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Clinical and cost-effectiveness of a guided internet-based Acceptance and Commitment Therapy to improve chronic pain–related disability in green professions (PACT-A): study protocol of a pragmatic randomised controlled trial

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ABSTRACT

Introduction Chronic pain is highly prevalent, associated with substantial personal and economic burdens, and increased risk for mental disorders. Individuals in green professions (agriculturists, horticulturists, foresters) show increased prevalence of chronic pain and other risk factors for mental disorders. Available healthcare services in rural areas are limited. Acceptance towards face-to-face therapy is low. Internet and mobile-based interventions (IMIs) based on Acceptance and Commitment Therapy (ACT) might be a promising alternative for this population and may enable effective treatment of chronic pain. The present study aims to evaluate the clinical and cost-effectiveness of an ACT-based IMI for chronic pain in green professions in comparison with enhanced treatment as usual (TAU+).

Methods and analysis A two-armed pragmatic randomised controlled trial will be conducted. Two hundred eighty-six participants will be randomised and allocated to either an intervention or TAU+ group. Entrepreneurs in green professions, collaborating spouses, family members and pensioners with chronic pain are eligible for inclusion. The intervention group receives an internet-based intervention based on ACT (7 modules, over 7 weeks) guided by a trained e-coach to support adherence (eg, by positive reinforcement). Primary outcome is pain interference (Multidimensional Pain Interference scale; MPI) at 9 weeks post-randomisation. Secondary outcomes are depression severity (Quick Inventory Depressive Symptomology; QIDS-SR16), incidence of major depressive disorder, quality of life (Assessment of Quality of Life; AQoL-8D) and possible side effects associated with the treatment (Inventory for the Assessment of Negative Effects of Psychotherapy; INEP). Psychological flexibility (Chronic Pain Acceptance Questionnaire, Committed Action Questionnaire, Cognitive Fusion Questionnaire) will be evaluated as a potential mediator of the treatment effect. Furthermore, mediation, moderation and health-economic analyses from a societal perspective will be performed. Outcomes will be measured using online self-report questionnaires at baseline, 9-week, 6-month, 12-month, 24-month and 36-month follow-ups.

Ethics and dissemination This study was approved by the Ethics Committee of the University of Ulm, Germany (file no. 453/17—FSt/Sta; 22 February 2018). Results will be submitted for publication in peer-reviewed journals and presented at conferences.

Trial registration number German Clinical Trial Registration: DRKS00014619. Registered on 16 April 2018.

Strengths and limitations of this study

- This protocol is the first large-scale pragmatic randomised controlled trial, investigating the clinical and cost-effectiveness of a guided Acceptance and Commitment Therapy–based internet and mobile-based intervention (IMI) for chronic pain in green professions.
- Preventive effects of the IMI on mental health (eg, onset depression) will be investigated.
- The present study evaluates short-term and long-term effects over an extensive time period of 3 years.
- The study also focuses on effect moderating and mediating factors (eg, psychological flexibility, working alliance, technological alliance).
- All IMI outcomes are assessed through online self-report measures only and the generalisability of the results are limited to the target population of green professions.

INTRODUCTION

Chronic pain is highly prevalent worldwide and associated with major personal and societal burden.[1–5] For European countries, Breivik and colleagues[1] report prevalences from 12% (Spain) to 30% (Norway). In Germany, the prevalence is estimated at 17%.[1] In a more recent survey, an even higher proportion of the responders (28.3%) reported chronic pain.[6] Chronic pain leads

to substantial reduction in global functioning and the quality of life.[2 7] Besides the negative effects of chronic pain itself, chronic pain is highly linked to and promotes comorbid mental disorders,[1 8–11] which lead to further health burdens, reduced global functioning and greater expenses.[12–14] Given the high disease and economic burden of chronic pain, effective treatments are highly needed.

In the treatment of chronic pain, multidimensional and interdisciplinary therapies are the gold standard.[15] Elements of Cognitive-Behavioural Therapy or Acceptance and Commitment Therapy (ACT) are most often involved in those treatments.[16–18] According to a meta-analysis, the ACT-based approaches seem to be effective in the treatment of chronic pain, reducing both pain-related symptoms (d=0.43, 95% CI 0.22 to 0.64) and depression severity (d=0.69, 95% CI 0.47 to 0.92).[19] ACT assumes psychological flexibility as a mechanism of change. Psychological flexibility is defined as "the ability to contact the present moment more fully as a conscious human being, and to change or persist in behavior when doing so serves valued ends"[20] (p. 7). Although effective treatments are available for chronic pain, many affected individuals remain untreated.[1] This corresponds to one-third of the population in Europe.[1] Thus, the access to adequate treatments needs to be facilitated, especially for populations with an increased prevalence for chronic pain and a limited access to healthcare.

Individuals both in green professions (agriculturists, horticulturists, foresters) and rural regions might constitute an example to this population: They show an increased prevalence for pain.[7 21–23] In addition, they are exposed to risk factors for chronic pain, pain severity and mental disorders (eg, major depressive disorder (MDD)). Most of these risk factors comprise, for example, financial pressures, high administrative workload, long working hours, high stress levels, part-time jobs off the farm, health problems and preceding work accidents.[22–25] Hence, this population could considerably profit from effective treatments, reducing pain-related and mental health outcomes. Consequently, the risk for mental disorders (eg, MDD) might also be lowered.[1 8–11 24 25] However, agriculturalists show limited acceptance towards and utilisation of face-to-face therapeutic treatments.[26] Moreover, the availability of multidimensional and interdisciplinary therapies is limited.[27–29] Thus, alternative and new ways to deliver treatment might be beneficial.

Internet and mobile-based interventions (IMIs) can help overcome barriers of face-to-face treatments.[30–32] For example, IMIs are temporally and spatially flexible, can reduce the waiting time for treatment and foster anonymity.[31 33] IMIs have been shown to be effective in both intervention[34] and prevention.[32 35] In chronic pain samples, IMIs achieved effect sizes similar to their face-to-face counterparts.[36] For pain interference, a meta-analytic effect of Hedge's g=−0.42 (95% CI −0.55 to −0.28) and for pain severity of g=−0.35 (95% CI −0.54 to −0.17) favouring the intervention group was found when compared with wait-list or treatment-as-usual groups.[36] Furthermore, there were effects on variables unrelated to pain, such as mood ratings (eg, depression) g=−0.27 (95% CI −0.38 to −0.16) or catastrophising g=−0.65 (95% CI −0.95 to −0.36).[36]

Despite strong evidence for the general effectiveness of IMIs for chronic pain, the effectiveness of ACT-based IMIs in green professions is currently unclear. This is true for the effects on both pain-related and mental health variables. Sociodemographic factors in this population such as higher age, lower educational level or lower internet affinity might lead to different effects.[36–38] Moreover, it is unclear whether a reduction of pain-related symptoms and mental health burden would help prevent mental disorders (eg, MDD) in this population in the long term. This study is part of a nationwide prevention project targeting the health and well-being of individuals in green professions. The effects of an ACT-based IMI for chronic pain will be systematically investigated in this population. The following research questions will be examined in a 36-month follow-up pragmatic randomised controlled trial:

1. Is the IMI effective in the reduction of pain interference in comparison with an enhanced treatment as usual (TAU+) group?
2. Is the IMI effective in the reduction of mental health variables (eg, depression, stress, sleep quality, anxiety) compared with a TAU+ group?
3. Is the IMI effective in the prevention of MDD?
4. Which variables moderate and mediate the effect between the intervention group and TAU+group?
5. Is the IMI cost-effective compared with the TAU+group?
6. What are the levels of intervention satisfaction, adherence, acceptance and negative side effects for the intervention group?

METHODS AND ANALYSIS

Design

This is a two-armed randomised controlled trial comparing a guided internet-based intervention to an enhanced treatment as usual (TAU+) group. All assessments will be conducted online and will take place before the randomisation (at baseline T0), 9 weeks after the randomisation (T1), at 6-month follow-up (T2), at 12-month follow-up (T3), at 24-month follow-up (T4) and at 36-month follow-up (T5).

This trial will be conducted and reported according to the CONSORT 2010 statement[39 40] and to the guidelines for execution and reporting internet intervention research.[41]

Inclusion and exclusion criteria

We will include (a) agriculturists, foresters and horticulturists with sufficient insurance coverage from a health insurance company (SVLFG) in Germany. The study is accessible for entrepreneurs, collaborating spouses and family members, as well as pensioners with sufficient

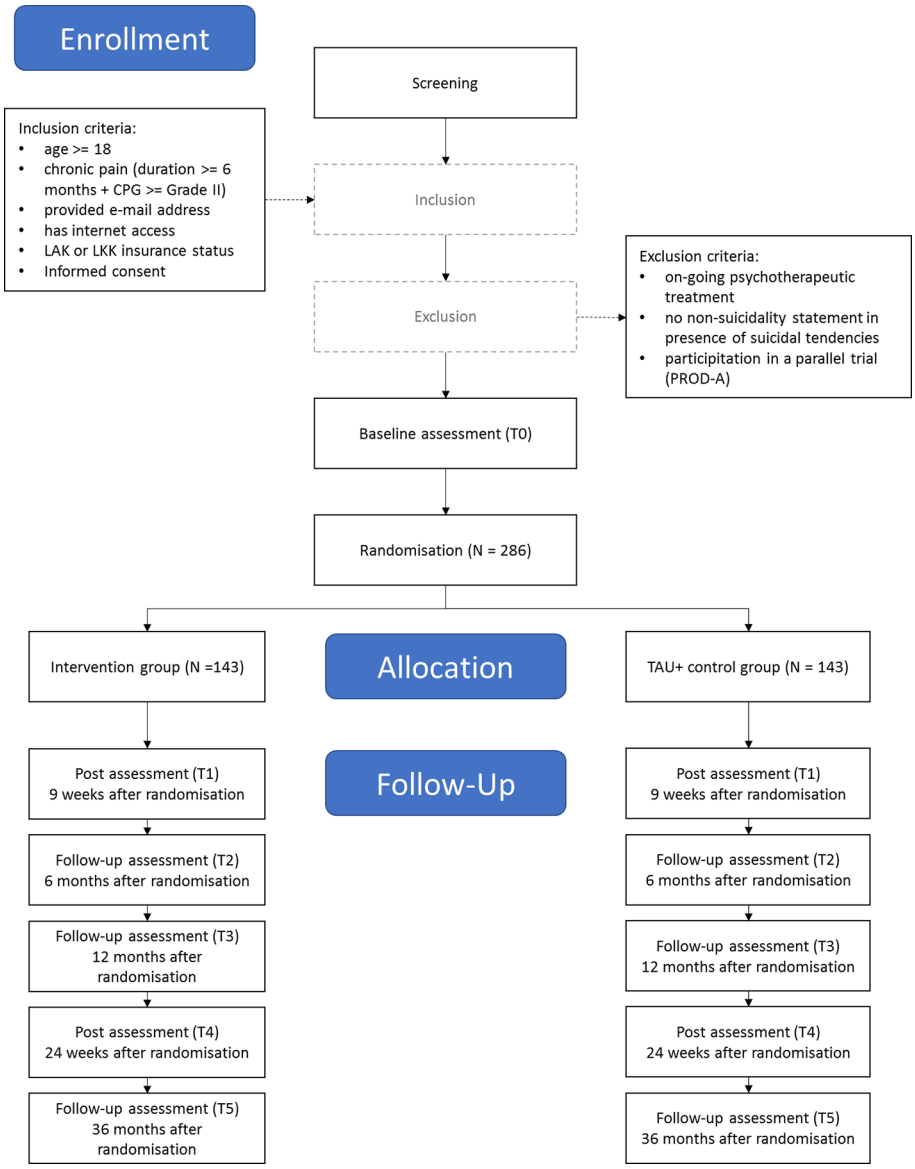

Figure 1 Flowchart of the study procedure.

insurance coverage who contribute to the production process ('Altenteiler'). Participants are required (b) to be aged 18 or above, (c) to report chronic pain, following the recommendations of the International Association of Pain in which the duration of pain is stated as ≥6 months,[42] (d) to experience considerable pain intensity (=at least grade II according to the Chronic Pain Grade questionnaire (CPG)[43–45]), (e) to provide an email address, (f) to have internet access and (g) be willing to give informed consent.

Participants are excluded if they (a) receive an on-going psychotherapeutic treatment, (b) are not able to distance themselves from suicidal ideation (not able to sign a non-suicide contract) and (c) if they are eligible for the parallel clinical trial PROD-A and would instead prefer to participate in it.[46] See figure 1 for a study flow chart. Inclusion and exclusion criteria are assessed in a self-report online survey, in which applicants' eligibility will be assessed prior to the trial inclusion and randomisation. The hand-signed informed consents and non-suicide contracts (see below) will be checked by the study team.

Suicidal ideation will be assessed with the PHQ-9 suicide item during the screening period and with the Quick Inventory Depressive Symptomology (QIDS-SR16; Rush *et al* 2003) suicide items during the assessments at T0–T5. If the participants score ≥1 on the PHQ-9 or QIDS-SR16 items, the BDI-II suicide item will additionally be administered since it is an efficient and more reliable screening instrument for suicidality.[47] All participants with an elevated suicide risk will receive an email with urgent advice to seek help and relevant information on available help services (eg, their general practitioner, local psychiatric emergency units or the national emergency number). The wording of the information material is adapted in emphasis, depending on the severity of suicidal ideation. In case of a BDI-II item score of >1, participants will be asked for a non-suicide contract. Participants refusing the non-suicide contract will be excluded from the study. If a

score of BDI-II ≥2 is reported, a more detailed clarification of self-endangerment will be performed by a psychological psychotherapist which is independent of the study inclusion status and assessment point. This procedure on suicidal ideation is adapted from prior studies[45 48] and was approved by the Ethics Committee of the University of Ulm.

Recruitment and procedure

The study population will be recruited via a journal for green professions and policy-holders of SVLFG with a quarterly circulation of 1.3 million. The journal article contains key information about the study protocol and describes various ways to participate in or get further information about the study (eg, postal return, fax, email, telephone and internet links). In addition, postal mailings and newsletter articles are being used to recruit participants. The recruitment has started in February 2018 and takes place nationwide in Germany.

All recruitment ways lead to an initial online screening survey, in which the applicants' eligibility will be assessed. If applicants are eligible for the present trial (acronym: PACT-A) or the parallel study focusing on the prevention of depression in green professions (acronym: PROD-A), they can choose between the trials as long as the recruitment for both trials is open. The participation is limited to one of the trials. The participants who are eligible for PACT-A will be asked to sign an informed consent and forwarded to the baseline assessment (T0). After the baseline assessment, the participants will be randomised and will receive either a guided internet-based intervention or an enhanced TAU. The participants will be contacted and reminded on the follow-up assessments (T1–T5).

Randomisation and blinding

The randomisation will take place at an individual level. It will be conducted by a person, blinded on all processes throughout the intervention. The blinding of the participants is not possible due to the nature of the intervention. Data collectors and data analysts are blinded regarding the participant's group membership. Group membership is only known by the persons administering the allocated treatments to the participants. The randomisation and allocation will be performed using permuted block randomisation with randomly arranged variable block sizes of (2, 4, 6) and an allocation ratio of 1:1. The randomisation list was created using a web-based randomisation program (https://sealedenvelope.com/). The randomisation will be carried out after the baseline assessment.

Power calculation and sample size

The primary outcome of the present study is the standardised mean difference between the intervention group and the TAU+ control group in pain interference at T1. For internet interventions targeting chronic pain, Buhrman and colleagues[36] reported an average effect of Hedges' g=−0.42 (−0.55 to −0.28). An a priori power calculation, targeting an effect of d=0.42 at an alpha level of 5% (one-tailed) and a power of 90%, has yielded a total sample size of 196. A t-test was used for power calculation. The calculations were conducted using G*Power (V.3.1.9.2).[49]

Several reviews and studies show high drop-out rates for internet interventions.[36 50 51] For instance, Melville and colleagues reported an average drop-out rate of 31% in a systematic review.[50] Since the present study aims for long-term follow-up and drop-out is assumed, the estimated sample size of 196 will be increased to be able to compensate a drop-out rate of 31%. Thus, the targeted total sample size of this study is going to be 286. However, the drop-out rate or effect in this study might differ from the assumed values and thus, a post hoc power analysis will be conducted to determine the actual power at T1 and follow-ups at T2–T5.

Intervention development

The online intervention is based on an effective internet intervention against chronic pain (d=0.58) called ACTonPAIN[51] and was adjusted to the targeted population by an IMI-providing company named GET.ON Institute. The present study team has not been involved in the intervention adjustments by the GET.ON Institute and are only engaged in the evaluation of this intervention.

Intervention content

The structure of the intervention follows the recommendations by Hayes and colleagues[52] and the structure of ACTonPAIN (for further information about ACTonPAIN, see[45 51]). The intervention is structured in seven sessions. In the first session, basic information about the intervention like acute pain, chronic pain and the effects of pain are presented, and the participants will be introduced to the concept of mindfulness and key concepts of ACT. Session 2 focuses on acceptance, session 3 on defusion, session 4 on self-concept, session 5 on values, session 6 on committed actions and session 7 summarises all sessions and fosters the sustainability of the learned content. Throughout the intervention, mindfulness and mindfulness exercises are going to be part of all sessions. The mindfulness exercises are aiming to encourage participants to perceive the here-and-now without judging or trying to change and alter it. Participants are advised to work on the sessions on a weekly basis.

All sessions are interactive, containing audios, videos, illustrated examples and exercises. In addition to the exercises within the sessions, participants receive homework assignments between each session. Throughout the intervention, participants will be guided by an e-coach. All e-coaches are trained psychologists, who are supervised by a licensed psychotherapist and paid by the GET.ON Institute. The e-coaches give feedback via email or telephone, based on the participant's preference to each session during the intervention phase (=weekly feedback, if participants adhere to the treatment protocol). The content of the feedback matches the assignments of the participants and supports treatment adherence (eg, by

positive reinforcement). The e-coaches will contact the participants on a monthly basis for over a year after the end of the intervention to monitor and maintain their current state. The duration of feedback can vary across participants and will be monitored to enable post hoc analysis on guidance time.

In addition to the intervention, all participants in the intervention group will have unrestricted access to TAU.

TAU+ content

The control group has full access to TAU. Based on the strong evidence for the effectiveness of ACT and internet-based ACT, it is unethical to withhold improved treatment from the control group.[36 53 54] Hence, the control group will be provided with psychoeducation as a minimal support treatment (TAU+).[54 55] The participants of the control group will receive an information letter with psychoeducation about stress, depression and chronic pain (pdf via email). The control group will receive a link to a free online audio CD with further information about stress and stress reduction. In addition, they will also be provided with information about different treatment options available in routine care.

TAU may vary across individuals since they have unrestricted access to it. We obtain information about the TAU in the economic evaluation with the help of the TiC-P[56 57] (see below). The TAU utilisation will be reported, and potential systematic differences will be examined.

Patient and public involvement

Patient and public involvement (PPI) representatives have provided input to the present study in several stages. First, PPI representatives were included in the intervention development by the GET.ON Institute to identify core symptoms, improve the usability, design and the overall tailoring of the intervention for the target population. Second, the PPI representatives gave feedback on the study materials to ensure the comprehensibility of the materials. The outcomes were defined according to international standards and the expertise of the research group. The PPI representatives, the SVLFG insurance company and the GET.ON Institute had no influence on the outcomes, data analysis methods or study design. However, the burden of the intervention from the patients' perspective is a crucial outcome of the study and both quantitative and qualitative methods will be applied to capture the burden and side effects. The dissemination plan of the study results includes publications in peer-reviewed journals, conferences as well as special reports for SVLFG, the GET.ON Institute and the PPI representatives.

Outcomes

For the primary and secondary outcomes, the recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT[58 59]) are considered. In addition, the ACT-related, other health-related indicators (eg, sleep quality or alcohol use), health-related quality of life, intervention costs and participants' satisfaction will be assessed. Demographic and medical variables will be examined as potential moderating and mediating variables. For an overview of all variables and respective measures, see table 1. All questionnaires will be transferred to an online survey platform (https://www.unipark.com/) and completed online. The online administration of assessments can yield psychometric properties equivalent to their paper-and-pencil counterparts.[60]

Primary outcome

The primary outcome is the standardised mean difference in pain interference between the intervention group and the control group at 9 weeks after randomisation (T1), as measured by the Multidimensional Pain Interference scale (MPI).[61 62] The MPI[61 62] measures the degree in which everyday activities are hampered. The German version of the MPI consist of ten 7-point Likert items (0="no interference/change" to 6="extreme interference/change"). The internal consistency is reported to be excellent (α=0.94) and the retest reliability (r=0.78) as good.

Secondary outcomes

Pain interference

Pain interference will also be assessed with the MPI at T2–T5. As recommended by the IMMPACT,[58 59] the Brief Pain Inventory (BPI)[63 64] will additionally be used at T0–T5 for the assessment of pain interference. The BPI measures pain interference with regard to mood, sleep, social relations and enjoyment of life.[63 64] On seven items, the participants have to indicate, on an 11-point scale (0="does not interfere" to 10="completely interferes") to what extent the intensity of pain affects their daily functioning. The internal consistency of the scale (α=0.88) is reported to be good.[65]

Pain intensity

Pain intensity will be measured by an 11-point numerical rating scale. The participants have to rate their worst, least and average pain during the last week, from 0 ("no pain") to 10 ("pain as bad as you can imagine").

Overall improvement

The Patient Global Impression of Change scale (PGIC[66]) measures the participants' global improvement after treatment on a 7-point scale from "very much improved" to "very much worse".[58 59]

Depression

The German version of the Quick Inventory Depressive Symptomology (QIDS-SR16[67]) assesses the symptom severity of depression. The 16-item self-report inventory covers all nine DSM-5 symptom criteria of MDD. The QIDS-SR16 is characterised by high internal consistency of α=0.86.[67] The items are rated on a 4-point scale ranging between 0 and 3. The total score ranges between 0 and 27, with a higher score indicating higher depressive

Table 1 Summary of assessments

Instrument		Time of measurement						
		Screening	T0	T1	T2	T3	T4	T5
Screening instruments								
CPG	Chronic Pain Grade questionnaire	✔						
Chronicity of Ppain	Pain longer for 6 months (yes/no)	✔						
PHQ-9	Patient Health Questionnaire	✔						
Primary outcome								
MPI	Multidimensional Pain Inventory		✔	✔*	✔	✔	✔	✔
Secondary outcomes								
BPI	Brief Pain Inventory		✔	✔	✔	✔	✔	✔
QIDS-SR16	Quick Inventory for Depressive Symptomatology		✔	✔	✔	✔	✔	✔
PSS-10	Perceived Stress Scale		✔	✔	✔	✔	✔	✔
ISI	Insomnia Severity Index		✔	✔	✔	✔	✔	✔
Numeric rating scale	Pain Intensity (0–10)		✔	✔	✔	✔	✔	✔
Perceived improvement	Improvement (1–7)		✔	✔	✔	✔	✔	✔
AUDIT-10	Alcohol Use Disorder Identification Test		✔	✔	✔	✔	✔	✔
GAD-7	Generalized Anxiety Disorder		✔	✔	✔	✔	✔	✔
Adapted items from CIDI 3.0, CIDI-SC and Epi-Q Screening Survey	Prevalence of major depression		✔	✔	✔	✔	✔	✔
AQoL-8D	Adjusted Quality of Life		✔	✔	✔	✔	✔	✔
SPE	Subjective prognosis of employment		✔	✔	✔	✔	✔	✔
Intervention-related outcomes								
WAI-SR†, WAI-SRT‡	Therapeutic relationship			✔		✔		
TAI-OT†	Technological alliance			✔	✔			
CSQ-I†	Patient satisfaction			✔				
INEP†	Inventory of negative effects in psychotherapy			✔	✔	✔		
Negative effects†	Negative effects in psychotherapy			✔	✔	✔		
ACT-related variables								
CPAQ	Chronic Pain Acceptance Questionnaire		✔	✔	✔	✔	✔	✔
CFQ	Cognitive Fusion Questionnaire		✔	✔	✔	✔	✔	✔
CAQ	Committed Action Questionnaire		✔	✔	✔	✔	✔	✔
Cost measurement								
TiC-P	Utilisation of health services, work-related productivity		✔	✔	✔	✔	✔	✔
Other assessments								
Sociodemographics			✔					
Predictors of major depression			✔					
BDI-II	Suicidality item	✔	✔	✔	✔	✔	✔	✔

T0, baseline; T1, 9 weeks after randomisation; T2, 6 months after randomisation; T3, 12 months after randomisation; T4, 24 months after randomisation; T5, 36 months after randomisation.
*The primary outcome is the standardised mean difference between intervention and control group at T1. MPI will also be assessed at T0 and T2–T5 as secondary outcome.
†To be completed by the intervention group only.
‡To be assessed by the e-coaches only.

symptom severity. The QIDS can also be analysed categorically: A comparison of QIDS-SR16 scores with current and lifetime diagnosis based on Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID) as a measure criterion showed that QIDS-SR16 is a reliable screening instrument for the diagnosis of MDD.[68] The cut-off scores of 13 and 14 yielded best results for sensitivity (76.5%) and specificity (81.8%), leading to correct classification

of over 80% of the participants.[68] In this study, the cut-off score in QIDS-SR16 for clinical depression is set to 13 for all measurement points within the 36-month follow-up period.

In addition, items which have been adapted from the Composite International Diagnosis Interview version 3.0 (CIDI 3.0), the Screening Scales (CIDI-SC)[69] and the Epi-Q Screening Survey[70] will be used to assess the prevalence of major depressive episode.

Stress

The 10-item version of the perceived stress scale (PSS-10[71]) measures the perception of stress in participants. The scale particularly assesses how "unpredictable, uncontrollable, and overloading respondents find their lives".[72] High values indicate a higher stress level. The German PSS-10 has a good reliability of ω=0.89.[73] The PSS-10 will be modified to address the perception of stress load in the last week instead of the last month.

Anxiety

The seven-item Generalized Anxiety Disorder questionnaire (GAD-7)[74] is a short self-report measure to assess the likelihood of generalised anxiety disorder. Higher values indicate higher anxiety levels. The German version has an excellent internal consistency of α=0.89.[75] Overall, the GAD-7 is a valid and reliable instrument to screen for generalised anxiety disorder.[74 75]

Sleep quality

Sleep quality will be measured using the Insomnia Severity Index (ISI).[76] The ISI is a brief self-report scale composed of seven items to identify clinical insomnia. Severe insomnia or low sleep quality is indicated by high values. The questionnaire has been validated in clinical and community samples and is characterised by high internal consistency (α=0.90 to 0.92) and adequate discriminative validity of the individual items.[77 78] The German version of the ISI was validated in three different samples and shows satisfactory internal consistency across all three (α=0.76 in adolescents, α=0.77 in young adults, α=0.81 in adult workers).[79]

Alcohol consumption

The Alcohol Use Disorder Identification Test (AUDIT)[80] will be applied to screen for hazardous alcohol use. The AUDIT has been validated in six different countries and therefore is cross-culturally applicable.[81 82] The 10-item self-report questionnaire measures a unidimensional construct with adequate internal consistency ranging between α=0.80 and α=0.83.[83 84] In the present study, the German Münster Version of the AUDIT following S3 guideline was applied.

Quality of life

Health-related quality of life will be assessed with the self-report questionnaire entitled Assessment of Quality of Life (AQoL-8D). This questionnaire consists of 35 items, covering the three physical dimensions 'independent living', 'pain' and 'senses', as well as the five psychosocial dimensions 'mental health', 'happiness', 'coping', 'relationships' and 'self-worth'.[85] Higher values indicate a lower quality of life. The AQoL-8D is characterised by a high Cronbach's alpha of 0.96 and good psychometric properties[85] and will be applied for cost-utility analyses.

Reliable change index

The procedure by Jacobson and Truax[86] will be used to calculate reliable change in the primary outcome.[87] Both reliable improvement and reliable deterioration will be calculated.

ACT-related variables

The German version of the Chronic Pain Acceptance Questionnaire (CPAQ[88]) will be used to measure psychological flexibility in respect to their activity engagement and pain willingness. Participants have to indicate their activity engagement (CPAQ-AE) and their pain willingness (CPAQ-PW) on a 20-item, 7-point Likert scale ranging from 0 ("never true") to 6 ("always true"). The German CPAQ has a good internal consistency (α=0.84–0.87).

The German version of the Cognitive Fusion Questionnaire (CFQ-D)[89] will be administered to measure cognitive fusion as a facet of psychological flexibility. The CFQ-D consists of seven items ranging from "never true (1)" to "always true (7)". All items are positively keyed and higher scores indicate a higher level of cognitive fusion. The internal consistency is excellent (α=0.94).[89]

To measure the facet Committed Actions, the German version of the Committed Action Questionnaire (CAQ-D)[90] will be used. The CAQ-D consists of 18 items: 9 positively keyed items and 9 negatively keyed items. Responders have to indicate to what extent an item applies to them on a scale from 0 (never true) to 6 (always true). The internal consistency of the CAQ-D is good (α=0.87).[90]

Work capacity

Work capacity will be measured with the German version of the Subjective Prognostic Employment Scale (SPE[91]). The SPE is a validated short self-report scale composed of three items with high internal consistency (Guttman scaling: rep=0.99). The SPE was developed to assess the subjective endangerment and prognosis of work capacity.[91]

Intervention-related variables

Intervention satisfaction will be assessed using the German version of the Client Satisfaction Questionnaire (CSQ-8[92]; German version: ZUF-8[93]), specifically adapted for assessing patient satisfaction with internet-based interventions (CSQ-I).[94] The CSQ-8 is a self-report questionnaire consisting of eight items characterised by high internal consistency (α=0.93).[92] The adapted German version CSQ-I has been validated for the assessment of patient satisfaction with internet-based interventions and is characterised by equally high internal consistency.[94 95] CSQ-I will be applied to assess satisfaction with online

trainings in the intervention group. An adapted version of the CSQ-I will be applied to the control group to evaluate satisfaction with information material.

The short version of the Working Alliance Inventory (WAI-SR)[96] will be applied to measure the therapeutic alliance between the client and e-coach. The 12-item self-report questionnaire covers the three subscales: (a) agreement on tasks, (b) agreement on goals and (c) development of an affective bond. For the German version, internal consistencies between α=0.81 and α=0.91 were reported for the subscales and internal consistencies between α=0.90 and α=0.93 for the total score.[96 97] The participants in the intervention group will complete the WAI-SR at T2 and T4. In addition, the e-coaches will be requested to complete the 10-item therapist version (WAI-SRT, developed by Adam O Horvath, http://wai.profhorvath.com/) at T1 and T3. This will allow us to compare how the therapeutic relationship is experienced by the client and e-coach, to gain a differentiated and comprehensive picture of the experienced working alliance. The WAI-SR and the WAI-SRT were adapted in wording for the current study investigating therapeutic alliance in guided internet-based interventions. The items were changed to refer to e-coaches instead of therapists and to online trainings instead of therapy. Due to a lack of suitable normative data for the interpretation of WAI, we will follow Jasper and colleagues[98] for interpretation: the mean scores of WAI will be labelled as low (score: 1.00–2.44), medium (score: 2.45–3.44) and high/positive (score: 3.45–5.00).[98]

In addition, the Technological Alliance Inventory—Online Therapy (TAI-OT) will be administered to assess the technological alliance between the client and online intervention. The TAI-OT is a new self-report questionnaire developed by Labpsitec consisting of 12 items and measures the degree to which the online programme is perceived as helpful in achieving therapeutic goals (http://www.labpsitec.uji.es/esp/index.php). Based on the similarity between TAI and WAI, the same cut-off values for interpretation will be applied to TAI.[98]

Side effects of psychotherapy will be assessed with the Inventory for the Assessment of Negative Effects of Psychotherapy (INEP). The INEP records whether any negative changes, which are experienced during or after the treatment in the social and/or work environment, are attributed on the psychotherapeutic intervention.[99] In this trial, an adapted 22-item version covering possible negative effects associated specifically with online trainings (eg, concerns about data protection) is applied.

In addition, an open question will be included for qualitative assessments of negative side effects of internet-based interventions. Participants will describe experienced negative events and side effects, their time of beginning, their frequency and their duration. Two further questions rate the negative impact of these events in the past and at present time.

Adherence, usage time and other usage variables will be tracked by the healthcare provider GET.ON. Under compliance with the European General Data Protection Regulation and data sharing agreements, these data will be merged with data from the assessments to explore the influence of adherence.

Cost measures

Cost evaluation will be based on the German version of the Dutch cost questionnaire entitled "Trimbos Institute and Institute of Medical Technology Questionnaire for Costs Associated with Psychiatric Illness" (TiC-P[57]). In this self-report questionnaire, the usage of healthcare services (eg, general practice services, sessions with psychotherapists or psychiatrists) and productivity loss (eg, hospital days, absenteeism, presenteeism) are registered. The German version of the TiC-P has been used in several studies (eg, see refs. 48 100 101). We adapted the questionnaire for the population of agriculturists, foresters and horticulturists.

Covariates

As potential moderating variables, demographic information (eg, gender, age, education), information about the agricultural farm (eg, farm size, area cultivated, number of workers) and about the situation of the entrepreneurial family (eg, financial situation, number of relatives living and working together, general work load) will be recorded at baseline. Furthermore, a variety of predictors (eg, personality, prior experience of violence and aggression, childhood experiences) will be included to assess relevant factors for development of depressive symptomology.

Screening instruments

Three questionnaires are used in the screening. The German version of the Patient Health Questionnaire (PHQ-9[102]) will be administered as a depression screening inventory to detect subthreshold depression (PHQ-9 ≥5). The PHQ-9 consists of nine items on a 4-point scale with a rating scale ranging from 0 to 3 (0="not at all", 1="several days", 2="more than half the days", 3="nearly every day"). Each item assesses one symptom of MDD. In addition, an item is included to register severity of daily life limitations associated with depressive symptoms. The computerised version (α=0.88) of the PHQ-9 shows an equally high internal consistency as the paper-and-pencil version (α=0.89).[103]

In addition to the PHQ-9, the BDI-II suicide item is used,[104] if applicants show elevated suicidal tendency based on PHQ-9 or QIDS-SR16 (see previous section for a more detailed procedure on suicidal tendency). On the BDI-II item, applicants have to indicate their suicidality on a 3-point scale (BDI-II item 1: "I have thoughts of killing myself, but I would not carry them out"; BDI-II item 2: "I would like to kill myself"; BDI-II item 3: "I would kill myself if I had the chance").

During the screening phase, considerable pain intensity will be measured with the German version of the Chronic Pain Grade questionnaire (CPG).[43] The CPG is a 14-item

questionnaire assessing pain disability and pain intensity. Based on the disability and intensity score, four different severity grades are given (see refs. 43 44). The internal consistency of the German CPG is good (α=0.82).

Statistical analyses

All statistical analyses will be conducted on an intention-to-treat basis. In addition, for those who have adhered to the study protocol and completed most of the intervention sessions (at least 80% of the modules), per-protocol (PP) analyses will be conducted. Data will be checked regarding missingness patterns and mechanisms. Analyses will be adapted accordingly (eg, using multiple imputation by chained equations[105]). All analyses will be carried out in the software R.[106] R packages used for analyses will be reported.

Clinical analyses

Regression analyses will be used as the primary method. The estimates will be adjusted for baseline in regression analyses. For continuous outcomes (eg, pain interference), linear regression will be carried out, and for dichotomous outcomes (eg, onset of depression), a Poisson regression will be employed. To quantify the effect of the intervention, group allocation will be inserted as a dummy-coded predictor in all regression models. All continuous variables will be z-standardised. Based on the data structure, the regression analyses will be adjusted (eg, use of robust estimation or use of multilevel regression analysis in case of substantial intraclass correlation). For all analyses, the alpha level will be set at 5%. Except for the primary outcome, two-sided tests will be conducted. Between-group differences in the primary outcome will also be tested without an adjustment for baseline using one-sided t-test (see power calculation) and the effect size will be reported as Cohen's *d*.

Moderator and mediator analyses

To examine for whom the intervention is best suited, exploratory moderation analyses will be conducted. Based on previous findings,[37 38] sociodemographic (eg, gender) and health-related variables (eg, baseline pain severity) will be analysed. Regression analyses will be employed wherein group will be included as a dummy-coded predictor along with the main effects of moderator variables and their interaction effects with group. Effect coding will be applied to all categorical (eg, gender) and z-standardisation to continuous (eg, baseline severity) moderator variables. Each moderator will be tested in a separate regression model. Furthermore, a holistic model including all identified moderators will be estimated.

Mediation analyses will be conducted to examine which processes might explain effects on health outcomes. The three facets of psychological flexibility (acceptance, cognitive fusion and committed action) measured within the present study as well as therapeutic alliance and technological alliance will be analysed as potential mediators. We will use time-lagged mediation models according to Cole and Maxwell.[107]

Economic evaluation

The health-economic evaluation will include both a cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). The evaluation will be performed from a societal (eg, all relevant costs) and a public healthcare perspective (eg, only direct medical costs) within a time horizon of 12 and 36 months. Missing cost and effect data will be imputed, using multiple imputation by chained equations. The CEA will include an assessment of the value of PACT-A by calculating the difference in costs between PACT-A and TAU+ and dividing this by the difference in effectiveness of both treatment options (ie, calculating the incremental cost-effectiveness ratio (ICER)). In the CUA, the ICER will be expressed as incremental costs per quality-adjusted life year gained.[108 109] We will use a SURE model (seemingly unrelated regression equations) to allow for correlated residuals of the cost and effect equations while adjusting for potential confounders (eg, baseline differences in utility scores).[110] Based on these non-parametric bootstrapped simulations of the ICER (n=2500), 95% bias-corrected and accelerated CIs will be obtained for incremental costs and effects, respectively, as well as a 95% CI around the ICER based on the bootstrap acceptability method.[111] The bootstrapped ICERs will be graphically displayed in a cost-effectiveness plane and will also be shown in a cost-effective acceptability curve disclosing the probability that PACT-A is cost-effective for a range of willingness-to-pay thresholds.[112] To test the robustness of the base-case findings, probabilistic sensitivity analyses will be done by changing several assumptions made in the base-case scenario (eg, about cost prices and volumes). An incremental net benefit regression analysis will be performed to ascertain which subgroups benefit more from PACT-A in terms of superior cost-effectiveness.[110 113]

DISCUSSION

In this study protocol, we described the design of a pragmatic randomised controlled trial, which evaluates the (cost-)effectiveness of a guided internet-based Acceptance and Commitment Therapy for chronic pain in individuals in green professions. The effects of the intervention on pain and mental health–related outcomes will be evaluated over an extensive follow-up period of 36 months. The preventive effects on mental health (eg, depression) in individuals with chronic pain in agricultural professions will be investigated.

Some limitations of the current study should be considered. Prior studies have shown that IMIs mainly reach female and higher-educated individuals.[51 114] If only female and highly educated people from the target population were reached, the generalisability of this study would be restricted. To overcome this selection bias, we are using multiple recruitment strategies to reach individuals from

both sexes and different educational levels. In addition, prior studies have shown that IMIs are frequently accompanied by high drop-out rates,[36 50 51] which can lead to a significant loss of power. Studies with guided IMIs show a lower drop-out rate.[115] To avoid a loss of power, the sample size was increased for this study, taking into account an average drop-out rate of 31%.[50] However, drop-out rates vary greatly across studies.[36 50 51] Consequently, this study could also be underpowered or overpowered. To quantify the actual power, post hoc power analyses will be conducted and the limitations on the statistical power of the study will be discussed.

Within this study, categorical analyses are planned to determine the prevalence and incidence of MDD within the target population. For this purpose, cut-off scores for QIDS will be used to define MDD (eg, QIDS ≥13 indicates MDD[68]). In-depth diagnostic procedures (eg, SCID interviews) could be more reliable to determine such estimates, but these are rather cost and time intensive. As a result, the reliability of the prevalence and incidence rates estimated in this study might be restricted. Using a QIDS cut-off score of 13 leads to high sensitivity (76.5%), high specificity (81.8%) and a correct classification of 80.7%.[68] Moreover, it has been shown that SCID interviews have a rather fair than perfect inter-rater reliability (kappa=0.66).[116] Thus, instead of the SCID, we consider the use of QIDS as a more appropriate approach, especially since the results will also be verified by items adapted from the CIDI[69] and Epi-Q Screening Survey.[70] The absence of structured clinical interviews should also be discussed regarding the inclusion criteria of chronic pain. Chronic pain is only assessed by self-report measurements (CPG+duration greater than 6 months). Since self-reported chronic pain is not verified by a clinical diagnosis, it can be questioned whether the participants included in this study indeed suffer from chronic pain. The International Association for the Study of Pain highlighted that chronic pain is seen as a disease of its own right which can be validly assessed by self-report measures and targeted, despite the individual syndromes of a person.[117] Thus, the self-report is assumed to be a suitable measurement for chronic pain. Lastly, based on the strong evidence for the effectiveness of internet-based and ACT-based interventions as well as results indicating a moderate effectiveness of a previous version of the present intervention, we strongly assume effects on pain interference. Thus, we decided on a one-sided testing of the primary outcome.[36 51 53] As commonly done in psychotherapeutic research, we set the alpha level at 5% for all analyses. However, the alpha could have been set to 2.5% for the one-sided test to provide a more conservative evaluation of the primary outcome.

Despite the limitations, several strengths should be highlighted. First, to our best knowledge, the effectiveness of ACT-based IMIs on chronic pain in green professions is currently obscure. This study will give first insights into the effectiveness of ACT-based IMIs in green professions with chronic pain. Moreover, by the long-term evaluation, this study can make a valuable addition to the current evidence base. Besides positive effects (eg, decrease of symptom severity), IMIs can also have negative side effects (eg, time pressure).[118] This study will also investigate the negative short-term and long-term effects of the IMI.

Another major strength of this study results from the routine care setting. Based on the setting, this study will provide information about the actual effectiveness of this IMI rather than its efficacy. It can be argued that this study is characterised by a strong external validity, regarding the generalisability of the intervention to green professions in Germany. In this vein, this study will give a robust estimation of the (cost-)effectiveness, side effects, treatment satisfaction and feasibility in the target population of green professions.

Lastly, the investigation of potential effect moderators and mediators should be highlighted. Those analyses will give us a deeper understanding of how certain processes contribute to the effectiveness of ACT-based IMIs as well as for whom this IMI is best suited for.

Overall, we consider the present study design well suited to answer the stated research questions. Based on the existing evidence,[32 36 48] we expect the IMI to be effective. If proven to be so, the implementation of this IMI in the preventive routine care of green professions will have a major impact on public health.

Ethics and dissemination

Written informed consent for participation in the study will be obtained from all participants prior to their involvement. All participant information will be stored securely in locked file cabinets and/or password protected in a secured cloud storage with restricted access. All reports, data collection and administrated forms will be only identified by a coded ID number to maintain participant confidentiality. All records that contain names or other personal identifiers, such as informed consent forms, will be stored separately from the study records identified by ID number. Listings that link participant ID numbers to other identifying information will be stored in separate, password-protected files with limited access.

Trial results will be presented on international conferences and published in peer-reviewed journals. Central results will be communicated to SVLFG and can be further used by SVLFG for information of insured persons, dissemination of health offers and further improvement of the healthcare offer.

Trial status

The trial is currently ongoing. The recruitment of participants has started in January 2018.

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Competing interests DE reports to have received consultancy fees and served in the scientific advisory board of several companies such as Minddistrict, Lantern, Novartis, Sanofi, Schoen Kliniken and German health insurance companies. He is a stakeholder of the Institute for Online Health Training (GET.ON), which aims to implement scientific findings related to digital health interventions into routine care. HB reports to have received consultancy fees and fees for lectures/workshops from chambers of psychotherapists and training institutes for psychotherapists in the e-mental-health context. IT reports to have received fees for lectures/workshops in the e-mental-health context from educational institutions for psychotherapists. She is implementation lead and project lead for the EU-research project ImpleMentAll at the Institute for Online Health Training (GET.ON). All other authors reported no competing interests.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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