Effects of a tailored lifestyle self-management intervention (TALENT II) on stress reduction: a randomised controlled trial

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Abstract

Background and objective: Stress, a pervasive challenge of modern life, contributes to serious health problems and affects a significant portion of the population. As a possible solution, this study examines the effectiveness of a lifestyle intervention called 'Individual Health Management' (IHM) in reducing stress.

Subjects and methods: 77 participants were enrolled in a monocentric randomised controlled trial. The IHM intervention group (n=38) was compared to a 6-month IHM waiting list (n=39). In addition, the lifestyle-group was followed up for six months and the patients in the waiting group were investigated in a cross-over design. The IHM includes a 12-month lifestyle programme with a blended learning approach. In the first 3 months, participants receive intensive counselling through health days and weekly evening seminars. This is followed by a 9-month maintenance phase with continuous monitoring by health coaches, remote counselling and refresher seminars.

Results: In the ITT-population, the IHM intervention significantly reduced perceived stress after 6 months compared to the CG, adjusting for gender and baseline values (mean difference= -20.50 [CI: -26.41; -14.59]; F= 47.78, p< 0.001, η^2 =0.36). The intervention group achieved clinically normal stress levels, with a stress reduction of 40% (m= -24.71; SD= 15.31), while the control group experienced an 8% reduction (m= -5.06; SD=10.87). These differences correspond to a significant and substantial effect size between the groups (t(66.63)=-6.48, p<.001, d=-1.48). In addition to stress reduction, other indicators of mental health, such as general mood, burnout, life satisfaction, well-being and vitality, also improved significantly. Remarkably, these positive results lasted for up to a year and continued to improve beyond this period. The supplementary crossover analysis confirmed the effectiveness of the IHM for the control group after their waiting period.

Conclusion: IHM demonstrates its multifaceted and enduring impact on mental health—achieving clinically normal stress values that persist for up to a year.

Trial registration: German Clinical Trial Register Freiburg (DRKS): DRKS00013040 (date registered 2017–10-1).

Keywords: Stress, Burnout, Prevention, Intensive lifestyle intervention, Individual health management (IHM), E-health, Traditional Chinese medicine (TCM)

Background and objective

Perceived chronic stress is known to contribute to the development of a variety of serious diseases (Mariotti, 2015), including coronary heart diseases (Richardson et al., 2012), cancer (Tausk, 2023), Alzheimer's disease (Machado et al., 2014), as well as depression and other mental health disorders (i.e. Marin et al., 2014). In Germany, only around half of the population display healthy stress behaviour (DKV, 2023) and the proportion of people who feel stressed has risen from 57% to 64% between 2013 and 2021 (TK, 2021). To reduce the stress load, an intervention approach is currently mainly being implemented to counteract the stress already present. Applied methods include mindfulness practices (Grossman et al., 2004; Chiesa & Serretti, 2009; Khoury et al., 2015), cognitive behavioural therapies (Romero-Gonzales et al., 2020; Granath et al., 2006; Khoo et al., 2019) and various direct coping strategies or stress management (Alkhawaldeh et al., 2020; Panahi et al., 2022). Holistic and lifestyle-changing methods to avoid the development of stress instead treating it in the sense of effective prevention would be an important addition to existing therapeutic approaches.

In this context, a randomised controlled study was conducted by Stier-Jarmer and colleagues (2016) to test such a multimodal stress prevention programme which showed remarkable positive effects after 6 months. Comprehensive lifestyle interventions have also been shown to be effective in reducing the risk of type 2 diabetes (Uusitupa et al., 2019; Galaviz et al., 2022), risk of dementia (Meng et al., 2022), depressive symptoms (Simjanoski et al., 2023; Wong et al., 2021), or sedentary behaviour (Nieste et al., 2021).

An additional aspect to consider in mental health interventions is the delivery method—whether it's digitized or in presence face-to-face. So far, there is evidence supporting both approaches (Goh et al., 2021; Ierardi et al., 2022). However, while purely internet-based interventions offer certain advantages, a meta-analysis revealed that internet-based cognitive therapies against depression did not have lasting effects after six or twelve months (Karyotaki et al., 2021). Another meta-analysis of stress intervention for internet-based cognitive therapies revealed that the initially strong effects observed after the intervention diminish to a small effect size during the final follow-up assessment (Svärdman et al., 2022). Similarly, other self-guided stress management programmes—such as those including cognitive behavioural therapy, mind-body components, or skills training—also demonstrated only modest effects on stress reduction immediately after the intervention, with no sustained impact during follow-up periods (Amanvemez et al., 2022). Interestingly, a recent meta-analysis that investigated the efficacy of various cognitive-behavioural therapies found that combining guidance via email and telephone can be more effective than using singular approaches (Mamukasjvili-Delau et al., 2022). The promising effects of integrating face-to-face interactions with digitized methods in psychotherapy have also been recently put forward by Bielinski et al. (2021).

Previously we used such a blended approach that combines the strengths of face-to-face and digitized components to develop a broad and multifaceted intervention called Individual Health Management (IHM) (Melchart et al., 2016). The IHM is designed to improve various aspects of lifestyle to prevent mental health issues. This comprehensive program integrates initial face-to-face components with recurring digitized elements, promoting extended effectiveness and sustainability. The main objective of this study is to test the effectiveness of the IHM for the parameter of stress reduction. As a local pilot project, the study is supported by the major statutory health insurance, AOK Bayern (Allgemeine Ortskrankenkasse -General Health Insurance, Bavaria) in cooperation with the TCM Clinic Bad Kötzting. This stress prevention study (TALENT II study) is part of a comprehensive network programme aimed

at enhancing health services in specific spa regions within Bavaria. The sustainability of IHM has already been proven in the context of weight reduction due to an all-embracing change in lifestyle (Melchart et al., 2017a; Melchart et al., 2017b). In the associated randomised control study on weight reduction (TALENT I study), which was conducted by our group, the IHM intervention led to a significant weight reduction of 10% of the initial weight after one year (Melchart et al., 2017a). Similarly, the web-based lifestyle intervention programme, as applied in the IHM, has now been successfully implemented in a specialized spa region for persons with perceived stress (Melchart et al., 2017c). This programme operates in Bad Kötzting, a Bavarian health resort known for its focus on preventive medicine and as the home of Germany's first Traditional Chinese Medicine (TCM) hospital. Developed by the Competence Centre for Complementary Medicine and Naturopathy (CoCoNat) at TU Munich, the IHM lifestyle intervention combines mainstream and complementary approaches to promote natural healing and self-regulation in stress management. The TALENT II study aims to evaluate the efficacy of the IHM lifestyle intervention in reducing perceived stress.

Subjects and methods

Study design

The study is a randomised, 2-arm, controlled, monocentric, interventional, clinical study and was performed at the SINOCUR prevention centre in Bad Kötzting, Germany. The centre is part of a centrally coordinated network for health promotion called "IHM Campus". The study compares an intervention group (IHM= Individual Health Management) with a control group (6 months waiting list for IHM). The main observation period for each participant was 6 months with additional longitudinal examinations for the intervention group up to the end of the 12-month lifestyle programme. In addition, the patients in the waiting group were compared with themself after receiving the intervention in form of a cross-over design. The study was registered in advance at German Clinical Trials Register Freiburg (DRKS, file number DRKS00013040, date registered October 01, 2017). Participants had to give a written informed consent. The study protocol was submitted to the ethics committee of the Medical Faculty of the Technical University of Munich (TUM) responsible for the principal investigator for examination of ethical and legal compliance

Recruitment and participants

Participants were recruited via written correspondence by the AOK Bayern health insurance. Contacted people were invited to conduct a short health survey in the e-health portal VITERIO® which is part of the IHM. All individuals who met the initial requirements of the study were invited to an appointment with the trial physician to obtain full information and to undergo a comprehensive examination of the study criteria. Main inclusion criteria were a Tedium-Measure ≥3,20 (=moderate stress, pre-burnout), a Perceived Stress Questionnaire (PSQ) total score > 41, and subjective feeling of stress exposure for more than 3 months. Participants were excluded if one of the following criteria was present: no legal capacity, insufficient proficiency in German, no private Internet access, a body mass index (BMI) < 17,5, psychiatric or psychotherapeutic treatment requirements, known health issues (e.g., diabetes, heart disease, liver or kidney diseases), known pregnancy (or lactation) or planned in the next year, participation in another clinical trial within the last 6 months. Randomisation, calculation of sample size and further details of the study protocol were described by Melchart et al. (2015). Due to the difficulties of COVID-19 the estimated sample size of 136 (α = 0.05, two-sided, power 80%,

expected drop-out rate of 5%) could not be achieved. The recruitment and allocation of participants is illustrated in the consort study flowchart (Figure 1).

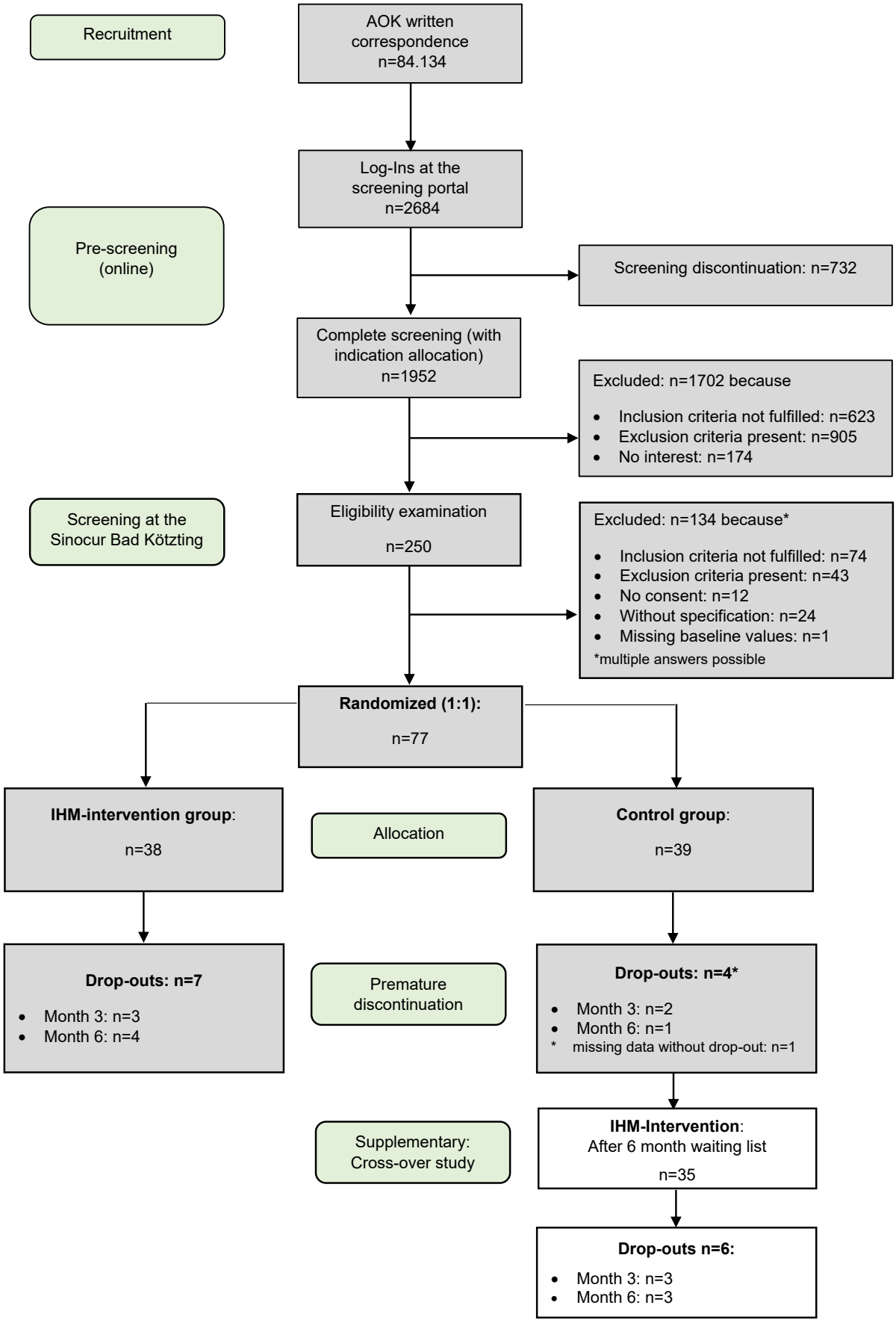

Figure 1. Consort flowchart

Intervention

The lifestyle intervention programme IHM has an overall duration of 12 month consisting of different phases and training packages. Participants will have access to a web-based health portal (viterio.de). During the first 3 months the participants receive an intensive lifestyle counselling consisting of 3 initial health days (introduction phase) and 10 weekly after-work group seminars (training phase). This is followed by a 9-month maintenance phase, which includes weekly monitoring by specially trained health coaches, remote lifestyle counselling as required and a half-day refresher course every 3 months to consolidate and deepen the teaching and learning content (Figure 2). Participation in at least 7 of the 10 after-work seminars and at least 3 of the 4 refresher days in months 3 to 12 was counted as successful participation.

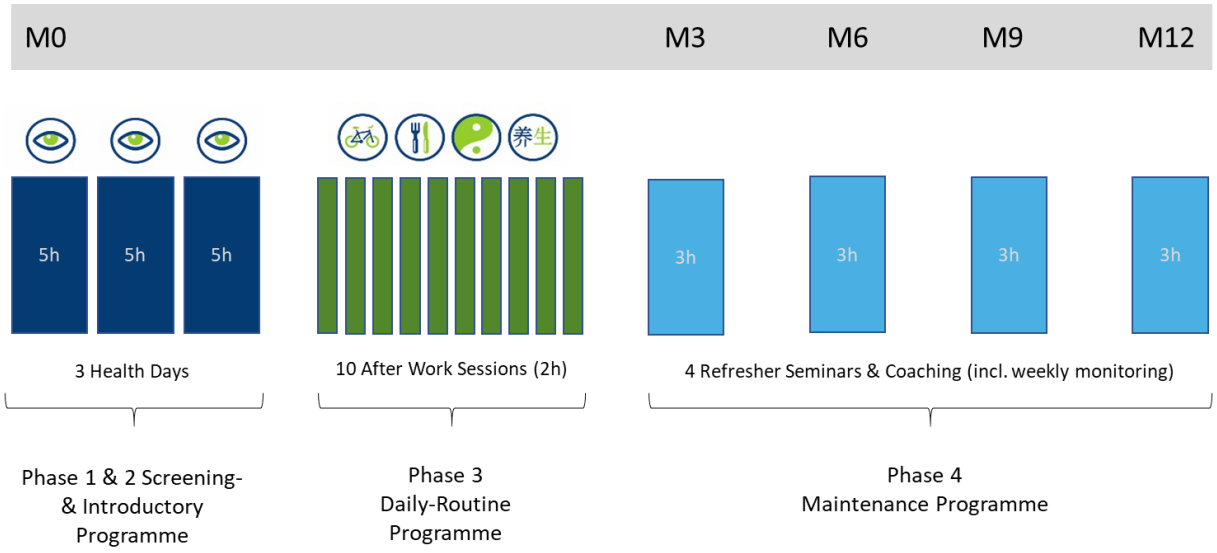

Figure 2. Schematic course of IHM

The intervention consists of a blended-learning concept with a combination of group interventions, single face-to-face counselling, and an individual web-based health portal (www.viterio.de). Through the online portal, participants can access personalised feedback, including written reports and graphs, detailing their progress. This feedback encompasses a time-and-mood analysis, as well as information on lifestyle changes, behavioural adjustments, and emotional regulation. The training content of the intervention includes self-awareness practices, quality of life optimisation, a 6-minute and 2-kilometre walking test, '3-1-2' Qi-Gong relaxation techniques, time management, stress and resilience information, mood regulation, dietary days for stress reduction, health behaviour related to physical activity, nutrition, and individual goal-setting. A more detailed elaboration of the IHM-intervention programme can be found in a previous publication by Melchart et al. (2016).

Outcomes

The primary outcome measure is the reduction of subjective stress (PSQ total score) after 6 months compared to the baseline at M0 (Perceived Stress Questionnaire total score PSQ-20; developed by Levenstein et al. (1993) and modified by Fliege et al. (2001)).
Secondary outcome parameters are the Tedium-Measure (Pines et al., 1981), ICD-10-Symptom-Rating (ISR; Tritt et al., 2008), severity of mood state in general (VAS), life satisfaction (FLZ; Heinrich & Herschbach, 2000), well-being and vitality (WHO-5, Topp et al., 2015; SF-36, Bullinger et al., 1995), and

the sense of coherence (SOC-13; Abel et al., 1995; Feldt et al., 2007). At baseline examination, socio-demographic data such as education, employment status, smoking and drinking habits were documented. The occurrence of adverse events (AEs) were systematically recorded at each physical examination following the baseline test.

Statistical analysis

We evaluated perceived stress as the primary outcome after 6 months (PSQ total score). Employing ANCOVA, we examined the intervention effect while adjusting for baseline values and gender (5% significance level, two-sided). The intention-to-treat (ITT) population included participants who completed the PSQ questionnaire at baseline. For missing data in month 6 within the IHM group, we realistically imputed using linear regression terms from the same group. Sensitivity analyses included a per-protocol analysis with only those subjects who completed the study as randomised without missing data. Additional *t*-test analyses examined differences from baseline values within and between groups at various time points. The secondary endpoints were analysed analogously using the per-protocol sample. All statistical tests were two-sided with a significance level of 5%. The secondary outcomes were performed in the sense of an exploratory approach, therefore, no imputations or corrections for multiple testing were applied. Demographic and baseline values were compared between groups using the t-test for continuous data and with the Mann-Whitney-U test for categorical data. Furthermore, the Central Limit Theorem justifies the use of the t-test for larger sample sizes (Moore et al., 2018). Therefore, the t-test was employed even when the data did not conform to a normal distribution, as long as the sample size was greater than 30. Non-parametric tests (Wilcoxon rank-sum or Mann-Whitney-U) were used when appropriate.

Results

Sociodemographic and baseline characteristics

77 participants were included in the study, 38 (49%) were assigned to the intervention group, and 39 (51%) to the control group. The control group had 89.7% females, while the intervention group had 76.3% females, resulting in a significant difference between the groups (p<.001). The mean age was 45.18 years (SD=11.35) in the control group and 44.32 years (SD=10.05) in the intervention group (p=.725). The total PSQ score at baseline was similar, with 62.11 (SD=11.30) in the IHM group and 62.74 (SD=13.19) in the control group (p=.822). However, the groups differed in the PSQ-subscale ‘joy’ (IHM: m=36.67, SD=14.52; CG: m=28.03, SD=15.83; p=.015, d=.57). Other parameters (education, employment status, living condition, smoking, alcohol consumption, and all secondary parameters) showed no significant difference between the groups (see Table 1).

Table 1. Baseline demographic and clinical characteristics

	Intervention Group (n=38)		**Control Group (n=39)**		**Between group differences**	**In total (n=77)**	
	mean	**SD**	**mean**	**SD**	**p**	**mean**	**SD**
Age (years)	44.32	10.05	45.18	11.35	.725	44.75	10.67
	n	**%**	**n**	**%**	**p**	**n**	**%**
Female	29	76.3	35	89.7	<.001***	64	83.1
Male	9	23.7	4	10.3		13	16.9
School education					.529		

No school-leaving certificate	0	0.0	1	2.6		1	1.3
Secondary general school certificate	15	40.5	11	28.2		26	34.2
Intermediate school certificate	15	40.5	19	48.7		34	44.7
University entrance qualification	6	16.2	8	20.5		14	18.4
Other degree	1	2.7	0	0.0		1	1.3
Vocational education					.207		
No completed vocational training	4	10.8	4	10.3		8	10.5
Completed apprenticeship	23	62.2	18	46.2		41	54.0
Vocational School	7	18.9	11	28.2		18	23.7
University of applied science	1	2.7	3	7.7		4	5.3
University degree	0	0.0	2	5.1		2	2.6
Other degree	2	5.4	1	2.6		3	3.9
Employment status					.748		
Employed	34	91.9	35	89.7		69	90.8
Temporarily retired	1	2.7	0	0.0		1	1.3
Retired	0	0.0	2	5.1		2	2.6
Employed without remuneration	1	2.7	1	2.6		2	2.6
Without specification	1	2.7	1	2.6		2	2.6
Living condition					.286		
Individual household	5	13.5	9	23.1		14	18.4
Multi-person household	32	86.5	30	76.9		62	81.6
Smoking					.720		
No	35	92.1	35	89.7		70	90.9
Yes	3	7.9	4	10.3		7	9.1
Alcohol					.417		
No	36	94.7	35	89.7		71	92.2
Yes	2	5.3	4	10.3		6	7.8
PSQ	**mean**	**SD**	**mean**	**SD**	**p**	**mean**	**SD**
Total score	62.11	11.30	62.74	13.19	.822	62.42	12.22
Worries	51.23	18.61	51.97	17.58	.859	51.60	17.98
Demands	64.03	22.49	57.78	18.88	.191	60.87	20.84
Joy	36.67	14.52	28.03	15.83	.015*	32.29	15.71
Tension	69.82	14.35	69.23	18.14	.874	69.52	16.27
Secondary outcomes							
General mood state severity (VAS)	58.82	15.24	53.69	15.12	.143	56.22	15.30
Tedium-Measure Burnout	4.19	0.54	4.33	0.54	.266	4.26	0.54
ISR score	1.13	0.51	1.07	0.42	.560	1.10	0.47
Life satisfaction (FLZ)	33.34	27.37	29.97	26.70	.587	31.64	26.91
Sense of Coherence (SOC)	54.53	9.16	54.54	9.44	.995	54.53	9.25
Well-being (WHO-5)	7.89	3.65	10.56	10.48	.140	9.25	7.95
Vitality (SF-36)	35.00	15.55	37.69	15.34	.447	36.36	15.40

Note. Due to a technical error, the data of one participant (IHM) is missing for education, employment details, living condition.

Dropouts and missing data

In the intervention group the dropout rate at month 6 was 18.4% (7 of 38). Three participants discontinued the study before month 3, and four more until month 6. Two additional participants discontinued until month 12. By the end of the 12-month intervention, 29 out of 38 participants completed the study. In the control group, dropout rate until month 6 was 7.7% (3 of 39). Due to technical difficulties, PSQ data for one participant was lost, resulting in 35 complete PSQ observations at month 6 in the control group and 31 in the IGM group. The main reasons for the study failures are attributable to the Covid-19 pandemic. Adherence rate to intervention?

Primary outcome

Analysis of variance

Using the ITT-population with a realistic imputation method, the intervention had a significant impact on the perceived stress outcome as shown by the analysis of variance ($F(1,73)=47.78$, $p<.001$). The group variable accounted for 36% of the variance (η2= 0.36). In addition, gender ($F(1,73)=1.63$, $p=.206$) had no significant influence on the variance, while the severity of the covariate PSQ total score at baseline ($F(1,73)=5.01$, $p=.028$, η2=0.05) showed a small significant impact. However, the p-value for the baseline value turned non-significant when using the PP population (see Table 2).

Table 2. ANCOVA results for the differences between month 6 and month 0 adjusted for gender and baseline values

	Intent-to-treat sample					Per-protocol sample				
	Sum of squares	**df**	**F**	**Sig.**	**η2**	**Sum of squares**	**df**	**F**	**Sig.**	**η2**
PSQ total score M0	820.6	1	5.01	.028 *	0.05	734.7	1	3.83	.055	0.04
Gender	266.5	1	1.63	.206	0.01	273.6	1	1.43	.237	0.01
Group (IHM/CG)	7828.9	1	47.78	< .001***	0.36	6636.5	1	34.63	< .001***	0.33
Residuals	11960.4	73				11880.9	62			

PSQ-total score

Based on our pilot study, we expected a significant group difference with an average reduction of 18 points in the IHM group and 9 points in the control group (Melchart et al., 2017c; Melchart et al., 2018). Although we could only recruit 78 participants for the study, the conservative ITT still showed a significant group difference in the main outcome variable PSQ after 6 months with a large effect size ($t(66.63)=-6.48$, $p<.001$, $d=-1.48$). Specifically, the IHM group's PSQ total score decreased by an average of 24.71 points ($SD=15.31$), corresponding to a 40% reduction. In contrast, the control group experienced a decrease of 5.06 points (8%, $SD=10.87$) in perceived stress scores. Furthermore, participants in the intervention group achieved a significant reduction in their PSQ total score, from an average of 62.11 ($SD=11.30$) to 37.39 ($SD=15.30$), corresponding to a large effect size ($t(37)=-9.95$, $p<.001$, $d=-1.81$). Notably, the average score of 41.20 is below the clinically normal threshold of 41.5. In comparison, the control group's reduction from 62.74 points ($SD=13.19$) to 57.67 ($SD=15.64$) corresponds to a small effect size ($t(38)=-2.91$, $p=.006$, $d=-0.34$), and the average score remains clinically abnormal.

To comprehensively assess the impact of the intervention over a 12-month period, we conducted an intra-group comparison within the IHM group. Remarkably, the intervention demonstrated continued effectiveness, culminating in significant improvement by month 12 ($t(37)=-11.14$, $p<.001$, $d=-2.23$). On average, the PSQ total score decreased by 40% at month 6 and further decreased by 45% at month 12. Similar results were observed in the PP population (see Table 3). Overall, the IHM group derived substantial benefits from the intervention, while the control group exhibited natural improvement without reaching clinical significance. Figure 3 gives an overview of the difference in PSQ total score for each time point.

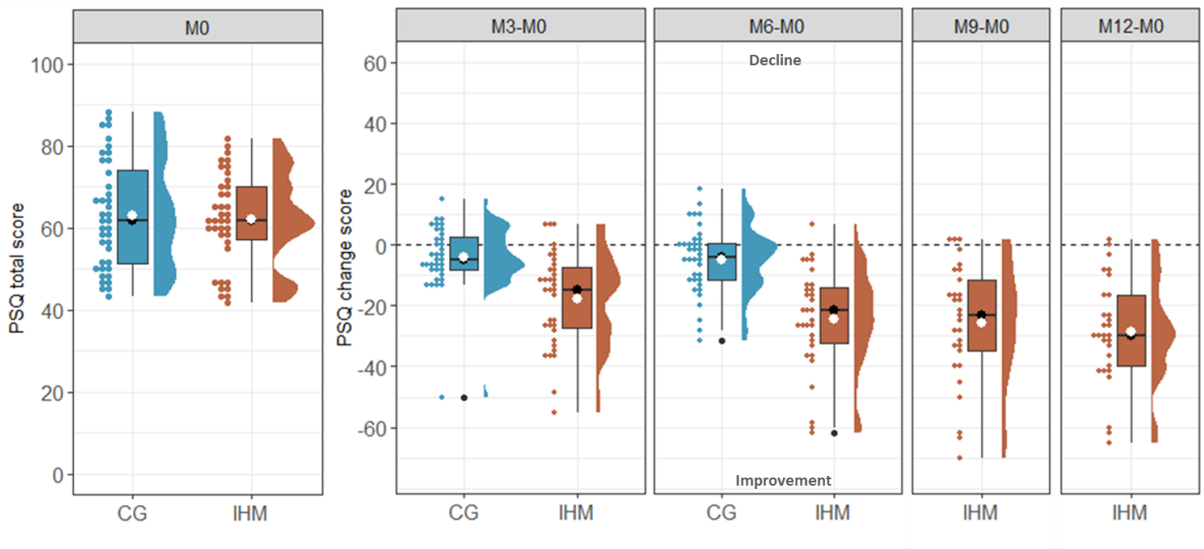

Figure 3. Perceived Stress: Distribution of mean differences at each time point per group (without imputation). The dashed line represents no change, values above the line indicate a decline, and values below the line show improvement. White circles indicate the mean, black lines and circles the median.

PSQ subscales

When taking a closer look at the mean differences between the IHM group and the CG after 6 months regarding the subscales, there were significant differences with large effect sizes for all sub-dimensions (*worries*: *p*<.001, *d*=-0.99; *demands*: *p*<.001, *d*=-1.00; *joy*: *p*<.001, *d*=1.13; *tension*: *p*<.001, *d*=-1.18). Furthermore, the within group analyses indicated that the IHM group experienced significant improvements with large effect sizes in all dimensions after 6 months (*worries*: p<.001, d=-1.26; *demands*: *p*<.001, *d*=-0.95; *joy*: *p*<.001, *d*=1.22; *tension*: *p*<.001, *d*=-1.80) as well as after 12 months (*worries*: *p*<.001, *d*=-1.52; *demands*: *p*<.001, *d*=-1.20; *joy*: *p*<.001, *d*=1.33; *tension*: *p*<.001, *d*=-2.26). In contrast, the CG showed only significant changes for the subscale tension (*p*=.012, *d*=-0.33). For a more detailed overview of the statistical results see Table 3.

Secondary outcomes

After 6 months, the IHM group demonstrated significant improvements compared to the CG for all secondary outcomes in the area of general well-being. The severity of mood state in general (*t*(63.17)=-6.19, *p*<.001, *d*=-1.53), Burnout symptoms (*t*(50.00)=-4.88, *p*<.001, *d*=-1.24), ISR total score (*t*(49.06)=-3.46, *p*=.001, *d*=-0.88), life satisfaction (*t*(44.81)=3.42, *p*=.001, *d*=0.87), sense of coherence (*t*(58.76)=4.39, *p*<.001, d=1.09), vitality (*t*(50.22)=4.89, *p*<.001, *d*=1.24), and WHO-5 well-being (*t*(55.51)=3.73, *p*<.001, *d*=0.94) showed significant differences between the two groups with large effect sizes in favour of the IHM group. The within-group analyses for the intervention in the IHM, comparing the values after 12 months, consistently revealed significant effects across all mental and psychological factors. These effects were even more pronounced than those observed after 6 months, with the exception of well-being and life satisfaction. Table 3 provides a concise summary of the statistical results, including intra-group comparisons and ANCOVA analyses. Furthermore, Figure 4 show a visual summary of the findings related to all outcome variables.

Table 3. Statistical results for the comparison between and within groups

	Intervention Group				Control Group				Difference between groups: Change from baseline		Effect size	Between group ANCOVA [1]
		Change from baseline		Effect size		Change from baseline		Effect size				
	N	**Mean**	**SD**	**Cohen's d**	**N**	**Mean**	**SD**	**Cohen's d**	**Mean difference [95%CI]**	**Pooled SD**	**Cohen's d**	**Parameter estimate for group [95%CI]**
PSQ total ITT												
M 3	38	-17.53	14.96	-1.31***	39	-4.17	10.31	-0.28*	-13.36 [-19.18; -7.54]	12.81	-1.04***	-14.03 [-19.80; -8.27]
M 6	38	-24.71	15.31	-1.81***	39	-5.06	10.87	-0.34**	-19.65 [-25.67; -13.63]	13.25	-1.48***	-20.50 [-26.41; -14.59]
M 9	38	-26.03	17.85	-1.94***								
M 12	38	-28.38	15.70	-2.23***								
PSQ total PP												
M 3	35	-17.71	15.41	-1.31***	35	-4.24	10.89	-0.27*	-13.48 [-19.84; -7.11]	13.35	-1.01***	-14.20 [-20.54; -7.85]
M 6	31	-24.46	16.71	-1.70***	35	-5.05	11.48	-0.34*	-19.42 [-26.10; -12.43]	14.18	-1.37***	-20.51 [-27.48; -13.54]
M 9	29	-25.80	19.51	-1.78***								
M 12	29	-28.79	17.19	-2.13***								
PSQ subscales												
PSQ worries PP												
M 3	35	-16.57	17.37	-0.99***	35	-4.19	16.50	-0.22	-12.38 [-20.46; -4.30]	16.94	-0.73**	-13.42 [-20.61; -6.22]
M 6	31	-22.37	19.82	-1.26***	35	-4.00	17.28	-0.20	-18.37 [-27.49; -9.25]	18.51	-0.99***	-20.68 [-29.06; -12.31]
M 9	29	-24.37	19.94	-1.39***[a]								
M 12	29	-26.44	18.98	-1.52***								
PSQ demands PP												
M 3	35	-18.86	19.83	-0.85***	35	-2.48	16.17	-0.11	-16.38 [-25.01; -7.75]	18.10	-0.91***	-15.45 [-23.92; -6.97]
M 6	31	-22.37	17.93	-0.95***	35	-4.95	16.83	-0.25	-17.41 [-25.97; -8.86]	17.36	-1.00***	-16.24 [-24.72; -7.77]
M9	29	-22.53	23.80	-0.92***								
M 12	29	-26.67	17.37	-1.20***								
PSQ joy PP												
M 3	35	13.91	18.03	0.80***	35	6.29	13.33	0.37**	7.62 [0.06; 15.18]	15.86	0.48*	10.61 [2.93; 18.29]
M 6	31	22.37	17.68	1.22***	35	4.19	14.47	0.23	18.18 [10.26; 26.09]	16.06	1.13***	21.01 [12.73; 29.28]
M 9	29	25.29	21.41	1.39***[a]								
M 12	29	25.29	21.63	1.33***[a]								
PSQ tension PP												
M 3	35	-21.52	21.94	-1.30***	35	-4.00	15.44	-0.20	-17.52 [-26.57; -8.48]	18.97	-0.92***	-18.05 [-26.50; -9.60]
M 6	31	-30.75	24.02	-1.80***	35	-7.05	15.67	-0.33*	-23.71 [-33.57; -13.84]	20.02	-1.18***	-24.61 [-36.20; -15.02]
M 9	29	-31.03	26.14	-1.66***								
M 12	29	-36.78	23.94	-2.26***								
Secondary Outcomes [2]												
Tedium-Measure (Burnout) PP												
M 3	35	-0.78	0.67	-1.13***	34	-0.17	0.54	-0.24	-0.61 [-0.91; -0.32]	0.61	-1.01***	-0.66 [-0.96; -0.35]
M 6	31	-1.18	0.85	-1.77***	35	-0.31	0.55	-0.47**	-0.87 [-1.22; -0.52]	0.71	-1.24***	-1.01 [-1.35; -0.67]
M 9	29	-1.34	0.88	-2.10***								
M 12	29	-1.43	0.90	-2.04***								
ISR PP												
M 3	35	-0.29	0.38	-0.57***	34	-0.08	0.25	-0.17	-0.21 [-0.36; -0.05]	0.32	-0.65**	-0.34 [-0.39; -0.09]
M 6	31	-0.47	0.47	-0.94***	35	-0.13	0.30	-0.33*	-0.36 [-0.52; -0.20]	0.39	-0.88**	-0.34 [-0.53; -0.15]
M 9	29	-0.50	0.46	-1.05***								
M 12	29	-0.66	0.51	-1.38***[a]								
General Mood State Severity (VAS) PP												
M 3	35	-22.20	19.00	-1.41***	35	-3.20	21.57	-0.18	-19.00 [-28.70; -9.31]	20.33	-0.94***	-17.32 [-26.01; -8.62]
M 6	31	-28.65	20.81	-1.84***	35	3.26	20.99	0.20	-31.90 [-42.20; -21.60]	20.90	-1.53***	-29.90 [-38.07; -21.74]
M 9	29	-26.59	24.45	-1.52***								
M 12	29	-31.31	23.77	-1.96***								
Life satisfaction (FLZ) PP												
M 3	35	12.29	25.53	0.47**	34	9.71	19.20	0.36**	2.58 [-8.30; 13.46]	22.64	0.11	2.51 [-7.61; 12.63]

M 6	31	28.39	35.23	1.01***	35	4.11	19.00	0.15	24.27 [10.57; 37.98]	27.81	0.87**	27.86 [15.63; 40.09]
M 9	29	31.83	32.17	1.10***								
M 12	29	31.59	36.07	1.00***								
Sense of Coherence (SOC) PP												
M 3	35	5.54	10.93	0.51**	35	0.80	8.50	0.07	4.74 [0.07; 9.41]	9.79	0.49*	5.11 [0.48; 9.74]
M 6	31	9.87	9.91	0.88***	35	-0.06	8.28	-0.01	9.93 [5.46; 14.40]	9.08	1.09***	10.07 [5.53; 14.62]
M 9	29	10.90	11.03	1.07***								
M 12	29	11.17	11.70	1.03***								
Well-being (WHO-5) PP												
M 3	35	8.03	12.91	0.78***	35	1.89	5.43	0.17*	6.14 [1.42; 10.67]	9.91	0.62*	6.12 [1.22; 11.02]
M 6	31	10.23	10.77	1.28***	35	1.37	8.16	0.13	8.85 [4.19; 13.52]	9.47	0.94***	8.16 [3.62; 12.69]
M 9	29	11.03	16.40	0.88** [a]								
M 12	29	14.00	17.38	1.05*** [a]								
Vitality (SF-36) PP												
M 3	35	18.57	20.09	1.02***	35	2.86	14.92	0.15	15.71 [7.27; 24.16]	17.70	0.89***	15.66 [7.10; 24.21]
M 6	31	27.10	23.30	1.57***	35	3.14	15.05	0.18	23.95 [14.41; 33.49]	19.36	1.24***	22.97 [13.70; 32.24]
M 9	29	26.21	24.63	1.30***								
M 12	29	32.07	23.62	1.87*** [a]								

[1] Between group ACNOVA adjusted for baseline values and gender.

[2] Due to the Corona virus pandemic a participant in the CG is missing for some secondary outcomes.

Significance: p<.05*, p<.01**, p<.001***; Effect size d: <.05 small effect, 0.5-0.8 medium effect, >0.8 large effect.

PP: per-protocol; ITT: Intent-to-treat; PSQ: Perceived Stress Questionnaire

[a] for not normally distributed complete observations (M9-M0 or M12-M0), the Wilcoxon signed rank test was additionally performed: Worries M9 (PSQ): z=-3.82, p<.001, r=0.84; Joy M9 (PSQ): z=4.27, p<.001, r=0.81; Joy M12 (PSQ): z= 4.08, p<.001, r=0.77; ISR: z= -4.65, p<.001, r=0.87; WHO-5 M9: z= 4.52, p<.001, r=0.85; WHO-5 M12: z= 4.62, p<.001, r=0.87; Vitality: z= 4.40, p<.001, r=0.83; SSS: z= 3.48, p<.001, r=0.66; Optimism: z= 3.79, p<.001, r=0.72; Pessimism: z= 3.69, p<.001, r=0.68. Wilcoxon signed rank test: Effect size r<.03 small effect, 0.3-0.5 medium effect, >0.5 large effect

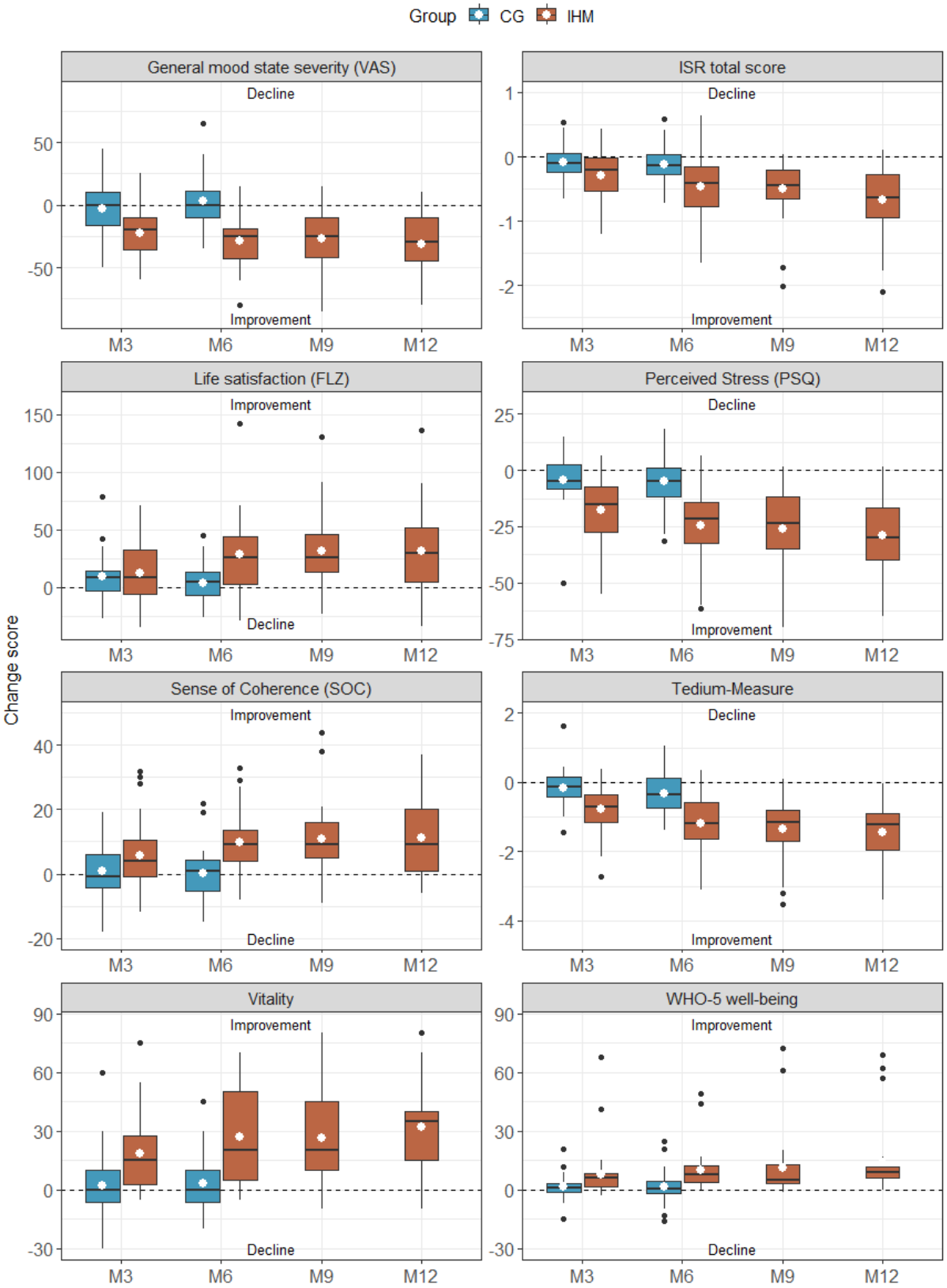

Figure 4. All outcomes: Distribution of mean differences at each time point per group (without imputation). The dashed line represents no change. White circles indicate the mean, black lines the median.

Adverse events

Participants who discontinued the study before month 3 are not included in the list. This leaves 35 participants for the IHM group and 37 for the CG. A total of 26 adverse events (AE) were reported, 11 in the IHM group and 15 in the CG group. None were considered to be severe adverse events. In 22 of the 26 AE there was no connection with the study (IHM: 8; CG: 14), and 4 AE were classified as not assessable in relation to a connection (IHM: 3; CG: 1).

Cross-over analysis

Given the small sample size, we conducted an additional single-group cross-over study. In this study, the original control group (previously on a waiting list) was compared with itself after receiving the intervention (new IHM group). We performed the same statistical analysis for the primary outcome as in the RCT described earlier.

The results of the cross-over (CO) analysis are slightly less strong but align with those obtained from the RCT. Utilizing the intention-to-treat (ITT) population with realistic imputation, we observed an 8% reduction in the PSQ total score for the CG after six months (mean change= -5.06, *SD*= 10.87). Following the intervention, the PSQ total score decreased by an additional 33% for the same group (mean change= -19.15, *SD*= 17.81). During the waiting period, the PSQ score declined from 62.74 (*SD* = 13.19) to 57.67 (*SD* = 15.64). Conversely, active participation in the intervention resulted in a reduction of the PSQ score from 57.57 (*SD*= 16.06) to 38.42 (*SD*= 20.69). Although both reductions were statistically significant, the effect size was small during the waiting period and substantial after the intervention (CG: *t(38)*=-2.91, *p*= .006, *d*=-0.34; IHM: *t(34)*=-6.36, *p* < .001, *d*= -1.01; *t*-test for paired samples). When comparing the mean difference after six months between the groups, we observed a significant improvement in the IHM group, characterised by a large effect size (*t*(34)=-3.86, *p*<.001, *d*=-0.94; *t*-test for paired samples). Notably, the values returned to clinically normal levels on average after 6 months of intervention, mirroring the experience observed in the IHM group of the RCT. For the PP population, the analyses revealed similar results (see Table 4). Figure 5 and 6 illustrate the results graphically.

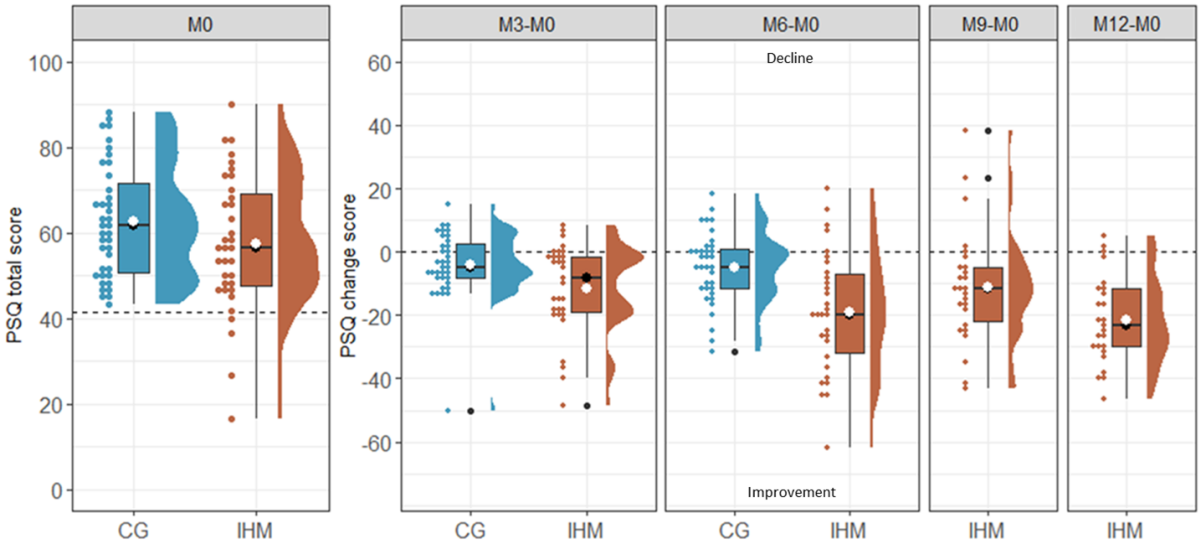

Figure 5. Cross-over analysis: Comparisons of mean differences for all time points (without imputation). The dashed line represents no change, values above the line indicate a decline, and values below the line show improvement. White circles indicate the mean, black lines/ circles the median. The mean differences after M6 for the CG are the baseline values for the new IHM group.

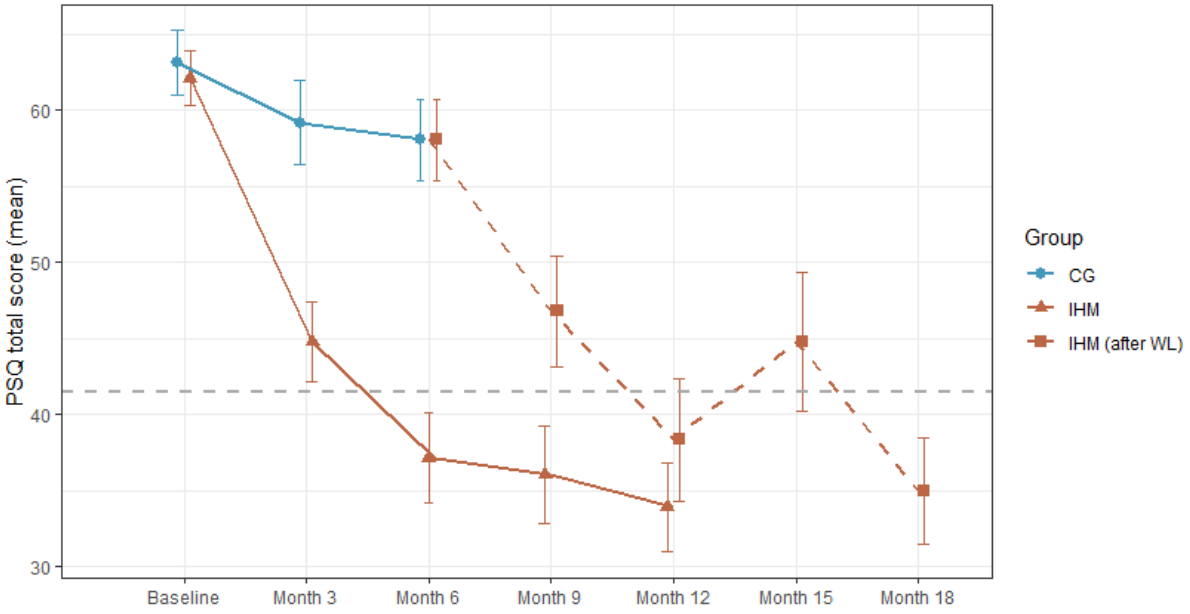

Figure 6. Mean total PSQ values at each time point per group (without imputation). The grey line represents the threshold value below which the values are considered clinically normal. The solid line indicates the mean values for the RCT groups (IHM and CG), while the dashed line represents the values for the CG when receiving the IHM after being on the waiting list (WL).

Table 4. Cross-over: Statistical results for the comparison between and within groups

	Intervention Group				Control Group				Difference between groups: Change from baseline		Effect size	Between group ANCOVA [1]
	Change from baseline			Effect size	Change from baseline			Effect size				
	N	**Mean**	**SD**	**Cohen's d**	**N**	**Mean**	**SD**	**Cohen's d**	**Mean difference [95%CI]**	**Pooled SD**	**Cohen's d**	**Parameter estimate for group [95%CI]**
PSQ total ITT												
M 3	35	-11.59	13.35	-0.63***	39	-4.17	10.31	-0.28*	-7.41 [-12.91; -1.92]	11.84	-0.59**	-7.89 [-13.42; -2.37]
M 6	35	-19.15	17.81	-1.01***	39	-5.06	10.87	-0.34**	-14.08 [-20.85; -7.32]	14.57	-0.94***	-15.21 [-21.94; -8.49]
M 9	35	-11.38	15.69	-0.59***								
M 12	35	-22.03	11.86	-1.38***								
PSQ total PP												
M 3	31	-11.61	14.21	-0.59***	35	-4.24	10.89	-0.27*	-7.38 [-13.56; -1.19]	12.56	-0.55*	-7.91 [-14.10 -1.71]
M 6	30	-19.11	19.23	-0.96***	35	-5.05	11.48	-0.34*	-14.06 [-21.79; -6.34]	15.53	-0.89**	-15.52 [-23.23 -7.81]
M 9	26	-11.16	18.27	-0.52**								
M 12	25	-21.60	13.94	-1.22***								

[1] Between group ACNOVA adjusted for baseline values and gender.
Significance: p<.05*, p<.01**, p<.001***; Effect size d: <.05 small effect, 0.5-0.8 medium effect, >0.8 large effect.
PP: per-protocol; ITT: Intent-to-treat; PSQ: Perceived Stress Questionnaire

Discussion

After six months of intervention, the IHM yielded remarkable results in reducing participants' perceived stress levels. Although decreased PSQ values were experienced in both groups after six months, the effect was significantly more pronounced in the IHM group. Furthermore, 33-36% of the variance in the difference of the total PSQ score could be explained solely by the group allocation. In comparison, the baseline values, which ranged from 41.67 to 81.67, only had a small significant impact on the variance (4%), and turned non-significant when using the PP instead of the ITT-population. This implies that the intervention is appropriate for a wider range of patients with varying stress levels. Moreover, the absence of significant gender-related differences in the variances suggests that the results were not substantially affected by the unequal distribution of genders among the groups. However, it's important to note that the potential impact of gender and baseline stress severity on the observed effects requires further investigation.
Furthermore, sensitivity analyses and the cross-over analysis confirmed the primary hypothesis, revealing a significant difference between groups regardless of the method used. In all cases, the mean perceived stress (PSQ) value in the IHM group decreased significantly, reaching a clinically normal level after 6 months (≤ 41.5). Remarkably, these low values persisted for up to twelve months and even demonstrated additional improvement (month 6: -40%; month 12: -45%).

The results are comparable to another lifestyle intervention that aimed to reduce stress (Stier-Jarmer et al., 2016). In this study, a 3-week intervention demonstrated remarkable effects with a large effect size immediately after the intervention, which persisted up to a six-month follow-up period. However, the effect declined over time. Our study reveals that a prolonged lifestyle intervention, including frequent refresher seminars, can consistently enhance the intervention's effectiveness over the course of one year. In our study, participants in the control group also demonstrated significant improvements in the total perceived stress (PSQ) score, corresponding to an 8% decrease. Although the previously mentioned study did not analyse within-group differences, the mean difference observed in the control group at month 3 aligns with the mean difference seen in our study at month 6. However, despite this improvement, it remains insufficient to reach a clinically normal value. A closer examination of the subscales revealed that the only significant change for the control group was related to tension. It appears that tension levels can naturally decrease over time to a small extent (11%). Nevertheless, our intervention effectively helped participants reduce tension, worries, and demands by 43%, 43%, and 36%, respectively, while increasing joy by nearly 75%.

In addition, our secondary analyses revealed that the comprehensive approach of our lifestyle intervention not only effectively reduces stress but also enhances various mental health aspects. These included depression, ISR symptoms, well-being, vitality, life satisfaction, sense of coherence, and the overall severity of mood state. Compared to a meta-analysis by Khoury et al. (2015) on mindfulness-based stress reduction interventions, our approach demonstrated comparable efficacy in improving mental health. Our comprehensive lifestyle intervention, which targets various behaviours contributing to health issues, offers potential benefits beyond stress reduction alone. The IHM's ability to address multiple health aspects becomes evident when we combine the results of our stress reduction study with a separate investigation on weight reduction. In that study, participants also received the IHM intervention and were able to reduce their weight by 10% (Melchart et al., 2017a). Thus far, the IHM has demonstrated efficacy in reducing mental health aspects and weight for participants coping with high stress levels or overweight conditions.

Besides assessing subjective mental health and weight, future studies should also evaluate the IHM in terms of physiological parameters. As previous research indicated that subtle physiological differences may not be easily detectable in physiologically healthy individuals, focusing on subgroups with abnormal physiological parameters could yield more valuable insights than a general analysis. For instance, one study explored a three-week intervention involving cold exposure, breathing exercises, and meditation in physically healthy participants and no significant changes were observed in cardiovascular parameters (Ketelhut et al., 2023). In contrast, a separate study examining the effects of mindfulness-based stress reduction in patients with acute myocardial infarction found significant improvements in hemodynamic parameters, particularly blood pressure (Gu et al., 2023). Thus, as a next step, investigating physiological differences in participants who displayed clinically abnormal values before the intervention would be valuable.

Another dimension of the IHM framework involves a blended learning approach, which combines a web-based portal with face-to-face seminars. Previous studies (e.g., Goh et al. 2021; Ierardi et al., 2022; Karyotaki et al., 2021) have shown that purely internet-based interventions offer short-term stress reduction but lack lasting effects. In contrast, our strategy—integrating initial face-to-face teaching with ongoing web-based support and regular refresher seminars over a year—appears more effective. However, longer interventions with refresher seminars come with a trade-off: they demand greater commitment from participants. This heightened commitment likely contributed to higher drop-out rates, which exceeded our expectations. Challenges related to COVID-19 regulations and caution also played a role and generally made it difficult to recruit participants for the study. Consequently, the randomization process did not involve the desired number of participants, resulting in an unbalanced gender distribution. Despite falling short of our intended sample size due to pandemic-related restrictions, the IHM group still achieved the expected reductions in perceived stress. Remarkably, they even exceeded the expectations we had based on the pilot study, highlighting the impact of the IHM intervention.

In summary, the IHM proves to be an effective intervention for reducing perceived stress and addressing various other mental health indicators. The comprehensive strategy leads to enhanced mental health factors, with positive outcomes persisting for up to a year and continuing to improve beyond that timeframe. Future research should explore the specific intervention parameters associated with stress reduction, as well as investigate the long-term effects beyond a one-year intervention period.

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