

Effectiveness of Lifestyle Modification on Health-Related Quality of Life among Women with Polycystic Ovary Syndrome

Abstract

Background: Polycystic Ovary Syndrome (PCOS) is the most common reproductive endocrine disorder, which affects approximately one in every five women at the age of reproduction. The first line of PCOS management is recommended to be lifestyle modification. This study aimed to evaluate the effectiveness of lifestyle modification on Health-Related Quality of Life (HRQoL) among women with PCOS. **Materials and Methods:** This quasi-experimental study was conducted on 124 women with PCOS recruited from the outpatient clinic at El-Takhassosy Obstetrics Hospital, Port-Said, Egypt, in 2021 and allocated to two groups; an educational group ($n = 62$) and a control group ($n = 62$). For data gathering, two tools were used; an interviewing questionnaire for assessing the demographic characteristics and a standardized HRQoL questionnaire. Healthy lifestyle modification educational sessions included nutritional guidelines for PCOS, physical exercise (walking for 30 min five times weekly), and instructions to relieve stress. **Results:** The mean (SD) of HRQoL score was 97.52 (8.75) in the educational group higher than the control group 87.32 (18.68) at 3 months postintervention and at 6 months postintervention; it reached 106.74 (11.53) in the educational group and 89.47 (22.14) in the control group. They were statistically significant after intervention (3 and 6 months) between studied groups (after 3 months was $t_{86,563} = 3.891, p < 0.001$ and after 6 months was $t_{91,826}$). **Conclusions:** Women with PCOS should receive structured education about lifestyle modification next to treatment to ensure improvement, particularly in patient-centered care.

Keywords: Education, health, quality of life, polycystic ovary syndrome

Introduction

Polycystic Ovary Syndrome (PCOS) is the most common reproductive endocrine disorder.^[1] Worldwide, the prevalence of PCOS is 6–13%. In Egypt, PCOS prevalence is estimated to be 13% in fertile women and 37.5% in secondary infertile women.^[2] Hirsutism, irregular menses, and failure to conceive were clinically presented with PCOS and negatively affected an individual's psychological well-being and interpersonal functioning.^[3] Moreover, it has several serious complications, such as endometrial hyperplasia and cancer due to high estrogen levels, hirsutism, and metabolic disorders because of the high androgen levels. In addition, insulin resistance causes hyperinsulinemia, which stimulates the ovary to secrete large amounts of androgens. As a result, having high androgen levels for an extended period of time increases the risk of developing cardiovascular diseases, including

hypertension. Furthermore, it increases the risk of gestational diabetes mellitus and hypertensive disorders during pregnancy.^[4]

Health-Related Quality of Life (HRQoL) refers to the individual's perception of their health and well-being, and the consequences and treatments of any disease that may affect their life condition.^[5] PCOS is a chronic condition with clinical manifestations that can deteriorate self-esteem, self-image, and psychosocial dimensions and negatively affect the HRQoL.^[6] The management of PCOS should be focused on support and education and needs to strongly emphasize a healthy lifestyle, with targeted medical therapy as required. Lifestyle modification is recommended as the first course of action for the nonpharmacological and noninvasive management of PCOS.^[7] It helps in weight loss and reduces endocrine disorders and metabolic syndrome. In addition, it could help to restore spontaneous ovulation,

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enhance the natural pregnancy rate, improve the outcome of assisted pregnancy, increase the success rate of assisted pregnancy, and reduce the risk of pregnancy complications.^[8]

Furthermore, the treatment of PCOS should include the physiological and psychosocial aspects to be effective in management.^[9] The care team has an essential role in positively impacting women with PCOS through counseling and education and providing support for dealing with the negative secondary self-image associated with the physical manifestations of PCOS. Through education, the woman understands the syndrome and its associated risk factors to prevent long-term health problems. In addition, nurses encourage women to make appropriate lifestyle changes and referrals to local support groups to help build coping skills.^[10] A healthy lifestyle is a way of life that promotes, maintains, and improves an individual's health, well-being, and overall quality of life. The influence of polycystic ovarian syndrome in women is currently an area of research in middle- and low-income nations. Aripin *et al.*^[11] reported a lack of knowledge and awareness about polycystic ovarian syndrome's causes and lifestyle modifications. At the reproductive age, lifestyle education is crucial for a better life in the future. Women with healthy lifestyles can manage any illness, including PCOS. An essential setting for recognizing and changing women's lifestyles can be found in outpatient clinics. Furthermore, there are certain aspects of PCOS about which health-care practitioners should educate women so that they may make the best health decisions. As a result, the current study aimed to evaluate the effectiveness of lifestyle modification on health-related quality of life among Women with Polycystic Ovary Syndrome.

Materials and Methods

This quasi-experimental study, two study-control groups, was carried out on 124 women from the outpatient clinic of El-Takhassosy Obstetrics Hospital, Port-Said, Egypt, from January 2021 to August 2021. A nonprobability convenience sampling technique was used for this study. We recruited 124 women according to predetermined inclusion and exclusion criteria. Inclusion criteria were (a) women aged 18–45 years and (b) diagnosed with PCOS according to Rotterdam criteria.^[a] Exclusion criteria were (a) chronic medical diseases, (b) psychiatric problems, and (c) women refusing to participate in the study. The sample size was calculated according to power analysis 80% with $z1 = 95$, $z2 = 79$, and $r = 1$. Women were randomly assigned into two groups (educational and control groups).

Randomization was factorial and balanced in a 1:1 manner using a computer-generated randomization list. It was performed after determining the participants' eligibility. The researchers did not make the allocation sequence aware when enrolling and assessing participants using opaque-sealed envelopes. Patients and researchers were aware of group allocation, but outcome assessors and data analysts were blinded.

Two tools were used for data collection. Tool 1: a structured interviewing questionnaire to collect personal data (age, education level, residence, occupation, and income) and Tool 2: a standardized HRQoL questionnaire for women with PCOS was adapted from Cronin *et al.*^[13] It contains 55 items and 4 domains; physiological, psychological, social, and sexual functions. The physiological function included body hair (7 items), weight (6 items), and menstrual problems (8 items). At the same time, the psychological function included emotional disturbances (12 items) and infertility's impact on psychological status (5 items). In addition, a social function included 12 items, and the sexual function included 5 items. Each statement has three answers ranging from severe to no problem, scoring 55–165. A high score indicates no problem, while a low score indicates maximum impairment of HRQoL. Tools validity and reliability were ascertained by a jury of six medical and nursing experts and assessed by piloting and measuring Cronbach's alpha value of 0.936.

The educational group gained knowledge regarding the proper lifestyle for PCOS alongside medical treatment. The control group was offered medical treatment only. Eligible women were individually interviewed to collect their data and initial HRQoL. The educational group attended three sessions in small groups of 4–6 women on three consecutive days weekly. The duration of each session was approximately 60 min. In the first session, they were educated about PCOS (definition, manifestations, and complications), the importance of weight reduction, and lifestyle modification (low glycemic index diets, moderate carbohydrate, high protein and low-fat diets, very low carbohydrate and high-fat diets, and moderate carbohydrate and high monounsaturated fat diets). In the second and third sessions, they were educated about how to perform physical exercises (walking for 30 min five times weekly) and given instructions to relieve stress, such as practicing relaxation techniques (e.g., breathing exercises).^[14] The session was presented using PowerPoint on a laptop, and an instructional brochure was given to each woman to guide lifestyle modification. All participants were interviewed after 3 and 6 months to assess the dimensions of HRQoL by using the standardized HRQoL questionnaire for women. The researchers maintained contact with the women through phone and WhatsApp weekly and during their monthly visits to the gynecological clinics to confirm that they strictly followed the diet and physical activity instructions. Each participant was interviewed in a private room. The questionnaire took 30–45 min to be completed. A researcher was available to help women in the control group who were educated about the lifestyle modification of PCOS after the study period ended.

Data were gathered and entered into the computer for statistical analysis using Statistical Package for Social Science program (SPSS) (ver. 21).^[24,25] SPSS Statistics is a statistical software suite developed by IBM for data management, advanced analytics, multivariate analysis, and business intelligence.^[15] Depending on the situation, data were input as numerical or categorical. No significant difference in the

distribution of the variables was found using the Kolmogorov–Smirnov test of normality; hence, parametric statistics were used.^[16] Data were described using mean and standard deviation. Categorical variables were defined using frequency and percentage. Comparisons were made between two studied independent, normally distributed variables, using the independent sample *t*-test.^[17] We utilized Levene’s test when the equality of variances is significant,^[12] while Welch’s *t*-test was applied when the two samples have unequal variances.^[18]

Repeated measures’ analysis of variance was used.^[19] When Mauchly’s test of sphericity^[20] was statistically significant, denoting the violation of the assumption of sphericity, the Greenhouse–Geisser correction was used.^[21] A pairwise comparison was conducted with the Bonferroni correction. The Chi-square test was used to test the association between qualitative variables.^[22] Monte Carlo corrections^[23] were carried out when indicated (i.e., $n \times m$ table and >25% of expected cells were less than 5). An alpha level was set at 5% with a significance level of 95%.

Ethical considerations

The Research Ethical Committee of the Faculty of Nursing, Port Said University, approved the study protocol on 4/12/2020 (Code 24). Participant informed consent was obtained after explaining the aim of the study. The researchers assured the women that the research was safe and that the information they collected would be kept confidential and only used for the study. They also explained the nature of the study, its process, and anticipated results. Throughout the research, they were advised of their right to object. The data were de-identified before being sent for study processing.

Results

One hundred and thirty-two patients were eligible for the study. Two patients declined to participate, and 6 were lost during follow-up, leaving 124 patients for the final analysis [Figure 1].

Regarding sociodemographic characteristics, there were no statistically significant differences between both groups; the educational and the control groups were homogeneous ($P > 0.05$) [Table 1]. It was noticed that there were no statistically significant differences between both groups in the pre-intervention phase. At the same time, both groups had statistically significant differences in the postintervention phase after 3 and 6 months. The educational group had higher means in all dimensions of quality of life and total HRQoL than the control group [Table 2 and Figure 2].

Discussion

This study aimed to evaluate the effect of structured educational sessions regarding lifestyle modification on HRQoL among women with PCOS. The current study

showed that education about lifestyle modification improved the mean scores of all dimensions of HRQoL and the overall score significantly. Improvements in body image and HRQoL were closely related to changes in weight. Also, lifestyle modification positively affects the hormonal disturbance and symptoms of PCOS, subsequently improving the HRQoL; Hukire and Devi supported these findings.^[26] Women with PCOS had significantly higher scores regarding the quality of life (emotion, weight, body hair, menstrual irregularities, and infertility) and postlifestyle modification assessment than pre-intervention. In addition, Ramos *et al.*^[27] stated that a resistance exercise training program improved the quality of life among women with PCOS after 16 weeks. Furthermore, Stener-Victorin *et al.*^[28] reported that 16 weeks of physical exercise improved the HRQoL among women with PCOS. Also, Stefanaki *et al.*^[29] found that the quality of life was improved among women with PCOS after 8 weeks of a stress management program. Moreover, Cooney LG *et al.*^[30] revealed that lifestyle modification and cognitive–behavioral therapy improved the quality of life among overweight and obese women with PCOS.^[30]

The current study’s findings showed that exercise intervention (yoga) was associated with significantly improving manifestations of PCOS, including menstrual cycle irregularity and mood swings. In addition, the exercise showed significant weight loss in the educational group. Similar to our findings, two studies showed that weight loss through increasing physical exercise alone could effectively regulate menstrual cycles.^[6,30] In the same line, Ribeiro *et al.*^[31] added that continuous or intermittent aerobic exercise was an effective method to improve the clinical presentation of PCOS and the quality of life among women with PCOS. On the contrary, according to Thomson *et al.*,^[32] the lifestyle program, including nutrition and physical exercise, significantly improved the HRQoL scores, except for the body hair among overweight and obese women with PCOS. These differences might be because of the different populations in their study on overweight and obese women with PCOS. From the researchers’ point of view,

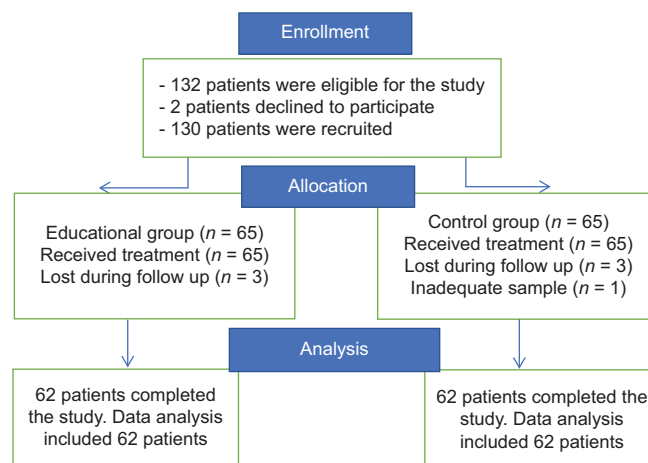


Figure 1: Patients’ flow chart

Table 1: Sociodemographic characteristics of the studied groups (n=124)

Variables	Mean (SD) n (%)		Statistical tests
	Educational group (n=62)	Control group (n=62)	
Age (years)	25.65 (4.44)	26.71 (5.57)	t^* (df**=122) = 1.176, P^{***} = 0.242
Residence			χ^{2****} (df**=1) = 0.367, p^{***} = 0.544
Rural	7 (11.29)	5 (8.06)	
Urban	55 (88.71)	57 (91.94)	
Educational level			χ^{2****} (df**=4) = 6.43, p^{***} (MC****) = 0.166
Illiterate	2 (3.23)	1 (1.62)	
Read and write	4 (6.45)	6 (9.68)	
Basic education	2 (3.23)	1 (1.61)	
Secondary education	35 (56.45)	23 (37.10)	
High education	19 (30.65)	31 (50.00)	
Occupation			χ^{2****} (df**=2) = 1.954, p^{***} (MC****) = 0.399
Housewife	37 (59.68)	31 (50.00)	
Working	21 (33.87)	23 (37.10)	
Student	4 (6.45)	8 (12.90)	
Income			χ^{2****} (df**=2) = 2.095, p^{***} (MC****) = 0.378
Not enough	15 (24.19)	10 (16.13)	
Enough	46 (74.19)	49 (79.03)	
Enough and exceed	1 (1.61)	3 (4.84)	
Total	62 (100)	62 (100)	

*Independent sample *t*-test. **Degree of freedom. ***Indicates statistically significant difference ($p < 0.05$). ****Pearson Chi-square. *****Monte Carlo correction for *p*

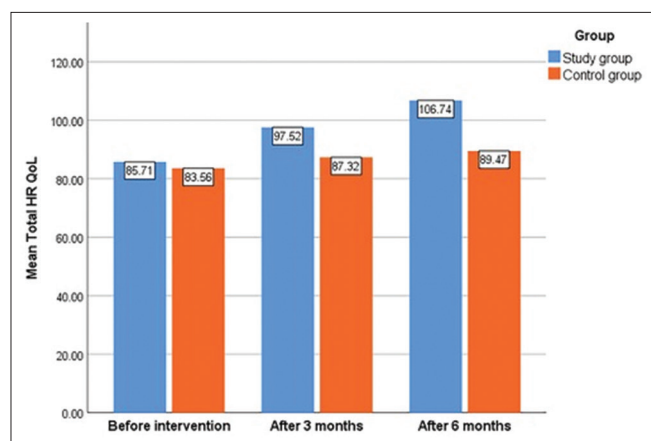


Figure 2: Total mean of the quality of life score among the studied groups (n = 124)

the program results did not appear immediately after the women applied the instructions. However, with time, especially after 3 months, noticeable results occurred for the woman, which encouraged the woman to follow the instructions carefully during the remaining 3 months to get the best results, reduce symptoms, and increase her quality of life. These data will better understand the unique barriers and enablers to dietary change and healthy behavior from the perspective of women with PCOS. This study's additional strength is that it offered a healthy intervention that positively impacted women's lives. While the proposed research has several strengths, it is also essential to acknowledge its limitations. Specifically, the study

was limited by the low number of women involved, timing, and implementation duration. A longer time period of follow-up would be informative. Moreover, we have not included an assessment of psychological distress, particularly depression and anxiety, which are particularly pertinent in women with PCOS.

Conclusion

Our study showed that a 6-month education intervention could enhance the understanding of diet and physical exercise. In light of the findings of this study, the teaching module may be regarded as an effective intervention for PCOS-affected women. Structured educational sessions about lifestyle modification effectively improve the HRQoL among women with PCOS. We suggest continuous health education for girls in schools about a healthy lifestyle to avoid the occurrence of PCOS, and women with PCOS should receive structured education about lifestyle modification alongside treatment to ensure improvement, particularly in the context of patient-centered care.

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Table 2: Mean score of the quality of life among the studied groups (n=124)

Variables	Mean (SD)		Test of significance
	Educational group (n=62)	Control group (n=62)	
Hirsutism			
Before intervention	8.53* (1.53)	8.79* (2.67)	$t^{****} (W^{*****}) (dF^{*****}=97.198)=0.659, P^{*****}$ $(W^{*****})=0.511, t^{****} (W^{*****}) (dF^{*****}=2.042)$ $p^{*****} (W^{*****})=0.044^{*****}, t^{****}$ $(W^{*****}) (dF^{*****}=85.843)=3.647, p^{*****}$ $(W^{*****}) < 0.001^{*****}$
After 3 months	11.15** (2.26)	10.05* (3.57)	
After 6 months	12.84*** (2.04)	10.58*** (4.43)	
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.787)=99.53 $p^{*****} < 0.001^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} = 1.677)=8.981 $p^{*****}=0.001^{*****}$	
% Change 3 vs. before	32.47 (26.59)	17.58 (40.22)	$t^{****} (W^{*****}) (dF^{*****}=2.430, P^{*****}$ $(W^{*****})=0.017^{*****}, t^{****} (W^{*****})$ $(dF^{*****}=94.072)=4.208, P^{*****} (W^{*****}) <$ 0.001^{*****}
% Change 6 vs. before	53.02 (26.72)	23.08 (49.24)	
Body weight			
Before intervention	8.97* (1.70)	8.26* (2.92)	$t^{****} (W^{*****}) (dF^{*****})=0.1652,$ $P^{*****} (W^{*****})=0.101, t^{****} (W^{*****})$ $(dF^{*****}=76.416)=2.494, P (W)=0.015^{*****},$ $t^{****} (W^{*****}) (dF^{*****}=121.047)=3.029,$ $p^{*****} (W^{*****})=0.003^{*****}$
After 3 months	20.87** (2.25)	18.76** (6.28)	
After 6 months	23.03** (7.25)	18.90*** (7.92)	
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.806)=13.915 $p^{*****} < 0.001^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} = 6.763 $p^{*****}=0.003^{*****}$	
% Change 3 vs. before	21.78 (0.91)	13.98 (35.45)	$t^{****} (dF^{*****}=122) = 1.103,, P=0.272, t^{****}$ $(dF^{*****}=122)=0.999,, P^{*****}=0.320$
% Change 6 vs. before	33.11 (45.96)	24.66 (48.13)	
Menstrual problems			
Before intervention	12.60* (2.05)	11.71 (3.95)	$t^{****} (W^{*****}) (dF^{*****}=91.668)=1.569,$ $P^{*****} (W^{*****})=0.120, t^{****} (W^{*****})$ $(dF^{*****} 110.636)=3.304, p^{*****}$ $(W^{*****})=0.001^{*****}, t^{****} (W^{*****})$ $(dF^{*****} 118.717)=2.781, p^{*****}$ $(W^{*****})=0.006^{*****}$
After 3 months	12.90* (1.50)	11.82 (2.09)	
After 6 months	14.48** (5.13)	12.11 (4.33)	
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.269)=6.464 $p^{*****}=0.008^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} =1.578)=0.628 $p^{*****}=0.449$	
% Change 3 vs. before	4.50 (17.64)	8.99 (29.11)	$t^{****} (W^{*****}) (dF^{*****} 100.489) = 1.040,$ $p (W)=0.301, t^{****} (W^{*****}) (dF^{*****}$ $74.858)=2.274, p^{*****} (W^{*****})=0.026^{*****}$
% Change 6 vs. before	17.57 (45.55)	3.68 (15.45)	
Emotions			
Before intervention	17.10* (1.62)	17.68*,** (5.89)	$t^{****} (dF^{*****}= 122)=0.749, p=0.455,$ $t^{****} (dF^{*****}= 76.416)=2.494, p^{*****}$ $(W^{*****})=0.015^{*****}, t^{****} (dF^{*****}=$ $122)=3.029,, P^{*****}=0.003^{*****}$
After 3 months	20.87** (2.25)	18.76*,** (6.28)	
After 6 months	23.03*** (7.25)	18.90** (7.92)	
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.165)=33.002 $p^{*****} < 0.001^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} =2)=4.470 $p^{*****}=0.013^{*****}$	
% Change 3 vs. before	22.74 (14.26)	8.08 (18.38)	$t^{****} (dF^{*****}= 122)=4.961,, p^{*****} (W^{*****})$ $< 0.001^{*****}, t^{****} (dF^{*****}= 79.842)=5.228,$ $p^{*****} (W^{*****}) < 0.001^{*****}$
% Change 6 vs. before	34.52 (40.88)	5.31 (16.26)	
Infertility			

Contd...

Table 2: Contd...

Variables	Mean (SD)		Test of significance
	Educational group (n=62)	Control group (n=62)	
Before intervention	8.42* (2.83)	7.94 (3.39)	$t^{****}(dF^{*****}=122)=0.862, P=0.390,$
After 3 months	10.11** (3.06)	8.32 (3.10)	$t^{****}(dF^{*****}=122)=3.233,$
After 6 months	10.42*** (2.63)	8.55 (3.49)	$p=0.002^{*****}, t(W)(dF=113.321)=3.372,$
%Change 3 vs. before	21.95 (15.74)	7.55 (12.09)	$p^{*****}(W^{*****})=0.001^{*****}$
%Change 6 vs. before	31.52 (32.22)	13.48 (45.85)	$t^{****}(dF^{*****}=122)=5.711 P^{*****}(W^{*****})$ $< 0.001^{*****}, t^{****}(dF^{*****}=122)=3.534,$ $p^{*****}(W^{*****})=0.013^{*****}$
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.276)=31.332 $p^{*****}< 0.001^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} =1.108)=3.186 $p^{*****}=0.075$	
Social function			
Before intervention	21.23* (3.93)	20.32 (3.32)	$t^{****}(W)^{****}(dF^{*****}=118.689)=1.383,$
After 3 months	21.97*, **, *** (5.19)	20.26 (3.35)	$p^{*****}(W^{*****})=0.169, t^{****}(W)$ $^{****}(dF^{*****}=104.227)=2.178,$
After 6 months	23.81*** (6.95)	20.42 (3.56)	$p^{*****}(W^{*****})=0.032^{*****}, t^{**}$ $^{**}(W)^{****}(dF^{*****}=90.888)=3.417,$ $p^{*****}(W^{*****})=0.001^{*****}$
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.566)=3.827 $p^{*****}=0.024^*$	F^{*****} (GG ^{*****}) (dF ^{*****} =1.221)=1.072 $p^{*****}=0.318$	
% Change 3 vs. before	5.54 (27.50)	-0.33 (2.08)	$t^{****}(W)^{****}(dF^{*****}=61.700)=1.674,$
% Change 6 vs. before	16.77 (43.49)	0.44 (5.13)	$p^{*****}(W^{*****})=0.099^*, t^{****}(W)$ $^{****}(dF^{*****}=62.700)=2.937,$ $p^{*****}(W^{*****})=0.005^{*****}$
Sexual function			
Before intervention	8.87* (1.12)	8.87 (1.70)	$t^{****}(W)^{****}(dF^{*****}=105.620)=0.000,$
After 3 months	9.92** (1.67)	8.89 (1.71)	$p^{*****}(W^{*****})=1.000, t^{****}(dF$ $^{*****}=122)=3.399, P=0.001^*, t^{****}(dF^{*****}=$ $122)=3.482., p^{*****}(W^{*****})=0.001^{*****}$
After 6 months	10.77*** (2.42)	9.23 (2.53)	
	F^{*****} (GG ^{*****}) (dF ^{*****} =1.551)=15.741 $p^{*****}< 0.001^{*****}$	F^{*****} (GG ^{*****}) (dF ^{*****} =1.023)=2.391 $p^{*****}=0.127$	
% Change 3 vs. before	13.86 (27.79)	0.20 (2.41)	$t^{****}(W)^{****}(dF^{*****}=61.916)=3.854,$
% Change 6 vs. before	23.39 (30.99)	3.81 (20.00)	$p^{*****}(W^{*****})< 0.001^{*****}, t^{****}(W)$ $^{****}(dF^{*****}=104.318)=4.180, p^{*****}$ $(W^{*****})< 0.001^{*****}$
Total HRQoL			
Before intervention	85.71* (7.51)	83.56* (18.37)	$t^{****}(W)^{****}(dF^{*****}=80.836)=0.851,$
After 3 months	97.52** (8.75)	87.32** (18.68)	$p^{*****}(W^{*****})=0.397, t^{****}(W)^{****}$ $(dF^{*****}=86.563)=3.891, p^{*****}$ $(W^{*****})< 0.001^{*****}, t^{****}(W)^{****}$ $(dF^{*****}=91.826)=5.450, p^{*****}(W^{*****})$ $< 0.001^{*****}$
After 6 months	106.74*** (11.53)	89.47*** (22.14)	

****Independent sample *t*-test, *****Welch's *t*-test (unequal variances *t*-test). *****Degree of freedom; *****Indicates *p*.

*****Analysis of variance (general linear model: repeated measures analysis) (performed only among the three time intervals of measurements: before the intervention, after 3 months, and after 6 months). *****Indicates statistically significant difference ($p<0.05$). *****Greenhouse-Geisser (Mauchly's test of sphericity was significant $p<0.05$). Superscript letters: *Assigned to before intervention, **assigned to after 3 months, and ***assigned to after 6 months. Different superscript letters indicate a pairwise statistically significant difference; adjustment for multiple comparisons was achieved using the Bonferroni method

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Conflicts of interest

Nothing to declare.

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