that only a few people were incorrectly classified as depressed, which indicates a high specificity. As in every model, there are also subjects who were incorrectly classified as *false negatives*, although they belong to

the depressive cohort. For the 49 true positives, the model shows a high sensitivity. The classification performance of the training shows for the socio-demographic data for non-depressive cases that the sensitivity is .79, which means that the model correctly identified .79 of the actual instances of this cases. The specificity for these cases is also .79, indicating that the model correctly identified .79 of the actual non-depressed as such. For depressive cases, the sensitivity is .59, indicating that the model correctly identified .59 of the actual depressives in this class. The specificity for depressive cases is .59, meaning that the model correctly identified .59 of the actual non-depressives as such. In summary, the results show that the model has a good ability to identify class 0 and is minimally more limited in identifying class 1. The specificity is identical to the sensitivity for both classes. With an AUC score of .75, it is shown that the model has a good overall ability to distinguish between the classes. In other words, the socio-demographic data show a difference between depressed subjects and healthy subjects. If the model is considered in relation to the PHQ9, a high performance in sensitivity and specificity could be demonstrated. The AUC score of .89 shows a very good ability to distinguish between the classes. The WHO-5 model shows good performance with a sensitivity for non-depressive cases of .78 and for depressive cases of .72. The specificity reflects the ability of the model to correctly classify non-depressive. The AUC score of .86 underlines the overall good discriminatory ability of the model between the classes. When all three areas are compared with each other, it is noticeable that two standardized and established test procedures such as the PHQ9 and the WHO-5 are only minimally better at predicting depression than the sociodemographic data. The PHQ9 and the WHO5 were developed specifically for the diagnosis of depression and are based on diagnostic criteria. In contrast, the sociodemographic survey does not contain any questions on symptoms. These results underline the key function of sociodemographic data in communication between GPs and their patients. While questionnaires should certainly continue to be completed in the waiting area, the present results make it clear that sociodemographic data are just as important. With an accuracy of .77 on the WHO-5, the sociodemographic scores show an almost similar accuracy of .74. The integration of sociodemographic data into the diagnostic process can provide valuable insights that go beyond the purely symptom-oriented questionnaires. Especially when it comes to capturing a more comprehensive picture of the patient's life circumstances. These findings can be directly incorporated into treatment planning, which standardized tests such as the PHQ9 and the WHO-5 cannot do in the same way. The results suggest that the inclusion of information such as loneliness, well-being, unemployment and physical activity is of great importance, especially for psychotherapeutic practice. This indicates that a stronger focus on socio-demographic factors is essential in primary care. Not only does the accuracy of diagnosis improve, but the therapeutic relationship is also strengthened and individualized treatment approaches can be created.

The logistic regression analysis revealed significant correlations between certain variables and the probability of depressive disorders in the outpatient setting. Regarding the hypotheses, the following conclusions were drawn: a non-significant p-value (p > .05) indicates that age at study inclusion has no statistically significant influence on the occurrence of depressive disorders. The OR of .06 suggests that an increase in age is associated with a lower likelihood of depression, but this relationship is not significant. Regarding the variable gender, the p-value indicates that gender has no significant effect on the occurrence of depressive disorders. We found an OR of 1.2, indicating that women have a slightly higher probability of depression, but this relationship is not statistically significant. Hypothesis 1a is therefore rejected. Hypothesis 1b regarding the relationship status of the test subjects has no significant influence on the probability of a current depressive illness (p = .51) and is therefore also rejected. The coefficient is positive, suggesting that individuals who are in a committed relationship and living with their partner may have a slightly higher likelihood of having a depressive disorder compared to other categories ("No" and "In a committed relationship but not living together"). However, this effect is not significant and therefore the influence cannot be confirmed. Unemployment is significantly positively associated with depression (p < .01). We found an OR of 0.51, indicating that unemployed people are 1.7 times more likely to be depressed, suggesting that unemployment is a risk factor for depression. Hypothesis 1c is therefore confirmed. The analysis shows that the number of inhabitants of the place where the participants grew up is significantly negatively associated with the probability of depression (p < .05). The odds ratio of .71 indicates that people from larger towns are about 29% less likely to suffer from depression. This suggests that hypothesis 1d can be confirmed. Hypothesis 2a, that discrimination at school has a significant influence on depressive symptoms, was confirmed. The analysis shows that discrimination at school is significantly negatively associated with the probability of depressive disorders (p = .01). The odds ratio of .48 suggests that experiencing discrimination at school may be associated with an approximately 52% lower likelihood of depressive illness. This suggests that experiencing discrimination at school may be associated with a lower likelihood of current depressive illness, but this seems contradictory and should be investigated further. Experiencing discrimination at work has no significant effect (p = .93) on the likelihood of current depressive illness. Financial problems show a significant influence (p = .03) on the probability of a current depressive illness. Hypothesis 2b is rejected, whereas hypothesis 2c is confirmed. Hypothesis 2d, which asks about previous family illnesses, is significant (p = .01). This indicates that a family history of mental illness is associated with a higher probability of a depressive illness and the hypothesis can be confirmed. Physical activity is not significantly associated with depression (p > 0.05) and hypothesis 2e is therefore rejected. The OR of .20 indicates that physical activity may have a slightly protective effect, but this effect is not statistically significant. The results of the logistic regression for loneliness (Lonliness_total) (p = .01) show that a coefficient of .76 is significantly positively associated with the occurrence of depressive symptoms. This indicates that people who report a higher level of loneliness are more likely to be classified as depressed. Social support (LSNS6 total) has a significant negative impact on the occurrence of depression (p < .04). An OR of .57 indicates that greater social support is associated with a reduction in the likelihood of depression, suggesting that social networks have a protective effect. Hypothesis 2f and 2g can therefore be successfully confirmed.

Finally, a new regression was run on the entire dataset to ensure comparability across different approaches. Loneliness is the most important feature in the model in terms of both coefficients and permutation importance, suggesting that it is a strong predictor of depression. People who feel lonely are more likely to be categorized as depressed social support from the (LSNS6) also plays a significant role. Its influence is negative, which means that stronger social networks reduce the risk of depression. People with stronger social networks and more social support are less likely to be classified as depressed. Population size and unemployment are also relevant, but less influential. The number of inhabitants indicates that people in larger towns are less likely to be classified as depressed. One possible reason for this could be the better social and economic conditions. Although unemployment in particular is positively associated with the prediction of depression, it plays a lesser role overall in the model prediction. The unemployment results indicate that unemployment is a risk factor for depression, as people without a job are more likely to be classified as depressed. Physical activity in particular plays a minor role in the model prediction. The results for physical activity show that increased activity can be associated with a reduction in depressive symptoms. This

interpretation sheds light on which factors the model has identified as important predictors for the states to be classified and how strongly these factors influence the model's decisions. The Importance of LSNS6 indicates that social support and networks play a significant role in model prediction but are less important than loneliness. The number of inhabitants influences the model, but not as strongly as loneliness and social support. Unemployment and physical activity are less decisive for the prediction than the other characteristics.

5.2 Discussion of the results considering the current state of research

The present results extend the correlations documented in the literature between demographic, psychosocial factors and depressive symptoms. The gender differences reported in the literature (Bebbington (1996); Piccinelli & Wilkinson (2000), Kühner (2003)) could not be confirmed in this study. There are still inconsistent findings in the literature (Hammarström et al. 2009). Empirical evidence has already shown that the low treatment rate among men is not due to a better state of health, but rather, for example, to the discrepancy between the perception of need and behavior when seeking help. This is probably still due to outdated traditional social norms (Möller-Leimkühler, 2002). In comparison to the sample recruited here, this problem can be illustrated: 46% of women fulfil depressive symptoms and only 26% of men. In our machine learning model presented here, gender did not show any significance, but future studies should confirm these results. Other studies (Weissman and Klerman, 1977; Krönke & Spitzer, 1998; Williams et al, 1995; Stage & Kragh-Sørensen et al, 2003; Poutanen et al, 2009; Müller et al, 2024) have shown a wide variety of results on this for decades and it will probably take much larger, longitudinal studies to clarify the question of whether there are gender-specific differences in prevalence or whether depressive symptoms determine the response behavior to the therapy. In all researched studies (Busch et al., 2013; Hapke, Cohrdes, & Nübel, 2019; Strine et al., 2006), the highest prevalence of depressive symptoms in both genders was between 18 and 29 years of age. This cannot be reflected in the outpatient setting here, as the average age is 41 years. The results of Beesdo-Baum and colleagues (2017) point in the same direction, the participating patients were on average 53.8 years old, with a range of 18-95 years and 60.4 % were female. Therefore, it is pointed out that also other psychosocial parameters should be addressed. Overall, Allen and colleagues (2014) discovered that mental disorders most heavily impact disadvantaged and impoverished populations. This can also be shown here by the net household income per person. In our study, the subjects with depressive symptoms had the lowest income with an average of 2.500€. The analysis shows the significant role of unemployment as a risk factor for depression. This is in line with previous studies that have shown a strong link between unemployment and mental illness (Hans & Lee, 2015; Reibling et al., 2017). Our calculations show that the size of the place of residence is also a relevant factor. People who grew up in larger towns are significantly less likely to suffer from depression. However, the researched studies report that the lowest prevalence of depressive symptoms was found in small towns (Robinson et al., 2017 & Busch et al., 2013). The correlation we found could be explained by several factors. Larger cities may offer better access to health services, social networks and employment opportunities, which could act as protective factors against depression. It should also be noted that, on average, participants live in larger cities than they grew up in. This indicates that changes in city size across the lifespan may play a role in mental health (Lederbogen et al., 2011). These results suggest that the city size in which the subjects grew up may have a long-term influence on mental health. This should be investigated further in future studies. One caveat is that our study largely took place in the greater Munich area and therefore fewer patients came from small towns.

We found that family history was significantly associated with an increased likelihood of depressive illness. This finding is consistent with previous studies that emphasize the importance of family influences on mental health (Han & Lee, 2015; Brydsten, Hammarström & San, 2018). When considering educational status, we were also able to recognize that a lower prevalence was shown in the upper education group than in the middle or lower education group, which has also been documented in the literature (Heidemann, 2021). An unexpected finding of our study is the relationship between experiencing discrimination at school and a lower likelihood of depression. At first glance, this relationship appears contradictory, as discrimination is typically considered a risk factor for mental illness (Benner et al., 2018). One possible explanation could be that the difficulties experienced at school may promote resilience or that the adult test subjects subsequently developed stronger coping strategies. In addition, the average age in our study was 42 years and we cannot draw any conclusions about the presence of depression in childhood and adolescence. Further research is needed to better understand this relationship. Studies related to discrimination in school and depression in adulthood were not found in the literature. Smyth and colleagues (2015) identified the impact of perceived emotional support and the size of the friend and family network as protective factors against mental health disorders. This may also be reflected by the LSNS6 in the cohort. Our results showed a negative influence on the occurrence of depression (p < .01). This means that stronger social support is associated with a reduction in the likelihood of depression, indicating that social networks have a protective effect. In terms of society, there has been an increased focus on safety in the neighborhood (Chen et al., 2017; Stansfeld et al., 2017). A study in China showed that a lower level of depression can be associated with satisfaction in the living environment and safety in the neighborhood (Fu, 2018). The neighborhood connection was also surveyed in this sample and the questions correlated strongly with the severity of depressive symptoms. Further studies, especially in German-speaking countries, are needed to substantiate our findings.

The results presented in relation to loneliness show that it has remained high even after the COVID-19 pandemic. The presence of loneliness shows that it is a key predictor of the onset of depressive symptoms in outpatients. These findings are consistent with the growing literature that identifies loneliness as a significant risk factor for depression, particularly in post-pandemic contexts (Entringer, 2022; Kirkland et al., 2023). The importance of social support for mental well-being is again underpinned by our findings. People with a strong social network are significantly less likely to suffer from depression. This is confirmed by numerous studies that emphasize the protective factor of social support for mental health (Smyth et al., 2015).

Henkel and colleagues (2003) have pointed out that the use of the WHO-5 scale can help GPs to recognize depression at an early stage. The results here confirm this, but the sociodemographic data should not only be seen as a supplement to established test procedures but should be investigated as an essential component of the diagnosis and treatment of depression. Our results could have an impact on the design of future diagnostic tools and therapeutic treatment approaches. For example, the waiting room in GP surgeries should serve as a tool here, in which patients can fill out a PHQ9 in a resource-saving manner and socio-demographic data can be determined. The GPs could already be provided with valuable information and the personal discussion could clarify any unanswered questions. In our recruited cohort, 16.2% of depressed patients were interviewed. The literature confirms that up to 20% of patients treated as outpatients in primary health care have depression (Burnham et al., 1989; Coulehan et al. 1990; Gerber et al., 1992). If more recent studies that relate the diagnostic criteria specifically to the ICD-10 are included, the prevalence indicates 10 - 14% of depressed patients in GP practices (Winter et al., 2000; Beesdo-Baum et al., 2017 & Jacobi et

al., 2002). Research is also already being conducted worldwide on the topic of social determination in the outpatient setting (Müller et al., (2024); Hildebrandt, Stage & Kragh-Sørensen (2003); Bertakis et al. (2001); Poutanen and colleagues (2009)), but the comparability of the data is limited. This supports the argument that it is important to conduct further studies on this topic in order to enable comparability. It is difficult to compare studies across countries, as there is no standardized global approach to primary care. For example, the system of a general practitioner differs between countries and some also offer disorder-specific consultation hours or support services (Müller et al., 2024).

Screening for mental illness is often challenging for primary care providers. This is due to various factors such as insufficient specialist knowledge in the field of psychiatric care (Beesdo-Baum et al., 2017; Jacobi et al., 2002), potentially negative reactions from patients to the screening, as well as the perception and getting to know the patients personally. However, time constraints and a lack of familiarity of primary care providers with the treatment of psychiatric disorders also play an essential role (Wittchen & Pittrow, 2002). GPs who have completed an additional qualification in psychotherapy had significantly better scores in the recognition of depression (Beesdo-Baum et al., 2017). This shows the importance of specific training for GPs, especially with the prevalence of 9.2% for depression in Germany, which is higher than the European average of 6.6% (Hapke, Cohrdes, & Nübel, 2019). Given the considerable importance of early and specialized treatment for depressed patients, it is surprising that only a small proportion of doctors (7.5%) report consistently referring their patients to psychiatrists. This is mainly due to the fact that the doctors surveyed emphasized the difficulty of referring patients to psychotherapists (49.6%) or psychiatrists (31.9%) (Wittchen & Pittrow, 2002). These figures highlight a worrying gap in care. This may be due to a lack of resources, time pressure or inadequate training in dealing with mental illness in primary care.

Particularly alarming is the fact that two thirds of depressed adults in Germany continue to be underserved, which underlines the urgency of improving care structures (Thornicroft et al., 2017). This undersupply is reflected both in the limited availability of specialists and in the limited variety of treatment options offered in primary care (Robert Bosch Stiftung (2021) & Kassenärztliche Bundesvereinigung (2024)). Primary care, which for many patients is the first and often only point of contact with the healthcare system, therefore does not appear to be adequately prepared for the complex needs of depressed patients. This situation highlights the urgent need for increased efforts to improve collaboration between GPs and mental

health specialists. Training for primary care physicians must be expanded and the availability of specialized services (e.g. psychotherapy) must be increased. Only through integrated care that addresses the individual needs of patients can the problem be countered.

In order to strive for an improvement in one's own country, a wide variety of concepts should be examined to enable the practitioner to provide patient-oriented care. In the overall comparison of the studies presented, particular attention should be paid to the fact that every depression has an individual course. In addition, the age differences between patients must be taken into account, as the perception and weighting of depression can differ (Beesdo-Baum et al., 2017). In order to obtain an overall view, large samples of data on psychosocial factors should be collected in order to integrate these aspects. The measures recommended in the S3 guidelines, such as the use of screening questionnaires and flow charts or individual training courses on depression, appear to play a subordinate role in GP depression diagnostics to date (AWMF, 2022).

5.3 Strengths and limitations

It is a cross-sectional outpatient study in which information on the course of the disorder could not be considered retrospectively, or only to a limited extent. A follow-up by a longitudinal study is advisable to be able to depict the prospective course. Due to the time and administrative effort required for the study, practices were selected in the vicinity of the LMU University Hospital working and residential cities. The participating medical practices that have registered to take part in the study already show an intrinsic motivation for the topic. The motivation of the participants could have been influenced by the awarding of the trial vouchers. Due to the lack of specific laboratory parameters as a basis for the diagnosis of depression, a detailed anamnesis and the use of diagnostic procedures as well as careful evaluation of the results are required. A major limitation of this study is the fact that the sample of depressive patients is small. This can be seen, for example, in the lack of correlation between gender and the occurrence of depression. The result is not statistically significant in the regression, despite a clear majority of depressed women in the sample. This indicates an inadequate sample size, which may not be sufficient to reliably recognize the differences between the genders. The lack of significance indicates that the observed distribution may have come about by chance and does not necessarily point to an actual correlation. A larger sample or additional analyses may be required to be able to make clearer statements about the influence of gender on the development of depression. This also applies to age and relationship status. However, it is even more significant that unemployment, the number of inhabitants and discrimination at school showed significant results despite the smaller sample. It also relates to loneliness and well-being, which are particularly important for future studies in therapeutic settings. Preventive measures based on psychosocial parameters could have an influence on reducing the incidence of depression in patients in general practice. This aspect could not be researched and was not included in the study. Not only the specific focus on psychosocial factors, as presented in our work, is new in the GP setting, but also the statistical approach shows a new and innovative side of this work. Machine learning was added to classical statistics to identify extended correlations and patterns.

5.4 Outlook

The studies from the literature are usually conducted using outdated questionnaires and methods and cannot be explicitly compared with today's measurement instruments. Socio-cultural aspects are not included enough; these should also be considered across the board and most studies do not imply this. It is also important to recognize that differences in mental health in relation to characteristics such as race, gender and ethnicity often stem from experiences of oppression or discrimination. A difficult component is to implement a focus on mental illness in GP practices. A calm setting in which the practitioner and patient can fully open is usually required for the enquiry into mental well-being. The time pressure and the large number of patients in GP surgeries usually do not allow this.

Future studies should replicate our results in GP practices. In other words, large samples should be aimed for, a longitudinal research design should be chosen, and the use of machine learning methods should be included. This may lead to the improvement of diagnostic criteria for GPs based on simple screening tools. This could provide a new perspective on the diagnosis of depression and clarify early warning signs by including psychosocial parameters. Those affected could thus receive more effective treatment and support.

V Literature

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1. Soziodemographische Informationen

Vorname, Familiennan	ne						
Wann sind Sie geboren?			/ Tag /	Tag / Monat / Jahr			
In welcher Stadt/ welc	hem Ort sind S	ie geboren?					
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laben Sie leibliche Kind	ler?						
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_	Aufbau-, Fachschule o.ä.	[z.B. Gymnasium, FOS-13]
	Von der Schule abgegangen ohne	☐ Abschluss der Polytechnischen Oberschule 10.
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nie Im Alter vor	n 0-5 Ja n 5-10 Ja	ahren.	Anzahl Umzüge: Anzahl Umzüge: Anzahl Umzüge:				

2. Psychiatrische Vorgeschichte

Befinden Sie	sich <u>aktuell</u> in psychia	trischer Behandlun	g?	
🗖 ja, ambu	lant 🗆] ja, teilstationär	🗖 ja, stationär	nein.
	nden Sie sich derzeit in Probleme? [Mehrfachne		ndlung aufgrund Ihrer psychisch	en
☐ Neurolog ☐ Hausarz		Andere:	peut/in (psychologische/r oder a	árztliche/r)
			sche / psychiatrische Symptome ste bei Angststörungen]	e auftraten?
		*	cher/psychischer Beschwerden und / oder psychologischer Hilf	
	_ (Jahre)			
An wen haber	n Sie sich bei diesem E	rstkontakt aufgrun	d ihrer psychischen Beschwerde	en gewendet?
Psychoth ärztliche/r) Psychiati (stationär) Neurolog	er/-in / Nervenarzt/-in nerapeut/in (psycholog rische / psychosomati ge/-in nge/in/Beratungsstelle	gische/r oder sche Klinik	☐ Hausarzt/-in ☐ andere Arzt/Ärztin ☐ andere Klinik (stationär) ☐ Andere: ☐ heutige/derzeitige Behanderstkontakt	flung ist der
Wie alt waren	Sie bei der ersten (teil	-) stationären psyc	hiatrischen Behandlung?	
-	_ (Jahre)			
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mal				
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nein	☐ ja, zur Mutter Mein Alter:	☐ ja, zum \ Mein Alt	• • • • • • • • • • • • • • • • • • • •	

Wie viele Geschwister haber	Sie?							
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Anzahl der Halbgeschwiste	er 🗆 0	□ 1	□ 2	□3	□ 4	□ >4		
Leidet oder litt einer Ihrer le	iblichen Ange	hörigen an e	einer der folger	den psychi	schen Erkran	kungen?		
Angststörung (z.B. Panikstör	rung, Phobien	, andere Ang	ststörungen)					
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Anzahl der Halbgeschwister		ekannt						
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Alkohol- oder Drogenabhäng	igkeit							
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☐ eigenes Kind	☐ Zweieiig	e Zwillingsge	eschwister	□n	ein / nicht be	ekannt		
Medikamentenabhängigkeit								
☐ Mutter	☐ Geschwi	ster 🗆 Hai	bgeschwister	□G	roßeltern			
				-				
Anzahl der Geschwister 0								
Schizophrenie oder Psychose)							
☐ Mutter	☐ Geschwi	ster 🗆 Hal	bgeschwister	□G	roßeltern			
	☐ Eineiige	Zwillingsges	chwister					
☐ eigenes Kind	☐ Zweieiig	e Zwillingsge	schwister	∐ n	ein / nicht be	kannt		
Manisch-depressive (bipolare	e) Erkrankung							
☐ Mutter	☐ Geschwi	ster 🗆 Hall	ogeschwister	☐ Gi	roßeltern			
	☐ Eineiige 2	Zwillingsges	chwister	-				
☐ eigenes Kind	☐ Zweieiige	Zwillingsge	schwister	□ ne	ein / nicht be	kannt		
Demenz / demenzielle Erkran	kung							
☐ Mutter	☐ Geschwis	ster 🗆 Hall	geschwister	□ Gr	oßeltern			
	☐ Eineiige 2	Zwillingsgeso	hwister	-				
☐ eigenes Kind	Anzahl der Halbgeschwister							
Autismus								
Mutter	☐ Geschwis	ster 🗆 Hall	geschwister	□ Gr	oßeltern			
eigenes Kind	_							

Geistige Behinderung					
☐ Mutter ☐ Vater ☐ eigenes Kind	☐ Geschwister ☐ Halbgeschwis ☐ Eineiige Zwillingsgeschwister ☐ Zweieiige Zwillingsgeschwister	☐ Tante / Onkel			
Nicht definierte psychische	Erkrankung /starker Verdacht auf psy	chische Erkrankung			
☐ Mutter ☐ Vater ☐ eigenes Kind	☐ Geschwister ☐ Halbgeschwis ☐ Einelige Zwillingsgeschwister ☐ Zweielige Zwillingsgeschwister	☐ Tante / Onkel			
Suizide in Ihrer Verwandtsch	naft				
☐ Mutter ☐ Vater ☐ eigenes Kind	☐ Geschwister ☐ Halbgeschwis ☐ Eineiige Zwillingsgeschwister ☐ Zweieiige Zwillingsgeschwister	☐ Tante / Onkel			
Leidet oder litt einer Ihrer le folgenden körperlichen Erki		rn, Geschwister, eigene Kinder) an einer der			
☐ Diabetes mellitus ("Zuckerkrankheit") ☐ Bluthochdruck ☐ Übergewicht	☐ Herzinfarkt ☐ Schlaganfall	☐ Krebsleiden ☐ Rheuma/Autoimmunerkrankung			
Hatte ein Verwandter von Ih	nen vor seinem 60. Lebensjahr einen	Herzinfarkt?			
☐ Mutter ☐ Vater ☐ eigenes Kind	☐ Geschwister ☐ Halbgeschwis ☐ Eineiige Zwillingsgeschwister ☐ Zweieiige Zwillingsgeschwister	ter Großeltern Tante / Onkel nein / nicht bekannt			
4. Psychopharma	aka				
Haben Sie bereits einmal Ps □ nein □ ja → Wenn ja, welche	***************************************	r psychischen Symptome genommen?			
Nehmen Sie aktuell Psychop	harmaka zur Verbesserung Ihrer psyc	hischen Symptome?			
□ nein □ ja → Wenn ja, welche					
Haben Sie in den letzten 12 leingenommen?	Monaten Beruhigungsmittel, Schlafmit	ttel, Sedativa, Hypnotika benötigt bzw.			
□ nein □ ja → wenn ja, welche un	d wie oft? 2- bis 4				

Loneliness Scale aus dem Socio-Economic Panel Die folgenden Fragen beziehen sich auf Ihr soziales Umfeld. Gar nicht Sehr Selten Häufig häufig Wie oft haben Sie das Gefühl, dass Ihnen die П Gesellschaft anderer fehlt? П Wie oft haben Sie das Gefühl, außen vor zu sein? П Wie oft haben Sie das Gefühl, dass Sie sozial П isoliert sind? **Lubben Social Network Scale** Unser soziales Umfeld bietet uns Gesellschaft und Freizeitkontakte, aber auch Hilfe und Unterstützung in ernsten Situationen. Zunächst fragen wir nach Kontakten zu Familienangehörigen und Verwandten (Eheparter, Kinder, Enkelkinder, Verschwägerte und andere Verwandte). 9 oder 5 bis 3 oder 2 keine mehr 8 4 Mit wie vielen Familienangehörigen treffen Sie sich mindestens einmal im Monat oder haben Sie mindestens einmal im Monat sonstigen Kontakt (z.B. telefonisch)? Mit wie vielen Familienangehörigen sind Sie so vertraut, dass П Sie sie um Unterstützung bitten können? Mit wie vielen Familienangehörigen sind Sie so vertraut, dass Sie private Angelegenheiten mit ihnen besprechen können? Jetzt fragen wir nach Kontakten zu Freunden und Nachbarn. 3 oder keine 9 oder 5 bis 2 8 mehr 4 Mit wie vielen Freunden oder Nachbarn treffen Sie sich mindestens einmal im Monat oder haben Sie mindestens einmal im Monat sonstigen Kontakt (z.B. telefonisch)? Mit wie vielen Freunden oder Nachbarn sind Sie so vertraut, п dass Sie sie um Hilfe bitten können? Mit wie vielen Freunden oder Nachbarn sind Sie so vertraut, dass Sie private Angelegenheiten mit ihnen besprechen können? WHO-5 Fragebogen zum Wohlbefinden Die folgenden Aussagen betreffen Ihr Wohlbefinden in den letzten zwei Wochen. Bitte markieren Sie bei jeder Aussage die Antwort, die Ihrer Meinung nach am besten beschreibt, wie Sie sich in den letzten zwei Wochen gefühlt haben. Meistens Etwa Etwas Ab In den letzten zwei Wochen... Die ganze mehr als weniger und keine Zeit die als die m Zeit-711 Hälfte Hälfte punkt der Zeit der Zeit ...war ich froh und guter Laune ...habe ich mich ruhig und entspannt gefühlt П ...habe ich mich energisch und aktiv gefühlt ...habe ich mich beim Aufwachen frisch und

ausgeruht gefühlt

interessieren

...war mein Alltag voller Dinge, die mich

Patient Health Questionnaire -9

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?

	Überhaupt nicht	An einzelnen Tagen	An mehr als der Hälfte der Tage	Beinahe jeden Tag
Wenig Interesse oder Freude an Ihren Tätigkeiten				
Niedergeschlagenheit, Schwermut oder Hoffnungslosigkeit		_	Ġ	
Schwierigkeiten ein- oder durchzuschlafen oder vermehrter Schlaf				
Müdigkeit oder Gefühl, keine Energie zu haben				
Verminderter Appetit oder übermäßiges Bedürfnis zu essen	_			
Schlechte Meinung von sich selbst; Gefühl, ein Versager zu sein oder die Familie enttäuscht zu haben	0		0	
Schwierigkeiten, sich auf etwas zu konzentrieren, z.B. beim Zeitunglesen oder Fernsehen		0		0
Waren Ihre Bewegungen oder Ihre Sprache so verlangsamt, dass es auch anderen auffallen würde? Oder waren Sie im Gegenteil "zappelig" oder ruhelos und hatten dadurch einen stärkeren Bewegungsdrang als sonst?				
Gedanken, dass Sie lieber tot wären oder sich Leid zufügen möchten?		_	_	_

Pokal -	· ID:	Aktuelles Datum:	
Phase:	o Studienbeginn	o 4-Wochen Follow-up	o 1 Jahres Follow-up
vELSA	Fragebogen		
	en Sie Ihr Geschlecht an: vählen Sie eine der folgender	n Antworten:	
。 M	ännlich		
o W	eiblich eiblich		
o Di	vers		
zusamr		n einer Beziehung und leben Sien Antworten:	mit Ihrem Partner
o Ja	ı		
o Ne	ein (Sie können Frage 3. über	rspringen)	
o In	einer festen Partnerschaft, a	ber nicht zusammenlebend	
	hr Partner eine andere ethnis ählen Sie eine der folgenden	che Herkunft oder Nationalität a Antworten:	ls Sie?
o Ja			
o Ne	ein		
Scheidu	re feste Beziehung in den let: ung, Trennung oder Auszug? ählen Sie eine der folgenden		egangen, z.B. durch
o Ja			
o Ne	ain		
geistig),	mern Sie sich um jemanden r der auf besondere Pflege ar ählen Sie eine der folgenden		rung (körperlich oder
o Ja			
o Ne	in		
	n Sie mindestens einmal pro ählen Sie eine der folgenden	Woche einer sportlichen Aktivitä Antworten:	it nach?
o Ja			
o Ne	in		

Phas	e: o Studienbeginn o 4-Wochen Follow-up o 1 Jahres Follow-up
7. W Bitt	ie groß ist der Unterschied zwischen ihrem Traumkörper und ihrer aktuellen Figur? e wählen Sie eine der folgenden Antworten:
0	Kein Unterschied
0	Klein
0	Moderat
0	Groß
0	Sehr groß
/ask	atten Sie schon einmal einen Herzinfarkt, einen Schlaganfall oder ein anderes kardio- uläres Ereignis (etwa eine Durchblutungsstörung an den Beinen oder andere Organe)? wählen Sie eine der folgenden Antworten:
0	Ja
0	Nein
	utten sie innerhalb der letzten 12 Monate Kopfschmerzen, wenn ja, wie häufig? wählen Sie eine der folgenden Antworten:
0	Nie oder fast nie (in dem Fall können Sie Fragen 12, 13 und 14 überspringen)
0	Seltener als einmal pro Monat
0	Ein oder zweimal im Monat
0	Etwa einmal pro Woche
0	Häufiger als einmal pro Woche
0	Täglich
	sewerten Sie die Intensität der Kopfschmerzen: wählen Sie eine der folgenden Antworten:
0	Leicht (stört nur geringfügig bei der Erledigung Ihrer täglichen Aufgaben)
0	Mäßig (behindert, aber verhindert nicht die Ausführung ihrer täglichen Aufgaben)
0	Schwer (verhindert die Ausführung zahlreicher täglicher Aufgaben)
neis	Venn Sie innerhalb der letzten 12 Monate unter Kopfschmerzen litten, haben Sie dabei die te Zeit auf Licht sensibel reagiert? wählen Sie eine der folgenden Antworten:
0	Ja
0	Nein

Pokal - ID:		Aktuelles Datum:	
Phase:	o Studienbeginn	o 4-Wochen Follow-up	o 1 Jahres Follow-up

12. Litten Sie innerhalb der letzten 12 Monate auch unter Migräneanfällen, wenn ja wie häufig? (Ein Migräneanfall zeichnet sich durch einseitigen pulsierenden Kopfschmerz aus, der durch Bewegung verstärkt wird. Der Schmerz wird häufig von Symptomen wie Übelkeit, Appetitlosigkeit, Erbrechen, Lichtund Geräuschempfindlichkeit oder Reizbarkeit begleitet. Die Schmerzen halten in etwa 4-72h an.) Bitte wählen Sie eine der folgenden Antworten:

- o Nie oder fast nie
- o Seltener als einmal pro Monat
- o Ein oder zweimal im Monat
- o Etwa einmal pro Woche
- Häufiger als einmal pro Woche
- Täglich

13. Bestand bei Ihnen jemals eine Schwangerschaft?

Bitte wählen Sie eine der folgenden Antworten:

- o Ja
- Nein

Bitte Beantworten Sie die folgenden zwei Fragen, falls bei Ihnen jemals eine Schwangerschaft bestanden hat:

13a. Litten Sie während einer Schwangerschaft an einer Präeklampsie, Eklampsie oder dem HELLP-Syndrom? (Schwere Erkrankung während einer Schwangerschaft, die mit hohem Blutdruck und Wassereinlagerungen einhergeht.)

Bitte wählen Sie eine der folgenden Antworten:

- o Ja
- Nein

13b. Haben Sie dabei eines oder mehrere der folgenden, genannten Ereignisse erlebt? Bitte wählen Sie die zutreffenden Antworten aus (Mehrfachauswahl):

- o Totgeburt nach der 24. Schwangerschaftswoche
- o Abtreibung einer Schwangerschaft
- Fehlgeburt (Abort), der vorzeitige Abgang einer Schwangerschaft vor der 20.
 Schwangerschaftswoche
- Trotz regelmäßigen, ungeschützten Geschlechtsverkehrs über ein Jahr ausbleibende Schwangerschaft
- Deutliche Gewichtszunahme von über 30 kg während der Schwangerschaft
- Keine der genannten Optionen

Pokal - ID:	- 4 77	Aktuelles D		1 Johnson Pollows von
Phase: o Studienbegin		ochen Follow-	•	1 Jahres Follow-up
14. Haben Sie sich jemals in genannten Situationen bena Bitte kreuzen Sie pro Zeile e	chteiligt gefühlt?	Wann zuletzt?	riminierung in	einer der nier
	Vor weniger als einem Monat	Vor mehr als einem Monat	Vor mehr als 12 Monaten	Noch nie
Am Arbeitsplatz				
In der Schule				
An öffentlichen Plätzen (Banken, Handelseinrichtungen, Krankenhäuser, Ämter usw.)		I		
Bezüglich des Wohnens (Schwierigkeiten beim Mieten/Kaufen einer Wohnung, Probleme in der Nachbarschaft usw.)		;		
15. Gab es innerhalb der letz Schwierigkeiten litten? Bitte wählen Sie eine der fol			n Sie unter em	sten finanziellen
o Nein				
o Einmal				
o Mehrmals				
16. Wie hoch ist Ihr monatlick Bitte wählen Sie eine der folg			kommen?	
 Bis 500 Euro netto im 500,01€-1500 € Euro 1000,01€-1500 € Euro 1500,01 € - 2000 € Euro 2000,01€-2500 € Euro 	netto im Monat o netto im Mona uro netto im Mor	at		

2500,01€-3000 € Euro netto im Monat
 3000,01€-3500 € Euro netto im Monat
 3500,01€-4000 € Euro netto im Monat
 4000,01€-4500 € Euro netto im Monat
 4500,01€-5000 € Euro netto im Monat
 mehr als 5000 Euro im Monat

_	okal - ID:		٠.		lles Datum:	171	T. 11	
P	hase:	o Studienbeginn	o 4-	Wochen Fo	llow-up	o I Jahres	Follow-up	
		ie innerhalb der letzten zw en En Sie eine der folgenden A			fstätig?			
	o Ja							
	o Nein (i	n dem Fall können Sie die l	Frag	en 18-22 üb	erspringen und	auf Seite 8	fortfahren)	
b	erufstätig	antworten Sie die folgende gewesen sind. Lesen Sie di en Sie pro Zeile eine der folg	e Fra	agen durch	und kreuzen Sie	letzten 12 N Zutreffend	Monate es an:	
			P. S. San S.	Häufig	Manchmal	Selten	Niemals oder fast nie	Keine Antwort
	Können S Neues er	Gie an ihrem Arbeitsplatz lernen?						
		ihre Arbeit einen hohen Gra tise oder besondere en?	ad					
	Ist es in I Initiative	hrem Job wichtig die zu ergreifen?						
		Sie in ihrem Beruf bestimme acht werden muss?	en		salge	MANISTER PROPERTY OF THE STATE		
		Sie in ihrem Beruf bestimme aben erledigt werden	en					
!		e ausreichend Zeit, um ihre n zu erledigen?	•					
		ig müssen Sie ihre Arbeit h ausführen?						
		Sie in ihrer Arbeit die gleich sehr häufig ausführen?	e					
	arbeiten (g müssen Sie sehr hart sehr viel in einem kurzen umsetzen)?						

Pokal - ID Phase:	o Studienbeginn	Aktuel o 4-Wochen Fo	o 1 Jahres			
		Häufig	Manchmal	Selten	Niemals oder fast nie	Keine Antwork

Verlangt ihr Beruf zu viel von Ihnen?

Wie häufig begegnen ihnen in ihrer Arbeit sich wiedersprechende Anforderungen?

Wie häufig werden sie durch Arbeit und häusliche Verpflichtungen davon abgehalten Zeit für sich selbst zu nehmen?

Wie häufig werden sie durch berufliche Verpflichtungen davon abgehalten sich Zeit für ihre Familie zu nehmen?

Wie häufig beeinträchtigen Familienangelegenheiten ihre Verpflichtungen gegenüber ihrer Arbeit (z.B pünktlich zur Arbeit erscheinen, Aufgaben ausführen, Teilnahme an Meetings auch zu ungewöhnlichen Arbeitszeiten)?

Wie häufig erschwert ihre berufliche Situation den häuslichen Verpflichtungen nachzukommen?

19. Geben Sie an inwiefern sie den gegebenen Aussagen zustimmen oder nicht zustimmen. Bewerten Sie ihre berufliche Situation innerhalb der letzten 12 Monate.

Bitte kreuzen Sie pro Zeile eine der folgenden Antworten an:

Stimme zu Stimme eher Stimme eher Stimme nicht zu nicht zu

Wenn Sie keinen guten Tag haben, zeigen ihre Arbeitskollegen hierfür Verständnis.

An ihrem Arbeitsplatz treffen Sie eine ruhige und

Pokal - ID:					
Phase	o Studienbeginn	o 4-W	ochen Follow-up	o 1 Jahr	es Follow-up
		Stimme zu	Stimme eher zu	Stimme eher nicht zu	Stimme nicht zu
ang an.	enehme Umgebung				
kon	ihrem Arbeitsplatz nmen die Kollegen gut einander aus.				
	genießen die Arbeit ihren Arbeitskollegen.	eriforme as			
Unt	können auf die erstützung ihrer egen zählen.				
Verl	haben ein gutes nältnis zu ihren gesetzten.				
außerl E-mai Grund kontal	urden Sie innerhalb der letzt halb ihrer gewöhnlichen Arb I, oder andere Kommunikati I irgend-welcher Arbeits-ang ktiert. vählen Sie eine der folgende	eitszeiten, via To ons-medien auf Jelegenheiten	elefon, zwischen i Familienleb	hren beruflichen en zu kämpfen?	12 Monaten mit Konflikten Anforderungen und Ihrem genden Antworten:
0	Täglich		о Та	glich	
٥	Mindestens einmal pro W	oche	o Mi	ndestens einmal p	oro Woche
0	Zweimal pro Monat oder	etwas häufiger	o Zw	eimal pro Monat	oder etwas häufiger
	Seltener als zweimal pro l	Monat	o Se	Itener als zweimal	pro Monat

22. Geben Sie auf einer Skala von 1 bis 10 (1 = kein Stress, 10 = maximal vorstellbarer Stress) an, wie belastet sie durch ihre berufliche Situation innerhalb der vergangenen 12 Monaten waren. Bitte wählen Sie eine der folgenden Optionen:

o Niemals oder fast nie

o Seltener als zweimal pro Monat

o Niemals oder fast nie

1	2	3	4	5	6	7	8	9	10

Pokal - ID:		Aktuelles Datum:	
Phase:	o Studienbeginn	o 4-Wochen Follow-up	o 1 Jahres Follow-up
Fragen zum	Zusammenhalt in der	Nachbarschaft	

Die Nachbarschaft bezieht sich auf den Ort der Gemeinschaft, in der Sie in den letzten 12 Monaten hauptsächlich gewohnt haben. Konkret meinen wir den Ort, an dem sich Ihr Haus befindet, und die Umgebung, in der Sie Ihren täglichen Aktivitäten nachgehen, z. B. Einkaufen. Dazu kann auch der Ort gehören, an dem sich religiöse, öffentliche oder kommerzielle Einrichtungen befinden.

23. Welche Größe hat ihr aktueller Wohnort?

wir haben gemeinsame Interessen, die uns verbinden.

Bitte wählen Sie eine der folgenden Antworten:

o bis 100 000 o bis 100

o bis 500 000 o bis 5000

bis 1 000 000 o bis 20 000

mehr als 1 000 000 o bis 50 000

Folgende Aussagen handeln thematisieren ihre Nachbarschaft und wie sie sich dort fühlen.

24. Beurteilen Sie wie diese Fragen auf ihre aktuelle Wohnsituation zutreffen.

	Trifft zu	Trifft eher zu	Teils / teils	Trifft eher nicht zu	Trifft nicht zu
Die Menschen in meiner Nachbarschaft teilen NICHT die Igleichen kulturellen, ethischen und moralischen Standards, sowie Verhaltensweisen.				1	
Die Menschen in meiner Nach- barschaft sind vertrauenswürdig.					
In meiner Nachbarschaft hilft man sich gegenseitig.					
Generell kommen die Menschen in meiner Nachbarschaft nicht miteinander aus.					
Unsere Nachbarschaft genießt einen engen Zusammenhalt und					

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MADRS

(Montgomery und Asberg Depressions-Skala)

1.) Sichtbare Traurigkeit

(Dieses Item beinhaltet die sich in Sprache, Mimik und Haltung ausdrückende Mutlosigkeit, Niedergeschlagenheit und Verzweiflung)

Keine Traurigkeit	0
	1
Sieht niedergeschlagen aus, ist aber ohne Schwierigkeiten aufzuhellen.	2
	3
Wirkt die meiste Zeit über traurig und unglücklich	4
	5
Sieht die ganze Zeit über traurig und unglücklich aus. Extreme Niedergeschlagenheit	6

2.) Berichtete Traurigkeit

(Beinhaltet die vom Patienten berichtete traurige Stimmung, gleichgültig ob sich diese sichtbar ausdrückt oder nicht, einschließlich Entmutigung, Niedergeschlagenheit, dem Gefühl der Hilflosigkeit und Hoffnungslosigkeit. Bewerten Sie nach Stärke, Dauer und dem Ausmaß der Stimmungsbeeinflußbarkeit durch äußere Ereignisse)

Vorübergehende Traurigkeit je nach den Umständen	0
	1
Traurig oder mutlos, jedoch ohne Schwierigkeiten aufzuheitern.	2
	3
Intensives Gefühl der Traurigkeit und Hoffnungslosigkeit. Die Stimmung ist jedoch immer noch durch äußere Umstände beeinflußbar.	4
	5
Ausdauernde oder unveränderliche Traurigkeit, Mutlosigkeit oder Hoffnungslosigkeit	6

3.) Innere Spannung

(Beinhaltet sowohl ein schwerdefinierbares Gefühl von Missbehagen als auch Gereiztheit, Unruhe, innere Erregung bis hin zu Angst und Panik. Bewerten Sie nach Stärke, Häufigkeit, Dauer und dem Ausmaß, in dem Beruhigung gesucht wird)

Leicht. Nur vorübergehende innere Spannung.	0
	1
Gelegentlich Gefühl von Missbehagen und Gereiztheit.	2
	3
Anhaltendes Gefühl innerer Spannung oder Erregung.	4
Kurzzeitige Panikanfälle, die der Patient nur mit Mühe beherrscht.	
	5
Nicht beherrschbare Angst oder Erregung. Überwältigende Panik.	6

4.) Schlaflosigkeit

(Beinhaltet die subjektive Erfahrung verminderter Schlafdauer oder –tiefe, verglichen mit dem vorher normalen Schlafverhalten)

Schläft wie gewöhnlich.	0
	1
Leichte Schwierigkeiten einzuschlafen. Oberflächlicher, unruhiger Schlaf. Geringfügig verkürzte Schlafdauer.	2
	3
Schlaf mindestens 2 Stunden verkürzt oder unterbrochen.	4
	5
Weniger als 2-3 Stunden Schlaf.	6

5.) Appetitverlust

(Beinhaltet das Gefühl der Abnahme des Appetits, verglichen mit dem vorherigen normalen Zustand. Bewerten Sie nach Stärke des Appetitverlusts oder dem zum Essen benötigten Zwang)

Normaler oder verstärkter Appetit.	0
	1
Geringfügige Appetitminderung.	2
	3
Kein Appetit. Nahrung wie ohne Geschmack.	4
	5
Nur mit Überredung zum Essen zu bewegen.	6

6.) Konzentrationsschwierigkeiten (Beinhaltet Schwierigkeiten der Konzentration, angefangen vom einfachen Sammeln der eigenen Gedanken bis zum völligen Verlust der Konzentrationsfähigkeit. Bewerten Sie nach Stärke, Häufigkeit und Ausmaß der Unfähigkeit zur Konzentration)

Keine Konzentrationsschwierigkeiten. Gelegentliche Schwierigkeiten, die eigenen Gedanken zu sammeln. Schwierigkeiten, sich zu konzentrieren und einen Gedanken festzuhalten. Nicht in der Lage, ohne Schwierigkeiten zu lesen oder ein Gespräch zu führen.		
Schwierigkeiten, sich zu konzentrieren und einen Gedanken festzuhalten.	Keine Konzentrationsschwierigkeiten.	0
Schwierigkeiten, sich zu konzentrieren und einen Gedanken festzuhalten.		1
	Gelegentliche Schwierigkeiten, die eigenen Gedanken zu sammeln.	2
		3
Nicht in der Lage, ohne Schwierigkeiten zu lesen oder ein Gespräch zu führen.	Schwierigkeiten, sich zu konzentrieren und einen Gedanken festzuhalten.	4
Nicht in der Lage, ohne Schwierigkeiten zu lesen oder ein Gespräch zu führen.		5
	Nicht in der Lage, ohne Schwierigkeiten zu lesen oder ein Gespräch zu führen.	6

7.) Untätigkeit (Beinhaltet Schwierigkeiten "in Schwung zu kommen" oder Verlangsamung bei Beginn oder Durchführung der täglichen Arbeiten)

Nahezu keine Schwierigkeiten "in Schwung zu kommen". Keine Trägheit.	0
	1
Schwierigkeiten, aktiv zu werden.	2
	3
Schwierigkeiten, einfache Routinetätigkeiten in Angriff zu nehmen, Ausführung nur mit Mühe.	4
	5
Vollständige Untätigkeit. Unfähig, ohne Hilfe etwas zu tun.	6

8.) Gefühllosigkeit (Beinhaltet das subjektive Empfinden des verminderten Interesses für die Umgebung oder Aktivitäten, die vorher Freude bereiteten)

Normales Interesse für Umgebung oder für andere Menschen.	0
	1
Vermindertes Interesse für Aktivitäten, die vorher Freude bereiteten.	2
	3
Verlust des Interesses für die Umgebung. Verlust der Gefühle für Freunde und Angehörige.	4
	5
Die Erfahrung der Gefühllosigkeit, Unfähigkeit, Ärger, Trauer oder Freude zu empfinden. Vollständiger oder schmerzhaft empfundener Verlust des Gefühls für nahe Verwandte und Freunde.	6

9.) Pessimistische Gedanken (Beinhaltet Schuldgefühle, Minderwertigkeitsgefühle, Selbstvorwürfe, Versündigungsideen, Reuegefühle und Verarmungsideen)

Keine pessimistischen Gedanken.	0
	1
Zeitweise Gedanken "versagt zu haben", Selbstvorwürfe oder Selbsterniedrigungen.	2
	3
Beständige Selbstanklagen. Eindeutige, aber logisch noch haltbare Schuld- und Versündigungsideen. Zunehmend pessimistisch in Bezug auf die Zukunft.	4
	5
Verarmungswahn, Reuegefühl, nicht wiedergutzumachende Sünden und Schuld. Selbstanklagen, die logisch absurd, jedoch unkorrigierbar sind.	6

10.) Selbstmordgedanken

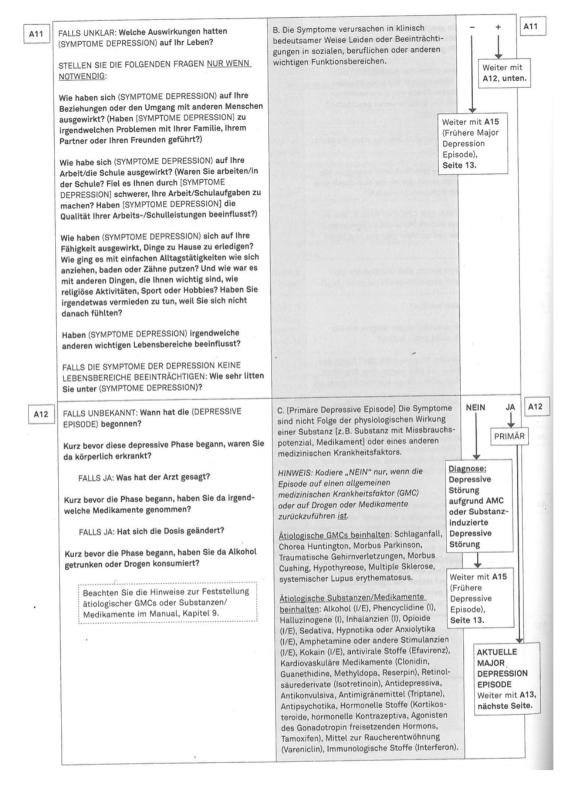
(Beinhaltet das Gefühl, das Leben sei nicht mehr lebenswert, der natürliche Tod sei eine Erlösung. Selbstmordgedanken und Vorbereitung zum Selbstmord. Selbstmordversuche sollten die Bewertung nicht direkt beeinflussen)

Constitute solitori die Dewortung nicht die Keit beennidssen)	
Freude am Leben oder die Ansicht, dass man im Leben die Dinge nehmen muss, wie sie kommen.	0
	1
Lebensmüde. Nur zeitweise Selbstmordgedanken.	2
	3
Lieber tot. Selbstmordgedanken sind Häufig. Selbstmord wird als möglicher Ausweg angesehen, jedoch keine genauen Pläne oder Absichten.	4
	5
Deutliche Selbstmordpläne und -absichten, falls sich eine Gelegenheit bietet. Aktive Vorbereitung zum Selbstmord.	6

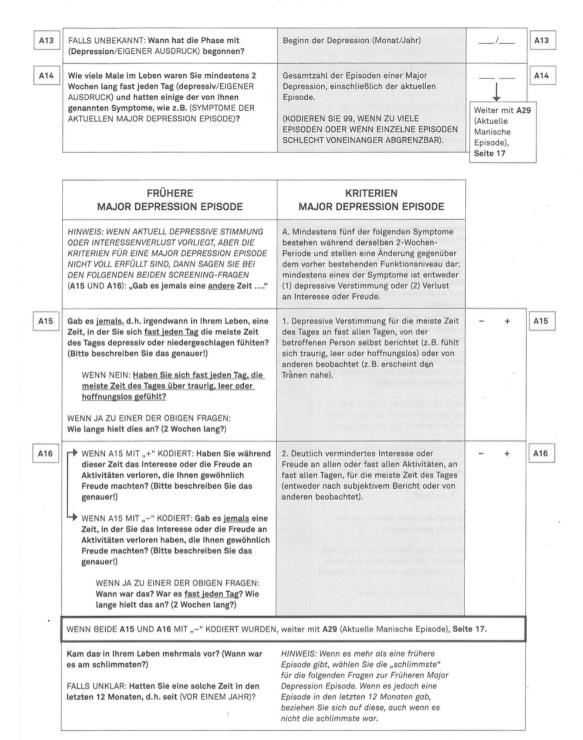
A. AFFEKTIVE EPISODEN

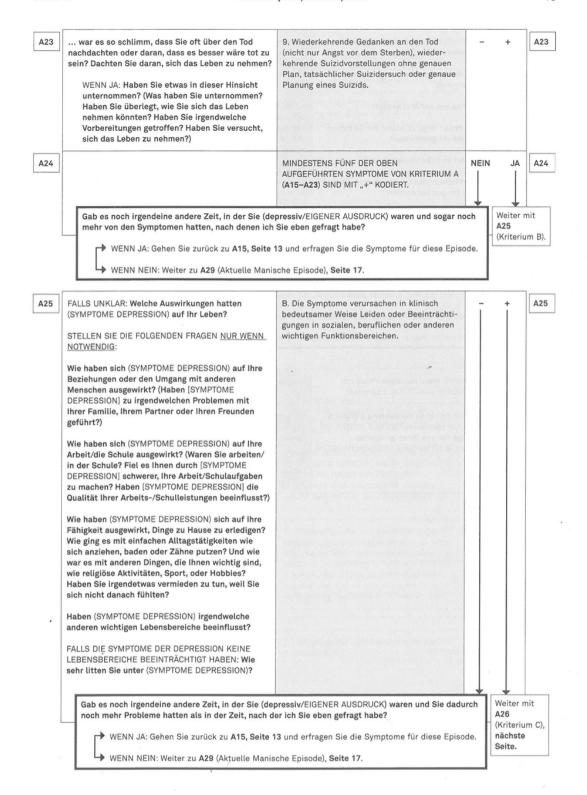
	AKTUELLE MAJOR DEPRESSION EPISODE	KRITERIEN MAJOR DEPRESSION EPISODE				
	Ich möchte Ihnen nun einige Fragen zu Ihrer Stimmung stellen.	A. Mindestens fünf der folgenden Symptome bestehen während derselben 2-Wochen- Periode und stellen eine Änderung gegenüber dem vorher bestehenden Funktionsniveau dar; mindestens eines der Symptome ist entweder (1) depressive Verstimmung oder (2) Verlust an Interesse oder Freude.				
	Während des letzten Monats, d.h. selt (VOR EINEM MONAT), gab es da eine Zeit, in der Sie sich fast jeden Tag die meiste Zeit des Tages depressiv oder niedergeschlagen fühlten? (Hat Irgendjemand gesagt, dass Sie niedergeschlagen oder depressiv aussehen?) WENN NEIN: Haben Sie sich fast jeden Tag, die meiste Zeit des Tages über traurig, leer oder hoffnungslos gefühlt? WENN JA ZU EINER DER OBIGEN FRAGEN: Bitte beschreiben Sie das genauer! Wie lange hielt	Depressive Verstimmung für die meiste Zeit des Tages an fast allen Tagen, von der betroffenen Person selbst berichtet (z. B. fühlt sich traurig, leer oder hoffnungslos) oder von anderen beobachtet (z. B. erscheint den Tränen nahe).	- +			
!	dies an? (2 Wochen lang?) WENN A1 MIT "+" KODIERT: Hatten Sie während dieser Zeit weniger Interesse oder Freude an Aktivitäten, die Ihnen gewöhnlich Freude machten? (Bitte beschreiben Sie das genauer!) WENN A1 MIT "-" KODIERT: Gab es während des letzten Monats, d.h. seit (VOR EINEM MONAT) eine Zeit, in der Sie das Interesse oder die Freude an Aktivitäten verloren haben, die Ihnen gewöhnlich Freude machten? (Bitte beschreiben Sie das genauer!) WENN JA ZU EINER DER OBIGEN FRAGEN: War das fast jeden Tag der Fall? Wie lange hielt das an? (2 Wochen lang?)	Deutlich vermindertes Interesse oder Freude an allen oder fast allen Aktivitäten, an fast allen Tagen, für die meiste Zeit des Tages (entweder nach subjektivem Bericht oder von anderen beobachtet).	- +			
	WENN BEIDE A1 UND A2 FÜR DEN AKTUELLEN MONAT MIT "—" KODIERT WURDEN, weiter mit A15 (Frühere Major Depression Episode), Seite 13.					
	BEZIEHEN SIE SICH BEI DEN FOLGENDEN FRAGEN AUF DIE SCHLIMMSTEN 2 WOCHEN WÄHREND DES VERGANGENEN MONATS.					
3	Während dieser Zeit (2-WÖCHIGER ZEITRAUM) wie war Ihr Appetit? (Im Vergleich zu sonst? Mussten Sie sich zum Essen zwingen? Haben Sie [weniger/mehr] als sonst gegessen? War das fast jeden Tag? Haben Sie an Gewicht ab- oder zugenommen?) WENN JA: Wie viel? (Haben Sie versucht, [abzunehmen/zuzunehmen]?)	Deutlicher Gewichtsverlust ohne Diät oder Gewichtszunahme (z.B. mehr als 5 % des Körpergewichtes in einem Monat) oder verminderter oder gesteigerter Appetit an fast allen Tagon.	- +			

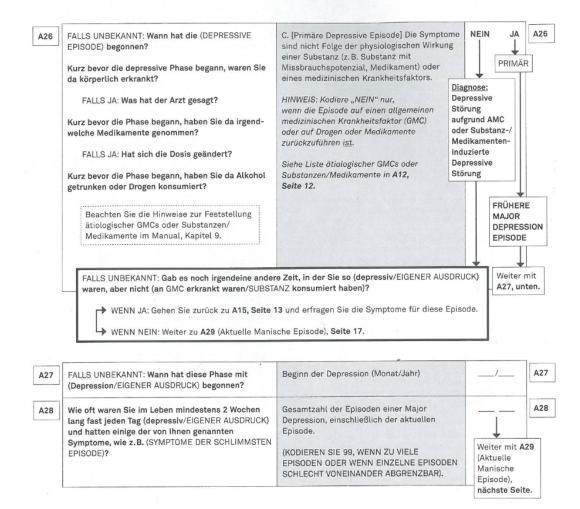
A4	wie haben Sie geschlafen? (Ein- oder Durchschlafprobleme, häufiges oder zu frühes Erwachen, ODER gesteigertes Schlafbedürfnis?)			-	+	A4
	Wie viele Stunden haben Sie geschlafen. (einschließlich Nickerchen)? Wie viele Stunden haben Sie vor dieser Phase von (Depressivität/ EIGENER AUSDRUCK) üblicherweise geschlafen? War das fast jede Nacht?	and the miles	no de religion Ossiano 30 Describera Una Ambridan I describ 21 Totalis (* 1122) desc			
A5	waren Sie so nervös oder unruhig, dass Sie nicht stillsitzen konnten? Oder das Gegenteil – sprachen oder bewegten Sie sich langsamer als sonst (als ob Sie sich durch eine zähe Masse oder Schlamm bewegten)? WENN JA ZU EINER DER OBIGEN FRAGEN: War es so schlimm, dass andere Personen es bemerkten? Was haben diese beobachtet? War das fast jeden Tag?)	5. Psychomotorische Ur samung an fast allen Ta beobachtbar, nicht nur von Rastlosigkeit oder V HINWEIS: ACHTEN SIE A WÄHREND DES INTERVI	agen (durch andere das subjektive Gefühl Verlangsamung).	-	+	A5
A6	wie viel Energie hatten Sie? (Fühlten Sie sich ständig müde und abgeschlagen? <u>Fast jeden Tag?</u>)	6. Müdigkeit oder Energieverlust an fast allen Tagen.			+	A6
47	fühlten Sie sich wertlos? Fühlten Sie sich schuldig wegen Dingen, die Sie getan oder auch nicht getan haben? WENN JA: Welche Dinge betrifft das? (Liegt das nur daran, dass Sie sich wegen Ihrer Krankheit nicht mehr um solche Dinge kümmern konnten?) WENN JA ZU EINER DER OBIGEN FRAGEN: Fast jeden Tag?	7. Gefühle von Wertlosigkeit oder übermäßige oder unangemessene Schuldgefühle (die auch ein wahnhaftes Ausmaß annehmen können), an fast allen Tagen (nicht nur Selbstvorwürfe oder Schuldgefühle wegen des Krankseins).			+ 1	A7
18	hatten Sie Schwierigkeiten beim Denken oder Konzentrieren? Fiel es Ihnen schwer, alltägliche Dinge zu entscheiden? (In welchen Situationen hat sich das ausgewirkt? <u>Fast jeden Tag</u> ?)	8. Verminderte Fähigkeit zu denken oder sich zu konzentrieren oder verringerte Entschei- dungsfähigkeit an fast allen Tagen (entweder nach subjektivem Bericht oder von anderen beobachtet).		-	+	A8
	war es so schlimm, dass Sie oft über den Tod nachdachten oder daran, dass es besser wäre tot zu sein? Dachten Sie daran, sich das Leben zu nehmen? WENN JA: Haben Sie etwas in dieser Hinsicht unternommen? (Was haben Sie unternommen? Haben Sie überlegt, wie Sie sich das Leben nehmen könnten? Haben Sie irgendwelche Vorbereitungen getroffen? Haben Sie versucht, sich das Leben zu nehmen?)	9. Wiederkehrende Gedanken an den Tod (nicht nur Angst vor dem Sterben), wieder- kehrende Suizidvorstellungen ohne genauen Plan, tatsächlicher Suizidersuch oder genaue Planung eines Suizids.		_	+	A9
110		MINDESTENS FÜNF DER OBEN AUFGEFÜHRTEN SYMPTOME VON KRITERIUM A (A1-A9) SIND MIT "+" KODIERT.			JA 🗼	A10
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		Weiter mit A15 (Frühere Major Depression Episo		leiter m ächste	



٦	FALLS UNKLAR. Während (MAJOR DEPRESSION EP AUSDRUCK)?	PISODE), wann waren Sie am meisten (depressiv/EIGENER			
17	Während dieser Zeit (SCHLIMMSTE 2-WÖCHIGE ZEITSPANNE) wie war Ihr Appetit? (Im Vergleich zu sonst? Mussten Sie sich zum Essen zwingen? Haben Sie [weniger/mehr] als sonst gegessen? War das fast jeden Tag? Haben Sie an Gewicht ab- oder zugenommen? Wie viel? Haben Sie versucht ab- oder zuzunehmen?)	3. Deutlicher Gewichtsverlust ohne Diät oder Gewichtszunahme (z.B. mehr als 5% des Körpergewichts in einem Monat) oder vermin- derter oder gesteigerter Appetit an fast allen Tagen.	- +		
18	wie haben Sie geschlafen? (Ein- oder Durchschlafprobleme, häufiges oder zu frühes Erwachen, ODER gesteigertes Schlafbedürfnis?) Wie viele Stunden haben Sie geschlafen (einschließlich Nickerchen)? Wie viele Stunden haben Sie vor dieser Phase von (Depressivität/EIGENER AUSDRUCK) üblicherweise geschlafen? War das fast jede Nacht?	4. Insomnie oder Hypersomnie an fast allen Tagen.	- +		
19	waren Sie so nervös oder unruhig, dass Sie nicht stillsitzen konnten? Oder das Gegenteil – sprachen oder bewegten Sie sich langsamer als sonst (als ob Sie sich durch eine zähe Masse oder Schlamm bewegten)? WENN JA ZU EINER DER OBIGEN FRAGEN: War es so schlimm, dass andere Personen es bemerkten? Was haben diese beobachtet? War das fast jeden Tag?)	5. Psychomotorische Unruhe oder Verlangsamung an fast allen Tagen (durch andere beobachtbar, nicht nur das subjektive Gefühl von Rastlosigkeit oder Verlangsamung). HINWEIS: ACHTEN SIE AUF DAS VERHALTEN WÄHREND DES INTERVIEWS.	- +	Α	
20	wie viel Energie hatten Sie? (Fühlten Sie sich ständig müde und abgeschlagen? <u>Fast jeden Tag</u> ?)	6. Müdigkeit oder Energieverlust an fast allen Tagen.	- +	- 4	
1	fühlten Sie sich wertlos? Fühlten Sie sich schuldig wegen Dingen, die Sie getan oder auch nicht getan haben? WENN JA: Welche Dinge betrifft das? (Liegt das nur daran, dass Sie sich wegen Ihrer Krankheit nicht mehr um solche Dinge kümmern konnten?) WENN JA ZU EINER DER OBIGEN FRAGEN: Fast jeden Tag?	7. Gefühle von Wertlosigkeit oder übermäßige oder unangemessene Schuldgefühle (die auch ein wahnhaftes Ausmaß annehmen können), an fast allen Tagen (nicht nur Selbstvorwürfe oder Schuldgefühle wegen des Krankseins).	- +	-	
22	hatten Sie Schwierigkeiten beim Denken oder Konzentrieren? Fiel es Ihnen schwer, alltägliche Dinge zu entscheiden? (In welchen Situationen hat sich das ausgewirkt? <u>Fast jeden Tag</u> ?)	Verminderte Fähigkeit zu denken oder sich zu konzentrieren oder verringerte Entschei- dungsfähigkeit an fast allen Tagen (entweder nach subjektivem Bericht oder von anderen beobachtet).	- 1	-	







VII Acknowledgements

At this point, I would like to express my sincere thanks to all those who have supported and accompanied me on the way to this dissertation.

My special thanks go first and foremost to my supervisors, Prof. Dr. Peter Falkai and Prof. Dr. Andrea Schmitt, whose professional expertise and constant support were invaluable to me. I thank you very much for your time, your patience and the constructive discussions, which always showed me a clear direction.

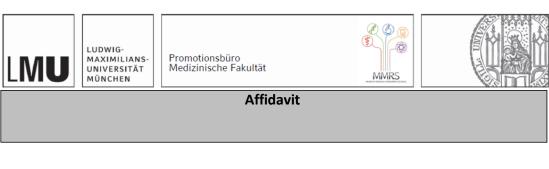
I would like to thank my beloved husband from the bottom of my heart. Without your unwavering love, patience and constant encouragement, this path would not have been possible. You have been my greatest support and my anchor in times of doubt. Thank you for always standing by my side.

Of course, I would also like to express my sincere thanks to the rest of my family, who have given me unconditional support and trust. Your love and patience have always encouraged me to give my best and given me strength in difficult moments.

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To all those who stood by my side along the way – thank you very much.

VIII Affidavit



	MÜNCHEN			IN IIV IIV IIV IIV IIV IIV IIV IIV IIV I	
		P	Affidavit		
Pfeiffer, Lis	a Monika				
Surname, first nan	ne				
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I hereby deck	are, that the s	ubmitted thesis e	entitled:		
Prediction o	of depressive		d on psycho in an outpat	•	ers in a naturalistic cohor
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I further dec	lare that the	•			bmitted in the same or academic degree.
Munich 24.0	06.2025				

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IX Confirmation of congruency



LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Promotionsbüro Medizinische Fakultät





Confirmation of congruency between printed and electronic version of the doctoral thesis

Pfeiffer, Lisa Monika	
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I hereby declare, that the submitted thesis entitled:	
Prediction of depressive disorders based on psycho recruited in an outpat	
is congruent with the printed version both in content and for	ormat.
Munich, 24.06.2025	
	Lisa Pfeiffer
place, date Si	gnature doctoral candidate

XI List of publications

Eder, J., Pfeiffer, L., Wichert, S. P., Keeser, B., Simon, M. S., Popovic, D., Glocker, C., Brunoni, A. R., Schneider, A., Gensichen, J., Schmitt, A., Musil, R., Falkai, P., & POKAL Group (2024). Deconstructing depression by machine learning: the POKAL-PSY study. *European archives of psychiatry and clinical neuroscience*, *274*(5), 1153–1165. https://doi.org/10.1007/s00406-023-01720-9

Eder, J., Glocker, C., Barton, B., Sarisik, E., Popovic, D., Lämmermann, J., Knaf, A., Beqiri-Zagler, A., Engl, K., Rihs, L., Pfeiffer, L., Schmitt, A., Falkai, P., Simon, M. S., & Musil, R. (2024). Who is at risk for weight gain after weight-gain associated treatment with antipsychotics, antidepressants, and mood stabilizers: A machine learning approach. *Acta psychiatrica Scandinavica*, 10.1111/acps.13684. Advance online publication. https://doi.org/10.1111/acps.13684