Enhanced self-efficacy after a self-management programme in pituitary disease: a randomized controlled trial

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Abstract

Context: Patients with pituitary disease report impairments in Quality of Life (QoL) despite optimal biomedical care. Until now, the effects of a self-management intervention (SMI) addressing psychological and social issues for these patients and their partners have not been studied.

Objective: To examine the effects of a SMI i.e. Patient and Partner Education Programme for Pituitary disease (PPEP-Pituitary).

Design and subjects: A multicentre randomized controlled trial included 174 patients with pituitary disease, and 63 partners were allocated to either PPEP-Pituitary or a control group. PPEP-Pituitary included eight weekly sessions (90 min). Self-efficacy, bother and needs for support, illness perceptions, coping and QoL were assessed before the intervention (T0), directly after (T1) and after six months (T2). Mood was assessed before and after each session.

Results: Patients in PPEP-Pituitary reported improved mood after each session (except for session 1). In partners, mood only improved after the last three sessions. Patients reported higher self-efficacy at T1 ($P=0.016$) which persisted up to T2 ($P=0.033$), and less bother by mood problems directly after PPEP-Pituitary ($P=0.01$), but more bother after six months ($P=0.001$), although this increase was not different from baseline ($P=0.346$). Partners in PPEP-Pituitary reported more vitality ($P=0.008$) which persisted up to T2 ($P=0.034$). At T2, partners also reported less anxiety and depressive symptoms ($P\leq0.014$).

Conclusion: This first study evaluating the effects of a SMI targeting psychosocial issues in patients with pituitary disease and their partners demonstrated promising positive results. Future research should focus on the refinement and implementation of this SMI into clinical practice.

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Introduction

Patients with long-term biochemical remission of pituitary disease report impairments in Quality of Life (QoL) (1). Until now, little attention has been paid to interventions aiming at improving psychosocial aspects of QoL (2). The need for a psychosocial intervention in patients with pituitary disease was supported by results of recent focus group conversations reporting unmet needs regarding psychosocial care. Other reported issues in these focus groups were fatigue, increased sensitivity to stress, anxiety, depressive symptoms, difficulties

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communicating about the disease and a reduced social network (3). In addition, a focus group study in partners of patients with pituitary disease reported that partners sometimes became annoyed by the tiredness and mood swings of their ill partner. Some partners felt they had to take on extra responsibilities at home (e.g., taking care of the children). They were aware of the negative consequences of the disease on their family, but they felt unable to cope emotionally or physically (4).

For patients with other chronic somatic diseases, psychosocial interventions, i.e., self-management interventions (SMIs), have been developed aiming to improve well-being of patients (5). Self-management is defined by Barlow *et al*. as 'the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and life style changes inherent to living with a chronic condition. Efficacious self-management encompasses the ability to monitor one's condition and to affect the cognitive, behavioural and emotional responses necessary to maintain a satisfactory QoL' (6). SMIs in several chronic conditions (e.g., asthma, diabetes and arthritis) have demonstrated a positive effect on well-being of patients (6). Martire *et al*. (2010) demonstrated that couple-oriented interventions were more efficacious than psychosocial interventions that only included the patient or usual care (7). Although SMIs for any chronic disease may be based on general theoretical constructs, the composition and focus of the SMI depends on the type of disease and self-management aims, e.g., focus on the prevention of exacerbations in asthma, or focus on lifestyle habits in diabetes (8).

There are only a few studies evaluating the effect of a SMI in patients with neuroendocrine disease. Martinez-Momblan *et al*. evaluated the effects of a 9-month educational nursing programme (5 visits) for patients with Cushing's syndrome in a randomized controlled trial ($n = 61$). This educational programme included knowledge on Cushing's syndrome, comorbidities, treatment, general management and autonomy in healthy lifestyles. Patients who followed this educational programme reported better disease-specific QoL, reduced pain, improved physical activity and a healthier lifestyle, compared to controls (9). Furthermore, Haugland *et al*. evaluated a 26-week educational programme in patients undergoing medical treatment for a neuroendocrine tumour in the gastrointestinal tract ($n = 37$), and demonstrated improvement in physical components of QoL, reduced stress and increased self-efficacy (10). These available SMIs focus primarily on education about Cushing's disease and its treatment and management (9) or education in patients with a neuroendocrine tumour in the gastrointestinal tract (10). Currently, a SMI for patients with pituitary disease and their partners addressing the psychosocial consequences and management of these consequences of the disease is lacking.

Considering the patient- and partner-reported need for psychosocial care in pituitary disease, and the current lack of a SMI addressing psychological and social issues in these patients and their partners, the aim of the present study was to evaluate the effects of such a SMI in a randomized controlled trial in a large cohort of patients with pituitary disease and their partners.

Participants and methods

Design

This multicentre two-arm randomized controlled trial was initiated by researchers at the Department of Medicine of the Leiden University Medical Centre (LUMC). Patients were randomized for the SMI or the control group; 1:1 randomization was performed by the first author (CDA). Partners of patients who agreed to participate ($n = 63$) were allocated to the same condition as their ill partner.

For ethical reasons, patients and partners who were randomized to the control group were also offered the SMI after the last measurement. The medical ethical committee of the LUMC approved the study, and written informed consent was obtained from all participants.

Participants

The recruitment was coordinated by the outpatient departments of Medicine of the LUMC and the Radboud University Medical Centre (Radboudumc). Exclusion criteria were: <18 or >75 years of age since older patients might have more comorbidity, current psychological treatment, current intensive medical treatment (e.g., radiotherapy, recovery from surgery) and psychiatric illness. A total number of 931 patients (and their partner when applicable) were informed about the study and were invited to participate (i.e., 462 from the LUMC; 469 from the Radboudumc). Reasons for not participating in the study were not speaking Dutch, not feeling comfortable talking in a group, too time-consuming, burden too large (physically and/or mentally), not able to come due to other obligations (e.g. work, staying abroad, pregnancy, surgery), long travel distance, not perceiving problems and no need for support (anymore), because patients already receive psychological counselling or previously received

it, or learned to cope with their illness by themselves. One hundred and eight patients (LUMC) and 80 patients (Radboudumc) agreed to participate. From the initial 188 incorporated patients, fourteen patients (7%) did not fill out the questionnaires. Therefore, a total number of 174 patients were included (Fig. 1).

Development of the SMI

The SMI was based on the standardized Patient (and Partner) Education Programme initially developed for Parkinson's disease (PEPP), and evaluated in seven European countries (11, 12) including the Netherlands (13, 14, 15), and is currently operational in patient care. The programme was then adapted for Huntington's disease (PEP-HD) (16) and was further developed and clinically tested in patients with chronic disease with psychiatric comorbidity (17). Since the self-management techniques seemed to be generally applicable, the programme has recently been developed for patients with chronic disease in general (PPEP4ALL) (18). PPEP4ALL addresses psychological and social issues related to all chronic disease and uses techniques from cognitive behavioural therapy such as cognitive restructuring, systematic relaxation training, situational behavioural analyses and training in social skills.

In order to assess whether PEPP was also suitable for patients with pituitary disease, focus group conversations in patients with pituitary disease were performed (3). The focus group guided us in laying the priorities and preferred options (e.g. fatigue, cognitive complaints and problems with sexuality) within the PPEP4ALL. Based on these results, we hypothesized that PEPP/PPEP4ALL (Fig. 2) would also be of relevance for patients with pituitary disease and their partners (when applicable). Then, we pilot tested it in 28 patients and 6 partners. Patients and partners reacted positively to the programme. Therefore, we decided to evaluate PPEP4ALL with the preferred options: fatigue, cognitive complaints and problems with sexuality. It was not necessary to drop any of the other components of PPEP4ALL, and considering the patient group, we named it the 'Patient

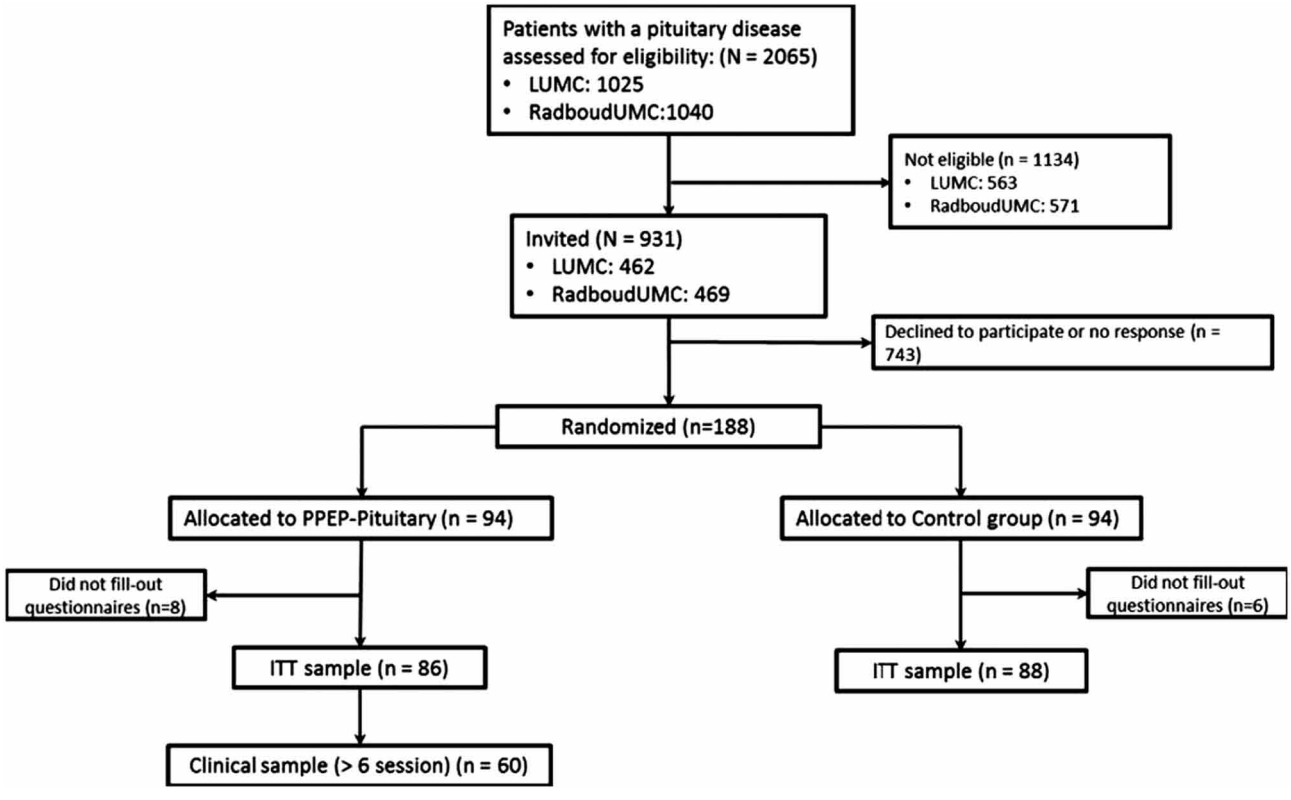

Figure 1
Flow chart of patients.

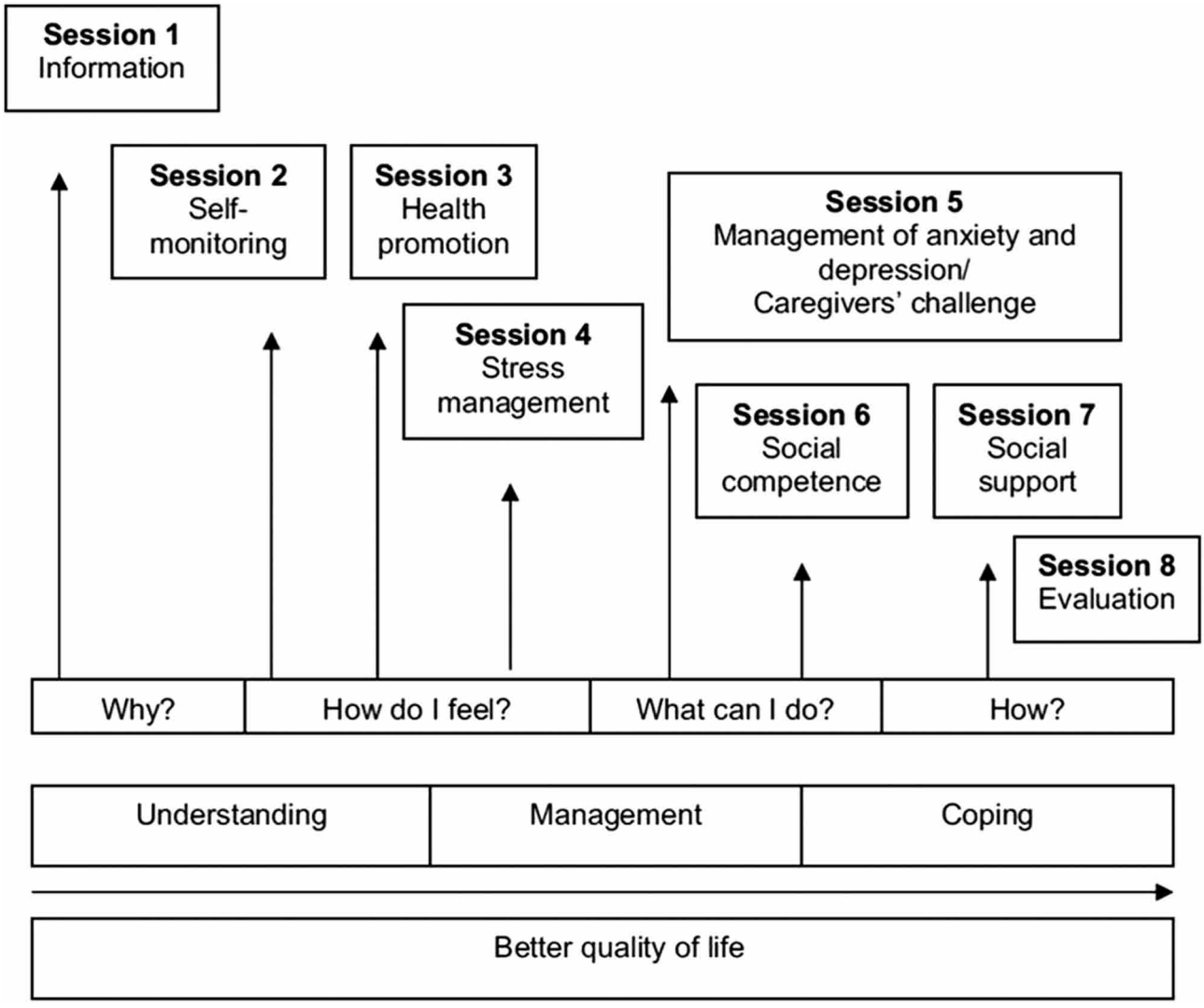

Figure 2
The themes and aims of the PPEP-Pituitary.

and Partner Education Programme for Pituitary disease (PPEP-Pituitary)'.

PPEP-Pituitary

PPEP-Pituitary includes self-management components of potential relevance for pituitary disease, i.e., fatigue management, stress management, dealing with anxiety and depression, and communication training (Supplementary Data 1, see section on supplementary data given at the end of this article). The programme consisted of eight weekly sessions of 90 min moderated by psychologists and medical social workers. Patients and partners participated separately and from their own perspective, in groups of 5–7 participants at the LUMC or at the Radboudumc. The same one or two trainers guided each group for 8 weeks (CDA, SM, RM, NF, MP-D, RG, JL, MS and MV). All trainers were trained in/experienced with the PPEP/PPEP4ALL, and followed a one-day training to get familiar with the disease-specific focus on pituitary disease.

Procedure

All included participants were asked to fill out questionnaires prior to the programme (T0). Next, participants in PPEP-Pituitary followed the 8-week SMI, while the participants in the control group were invited

for a single (optional) information meeting in week 4 or 5. For the formation of the patient groups, groups were stratified by disease in 3 groups i.e., 1) Cushing's disease (CD), 2) acromegaly or 3) prolactinoma/non-functioning pituitary adenoma (NFA)/FSH-adenoma/craniopharyngioma/hypopituitarism due to other causes. Partners in PPEP-Pituitary were not stratified by pituitary disease of their partner. Participants were asked to fill out the questionnaires again after the 8-week intervention (T1) and 6 months later (T2). Demographic characteristics (i.e., age, gender, marital status and education) and medication use were assessed by a self-report. Clinical characteristics of patients (e.g., type of pituitary disease and duration of follow-up) were derived from medical records.

Measures

For an overview of the used measures, see Table 1.

Based on the preference of participants, questionnaires were sent by email (online survey) or by regular mail to increase the response rate. One hundred and nine patients and 53 partners completed the questionnaires online, and 65 patients and 10 partners by postal survey. Previous research demonstrated that paper-and-pencil and online surveys do not lead to different results (19). Partners completed the same questionnaires except the LBNQ-Pituitary, the EQ-5D, the IPA and the disease-specific QoL questionnaires (i.e., AcroQoL, CushingQoL). In addition, patients and partners in the PPEP-Pituitary group were asked to fill out an evaluation form about PPEP-Pituitary (Supplementary Data 2).

Statistical analyses

Data were analysed using PASW Statistics version 20.0.0 (SPSS Inc.). To check the normality of data, the Kolmogorov–Smirnov test was used. Demographic characteristics and the baseline scores (Supplementary Data 3) were compared using independent sample t-test and chi-square test when data were normally distributed and by using Mann–Whitney U test and Fisher's exact when data were not normally distributed. To compare pre- and post-session mood ratings, paired sample t-tests were used. A linear mixed model with random participant effect, and fixed time and group effects, as well as group by time interactions measured the effects of the programme. The linear mixed model enables accommodating missing data points (38), and corrects for potential baseline differences. The effects of the programme were evaluated following intention to treat (ITT) principles, including all participants. Although ITT analysis is the golden standard for analysing an RCT, it is also considered conservative (39) since not all participants in PPEP-Pituitary attended all sessions. Therefore, the *post hoc* analyses comprised the clinical sample analyses including only the patients that attended at least six sessions, since this is the minimum amount of sessions to consider that someone completed PPEP-Pituitary, and since this situation will be more similar to the clinical situation. This analysis was performed using the same linear mixed model. The data from the evaluation were analysed descriptively. Due to the explorative nature of this study, the level of significance was set at $P<0.05$. However, to take into account the effect of multiple testing, a Bonferroni correction was applied, and a level of significance of $P<0.005$ was also used.

Results

Baseline characteristics

Of the 188 patients incorporated, 94 patients were allocated to PPEP-Pituitary and 94 patients to the control group. Fourteen patients (8 in PPEP-Pituitary and 6 in the control group) did not complete any of the questionnaires and were not included in the ITT analysis. Therefore, a final number of 174 patients were included in the ITT analysis (PPEP-Pituitary: $n = 86$ and control group: $n = 88$). Seventy per cent of the patients ($n = 60$) in PPEP-Pituitary attended at least 6 sessions i.e., the clinical sample.

From this clinical sample, 12 patients (20%) attended 6 sessions, 24 patients (40%) attended 7 sessions and another 24 patients (40%) attended all 8 sessions.

From the patients in the control group, 42 patients (48%) attended the optional information meeting. Furthermore, 70% of the patients were married or in a relationship ($n = 122$), and 63 partners (52%) were willing to participate. Twenty-five partners were in the PPEP-Pituitary group, and 38 partners were in the control group. From the partners in PPEP-Pituitary, 52% ($n = 13$) attended at least 6 sessions (i.e., the clinical sample). From the partners in the control group, 16 (42%) attended the optional information meeting (Table 2).

Mood changes after each PPEP-Pituitary session

Patient reported mood improved significantly after each session (all $P < .001$), except for session 1. Partners' mood

Table 1 Measures.

Questionnaire	Outcome	Subscales	Number of items	Range	Measurement time	Participants
Visual analogue scale-Mood (VAS-Mood)	Mood	1	1	0–100, 0 = extremely bad mood to 100 = extremely good mood	Before and after each session	Patients and partners in PPEP-Pituitary
General self-efficacy scale (GSE) (20, 21)	Self-efficacy	1	10	10–40, ↑scores indicate ↑self-efficacy	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
Leiden bother and needs questionnaire for pituitary diseases (LBNQ-Pituitary) (22)	Bother and need for support	5: Mood, Negative illness perceptions, Issues in sexual functioning, Physical and cognitive complaints, Issues in social functioning	26	0–100, ↑scores indicate ↑bother and need for support	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
Brief Illness perception questionnaire (B-IPQ) (23)	Illness perceptions	8: Consequences, Personal control, Timeline, Treatment control, Identity, Concern, Coherence, Emotional response	8	0–10, 0=not at all to 10=very much	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
the Utrecht coping list (UCL) (24)	Coping strategies	7: Active coping, Seeking distraction, Avoiding, Seeking social support, Passive coping, Expressing emotions, Fostering reassuring thoughts	47	Active coping (7–28) Seeking distraction (8–32), Avoiding (8–32), Seeking social support (6–24), Passive coping (7–28), Expressing emotions (3–12), Fostering reassuring thoughts (5–20).↑scores indicate ↑more frequent performance of that coping	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
Impact on participation and autonomy (IPA) (25)	Participation and autonomy	5: family role, autonomy outdoors, autonomy indoors, social life and relationships, work and education	32	0–4, ↓scores indicate ↑participation and autonomy	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
EuroQoL-5D (EQ-5D) (26)	QoL	5: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression	5	1–3, ↑scores indicate ↓QoL	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
Short form 36 (SF-36) (27, 28)	QoL	9: physical functioning, social functioning, role limitation (physical), role limitation (emotional), mental health, vitality, pain, general health perception, general perception of change in health	36	0–100, ↑scores indicate ↑QoL	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group

Continued)

Table 1 Continued.

Questionnaire	Outcome	Subscales	Number of items	Range	Measurement time	Participants
Multidimensional fatigue inventory (MFI-20) (29)	Fatigue	5: General fatigue, Physical fatigue, Reduced activity, Reduced motivation, Mental fatigue	20	0–20, ↑scores indicate ↑fatigue	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
Hospital anxiety and depression scale (HADS) (30, 31)	Anxiety and depression	2: anxiety, depressive symptoms	14	0–21, ↑scores indicate ↑anxiety/ depressive symptoms	T0, T1, T2	Patients and partners in PPEP-Pituitary and control group
AcroQoL (32, 33, 34)	Disease-specific QoL	3: physical, psychological-appearance, psychological-personal relations	22	0–100, ↓scores indicate ↓QoL	T0, T1, T2	Patients with acromegaly in PPEP-Pituitary and control group
CushingQoL (35, 36, 37)	Disease-specific QoL	2: Psychosocial issues, physical problems	12	0–100, ↓scores indicate ↓QoL	T0, T1, T2	Patients with CD in PPEP-Pituitary and control group

improved only after sessions 6, 7 and 8 (all $P \leq .030$) (Table 3).

Effects of intervention: Intention to treat analysis

Self-efficacy

For patients a significant interaction was found for self-efficacy (GSE) ($P = 0.002$), with PPEP-Pituitary reporting more self-efficacy compared to controls (difference 1.35, $P = 0.016$) (T1 vs T0), which persisted up to the 6-month follow-up (difference 1.74, $P=0.033$) (T2 vs T0). No significant difference in self-efficacy was observed in partners (Table 4).

Bother and needs for support

An interaction was found for being bothered by mood problems (LBNQ-Pituitary) ($P=0.002$) with PPEP-Pituitary, reporting to be less bothered by mood problems compared to controls (difference −6.27, $P=0.010$) (T1 vs T0). At T2 relative to T1, PPEP-Pituitary reported more bother by mood problems compared to controls (difference 8.71, $P=0.001$), but this increase at T2 was not significantly different from baseline (difference 2.44, $P=0.346$). Furthermore, an interaction was observed on the total score of the bothered by items of the LBNQ-Pituitary ($P=0.028$), with PPEP-Pituitary reporting more overall bother (total score) at T2 relative to T1 compared to controls (difference 4.58, $P = 0.008$), but this increase at T2 was also not significantly different from baseline (difference 2.20, $P = 0.219$).

Illness perceptions

No significant differences in illness perceptions (B-IPQ) were observed for patients over time.

For partners, an interaction was found for perceived treatment control ($P=0.025$), with PPEP-Pituitary perceiving more treatment control compared to controls (difference 3.12, $P=0.008$) (T2 vs T1), but this increase at T2 was not significant from baseline (difference 1.43, $P=0.230$)

Coping

No significant differences in coping styles (UCL) were found for patients and partners over time.

Participation and autonomy

No significant differences in participation and autonomy (IPA) were found for patients over time.

Quality of life

For patients, no significant differences were found for QoL (i.e., EQ-5D, SF-36, MFI-20, HADS, CushingQoL, AcroQoL).

Table 2 Demographic variables of patients and partners.

	Patients ($n=174$)			**Partners** ($n=63$)		
	PPEP-Pituitary group ($n=86$)	Control group ($n=88$)	*P* value	PPEP-Pituitary group ($n=25$)	Control group ($n=38$)	*P* value
Gender (M/F)	33/53	31/57	0.667	17/8	18/20	0.107
Age (years)	52.7 (11.9)	53.4 (12.7)	0.600	55.7 (10.6)	58.9 (9.9)	0.298
Condition/condition of ill partner, *n* (%)			0.866			0.835
Cushing's disease	21 (24%)	19 (22%)		7 (28%)	6 (16%)	
Acromegaly	12 (14%)	10 (11%)		5 (20%)	7 (18%)	
Prolactinoma	18 (21%)	20 (23%)		3 (12%)	9 (24%)	
NFA	27 (31%)	30 (34%)		8 (32%)	13 (34%)	
FSH-adenoma	0 (0%)	1 (1%)		0 (0%)	0 (0%)	
Craniopharyngioma	5 (6%)	3 (3%)		2 (8%)	0 (0%)	
Hypopituitarism due to other causes	3 (4%)	5 (6%)		0 (0%)	1 (3%)	
Education, *n* (%)			0.219			0.238
Low	20 (23%)	27 (31%)		4 (16%)	13 (34%)	
Medium	23 (27%)	29 (33%)		11 (44%)	11 (29%)	
High	42 (49%)	32 (36%)		10 (40%)	14 (37%)	
Unknown	1 (1%)	0 (0%)		0 (0%)	0 (0%)	
Marital status, *n* (%)			0.027			NA
Single	16 (19%)	11 (13%)		0 (0%)	0 (0%)	
Relationship/marriage	55 (64%)	67 (76%)		25 (100%)	38 (100%)	
Divorced	8 (9%)	9 (10%)		0 (0%)	0 (0%)	
Widow	7 (8%)	0 (0%)		0 (0%)	0 (0%)	
Unknown	0 (0%)	1 (1%)		0 (0%)	0 (0%)	
Pituitary surgery, *n* (%)	60 (70%)	63 (72%)	0.792	NA	NA	NA
Radiotherapy, *n* (%)	19 (22%)	21 (24%)	0.781	NA	NA	NA
Duration since diagnosis (years)	11.7 (10.8)	13.0 (13.5)	0.884	NA	NA	NA
Hypopituitarism, *n* (%)						
ACTH	40 (47%)	50 (57%)	0.174	NA	NA	NA
TSH	42 (49%)	46 (52%)	0.650	NA	NA	NA
LH/FSH	40 (47%)	41 (47%)	0.992	NA	NA	NA
GH	36 (42%)	40 (46%)	0.633	NA	NA	NA
ADH	6 (7%)	8 (9%)	0.608	NA	NA	NA

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For partners, an interaction was found for vitality (SF-36) ($P=0.026$), with PPEP-Pituitary reporting more vitality compared to controls (difference 14.03, $P=0.008$) (T1 vs T0), which persisted up to the 6-month follow-up (difference 15.45, $P=0.034$) (T2 vs T0). Furthermore, an interaction was found for anxiety (HADS) ($P=0.035$), with PPEP-Pituitary reporting less anxiety at T2 relative to T0 (difference –2.65, $P=0.014$). In addition, an interaction was found for depressive symptoms (HADS) ($P = 0.012$), with PPEP-Pituitary reported less depressive symptoms at T2 relative to T0 (difference –3.47, $P = 0.003$), as well as at T2 relative to T1 (difference –2.60, $P = 0.012$). Finally, an interaction was found for the HADS total score ($P = 0.005$), with PPEP-Pituitary reporting a lower total HADS score at T2 relative to T0 (difference –6.51, $P = 0.002$), as well as at

Table 3 Pre- and post-session mood-VAS ratings (range 0–100) of patients and partners. Data are presented as mean (s.d.).

	Patients ($n=54$–70)			**Partners** ($n=10$–15)		
Session	Before session	After session	*P* value	Before session	After session	*P* value
1	69.91 (13.14)	70.94 (12.09)	0.384	71.15 (10.24)	71.92 (12.17)	0.776
2	68.03 (14.83)	74.32 (12.27)	**<0.001***	72.00 (9.02)	73.13 (10.46)	0.687
3	65.27 (14.48)	73.11 (12.41)	**<0.001***	68.75 (14.32)	74.83 (9.11)	0.090
4	68.96 (12.93)	75.39 (10.32)	**<0.001***	70.58 (8.37)	73.42 (7.83)	0.055
5	68.77 (10.55)	73.55 (11.94)	**<0.001***	73.60 (8.51)	73.40 (7.90)	0.920
6	67.96 (12.81)	73.18 (11.22)	**<0.001***	73.00 (6.95)	77.17 (6.46)	**0.005***
7	70.76 (10.02)	75.25 (9.43)	**<0.001***	75.08 (7.32)	78.15 (7.03)	**0.025***
8	70.65 (10.48)	77.93 (9.33)	**<0.001***	73.08 (6.09)	77.54 (7.66)	**0.030***

*$P<0.05$.

Table 4 Changes in the outcome measures in patients and partners (ITT sample).

	Patients (n = 174)				**Partners** (n = 63)			
	ΔPPEP-control T0-T1	ΔPPEP-control T1–T2	ΔPPEP-control T0–T2	P value group × time	ΔPPEP-control T0–T1	ΔPPEP-control T1–T2	ΔPPEP-control T0–T2	P value group × time
LBNQ-Pituitary								
Bother by								
Mood problems	−6.27*	8.71#	2.44	0.002#	NA	NA	NA	NA
Negative illness perceptions	−2.14	4.03	1.89	0.176	NA	NA	NA	NA
Issues in sexual functioning	2.92	2.02	4.94	0.272	NA	NA	NA	NA
Physical and cognitive complaints	−0.77	4.66	3.89	0.127	NA	NA	NA	NA
Issues in social functioning	−3.06	1.54	−1.52	0.347	NA	NA	NA	NA
Total score	−2.37	4.58*	2.20	0.028*	NA	NA	NA	NA
Need for support								
Mood problems	−4.69	8.26	3.57	0.073	NA	NA	NA	NA
Negative illness perceptions	−1.92	6.33	4.41	0.131	NA	NA	NA	NA
Issues in sexual functioning	4.09	2.03	6.12	0.309	NA	NA	NA	NA
Physical and cognitive complaints	0.79	5.85	6.63	0.077	NA	NA	NA	NA
Issues in social functioning	−4.38	2.75	−1.64	0.199	NA	NA	NA	NA
Total score	−1.65	5.17	3.53	0.078	NA	NA	NA	NA
EQ-5D								
Mobility	−0.07	0.04	−0.03	0.509	NA	NA	NA	NA
Self-care	0.01	0.01	0.02	0.904	NA	NA	NA	NA
Daily activity	−0.15	0.05	−0.10	0.167	NA	NA	NA	NA
Pain	−0.03	−0.04	−0.06	0.781	NA	NA	NA	NA
Mood	−0.06	−0.05	−0.10	0.408	NA	NA	NA	NA
VAS	−3.63	0.84	−2.79	0.352	NA	NA	NA	NA
SF-36								
Physical functioning	3.45	−4.82	−1.37	0.211	1.95	7.66	9.62	0.302
Social functioning	2.08	−1.92	0.17	0.722	3.04	14.71	17.75	0.084
Role limitations-Physical	2.39	−12.03	−9.64	0.203	−6.87	29.52	22.65	0.111
Role limitations-Emotional	−3.31	3.19	−0.12	0.831	−15.99	30.92	14.93	0.156
Mental Health	1.63	−2.18	−0.55	0.480	−6.26	11.61	5.35	0.330
Vitality	3.14	−3.43	−0.29	0.284	14.03*	1.42	15.45*	0.026*
Pain	−2.62	−0.79	−3.40	0.505	−4.42	9.57	5.15	0.281
General Health	−0.62	3.77	3.14	0.179	2.82	−2.66	0.17	0.729
Health change	0.03	−7.79	−7.50	0.234	12.72	8.74	21.46	0.083
MFI-20								
General fatigue	−0.37	0.40	0.03	0.441	1.18	−0.58	0.61	0.215
Physical fatigue	0.20	−0.42	−0.22	0.389	−0.13	−0.10	−0.23	0.932
Reduced activity	−0.20	0.27	0.07	0.731	0.44	−0.70	−0.26	0.700
Reduced motivation	0.07	0.02	0.10	0.961	−0.40	−0.48	−0.88	0.373
Mental fatigue	0.37	1.44	1.82	0.107	−0.16	−0.88	−1.04	0.152
HADS								
Anxiety	−0.09	0.07	−0.02	0.976	−0.91	−1.74	−2.65*	0.035*
Depression	−0.36	0.99	0.63	0.056	−0.87	−2.60*	−3.47#	0.012*
Total score	−0.50	1.20	0.71	0.221	−1.97	−4.54*	−6.51#	0.005#
B-IPQ								
Consequences	0.03	0.50	0.54	0.221	0.64	−0.23	0.41	0.770
Timeline	−0.28	0.27	−0.01	0.662	−0.42	0.38	−0.04	0.712
Personal control	−0.46	−0.22	−0.68	0.430	1.07	0.45	1.53	0.504
Treatment control	−0.11	0.43	0.32	0.547	−1.69	3.12*	1.43	0.025*
Identity	−0.25	0.07	−0.18	0.773	−0.24	0.79	0.55	0.589
Coherence	−1.12	0.47	−0.65	0.491	−1.13	0.29	−0.83	0.142
Emotional representations	0.68	0.05	0.73	0.133	0.29	0.57	0.86	0.737
Concerns	−0.51	0.77	0.26	0.108	−0.63	1.30	0.67	0.359
UCL								
Active coping	−0.26	−0.27	−0.53	0.808	1.25	0.84	2.09	0.628
Seeking distraction	0.99	−0.16	0.83	0.348	−0.88	2.48	1.60	0.191
Avoiding	0.31	0.27	0.58	0.711	0.35	0.36	0.71	0.834

(Continued)

Table 4 Continued.

	Patients (n = 174)				Partners (n = 63)			
	ΔPPEP-control T0-T1	ΔPPEP-control T1–T2	ΔPPEP-control T0–T2	P value group × time	ΔPPEP-control T0–T1	ΔPPEP-control T1–T2	ΔPPEP-control T0–T2	P value group × time
Seeking social support	−0.48	0.21	−0.26	0.544	0.71	−1.63	−0.92	0.501
Passive coping	0.41	0.64	1.05	0.281	−0.96	0.20	−0.76	0.503
Expression of emotions	0.07	−0.07	0.00	0.944	−0.35	0.38	0.03	0.771
Fostering reassuring thoughts	−0.16	−0.04	−0.20	0.907	−1.31	1.63	0.33	0.111
GSE								
Total score	1.35*	0.39	1.74*	0.020*	0.45	−0.77	−0.32	0.830
IPA								
Autonomy indoors	−0.01	.12	0.11	0.247	NA	NA	NA	NA
Family role	−0.00	−0.03	−0.03	0.956	NA	NA	NA	NA
Autonomy outdoors	−0.08	0.01	−0.07	0.657	NA	NA	NA	NA
Social life and relationships	0.06	−0.34	0.02	0.694	NA	NA	NA	NA
Work and education	−0.07	0.26	0.19	0.869	NA	NA	NA	NA
CushingQoL†								
Psychosocial issues	4.16	−4.36	−0.20	0.337	NA	NA	NA	NA
Physical problems	3.68	−1.06	2.63	0.666	NA	NA	NA	NA
Total score	3.83	−4.07	−0.24	0.304	NA	NA	NA	NA
AcroQoL‡								
Physical score	3.32	−15.64	−12.31	0.101	NA	NA	NA	NA
Psychological-appearance	−6.72	−2.05	−8.77	0.504	NA	NA	NA	NA
Psychological-personal relations	5.65	−18.17	−12.52	0.124	NA	NA	NA	NA
Total score	1.25	−12.16	−10.91	0.149	NA	NA	NA	NA

*P<.05, #P<.005. †Only patients with Cushing's disease; ‡Only patients with acromegaly. LBNQ-Pituitary, Leiden Bother and Needs Questionnaire for pituitary diseases; EQ-5D, EuroQoL-5D; SF-36, Short Form 36; MFI-20, Multidimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; B-IPQ, Brief Illness Perception Questionnaire; UCL, Utrecht Coping List; GSE, General Self-Efficacy Scale; IPA, Impact on Participation and Autonomy questionnaire. P value group x time: significance of the interaction i.e., PPEP-Pituitary vs. control group x time point (i.e., baseline (T0), directly after PPEP-Pituitary (T1), 6 months follow-up (T2)).

T2 relative to T1 (difference −4.54, P=0.034) compared to controls.

Post hoc analysis: Clinical sample

All findings from the ITT analyses were also observed in the clinical sample analysis (Supplementary Data 4). However, some new findings were observed. Patients in PPEP-Pituitary reported a higher need for support for coping with negative illness perceptions (LBNQ-Pituitary) than those in controls (difference 7.88, P=0.018) at T2 relative to T1, but this increase at T2 was not significantly different from baseline (difference 3.14, P=0.422). Furthermore, PPEP-Pituitary reported a higher need for support for physical and cognitive problems (LBNQ-Pituitary) at T2 relative to T1 (difference 7.01, P=0.023), which was also significantly different from baseline (difference 7.43, P=0.036). PPEP-Pituitary reported more depressive symptoms (HADS) (difference 1.17, P=0.008) at T2 relative to T1, but this increase at T2 was not significantly different from baseline (difference 0.67, P=0.191). Partners in PPEP-Pituitary reported better social functioning (SF-36) at T2 relative to T1 (difference 19.70, P=0.023) compared to controls, which was also significantly different from baseline (difference 22.30, P=0.012).

Patient and partner evaluation

Of the patients who followed at least 6 sessions i.e., the clinical sample (n=60), 55 patients filled out the evaluation form (92%). Ninety-five per cent of the patients agreed that the exchange of experiences within the group was helpful, and over half of the patients (53%) reported a better understanding of the psychological effects of their disease. Two-thirds of the patients (67%) reported their expectations were fulfilled, and 84% would recommend the programme to other patients. All partners who followed at least 6 sessions (n=13) filled out the evaluation form. All partners agreed that the exchange of experiences was helpful; two-thirds of the partners (62%) reported a better understanding of the psychological effects of the disease. In 54% of the partners, their expectations were fulfilled, and 77% would recommend the programme to other partners.

Discussion

PPEP-Pituitary resulted in enhanced self-efficacy in patients which persisted after the 6-month follow-up. Perceived bother by mood problems decreased directly after PPEP-Pituitary, but returned to baseline level after 6-month follow-up. Partners reported more vitality immediately after PPEP-Pituitary, which was still present after 6 months. Partners also reported less anxiety and depressive symptoms after 6 months. Furthermore, mood improved after each session (except for session 1) in patients and after the last three sessions in partners.

Similar to the results of the SMI described by Haugland *et al.* (10), PPEP-Pituitary enhanced self-efficacy in patients. The term self-efficacy is described in the 'Social Cognitive Theory' of Bandura (40) and defined as the person's beliefs in his or her own capabilities to perform a certain action, in a certain environment. Following this model, behaviour is directly influenced by goals and self-efficacy expectations. In line with this model, several studies demonstrated that self-efficacy influences self-management behaviour (41, 42), as well as SMIs improving self-efficacy in patients with chronic disease (43, 44). For instance, Steed *et al.* evaluated a SMI which was based on the Social Cognitive Theory and demonstrated a positive effect on diabetes self-management behaviour, i.e., diabetes-specific diet, exercise and blood glucose monitoring (45). Following Bandura, self-efficacy can be increased and behaviour change is enhanced by four components: 1) mastery, which refers to the direct experience of success in performing a certain behaviour; 2) vicarious experience, which refers to modelling gained by successful behaviour of a person with whom one identifies (e.g., person with the same illness); 3) social persuasion e.g., encouragement from health professionals or members of the self-management group; and 4) reducing feelings of stress and altering negative emotional tendencies, since this may lead to reducing misinterpretations of physical symptoms or one's physical state (46). All four components were used in PPEP-Pituitary.

The results of the ITT analysis were further confirmed by the analyses including only participants that followed at least six sessions (i.e., the clinical sample). In the clinical sample analysis as well as in the ITT analysis, we observed that depressive symptoms and bother by mood problems increased during 6-month follow-up after PPEP-Pituitary, although not different from baseline levels. Furthermore, the clinical sample analysis complemented the ITT results by observations that patients reported a higher need for support for coping with negative illness perceptions and physical and cognitive problems. This finding might be explained by the fact that patients in PPEP-Pituitary learned skills to concretize/verbalize their healthcare needs, but also suggests that it might be useful to implement one or two additional refreshing/booster sessions during follow-up e.g., after 6 months or even over 12 months. On the other hand, partners reported an increase in social functioning 6 months after PPEP-Pituitary. This seems to indicate that partners needed time to implement the newly learned skills in their daily lives. It could also be that aspects of QoL improved in partners as a result of the improvement in self-efficacy in their ill partners.

In the present study, we did not observe any effects in patients on QoL, illness perceptions, coping, and autonomy and participation in different life domains. It should, however, be noted that there was a relatively long duration since diagnosis (i.e., PPEP-Pituitary: 12 years, control group: 13 years). It is conceivable that during this long period of living with the disease, patients and partners adapted to the consequences of the disease and/or already had received appropriate support, which may have limited the beneficial effects of our programme in improving psychosocial aspects. It should also be realized that although some aspects did not change during the time of the study, it could be that due to the learned psychosocial skills, patients and partners became more resilient to develop psychosocial morbidity, and future research into this area is warranted.

Due to the explorative nature of the present study, a large number of outcome parameters was used which could have led to a higher chance of type I error. After the *post hoc* Bonferroni correction, the effect on mood problems in patients and the effect on anxiety and depressive symptoms could still be observed. Furthermore, the large number of outcome parameters could also have influenced the response rate of the participants, considering the duration of filling out the questionnaires. In addition, it should be acknowledged that self-management is, by definition, largely implemented by the participants themselves with limited external supervision. For instance, it is not known how often participants practised the learned skills at home. This information could have provided additional insight into the effects of the program, and should therefore be taken into account in future research by, for instance, asking participants to keep up a diary. Another limitation related to research

in SMIs is that they largely rely on self-report measures. The measures used in this study were all validated, but probably not equal to direct observation.

A strength of the present study is the inclusion of both patients and partners, and the relatively large sample size. In addition, the variability in included centres as well as in trainers ($n=9$) (i.e. psychologist, medical social workers) increases the validity of the effect of PPEP-Pituitary. For future implementation of the programme in (other) medical centres, PPEP-Pituitary can be provided by psychologist and social workers, but also by other healthcare professionals such as endocrine nurses as long as they are trained in the principles of PPEP-Pituitary and have an appropriate level of knowledge about pituitary disease. Sixty-seven per cent of the patient reported that their expectation about PPEP-Pituitary were met. From the notes written on the evaluation forms it became apparent that patients would have liked more (practical, medical) information about their disease (i.e. bodily changes due to disease, medication, side-effects). Therefore, we are considering the invitation of an endocrine nurse to the first session to provide (practical) information about the disease. For future implementation of PPEP-Pituitary, it is very difficult to form separate groups per disease (i.e., CD, acromegaly, NFA/PRL), considering the low incidence of pituitary adenomas. Therefore, we postulate that groups can be formed with patients with different pituitary diseases. This seems to be suitable considering the overlapping symptoms (i.e. hypopituitarism, fatigue), but on the other hand, it can be imagined that for a patient it can be helpful to have at least one other person in the group with the same disease. Future implementation of PPEP-Pituitary groups of patients with different pituitary diseases can be formed, but with taking into account the distribution of diseases per group. Furthermore, a question that needs to be further clarified in future research is determining the best moment to offer PPEP-Pituitary during the disease process. We believe that directly after biomedical treatment is not the right moment, because patients need their time and energy to recover from treatment, but also because patients will not have a clear idea about the psychosocial consequences of the disease, making it difficult to work on during PPEP-Pituitary. On the other hand, when the programme is offered years after biomedical treatment, patient may have learned to cope with the consequences and/or they had to search for psychological care by themselves. Therefore, we postulated that the ideal moment to offer the programme will be between 6 and 12 months after biochemical remission. It is speculated that offering the programme at that time might lead to less healthcare consumption. Therefore, for future research, it would be interesting to assess the effects of PPEP-Pituitary in a clinical setting that also includes patients that have recently obtained a stable medical situation.

In conclusion, this first study about the effects of PPEP-Pituitary in a large cohort of patients with, on average, a relatively long duration since diagnosis demonstrated that PPEP-Pituitary enhances self-efficacy in patients, and their partners report better QoL in the long term. We postulate that implementing PPEP-Pituitary in clinical care will (at least partly) meet the current unmet needs regarding psychosocial care in patients with pituitary disease and their partners. For the implementation of PPEP-Pituitary, we are currently evaluating the approach to schedule one or two additional refreshing/booster sessions after 6 months or 12 months. Future research will need to focus on the implementation of this programme into clinical care trajectories.

Supplementary data

This is linked to the online version of the paper at http://dx.doi.org/10.1530/EJE-16-1015.

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