A transdiagnostic group exercise intervention for mental health outpatients in Germany (ImPuls): results of a pragmatic, multisite, block-randomised, phase 3 controlled trial

Sebastian Wolf, Britta Seiffer, Johanna-Marie Zeibig, Anna Katharina Frei, Thomas Studnitz, Jana Welkerling, Edith Meinzinger, Leonie Louisa Bauer, Julia Baur, Stephanie Rosenstiel, David Victor Fiedler, Florian Helmhold, Andreas Ray, Eva Herzog, Keisuke Takano, Tristan Nakagawa, Mia Maria Günak, Saskia Kropp, Stefan Peters, Anna Lena Flagmeier, Lena Zwanzleitner, Leonie Sundmacher, Ander Ramos-Murguialday, Martin Hautzinger, Gorden Sudeck, Thomas Ehring

Summary

Background Globally, mental health conditions pose a substantial burden of disease. Despite the availability of evidence-based pharmacological and psychological treatments, the symptoms of a substantial subgroup of patients do not respond to these interventions, and only a minority of patients have access to them. This study aimed to assess the efficacy of ImPuls, a 6-month transdiagnostic group exercise intervention, plus treatment-as-usual, compared with treatment-as-usual alone in outpatients with various mental disorders.

Methods In this pragmatic, two-arm, multisite, randomised controlled trial in Germany, ten outpatient rehabilitative and medical care facilities were involved as study sites. Participants were outpatients diagnosed according to ICD-10 with one or more of the following disorders based on structured clinical interviews: moderate or severe depression, primary insomnia, post-traumatic stress disorder (PTSD), panic disorder, or agoraphobia. Participants were required to be aged between 18 years and 65 years, insured by the health insurers Allgemeine Ortskrankenkasse Baden-Württemberg or Techniker Krankenkasse, fluent in German, and without medical contraindications for exercise. Blocks of six participants were randomly allocated to ImPuls plus treatment-as-usual or treatment-as-usual alone (allocation ratio: 1:1), stratified by study site. The randomisation sequence was generated by an external data manager. The team responsible for data collection and management was masked to the randomisation sequence. The ImPuls intervention comprised evidence-based outdoor exercises lasting 30 min, and aimed at achieving at least moderate intensity. It also incorporated behavioural change techniques targeting motivational and volitional determinants of exercise behaviour. Treatment-as-usual was representative of typical outpatient health care in Germany, allowing patients access to any standard treatments. The primary outcome was global symptom severity at 6 months after randomisation, measured using self-report on the Brief Symptom Inventory (BSI-18) and analysed in the intention-to-treat sample. No individuals with lived experience of mental illness were involved in conducting the study or writing the final publication. Safety was assessed in all participants. The trial was registered with the German Clinical Trials Register (DRKS00024152) with a completion date of June 30, 2024.

Findings 600 patients provided informed consent, were recruited to the study, and underwent a diagnostic interview between Jan 1, 2021, and May 31, 2022. Following this, 199 were excluded on the basis of inclusion and exclusion criteria and one withdrew consent during the baseline assessment. Of the 400 eligible participants, 284 (71%) self-identified as female, 106 (27%) self-identified as male, and nine (2%) self-identified as other. The mean age was 42·20 years (SD 13·23; range 19–65). Ethnicity data were not assessed. 287 (72%) participants met the criteria for moderate or severe depression, 81 (20%) for primary insomnia, 37 (9%) for agoraphobia, 46 (12%) for panic disorder, and 72 (18%) for PTSD. 199 participants were allocated to the intervention group of ImPuls plus treatment-as-usual and 201 to the control group of treatment-as-usual alone. 38 (19%) participants did not receive the minimum ImPuls intervention dose. ImPuls plus treatment-as-usual demonstrated superior efficacy to treatment-as-usual alone in reducing global symptom severity, with an adjusted difference on BSI-18 of 4·11 (95% CI 1·74–6·48; d=0·35 [95% CI 0·14–0·56]; p=0·0007) at 6 months. There were no significant differences in the total number of adverse events or serious adverse events between the two groups. There was one serious adverse event (male, torn ligament) related to the intervention.

Interpretation ImPuls is an efficacious transdiagnostic adjunctive treatment in outpatient mental health care. Our findings suggest that exercise therapy should be implemented in outpatient mental health care as an adjunctive transdiagnostic treatment for mental disorders such as depression, insomnia, panic disorder, agoraphobia, and PTSD. Transdiagnostic group exercise interventions might ameliorate the existing disparity in care provision between the many individuals in need of evidence-based treatment and the few who are receiving it.

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Faculty of Economics and Social Sciences, Institute of Sports Science, Department of Education & Health Research (S Wolf PhD, B Seiffer MSc, J-M Zeibig PhD, A K Frei MSc, T Studnitz MSc, J Welkerling MSc, E Meinzinger BSc, L L Bauer MSc, S Rosenstiel PhD, D V Fiedler MSc, Prof G Sudeck PhD), **Faculty of Science, Psychological Institute, Department of Clinical Psychology and Psychotherapy** (J Baur PhD, Prof M Hautzinger PhD), **Medical Faculty, Institute of Medical Psychology and Behavioural Neurobiology** (F Helmhold MSc, A Ray PhD, A Ramos-Murguialday PhD), **and Department of Neurology & Stroke** (A Ramos-Murguialday), **University of Tübingen, Tübingen, Germany; Department of Psychology, Division of Clinical Psychology and Psychological Treatment, LMU Munich, Munich, Germany** (E Herzog MSc, K Takano PhD, T Nakagawa PhD, M M Günak MSc, Prof T Ehring PhD); **Chair of Health Economics, Technical University Munich, Munich, Germany** (S Kropp MSc, Prof L Sundmacher PhD); **German Association for Health-Enhancing Physical Activity and Exercise Therapy, Hürth-Efferen, Germany** (S Peters PhD); **AOK Baden-Württemberg, Stuttgart, Germany** (A L Flagmeier MSc); **Techniker Krankenkasse,**

Hamburg, Germany (L Zwanzleitner BSc); Tecnalia, Basque Research and Technology Alliance, San Sebastián, Spain (A Ramos-Murguialday); Athenea Neuroclinics, San Sebastián, Spain (A Ramos-Murguialday); German Center for Mental Health, Munich, Germany (T Ehring); International Max Planck Research School for Cognitive and Systems Neuroscience, Tübingen, Germany (F Helmhold); Human Informatics and Interaction Research Institute, National Institute of Advanced Industrial Science and Technology, Tsukuba, Japan (K Takano); Department of Human Sciences, Institute of Sport Science, Bundeswehr University Munich, Munich, Germany (S Peters)

Correspondence to Dr Sebastian Wolf, Faculty of Economics and Social Sciences, Institute of Sports Science, Department of Education & Health Research, University of Tübingen, 72074 Tübingen, Germany
sebastian.wolf@uni-tuebingen.de

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Introduction

Globally, mental health conditions are a major health concern, accounting for 4·9% of all disability-adjusted life-years (DALYs) and ranking as the seventh leading cause of all DALYs.[1,2] Depression, insomnia, anxiety, and stress-related disorders are some of the most prevalent mental health conditions worldwide. They frequently overlap and share aetiological and maintenance factors.[3]

Although evidence-based interventions exist, several challenges remain. First, the symptoms of a substantial subgroup of patients do not respond to pharmacotherapy and psychological treatment, with non-response rates

Research in context

Evidence before this study

There is strong evidence that exercise interventions are efficacious in reducing the symptoms of a range of highly prevalent mental health conditions, including depression, insomnia, agoraphobia, panic disorder, and post-traumatic stress disorder (PTSD). However, most research to date has focused on disorder-specific outcomes and interventions in patient samples with specific mental health conditions. By contrast, there is a lack of evidence on transdiagnostic exercise interventions and their effects on global symptom severity in samples of patients with various mental health conditions. Furthermore, evidence on the disorder-specific effects of exercise interventions is mostly based on studies without long-term follow-up assessments and with small sample sizes, making it difficult to draw conclusions about their long-term efficacy. Before conducting the present study, we searched PubMed in March, 2020 using the following search terms: ((exercise[Title/Abstract]) OR (physical activity[Title/Abstract])) AND ((transdiagnostic[Title/Abstract])) AND ((intervention) OR (treatment)) AND ((depression) OR (anxiety) OR (panic) OR (agoraphobia) OR (insomnia) OR (PTSD)). Our search had no date or language restrictions, and it used the filter for randomised controlled trials. Three relevant papers were identified: two consisted of study protocols published in 2015 and 2016, and one from 2017 reported the results of a clinical trial. The study protocols described trials designed to evaluate the efficacy of transdiagnostic interventions in which physical activity constituted only one component. The clinical trial investigated the effects of exercise and strength training on disorder-specific and transdiagnostic outcomes, albeit only in patients with anxiety-related disorders. Both exercise types (ie, aerobic exercise and strength training) improved disorder status. Aerobic exercise improved general psychological distress and anxiety. Resistance training improved disorder-specific symptoms, anxiety sensitivity, distress tolerance, and intolerance of uncertainty. After concluding this study in September, 2023, we updated our literature search. Apart from our own feasibility study, we found no additional studies specifically evaluating the efficacy of exercise on global symptom severity in a sample of patients diagnosed with depression, insomnia, anxiety disorders, or PTSD.

Added value of this study

Our large randomised controlled trial assessed the efficacy of a 6-month group exercise intervention (ImPuls) plus treatment-as-usual compared with treatment-as-usual alone in reducing global transdiagnostic symptom severity in a real-world outpatient context for physically inactive adult patients diagnosed with moderate or severe depression, insomnia, agoraphobia, panic disorder, or PTSD. Of the 400 patients randomly assigned to the intervention or control group, 77% were already receiving a standard outpatient treatment (pharmacotherapy or psychological treatment) at baseline. We found larger improvements in global symptom severity in the intervention group than in the control group at 6 months after baseline, with persistent benefits seen at the 12-month follow-up assessment. An evaluation of reliable clinical change showed that the effects were clinically meaningful at both 6 months and 12 months. We also found indications of benefits for disorder-specific mental health symptoms, including those of depression, panic disorder, general anxiety, and PTSD. These clinical effects were maintained for depression, general anxiety, and panic disorder up to the 12-month assessment. Mean self-reported exercise increased in the intervention group from 17 min weekly on average to the intended dose of more than 90 min weekly at 6 months and dropped to 69 min at 12 months. Increases in self-reported exercise partially explained the treatment effects for participants who adhered to the minimum intervention dose. Our results provide strong evidence that exercise therapy is a feasible and efficacious transdiagnostic adjunctive treatment in real-world mental health care contexts for outpatients with various mental disorders.

Implications of all the available evidence

Strong evidence that exercise is efficacious in treating specific mental health conditions, as well as new evidence from our study that exercise has transdiagnostic effects when combined with treatment-as-usual, suggests that exercise therapy should be used in outpatient mental health care as an alternative to standard treatment or as an adjunctive treatment for disorders such as depression, insomnia, panic disorder, agoraphobia, and PTSD. Transdiagnostic group exercise interventions hold great promise because they allow for the simultaneous treatment of multiple patients. By optimising the use of health-care resources and potentially reducing waiting times for treatment, these interventions could ameliorate the existing disparity in care provision between the many individuals in need of evidence-based treatment and the few who are receiving it.

ranging from 30% to 50% across mental health conditions.[4,5] Second, only a minority of patients have access to evidence-based standard treatments.[6] Even in a high-income country such as Germany, only 10% of individuals with mental health conditions receive evidence-based treatment, and only 2·5% receive psychological treatment, often waiting for up to 9 months.[7] Third, psychological treatment is usually administered as individual rather than group therapy, which can be considered inefficient from a public health perspective. Finally, the use of psychotropic medication can have detrimental effects on physical health, such as weight gain, sedation, or extrapyramidal side-effects.

Exercise of moderate-to-vigorous intensity has demonstrated disorder-specific therapeutic effects in patients with specific mental health conditions.[8] Previous meta-analyses investigating the effects of exercise on depression have found large effects compared with treatment-as-usual.[9,10] Furthermore, moderate effects have been reported for exercise in addition to treatment-as-usual for depression.[11] In the case of post-traumatic stress disorder (PTSD) and insomnia, meta-analyses have found small-to-moderate effects and large effects, respectively, for exercise interventions compared with passive control groups or treatment-as-usual.[12,13] For anxiety and stress-related disorders, combined meta-analytic evidence indicates small-to-moderate anxiolytic effects.[14] Although the evidence derived from the cited meta-analysis supporting the disorder-specific effects on depression is strong, with almost universally positive results, the evidence for the other disorders, particularly PTSD, insomnia, and anxiety disorders, is positive but based on few studies. The efficacy of exercise across these disorders might be explained by its effects on transdiagnostic aetiological and maintenance mechanisms, such as anxiety sensitivity, self-efficacy, and stress reactivity.[15,16]

To date, there is a lack of evidence on the efficacy of transdiagnostic group exercise programmes in reducing global symptom severity among patients with various mental health conditions. This is unfortunate given that such programmes allow for the simultaneous treatment of multiple patients in heterogeneous groups, optimising the use of health-care resources. Evaluating these programmes in real-world outpatient settings is crucial to assess their potential as alternatives or adjuncts to standard treatment and help bridge the current treatment gap.

The ImPuls programme, a recent transdiagnostic group exercise intervention, was developed for outpatients with various mental health conditions based on current evidence regarding the efficacy of exercise and its long-term maintenance.[17] Because patients with mental health conditions often have difficulties motivating themselves to perform regular exercise, ImPuls explicitly included motivational and volitional elements based on evidence that these can increase exercise maintenance.[18] A feasibility study of ImPuls demonstrated large immediate and moderate long-term effects compared with a passive control group in patients awaiting psychological treatment.[19,20] In this Article, we report the results of a large-scale, multisite, pragmatic randomised controlled trial that aimed to investigate the long-term efficacy of ImPuls plus treatment-as-usual compared with treatment-as-usual alone in a real-world outpatient mental health-care setting in Germany. We tested the following pre-registered hypotheses.[21] First, that participants in the intervention group receiving ImPuls plus treatment-as-usual will show reduced global symptom severity and more instances of clinically significant change at 6 months and 12 months compared with a control group receiving treatment-as-usual only (primary outcome), with global symptom severity at 6 months being the primary endpoint. Second, that the intervention will lead to significantly higher volumes of self-reported exercise and moderate-to-vigorous intensity physical activity, as measured by accelerometry at 6 months and 12 months, compared with the control group. Third, that participants in the intervention group will show reduced disorder-specific symptoms compared with participants in the control group at 6 months and 12 months. Finally, that the effect of the intervention in reducing the primary outcome, global symptom severity, from baseline to 6 months and from baseline to 12 months will be mediated by increases in self-reported exercise and moderate-to-vigorous intensity physical activity.

Methods

Study design and participants

We conducted a pragmatic, multisite, block-randomised, phase 3 controlled trial with two treatment groups (ImPuls plus treatment-as-usual *vs* treatment-as-usual alone) and three points of assessment (baseline, 6 months, 12 months). The trial was carried out across ten different outpatient rehabilitative and medical care facilities in southwest Germany (appendix p 58).

See Online for appendix

Eligible participants were adults who were: (1) aged between 18 years and 65 years; (2) insured by one of the two cooperating statutory health insurers, Allgemeine Ortskrankenkasse Baden-Württemberg or Techniker Krankenkasse; (3) fluent in German; (4) without medical contraindications for exercise; and (5) diagnosed according to ICD-10 with at least one of the following disorders: major depressive disorders of at least moderate severity (F32.1, F32.2, F33.1, F33.2), insomnia (F51.0), agoraphobia (F40.0, F40.01), panic disorder (F41.0), or PTSD (F43.1). Participants were excluded if they had: (1) engaged in at least 30 min of exercise of at least moderate intensity more than once a week for 6 weeks within the 3 months before study diagnosis; or (2) a current diagnosis of mental and behavioural disorders caused by psychotropic substances, eating disorders, bipolar disorder, schizophrenia, or acute

suicidality (appendix pp 16–17). Gender data were collected via self-report (female, male, other).

Patients were recruited from various settings (appendix pp 39, 60) and screened for somatic contraindications to exercise using the Physical Activity Readiness Questionnaire. Additionally, patients had to provide a health provider's referral for ImPuls before the baseline assessment. After obtaining written informed consent from patients to participate in the study, qualified psychologists conducted a structured clinical interview, termed SCID-5-CV, to confirm eligibility. Once six patients at a study site were found to be eligible, they received online questionnaires covering all primary, secondary, and further outcomes, as well as demographic data, through the web-based data management system REDCap. Additionally, participants were given an accelerometer-based physical activity sensor (MOVE 4; movisens) to wear for 7 consecutive days (appendix pp 23–24, 39–41). The study was conducted according to the guidelines of the Declaration of Helsinki of 2010 and was approved by the local ethics committee for medical research at the University of Tübingen (888/2020B01; Nov 2, 2020). The study protocol has been published previously.[21]

Randomisation and masking

Each group of six eligible patients was randomly assigned to ImPuls plus treatment-as-usual or treatment-as-usual alone with a randomisation ratio of 1:1. The randomisation sequence was generated by an external data manager using a varying-size permuted block design, stratified by study site. Randomisation codes were generated digitally and concealed on a secure system. The team responsible for data collection and management, who were in direct contact with patients, were masked to the randomisation sequence. The data analyst remained masked to treatment allocation until the primary statistical analyses were complete.

Procedures

Within 14 days after randomisation, global symptom severity was reassessed to verify that patients met the cutoff criteria for a mental disorder. All measures taken during the baseline assessment were repeated at 6 months and 12 months after randomisation. The intervention group received ImPuls plus treatment-as-usual, whereas the control group received treatment-as-usual only. Treatment-as-usual consisted of any available standard intervention typically provided in the German outpatient setting. Available standard interventions include psychological (cognitive behavioural therapy, psychoanalysis, systemic therapy) and pharmacological treatments. The prescription or use of standard interventions during the study period was not assessed. Patients might have learned about such interventions through their treating physicians or psychotherapists, or they might have sought standard therapy on their own, such as by consulting a psychotherapist. Differences between groups were documented only at baseline. Upon completing all assessments, patients in the control group were compensated with €450.

The design and components of ImPuls are shown in figure 1 and the appendix (pp 18–21).[17,20,21] Exercise therapists were required to have an academic degree or comparable qualification with at least 3 years of training as physical activity or exercise professionals, along with a specific therapeutic qualification. All therapists also received training in ImPuls (appendix pp 17–18, 59).

Treatment dropout criteria were defined as missing 2 entire weeks during weeks 1–4. Attendance during the supervised (weeks 0–4) and partially supervised (weeks 5–24) periods was tracked. Study dropouts were defined as intentional discontinuation of the entire study or of all assessments (appendix pp 22, 30).

The fidelity of the therapists' delivery of the intervention was evaluated through video recordings. Ten per cent of all recorded sessions were randomly selected for evaluation. Randomisation was conducted by the external data manager. All supervised sessions (weeks 0–4) were recorded by the exercise therapists themselves. For the final evaluation, one video session from each group was selected out of the eight recorded sessions that included the core elements of the intervention. These core elements of the manualised ImPuls intervention were determined a priori. To assess adherence, rating forms were developed for each of the recorded sessions, with items divided into general adherence questions and questions focusing on the core elements of the intervention. Therapist adherence to the treatment manual was assessed independently by two reviewers. A general adherence score and an adherence score focusing only on core elements were calculated and then averaged to compute the overall fidelity score. The expected overall fidelity score was set at a minimum of 90%. Further details of the assessment and evaluation process can be found in the appendix (pp 29–30, 61–62).

Outcomes

Global symptom severity served as the primary outcome and was measured using the Global Severity Index (GSI) derived from the validated German version of the Brief Symptom Inventory (BSI-18) at 6 months.[22] The GSI encompasses ratings of general mental distress across symptom scales for somatisation, depression, and anxiety. Each scale consists of six items, contributing to a total of 18 items in the assessment. Participants rate each item on a 5-point Likert scale (range: 0–4). The total score is calculated for each of the three scales, and the GSI is determined by summing these three scores. Higher scores on the GSI indicate greater levels of distress, with a clinical cutoff set at 12.[22] The primary outcome was assessed in the intention-to-treat sample.

Secondary outcomes were the GSI (BSI-18) at 12 months, depressive symptoms assessed with the Patient Health

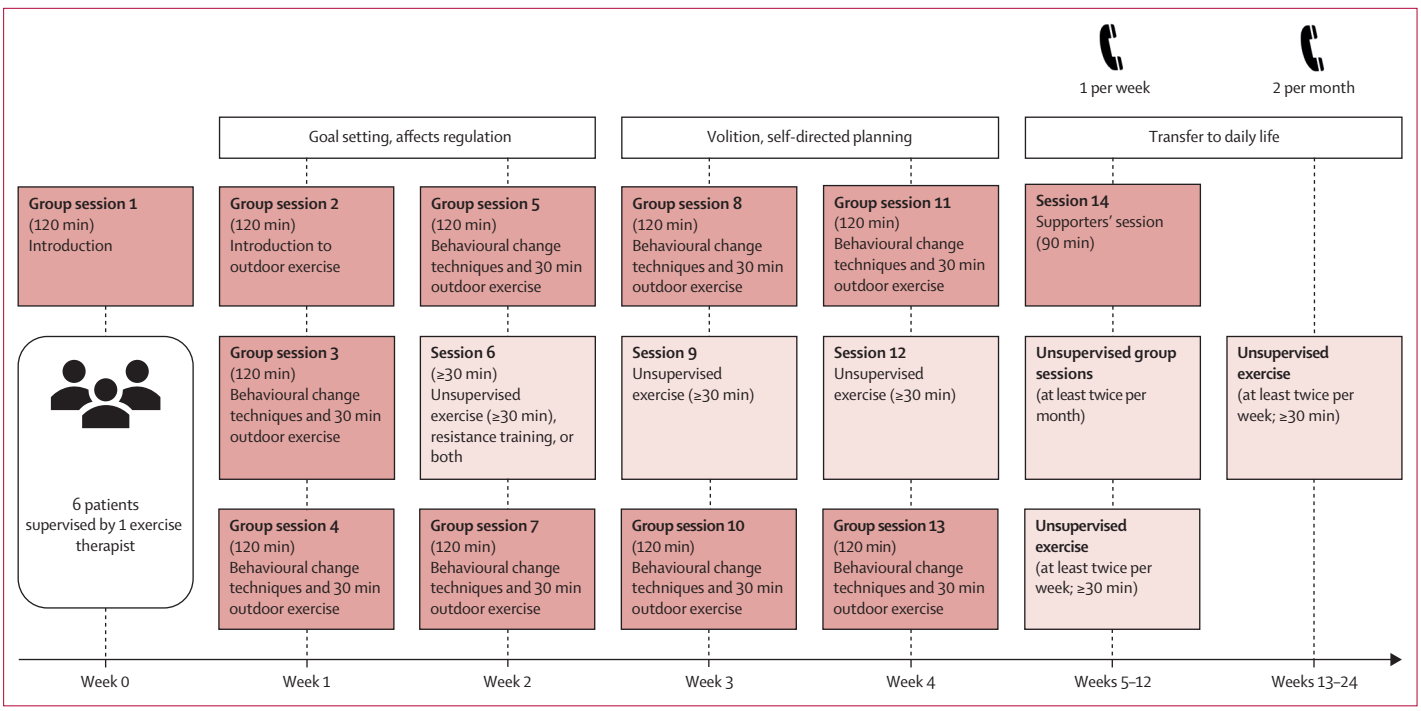

Figure 1: **Design and components of the ImPuls intervention**

The dark red boxes indicate supervised sessions with group meetings (group sessions) and 30 min of moderate-to-vigorous aerobic exercise performed as outdoor running along with a supporters' session in week 5. The aim of the supporters' session was to enable the patients' supporters (eg, family or friends) to help patients permanently integrate physical activity into their daily lives. For example, patients and supporters jointly developed plans to overcome specific barriers. Intensity was controlled by a heart rate monitor (SIGMA iD.FREE) combined with a chest strap (SIGMA R1 Bluetooth Duo Comfortex+) and the Borg Rating of Perceived Exertion Scale. Moderate-to-vigorous intensity was defined as at least 64% of maximum heart rate, subtracting age from 220, and a self-report of at least 13 points of the Rating of Perceived Exertion Scale. Behavioural change techniques such as goal-setting and barrier management were integrated to improve motivational and volitional skills for exercise maintenance. These were delivered by exercise therapists in the group sessions and supported by the ImPuls smartphone application. The medium red boxes depict non-supervised aerobic exercise, allowing patients to choose type of exercises independently based on their own interests. Telephone calls in combination with the ImPuls smartphone application were used for long-term exercise monitoring. The participants had access to the ImPuls smartphone application during the whole trial, which could be used to track exercise duration and intensity.

Questionnaire-9, non-organic insomnia symptoms assessed with the Insomnia Severity Index, sleep quality assessed with the global sleep quality score of the Pittsburgh Sleep Quality Index, anxiety symptoms assessed with the Generalized Anxiety Disorder Scale-7, panic disorder and agoraphobia symptoms assessed with the three-item panic subscale of the BSI-18, and symptoms of PTSD assessed with the PTSD Checklist for DSM-5 (PCL-5; appendix pp 25–29). Self-reported exercise was measured in minutes per week using the Exercise Activity Index of the Physical Activity, Exercise, and Sport Questionnaire. Weekly minutes spent in moderate-to-vigorous physical activity were measured using accelerometer-based sensors (Move 4, movisens). Moderate-to-vigorous physical activities were defined as those with energy expenditures of at least three metabolic equivalents of task (appendix pp 27–28). Metabolic equivalents of task serve as an objective metric for assessing the ratio of energy expenditure relative to an individual's mass during physical activities, in comparison to the energy expended during sedentary periods. In addition to the secondary outcome of global symptom severity at 12 months, all other secondary outcomes were assessed at 6 months and 12 months in the intention-to-treat sample.

Additional prespecified assessments, which took place during the supervised period (weeks 1–4; appendix pp 18–19, 31), included calculating mean objective exercise intensity, expressed as a percentage of maximum heart rate (HRmax). HRmax is calculated by subtracting the participant's age from 220. Heart rate data were collected using heart rate monitors (SIGMA iD.FREE). Using the ImPuls smartphone application, perceived exertion was rated by participants with the Borg Rating of Perceived Exertion scale and mean session duration (min per session) was tracked during the supervised period (weeks 1–4; appendix pp 18–19, 31). These additional assessments were conducted exclusively in the intervention group based on an intention-to-treat approach.

Patients' outcome expectations, motivation, and satisfaction with the intervention, as well as exercise therapists' motivation and satisfaction with the intervention, were assessed with validated scales (appendix pp 31–37). On these scales, means falling into the upper quartile, the second or third quartiles, or the lowest quartile were considered high, moderate, and low scores, respectively. Patients' outcome expectations and motivation were assessed in all patients on an intention-to-treat basis,

whereas patients' satisfaction with the intervention was assessed only in the intervention group. Therapists' motivation and satisfaction were assessed using an intention-to-treat approach in all therapists treating at least one group.

Adverse events were assessed at baseline, 6 months, and 12 months in all patients on an intention-to-treat basis. Serious adverse events could be reported at any time and were assessed through structured interviews at each assessment point. All serious adverse events were reported to an independent Data Safety and Monitoring Board (appendix pp 48–51).

Choice of primary outcome measure

The BSI-18 is a short and resource-efficient version of the Symptom Checklist-90, which internationally is the most frequently used questionnaire for assessing general psychological distress and is validated in several languages. Using the BSI-18 requires the purchase of a licence. The completion time of the BSI-18 is approximately 4 min. The questionnaire showed excellent fit with the composition of our transdiagnostic sample because the GSI derived from it encompasses ratings across depression, anxiety, and somatisation symptoms. In German outpatients with various mental disorders, the GSI has shown good internal consistency (Cronbach's alpha, 0·89). Moreover, it has demonstrated construct validity in patients with affective disorders and anxiety disorders, with correlation coefficients of r=0·71 for affective disorders and r=0·67 for anxiety disorders.[23] To assess clinically meaningful change, we used the Reliable Change Index according to the Jacobson–Truax method using a cutoff of 12.

To evaluate transdiagnostic efficacy, it is important to use a global index that is sensitive to each disorder in a transdiagnostic sample. This approach enables direct assessment of the relationship between transdiagnostic mechanisms, such as increased exercise, and a psychopathological outcome across different disorders. Using disorder-specific measures to assess mechanisms of change would lower sensitivity across the full sample and necessitate numerous discrete analyses. Furthermore, conducting analyses of efficacy and mechanisms of impact in each diagnostic subgroup would diverge from our transdiagnostic approach and reduce statistical power.

Statistical methods

The minimum sample size (n=375) was determined a priori through a power analysis. This analysis was based on the smallest post-treatment effect size of exercise versus treatment-as-usual or waiting list as control conditions reported in earlier meta-analyses, which was d=–0·348 for PTSD symptoms.[13] We assumed a two-sided *t* test, alpha level of 0·05, test power of 80% based on 1:1 allocation (equal group size), and a dropout rate of 30%. To ensure sufficient statistical power for further predefined analyses, as published in a separate study protocol for the process evaluation of ImPuls, a maximum sample size of n=600 was pre-registered.[24] Due to recruitment delays caused by the COVID-19 pandemic, the original target of 600 participants was not met. However, we ultimately recruited 400 participants, which means that the study was sufficiently powered for the main analyses.

All analyses adhered to the pre-established statistical analysis plan published before database lock and were conducted using R (version 4).[21] Descriptive statistics were calculated for baseline characteristics and outcome measures at 6 months and 12 months, and they were presented as means and standard deviations. The primary and secondary outcomes were analysed using linear mixed models (restricted maximum likelihood estimation; appendix p 45). These models incorporated categorical fixed factors for time (baseline, 6 months, 12 months), groups (ImPuls plus treatment-as-usual and treatment-as-usual alone), and their interaction. Also, random intercepts to account for between-person and between-site variation and random slopes for time-related between-person variation were included. The analysis for the primary and secondary outcomes included data from all randomised participants on an intention-to-treat basis. Data are presented as adjusted differences with 95% confidence intervals, p values, and standardised between-group effect sizes based on 95% CIs. Missing values were addressed using multilevel multiple imputation. The significance level was set at alpha=0·05. Exploratory analyses (not pre-registered; appendix p 67) were performed to investigate associations between treatment responses (ie, changes in the primary and all secondary outcomes) and motivation (at baseline) and satisfaction (after the 4-week supervised period). An additional sensitivity analysis (not pre-registered; appendix p 68) tested whether the results of the primary outcome were unchanged after controlling for inclusion diagnosis.

The normality assumption of residuals was checked using QQ plots, and non-normally distributed data were log-transformed. Effect sizes for adjusted group differences at each follow-up timepoint were calculated, divided by the standard deviation estimated through the mixed models (Cohen's d: 0·2 small, 0·5 medium, and 0·8 large effect). A reliable change index based on the Jacobson–Truax method was calculated for the GSI score at 6 months and again for the GSI score at 12 months on the non-imputed dataset (appendix pp 45–46). The Mann–Whitney *U* test was performed to assess differences in ordinal scores (recovered, improved, unchanged, deteriorated) between groups. Analyses for primary and secondary outcomes were repeated on the completer sample, defined as those who completed at least 2 full weeks of the supervised intervention period (weeks 1–4; appendix p 22).

To test the fourth hypothesis, mediation analyses were performed on the simple change scores of GSI (outcome) and of moderate-to-vigorous physical activity and self-reported exercise (as the mediators). Two path models were estimated: one for changes from baseline to

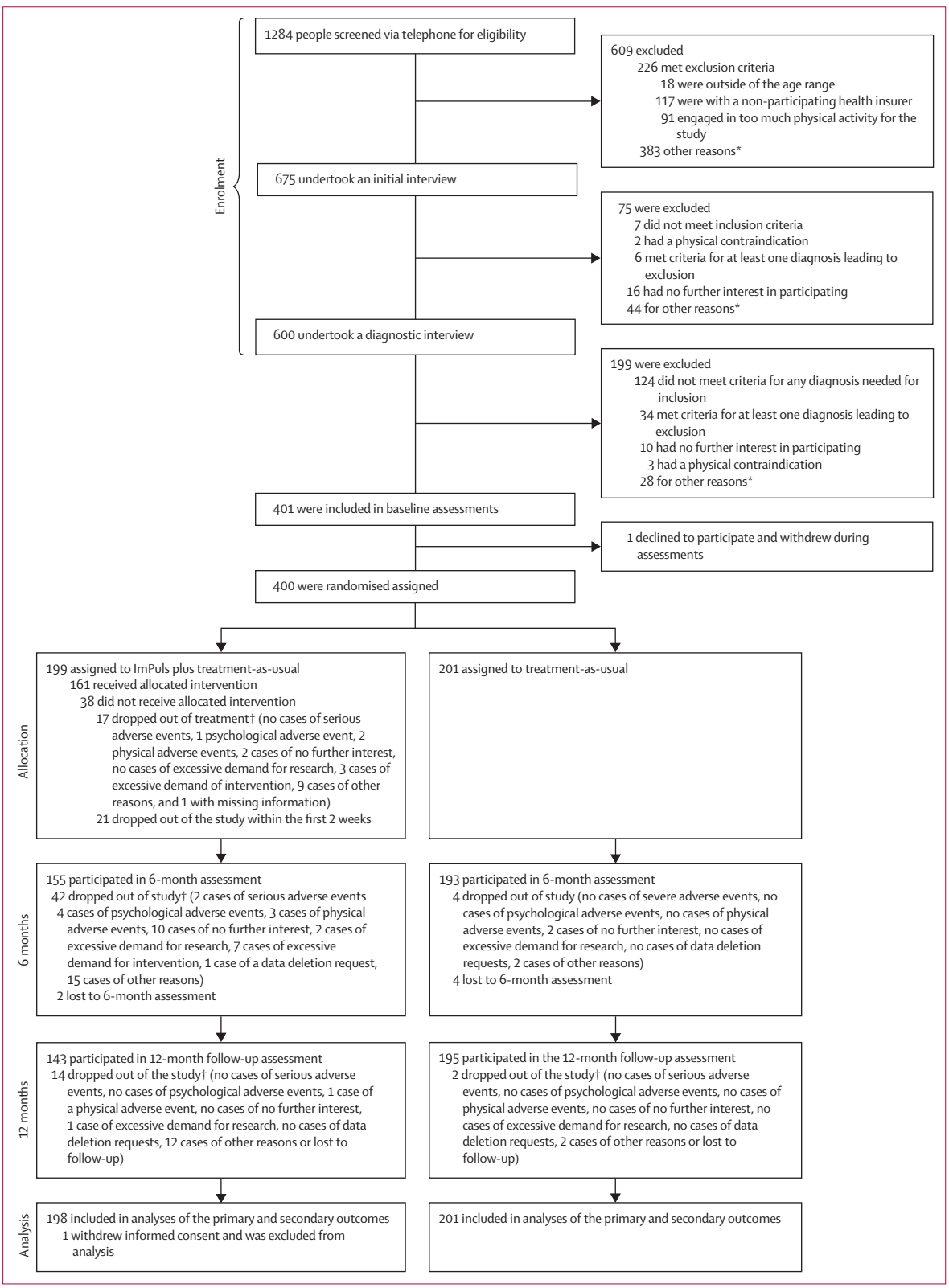

Figure 2: **Trial profile**
Excessive demand (research) refers to patients finding tasks related to research aspects burdensome (for example, too many questionnaires, excessively long completion time of questionnaires); the research aspects of study participation were too onerous. Excessive demand (intervention) means that patients considered tasks or efforts related to the intervention as too demanding (for example, too high intervention frequency, too long a distance to travel to the centre for therapy sessions); the intervention itself was too onerous. *Other reasons include organisational problems, relocation, no more contact possible, physical constraints, language problems, or unknown. †Multiple answers possible; study dropout details have been presented as number of cases rather than number of participants and therefore might not total the number of participants who dropped out of the study at each point.

	ImPuls plus treatment-as-usual (n=199)	Treatment-as-usual (n=201)
Age, years		
Mean age	41·73 (12·80)	42·65 (13·65)
Missing	3 (2%)	2 (1%)
Gender		
Female	141 (71%)	143 (71%)
Male	56 (28%)	50 (25%)
Other	1 (<1%)	8 (4%)
Missing	1 (<1%)	0
Highest level of education		
None	1 (<1%)	0
Primary (Grundschule)	0	0
Basic or intermediate secondary (Hauptschule or Realschule)	48 (24%)	49 (24%)
Vocational	9 (5%)	16 (8%)
Secondary qualifying for university admission (Abitur)	59 (30%)	71 (35%)
University	72 (36%)	64 (32%)
Other	9 (5%)	1 (<1%)
Missing	1 (<1%)	0
Employment status		
Employed (full-time or part-time)	73 (37%)	90 (45%)
In education (with or without part-time job)	29 (15%)	23 (11%)
Fully or partially unable to work	36 (18%)	32 (16%)
Permanently fully or partially limited in work capacity due to a long-term health condition or disability	17 (9%)	17 (8%)
Unemployed	9 (5%)	5 (2%)
Stay-at-home partner or spouse (with or without part-time job)	13 (7%)	6 (3%)
Retired	1 (<1%)	0
Other	18 (9%)	26 (13%)
Missing	3 (2%)	2 (1%)
Relationship status		
Single, separated, or widowed	83 (42%)	78 (39%)
Married or living with a partner	115 (58%)	123 (61%)
Missing	1 (<1%)	0
Number of children		
0	107 (54%)	107 (53%)
1	28 (14%)	28 (14%)
2	41 (21%)	40 (20%)
3	19 (10%)	18 (9%)
4	3 (2%)	2 (1%)
5	0	3 (1%)
Missing	1 (<1%)	2 (1%)

(Table 1 continues in next column)

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	ImPuls plus treatment-as-usual (n=199)	Treatment-as-usual (n=201)
Housing situation		
With others (family, partner, shared apartment) without children	84 (42%)	95 (47%)
With others and with children	36 (18%)	32 (16%)
Assisted living without children	2 (1%)	3 (1%)
Assisted living and with children	0	0
Alone without children	48 (24%)	51 (25%)
Alone with children	24 (12%)	16 (8%)
Other	4 (2%)	3 (1%)
Missing	1 (<1%)	1 (<1%)
Current diagnosis		
Moderate or severe depression (ICD-10 F32·1, F32·2, F33·1, F33·2)	146 (73%)	141 (70%)
Panic disorder (ICD-10 F41·0)	25 (13%)	21 (10%)
Agoraphobia (ICD-10 F40·0, F40·01)	19 (10%)	18 (9%)
Post-traumatic stress disorder (ICD-10 F43·1)	31 (16%)	41 (20%)
Primary insomnia (ICD-10 F 51·0)	44 (22%)	37 (18%)
Comorbidity: any other inclusion diagnosis	53 (27%)	45 (22%)
Comorbidity: any other non-inclusion psychiatric diagnosis	92 (46%)	104 (52%)
Comorbidity: any other inclusion diagnosis or any further psychiatric diagnosis	125 (63%)	121 (60%)
Health insurance provider		
AOK Baden-Württemberg	90 (45%)	90 (45%)
Techniker Krankenkasse	108 (54%)	111 (55%)
Missing	1 (<1%)	0

(Table 1 continues in next column)

6 months and the other for changes from baseline to 12 months. We used full-information maximum likelihood estimation to handle missingness and bootstrapped standard errors for direct, indirect, and total effects. The same mediation analyses were repeated on the completer sample (appendix p 45).

The study was registered with the German Clinical Trial Register (DRKS00024152; Feb 5, 2021). The progress of the study and its final results were discussed with the Data Safety and Monitoring Board.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 1, 2021, and May 31, 2022, a total of 600 patients provided informed consent, were recruited to the study, and undertook a diagnostic interview. Of these patients, 199 were excluded on the basis of inclusion and exclusion criteria and one patient withdrew consent during the baseline assessment. The remaining 400 patients were randomly assigned to ImPuls plus treatment-as-usual (n=199) or treatment-as-usual alone (n=201; figure 2).

Demographic and baseline data for these 400 participants are shown in table 1 (appendix pp 55–56). Their mean age

	ImPuls plus treatment-as-usual (n=199)	Treatment-as-usual (n=201)
(Continued from previous column)		
Treatments		
Psychological treatment		
Receiving outpatient psychological treatment	103 (52%)	116 (58%)
Missing	55 (28%)	44 (22%)
Pharmacological treatment		
Receiving outpatient pharmacological treatment	108 (54%)	108 (54%)
Missing	2 (1%)	1 (<1%)
Outpatient standard care		
Receiving any outpatient standard care (psychological or pharmacological treatment)	152 (76%)	155 (77%)
Missing	29 (15%)	23 (11%)
Alternative treatment		
Receiving alternative treatment (online or application-based therapy)	12 (6%)	8 (4%)
Missing	2 (1%)	2 (1%)
Previous psychological treatment		
Previous outpatient psychological treatment	140 (70%)	144 (72%)
Missing	2 (1%)	2 (1%)
Previous pharmacological treatment		
Previous outpatient pharmacological treatment	105 (53%)	98 (49%)
Missing	2 (1%)	0
Previous outpatient standard care		
Any previous outpatient standard care (psychological or pharmacological treatment)	153 (77%)	159 (79%)
Missing	2 (1%)	1 (<1%)
Previous inpatient psychiatric treatment		
Previous inpatient psychiatric treatment or hospital day unit care	114 (57%)	101 (50%)
Missing	1 (<1%)	0

Data are n (%) or mean (SD).

Table 1: **Baseline characteristics**

was 42·20 years (SD 13·23; range 19–65), and 284 (71%) of the 400 participants reported being female, 106 (27%) reported being male, and nine (2%) reported being of other gender. Gender data was missing in one participant who was randomly assigned to the ImPuls plus treatment-as-usual group. Regarding diagnoses, 287 (72%) of the 400 participants were diagnosed with moderate or severe depression, 81 (20%) with primary insomnia, 37 (9%) with agoraphobia, 46 (12%) with panic disorder, and 72 (18%) with PTSD. 98 (25%) participants had at least one of the other inclusion diagnoses, and 196 (49%) had at least one additional psychiatric diagnosis not among the inclusion diagnoses.

Regarding treatment history, 307 (77%) of the 400 participants were receiving a standard pharmacological or psychological treatment at baseline. 312 (78%) reported a previous standard treatment, and 215 (54%) had a history of inpatient or hospital day unit treatment. Directly after randomisation, global symptom severity in both groups (mean 20·67 [SD 11·55]) was comparable to the German clinical norm sample (mean 20·23 [SD 12·19]).[22,25]

Treatment fidelity achieved an overall score of 87%, which was only slightly lower than intended (>90%) and can still be considered high (appendix pp 61–62). Demographic characteristics of the exercise therapists are presented in the appendix (p 59). Therapist motivation (scale 1–5; mean 4·25 [SD 0·57]; n=19), satisfaction with the intervention (scale 1–5; mean 3·39 [SD 0·91]; n=15), and expectations of intervention success (scale 1–5; mean 3·88 [SD 0·55]; n=19) at baseline were moderate to high. Patient motivation (scale 4–16; mean 14·05 [SD 2·50]; n=354) and expectations of intervention success (scale 1–5; mean 3·03 [SD 0·96]; n=350) were also moderate to high for the entire sample. Satisfaction with the intervention after the 4-week supervised period (scale 6–30; mean 21·96 [SD 3·88]; n=156) and after the 6-month intervention period (scale 6–30; mean 22·28 [SD 5·11]; n=135) was moderate. The overall attendance rate was high at 84%. Mean objective exercise intensity, indexed by percentage of individual maximum heart rate, was 71% (SD 14%; n=38) and thus aligned with expectations, as did the mean subjective rating of perceived exertion (scale 6–20; mean 13·96 [SD 1·44]; n=79) and mean exercise session duration (32·88 min [SD 9·19]; n=82), averaged across all exercise sessions within the supervised period (appendix p 62).

In total, 62 participants (16%) of 400 dropped out of the study (ImPuls plus treatment-as-usual: 56 [28%] of 199; treatment-as-usual: six [3%] of 201). In the ImPuls plus treatment-as-usual group, 161 patients (81%) of 199 completed the minimum intervention dose, indicating a treatment dropout rate of 19%. Data for the primary outcome (GSI) were available for 398 participants at baseline (197 in the ImPuls plus treatment-as-usual group and 201 in the treatment-as-usual group), 338 participants at 6 months (148 in the ImPuls plus treatment-as-usual group and 190 in the treatment-as-usual group), and 329 participants at 12 months (135 in the ImPuls plus treatment-as-usual group and 194 in the treatment-as-usual group). Performing Little's test on the primary and secondary outcomes led to the rejection of the missing completely at random assumption (χ^2 [179]=352; p<0·0001). Baseline predictors of attrition in the ImPuls plus treatment-as-usual group indicated a higher likelihood of study discontinuation among individuals with agoraphobia and those who had received previous psychiatric treatment (appendix p 71).

Descriptive statistics were calculated for the primary and secondary outcome measures at all assessment points, along with the results of the mixed model analyses, and are summarised in table 2. In the primary intention-to-treat analysis of 399 participants, ImPuls plus treatment-as-usual was superior to treatment-as-usual alone, showing an adjusted difference on the BSI-18 of 4·11 (95% CI 1·74–6·48; *d*=0·35 [95% CI 0·14–0·56]; p=0·0007) at 6 months (for our primary endpoint) and 3·29 (95% CI 0·86–5·72; *d*=0·28 [95% CI 0·07–0·50]; p=0·0080; table 2) at 12 months (first hypothesis). Based on the Jacobson–Truax method, a greater number of participants in the intervention group achieved clinically significant changes from baseline to 6 months (W=11551; p=0·0017) and from baseline to 12 months (W=11084; p=0·0095; appendix pp 45–46, 63) compared with treatment-as-usual alone.

	Unadjusted mean (SD); N		Adjusted difference (95% CI)	p value	Standardised between-group effect size (95% CI)
	ImPuls plus treatment-as-usual	Treatment-as-usual			
Global Severity Index (BSI-18)					
Baseline	22·08 (11·75); 197	22·01 (10·55); 201	..	..	..
6 months	14·03 (11·28); 148	19·61 (12·36); 190	4·11 (1·74 to 6·48)	0·0007	0·35 (0·14 to 0·56)
12 months	12·65 (11·20); 135	18·40 (12·45); 194	3·29 (0·86 to 5·72)	0·0080	0·28 (0·07 to 0·50)
Depression (PHQ-9)					
Baseline	13·76 (5·04); 197	13·79 (4·99); 200	..	..	..
6 months	10·33 (5·61); 147	12·15 (5·92); 190	1·26 (0·11 to 2·41)	0·032	0·23 (0·01 to 0·44)
12 months	9·07 (5·67); 134	11·72 (6·26); 192	1·47 (0·24 to 2·70)	0·020	0·27 (0·04 to 0·49)
Insomnia (ISI)					
Baseline	15·14 (5·68); 197	14·50 (6·37); 201	..	..	..
6 months	11·51 (5·50); 148	13·19 (6·55); 190	1·25 (–0·02 to 2·52)	0·054	0·20 (–0·02 to 0·42)
12 months	10·51 (6·09), 135	12·46 (6·26); 194	0·96 (–0·33 to 2·24)	0·15	0·16 (–0·07 to 0·38)
Sleep quality (PSQI)					
Baseline	10·10 (3·74); 182	9·93 (3·87); 196	..	..	..
6 months	8·67 (3·81); 125	9·02 (3·59); 167	0·42 (–0·44 to 1·27)	0·34	0·11 (–0·12 to 0·34)
12 months	8·27 (3·87); 115	9·10 (4·02); 166	0·44 (–0·39 to 1·27)	0·30	0·11 (–0·11 to 0·34)
Anxiety (GAD-7)					
Baseline	10·54 (4·87); 196	10·67 (4·78); 201	..	..	..
6 months	7·49 (4·58); 148	9·40 (4·92); 190	1·28 (0·27 to 2·30)	0·013	0·26 (0·05 to 0·47)
12 months	6·56 (4·64); 133	8·93 (5·12); 192	1·22 (0·14 to 2·30)	0·027	0·25 (0·02 to 0·47)
Panic (BSI-18)					
Baseline	2·81 (2·79); 197	2·59 (2·47); 201	..	..	..
6 months	1·38 (2·16); 148	2·18 (2·42); 190	0·60 (0·10 to 1·09)	0·020	0·25 (0·04 to 0·46)
12 months	1·16 (2·03); 135	2·13 (2·33); 194	0·57 (0·08 to 1·07)	0·024	0·24 (0·03 to 0·45)
Post-traumatic stress disorder (PCL-5)					
Baseline	29·10 (16·59); 196	30·08 (14·94); 200	..	..	..
6 months	20·20 (16·37); 148	26·27 (17·09); 187	3·94 (0·63 to 7·24)	0·020	0·24 (0·03 0·45)
12 months	18·37 (16·22); 133	24·15 (16·40); 192	3·09 (–0·38 to 6·56)	0·081	0·19 (–0·03 to 0·41)
Self-reported exercise (BSA)*					
Baseline	17·90 (55·54); 196	19·67 (84·13); 200	..	..	..
6 months	92·06 (109·58); 145	37·77 (79·92); 189	–1·11 (–1·58 to –0·64)	<0·0001	–0·65 (–0·94 to –0·37)
12 months	68·51 (107·73); 131	54·35 (125·80); 192	–0·44 (–1·00 to 0·12)	0·12	–0·26 (–0·59 to 0·07)
Moderate-to-vigorous physical activity (accelerometry data)*					
Baseline	325·78 (204·41); 172	336·93 (233·84); 184	..	..	..
6 months	341·40 (239·38); 114	336·75 (234·98); 146	–0·02 (–0·20 to 0·16)	0·80	–0·03 (–0·27 to 0·21)
12 months	342·33 (226·19); 111	357·40 (240·70); 172	0·03 (–0·15 to 0·20)	0·76	0·04 (–0·20 to 0·27)

Data are mean (SD); N, unless otherwise indicated. p<0·05 indicates significance. BSI-18=Brief Symptom Inventory-18. PHQ-9=Patient Health Questionnaire-9. ISI=Insomnia Severity Index. PSQI=Pittsburgh Sleep Quality Index. GAD-7=Generalized Anxiety Disorder scale. PCL-5=Posttraumatic Stress Disorder Checklist 5. BSA=self-reported exercise in min per week based on the athletic exercise index of the Physical Activity, Exercise, and Sport Questionnaire. Accelerometry data indicates weekly minutes spent in moderate-to-vigorous physical activity. Moderate-to-vigorous physical activities were defined as those with energy expenditures of at least 3 metabolic equivalents of task derived from accelerometry sensors worn for 7 consecutive days. *Unadjusted means are based on raw data and adjusted and standardised estimates are based on log-transformed data due to a skewed distribution of raw data.

Table 2: **Descriptive summaries of primary and secondary outcome measures and results of the mixed models on the intention-to-treat sample**

Across secondary outcomes, ImPuls plus treatment-as-usual resulted in improvements compared with treatment-as-usual alone in measures of depression, panic, general anxiety, PTSD, and self-reported exercise up to 6 months (table 2). At 12 months, the superiority of ImPuls plus treatment-as-usual persisted regarding symptoms of depression, general anxiety, and panic. The analysis of treatment completers showed significant between-group differences, with increased effect sizes compared with the primary analysis at both 6 months (4·69 [95% CI 2·20–7·17]; *d*=0·40 [95% CI 0·18–0·63]; p<0·0002) and 12 months (3·84 [95% CI 1·13–6·55]; *d*=0·33 [95% CI 0·09–0·57]; p=0·0055; appendix pp 72–79). Significant long-term differences between the two groups at the 12-month assessment were seen for depression, general anxiety, panic, and PTSD symptoms. Results of the sensitivity analysis are reported in the appendix (pp 67–68).

The results of the mediation analysis indicated only marginally significant mediation effects of changes in self-reported exercise on changes in global symptom severity for both the 6-month and 12-month assessments (appendix p 69). However, in the completer sample, a significant indirect effect was identified on changes in global symptom severity from baseline to 6 months (ß=–0·04; p=0·033), mediated by increases in self-reported exercise. The direct effect of the intervention remained statistically significant (ß=–0·14; p=0·0056), suggesting partial mediation (appendix pp 78–79).

Over the 12-month follow-up period, a total of 220 participants reported adverse events, including 85 (63%; 26 male, 58 female, and one other) of 136 patients with complete answers in the ImPuls plus treatment-as-usual group and 135 (71%; 35 male, 96 female, and four other) of 190 participants with complete answers in the treatment-as-usual group. A prevalent example of reported adverse events was the occurrence of new physical symptoms in the context of a SARS-CoV-2 infection. 14 (7%; seven male and seven female) of 199 patients in the ImPuls plus treatment-as-usual group reported 15 serious adverse events and 22 (11%; four male, 17 female, and one other) of 201 patients in the treatment-as-usual group reported 24 serious adverse events (table 3). There were no significant differences in the total number of adverse events or serious adverse events between the two groups. Eight participants who dropped out of the study indicated that their withdrawal was due to reported adverse events, whereas two indicated that their withdrawal was due to serious adverse events. There was one serious adverse event (torn ligament) related to the intervention (appendix pp 80–81).

	ImPuls plus treatment-as-usual (n=199)		Treatment-as-usual (n=201)	
	Events	Participants	Events	Participants
Type of adverse event				
Related to intervention	1	1 (1 male)	NA	NA
Related to psychiatric events	10	9 (5 male, 4 female)	15	14 (2 male, 11 female, 1 other)
Related to physical events	5	5 (2 male, 3 female)	9	9 (3 male, 6 female)
Total*	15	14 (7 male, 7 female)	24	22 (4 male, 17 female, 1 other)
Severity				
Low	0	0	0	0
Moderate	3	3 (3 male)	4	4 (2 male, 2 female)
High	12	11 (4 male, 7 female)	20	19 (3 male, 15 female, 1 other)

Severity was rated by the external Data Safety and Monitoring Board. NA=not available. *Multiple serious adverse events per participant possible.

Table 3: **Serious adverse events during the ImPuls trial**

Discussion

This large pragmatic randomised controlled trial demonstrated the efficacy of ImPuls, a transdiagnostic group exercise intervention, plus treatment-as-usual, in reducing global symptom severity and symptoms of depression, general anxiety, panic, and PTSD at 6 months after baseline compared with the control group receiving treatment-as-usual alone. Treatment effects were maintained up to 12 months after baseline for global symptom severity, depression, general anxiety, and panic. Notably, the intervention group showed better clinical recovery and improvement at both the 6-month and 12-month assessments compared with the control group. Although the intervention resulted in a substantial increase in self-reported exercise, this was not reflected in the accelerometer-based moderate-to-vigorous physical activity results at 6 months.

A sensitivity analysis focusing exclusively on patients who adhered to the minimum intervention dose confirmed the main analysis and yielded slightly larger effect sizes. The increase in self-reported exercise from baseline to 6 months partially mediated the treatment effects on global symptom severity in the analysis of completers, thus supporting the rationale behind the exercise intervention. The treatment dropout rate of 19% was comparable to rates reported in other randomised controlled trials involving exercise interventions for outpatients with depression in mental health-care services (19%) and anxiety and stress-related disorders (18%), as well as to rates observed for psychological treatments in real-world contexts (26%).[10,26,27] The probability of study dropout in the intervention group was higher among patients diagnosed with agoraphobia, which might be due to group outdoor exercise provoking anxiety in this patient population.

In existing meta-analyses, the focus has typically been on disorder-specific interventions in disorder-specific samples. Moreover, to date, only a few meta-analyses have investigated the efficacy of exercise as an adjunct to treatment-as-usual in patients with depression.[11,12,14] Our study replicates the positive findings of these analyses but shows considerably smaller effect sizes. This discrepancy could partly result from the comparison in our study between exercise as an adjunct to treatment-as-usual and treatment-as-usual alone, which constitutes a more stringent test than comparisons involving waiting

lists or passive control groups. Such control groups have often been used as comparator groups in the earlier studies underlying the meta-analyses published to date, often without clear differentiation between passive and active controls. The use of transdiagnostic measures in our study, which tend to be less specific than disorder-specific measures, especially in samples of patients with various mental disorders, might also have contributed to our smaller effect sizes. A recent meta-analysis of studies comparing transdiagnostic psychological treatments against passive control groups or treatment-as-usual in patients with major depression and anxiety disorders reported small-to-moderate effects, similar to those found in our study.[28]

In our study, the intervention group saw an increase in self-reported exercise to more than 90 min at 6 months, which aligned with our intervention manual and recent evidence on the disorder-specific efficacy of exercise in mental disorders.[8,9] At 12 months, the average weekly exercise duration remained high at 69 min, indicating that patients in the intervention group, on average, continued to maintain the necessary exercise volume. Contrary to our expectations, the treatment-as-usual group also experienced a substantial increase in exercise volume from baseline to 12 months, possibly reflecting heightened motivation for exercise stimulated either by participation in the study or through the effects of treatment-as-usual itself.

The existing literature lacks trials that simultaneously report on exercise volume, its long-term sustainability, treatment efficacy, and the role of exercise volume as a mediator of treatment effects.[8] Among the few trials that have considered exercise volume as an outcome, changes in exercise volume, regardless of group allocation, have been correlated with symptom reduction.[20,29] In this context, our study adds new insights by identifying a partial mediation effect of treatment outcomes through increases in self-reported exercise. However, this partial mediation was significant only in the completer analysis and from baseline to 6 months, suggesting that other factors contributed to the clinical efficacy observed. Evidence from our earlier feasibility study suggests that the long-term effects of ImPuls are due not solely to increased exercise volume but also to the deliberate use of exercise for affect regulation, which might also be true in the current trial.[19] Notably, accelerometry-based physical activity data did not show differential increases and were not associated with changes in global symptom severity. This could be due to the physical presence of the accelerometer motivating all patients to engage in exercise, as reflected in the consistently high activity levels across all measurement timepoints. Additionally, the data captured by accelerometers lack specificity because they include routine daily activities, such as domestic and occupational tasks, which have inconsistent associations with mental health.[30] Furthermore, although moderate-to-vigorous physical activity and self-reported exercise, as well as their changes from baseline to the 6-month assessment, correlated with each other in our study, patients might have overestimated their increases in exercise through self-reports, a tendency that has been demonstrated in the literature.[31] This tendency may be particularly pronounced when positive outcomes, such as achieving personal goals, are incorrectly attributed to increased exercise. However, self-reported exercise may serve as a strong predictor of treatment effects, as it more validly captures the primary objective of ImPuls, which is to increase exercise behaviour. The self-perception of being physically active mediates treatment effects of exercise on mental health.[32] Recent studies have shown that increases in self-efficacy and self-esteem through exercise seem to mediate effects on mental health.[33,34] Other psychosocial and neurobiological factors are discussed as mechanisms of impact, but the evidence remains inconclusive.[33,34]

Our study has several important limitations. First, we encountered differential drop-out rates between the groups. Comparing these rates is challenging due to the compensation provided exclusively to the control group, which might have contributed to its lower attrition rate. Patients diagnosed with agoraphobia and those who had received previous psychiatric treatment were more likely to drop out of the intervention group. To mitigate the influence of attrition bias, we incorporated both variables as predictors in our missing data imputation procedures. Second, similar to existing evidence-based standard treatments, our study identified a substantial proportion of participants whose symptoms did not respond, indicating that a subgroup of patients did not benefit from the exercise intervention. Various factors, such as a mismatch with the intervention (eg, group *vs* individual format), might account for non-response and warrant investigation in future studies. Third, we only included patients from two statutory health insurance providers, limiting the representativeness of our sample. Fourth, we were unable to systematically identify or assess any interventions that participants might have received alongside our study as part of treatment-as-usual and thus were unable to control for these. Fifth, we did not involve people with lived experience in the research and writing process, which would have contributed informed personal insights into the effectiveness and practicality of the intervention under study. Sixth, gender-based analysis was not conducted, as this was not included in the pre-registration of the study. Seventh, since ethnicity data were not collected, we cannot draw conclusions about potential differential effects based on ethnicity. Finally, our research design does not allow us to determine whether non-specific factors, such as daily routine or social support, contributed to the observed effects.

Overall, the findings of our study suggest that group interventions that combine exercise with behaviour change techniques, such as ImPuls, offer a viable and promising adjunctive treatment for moderate or severe

depression, insomnia, agoraphobia, panic disorder, and PTSD. Future research should analyse the reasons for non-response to refine ImPuls and similar interventions and to improve response rates. Comparative studies are warranted to compare ImPuls with standard transdiagnostic psychological interventions, as well as other pharmacological, behavioural, and psychosocial interventions. Such research could determine whether ImPuls might also serve as an alternative to standard treatment in routine care settings.

Contributors

SW, J-MZ, BS, ALF, LZ, LS, AR-M, MH, GS, and TE contributed to the conception and the design of the study and acquisition of funding. SW was responsible for the administration of the entire project. TE, AR, LZ, ALF, SP, GS, TE, and LS were responsible for project administration as consortium partners. SW, J-MZ, BS, JW, LLB, TS, AKF, EM, SR, and DVF were responsible for study organisation, recruitment and assessment, training of the exercise therapists, and data management. SR, DVF, SW, and GS were responsible for the process evaluation, development of treatment fidelity score, data management, and training of the exercise therapists. FH, AR, and AR-M were responsible for the application design, development, and maintenance. SP was responsible for the recruitment of the study sites and the qualification of the exercise therapists. ALF and LZ were the representatives of the two statutory health insurers, providing the routine data for the health economics analysis and supporting patient recruitment. EH, MMG, KT, TN, and TE were responsible for data management, data handling, the randomisation procedure, data pre-processing, and analysis of treatment fidelity. EH, MMG, TE, and TN verified the data, and had access to the raw study data. KT was the masked external statistician responsible for the formal statistical analysis, SK and LS were responsible for the health economic analysis. JB was responsible for study organisation, recruitment and assessment; training of the exercise therapists; and data management. Original draft preparation was done by SW. All authors contributed to the drafting and revision of the final study protocol. SW, TE, and KT had final responsibility for the decision to submit for publication. All authors confirm that they had full access to all data in the study and confirm responsibility for the decision to submit for publication.

Declaration of interests

SP declares that the German Association for Health-Enhancing Physical Activity and Exercise Therapy maintains a training programme for psychiatry, psychosomatics, and addiction. All other authors declare no competing interests.

Data sharing

Individual participant data that underlie the results reported in this Article will be published after de-identification. Documents that will be shared further are the study protocol, analytic code, and aggregated individual study data. Routine and administrative data from the participating statutory health insurers will not be made available. Access to data will be provided to anyone legitimately interested in it. Analytic code and aggregated individual study data are available on OSF. Participants gave informed consent for their data to be published after de-identification (except for the routine and administrative data from the statutory health insurers).

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