Quality of life and mood problems: gender differences among individuals in treatment for co-morbid substance use disorder and psychiatric comorbidities

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Master Thesis

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Abstract

Background and aim: Although literature suggests that quality of life (QoL) in women with substance use disorders (SUDs) is lower than in men, it remains unknown whether this 1) applies to SUD patients with psychiatric comorbidities in the Netherlands; and 2) whether there is a gender difference in QoL gain during treatment. This study therefore aimed to compare QoL (gain) between genders. Because research linked mood problems to worse QoL and substance usage in women, it was also the aim to compare genders in the association between (change in) mood problems and (change in) QoL. *Methods*: The longitudinal design involved data of day-patient treatments between 2018-2020. Sixty nine females and one hundred and thirty males with SUDs and comorbidities were assessed, using the EQ-5D-3L and the ICECAP-A. Analysis of variance and moderation analyses were performed with multiple imputation, controlling for treatment group. *Results:* At pretest, QoL in women was significantly lower when compared to men. There was no significant gender difference concerning gain in QoL, as well as regarding the association between mood problems and QoL at pretest and posttest. *Conclusions*: Women with SUDs and comorbidities experience lower QoL than men, a gender gap that is less profound in the normal population. Stigma and adverse life conditions arguably play a role. There is no evidence that men and women profit differently from treatment. In any case, mood problems, trauma experiences and meaningful activities could be considered more in future studies, as their association with QoL seems to be critical.

1 Introduction

1.1 Substance use disorder: prevalence and differences men and women

Drug and alcohol addiction is an ongoing problem across the world. In the United States, drug overdoses have increased by 35% between 2015 and 2019 and new data suggests that this number has risen even more since the COVID-19 pandemic (Psychiatric Times, 2021). There are also growing concerns in the Netherlands. Only recently it has been advised by the Dutch National Institute of Public Health (RIVM) to refrain from selling alcohol in supermarkets, in order to lower mortality of problematic drinking (De Telegraaf, 2021). This conclusion may not be surprising, given the relatively high prevalence of substance use disorders (SUDs) in and outside the Netherlands. Although recent numbers are unfortunately not available, 1 in every 14 adults in the US were dealing with SUDs in 2017 (SAMHSA, 2017). In the Netherlands, the prevalence of SUDs was estimated around 10% in 2015 (Trimbos Instituut, 2015). According to Trimbos Instituut (2015), there may be less under-reporting of problematic use in the Netherlands than in other countries. This is because of the relative tolerance to drug use, especially cannabis use, as it is legal.

Important to consider is that SUDs have always been more prominent in men than in women. In 2017, 9.4% of men and 5.2% of women from an age of 12 in the United States were dealing with a SUD. Although the prevalence in men remains higher than in women, the gap is slowly narrowing. McHugh and colleagues (2018) explain that the prevalence of SUDs in younger generations is much smaller than before, which they think is associated with lower role traditionality (in e.g. work and childcare) and access to drugs and alcohol. Nowadays, women of younger generations have more access to drugs and alcohol and they perceive less stigma than before (McHugh et al., 2018). Although stigma is decreasing, it still makes women feel more reluctant to seek treatment when compared to men. For example, they fear their family opinion and worry about child care responsibilities (Greenfield, 2007). Consequently, women feel barriers to seek treatment for substance use problems. Moreover, when compared to men, women with SUDs more frequently perceive their co-occurring psychiatric problems as their main problems (Greenfield, 2007). Accordingly, women with SUDs tend to go into treatment at other mental health care institutions than traditional addiction clinics, which are frequented by men (Greenfield, 2007).

1.2 Substance use disorder and comorbidities

The co-occurring psychiatric problems we are talking about are indeed a central problem in people suffering from SUDs, not only for women. According to Dom et al. (2013), around 41% of people with mental health disorders engage in substance abuse. Vice versa, in an European epidemiological study it was found that 30-60% of SUD patients also had another psychiatric disorder (Torrens, Mestre-Pintó & Domingo-Salvany, 2015). The most common were depression (30-50%), anxiety (20-40%), and personality disorder (15-40%). They did not mention secondary or even tertiary SUDs, which are in the end the most common comorbidities for people with SUDs (American Psychiatric Association, 2013). In a study by Zuckermann et al. (2019), 50% of people using substances, engaged in poly-substance use.

There are slight differences in co-occurring psychiatric disorders between men and women with SUDs. Where co-occurring affective disorders such as anxiety, depression and panic disorder are more prevalent in women, disorders such as ADHD and antisocial personality disorder are more common in men (Brady & Randall, 1999; Chen et al., 2011). When it comes to poly-substance use, the longitudinal study of Zuckermann and colleagues (2019) shows that it is more likely for men to use a high amount of substances. For example, using four substances was twice as common in men when compared to women. However, the authors state that even though poly-substance use seems traditionally more probable around men, it is beginning to turn. They found that male students reported poly-substance use more often than female students until 2017/2018. After that, a higher proportion of females engaged in dual substance use than men, but using three or four substances was still more common around men.

1.3 Treatment of substance use disorders

Fortunately, some positive notes can be given about SUD treatment. Teesson and colleagues (2008) found that addiction treatment leads to less substance use, less crime, and an improvement in psychological and physical well-being, even after three years. SUD treatments that have been found effective in the Netherlands generally embody cognitive behavioral therapy (CBT) and motivational interviewing (MI) (LSMR, 2009). MI is aimed at bringing out intrinsic motivation for change in patients. Instead of a directive approach of the therapist in which arguments for change are presented, the technique is drew on reflective listening and asking motivational questions. MI has been found to be effective for alcohol, drug and gambling addictions in adolescents and adults. In less complex addictions, the intervention is sometimes used on its own. In patients with more complex psychiatric problems, MI is often combined with CBT (Van der Molen, Simon & Van Lankveld, 2015).

CBT is the most effective treatment for SUDs, preferably group-wise (LSMR, 2009). CBT has several objectives in the treatment of SUDs. The function of substance use and factors that perpetuate substance use are explored and altered. Furthermore, depending on the individual situation of the person, adaptive coping skills are taught and personal problems that are intertwined with the maintenance of psychiatric problems are tackled. In more complex cases in which patients suffer from severe withdrawal symptoms, patients are first admitted for detoxification (Van der Molen et al., 2015). This is withdrawing from substances under medical supervision, in order to prevent withdrawal symptoms from causing severe illness or death (Timko et al., 2016). Detoxification often requires drug treatment. However, in some cases drug treatment is also continued during psychotherapy, for example to reduce craving symptoms (Van der Molen et al., 2015).

It goes without saying that studying the effectiveness of addiction treatment is important in order to deliver the best possible care for people with SUDs. Additionally, there are cost considerations that further underline this importance. Altogether, SUDs in the Netherlands are responsible of 0.93% of general health care costs and 3.26% of mental health care costs, which is about 820 million euros. In comparison, this is about the same as all healthcare costs spent on breast cancer (Volksgezondheidzorg.info, 2017). Needless to say, it is important to gain insight of effectiveness of SUD treatment.

1.4 Quality of life as an outcome measure

Studies about the effectiveness of treatment of SUDs so far have typically considered abstinence or lower rates of substance use as a desired treatment outcome (Laudet, 2011; Pasareanu et al., 2015). In the past decennium this has started to change, since SUD is being acknowledged as a chronic disease (Laudet, 2011), in response to study results about altering brain structures as a consequence of addiction (Koob & Le Moal, 2008). Thus, as with other chronic diseases, other outcome measures were needed to evaluate whether the treatment is effective.

One of such outcome measures is quality of life (QoL). QoL is a well-known and widely-used construct to measure treatment effectiveness (De Maeyer et al., 2009; Versteegh, Knies & Brouwer, 2016; Adan et al., 2017). According to Testa and Simonson (1996, p. 835), QoL refers “to the physical, psychological and social domains of health, seen as distinct areas that are influenced by a person’s experiences, beliefs, expectations and perceptions”. In patients with SUDs, QoL is often impaired when compared to people without such problems (Smith & Larson, 2003). On top of that, most of the earlier studies suggest that QoL for female patients

is around 10% lower than their male counterparts (Foster et al., 2000; Griffin et al., 2015; Fernandez et al., 2016). Women may seek treatment less often than men, but when they do, they often do so with more serious medical, psychiatric (McHugh et al., 2018; Choi et al., 2015), social, and employment problems (Choi et al., 2015) when compared to men.

When it comes to treatment effectiveness, QoL studies about differences between men and women show mixed results. In their critical review, McHugh and colleagues (2018) found insufficient evidence that men and women differ in QoL gain after treatment. However, they emphasize that little research has accounted for study populations experiencing complex comorbidities alongside substance use. This is unfortunate, because research shows that women with SUDs show a greater vulnerability to comorbidity when compared to men (Stecker et al., 2007; Chen et al., 2011). Because comorbidities have a negative association with QoL in patients with SUDs (Pasareanu et al., 2015), it could be argued that QoL in women is lower than in men. On top of that, women with SUDs display a greater link between emotional problems and substance use, such as substance usage to cope with symptoms of depression or anxiety (McHugh et al., 2018). Muller, Skurtveit and Clausen (2016) also found evidence that depression in women suffering from SUDs, was more strongly associated to lower QoL when compared to men. These findings show a complex interplay between psychiatric comorbidity, substance use and QoL. Hence, it remains unknown whether this affects treatment effectiveness and how differences in QoL between men and women might come to light.

Moreover, Pasareanu and colleagues (2015) did find a gender difference in QoL after treatment. They studied predictors of change in QoL after substance abuse treatment, which relied on pharmacotherapy, MI, and cognitive behavior therapy in a group setting. They used the QoL-5, which was intended to measure subjective life-satisfaction in areas such as mental health, body, personal relationships, and self-image. The authors found that the female gender was significantly associated with higher positive change in QoL from pretest to posttest, meaning that women profited more from treatment. Notably, as far as we know, this was the only QoL study using logistic regression to measure differences between men and women. Logistic regression is generally not applied to continuous dependent variables. In such analyses, the dependent variable has to be divided into two groups. When a variable is continuous, this leads to lost information and the possibility that the cut-off values are arbitrary (Ranganathan, 2017). Indeed, this authors in this study do not explain what the cut-off values are based on. Thus, the proportion of change in QoL in women was greater than in men, but it is unclear if this is of clinical and practical importance.

In conclusion, there are reasons to believe that there are some differences in QoL between men and women suffering from SUD and psychiatric comorbidities, possibly triggered by mood problems such as anxiety and depression. However, the study results are mixed. There is also a lack of study results in similar populations in the Netherlands. It therefore remains unclear if there are differences in QoL between men and women undergoing treatment for SUDs and psychiatric comorbidities.

1.5 Study aim and practical implications

Based on the literature, in this study participants with both SUDs and psychiatric comorbidities are included. This will give more insight in this particular patient group in the Netherlands. The aim of the study is to explore possible differences in QoL between men and women suffering from SUD and psychiatric comorbidities in the Netherlands, before and after treatment. It will also be examined if gender moderates the relationship between anxiety and depression, in this study defined as mood problems, and QoL. Knowing in what way mood problems and gender are responsible for different levels of QoL before and after treatment, provides the opportunity to design tailor-made treatment programs, for example gender-specific treatments or treatments that focus more on mood problems. Not unimportantly, a broader understanding of women in addiction treatment could hopefully contribute to further reducing the earlier mentioned stigma of women as the broadcasting of knowledge could possibly motivate women to seek treatment earlier.

1.6 Research questions

This study sets out to answer the following research questions:

1a: *To what extend does QoL between men and women with SUDs and psychiatric comorbidities differ at the start of treatment?* Based on our literature review, it is expected that women experience lower QoL than men (Foster et al., 2000; Griffin et al., 2015; Fernandez et al., 2016).

1b: *Does gender moderate the relationship between mood problems and QoL in people with SUDs and psychiatric comorbidities at the start of treatment?* As mentioned before, the literature suggest that there is a stronger link between mood problems and QoL in women with SUDs when compared to men (McHugh et al., 2018). Therefore, it is expected that there is a stronger negative relationship between mood problems and QoL in women with SUDs and psychiatric comorbidities when compared to men with similar problems.

2a: *To what extend does change in QoL differ between men and women with SUDs and psychiatric comorbidities?* In the literature there are different findings. Pasareanu et al. (2015) found that women showed larger positive change in QoL than men, whereas McHugh et al. (2018) found no gender difference. This study aims to clarify if QoL change at posttest differs between men and women suffering from SUDs and psychiatric comorbidities.

2b: *Does gender moderate the relationship between change in mood problems and change in QoL in people with SUDs and psychiatric comorbidities at posttest?* In line with the expectation described in question 1b, it is predicted that change in mood problems is more strongly connected to positive change in QoL in women when compared to men.

1.7 Covariate

Since participants received treatment in 12 different treatment groups at 6 different locations in the Netherlands, many program factors could potentially play a role in the results. Therefore "treatment group" will be taken into account as a covariate in all of the analyses.

The researched variables are listed in a conceptual model below in Figure 1.

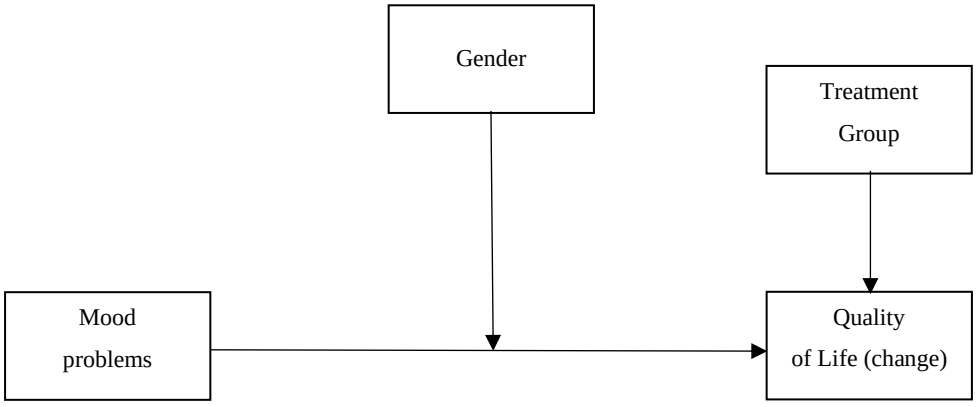

Figure 1.
Conceptual model

2 Methods

2.1 GGZ Momentum

The study took place at GGZ Momentum, a mental health care institution that specializes in co-morbid psychiatric disorders: mostly addiction, personality-, and eating disorders. GGZ Momentum is constituted at six different locations in the regions Noord-Brabant and Gelderland in the Netherlands. The institution offers different treatment programs that vary in intensity (days or hours a week) and duration (up to 18 months or more). This study will focus on the 12 part-time treatments that are one of the mental health care options offered by GGZ Momentum. All part-time treatments are a minimum of two and a maximum of five days per week. In addition, they are predominantly in a group setting, where the focus relies on CBT purposes such as coping with psychiatric complaints and learning new skills to deal with daily life (GGZ Momentum, 2021).

2.2 Study design and procedure

The current study had a longitudinal design, using archival data of the years 2018-2020 on day-patient treatment for SUD and psychiatric comorbidities. Both within- and between-subject data were considered. All participants were tested twice: before and after treatment. The variables were compared on pretest and on the difference scores between pretest and posttest. Time of measurements differed from subject to subject, since they went in and out treatment at different times. In general, the participants completed the questionnaires at the treatment location using a tablet. Some of the participants filled out the questionnaires at home. This was especially the case during the COVID-19 lockdowns. During this period, in 2020, less patients were reached to participate compared to the other years.

2.3 Participants

The research sample consists of 199 participants, of which 69 were female and 130 were male. They were aged between 20 and 71 (M = 37.15, SD = 10.43, M (female) = 38.13, SD = 11.57 and M (men) = 36.63, SD = 9.78). The participants were predominantly Caucasian (95%). They were in day-patient treatment for multiple days a week for a duration of 3-18 months, where they followed mainly group treatment but also individual treatment. About half of the participants had multiple SUDs. They were treated for substance abuse of alcohol (63%), cannabis (31%), cocaine (27%) and other substances like hypnotica/anxiolytica and amphetamine (25%). The participants were selected on having at least two DSM-5 diagnoses.

The most common comorbidities were other SUDs, personality disorders, and depressive disorders (see Table 1). Only the first three diagnoses were selected in order to obtain understanding of the psychiatric problems of participants in a feasible way, which means that some of the participants may have had more than three disorders. The ranking of the three diagnoses was based on clinical judgement. Because of the small sample size, SUD was allowed to be first, second or third disorder.

In all treatment groups, the representation of female and male patients was roughly the same, when relating to the gender group sizes. It was also checked if there were important differences in the representation of psychiatric disorders in the groups. There were two treatment groups specialized in eating disorders. These groups consisted out of less than three participants, that were only female. Therefore these two treatment groups were left out in the present study.

Table 1

DSM-5 disorders in the research sample (N=199)

Disorder DSM-5	*Men (N=130)*	*Women (N=69)*
Alcohol	79 (60.77%)	46 (66.67%)
Cannabis	46 (35.38%)	16 (23.19%)
Cocaine	46 (35.38%)	11 (15.94%)
Other substances	36 (27.70%)	24 (34.78%)
Personality disorder	50 (38.46%)	35 (50.72%)
Depressive disorder	25 (19.23%)	17 (24.64%)
Trauma-related disorders	12 (9.23%)	16 (23.19%)
Eating disorders	2 (1.54%)	16 (23.19%)
Anxiety	11 (8.46%)	3 (4.35%)
Other DSM-5 disorders	29 (22.31%)	10 (14.49%)
Psychosocial and environmental problems as mentioned in DSM-5	39 (30%)	15 (21.73%)

2.4 Measures

Quality of life In this study, two questionnaires were used to measure QoL: the EQ-5D-3L and the ICECAP-A. The EQ-5D-3L is a well-known self-report instrument in the Netherlands (Versteegh et al., 2016) and across the world (Rand et al., 2020), that focuses on health-related quality of life. The measurement has been found reliable and valid in the Netherlands, hence, it is the standard measure to evaluate health care interventions in the Netherlands (Versteegh et al., 2016; Zorginstituut, 2016). According to Engel et al. (2018) and Zorginstituut Nederland (2016), however, measurements of health-related QoL lack important psychological information that is needed to capture the full spectrum of ‘quality of life’ as a

construct. Engel et al. (2018) and Versteegh, Knies and Brouwer (2016) therefore proposed that the ICECAP-A, which measures capability well-being, should be used alongside the EQ-5D-3L. In the following sections the instruments and underlying constructs are further explained.

Health-related quality of Life The EQ-5D-3L was originally developed for economic evaluation of health care, by estimating quality-adjusted life-years (QALYs) (Devlin & Brooks, 2017). QALYs, in short, both consider the quantity and quality of life-years that patients have after an intervention. Nowadays, the EQ-5D-3L is generally used to measure health-related quality of life (hrQoL) independent of quantity of life-years, to assess the effectiveness of health care interventions (Zorginstituut Nederland, 2016).

The EQ-5D-3L focuses on perceived hrQoL around five health domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. These domains are displayed in five single-items. The participants indicate by means of the answer options that they do not experience any problems, some problems, or complete inability or extremity in these areas. For example, in the domain anxiety/depression participants can choose between "I am not anxious or depressed", "I am moderately anxious or depressed" or "I am extremely anxious or depressed". The EQ-5D-3L does also include a VAS-scale (visual analogue scale) that ranges from 0 "worst imaginable health state" and 100 "best imaginable health state" (Szende, Janssen & Cabase's, 2014, p. 23). Feng, Parkin & Devlin (2014) studied the EQ VAS for measuring hrQoL as a construct. Not only they write that the EQ VAS, as a stand-alone item, is a reliable and valid way to measure hrQoL, they also argue that this single item is possibly a better way to measure hrQoL than using the health domains of the EQ-5D-3L. According to these authors, the EQ VAS encompasses more than just health on these fixed domains. By using the EQ VAS, any health domains outside those of the EQ-5D-3L are better taken into account. Random examples are intimacy, mindfulness, social health, eating, and exercising. The EQ VAS can therefore be used to measure hrQoL as a broad construct that is closer to patients subjective experience (Feng et al., 2014). For these reasons, in this study only the EQ VAS will be used to measure hrQoL.

Capability well-being The ICECAP-A measures capability well-being, which is defined as the way people feel capable of construing a life that is personally valuable (Coast et al., 2015). It contains 5 items: stability ("feeling settled and secure"), attachment ("love, friendship and support"), autonomy ("being independent"), achievement ("achievement and progress") and enjoyment ("enjoyment and pleasure"). These items could be scored from 1 (no capability)

to 4 (full capability) in terms of "I can" or "being able to". For example "I am able to feel settled and secure in all areas of my life" (4), "in many areas of my life" (3), "in a few areas of my life" (2) or "I am unable to feel settled and secure in any areas of my life" (1) (University of Birmingham, 2021). In the analyses a tariff value was used according to the scoring manual of the ICECAP-A (University of Birmingham, 2021). Using the EQ-5D-3L together with the ICECAP-A, is recommend to asses treatment interventions in the Netherlands. This is especially in health problems such as addiction that generally require health care for longer periods of time (Versteegh et al., 2016; Zorginstituut Nederland 2016). Hence, both the EQ-5D-3L and the ICECAP-A are used in this study.

The ICECAP-A has shown good construct validity in a normal population sample (Al-Janabi et al., 2013). To our knowledge, there are no other studies that evaluated validity in a SUD patient group. The same applies to reliability. However, reliability has been investigated in other patient groups. Linton and colleagues found that the ICECAP-A had good internal consistency with a Cronbach's alpha of .83 in six physical illness patient groups and one depression group. In the current study the reliability of the ICECAP-A was adequate (Cronbach's alpha = .74 on pretest and .85 on posttest).

Mood problems Mood problems was measured by the item anxiety/depression of the EQ-5D-3L. Participants are asked if they experience anxiety or depression in general, as a opposed to using a questionnaire about specific diagnostic complaints. A Norwegian study (Rand et al., 2020) stated that this single item explained 37% of the variance of the Hopkins Symptom Checklist-25 (HSCL-25), which is an 25-item instrument used in clinical practice to screen for anxiety and depression (Sandanger et al., 1998).

2.5 Statistical analyses

The analyses were conducted in IBM SPSS Statistics, version 25. First, missing data were being evaluated. A total of 27 women (39%) and 22 men (17%) were lost at posttest, resulting in a final sample of 42 women and 73 men that completed the questionnaires. Because of the many missing values in independent and dependent variables that followed, multiple imputation was used to replace the values. Following the recommendations of Graham, Olchowski & Gilreath (2007), 20 imputations were used in order to ensure minimal power loss. In this way, the chance of finding a significant effect is greater if it is actually present in the population (Furr, 2018). The analyses of variance in this study did not provide pooled results in SPSS. In these analyses, the missing statistics were acquired by calculating the mean of the

20 imputations. SPSS did not provide all required pooled statistics in regression analyses either. Standardized coefficients were therefore obtained by transforming the data in Z-scores (standard scores) in SPSS and performing the regression analyses for the second time. Other missing statistics were acquired by drawing the mean from the 20 imputations.

Beforehand, assumptions were checked of the analyses described in this section. If applicable, adjustments were made. After that, the research variables were examined by analyzing descriptive statistics and correlations. Treatment groups consisting out of a minimum of 20 participants were correlated with the dependent variables: hrQoL and capability well-being. The nominal variable treatment group was dummy coded into seven variables that were treated as continuous variables in the analyses. The dummy variables that correlated significantly with hrQoL or capability well-being were included as covariates in the analyses.

To test the first research question about the differences in QoL between men and women at pretest, a multivariate analysis of variance (MANOVA) was performed with hrQoL and capability well-being as dependent variables. To examine whether gender had a moderating effect on the relationship between mood problems and QoL at pretest, a moderation analysis was conducted twice using the two QoL dependent variables. Any covariates were controlled for by including them in the first block. In the second block, mood problems was added as a predictor, after it was centered. In the third block, gender as a dummy variable and the interaction variable gender (dummy) X mood problems (centered) were added.

Subsequently, change scores from pretest to posttest of hrQol and capability well-being were computed. These change scores were used as dependent variables in the analyses at posttest. Because there were no treatment groups that correlated significantly with hrQoL, the difference between genders in change of hrQoL was tested by means of a *t*-test. There were, however, covariates involved concerning the variable capability well-being. Hence, an ANCOVA was executed to see if there was a gender difference in capability well-being change after treatment. To test whether gender moderated the relationship between change in mood problems and change in QoL at posttest, there was a third change score variable computed for mood problems. After this, the change scores of mood problems and the two QoL variables were used in the same way as in the above described moderation analysis, together with the variables gender and treatment group covariates.

In this study we chose to not correct for multiple testing, since the Bonferroni correction is considered extremely conservative, leading to many false negatives (Goldman, 2008).

3 Results

3.1 Preliminary analyses

First, descriptives were screened and assumptions were checked for the analyses used in this study. Normality distributions of the research variables were violated. Spearman correlations were therefore executed. The *F*-tests and *t*-tests in this study were robust against normality violations, because both gender groups consisted out of 20 or more participants (Furr, 2018).

Homogeneity assumptions were violated for hrQoL, but not for capability well-being. This has been taken into account when reading the output results of the *t*-tests. According to (Furr, 2018), the *F*-tests were not robust against heterogeneity because the male group was more than 1,5 larger than the female group. Since the largest variances were found in the female group, significant results concerning the variable hrQoL in this study could be too liberal (Furr, 2018). This should be taken into consideration when interpreting the results.

Finally, remaining extra assumptions for multiple regression were checked. No disturbing violations were found.

3.2 Descriptives and correlates

Descriptives of the research variables are summarized in Table 2 and correlations are summarized in Table 3. At pretest, the two-days treatment group "Veldhoven 2D" correlated significantly with hrQoL and capability well-being. Both associations were positive and weak. The Spearman-correlation also showed a weak, significant negative relationship between mood problems and "Veldhoven 2D". The dependent variables in this study, hrQoL and capability well-being, had a significant, moderate and positive association. Mood problems was negatively correlated to both hrQoL and capability well-being. These correlations were both significant and moderate.

After calculating change scores of hrQoL, capability well-being, and mood problems at posttest, Spearman correlations showed a significant positive association between hrQoL and capability well-being. This relationship was of moderate strength. Furthermore, hrQoL and capability well-being were both moderately and negatively related to mood problems. These associations were significant. The variables that were significantly related to hrQoL or capability well-being at pretest or posttest, were taken into account as covariates in this study.

Table 2

Descriptives study variables at pretest and on calculated change scores (posttest-pretest)

		Total		**Men**		**Women**	
	Variable name						
Pretest		*M*	*SD*	*M*	*SD*	*M*	*SD*
	1. hrQoL	62.11	17.37	64.59	1.33	57.44	2.45
	2. Capability well-being	.64	2.60	.66	.02	.59	.02
	3. Mood problems	2.00	.63	1.93	.06	2.13	.07
		M		*M*	*SD*	*M*	*SD*
Change scores	1. hrQoL	6.96	18.80	6.10	2.88	8.57	6.58
	2. Capability well-being	.07	2.83	.08	.03	.04	.05
	3. Mood problems	-.24	.78	-.25	.10	-.22	.21

Table 3

Correlations study variables at pretest and on calculated change scores (posttest-pretest)

	Variable name	**1**	**2**	**3**	**4**
Pretest	1. hrQoL	–			
	2. Capability well-being	.478**	–		
	3. Mood problems	-.538**	-.561**	–	
	4. Age	-.007	.100	-.196**	–
	5. Den Bosch support	-.062	-.123	.105	.151*
	6. Den Bosch schema	-.041	-.068	.028	.044
	7. Den Bosch narrative	.080	.028	-.097	-.101
	8. Nijmegen psych	-.104	-.111	.080	.084
	9. Nijmegen support	-.107	-.046	.044	-.086
	10. Veldhoven 2D	.158*	.265**	-.250**	-.010
	11. Veldhoven 4D	-.014	-.015	.126	.028
Change scores	1. hrQoL	–			
	2. Capability wellbeing	.389*	–		
	3. Mood problems	-.409**	-.405*	–	
	4. Age	-.005	-.097	.065	–
	5. Den Bosch support	-.025	.044	.018	.151*
	6. Den Bosch schema	-.061	-.121	.119	.044
	7. Den Bosch narrative	-.149	-.208*	.153	-.101
	8. Nijmegen psych	-.011	.080	-.053	.084
	9. Nijmegen support	.163	.200*	-.076	-.086
	10. Veldhoven 2D	.101	.103	-.054	-.010
	11. Veldhoven 4D	.009	.006	-.082	.028

***** $p < .05$ ** <.01

3.3 Gender difference hrQoL and capability well-being at pretest

To test the difference between men and women in hrQoL and capability well-being at pretest, a MANOVA was conducted. The multivariate tests of the covariate 'Veldhoven 2D' were significant ($\lambda = .950$, $F(2,195) = 5.303$, $p = .006$). The same applies to the variable gender ($\lambda = .964$, $F(2,195) = 3.609$, $p = .030$). Univariate tests are summarized in Table 4. It indicated

that there was a significant difference between genders in hrQoL at pretest. Pooled marginal means conveyed that women scored 6.428 points lower on hrQoL (M = 57.912 SD = 2.073) than men (M = 64.340, SD = 1.524). There was also a significant gender difference in capability well-being at pretest. Women (M = .60, SD = .310) scored .053 lower than men (M = .653, SD = .228) on capability well-being. Both significant effects of hrQoL and capability well-being were weak (see Table 4).

Table 4

ANCOVAs results comparing men and women on study variables at pretest and on change scores (posttest-pretest)

		F	*df*	*p*	*η2*
	Variable name				
Pretest					
	1. hrQoL	6.330	2,196	.013	.002
	2. Capability well-being	3.773	2,196	.049	.001
Change scores	1. hrQoL: *t*-test, see page 18				
	2. Capability well-being	1.145	2,196	.504	<.001

3.4 Gender difference in relationship between mood problems and hrQoL or capability well-being at pretest

As we were interested in the difference between men and women concerning the relationship between mood problems and quality of life, a moderator analysis was executed twice for both hrQoL and capability well-being at pretest. Test statistics for hrQoL are summarized in Table 5. Model 1 with the group variable 'Veldhoven 2D' predicted 2.5% of the variance of hrQoL. When mood problems was added in model 2, 27.7% more variance was explained (R^2_{change} = .277, F_{change} (1,196) = 77.753, p < .001). The change in model 3 was not significant (R^2_{change} = .021, F_{change} (2,194) = 3.008, p = .052).

The pooled coefficients of mood problems were significant. This indicates that higher levels of mood problems are responsible for lower levels of hrQoL. The pooled coefficients of gender and the interaction variable were not significant. In other words, the relationship between mood problems and hrQoL was not different for women when compared to men. Furthermore, the significant effect of gender that was found earlier in the earlier analyses, disappeared in the third step of the regression model. This conveys that the variable mood problems explained some of the same variance as gender. Indeed, the unique variance explained by mood problems was 27% in the second model and decreased to 13.46% in the third model.

Table 5

Results moderation analysis health-related quality of life at pretest (N =199)

	Variable	b (SE)	β	df	t	sr
Model 1	Veldhoven 2D	7.822 (3.455)	.159	197	2.264*	.159
Model 2	Veldhoven 2D	1.221 (3.044)	.025	196	.401	.024
	Mood problems	-14.867 (1.734)	-.537	196	-8.574***	-.520
Model 3	Veldhoven 2D	1.351 (3.082)	-.537	194	.438	.026
	Mood problems	-.12.704 (2.070)	.028	194	-6.136***	-.367
	Gender	7.936 (8.148)	.224	194	.974	.058
	Gender X mood problems	-.5823 (3.767)	-.359	194	-.1.546	.122

Model 1 R^2 = .025, Model 2 R^2 = .302, Model 3 R^2 = .325; * p < .05 *** p <.001

Similar results were found for capability well-being. Test statistics are summarized in Table 6. Model 1, with the predictor "Veldhoven 2D", predicted 5.9% of the variance of capability well-being. When mood problems was added in model 2, 24% more variance was explained (R^2_{change} = .240, F_{change} (1,196) = 67.141, p < .001). The change in model 3 was not significant (R^2_{change} = .005, F_{change} (2,194) = 3.008, p = .470).

The pooled coefficients of mood problems were significant, indicating that higher levels of mood problems lead to lower levels of capability well-being. The pooled coefficients for the gender variable and the interaction variable displayed no significant effect. In other words, there was no gender difference in the relationship between mood problems and capability well-being at pretest. Here as well the unique variance of mood problems was 24.01% in the second model and 15.05% in the third model, leaving no unique variance explained by gender.

Table 6

Results moderation analysis capability well-being at pretest (N =199)

	Variable	b (SE)	β	df	t	sr
Model 1	Veldhoven 2D	.127 (.036)	.245	197	3.531***	.245
Model 2	Veldhoven 2D	.061 (.032)	.118	196	1.907	.114
	Mood problems	-.148 (.018)	-.507	196	-8.145***	-.490
Model 3	Veldhoven 2D	.058 (.033)	.112	194	1.764	.106
	Mood problems	-.142 (.022)	-.484	194	-6.397***	-.388
	Gender	-.006 (.086)	-.015	194	-.067	-.004
	Gender X mood problems	-.012 (.040)	-.070	194	-.300	-.018

Model 1 R^2 = .059, Model 2 R^2 = .299, Model 3 R^2 = .305; *** p <.001

3.5 Gender difference hrQoL and capability well-being at posttest

After treatment, analyses were performed using change scores that were calculated for mood problems, hrQoL, and capability well-being. To measure the variable hrQoL, a *t*-test was executed because there were no significant covariates (see Table 2 for significant covariates). It indicated that there was no significant difference between men and women in how much they gained in hrQoL after treatment (t= -4.87, p = .628).

Subsequently, an ANCOVA was conducted, as we were interested in the difference between men and women in how much they gained in capability well-being during treatment. The results are summarized in Table 4. The treatment groups Den Bosch narrative and Nijmegen support were used a covariates, as they are significantly related to capability well-being change from pretest tot posttest. The results showed that the gender variable was not significant. This indicates that there was no difference between men and women in the amount of change in capability well-being after treatment.

3.6 Gender difference relationship between mood problems and hrQoL or capability well-being at posttest

To test whether gender is a moderator of the relationship between change in mood problems and change in quality of life after treatment, a moderator analysis was executed twice for hrQoL and capability well-being. Statistics for hrQoL are summarized in Table 7. Model 1 with the predictor mood problems explained 25.3% of the variance of hrQoL. When gender and the interaction variable were added in model 2, the extra variance explained was not significant (R^2_{change} = .007, F_{change} (2,195) = .912, p = .404).

Pooled coefficients showed that the change score of mood problems was a significant predictor of hrQoL. A decrease in mood problems was responsible for an increase in hrQoL. The coefficients of gender displayed no significant differences between men and women. The interaction variable was also not significant, indicating that the association between change in mood problems and change in hrQoL, is not different for women when compared to men. In other words, a decrease in mood problems after treatment, did not lead to a stronger increase of hrQoL in women when compared to men.

Table 7

Results change scores moderation analysis health-related quality of life at posttest (N =199)

	Variable	b (SE)	β	df	t	sr
Model 1	Mood problems	11.982 (3.337)	-.454	197	3.591***	.459
Model 2	Mood problems	11.460 (3.112)	-.435	195	3.683***	.336
	Gender	3.109 (4.193)	.068	195	.742	.068
	Gender X mood problems	1.319 (4.405)	-.032	195	.299	.024

Model 1 R^2 = .253, Model 2 R^2 = .007; *** p <.001

Similar results apply to capability well-being (see Table 8). Model 1 controlled for the covariates Den Bosch narrative and Nijmegen Support. This step predicted 3.1% of the variance of capability well-being. When mood problems was added in model 2, 17.3% more variance was explained (R^2_{change} = .240, F_{change} (1,195) = 42.323, p < .001). The change in model 3 was not significant (R^2_{change} = .007, F_{change} (2,193) = .909, p = .405).

Change in mood problems was the only predictor that significantly explained variance of capability well-being. The gender variable and interaction variable were not significant.

Table 8

Results moderation analysis change in capability well-being at posttest (N =199)

	Variable	b (SE)	β	df	t	sr
Model 1	Den Bosch narrative	.117 (.061)	-.185	196	1.917	.138
	Nijmegen support	-.098 (.045)	.173	196	-2.184*	-.171
Model 2	Den Bosch narrative	.079 (.063)	-.123	195	1.260	.120
	Nijmegen support	-.082 (.044)	.145	195	-1.873	-.142
	Mood problems	-.086 (.030)	-.353	195	-2.868**	-.348
Model 3	Den Bosch narrative	.073 (.063)	-.113	193	1.161	.109
	Nijmegen support	-.081 (.043)	.143	193	-.1876	-.140
	Mood problems	-.096 (.031)	-.392	193	-3.065**	-.296
	Gender	.023 (.033)	-.051	193	.694	.050
	Gender X mood problems	.023 (.042)	.060	193	.542	.046

Model 1 R^2 = .031, Model 2 R^2 = .204, Model 3 R^2 = .211; * p < .05 ** p <.01

4 Discussion

4.1 The current study

To our knowledge, the present study is the first study in the Netherlands that investigated QoL in a psychiatric complex group: people with SUDs and comorbidities. It aimed to explore whether men and women with these psychiatric problems differed in hrQoL and capability well-being. These constructs together represented the construct quality of life (QoL). The aim was also to examine if the relationship between mood problems – in this study anxiety and depression – and QoL was stronger for women compared to men. It was expected that women experience lower QoL and that the relationship between mood problems and QoL is stronger for women when compared to men at start of treatment. In line with these expectations, it was hypothesized that positive change in mood problems was associated with a greater change in QoL for women when compared to men. Finally, the current study aimed to clarify if there is a difference between men and women in the proportion of change in QoL after treatment. In all of these analyses, treatment groups that significantly related to QoL were kept into account as possible covariates.

The results indicated that women with SUDs and comorbidities experience lower QoL than men at start of treatment, as indicated by both lower hrQoL and capability well-being. This difference, however, ceased to exist after treatment. The gender groups did not differ significantly in the proportion of hrQoL and capability well-being gained during treatment. Furthermore, the relationship between mood problems and QoL was not different for women when compared to men at pretest. In line with this finding, change in mood problems was not more strongly linked to a larger proportion of QoL change in women when compared to men. In any case, however, mood problems was significantly related to higher QoL at pretest in both sexes. More positive change in mood problems was also significantly related to a larger gain in hrQoL and capability well-being.

4.2 Lower quality of life for women with SUDs and comorbidities at pretest

Based on findings outlined in the introduction, the lower QoL of women with SUDs at start of treatment came as no surprise. As already shortly mentioned, McHugh and colleagues (2018) underlined that women with SUDs generally seek treatment for addiction less often than men because of the perceived stigma. While not getting help, symptoms can possibly freely exacerbate. Moreover, Choi and colleagues (2015) found that women with SUDs experience

more problems in medical, employment, family/social, and psychiatric areas than men, while men experience more problems in drug, alcohol, and legal areas. Unfortunately, the authors do not further specify these problems. Insight of the content of the ASI (Alcohol and Drugs Abuse Institute, 2021) that they used to measure these problem areas, suggests that the gender difference in these problem areas is mainly in terms of quantity. After all, the ASI focuses on the presence and quantity of for example medical diseases, psychiatric symptoms, medication use, job and job duration, salary, charges and sentences, drug (types), and alcohol use. Hence, the higher score that Choi et al. (2015) found in the above mentioned problem areas for women, is arguably because of higher medical and psychiatric burden and worse job conditions. Only the area of family/social goes a little further than just presence of relationships, as the ASI also asks about the closeness/satisfaction of relationships and potential abuse situations (ASI, 2021). This implies that the higher experienced problems of family/social areas in women with SUDs, could mean more than just a lower presence and amount of relationships, which will be further discussed in the next section. Finally, when it comes to the medical area, earlier findings by McHugh et al. (2018) propose that women suffer from more medical consequences of their use as their metabolic systems differ from men. In any respect, all these problem areas are in line with the lower scores on hrQoL and all capability areas of the ICECAP-A, which shows that women with SUDs feel less attached to others, secure, autonomous, independent, and experience less achievement and enjoyment in life (University of Birmingham, 2021).

The V codes of the DSM-5 that have been ascribed to the participants in the present study could potentially give more insight in the family and social problems that are experienced by women (Choi et al., 2015). V codes are other life conditions that could impact the prognosis or diagnosis of someone (APA, 2013). In the current study, the percentage of men with V codes was actually higher. Strikingly, especially housing problems were ascribed more to men when compared to women. Indeed, Bretherton (2017) writes that for example homelessness around men is more common, since women seek support more often and are protected by community when children are living with them. Women in the current study, on the other hand, had 5 times more V codes than men regarding child adversity experiences like physical and sexual abuse. This is in line with Evans, Grella & Upchurch (2017). They say that women have more chance than men to have experienced more than three childhood adversity experiences and sexual abuse as a child. According to them, this increases the odds of developing a SUD in later life. Moreover, Mosley-Johnson et al. (2019) write that adverse childhood experiences are negatively associated with life satisfaction and well-being, in particular when it comes to abuse.

These findings underline the impact of childhood experiences and could potentially be one of the factors that explain why QoL of women with SUDs is lower than men.

That being said, it is important to note that the populations norms of the EQ VAS for 'average' women are already lower than men across the world and across all age groups (Szende et al., 2014). A Norwegian study by Rand et al. (2020), however, compared population norms of the EQ VAS against SUD populations and their data reveals that the difference in QoL between men and women in the SUD population, is much larger than in the normal population. In their country, in the age group 21-25, average females even exceeded their male counterparts in terms of QoL. This is the opposite in all age groups in the SUD group, suggesting that women with SUDs are more vulnerable than men with similar problems.

Unfortunately the only population norms of the ICECAP-A found, are those from a Hungarian study (Baji et al., 2020). The ICECAP-A score in the normal Hungarian population was only .01 lower for women when compared to men. Although these numbers may be less comparable to the Dutch population, it is striking that this difference between genders is about five times smaller than what was found in the SUD group in the current study. Hence, in summary, these findings suggests that QoL is already lower for women when compared to men, but the presence of SUDs seems to make QoL even lower for women than for men with SUDs. As mentioned, this could arguably be because of stigma, underlying group characteristics such as childhood adversity experiences, or because of other life difficulties in the areas of relationships, work and physical/mental health. Future research should focus on specifying the reasons of lower QoL for women with SUDs and comorbidities.

Contrary to the findings in the current study, Rand et al. (2020) found no gender difference in quality of life on the EQ VAS, but did find a lower score for women taking all the dimensions of the EQ-5D-3L. It could be that they had power issues of the EQ VAS considering the amount of female participants, that was even lower than in the present study, making it hard to find an effect (Furr, 2018). It could also be that the actual gender gap in hrQoL in Norway is smaller than in the Netherlands. This could be clarified by future research.

4.3 Relationship between mood problems and quality of life

In the current study, mood problems and QoL were not associated any stronger in women when compared to men. This applied to the pretest condition, as well as to the change scores after treatment. In other words, change in mood problems was also not more strongly associated with change in QoL in women. These findings are striking, as the earlier discussed results implied that women use substances to cope with depression or anxiety (McHugh et al.,

2018) and that depression in women is more strongly associated with QoL (Muller et al., 2016). Possibly, the operationalization of mood problems in the current study is a problem, since it was measured by only one item of the EQ-5D-3L. On the other hand, men could differ less from women in mood problems correlations with either QoL or amount of substance usage than is being insinuated by previous studies. Chen and colleagues (2011) for example found that men with SUDs and a co-occurring depression, ended up in critical situations such as hospitalization and admission to mental health care institutions more often than women suffering from the same disorders. Furthermore, Olivia et al. (2018) indicated that anxiety was a significant predictor of relapse in men and depression in women, respectively. These potentially different ways in which anxiety and depression in men and women play a role in exacerbating mental health conditions may complicate comparing the association between mood problems – in the present study measured as anxiety and depression in only one construct – and QoL in both sexes. Once again, however, the current study results prove that men and women with SUDs and comorbidities gain equally in QoL when mood problems during treatment are decreased, showing that mood problems is an essential area for treatment to focus on for both sexes.

More importantly, more insight into the coping mechanism involved in SUDs suggests a much simpler link between mood problems and QoL. Abulsoud and colleagues (2013) found that women engaged in heavy drinking more often when dealing with difficult emotional situations and were more tempted to use alcohol when compared to men. However, they also found that women scored higher on the Beck Depression Inventory (BDI). When controlling for the BDI-scores, the gender difference in coping mechanisms disappeared. It may therefore be that if men and women experience equally as much mood problems and comorbidity, QoL differences might not even be there.

In conclusion, the above discussion suggests that women perceive lower QoL than men and that this is especially true in the SUD population. It could be that women with SUDs experience depression and anxiety more often than men due to various mentioned circumstances, in addition to the difference in affective disorders that already exists between men and women (Chen et al., 2011). Subsequently, this may be the reason that women in the SUD population in particular perceive a lower QoL.

4.4 No gender difference in quality of life change after treatment

Although QoL for women was still lower than men after treatment, there is no difference in how much men and women with SUDs improved in QoL. Men and women gained equally in both capability well-being and hrQoL, showing that treatment was effective for both groups. Remarkable in the present study is the dropout rate of the female participants, which was more than twice as great (39%) than men (17%). Unfortunately, it is not known whether this difference has arisen because women quit treatment more often, because of motivational factors in filling out the questionnaires or because of organizational errors. Lappan, Brown & Hendricks (2020), however, reviewed studies of SUD treatment conducted between 1965 and 2016 and found that the average dropout rate is 30.4%. When taking men and women together, the dropout in the current study was 29.9%, which makes the dropout rate not any different from results in other studies. Unfortunately, Lappan et al. (2020) did not differentiate between men and women. Hence, it remains unknown why women in the present study were more often lost at pretest.

When it comes to treatment retention, Choi et al. (2015) found that women with SUDs and co-morbid disorders stayed in treatment longer than men. This study involved, however, participants in in-house treatment services, which is a different population than in the current study. The study was also funded privately by the research project, which is opposing the publicly funding nature of the present study. Arfken et al. (2001) found a lower retention rate for women in both residential settings and in intensive outpatient settings. It was not part of a funded research project and is therefore more alike the population and setting of the present study. Thus, potentially, women with SUDs and comorbidities in outpatient day treatment do dropout more often. Reasons for dropout should be investigated by future studies.

4.5 Effect of the treatment groups

At pretest, the two-day treatment group in Veldhoven was the only group that correlated significantly with both hrQoL and capability well-being. Both associations were positive, suggesting that people in this group already perceived a higher QoL at pretest. This is no coincidence given the significant negative correlation of the group in question with mood problems, showing that the participants in this group experienced less mood problems at pretest. This again stresses the importance of perceived mood problems in how much QoL one experiences.

At post-test, no treatment group was significantly associated with hrQoL. In other words, there is no indication that one of the treatment groups was more effective than the other in influencing hrQoL. Regarding capability well-being, however, two treatment groups made a difference compared to the other treatment groups. The narrative group in Den Bosch had a negative correlation with capability well-being, which means that this group performed significantly worse than the other groups regarding capability well-being. The support group in Nijmegen shows the opposite: people in this group have gained more in capability well-being compared to the other groups. Although it is impossible to draw any conclusions from this as a million factors could play a role, a noticeable element is that the narrative group is the only group that offered a treatment program of five days a week. Moreover, the group had no specific ending date. Looking at these circumstances it does not come as a surprise that people gained less in capability well-being during this treatment, since most of the participants in this group stayed in fulltime treatment for at least nine months of longer. After all, the ICECAP-A asks about capability in all areas of people's lives, for example "I can achieve and progress in all areas of my life" or "I can have a lot of enjoyment and pleasure" (University of Birmingham, 2021). Arguably, being in this treatment leaves less actual room for experiencing capability in these life areas.

Of course, we cannot ignore the fact that some clients probably need the structure of a full-time treatment program. Patients characteristics in more intensive groups could play a role as well in how much people gain in capability well-being, even though pretest differences were controlled for. In any case, it is doubtful whether fulltime treatment programs are the most favorable for patients. Best and colleagues (2013) showed that although it is traditionally thought that abstinence has the greatest impact on QoL gain, engaging in meaningful activity – like education, employment, volunteering, and training – is even more positively associated with QoL. This is further emphasized by the fact that, in their study, women at the start of treatment engaged less in meaningful activity than men, suggesting another possible reason of lower QoL in women at start of treatment. This difference in engaging in meaningful activity ceased during treatment, possibly partly explaining why women profit just as much from treatment as men.

Earlier research by the same author (Best, 2012) attempted to explain why meaningful activity has its benefits. It was argued that by engaging in meaningful activity, patients develop capability factors such as self-efficacy and self-esteem, which will help them to fully recover from their addiction. They also come in to contact with new social contacts that provide network opportunities to acquire for example jobs or housing in their future. In addition, these socials

contacts fulfill needs for connecting with other people while preventing patients to seek contact with co- substance users (Best, 2013).

Thus, the nature of the narrative group in which there may be little room for self-fulfillment in other areas of one's life, outside the therapy room, may be one of the reasons why clients improve less in capability well-being compared to the other groups. In contrast to the narrative group, the Nijmegen support group, which had a significantly positive correlation with capability well-being compared to the other groups, generally lasted three months for two days a week.

Outside of the structure of the groups, it might be that some of the core treatment principles influence capability well-being as well. Without the desire to being complete as all treatment groups of GGZ Momentum rely on many treatment principles, the Nijmegen support group seems to focus more on structuring as part of CBT, such as engaging in healthy daily activities and preventing relapse as compared to the narrative group. The narrative group also focusses on, as the name holds, principles like narrative therapy (GGZ Momentum, 2021). Shakeri et al. (2020) compared narrative therapy to treatment as usual in patients with amphetamine addiction and co-morbid anxiety and depression. They found that narrative therapy was more effective in reducing anxiety and depression, but not in improving QoL. The QoL scale that they used, the SF-36, relied on both health dimensions, mental health dimensions, vitality, and social dimensions (Shakeri et al., 2020), which makes the scale comparable to both scales used in the current study. Moreover, the authors also reviewed literature comparing CBT to narrative therapy and write that CBT is more favorable in increasing QoL in adolescents and adults with SUDs and comorbidities. According to them, narrative therapy can bring back painful memories as patients have to dive deep into their history in order to separate themselves from their problems. They write that narrative therapy is therefore not effective in improving QoL in patients with chronic conditions, especially, as these people want to look forward in their lives. Earlier it was argued that SUDs can be seen as chronic conditions (Laudet, 2011). Following these argumentations, it could be that elements of narrative therapy are effective for improving symptoms of anxiety and depression in people with SUDs, but that treatments relying on CBT principles are better in improving QoL. That being said, the study of Shakeri et al. (2020) was conducted in Iran. Their results should therefore be replicated in the Netherlands.

4.6 Strengths and limitations

Without being complete, the most important strengths and weaknesses in the present study are summarized. As earlier mentioned, the present study is the first research that focuses on QoL of patients with SUDs and psychiatric comorbidities in the Netherlands, with a particular angle on female patients. At the same time, by choosing this approach, the problem of a small group size of women was encountered. Moreover, the large drop-out percentage decreased the sample size, especially for women. The use of multiple imputation is a strength of this study. It is a valid and common way to solve the problem of low power that resulted from the small sample size (Kazdin, 2021). However, still only 69 women were compared to 130 men. According to Kazdin (2021), to be able to achieve power of .80 when comparing a group of 70 participants to another group, effect sizes have to be around .50. This is a medium effect. Thus, if the real effect in the population is small, power decreases to only .22 or less. This is a major problem in the present study.

Still, the target group of patients with SUDs and comorbidities in intensive day-treatment has hardly been studied in the Netherlands. Even at GGZ Momentum it was difficult to study these patients, since about 10-15 patients start in each group. Fortunately, the longitudinal design of the study guaranteed a reasonable sample size with the results not depending on one particular time point. At the same time, the longitudinal design was a disadvantage, because some of the participants followed treatment during the pandemic of COVID-19 and some of them did not. Therefore, it is not measurable in what way COVID-19 may have affected the results, threatening construct validity. For example capability well-being or hrQoL could hypothetically be influenced by COVID-19 measures or illnesses, as well as that some treatments were partly online. However, the main objective of the present study was comparing men and women. It is unknown whether one of the sexes has suffered more from COVID-19 than the other.

Unfortunately, the large attrition rate of especially women is a problem for the validity of the present study. As the reasons for dropout are not known, it could potentially be that the remaining or dropped out group of women had certain characteristics that are not known to the study. It is not known whether the dropped out women stopped treatment, did not have motivation to participate in the research at posttest or other reasons. These possible reasons could be a threat of construct validity, external validity and internal validity (Kazdin, 2021). Do women not differ from men at posttest because of no actual differences in hrQoL and capability well-being gain, or is another motivational construct at play that causes the results? The same question causes selection bias (Kazdin, 2021), because it could be that the remaining group of

women is different than the remaining group of men, especially because more than twice of women dropped out at posttest compared to men. Finally, the attrition causes external validity problems because the loss of such a large percentage (39%) of women, makes generalizing the results to the natural population of women with SUDs difficult (Kazdin, 2021). After all, women who were lost to follow up, belong to the population as well.

The use of a single item to measure anxiety and depression symptoms, was a strength and a weakness at the same time. At start and end of treatment, patients at GGZ Momentum have to fill out multiple questionnaires. Adding another questionnaire would have the potential of tiring the participants and making them fill out the questionnaire less seriously. At the same time, it may be a shortcoming that mood problems and QoL are items within the same EQ-5D-3L scale. Constructs may therefore not entirely be independent, which could be a problem for internal construct validity (Hadzibajramovic et al., 2015). However, the ICECAP-A is also filled out at the same time as the EQ-5D-3L, just like in most survey studies where multiple questionnaires are used. Hence, dependency of questionnaires and items is a problem that is inherent to many survey studies, but should be taken into account in the interpretation of the validity of this study. In addition to that, although earlier is mentioned that the single anxiety/depression item of the EQ-5D-3L explains almost 40% of the HSCL-25 questionnaire that screens for anxiety and depression (Sandanger et al., 1998), the single item is arguably less sensitive to compare smaller differences of anxiety/depression in participants. This is already the case for using the EQ-5D-3L compared to the EQ-5D-5L. Rand et al. (2020) argue that the limited answering options in the EQ-5D-3L by only three categories (no, moderate, and extreme), may be insufficient to detect small significant differences in QoL. They suggest that the EQ-5D-5L, which has five answering options, should be used for future studies.

4.7 Implications and recommendations for future research

First of all, the findings in this study should be replicated in similar patient groups in the Netherlands by using a larger sample size. Moreover, dropout reasons should be investigated in order to clarify if men and women really differ in dropout rates and more importantly, why.

Having said this, the finding that QoL for women is lower than men and that this gap is much larger in the SUD population than in the normal population, draws attention to the vulnerable group of women with SUDs and comorbidities. Future research can focus on the specific reasons for lower QoL of this particular psychiatric group in the Netherlands. It could be investigated if stigma is indeed one of these reasons. If so, government campaigns could focus on creating awareness around addiction for women specific, and promote seeking help.

Moreover, as was mentioned that women seek help for co-morbid psychiatric problems more often than for addiction, even though it might be their main problem (Greenfield, 2007), clinicians should pay attention to addiction problems in women. These problems may not show themselves on the surface.

Furthermore, the results in the present study and the discussed literature underline the importance of mood problems such as anxiety and depression. As found in the present study and in the discussed literature, women experience more co-morbid problems and mood problems. First, future studies should investigate if their might be other models responsible for lower QoL in women. By for example studying if mood problems is mediating the relationship between gender and QoL or by controlling for amount of mood problems. Second, studies should focus on the best content of treatment for patients with SUDs and co-morbid problems. In the introduction it was already mentioned that CBT in groups is the best treatment for patients with SUDs (LSMR, 2009). The results in the current study suggest that the same accounts for men and women with SUDs and comorbidities. Approaches such as narrative therapy may not necessarily be better for QoL gain. Still, it should be further investigated how concurrent emotional disorders or problems should be treated best alongside addiction.

Special attention should be paid to trauma experiences. The finding that higher prevalence of traumatic childhood experiences might play a role in lower QoL in women, should be further investigated. In an internal conversation at GGZ Momentum with a clinician (J.P., personal communication, July 17th, 2021) before sharing any results, it was shared that traumatic experiences are more common in female patients and that treatments of GGZ Momentum do not focus on these experiences much yet. Future research could clarify how and whether traumatic experiences influence QoL. RCTs (randomized controlled trials) could be used to determine whether the integration of trauma treatment in SUD treatment can help to further improve QoL, as well as to clarify what the content of multiple day-treatments should be like.

In any case, this study does not indicate that women benefit more or less from treatment than men. This is an important finding, as in the introduction was said that earlier studies found lower QoL in women with SUDs (Foster et al., 2000; Griffin et al., 2015; Fernandez et al., 2016), but studies about treatment effectiveness are limited and mixed (Pasareanu et al., 2015; McHugh et al., 2018). However, the finding that there is no gender difference in treatment effectiveness does not automatically mean that gender-specific treatments could not be better. According to multiple studies, female-only treatments that address problems and life circumstances of women in particular have been shown to be more effective for women

(Ashley, Marsden, & Brady, 2003; Greenfield et al., 2008; Greenfield, Cummings, Kuper, Wigderson, & Koro-Ljungberg, 2013). However, it is debatable how this would manifest itself in the LHBTIQ+ community these days, as men and women in transition or non-binary people are changing the perspective on gender. That being said, future research should focus on what works best for men, women and gender-independent people with SUDs and comorbidities in the Netherlands.

Finally, RCTs can also contribute to discovering whether meaningful activities are a valuable inclusion to SUD treatment groups of several days a week. For example, by offering internships, volunteer work or career training at various external locations, alongside therapy, it can be investigated whether this indeed contributes to a better QoL. If this is indeed the case, it could potentially decrease waiting lists and costs in mental health care, as more treatment time is made available.

References

Abulseoud, O. A., Karpyak, V. M., Schneekloth, T., Hall-Flavin, D. K., Loukianova, L. L., Geske, J. R., ... & Frye, M. A. (2013). A retrospective study of gender differences in depressive symptoms and risk of relapse in patients with alcohol dependence. *The American journal on addictions*, *22*(5), 437-442.

Adan, A., Marquez-Arrico, J. E., & Gilchrist, G. (2017). Comparison of health-related quality of life among men with different co-existing severe mental disorders in treatment for substance use. *Health and Quality of Life outcomes*, *15*(1), 1-12.

Alcohol and Drugs Abuse Institute. (2021). *Addiction Severity Index.* Retrieved from https://adai.washington.edu/instruments/pdf/Addiction_Severity_Index_Baseline_Followup_4.pdf

Al-Janabi, H., Peters, T. J., Brazier, J., Bryan, S., Flynn, T. N., Clemens, S., ... & Coast, J. (2013). An investigation of the construct validity of the ICECAP-A capability measure. *Quality of Life Research*, *22*(7), 1831-1840.

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

Arfken, C., L., Klein, C., di Menza, S., & Schuster, C. (2001). Gender differences in problem severity at assessment and treatment retention. *Journal of Substance Abuse Treatment*, *20*, 53–57.

Ashley, O. S., Marsden, M. E. and Brady, T. M. (2003). Effectiveness of substance abuse treatment programming for women: A review. *The American Journal of Drug and Alcohol Abuse*, *29*(1), 19–53.

Baji, P., Farkas, M., Dobos, Á., Zrubka, Z., Gulácsi, L., Brodszky, V., ... & Péntek, M. (2020). Capability of well-being: validation of the Hungarian version of the ICECAP-A and ICECAP-O questionnaires and population normative data. *Quality of Life Research*, *29*, 2863-2874.

Best, D. (2012). Addiction recovery: A movement for social change and personal growth in the UK. Brighton, UK: Pavilion.

Best, D., Savic, M., Beckwith, M., Honor, S., Karpusheff, J., & Lubman, D. I. (2013). The role of abstinence and activity in the quality of life of drug users engaged in treatment. *Journal of substance abuse treatment*, *45*(3), 273-279.

Brady, K. T., & Randall, C. L. (1999). Gender differences in SUDs. *Psychiatric Clinics of North America*, *22*(2), 241-252.

Bretherton, J. (2017). Reconsidering gender in homelessness. *European Journal of Homelessness _ Volume*, *11*(1).

Chen, K. W., Banducci, A. N., Guller, L., Macatee, R. J., Lavelle, A., Daughters, S. B., & Lejuez, C. W. (2011). An examination of psychiatric comorbidities as a function of gender and substance type within an inpatient substance use treatment program. *Drug and alcohol dependence*, *118*(2-3), 92-99.

Ciobanu, I., Di Patrizio, P., Baumann, C., Schwan, R., Vlamynck, G., Bédès, A., ... & Bourion-Bédès, S. (2020). Relationships between coping, anxiety, depression and health-related quality of life in outpatients with SUDs: results of the SUBUSQOL study. *Psychology, health & medicine*, *25*(2), 179-189.

Coast, J., Kinghorn, P., & Mitchell, P. (2015). The development of capability measures in health economics: opportunities, challenges and progress. *The Patient-Patient-Centered Outcomes Research*, *8*(2), 119-126.

De Maeyer, J., Vanderplasschen, W., & Broekaert, E. (2009). Exploratory study on drug Users' perspectives on quality of life: more than health-related quality of life?. *Social Indicators Research*, *90*(1), 107-126.

De Telegraaf. (2021). *Advies RIVM: alcohol alleen bij slijterij verkopen.* Retrieved from: https://www.telegraaf.nl/nieuws/1339479840/advies-rivm-alcohol-alleen-bij-slijterij-verkopen

Devlin, N. J., & Brooks, R. (2017). EQ-5D and the EuroQol group: past, present and future. *Applied health economics and health policy*, *15*(2), 127-137.

Dom, G. et al. (2013). *Handboek dubbele diagnose?* Utrecht, Nederland: De Tijdstroom.

Engel, L., Bryan, S., Noonan, V. K., & Whitehurst, D. G. (2018). Using path analysis to investigate the relationships between standardized instruments that measure health-related quality of life, capability wellbeing and subjective wellbeing: An application in the context of spinal cord injury. *Social Science & Medicine*, *213*, 154-164.

Evans, E. A., Grella, C. E., & Upchurch, D. M. (2017). Gender differences in the effects of childhood adversity on alcohol, drug, and polysubstance-related disorders. *Social psychiatry and psychiatric epidemiology*, *52*(7), 901-912.

Feng, Y., Parkin, D., & Devlin, N. J. (2014). Assessing the performance of the EQ-VAS in the NHS PROMs programme. *Quality of Life Research*, *23*(3), 977-989.

Fernandez, V. R., Fernandez, A. S., & Lopez, J. C. (2016). Quality of life from the perspective of addiction. *Revista de calidad asistencial: organo de la Sociedad Espanola de Calidad Asistencial*, *31*(1), 3-9.

Foster, J. H., Peters, T. J., & Marshall, E. J. (2000). Quality of life measures and outcome in alcohol-dependent men and women. *Alcohol*, *22*(1), 45-52.

Furr, R.M. (2018). Psychometrics: An introduction. Third Edition. Thousand Oaks, CA: Sage Publications.

GGZ Momentum. (2021). *Deeltijden overzicht.* Retrieved from https://www.ggzmomentum.nl/behandelingen/deeltijden

Goldman, M. (2008). *Why is multiple testing a problem?* Retrieved from https://www.stat.berkeley.edu/~mgoldman/Section0402.pdf

Greenfield, S. F., Brooks, A. J., Gordon, S. M., Green, C. A., Kropp, F., McHugh, R. K., ... Miele, G. M. (2007). Substance abuse treatment entry, retention, and outcome in women: A review of the literature. Drug and Alcohol Dependence, 86(1), 1–21.

Greenfield, S. F., Potter, J. S., Lincoln, M. F., Popuch, R. E., Kuper, L., & Gallop, R. J. (2008). High psychiatric symptom severity is a moderator of substance abuse treatment outcomes among women in single vs. mixed gender group treatment. *The American Journal of Drug and Alcohol Abuse, 34*(5), 594–602.

Griffin, M. L., Bennett, H. E., Fitzmaurice, G. M., Hill, K. P., Provost, S. E., & Weiss, R. D. (2015). Health-related quality of life among prescription opioid-dependent patients: Results from a multi-site study. *The American journal on addictions*, *24*(4), 308-314.

Hadzibajramovic, E., Ahlborg, G., Grimby-Ekman, A., & Lundgren-Nilsson, Å. (2015). Internal construct validity of the stress-energy questionnaire in a working population, a cohort study. *BMC public health*, *15*(1), 1-9.

Kazdin, A. E. (2021). *Research design in clinical psychology*. Cambridge University Press.

Koob, G. F., & Le Moal, M. (2008). Addiction and the brain antireward system. *Annu. Rev. Psychol.*, *59*, 29-53.

Landelijke Stuurgroep Multidisciplinaire Richtlijnontwikkeling in de GGZ. (2009). *Multidisciplinaire richtlijn stoornissen in het gebruik van alcohol.* Utrecht: Trimbos instituut.

Lappan, S. N., Brown, A. W., & Hendricks, P. S. (2020). Dropout rates of in-person psychosocial substance use disorder treatments: a systematic review and meta-analysis. *Addiction*, *115*(2), 201-217.

Laudet, A. B. (2011). The case for considering quality of life in addiction research and clinical practice. *Addiction science & clinical practice*, *6*(1), 44.

Levola, J., Eskelinen, S., & Pitkänen, T. (2020). Associations between self-rated health, quality of life and symptoms of depression among Finnish inpatients with alcohol and SUDs. *Journal of Substance Use*, *25*(2), 128-134.

Linton, M. J., Mitchell, P. M., Al-Janabi, H., Schlander, M., Richardson, J., Iezzi, A., ... & Coast, J. (2018). Comparing the German translation of the ICECAP-A capability wellbeing measure to the original English version: Psychometric properties across healthy samples and seven health condition groups. *Applied Research in Quality of Life*, 1-23.

McHugh, R. K., Votaw, V. R., Sugarman, D. E., & Greenfield, S. F. (2018). Sex and gender differences in SUDs. *Clinical psychology review*, *66*, 12-23.

Mosley-Johnson, E., Garacci, E., Wagner, N., Mendez, C., Williams, J. S., & Egede, L. E. (2019). Assessing the relationship between adverse childhood experiences and life satisfaction, psychological well-being, and social well-being: United States Longitudinal Cohort 1995–2014. *Quality of Life Research*, *28*(4), 907-914.

Muller, A. E., Skurtveit, S., & Clausen, T. (2016). Many correlates of poor quality of life among substance users entering treatment are not addiction-specific. *Health and quality of life outcomes*, *14*(1), 1-10.

Oliva, F., Nibbio, G., Vizzuso, P., Sodano, A. J., Ostacoli, L., Carletto, S., & Picci, R. L. (2018). Gender differences in anxiety and depression before and after alcohol detoxification: anxiety and depression as gender-related predictors of relapse. *European addiction research*, *24*, 163-172.

Pasareanu, A. R., Opsal, A., Vederhus, J. K., Kristensen, Ø., & Clausen, T. (2015). Quality of life improved following in-patient SUD treatment. *Health and quality of life outcomes*, *13*(1), 35.

Psychiatric Times. (2021). *Biden Administration Plan Tackles Drug Addiction Crisis.* Retrieved from https://www.psychiatrictimes.com/view/biden-administration-plan-narrows-in-on-drug-addiction-crisis

Rand, K., Arnevik, E. A., & Walderhaug, E. (2020). Quality of life among patients seeking treatment for SUD, as measured with the EQ-5D-3L. *Journal of Patient-Reported Outcomes*, *4*(1), 1-10.

Ranganathan, P., Pramesh, C. S., & Aggarwal, R. (2017). Common pitfalls in statistical analysis: logistic regression. *Perspectives in clinical research*, *8*(3), 148.

Sandanger, I., Moum, T., Ingebrigtsen, G., Dalgard, O. S., Sørensen, T., & Bruusgaard, D. (1998). Concordance between symptom screening and diagnostic procedure: the Hopkins Symptom Checklist-25 and the Composite International Diagnostic Interview I. *Social psychiatry and psychiatric epidemiology*, *33*(7), 345-354.

Shakeri, J., Ahmadi, S. M., Maleki, F., Hesami, M. R., Moghadam, A. P., Ahmadzade, A., ... & Elahi, A. (2020). Effectiveness of group narrative therapy on depression, quality of life, and anxiety in people with amphetamine addiction: a randomized clinical trial. *Iranian journal of medical sciences*, *45*(2), 91.

Smith, K. W., & Larson, M. J. (2003). Quality of life assessments by adult substance abusers receiving publicly funded treatment in Massachusetts. *The American Journal of Drug and Alcohol Abuse*, *29*(2), 323-335.

Stecker, T., Han, X., Curran, G. M., & Booth, B. M. (2007). Characteristics of women seeking intensive outpatient substance use treatment in the VA. *Journal of Women's Health*, *16*(10), 1478-1484.

Substance Abuse and Mental Health Services Administration.(2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (HHS Publication No. SMA 17-5044, NSDUH Series H-52). Rockville, MD: Center for Behavioral Health Statistics and Quality. https://www.samhsa.gov/data/

Szende, A., Janssen, B., & Cabase's, J. (2014). *Self-reported population health: an international perspective based on EQ-5D* (p. 212). Springer Nature.

Tarlow, E. M., & Haaga, D. A. (1996). Negative self-concept: Specificity to depressive symptoms and relation to positive and negative affectivity. *Journal of Research in Personality*, *30*(1), 120-127.

Testa, M. A., & Simonson, D. C. (1996). Assessment of quality-of-life outcomes. *New England journal of medicine*, *334*(13), 835-840.

Timko, C., Schultz, N. R., Britt, J., & Cucciare, M. A. (2016). Transitioning from detoxification to substance use disorder treatment: facilitators and barriers. *Journal of substance abuse treatment*, *70*, 64-72.

Torrens, M., Mestre-Pintó, J.I., & Domingo-Salvany, A. (2015). Comorbidity of substance use and mental disorders in Europe. *European Monitoring Center for Drugs and Drugs Addiction.*

Trimbos Instituut. (2015). *Nationale Drug Monitor.* Retrieved from https://www.trimbos.nl/docs/24dd30ba-464f-4dcd-a740-20ac058d310b.pdf

University of Birmingham. (2021). *ICECAP-A Questionnaire.* Retrieved from https://www.birmingham.ac.uk/research/activity/mds/projects/haps/he/icecap/icecap-a/index.aspx

Van der Molen, H.T., Simon, E. & Van Lankveld, J. (2015). *Klinische Psychologie: Theorieën en Psychopathologie.* Groningen/Houten, Nederland: Noordhoff Uitgevers.

Versteegh, M., Knies, S., & Brouwer, W. (2016). From good to better: new Dutch guidelines for economic evaluations in healthcare.

Volksgezondheidszorg. (2017). *Zorguitgaven alcohol- en drugsverslaving 820 miljoen euro.* Retrieved from https://www.volksgezondheidenzorg.info/onderwerp/drugsverslaving/kosten/zorguitgaven#node-zorguitgaven-alcohol-en-drugsverslaving-naar-sector

Zorginstituut Nederland. (2016). *Richtlijn voor het uitvoeren van economische evaluaties in de gezondheidszorg.* Retrieved from https://www.zorginstituutnederland.nl/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-gezondheidszorg

Zuckermann, A. M., Williams, G., Battista, K., de Groh, M., Jiang, Y., & Leatherdale, S. T. (2019). Trends of poly-substance use among Canadian youth. *Addictive behaviors reports*, *10*, 100189.