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Moderators of treatment effect of Prompt Mental Health Care compared to treatment as usual: Results from a randomized controlled trial

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A B S T R A C T

Background: In this exploratory study, we investigated a comprehensive set of potential moderators of response to the primary care service Prompt Mental Health Care (PMHC).

Methods: Data from an RCT of PMHC (n = 463) versus treatment as usual (TAU, n = 215) were used. At baseline mean age was 34.8, 66.7% were women, and 91% scored above caseness for depression (PHQ-9) and 87% for anxiety (GAD-7). Outcomes: change in symptoms of depression and anxiety and change in remission status from baseline to six- and 12- months follow-up. Potential moderators: sociodemographic, lifestyle, social, and cognitive variables, variables related to (mental) health problem and care. Each moderator was examined in generalized linear mixed models with robust maximum likelihood estimation.

Results: Effect modification was only identified for anxiolytic medication for change in symptoms of depression and anxiety; clients using anxiolytic medication showed *less* effect of PMHC relative to TAU (all $p < 0.001$), although this result should be interpreted with caution due to the low number of anxiolytic users in the sample. For remission status, none of the included variables moderated the effect of treatment.

Conclusion: As a treatment for depression and/or anxiety, PMHC mostly seems to work equally well as compared to TAU across a comprehensive set of potential moderators.

1. Background

All individuals do not benefit equally from treatment (Delgadillo et al., 2016; Hoyer et al., 2016; Joesch et al., 2013; Vittengl et al., 2016). In fact, for common mental disorders such as anxiety and depression, poor response or non-response is common across interventions (Hansen et al., 2002). In addition, some experience multiple episodes, as well as relapse after treatment (Bruce et al., 2005; Burcusa & Iacono, 2007; Hollon et al., 2002; Vittengl et al., 2007). When making decisions on inclusion or when tailoring treatment to various groups, knowledge of moderators (pre-treatment variables clarifying for whom or under what conditions a particular treatment is more likely to work (Baron & Kenny, 1986; Kazdin, 2007)) of treatment effect are of great importance. Large-scale randomized controlled trials (RCT) have the potential to provide valuable information on moderators (Kraemer et al., 2002).

In the present study, we explore moderators of effect of Prompt Mental Health Care (PMHC). PMHC aims at improving access to evidence-based primary care treatment for individuals with symptoms of mild to moderate depression and anxiety disorders (Knapstad et al., 2018; Knapstad et al., 2020; Smith et al., 2016; Smith et al., 2017; Helsedirektoratet and Psykisk Helsehjelp – 12 Pilotkommuner, 2013). The service is an adapted version of the English IAPT (Improving Access to Psychological Therapies (Community Mental Health team and H.a.S. C.I.C., 2019)) and was initiated as a pilot project commissioned by the Norwegian Ministry of Health and Care in 2012 (Helsedirektoratet and Psykisk Helsehjelp – 12 Pilotkommuner, 2013). Today, PMHC is employed in 59 Norwegian municipalities (Nasjonalt kompetansesenter for psykisk helsearbeid, 2021). PMHC is supposed to supplement exiting services, and should be low threshold, free of charge and without need of referral (Helsedirektoratet and Psykisk Helsehjelp – 12 Pilotkommuner, 2013; Lervik et al., 2020). All care is based on cognitive behavioral therapy (CBT) (Helsedirektoratet and Psykisk Helsehjelp – 12 Pilotkommuner, 2013; Lervik et al., 2020). Both low and high-intensity care is offered in matched care variants.

Both IAPT and PMHC have been found to substantially and

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Abbreviations

C(B)T	Cognitive (behavioral) therapy
DSM-V:	Diagnostic and Statistical Manual of Mental Disorders - 5
IAPT	Increasing access to psychological therapies
NCPHS	The Norwegian Counties Public Health Surveys
PMHC	Prompt mental health care
TAU	Treatment as usual

sustainably reduce symptoms of anxiety and depression in observational studies (Community Mental Health team and H.a.S.C.I.C., 2019; Knapstad et al., 2018; Myrtveit et al., 2019; Wakefield et al., 2021). PMHC has further proved effective compared to treatment as usual (TAU) in a randomized controlled trial (Knapstad et al., 2020; Sæther et al., 2020). Uncertainties about the effectiveness of PMHC remain though, in particular due to risk of performance, detection, and attrition bias. Moreover, not all individuals receiving PMHC recover or experience the same amount of improvement (Knapstad et al., 2020), and relapse was also experienced by some individuals (at 12 months follow-up, 10% of PMHC clients had relapsed, against 16% in TAU) (Sæther et al., 2020).

A range of systematic reviews have summarized previous research on moderators of treatment outcome in CBT ((Porter & Chambless, 2015; Schneider et al., 2015; Whiston et al., 2019)). The findings suggest that the evidence so far is inconclusive (Porter & Chambless, 2015; Schneider et al., 2015; Whiston et al., 2019). A major problem to study moderator effects have been the presence of underpowered studies (Porter & Chambless, 2015; Schneider et al., 2015). It is clear that more studies on effect modification based on larger samples are called for in the context of CBT (Porter & Chambless, 2015; Schneider et al., 2015), also with regards to services such as IAPT and PMHC (Wakefield et al., 2021). In this study, we follow the recommendation of Kraemer and colleagues (Kraemer et al., 2002) in making use of data from a large RCT to explore moderators of treatment effect.

2. Aim

In this exploratory study, we aimed to investigate a range of person specific potential moderators of PMHC treatment effect. Change in symptoms of depression (PHQ-9) and anxiety (GAD-7) as well as change in remission status, from baseline to six- and 12- months follow-up, were the considered outcome variables. A comprehensive set of potential moderators of treatment effect of PMHC versus TAU was investigated: Sociodemographic factors (sex, age, education, work status, marital status, immigration status), lifestyle and social factors at baseline (smoking, alcohol use, physical activity, obesity, negative life events, social support), as well as variables related to type of presenting mental health problem, cognitive factors, previous care, and self-reported cause of presenting mental health problem.

3. Methods

The current study is a secondary analysis of an RCT comparing PMHC to treatment as usual (TAU) (Knapstad et al., 2020). The study was conducted within routine care in two Norwegian municipalities; Kristiansand and Sandnes. Details about the trial design are provided in the primary evaluation (Knapstad et al., 2020) and are summarized in the following.

3.1. Trial design, inclusion procedures and eligibility criteria

The trial was reported according to the CONSORT statement and is registered at ClinicalTrials.gov (NCT03238872). No changes to the design were made after trial commencement. The trial protocol was approved by the regional ethics committee for Western Norway (REK-vest no. 2015/885).

The study was set up as a randomized controlled superiority trial with parallel assignment. The participants were randomized on a 70:30 ratio (PMHC vs. TAU) using a random number generator.

All clients contacting PMHC in Sandnes and Kristiansand, both GP- and self-referred, got an appointment for individual assessment at the PMHC clinic. In this detailed screening and assessment, one of the therapists conducted a clinical interview with the client. The therapist identified the relevance and severity of the mental health problems, the available client resources, and motivation for treatment. Eligible clients who agreed to participate gave written consent and registered to a secure online data-portal. All questionnaire data from both clients and therapists was collected through this portal.

Eligibility criteria were anxiety and/or mild to moderate depression (PHQ-9$\geq$10 and/or GAD-7$\geq$8, no formal diagnosis provided), being $\geq$18 years old, residing in Kristiansand or Sandnes, and having basic Norwegian language proficiency. The latter was added for practical purposes and resembles ordinary PMHC care. Clients were excluded if they were entitled to secondary health care due to suicide risk, eating disorder, bipolar disorder, severe depression, incapacitating anxiety, psychotic symptoms, severe substance abuse, or personality disorder. Additional exclusion criteria during the trial were having serious physical health problem as main problem or two or more previous treatment attempts in secondary services without effect (as such factors might indicate mental health problem outside the PMHC target). Scoring in the severe category of PHQ and/or GAD was not used as a formal exclusion criterion, neither in PMHC nor in the study. Excluded clients were referred to their GP or other relevant services.

In the current study, only clients scoring above cut-off on symptoms of depression or anxiety at baseline were included (see Fig. 1). This gave a total n of 678.

3.2. The PMHC intervention and TAU

Details on the interventions can be found in previous publications (Knapstad et al., 2020; Lervik et al., 2020; Sæther et al., 2020). A summary follows here.

The PMHC treatment is based on the IAPT treatment model and includes both low-intensity (guided self-help, psychoeducational courses) and high-intensity (individual treatment) treatment forms of CBT. PMHC uses variations of a "matched care" approach in which the treatment offered is based on a cooperative decision between client and therapist. In Sandnes, most clients started with a four-session psychoeducational course. This was common in Kristiansand as well, although not as systematically implemented as in Sandnes. Despite growing evidence of guided self-help as an effective treatment form for anxiety and depression (Knapstad et al., 2020; Kroenke et al., 2001; Porter & Chambless, 2015; Whiston et al., 2019) and the Directorate of Health's requirement to offer low-intensity treatments when indicated, self-help programs were to a little extent readily available during the trial period. Materials available throughout the trial were paper-based programs developed by other PMHC centers. Towards the end of the data collection period, various internet-based programs were increasingly used via a website developed by Norwegian psychologists (www.assistertselvhjelp.no). This website offers specific guided self-help programs for anxiety, depression, stress, and sleep difficulties. No extra resources were added to or amendments conducted of the PMHC service delivery during the trial.

The PMHC group received a median of five (IQR = 4–9) treatment sessions. A session could be either guided self-help, group-course psychoeducation or individual therapy. In total 85.8% received at least two treatment sessions (ex. assessment) and 76.9% completed treatment (defined as therapist reporting that treatment goal was fulfilled and/or having completed at least six sessions). Group-based psychoeducation

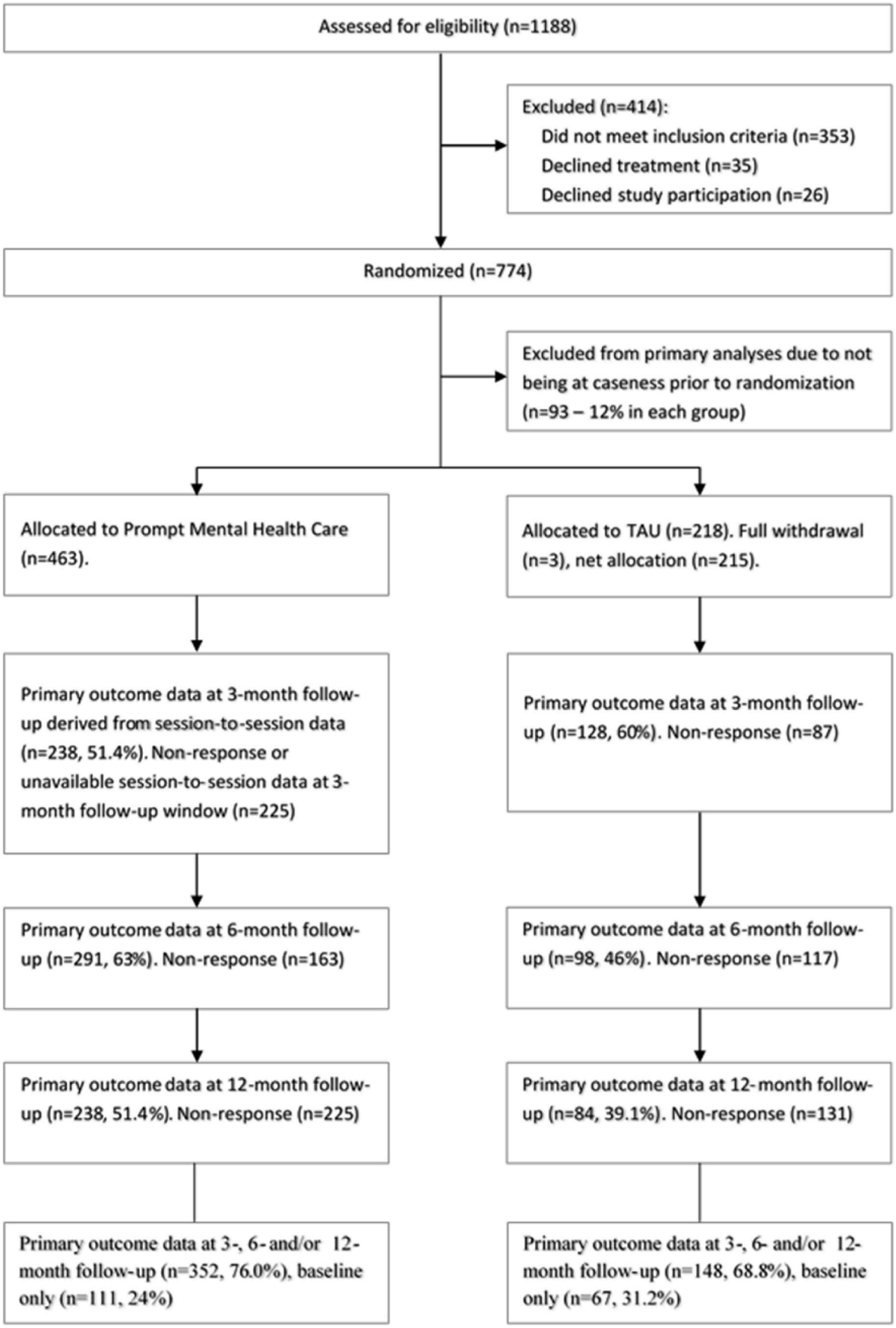

Fig. 1. Flow diagram of PMHC for the period between November 2015 and September 2018.

was the primary treatment form for 35.1%, individual CBT for 30.0%, and guided self-help for 0.9%. The remaining 34.0% received a combination of these treatment forms.

TAU included all ordinary services available to the target population. In the two included municipalities, this usually included follow-up by the GP, or alternatively by private psychologists or occupational health services. After randomization, the TAU group received a response letter in which they were encouraged to contact the GP for further follow-up as well as references to publicly available self-help resources (internet, books).

At 12-month follow-up, about 1 in 4 of respondents in the PMHC group reported to have received some form of additional care for their mental health problem outside of PMHC since baseline (Sæther et al., 2020). Care had been provided by other specialist health services for 12% of respondents. In the TAU group, 1 in 2 of respondents reported to have received care for their mental health problem since baseline, 42% from specialist health care services (Sæther et al., 2020).

4. Data availability

Data from measurements at baseline, 3 months, 6 months, and 12 months after baseline in both the PMHC- and TAU-group were used for the present study. Moderator effects are presented for six and 12-months follow-up only as these were our primary endpoints. As shown in Fig. 1, primary outcome data (PHQ and GAD) was at six months available for 63% in the PMHC group, and 46% in the TAU group. At 12 months, primary outcome data was available in 51.4% in the PMHC group, and 39.1% in the TAU group (Sæther et al., 2020).

On the 41 potential moderators of interest, information was available for at least 91.5% of respondents (information collected at baseline). The variable with the least available data was use of anxiolytic medication, with missing for 58 clients (missing for 8.6%). The average data availability on these 41 potential moderator variables was 98.8% (SD: 2.2, range 91.5–100).

4.1. Outcome measures

Symptoms of depression as measured by the Patient Health Questionnaire (PHQ-9) and symptoms of anxiety as measured by the Generalized Anxiety Disorder Assessment (GAD-7) were used as outcome variables.

The Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001, 2010) includes nine items based on each of the DSM-IV criteria for depression. Individuals indicate how often during the last two weeks they have experienced each of the symptoms. Response options are from 0 (“not at all”) to 3 (“nearly every day”), sum score ranges from 0 to 27. Caseness was defined PHQ $\geq$10. The PHQ has good psychometric properties (Kroenke et al., 2001). Cronbach’s alpha based on PMHC data was 0.80. For the moderator analyses, both the continuous scores and the dichotomous scores based on the cut-off value of 10 were used as outcomes. Participants with a PHQ-score below 10 were considered to be in remission for clinically significant symptoms of depression.

The Generalized Anxiety Disorder Assessment (GAD-7) (Kroenke et al., 2010; Spitzer et al., 2006) measures frequency of seven common anxiety symptoms. Response options are from 0 (“not at all”) to 3 (“nearly every day”), sum score ranges from 0 to 21. Caseness was defined GAD $\geq$8. In addition to measuring generalized anxiety disorder (Spitzer et al., 2006), there are indications that the GAD-7 also has good sensitivity and specificity for panic, social anxiety, and post-traumatic stress disorder (Kroenke et al., 2007). Cronbach’s alpha based on PMHC data was 0.83. For the moderator analyses, both the continuous scores and the dichotomous scores based on the cut-off value of 8 were used as outcomes. Participants with a PHQ-score below 8 were considered to be in remission for clinically significant symptoms of anxiety.

4.2. Moderators of interest

Potential moderators specific to the client were investigated. All variables were self-reported at baseline, prior to randomization. Continuous variables were categorized to augment their clinical relevance and to circumvent the assumption that moderators operate in a linear fashion (Cooper et al., 2016; Kraemer, 2016). If pre-defined cut-offs were not available, binary variables were created based on the highest or lowest tertile, depending on what was considered clinically most relevant. Tertiles were used to balance sample size on one hand and the identification of clinically relevant groups on the other hand. Most of the potential moderators included in the current study were also investigated in the analysis of predictors of change in the observational study of the first 12 PMHC pilots (Knapstad et al., 2018).

4.2.1. Socio-demographic variables

Sex (Female: y/n). Age ($\geq$30: y/n). This age cutoff was chosen as younger age has been found associated with poorer treatment outcome in IAPT (Delgadillo et al., 2016). Education (Higher education (university/university college): y/n). Two questions, one multi-response item about current work status and one about sources of income, assessed employment status. Based on these, we determined whether participants were in full- or part-time regular work without receiving benefits (y) or not (n). Marital status (Married/cohabiting: y/n). Immigration background (defined as being an immigrant or born in Norway by immigrant parents: y/n).

4.2.2. Lifestyle and social variables

Smoking was grouped as “daily/sometimes” (y) and not smoking (n)). Paralleling the measure used in The Norwegian Counties Public Health Surveys (NCPHS) (Knapstad et al., 2021), alcohol use was coded as using alcohol $\geq$2 days a week (y) or less than this (n). Again, inspired by the NCPHS (Knapstad et al., 2021), physically activity (defined as moderate intensity for at least for 30 min) was grouped as $\geq$4 days a week (y) or less than this (n). This was done in order to get close to the Norwegian Directorate of Health’s recommendations on physical activity (The Norwegian Directorate of Health, 2019). Obesity (BMI$\geq$ 30; y/n).

Negative life-events were measured by means of the Life-events scale (Havik et al., 1995). Clients are asked to rate the occurrence and impact of 24 specific life-events during the last year from −3 (very negative) to 3 (very positive). The total impact of life-events was estimated by calculating the sum score across all life events. A sum score $<$0 was coded as 1 (net negative effect of life events) and a sum score of $\geq$0 was coded as 0 (net zero or positive effect of life events).

Social support was assessed using the Oslo 3-items social support scale (OSS-3) (Dalgard et al., 2006). The items cover number of close confidants, the sense of concern or interest shown by others and perceived availability of practical help from neighbors. Cronbach’s alpha of the OSS-3 was relatively low in our sample (0.58). Following the operationalization from Bøen et al. (Bøen et al., 2012), a sum-score ranging from 3 to 14 was calculated. As in Bøen et al. (Bøen et al., 2012), clients scoring 3–8 were coded as 1 (low social support), whereas those scoring 9–15 were coded as 0 (medium to high social support).

4.2.3. Health-related problems

Functional status was measured using the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002). WSAS has been used in previous evaluations of PMHC (Smith et al., 2016) and IAPT (Clark et al., 2009), and has been found to have discriminant validity to, and comparable reliability and sensitivity to change as, the PHQ-9 and GAD-7 (Zahra et al., 2014). The measure contains 5-items, assessing impairment caused by mental health problems during the last month in five domains (0 = not impaired to 8 = severely impaired). A binary variable was created from the sum score; highest tertile impairment (low functional status): 1, lowest two tertiles: 0.

Health-related quality of life (HRQL) was measured using the EQ-5D (Rabin & Charro, 2001). HRCL measured by the EQ-5D is associated with depression among primary care clients, and improves when depression is treated (Sobocki et al., 2007). The paper version of EQ-5D was in large completed electronically; a dedicated digital version of the EQ- 5D was not used. We created a simple sum score (5–25), where higher scores indicate poorer HRCL. As with WSAS, a binary variable was created from the sum score; highest tertile (low health-related quality of life): 1, lowest two tertiles: 0.

Based on information from PHQ (Kroenke et al., 2001, 2010) and GAD (Kroenke et al., 2010; Spitzer et al., 2006), a three level diagnostic group variable was created. Clients were defined as having depression only (PHQ≥10, GAD<8), anxiety only (PHQ<10, GAD≥8), or both (PHQ≥10 and GAD≥8). For estimation purposes, this operationalization could only be used when PHQ/GAD outcome was based on continuous scores.

Moderate to severe symptoms of depression was defined as PHQ9 >14 when PHQ/GAD outcome was based on continuous scores. For estimation purposes, a continuous PHQ-score at baseline was examined as potential moderator when PHQ/GAD outcome was based on dichotomized scores.

Indications of dysthymia (y/n); Clients were asked whether or not they had felt depressed or sad most days during the last two years, even if they had felt ok sometimes.

Severe symptoms of anxiety were defined as GAD7 >14 when PHQ/GAD outcome was based on continuous scores. For estimation purposes, a continuous GAD-score at baseline was examined as potential moderator when PHQ/GAD outcome was based on dichotomized scores.

Symptoms of social anxiety were assessed by an abbreviated form of the Social Phobia Inventory (O'Connor & Rutter, 2000), SPIN-9. Five items regard avoidance and four regarding physiological discomfort (alpha = .86). The respondent are asked to what extent each symptom have been bothersome during the past week, from "not at all" (0) to "extremely" (4). Caseness (1) was defined by a SPIN-9 sum score>18 (O'Connor & Rutter, 2000; The IAPT data handbook version, 2011).

Symptoms of agoraphobia were measured by an abbreviated version of the Mobile inventory for Agoraphobia (Chambless et al., 1985), MI-9, suggested from a generalizability study carried out at Modum bad (Hoffart et al., 2018). The scale includes rating of avoidance due to anxiety or discomfort of nine places/situations, when alone and when accompanied, from "never" (1) to "always" (5) (alpha = .93). Caseness (1) was defined as sum-score ≥ 29 (Chambless et al., 1985).

Symptoms of insomnia were assessed by the Karolinska Sleeping Scale (Sivertsen et al., 2019). The scale has good psychometric properties and has been validated against clinical interviews in a Norwegian population sample (Engstrøm et al., 2011). Caseness (1) was defined according to DSM-V criteria of insomnia (difficulties in initiating or maintaining sleep, being sleepy at daytime ≥3 days a week, with problems lasting for ≥3 months).

4.2.4. Cognitive factors

Depressive cognitions were assessed using an abbreviated version of the Cognitions Check-List for depression, CCL-D. The three items carrying most information based on results from previous validation work were included in the abbreviated sample (Steer et al., 1994). Cronbach's alpha in our sample was 0.90. Participants in the highest tertile were categorized as having clinically significant levels of depressive cognitions (y) and were compared to those in the lowest two tertiles (n).

We assessed anxious cognitions using 11 questions from the Anxious Questionnaire, ATQ. Seven items from the ATQ relating to agoraphobia (ATQ-AP) (Chambless et al., 1984; Hoffart, 1995) and four items from the social anxiety ATQ (ATQ-SA) (Hoffart et al., 2009; McManus et al., 2000) were used. More details are available in our previous publication (Knapstad & Smith, 2021). As with the CCL-D, clients reporting the highest tertile (y)were compared to those reporting the lowest two (n).

Outcome expectancy: With regard to their symptoms of anxiety and/or depression, clients were presented with the statement "I expect to get well also without treatment". Subsequently, they were asked whether the statement fit them "very well", "rather well", "neither well nor poorly", or "poorly". Clients indicating "poorly" were grouped as "Expecting no recovery without treatment" (y) and compared to those expecting recovery (n).

4.2.5. Dispositional factors

Dispositional self-control was assessed by the "The Brief Self-Control Scale" (Tangney et al., 2004), (alpha = 0.76). This is a five-item scale measuring individual differences in self-regulatory behaviors, rated on a five-point scale from "not at all like me" (1) to "very much like me" (5). Scoring within the lowest tertile was coded as 1 (low self-control) and scoring in the two highest was coded as 0 (middle to high self-control).

Dispositional mindfulness was assessed by the "Mindfulness Attention Awareness Scale"-6, MAAS-6 (Brown & Ryan, 2003). (alpha = 0.82). MAAS-6 taps the tendency to be present in the moment in everyday activities, on a 6 point-scale from almost never (1) to almost always (6). A sum score is calculated and, like above, the lowest tertile was coded as 1 (low mindfulness) and the two highest tertiles as 0 (middle to high mindfulness).

4.2.6. Perceived cause of symptoms

The participants were asked to indicate their perceived cause of symptoms from a fixed list created for the investigation of PMHC. Multiple responses were allowed. Causes with sufficient number of responses (at least n = 25 reporting this cause in each group (PMHC/TAU)) were included in the analyses (yes = 1, no = 0): Relationship problems, family relations, eating problems, work/school related, overweight, somatic illness, difficult childhood, and/or bullying.

4.2.7. Mental health care related factors

Clients were asked whether they had had previous treatment attempts during last 12 months (yes = 1, no = 0). They were also asked whether they had used antidepressant medication (every day = 1, less than every day = 0), anxiolytic medication (every week = 1, less than every week = 0), or sleep medication (every week = 1, less than every week = 0) during the last 4 weeks. No details as to which medications were of interest were included. These variables can therefore include a combination of prescription and non-prescription medications.

4.2.8. Site

Clients were part of PMHC or TAU in one of two sites; the municipalities Kristiansand (0) or Sandnes (1). This is the only variable investigated as a moderator that is not person specific.

4.3. Statistical analyses

Generalized linear mixed models with robust maximum likelihood estimation, based on the available data from all participants (n = 678), were used to examine the effects of the potential moderator variables on the outcome variables. Raw PHQ and GAD scores were modelled as continuous variables (normal distribution, identity link function), whereas PHQ and GAD remission status were modelled as binary variables (binomial distribution, logit link function). Time was treated as a categorical variable (baseline, 3-, 6- and 12-months follow-up). Person ID was included as random effect.

Each potential moderator was examined in a separate model for change in PHQ and GAD scores and change in PHQ and GAD remission status. Each model contained main effects for the moderator of interest and time, two-way interactions for time * moderator of interest and time * affiliation, and a three-way interaction for time * moderator of interest * affiliation. The main effect of affiliation and the two-way interaction between moderator * affiliation were not included in the models as these represent baseline differences across the two intervention groups which have expected values of zero by design (see recommendations by Twisk

Table 1
Baseline characteristics by treatment group, n = 678.

	Prompt mental health care, n = 463 % (n)	Treatment as usual, n = 215 % (n)	Total, n = 678 % (n)
Demographic variables			
Sex: female	65.7 (304)	68.4 (147)	66.5 (451)
Age ≥30	60.3 (279)	57.2 (123)	59.3 (402)
High education	43.9 (202)	36.6 (78)	41.6 (280)
In regular work	37.2 (172)	38.1 (82)	37.5 (254)
Not married/cohabiting	44.9 (207)	41.1 (88)	43.7 (295)
Immigrant background	12.6 (58)	9.4 (20)	11.5 (78)
Lifestyle and social factors at baseline			
Smoker	24.2 (112)	28.4 (61)	25.5 (173)
Alcohol ≥2–3 days a week	15.8 (73)	16.7 (36)	16.1 (109)
Physical activity ≥4 days a week	26.8 (121)	21.8 (46)	25.2 (167)
BMI ≥30	16.6 (72)	15.7 (30)	16.4 (102)
Negative life events	71.9 (312)	78.8 (160)	74.1 (472)
Poor social support	34.8 (161)	33.5 (72)	34.4 (233)
Health-related problems			
Poor functional status (Highest tertile WSAS)	39.7 (184)	36.7 (79)	38.8 (263)
WSAS (mean, SD)	21.7 (7.8)	21.8 (7.7)	21.4 (8.1)
Poor health-rel. quality of life (Highest tertile EQ-5D)	38.7 (179)	34.4 (74)	37.3 (253)
EQ-5D (mean, SD)	10.9 (2.8)	10.9 (2.8)	10.9 (2.7)
Diagnostic group (PHQ and/or GAD above cut-off)			
Depression only	13.0 (60)	13.0 (28)	13.0 (88)
Anxiety only	9.9 (46)	7.4 (16)	9.1 (62)
Depression and anxiety	77.1 (357)	79.5 (171)	77.9 (528)
Mod. to severe symptoms of depression	52.3 (242)	51.6 (111)	52.1 (353)
Dysthymia	62.0 (287)	61.6 (130)	61.9 (417)
Severe symptoms of anxiety	29.6 (137)	31.2 (67)	30.1 (204)
Agoraphobia (MI-8)	50.3 (233)	53.5 (115)	51.3 (348)
Social anxiety (SPIN-9)	64.6 (299)	66.1 (142)	65.0 (441)
Insomnia	65.7 (304)	64.0 (137)	65.1 (441)
Having experienced presenting problem ≥6 months	86.8 (401)	88.8 (191)	87.4 (592)
Having experienced presenting problem at current level ≥6 months	66.6 (307)	68.5 (146)	67.2 (453)
Cognitive factors			
Depressive cognitions (Highest tertile CCL-D)	41.3 (191)	30.7 (66)	37.9 (257)
Anxious cognitions (Highest tertile)	34.6 (160)	36.7 (79)	35.3 (239)
Expect no recovery without treatment	46.2 (213)	41.7 (88)	44.8 (301)
Dispositional factors			
Self-control (Lowest tertile)	42.3 (196)	40.9 (88)	41.9 (284)
Mindfulness (Lowest tertile)	34.2 (158)	30.7 (66)	33.1 (224)
Mental health care factors at baseline			
Previous treatment attempt	22.5 (104)	20.5 (44)	21.9 (148)
Anxiolytic medication	7.6 (32)	6.0 (12)	7.1 (44)
Antidepressant medication	15.4 (67)	14.7 (30)	15.2 (97)
Sleep medication	16.4 (72)	17.4 (36)	16.7 (108)
Self-reported cause of presenting problem			
Relationship problems	35.4 (162)	33.0 (70)	34.6 (232)
Family relations	54.6 (250)	50.2 (107)	53.2 (357)
Eating problems	16.6 (76)	19.2 (42)	17.6 (118)
Work/school related problems	57.2 (262)	62.4 (133)	58.9 (395)
Overweight	14.0 (64)	12.7 (27)	13.6 (91)
Somatic illness	22.1 (101)	16.9 (36)	20.4 (137)
Difficult childhood	29.9 (137)	23.9 (51)	28.0 (188)
Bullying	19.9 (91)	18.3 (39)	19.4 (130)
Site			
Sandnes	58.1 (269)	54.4 (117)	56.9 (386)
Kristiansand	41.9 (194)	45.6 (98)	43.1 (292)

et al. (Twisk et al., 2018). As running multiple tests can increase the risk of detecting spurious associations, the significance level was set to $p < 0.01$. Moderation was considered to have occurred when the three-way interaction at 6- or 12-months follow-up was statistically significant ($p < 0.01$). For continuous outcomes, standardized effect sizes (ES) were calculated by dividing the unstandardized estimate with the standard deviation at baseline of PHQ (SD = 4.3) or GAD (SD = 4.2) (Sæther et al., 2020). Standardized effects were interpreted as respectively small (0.2), medium (0.5), or large (0.8).

Stata version 15 (StataCorp. and Stata Statistical Software, 2017) was used for all analyses.

5. Results

5.1. Baseline characteristics and participant flow

Details of the participant flow and characteristics are previously described (Knapstad et al., 2020). In the current sample, there were 463 participants in the PMHC group and 215 in the TAU group (Fig. 1). The mean age was 34.8 and two thirds were women. At baseline, the overall mean depression (PHQ) score was 14.9 (SD: 4.4), and 90.9% scored above level for caseness (PHQ-9 ≥ 10). For anxiety (GAD), the mean score was 12.0 (SD: 4.2) with 87.0% at caseness (GAD-7 ≥ 8) (Knapstad et al., 2020).

Table 1 gives a detailed overview of all baseline characteristics examined in the following, by treatment group. As expected, there were no statistically significant difference in distribution of characteristics between treatment groups.

5.2. Moderators of treatment effect on symptoms of depression (PHQ) and/or anxiety (GAD)

Table 2 shows results from the moderator analyses for the continuous outcomes. Results significant at the $p < 0.01$ level are marked in bold. PMHC treatment effect was not modified by demographic variables,

Table 2
Moderators of change in symptoms of depression and anxiety from baseline to 6- and 12-months follow-up (unadjusted).

	Symptoms of depression, PHQ								Symptoms of anxiety, GAD							
	6 months				12 months				6 months				12 months			
	Coeff.	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**
Demographic variables																
Sex: female	0.25	−2.36	2.86	0.06	1.17	−1.71	4.06	0.27	0.36	−1.63	2.35	0.09	0.07	−2.09	2.22	0.02
Age ≥30	−0.38	−2.85	2.09	−0.09	0.07	−2.54	2.68	0.02	−0.32	−2.14	1.51	−0.08	−0.78	−2.95	1.38	−0.19
High education	0.77	−1.69	3.22	0.18	1.34	−1.08	3.77	0.31	−0.52	−2.36	1.33	−0.12	1.17	−0.87	3.21	0.28
In regular work	0.18	−2.31	2.67	0.04	−0.42	−2.92	2.09	−0.10	0.10	−1.70	1.91	0.03	−0.64	−2.76	1.48	−0.15
Not married/cohabiting	−0.44	−2.92	2.04	−0.10	−0.94	−3.56	1.67	−0.22	−0.45	−2.27	1.37	−0.11	−0.51	−2.60	1.58	−0.12
Immigrant backgr.	2.18	−1.86	6.21	0.51	−0.33	−4.80	4.14	−0.08	1.94	−1.05	4.93	0.46	0.71	−2.61	4.03	0.17
Lifestyle and social factors																
Smoker	0.05	−2.64	2.73	0.01	0.21	−2.53	2.96	0.05	0.49	−1.65	2.63	0.12	0.65	−1.65	2.95	0.15
Alcohol≥2–3 d/week	0.15	−3.32	3.62	0.04	0.56	−2.60	3.71	0.13	−0.45	−2.98	2.09	−0.11	0.43	−2.24	3.11	0.10
Physical act.≥4 d/week	0.07	−2.78	2.91	0.02	0.59	−2.44	3.63	0.14	−0.03	−2.13	2.08	−0.01	−0.32	−2.74	2.09	−0.08
BMI ≥30	−3.11	−6.04	−0.19	−0.72	−1.87	−5.25	1.52	−0.43	−1.27	−3.52	0.99	−0.30	−0.16	−2.75	2.44	−0.04
Negative life events	−1.04	−4.14	2.05	−0.24	0.24	−2.63	3.11	0.06	−1.73	−4.07	0.60	−0.41	−0.34	−2.94	2.26	−0.08
Poor social support	0.87	−1.72	3.46	0.20	1.26	−1.50	4.01	0.29	−0.57	−2.43	1.28	−0.14	1.10	−0.95	3.16	0.26
Health-related problems																
Poor functional status (WSAS)	−0.87	−3.70	1.97	−0.20	−0.17	−3.23	2.90	−0.04	−0.36	−2.34	1.62	−0.09	0.06	−2.31	2.43	0.02
Poor health-related quality of life (EQ-5D)	−1.12	−3.81	1.58	−0.26	−0.64	−3.67	2.40	−0.15	0.01	−1.92	1.94	0.00	0.16	−2.35	2.67	0.04
Diagnostic gr. (PHQ,GAD)																
Depression only	1.34	−1.75	4.42	0.31	−1.40	−4.24	1.45	−0.33	0.96	−0.79	2.70	0.23	0.47	−1.59	2.54	0.11
Anxiety only	3.48	−0.20	7.15	0.81	−0.28	−4.22	3.67	−0.07	1.35	−1.97	4.67	0.32	1.35	−2.09	4.78	0.32
Depression and anxiety	Base															
Mod. to severe symptoms of depression (PHQ)	−0.74	−3.30	1.81	−0.17	−0.24	−2.85	2.36	−0.06	0.45	−1.37	2.28	0.11	−0.82	−2.93	1.29	−0.20
Dysthymia	−1.62	−4.05	0.81	−0.38	−0.77	−3.23	1.69	−0.18	−1.39	−3.17	0.40	−0.33	−1.13	−3.16	0.90	−0.27
Severe symptoms of anxiety (GAD)	1.61	−1.44	4.65	0.37	−0.70	−3.81	2.41	−0.16	1.19	−1.12	3.51	0.28	−1.00	−3.65	1.65	−0.24
Agoraphobia (MI-8)	−1.93	−4.34	0.49	−0.45	0.33	−2.21	2.86	0.08	−1.85	−3.62	−0.07	−0.44	−0.74	−2.84	1.37	−0.18
Social anxiety (SPIN-9)	−1.40	−4.05	1.24	−0.33	0.21	−2.38	2.80	0.05	−1.14	−3.07	0.78	−0.27	−1.59	−3.74	0.57	−0.38
Insomnia	−1.94	−4.42	0.55	−0.45	−1.17	−3.85	1.51	−0.27	−0.73	−2.45	0.99	−0.17	−0.95	−3.06	1.16	−0.23
Having experienced presenting problem ≥ 6m	−1.68	−4.96	1.61	−0.39	−2.54	−6.58	1.50	−0.59	−0.43	−3.12	2.27	−0.10	−1.09	−4.34	2.15	−0.26
Having experienced presenting problem at current level ≥ 6m	−1.49	−3.97	0.98	−0.35	−1.41	−3.97	1.16	−0.33	−1.36	−3.16	0.44	−0.32	−1.78	−3.85	0.29	−0.42
Cognitive factors																
Depressive cognitions (CCL-D)	−1.76	−4.24	0.73	−0.41	−0.85	−3.97	2.28	−0.20	−1.55	−3.37	0.27	−0.37	−1.14	−3.45	1.16	−0.27
Anxious cognitions (ATQ)	0.32	−2.27	2.91	0.08	−0.59	−3.33	2.15	−0.14	−0.06	−1.97	1.85	−0.01	−0.89	−3.18	1.41	−0.21
Expect no recovery without treatment	0.90	−1.59	3.39	0.21	0.22	−2.44	2.87	0.05	−0.26	−2.07	1.54	−0.06	−0.30	−2.49	1.88	−0.07
Dispositional factors																
Low self-control	−0.65	−3.20	1.89	−0.15	−2.33	−4.80	0.14	−0.54	−0.58	−2.49	1.34	−0.14	−2.08	−4.30	0.15	−0.49
Low mindfulness	−0.86	−3.59	1.86	−0.20	−1.02	−3.69	1.65	−0.24	−0.68	−2.65	1.30	−0.16	−1.54	−4.07	0.99	−0.37
Mental health care factors																
Previous treatment attempt	−0.22	−3.19	2.75	−0.05	1.51	−1.66	4.68	0.35	0.27	−1.74	2.27	0.06	0.49	−2.00	2.99	0.12
Anxiolytic medication	**9.12**	**5.74**	**12.51**	**2.12**	**9.62**	**4.81**	**14.42**	**2.24**	1.81	−0.60	4.21	0.43	**6.12**	**3.49**	**8.74**	**1.46**
Antidepressant medication	−1.04	−4.91	2.82	−0.24	−2.63	−6.80	1.54	−0.61	−1.22	−3.67	1.24	−0.29	−1.41	−4.21	1.38	−0.34
Sleep medication	2.36	−0.92	5.63	0.55	2.31	−1.74	6.36	0.54	0.70	−1.44	2.85	0.17	−0.30	−3.41	2.81	−0.07
Self-reported cause																

(*continued on next page*)

Table 2 (*continued*)

	Symptoms of depression, PHQ								Symptoms of anxiety, GAD							
	6 months				12 months				6 months				12 months			
	Coeff.	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**EV**
Relationship problems	0.42	−2.09	2.93	0.10	0.95	−1.54	3.43	0.22	−0.24	−2.26	1.79	−0.06	0.67	−1.50	2.84	0.16
Family relations	−0.67	−3.17	1.82	−0.16	−0.49	−3.11	2.12	−0.12	−0.02	−1.83	1.80	0.00	0.81	−1.36	2.98	0.19
Eating problems	1.15	−2.03	4.32	0.27	−0.38	−4.07	3.32	−0.09	−0.13	−2.41	2.16	−0.03	0.17	−2.80	3.14	0.04
Work/school related prob.	−1.65	−4.13	0.83	−0.38	−2.51	−5.03	0.01	−0.58	−0.14	−1.91	1.62	−0.03	−0.53	−2.66	1.61	−0.13
Overweight	−1.93	−5.57	1.71	−0.45	−2.71	−6.56	1.13	−0.63	−1.46	−3.86	0.94	−0.35	−0.88	−4.06	2.31	−0.21
Somatic illness	−0.48	−3.58	2.62	−0.11	1.12	−2.12	4.36	0.26	0.33	−1.60	2.26	0.08	1.18	−1.07	3.43	0.28
Difficult childhood	0.26	−2.81	3.33	0.06	−1.82	−4.87	1.24	−0.42	1.29	−0.79	3.36	0.31	−1.35	−3.86	1.16	−0.32
Bullying	−1.76	−4.69	1.17	−0.41	−1.67	−4.34	1.01	−0.39	−1.14	−3.20	0.93	−0.27	−0.01	−2.45	2.43	0.00
Site																
Sandnes	−0.31	−2.80	2.19	−0.07	1.96	−0.49	4.42	0.46	−0.39	−2.23	1.44	−0.09	0.35	−1.74	2.43	0.08

Results from generalized linear mixed models with robust estimation, based on the available data from all participants (n = 678). Independent variable: Potential moderator of treatment outcome. Dependent variable; change in PHQ and GAD from baseline to 6- and 12- months. The presented estimates are the coefficients of the 3-way interaction. Bold: model giving p-value of interaction "moderator variable*treatment type*time-point of interest" <0.01. All potential moderator variables measured at baseline.

lifestyle variables, variables related to health problems, cognitive factors, dispositional factors, causes of mental health problems or site. Effect modification was found only for use of anxiolytic medication. Table 3 and Fig. 2 show that individuals taking anxiolytic medications experienced less effect of PMHC compared to TAU for symptoms of depression at six and 12 months, and for symptoms of anxiety at 12 months.

Regarding symptoms of depression, 75.3% (n = 219) and 75.8% (n = 182) were in remission at 6- and 12-month follow-up in the PMHC group against 49.0% (n = 48) and 57.4% (n = 48) in the control group. As for symptoms of anxiety, 74.9% (n = 218) and 76.5% (n = 182) were in remission at 6- and 12-month follow-up in the PMHC group against 59.2% (n = 58) and 61.9% (n = 52) in the control group. As shown in Table 4, none of the examined variables moderated the effect of PMHC on remission status. The potential moderating effect of anxiolytic medication on remission status could not be estimated due to sparse data (see also Table 1).

6. Discussion

In this study, we explored moderators of treatment response of PMHC compared to TAU in a sample of adult clients with symptoms of anxiety or mild to moderate depression. The analyses are based on data from an RCT showing good effect of PMHC relative to TAU in terms of symptom reduction and recovery (Knapstad et al., 2020; Sæther et al., 2020). We found hardly any variable to moderate the effect of PMHC treatment both in terms of change in symptoms levels and change in remission status. The only variable found to modify treatment effect was use of anxiolytic medication, and only with regard to change in symptom levels.

As detailed by Kramer and colleagues (Kraemer et al., 2002), knowledge of moderators of treatment effect can suggest to clinicians and researchers who might benefit the most from specific treatments, who might be part of subpopulations with different causal mechanisms for illness, or what might be good inclusion/exclusion criteria when performing RCTs. However, previous studies have found CBT to work equally well across a range of potential moderators (Cooper et al., 2016), including demographic variables (Cuijpers et al., 2014; Schneider et al., 2015). It seems that finding easily identifiable variables that can indicate whom might benefit more – or less – from CBT is difficult. As such, it confirms that CBT is a useful approach for a wide section of individuals in need.

Also in our study, hardly any of the 41 investigated potential variables modified effect of PMHC compared to TAU. For example, baseline severity, which is a consistent predictor of poorer treatment outcome (Eskildsen et al., 2010; Haby et al., 2006), did not modify treatment effect. This is in line though with previous research that also failed to identify baseline severity as a moderator of treatment effect (Schneider et al., 2015; Vittengl et al., 2016). It should be noted that cases of severe depression are excluded from treatment in PMHC (Knapstad et al., 2020; Helsedirektoratet and Psykisk Helsehjelp – 12 Pilotkommuner, 2013), and this restriction of range could mask a potential moderating effect of disease severity, but within the target group, the effect of PMHC compared to TAU appears to be the same for both clients with low and higher severity levels of depression.

Naturally, effect of PMHC treatment might differ with type of mental health problem. In PMHC, no formal diagnoses are set (Lervik et al., 2020). During the trial period, provisional diagnoses were provided in the PMHC group, but not in the TAU group (Knapstad et al., 2020). Differences in treatment effect of PMHC compared to TAU could therefore not be investigated for different diagnoses. However, research has indicated that CBT works similarly well across disorders (Haby et al., 2006; Roshanaei-Moghaddam et al., 2011). To this end, we have previously found medium-sized effects of PMHC versus TAU among subgroups of clients with clinical relevant symptoms of social anxiety and agoraphobia (Knapstad & Smith, 2021). Our study adds to this by

Table 3
Unstandardized effectiveness of PMHC compared to TAU on symptoms of depression (PHQ) and anxiety (GAD) for clients using anxiolytic medication every week and clients not using anxiolytic medication every week.

	Symptoms of depression (PHQ-9)				Symptoms of anxiety (GAD-7)			
	Six months		12 months		Six months		12 months	
	Effectiveness (95%CI)	p-value	Effectiveness (95%CI)	p-value	Effectiveness (95%CI)	p-value	Effectiveness (95% CI)	P-value
Anxiolytic medication every week	5.25 (2.13–8.38)	0.001	6.20 (1.59–10.82)	0.008	−0.50 (−2.70 to 1.69)		3.79 (1.42–6.17)	0.002
Not anxiolytic medication every week	−3.87 (−5.17 to −2.57)	<0.001	−3.41 (−4.73 to −2.09)	<0.001	−2.31 (−3.28 to −1.33)		−2.32 (-3.43 to −1.21)	<0.001

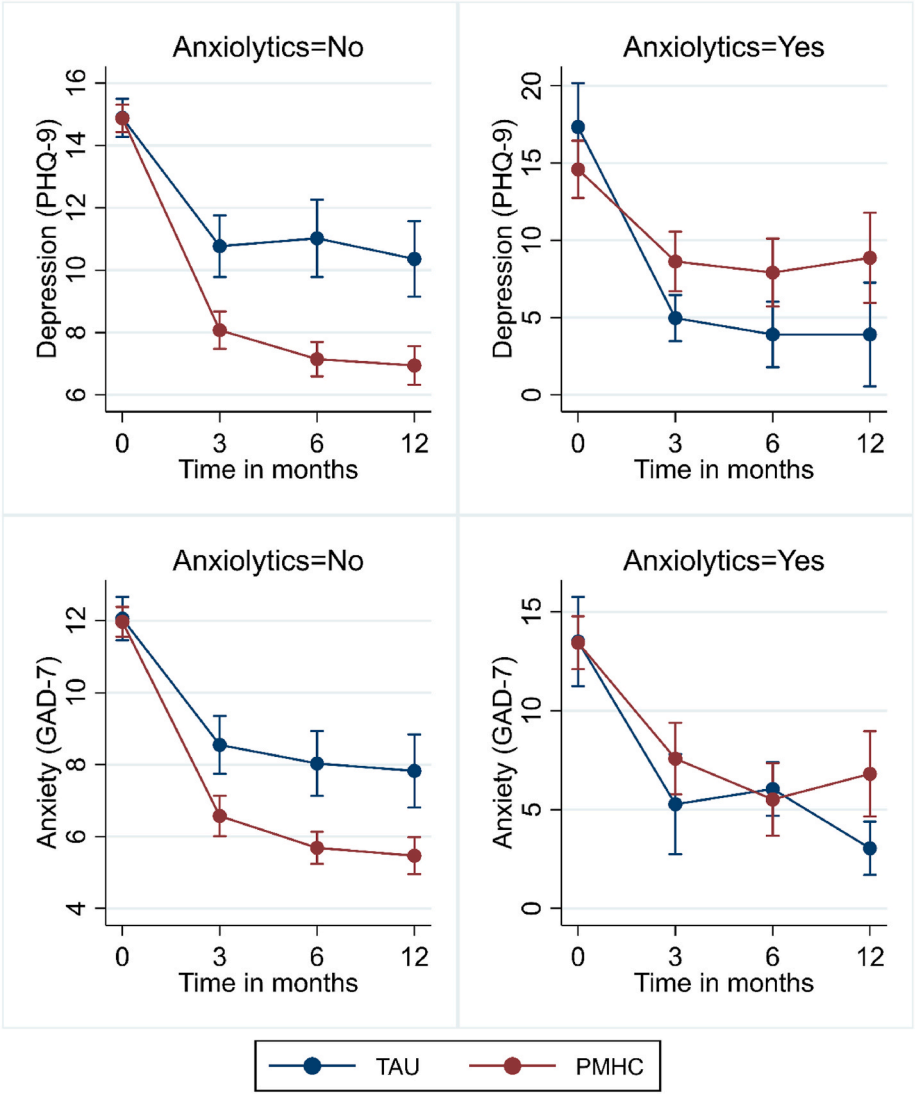

Fig. 2. Intervention effects by anxiolytic use on symptoms of depression (upper graphs) and symptoms of anxiety (bottom graphs).

indicating that PMHC works equally well compared to TAU for individuals with symptoms of agoraphobia, social anxiety, dysthymia and insomnia. Also, PMHC works equally well compared to TAU for individuals with symptoms of anxiety, symptoms of depression, or symptoms of both anxiety and depression. This is interesting, as these disorders tend to have different trajectories. For instance, spontaneous recovery is relatively common in depression (Posternak & Miller, 2001), while comorbid anxiety and depression seems more persistent than either anxiety or depression alone (Merikangas et al., 2003).

The only variable significantly modifying treatment effect in our study was use of anxiolytic medication once a week or more. Clients using anxiolytic medication experienced less symptom reduction with PMHC compared to TAU than clients not using anxiolytic medications. In fact, it suggested that anxiolytic users in the TAU group experienced larger symptom reductions compared to anxiolytic users in the PMHC group. This moderating effect could not be examined with regard to remission status due to sparse data as only 44 clients used anxiolytic medications. Due to the small number of anxiolytic users, the statistical power to detect a true moderating effect of anxiolytics was low, and the associated sampling distribution of this effect was relatively wide.

Table 4
Moderators of change in remission status for depression and anxiety from baseline to 6- and 12- months follow-up.

	Remission, PHQ						Remission, GAD					
	6 months			12 months			6 months			12 months		
	Coeff.	**95% CI, lower limit**	**95% CI, upper limit**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**	**Coeff.**	**95% CI, lower limit**	**95% CI, upper limit**
Demographic variables												
Sex: female	−0.49	−2.15	1.19	−0.75	−2.57	1.07	0.00	−1.49	1.49	0.16	−1.52	1.84
Age ≥30	0.70	−0.84	2.25	0.23	−1.50	1.96	0.21	−1.18	1.60	1.19	−0.42	2.80
High education	−0.65	−2.17	0.86	−1.11	−2.82	0.59	0.05	−1.37	1.47	−1.45	−3.10	0.20
In regular work	−0.80	−2.33	0.73	−0.93	−2.61	0.76	−0.49	−1.91	0.93	−1.36	−2.95	0.24
Not married/cohabiting	−0.09	−1.60	1.43	0.06	−1.63	1.75	−0.24	−1.66	1.17	−0.72	−2.36	0.92
Immigrant background	−0.55	−2.91	1.81	−0.80	−3.38	1.79	−0.62	−2.96	1.72	0.56	−1.90	3.02
Lifestyle and social factors												
Smoker	0.84	−0.94	2.61	1.06	−0.94	3.06	0.17	−1.44	1.78	−0.58	−2.62	1.45
Alcohol≥2–3 d/week	1.27	−0.85	3.39	−0.42	−2.95	2.11	0.94	−1.02	2.91	−1.02	−3.50	1.47
Physical act.≥4 d/week	0.14	−1.56	1.83	−0.54	−2.57	1.48	−0.08	−1.70	1.54	0.04	−1.87	1.95
BMI ≥30	1.68	−0.49	3.86	2.02	−0.31	4.36	0.24	−1.64	2.12	1.28	−0.78	3.34
Negative life events	0.24	−1.45	1.92	−0.38	−2.26	1.49	1.34	−0.23	2.92	0.23	−1.49	1.95
Poor social support	0.22	−1.42	1.85	−1.36	−3.13	0.42	0.54	−0.97	2.06	−1.66	−3.36	0.04
Health-related problems												
Poor functional status (WSAS)	0.48	−1.10	2.05	−0.02	−1.76	1.71	1.14	−0.31	2.59	0.44	−1.21	2.09
Poor health-related quality of life (EQ-5D)	0.37	−1.28	2.01	1.35	−0.62	3.31	0.53	−0.96	2.01	0.32	−1.53	2.18
PHQ-score baseline	nc	nc	nc	nc	nc	nc	0.11	−0.06	0.27	0.13	−0.06	0.32
dystymi	0.19	−1.30	1.69	−0.51	−2.19	1.17	0.69	−0.71	2.10	−0.55	−2.14	1.04
GAD-score baseline	−0.08	−0.26	0.10	0.09	−0.12	0.29	nc	nc	nc	nc	nc	nc
Agoraphobia (MI-8)	0.78	−0.71	2.26	0.04	−1.63	1.71	1.35	−0.06	2.77	−0.07	−1.63	1.49
Social anxiety (SPIN-9)	1.22	−0.41	2.84	−0.38	−2.18	1.43	0.48	−1.02	1.97	1.01	−0.69	2.71
Insomnia	1.13	−0.49	2.75	0.25	−1.46	1.97	1.15	−0.36	2.66	0.26	−1.37	1.90
Having experienced presenting problem ≥ 6m	−0.28	−2.71	2.15	0.07	−2.45	2.59	−0.98	−3.13	1.17	−0.92	−3.20	1.36
Having experienced presenting problem at current level ≥ 6m	0.69	−0.95	2.33	0.77	−1.07	2.61	0.89	−0.64	2.42	0.68	−1.08	2.43
Cognitive factors												
Depressive cognitions (CCL-D)	1.55	−0.16	3.26	−0.86	−2.66	0.95	0.70	−0.79	2.18	0.43	−1.25	2.11
Anxious cognitions (ATQ)	−0.25	−1.84	1.33	0.39	−1.35	2.13	0.50	−0.97	1.98	−0.03	−1.67	1.62
Expect no recovery without treatment												
Dispositional factors	0.01	−1.55	1.56	1.27	−0.49	3.03	0.74	−0.68	2.16	0.54	−1.06	2.14
Low self-control	0.04	−1.56	1.64	0.71	−1.20	2.62	1.16	−0.31	2.63	0.78	−1.11	2.67
Low mindfulness												
Mental health care factors	0.13	−1.41	1.67	−0.35	−2.07	1.37	−0.43	−1.83	0.96	−0.25	−1.87	1.38
Previous treatment attempt	−0.98	−2.74	0.79	−0.36	−2.34	1.62	−0.48	−2.11	1.15	0.49	−1.36	2.33
Anxiolytic medication	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc	nc
Antidepressant medication	−0.08	−2.30	2.13	0.09	−2.26	2.45	1.26	−0.85	3.38	−0.54	−3.02	1.95
Sleep medication	−1.56	−3.61	0.48	−1.88	−4.15	0.40	−1.15	−3.04	0.74	−0.22	−2.43	2.00
Self-reported cause												
Relationship problems	−0.06	−1.68	1.56	−0.37	−2.20	1.47	0.42	−1.13	1.97	−1.28	−3.10	0.55
Family relations	0.62	−0.89	2.14	0.08	−1.69	1.85	0.36	−1.05	1.77	−0.48	−2.10	1.13
Eating problems	−1.11	−3.03	0.82	−0.12	−2.29	2.05	−0.27	−2.16	1.63	−1.14	−3.24	0.97
Work/school related prob.	−0.32	−1.89	1.25	0.95	−0.79	2.69	−0.28	−1.78	1.21	−0.04	−1.70	1.61
Overweight	−0.06	−2.50	2.38	0.97	−1.60	3.54	0.53	−1.57	2.64	1.15	−1.16	3.46
Somatic illness	0.17	−1.78	2.12	−0.24	−2.27	1.79	−0.49	−2.15	1.18	0.07	−1.91	2.05
Difficult childhood	1.08	−0.76	2.91	−0.32	−2.45	1.81	−0.54	−2.27	1.18	0.86	−1.28	3.00
Bullying	1.78	−0.19	3.74	1.79	−0.71	4.29	1.32	−0.45	3.10	−0.29	−2.59	2.01
Site												
Sandnes	−0.39	−1.90	1.12	−1.55	−3.31	0.20	0.21	−1.18	1.60	0.58	−1.01	2.17

Results from generalized linear mixed models with robust estimation, based on the available data from all participants (n = 678). Independent variable: Potential moderator of treatment outcome. Dependent variable; change in remission status from baseline to 6- and 12- months. The presented estimates are the coefficients of the 3-way interaction (log-odds scale). Bold: model giving p-value of interaction "moderator variable*treatment type*time-point of interest" <0.01. All potential moderator variables measured at baseline; nc = no convergence.

Hence, the size of the moderating effect in this sample had to be large in order to become statistically significant. Low power is typically associated with inflated effect sizes and can distort research findings due to random and systematic errors. Therefore, the results for anxiolytic medication found in this study should be interpreted with caution. Clinically, our finding can be understood by the notion that when psychological symptoms are kept low by the anxiolytic medication, this in turn suppresses emotional engagement, which is considered a key

principle for CBT to work. Alternatively, some might rely on the medication to work, making them less motivated to engage in the CBT treatment. Yet, we have been unable to find literature to support our finding, and indeed some research indicates that the use of anxiolytic medication does not modify effect of CBT (CBT for social phobia) (Eskildsen et al., 2010). A larger future study will be needed to show whether this result is just an anomaly or not.

6.1. Strengths and limitations

The main strengths of the current study are the use of a randomized controlled study design, the long follow-up time, and the relatively large sample size. This contrast the bulk trials in the field; many studies have strict inclusion criteria and minimal power to examine treatment effects across groups (Porter & Chambless, 2015). The relatively large sample may have reduced the risk of chance findings, which is known to be more common in smaller trials (Porter & Chambless, 2015). At the same time, we did not reach the target N (Knapstad et al., 2020) and experienced a higher attrition-rate than anticipated, particularly at 12 months follow-up (Sæther et al., 2020). This loss in statistical power reduced the probability of identifying relevant moderating effects, but our findings can still be of great use for future meta-analyses. The attrition rate also increased the risk of bias and implies that the results of our study should be interpreted with caution. It should be noted though that several sensitivity analyses conducted in the primary evaluation of the RCT (Knapstad et al., 2020) indicated that accounting for differential attrition and other missing data not-at-random scenarios did not substantially alter the results. Naturally, it is not clear whether these results generalize to the moderator analyses of the present study, but it was considered beyond the scope of this study to test these more complex models in the context of the moderator analyses. The planned linkage of the collected RCT data to national registries will provide near complete information on some outcome variables of interest (e.g. employment, medication use), and will enable us to study the moderators of trial effectiveness on registry-based outcomes with greater statistical power and without attrition bias (Knapstad et al., 2020).

Other limitations include non-blinding of therapists and clients with regard to treatment assignment, and the fact that outcome data was based on self-report rather than more objective data (registry, diagnostic interview).

Finally, this study focuses on client characteristics at baseline as moderators of treatment effect. Other moderators might also be of importance. For instance, variables associated with the organization of services, such as percentage of referrals treated, have been shown to predict clinical outcomes in IAPT (Clark et al., 2018). In order to study the effect of service level variables, a sufficient number of care sites must be included in the study. Such variables could therefore not be investigated here.

6.2. Conclusion

Individuals using anxiolytic medications experienced less effect of PMHC compared to TAU, although this result should be interpreted with caution due to the low number of anxiolytic users in the sample. Apart from this, PMHC worked better than TAU, and equally so, across demographic variables, lifestyle variables, health-related variables, mental health care related variables, cognitive factors, and reported cause of problems. Our findings indicate that a wide and greatly differing population of individuals with symptoms of anxiety and/or mild to moderate depression experience better effect of PMHC than of TAU.

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CRediT authorship contribution statement

Solbjørg M.M. Sæther: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Marit Knapstad:** Conceptualization, Methodology, Investigation, Writing – review & editing, Project administration, Funding acquisition. **Nick Grey:** Writing – review & editing. **Otto R.F. Smith:** Conceptualization, Methodology, Software, Investigation, Resources, Data curation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

None.

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Further reading

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