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Development, evaluation, and implementation of a digital behavioural health treatment for chronic pain: Study protocol of the multi-phase DAHLIA project

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6 2 **health treatment for chronic pain: Study protocol of the multi-phase**
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8 3 **DAHLIA project**
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4 40 Development, evaluation, and implementation of a digital behavioural health
5 41 treatment for chronic pain: Study protocol of the multi-phase DAHLIA project
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8
9 43 **ABSTRACT**

10 44 **Introduction:** Chronic pain affects about 20-40% of the population and is linked to mental
11 45 health outcomes and impaired daily functioning. Pharmacological interventions are commonly
12 46 insufficient for producing relief and recovery of functioning. Behavioural health treatment is
13 47 key to generate lasting benefits across outcome domains. However, most people with chronic
14 48 pain cannot easily access evidence-based behavioural interventions. The overall aim of the
15 49 DAHLIA project is to develop, evaluate, and implement a widely accessible digital behavioural
16 50 health treatment to improve well-being in individuals with chronic pain.

17 51 **Methods and analysis:** The project follows the four phases of the mHealth Agile Development
18 52 and Evaluation Lifecycle: (i) *development and pre-implementation surveillance* using focus
19 53 groups, stakeholder interviews, and a business model; (ii) iterative *optimisation studies*
20 54 applying single case experimental design (SCED) method in 4-6 iterations with n=10 patients
21 55 and their health care professionals per iteration; (iii) a two-armed *clinical randomized*
22 56 *controlled trial* enhanced with SCED (n=180 patients per arm); (iv) and interview-based *post-*
23 57 *market surveillance*. Data analyses include multilevel modelling, cost-utility, and indicative
24 58 analyses.

25 59 In October 2021, inter-sectorial partners are engaged and funding is secured for four years. The
26 60 treatment content is compiled and the first treatment prototype is in preparation. Clinical sites
27 61 in three Swedish regions are informed and recruitment for phase one will start in autumn 2021.
28 62 To facilitate long-term impact and accessibility, the treatment will be integrated into a Swedish
29 63 health platform (www.1177.se), which is used on a national level as a hub for advice,
30 64 information, guidance, and e-services for health and healthcare.

31 65 **Ethics and dissemination:** The study plan has been reviewed and approved by Swedish
32 66 Ethical Review Authorities. Findings will be actively disseminated through peer-reviewed
33 67 journals, conference presentations, social media, and outreach activities for the wider public.

34 68 **Trial Registration number:** ClinicalTrials.gov Identifier: NCT05066087; Karolinska
35 69 Institutet Protocol Record Dnr 2021-02437.

36 70 **Keywords:** chronic pain; digital; behavioral health; protocol; intervention; single case
37 71 experimental design; diary; implementation; randomized controlled trial
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3 73 **Strength and limitations of the study**
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- 5 74 • An agile, iterative, and data-driven process is ideally suited to navigate the complex
6 75 challenges faced during the development, evaluation, and implementation of a digital
7 76 behavioural treatment.
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10 77 • Executing the project with a multi-disciplinary, inter-sectorial, and international team
11 78 brings expertise and insights from complementary views together.
12
13 79 • Patients and different stakeholders, such as health care professionals, managers and
14 80 digital developers, are involved in the project from the start, thus ensuring that
15 81 individual needs to use and/ or promote the treatment can be met.
16
17 82 • The richness of methodologies combining traditional clinical trial evaluations on the
18 83 population level, fine-graded momentary data collection on the individual level, explicit
19 84 focus on cost-effectiveness, and determinants of implementation allows for a treatment
20 85 evaluation from all angles.
21
22 86 • Due to the complexity and step-wise approach of this project, problems (e.g., delays in
23 87 recruitment) in earlier phases might negatively affect the execution of later phases, thus
24 88 calling for mitigation strategies to address potential delays.
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89 INTRODUCTION

90 Chronic pain (CP) affects 20 to 40 % of the adult population¹. Due to the COVID-19 pandemic,
91 prevalence rates may increase further since CP can develop as a post-viral syndrome, from
92 insufficient risk factor management during lockdown (e.g., inactivity, stress), or from
93 accumulated unmet rehabilitation needs in overburdened rehab services^{2 3}. Chronic pain
94 impacts not only individuals' daily activities and overall quality of life, but also social and
95 working contexts⁴. Thus, considerable direct and indirect health-related costs are associated
96 with CP⁵ and it represents a major issue for health care services and society at large.

97 A consensus exists regarding the importance of a holistic perspective integrating social,
98 psychological, and biological factors of CP to accommodate this condition and its implications,
99 and to guide interventions aimed at providing support⁶. Considering the typical complexity of
100 CP, pharmacological treatment alone is usually insufficient in producing sustained relief and
101 recovery of functioning⁷. Instead, management plans should target key behavioural, emotional,
102 cognitive, and social factors in everyday functioning and quality of life⁸.

103 To generate general and lasting benefits across outcome domains, person-centred,
104 behavioural health interventions are critical. The necessity to match the pain treatment with
105 specific needs of each patient has been the focus of discussion for the past decades⁹. Existing
106 evidence supports methods that stem from cognitive behavioural frameworks¹⁰, including the
107 fear-avoidance model of pain and disability¹¹ and the psychological flexibility model, the
108 model underlying acceptance and commitment therapy (ACT)^{12 13}. In this type of treatment,
109 the objective is to optimize effects by individualising treatment through evidence-based
110 therapeutic procedures¹⁴. In clinical practice, face-to-face therapy dominates in effectively
111 promoting well-being in patients with CP^{7 15}. Modes of treatment delivery are evolving,
112 however, as new models of care emerge.

113 Until now and despite the empirical support, interdisciplinary treatment, including
114 behavioural interventions, are commonly not available or difficult to access for most
115 individuals with CP^{16 17}. Digital solutions aiming at promoting health, also known as eHealth,
116 appear promising to bridge this gap as they appear cost-effective, can be tailored to individual
117 needs, applied in everyday life, and used at the patients' convenience¹⁸. Particularly in light of
118 the COVID-19 pandemic, distance approaches are gaining more attention in the management
119 of CP¹⁹. However, the development and implementation of evidence-based digital
120 interventions face challenges.

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3 121 Innovative digital treatments require an accurate scientific evaluation to ensure clinical
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5 122 effectiveness. As it is still seen as the “gold standard”, digital interventions for CP are often
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7 123 assessed through research-led randomized controlled trials (RCTs)^{18 20 21}. However, a call for
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9 124 real-world and n-of-1 evaluations of efficacy and safety of individual assessment and treatment
10
11 125 approaches is also being heard²². Compared to RCTs, n-of-1 study designs utilise repeated
12
13 126 measurements to provide a more fine-graded, time- and context-sensitive picture of individual
14
15 127 trajectories and pattern, thus allowing to evaluate effects at the within-person level²³.

16
17 128 Moreover, it has been shown that eHealth innovations purely originated from an
18
19 129 academic context are rarely sustainably implemented into health care practice due to a lack of
20
21 130 infrastructure, funding, and time²⁴. To avoid research waste when creating new eHealth
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23 131 solutions, a strong user-centred design and focus on implementation is suggested²⁵. A
24
25 132 framework that combines the scientific rigor of traditional research methods with a rapid and
26
27 133 iterative digital product development approach is needed. Then, the development of an
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29 134 evidence-based and user-friendly digital behavioural treatment is facilitated that is
30
31 135 implementation-ready for applied health care.

32
33 136 The ‘mHealth agile development and evaluation lifecycle’ (Figure 1) is a framework
34
35 137 created to promote the development of evidence-based, effective, and sustainable digital
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37 138 solutions²⁶. This framework emphasises practicality, flexibility, rapid evaluation, and the
38
39 139 possibility to adjust protocols to meet technological changes and insights that emerge as part
40
41 140 of the process. Therefore, Wilson, et al.²⁶’s framework will guide the present project with the
42
43 141 ultimate goal to develop, evaluate, and implement an effective and accessible behavioural
44
45 142 treatment to improve health in individuals with CP across Sweden.

46
47 143 --- FIGURE 1 NEAR HERE---

48 144 **Research objectives**

49
50 145 The overall aim of this project is to develop, evaluate, and implement a digital behavioural
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52 146 health treatment to improve well-being in individuals with CP. The treatment will be integrated
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54 147 into a nationally available health care web-platform, which facilitates large scale evaluations,
55
56 148 further development, dissemination, and long-term use in clinical practice across Sweden.
57
58 149 Within the project, we will (i) develop a prototype of the digital treatment matching the needs
59
60 150 of individuals with CP, using focus groups to assess user demands, and discuss possible
61
62 151 treatment structures and content, (ii) pilot the treatment in several iterations to evaluate its
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64 152 feasibility and acceptability, efficacy, and individual change processes by combining intensive
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66 153 (Single case experimental design (SCED)) and extensive methods; (iii) conduct a two-armed

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154 RCT enhanced with SCED to assess the clinical effectiveness, cost-effectiveness, and long-
155 term effects compared to treatment as usual (TAU) on a between- and within-person level; and
156 (iv) identify barriers and facilitators, and monitor the implementation process of the treatment,
157 through a business model and stakeholder interviews.

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158 **METHODS AND ANALYSIS**

159 Following the mHealth agile lifecycle²⁶, the DAHLIA (Acronym: Digital behaviourAI HeaLth
160 for chronIc pAin) project consists of an identification phase 0 and four main phases:
161 Development, optimisation, clinical trial evaluation, and post-market surveillance (See
162 overview of the DAHLIA project in Figure 2). Phase 1 includes two studies: focus groups with
163 patients and health care professionals (HCPs) to develop the treatment prototype (Study 1), and
164 stakeholder interviews to prepare for the implementation process by creating a business model
165 and identifying of barriers and facilitators (Study 2). Phase 2 (Optimisation) aims at optimising
166 the treatment and entails 4-6 iterations to test and gradually improve the prototype in a data-
167 driven manner (Study 3). Phase 3 consists of a large-scale clinical trial to evaluate the digital
168 treatment in comparison to TAU in a two-armed RCT enhanced with SCED (Study 4). Finally
169 in phase 4, a post-market surveillance is conducted using interviews with stakeholders from
170 different Swedish regions, also presenting lessons-learned (Study 5). Each phase may inform
171 and alter subsequent phases, in line with the agile approach. Details of the studies are described
172 in the following paragraphs.

173 --- FIGURE 2 NEAR HERE ---

174 **Project Identification**

175 **Involvement of inter-sectorial partners and international collaborators**

176 This project is a collaboration between academia, health care, and industry. The academic
177 partners come from seven universities in four countries (Sweden, Belgium, the Netherlands,
178 and the U.S.). The researchers contribute to the project with their scientific and clinical
179 experience in developing and evaluating digital treatments, implementation sciences, cost-
180 utilisation analysis, CP and related health issues, and the SCED method. The DAHLIA
181 treatment will be designed within the 1177.se platform in collaboration with health care
182 developers and digital designers in Region Kalmar and supported by the industry partner Inera,
183 who is responsible for the maintenance of the platform. The health care partners currently
184 represent three of the 21 regions in Sweden, and include primary care centres in Region
185 Kalmar, the Pain Clinic at Capio St. Göran Hospital, Region Stockholm, and the Rehabilitation
186 centre in Region Örebro.

187 **Personas as early user research**

188 Personas are typical patient- or user-profiles illustrating the target group of a treatment or
189 product and can be useful in the development of digital interventions to communicate user

1
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3 190 needs to the development team^{27 28}. By giving a narrative and name, personas facilitate a more
4
5 191 concrete discussion of patient needs, and to what extent the treatment might match those
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7 192 needs²⁹. In the DAHLIA project, three distinct patient personas evolved in an online workshop
8
9 193 and were edited over several months until the project partners were developed in a stepwise
10
11 194 manner. The personas originated from patient interviews in a previous study²⁷, and discussed
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13 195 in an online workshop to assess the relevance for the DAHLIA project. The personas were then
14
15 196 adjusted based on factors identified in research³⁰⁻³², other personas used in digital development
16
17 197 projects region Kalmar, and input from the clinical researchers (RW, IF, KB, LMcC, SP). The
18
19 198 personas were continuously edited over several months until the project partners agreed on the
20
21 199 final versions. The categories for each persona are: (i) *personal information*, including
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23 200 employment, education, family, background and social context, social support, and living area;
24
25 201 (ii) *patient pain profile*, including pain problem, consequences, pain behaviour, and attitude to
26
27 202 treatment; (iii) *health care and treatment*, including contact with health care, comorbidities,
28
29 203 and medicine; and (iv) *personal needs and goals*, specifically related to the treatment. Figure
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31 204 3 illustrates one of the personas used in the DAHLIA project.

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--- FIGURE 3 NEAR HERE ---

206 During the early development of the DAHLIA treatment prototype (version 1.0), and
207 prior to patient involvement, personas were used to ensure that relevant characteristics and
208 contextual factors were considered³³. The personas were presented at the start of treatment
209 workshops to discuss, for instance, if and how the treatment content and structure fit the
210 personas' characteristics and met their needs. Potential problems for a persona in relation to
211 treatment elements were identified, resulting in further discussions and consensus-based
212 adjustments.

213 **Guiding principles in the development process of the DAHLIA treatment**

214 Four three-hour online workshops took place between June 2020 and June 2021 to discuss the
215 theoretical framework, conceptual model, and treatment components. Project partners
216 presented their previous work related to behavioural treatment approaches and conferred on
217 the guiding principles for the prototype development. The group reached consensus on using
218 learning theory³⁴ as the theoretical framework for assessment and treatment. Furthermore, it
219 was agreed that the fear-avoidance model¹¹ and psychological flexibility model^{10 14 35} should
220 be used as conceptual models for the DAHLIA treatment. Conclusively, the primary objective
221 of the treatment is to increase resilience to pain and distress by promoting and training
222 behavioural skills of relevance to the individual's functioning and well-being. Furthermore, a

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3 223 self-guided micro-learning format³⁶ was chosen, including brief and frequent sessions (micro-
4 224 sessions), delivered digitally and accessible via a smartphone or desktop computer
5 225 (www.1177.se; details see ‘Stakeholder interviews (Study 2)').

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7
8 226 Based on the theoretical framework and conceptual models, values-oriented exposure
9 227 is considered to be the core procedure. Exposure implies the use of systematic contact with
10 228 negative experience such as pain and feelings of emotional distress that promotes avoidance,
11 229 in a way that reduces their adverse influence and produces more flexible, varied, and engaged
12 230 patterns of behaviour. Essentially, the function of exposure is to reduce negatively reinforced
13 231 behaviour focused on alleviating unwanted experiences, in favour of positively reinforced
14 232 behaviour focused on approaching goals in daily life. Exposure is enabled by several
15 233 behavioural processes, such as identifying life values and noticing own thoughts and emotions,
16 234 known as defusion (OPEN), flexible attention to the present (AWARE), and the building of
17 235 extended habits of engagement (ACTIVE)¹⁰.

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19
20 236 At the end of Phase 0, the following is envisioned: The DAHLIA treatment will run
21 237 over six weeks and includes four self-guided micro-sessions per week. Each session will
22 238 include a set of key elements (see Figure 4). The extent to which each of these elements will
23 239 be included in the session can vary. It should be noted that due to the agile process, data-driven
24 240 decisions might result in changes to this suggested structure.

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27 241 --- FIGURE 4 NEAR HERE---

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30 242 A chat function will enable patients to connect with their health care professionals
31 243 (HCPs, see details section ‘participants and recruitment’) for additional guidance,
32 244 asynchronous feedback, and further instructions. The role of the HCP is to encourage and
33 245 motivate patients to remain in the program and intervene in case the individual situation
34 246 worsens. At the start of the treatment, a specific weekday will be agreed on, during which the
35 247 HCP replies to the patient’s message. Potentially, the reply could also be a chat message, a
36 248 phone call, or a video call. The contact with the HCP will take place once a week, with a
37 249 minimum of six individual interactions between the HCP and patient. HCPs will receive
38 250 training, a manual, and supervision to provide the treatment.

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41 251 Furthermore, patients will be prompted to fill in a pre-scheduled digital diary twice a
42 252 day. The digital diary has the purpose to enable self-monitoring for increased self-awareness
43 253 of own behaviours, emotions, and routines, and thus enhanced orientation towards values and
44 254 goals³⁷, and data collection to gain insight into the individual change processes and effects of
45 255 the treatment in the context of the SCED. The full list of the daily diary items can be found in
46 256 the ‘Individual change processes’ section.

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3 257 After the main six-week intervention period, the treatment also entails booster-sessions
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5 258 delivered through the 1177 web-platform after two and four months. The participants get
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7 259 invited via SMS or emails to revisit the web-platform where they can engage in short
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9 260 behavioural exercises. Booster sessions are suggested in other contexts to support long-term
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11 261 behavioural changes³⁸ and reinforce patients learned coping strategies. Figure 5 summarises
12 262 the DAHLIA treatment components.

13 263 --- FIGURE 5 NEAR HERE ---

16 264 **Participants and recruitment**

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18 265 In the DAHLIA project, participants will be people who either use or deliver the digital
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20 266 treatment, or who facilitate the treatment implementation. Thus, study participants are (i)
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22 267 patients with CP, (ii) HCPs treating patients with CP, (iii) health care managers, (iv) developers
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24 268 of the 1177.se web platform, (v) other stakeholders identified in the process (e.g., policy
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26 269 makers, representatives from patient organisations). Health care professionals will be licensed
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28 270 psychologists or psychotherapists trained in cognitive behavioural therapy. Health care
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30 271 managers, developers, and other stakeholders need to be directly or indirectly connected with
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32 272 the treatment (e.g., decision-making on an organisational level; technical support etc.), but no
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34 273 other requirements apply.

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36 274 Patients are eligible for inclusion if they: are older than 18 years of age; report a pain
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38 275 duration of ≥ 3 months; are able to communicate in Swedish; and have access to a computer,
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40 276 smartphone, and internet in their home environment. The exclusion criteria are: injury or illness
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42 277 that require immediate assessment and treatment, or is expected to progress significantly during
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44 278 the next 6 months; unstable medication (based on self-report: changes in medication during the
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46 279 past 3 months or expected within the next 3 months that could influence well-being and
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48 280 functioning substantially, such as opioids, anti-epileptic drugs, antidepressants); previous CBT
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50 281 treatment (including ACT) during the past 6 months; severe psychiatric co-morbidity (for
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52 282 instance, high risk of suicide).

53
54 283 Information regarding the DAHLIA project and specific sub-studies will be provided
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56 284 to the clinics, including detailed instructions for eligibility. Regions recruiting patients are
57
58 285 Kalmar, Stockholm, and Örebro. Additional regions have expressed interest in participating
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60 286 and recruitment might be extended. Patients will be approached via their health care centres
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288 and once patients have expressed interest in study participation, a formal eligibility check will
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or online meeting by their treating care professionals, including psychologist and pain

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3 290 physicians. A short interview will be conducted to confirm eligibility and ensure that none of
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5 291 the exclusion criteria are met. Informed consent is then obtained from all participants prior to
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7 292 enrolment in the study. Sociodemographic and pain-descriptive information will be collected
8
9 293 from all participants including age, sex, level of education, occupation, location, level, and
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11 294 duration of pain, pain diagnosis (if applicable), and approaches to relief pain (e.g., medication,
12
13 295 heat, physiotherapy).

14 296 **Phase 1: Development**

17 297 **Focus groups (Study 1)**

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19 298 The aim of this study is to (i) identify the needs of patients and HCPs and (ii) match the
20
21 299 treatment content to their needs. At least three focus groups will be conducted in autumn 2021,
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23 300 one with HCPs (i.e., psychologists/ psychotherapists trained in CBT) and two with patients.
24
25 301 Per focus group, 6-8 participants will join³⁹. An attempt will be made to recruit a heterogeneous
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27 302 group of patients in terms of such characteristics as pain condition, sex, and socio-economic
28
29 303 background. The focus groups will be held online and take 90-120 minutes. A semi-structured
30
31 304 guide inspired by Gruters, et al.⁴⁰ will be followed. In addition to a general discussion around
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33 305 health and individual needs at the start, the focus group leader (i.e., research assistant and
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35 306 clinical coordinator) will ask participants to reflect on the design, set-up, content, and
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37 307 prospective feasibility of the DAHLIA treatment (details see Appendix 1). The group
38
39 308 conversations will be audio- and video-taped. Field notes will provide further insight into
40
41 309 relevant cues and observations.

42
43 310 The recordings will be transcribed verbatim and the data analysis will be performed by
44
45 311 two independent researchers. The information for the patient groups and HCP group will be
46
47 312 analysed separately. A combination of inductive and deductive content analysis will be used.
48
49 313 First, the deductive approach will determine the themes emerging from the semi-structured
50
51 314 guide: (i) health needs and determinants to live well with CP, and (ii) feedback on the DAHLIA
52
53 315 treatment. Then, an indicative analysis will be performed to identify categories within the
54
55 316 themes. The transcript will be read carefully and open coding will be used. A consensus
56
57 317 meeting with a third researcher will be conducted as a final step. This approach has been
58
59 318 described previously and appears valid to answer the research question^{40 41}. The results from
60
61 319 the focus groups will be integrated into the treatment prototype (version 2.0).

320 Stakeholder interviews (Study 2)

321 The aim of this study is to develop a preliminary business model for the digital behavioural
322 treatment and identify barriers and facilitators of the prospective implementation process. An
323 explicit focus on implementation early during treatment development has been
324 recommended⁴². Particularly, business modelling in the context of eHealth technologies can
325 help to create a set of success factors that will influence sustainability and effectiveness⁴³. To
326 build the knowledge base across the multiple studies and settings, the consolidated framework
327 for implementation research (CFIR)⁴⁴ will be used. The CFIR has five major domains:
328 intervention characteristics, outer setting, inner setting, characteristics of the individuals
329 involved, and the process of implementation. It is utilized as part of the analysis, as explained
330 below.

331 As a first step, a preliminary version of the business model canvas was filled in by the
332 research team (SB, SJ, RW, HC). As suggested by Osterwalder and Pigneur⁴⁵ ‘a business
333 model describes the rationale of how an organization creates, delivers, and captures value’
334 (p.14) and demonstrates the logic of how a company or organisation intends to generate profit
335 for a service or product. The nine blocks of the business model cover four areas of a business:
336 customers, offers, infrastructure, and financial viability. Figure 6 presents the template of the
337 business model canvas and short definitions for each segment, including example aspects
338 relevant for the DAHLIA project.

339 --- FIGURE 6 NEAR HERE---

340 In the present study, the treatment will be integrated into the national public health care
341 website (www.1177.se), using the digital platform for behavioural health (‘Stöd och
342 Behandling’). This digital platform is free from commercial interests, maintained by Inera,
343 which is owned by the county councils and regions. The general aim of this national website is
344 to increase access to healthcare, strengthen the position of the patient, and contribute to
345 improved public health. The website (www.1177.se) contains health care information,
346 inspiration, and e-services. Each of the 21 regions in Sweden is responsible for coordinating
347 activities and services provided on www.1177.se, which are conducted by own staff or
348 contracted providers. Through a national network, providers and regions can cooperate and
349 share licenses for services.

350 The business model will be discussed and refined as part of the stakeholder interviews.
351 Currently identified stakeholders are software developers, HCPs, and health care managers. A
352 semi-structured guide inspired by a previous study on eHealth implementation⁴⁶ will structure
353 the interviews and gather information on gatekeepers, barriers, and facilitators for prospective

1
2
3 354 dissemination and use. Questions are tailored to the different stakeholders and include, for
4
5 355 example, *'If/how is the interventions' content updated?'*, *'Who is responsible/ involved in the*
6
7 356 *maintenance of the intervention?'*, *'What could facilitate/ hinder the implementation process?'*,
8
9 357 and *'Do you think this intervention has the potential to become successful in your care*
10 358 *facility?'*. The full guide can be seen in Appendix 2. As part of the agile process, the guide may
11
12 359 be adjusted based on information collected during the interviews and tailored to additional
13
14 360 stakeholders including policy makers or representatives from patient organisations.

15 361 A minimum of eight interviews will be conducted and snow-ball sampling will identify
16
17 362 additional participants that can inform the process. Interviews will be conducted until data
18
19 363 saturation is achieved and no new topics seem to emerge. The interviews will be recorded, and
20
21 364 the qualitative data will be transcribed. Then, a qualitative thematic analysis will be
22
23 365 performed⁴⁷ with statements related to potential barriers and facilitators. An inductive approach
24
25 366 to group the information will applied in order to best scope the replies and map categories onto
26
27 367 the CFIR domains⁴⁴ as previously described.

27 368 Finally, implementation strategies matching the emerging topics will be formulated⁴⁸.
28
29 369 Together with the business model, these two elements represent the implementation plan for
30
31 370 the DAHLIA project. Findings from this study may furthermore influence the post- market
32
33 371 surveillance (Study 5, see details below).

35 372 **Phase 2: Optimisation (Study 3)**

36
37 373 The aim of the optimisation phase is to pilot the treatment and improve it through an iterative
38
39 374 data-driven process using small patient cohorts. The primary objective is to determine the
40
41 375 treatment feasibility and acceptability, and the secondary objectives are to examine individual
42
43 376 change processes, and efficacy across iterations on a group-level. The general procedures
44
45 377 include the eligibility check, and four assessment periods: baseline, main treatment period,
46
47 378 post-intervention, and 3- and 6-months follow-ups. Results from each iteration will be
48
49 379 integrated into the subsequent iteration, then tested again, until satisfaction is reached and no
50
51 380 new major issues seem to emerge. In the optimisation studies, different methodologies will be
52
53 381 combined namely momentary data collection using digital diaries, retrospective questionnaires,
54
55 382 and semi-structured interviews. The latter will be conducted by a research assistant, while the
56
57 383 diaries and questionnaires will be completed online. Figure 7 provides an overview of the
58
59 384 procedure in relation to the research objectives.

58 385 --- FIGURE 7 NEAR HERE ----

1
2
3 386 In total, 40 to 60 patients and their treating HCPs will be included, with n=10 patient-
4
5 387 HCP dyads each iteration. Four iterations have been seen as sufficient in a previous study to
6
7 388 optimise a digital treatment⁴⁹, therefore, a minimum of four iterations will be conducted in the
8
9 389 DAHLIA project. In accordance with the agile approach, additional iterations may be
10
11 390 performed if deemed necessary. The rationales for the approaches and methodological details
12
13 391 are described below.

14 392 **Feasibility and acceptability**

15
16 393 The procedure to evaluate the feasibility and acceptability of the treatment includes self-
17
18 394 reports, interviews, and technical data. Short self-reports will be collected after each micro-
19
20 395 and booster-session. Specifically, patients will be asked to rate the micro-session on its
21
22 396 usefulness, enjoyment, and comprehension (*'I experienced today's session as helpful/
23
24 397 enjoyable/ understandable.'*, rated on a 7-point numerical scale from 1=not at all, to 7=very
25
26 398 much).

27 399 Furthermore, at the end of the main intervention period, interviews will be conducted
28
29 400 following a semi-structured guide to assess the participants' general experience and different
30
31 401 treatment components, specifically the diary, micro-sessions, and chat function. Questions are
32
33 402 first rated on a 7-point numeric scale and participants are then encouraged to elaborate on their
34
35 403 response with further details, if possible. Examples of questions are *'Did the intervention
36
37 404 hinder your daily occupation?'*, *'Were the micro-sessions difficult or unclear?'*, *'Did you
38
39 405 experience the digital diary as burdensome?'*, or *'Would you recommend the treatment to a
40
41 406 friend?'* (details see Appendix 3). This guide is based on other feasibility studies^{49 50} and
42
43 407 tailored to the DAHLIA treatment components. The HCPs will also be interviewed using a
44
45 408 guide that follows the same structure (i.e., numeric scale and open elaborations), but the
46
47 409 specific questions will be informed by the focus groups (study 1).

48
49 410 Additionally, technical data generated from the 1177.se website will be collected. These
50
51 411 data include time and frequency of log-ins, duration of engagement with the treatment, and use
52
53 412 of components. Technical data will be used to describe the overall use and adherence, and
54
55 413 allows mediation analyses to determine the influence of engagement rates on treatment
56
57 414 outcomes.

58
59 415 Data from the feasibility assessments will be analysed using descriptive statistics and
60
416 qualitative synthesis to identify trends. The results will be presented reflecting the two core
417
418 variables from the Technology Acceptance Model (TAM): 'Perceived Usefulness' and
'Perceived Ease of Use'⁵¹. After each iteration, the insight gathered will be fed back to the

419 developers and integrated to gradually improve the feasibility and acceptability through data-
420 driven adjustments of the treatment.

421 **Individual change processes**

422 The optimisation studies implement a sequential replicated and randomized single case
423 experimental design (SCED) to gain detailed insight into within-person behavioural changes,
424 and to develop and test the DAHLIA intervention, which has been recommended in the context
425 of CP⁵². In SCEDs, each case functions as their own control and changes are evaluated
426 comparing levels of the outcome variables across different phases (e.g., baseline phase ‘A’ and
427 treatment phase ‘B’)⁵³. The methodology aims to demonstrate cause-effect relationships
428 between the treatment (independent variable) and the target behaviour (dependent variable)⁵⁴.

429 When planning a SCED study, the Risk of Bias in N-of-1 Trials (RoBiNT) Scale, a
430 critical appraisal tool that evaluates the methodological quality of intervention studies using
431 single-case methodology, can be followed as guidance^{54 55}. The design decision made in the
432 present study were based on this appraisal tool to ensure a scientifically robust approach. Table
433 1 provides details on the design elements.

434

435 Table 1. Methodological SCED approach of the DAHLIA study based on the RoBiNT Scale.

Item	RoBiNT Scale	SCED details, per optimisation iteration (<i>anticipated points</i>)
INTERNAL VALIDITY SUBSCALE		
1	Design	A replicated randomised AB-design with 10 x A-B (total of 20 phases), providing the opportunity to observe the experimental effect 10 times. (<i>2 points</i>)
2	Randomisation	The start of the treatment phase and therefore length of baseline phase will be determined randomly for each participant, with the baseline phase lasting between 5 to 10 days. This means that the treatment phase will start on any day between the 6 th and 11 th assignment. (<i>2 points</i>)
3	Sampling behaviour during all phases	The baseline phase will last at least 5 days, with twice daily sampling, resulting in 10 data points or more (phase A) (assuming 100% compliance to diary). The treatment phase will run over 6 weeks, with twice daily sampling on at least 4 days per week (6 weeks x 4 days x twice daily sampling), resulting in 48 data points or more (phase B) (assuming 100% compliance to diary). Even if the compliance rate should be lower, the amount of data points will lie >5 data points. (<i>2 points</i>)
4	Blinding of participants and HCP delivering the treatment	Blinding of the participant and practitioner is not feasible in the DAHLIA project. The behavioural treatment is delivered through a web-platform independently of the HCP; however, the HCP provides weekly, tailored support in addition to the online treatment. Neither the participant nor the HCP are blinded. (<i>0 points</i>).
5	Blinding (masking) of assessors	Patients complete self-report diaries and are not blinded to treatment phase, therefore, not independent of the therapy process. (<i>0 point</i>)
6	Inter-rater agreement	The measure of the target behaviour is a subject measure relying on self-reports from the digital diaries. (<i>0 points</i>)
7	Treatment adherence	The treatment is delivered through a web-platform following a standardized approach. Adherence to treatment (%) is calculated using digital log-in data . (<i>2 points</i>)
EXTERNAL VALIDITY AND INTERPRETATION SUBSCALE		

8	Baseline characteristics	A short interview by an HCP as part of the eligibility check will be conducted. Furthermore, a case formulation including information on age, sex, aetiology of CP, and severity of CP will be presented when presenting the results; this information will be based on a baseline assessment (online self-report). (2 points)
9	Setting	Information on the general location (Swedish region, hospital/ pain clinic) will be provided; however, the participant will engage with the online treatment in their everyday life, and therefore, it will not be possible to include details about the specific environment. (1 point)
10	Dependent variable (target behaviour)	Table 2 provides an overview of all diary items, which are scores on a 7-point Likert-Scale, except from the pain level item (0-100). Process outcome measures: 5 items on psychological (in)flexibility (see Table 2), 2 items on pain self-efficacy, 1 item on pain avoidance. Primary outcome measures: 1 item on pain level, 1 item on pain interference, 1 item on pain catastrophizing. Secondary outcome measures: 3 items on sleep, 2 items on affect, 1 item on stress, 1 item on fatigue. (2 points)
11	Independent variable (treatment)	A detailed description of the DAHLIA treatment is given above, including the treatment content, and number, duration, and frequency of sessions. (2 points)
12	Raw data record	Ten cases will be recorded (4-6 iteration with n=10 participants per iteration). Raw data will be presented with a data point for each diary entry. (2 points)
13	Data analysis	Data will be analysed and reported for each participant individually. Structured visual analysis, effect size measures and a randomization test wrapper for multilevel models will be applied. (2 points).
14	Replication	Ten participants will be included (per optimisation iteration). Across all iterations, data from n=40-60 participants will be available. (2 points)
15	Generalization	Patients will be heterogeneous in their characteristics. Furthermore, retrospective self-reports will be completed by each participant pre-post treatment , including two FUs (details see Table 3). (1 point)

436

437 Under the condition that all choices can be executed as intended, the internal validity
 438 of this SCED study will reach 8/14 points, and the external validity will reach 14/16 points.
 439 The total interpretation score will be 22/30 points. This score indicates a moderate
 440 methodological rigour⁵⁶.

441 Target behaviours will be assessed via self-reports collected through a digital diary.
 442 This diary will be prompted through the SMS function of REDCap, or a smartphone application
 443 (e.g., www.mpath.io). Both data collection methods will be piloted with participants to ensure
 444 that the diary works reliably. Participants will be prompted to complete the diary twice daily
 445 (for details see Table 2). Proposed diary items are based on traditional questionnaires and other
 446 diary studies⁵⁷, and were chosen as they assess relevant aspects in the context of CP.
 447 Furthermore, items should be short and easily to answer quickly⁵⁷. The order of the items will
 448 be the same in each prompt to allow participants to get used to the questions, minimise time to
 449 complete the diary, and thus limit interference with their daily flow. The reliability, validity,
 450 and sensitivity of the items will be explored as part of the optimisation studies using suggested
 451 statistics (e.g., P-technique factor analysis). Idiosyncratic items might also be discussed with
 452 patients, in line with the agile approach, to improve validity and potentially patient engagement
 453 and ownership. Based on user-input, scientific evidence, and insight gained, diary items might

454 be optimised and adjusted, and any adjustments made will be reported in prospective
455 publications.

456

457 Table 2. Proposed daily diary items.

LUNCH/ EVENING DIARY		
Instructions (Availability to fill out: Lunch diary 12-14h, evening diary 18-20h)	<p>LUNCH: Hello & welcome to your digital diary! Please reflect on last night and this morning, and rate the following statements. Self-reflections can help to understand your daily routines and needs better. Let's get started.</p> <p>EVENING: Welcome back to your daily diary. Please take 2-3 minutes to reflect on this afternoon.</p>	
Construct	Item	Answering scale
Last night, ...		
1 Sleep ¹	... I generally slept well.	7-point numeric scale
2 Sleep ¹	... I had problems falling asleep.	7-point numeric scale
3 Sleep ¹	... I woke up frequently or too early.	7-point numeric scale
During the morning/ During the afternoon...		
4 Positive affect	... I felt happy, energetic, at ease, or enthusiastic.	7-point numeric scale
5 Negative affect	... I felt down, irritated, depressed, or hopeless.	7-point numeric scale
6 Stress	... I felt stressed.	7-point numeric scale
7 Fatigue	... I felt tired.	7-point numeric scale
8 Experiential avoidance/ Acceptance ²	... I tried to distract myself when I felt unpleasant emotions. ... I opened myself to all my feelings, the good and the bad.	7-point numeric scale
9 Lack of contact with present moment/ Present moment awareness ²	... I did most things on "automatic" with little awareness of what I was doing. ... I was attentive and aware of my emotions.	7-point numeric scale
10 Self as content/ Self as context ²	... I criticized myself for having irrational or inappropriate emotions. ... I tried to see the larger picture, even when I was down, depressed, or hopeless.	7-point numeric scale
11 Fusion/ Defusion ²	... distressing thoughts tended to spin around in my mind like a broken record. ... I was able to notice my thoughts and feelings without getting overwhelmed by them.	7-point numeric scale
12 Lack of contact with values/ Values ²	... I didn't have time to focus on things that are important to me. ... I tried to connect with what is truly important to me.	7-point numeric scale
13 Inaction / Committed action ²	... negative feelings trapped me in inaction. ... I didn't quit working towards what is important even if it was though.	7-point numeric scale

14	Pain level	... my overall pain level was:	0 (no pain) to 10 (worst pain imaginable)
15	Pain interference	... my pain interfered with my...	7-point numeric scale <ul style="list-style-type: none"> ○ General activities ○ Mood ○ Walking abilities ○ Normal work (including housework) ○ Relations with others ○ Enjoyment of life
16	Pain catastrophizing	... I worry about whether my pain will stop or not.	7-point numeric scale
17	Pain avoidance	... I did not do things to avoid feeling my pain.	7-point numeric scale
18	Pain self-efficacy	... I could do some form of housework/ paid/ unpaid work, despite the pain.	7-point numeric scale
19	Pain self-efficacy	... I could live a normal lifestyle, despite the pain.	7-point numeric scale
20	Open question	I would also like to share this about my morning/ afternoon:	Free text
21	Treatment interaction ³	Today, I completed a treatment module.	<ul style="list-style-type: none"> ○ Yes. ○ No, because it was a 'module free day'. ○ No, but I will do it tonight. No, because: <i>free text</i>
	Instructions	LUNCH: Thank you & have a nice afternoon! EVENING: Thank you very much for taking the time to fill in your diary. Have a nice evening!	

458 *7-point numerical scale ranges from 1: not at all, to 7: very much.*

459 *Note: ¹Sleep items only as part of the morning questionnaire; ²Both psychological flexibility and*
460 *inflexibility items will be tested to determine with are more feasible and suitable to use; ³Treatment*
461 *interaction item only as part of the evening questionnaire.*

462

463 In addition to the information in Table 1, the analysis will be executed as follows. Diary
464 data have a multilevel structure because repeated measurements (level 1) are nested within
465 individuals (level 2). First, structured visual analysis will be conducted for each individual
466 separately following the four steps described in Kratochwill, et al. ⁵³ to examine the within-
467 and between-phase patterns in respect to the effects on level, trend, variability, immediacy,

1
2
3 468 overlap, and consistency. Additionally, effect size measures will be calculated at the individual
4
5 469 level using standardized mean difference and Tau-U, and at a group level using the between-
6
7 470 case standardised mean difference⁵⁸. Finally, to avoid making distributional and random
8
9 471 sampling assumptions, the randomization test wrapper for multilevel models will be used to
10
11 472 synthesise the data from the whole group of cases and evaluate treatment effects⁵⁹. Scientific
12
13 473 advisors of this project will provide expertise and support in the SCED analyses. Results will
14
15 474 be presented following the RoBiNT scale and SCRIBE guideline⁶⁰.

17 475 **Efficacy across iterations**

18
19 476 In the optimization studies, efficacy will be determined using both intensive (SCED) as well
20
21
22 477 as extensive methods (retrospective self-reports from baseline, post-intervention and FUs; see
23
24
25 478 Figure 7). The diary and questionnaire data will be aggregated across all iterations, thus include
26
27 479 data from 40-60 participants. This approach allows to investigate the generalisability of results
28
29 480 of the SCED and evaluate treatment effects in applied research⁶¹. MultiSCED will be used for
30
31 481 the SCED data ⁶².

32
33 482 The proposed retrospective questionnaires used can be separated into process, primary,
34
35 483 and secondary outcome measures (see Table 3). Additionally, negative treatment effects may
36
37 484 occur in the context of internet interventions, and therefore, need to be acknowledged and
38
39 485 systematically assessed⁶³. Negative treatment effects are here assessed post-treatment using the
40
41 486 negative effects questionnaire (NEQ), a tool with reliable and valid psychometrics⁶⁴.

42 487 Descriptive statistics of the retrospective questionnaires will summarize demographics
43
44 488 and pre-treatment clinical characteristics of the sample. To evaluate changes in treatment
45
46 489 outcomes over time, linear multilevel modelling (MLM) will also be used. MLM accounts for
47
48 490 repeated measures within subjects and can handle missing data, which will be addressed per
49
50 491 variable. Using a random intercept model, time will be treated as a categorical variable and pre-
51
52 492 treatment values will be specified as the reference point. Therefore, results will be interpreted
53
54 493 as a change from pre-treatment to post-treatment and, from pre-treatment to follow-up
55
56 494 assessments. Anchor-based methods will be applied to determine clinical significance of
57
58 495 changes in outcome measures⁶⁵. Separate linear growth models⁶⁶ will be computed for each
59
60 496 variable, while controlling for multiple testing. Significance level is set at Alpha (α)=0.05.

498 Table 3. Proposed outcome variables and tools used to assess efficacy using extensive methods.

Focus	Variables	Instrument	Supported psychometrics
Process outcome measures	Open/ Acceptance	Chronic Pain Acceptance Questionnaire (CPAQ)	Internal consistency and criterion validity (Swedish version) ⁶⁷
	Aware	5 items on, 'acting with awareness' from the Five Facets Mindfulness Questionnaire (FFMQ)	Internal consistency, reliability, and construct validity (Swedish version) ⁶⁸
	Engaged/ committed actions	(i) Valuing questionnaire; (ii) Committed action questionnaire	(i) Internal consistency and construct validity (Swedish version) ⁶⁹ ; (ii) Proven validity and reliability (Swedish version) ⁷⁰
	Psychological flexibility	Swedish translation of the Multidimensional psychological flexibility inventory (MPFI)	Convergent and discriminant validities (English version) ⁷¹
	Self-efficacy	General self-efficacy scale (S-GSE)	Reliable with high internal consistency (Swedish version) ⁷²
	Pain self-efficacy	Pain self-efficacy questionnaires (PSEQ-2)	Evidence for reliability and validity (English version) ⁷³ , translated into Swedish ⁷⁴
	Avoidance	Avoidance subscale of Psychological Inflexibility in Pain Scale (PIPS)	Internal validity and construct validity (Swedish version) ⁷⁵
Primary outcome measure	Catastrophizing	Subscale of coping strategies questionnaire (CSQ)	Internal consistency and sufficient test-retest reliability (Swedish version) ^{76 77}
	(Dis)ability/ pain screening	Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ)	Clinically reliable and valid (Swedish version) ⁷⁸
	Work ability	Work ability index (WAI)	Validated (Swedish version) ⁷⁹
	Functioning	Brief pain inventory (BPI-SF)	Reliable and valid in multiple languages (including Swedish version) ⁸⁰
Secondary outcome measure	Well-being/ depression	Patient Health Questionnaire (PHQ-9)	Satisfactory content validity and sufficient reliability (Swedish version) ⁸¹
	Perceived stress	Perceived Stress Scale (PSS)	Internal reliability and construct validity (Swedish version) ⁸²
	Sleep problems	Insomnia Severity Index (ISI)	Satisfactory factor structure, internal reliability, and concurrent validity (Swedish version) ⁸³
	Health-related quality of life	EQ-5D	Standardised measure of health-related quality of life developed by the EuroQol Group ⁸⁴

499 **Phase 3: Clinical evaluation (Study 4)**

500 **Randomized controlled trial enhanced by SCED**

501 To determine the clinical effectiveness of the DAHLIA treatment, a RCT enhanced with SCED
502 will be conducted. While RCTs provide estimates of between-subject treatment responses,
503 differences in average scores between groups, they are unable to indicate specific within-
504 subject responses. Simons, et al.⁸⁵ apply a similar design and argue that SCED is a valuable
505 addition to a traditional RCT design. One reason for this combined approach is that RCTs
506 provide information on the population level, whereas SCEDs focus on the individual level.
507 Furthermore, heterogeneity of treatment effects might remain undetected in a traditional RCT
508 design⁸⁶. Additionally, the need for large cohorts of patients for adequate sub-group analysis⁸⁷,
509 and a lack of feasibility to reach certain patient groups⁸⁸ limits the insights from a traditional
510 RCT. Applying SCED and multilevel modelling, even group results from small and distinct
511 cohorts can be performed on a meta-analysis level⁸⁵.

512 Outcome measures will be the same as in the optimisation studies, including the diary
513 items for the SCED (see Table 2), and retrospective questionnaires (see details Table 3;
514 including NEQ post-treatment⁶⁴). A priori computations based on a power of .95, four
515 questionnaire assessment points and a medium effect size shows that 360 participants (180 in
516 each arm) are sufficient to generate stable findings in the analyses of treatment effects. With
517 an estimated attrition rate of 18%, this implies that 295 participants will provide post-treatment
518 data, which is considered adequate also for moderator/ predictor and cost-effectiveness
519 evaluations. However, outcome measures and calculated sample size will be updated and might
520 be modified based on iterations in the prior phase.

521 Treatment arm randomization is conducted by a research assistant following the
522 decision on study inclusion by the HCP and after the baseline assessment (sociodemographic
523 information, questionnaires, A-phase of SCED) is completed. Participants are randomized to
524 the treatment arm or treatment as usual (TAU) using a block randomization strategy to ascertain
525 equal distributions across the arms. Randomization is conducted by a local project manager
526 who is not involved in the screening or intervention. Next, participants undergo treatment; then
527 all participants complete the post-intervention assessment (questionnaires and 5-day digital
528 diary). Booster-sessions will be sent to the participants in the intervention group at 2- and 4-
529 months. Finally, at the 3- and 6-month follow-ups (FUs), all participants complete the
530 questionnaires and 5-day digital diary period. In case participants decide to discontinue the
531 study at any point in time, they might choose to provide a reason.

1
2
3 532 To examine changes in process, primary and secondary outcome measures (Table 3),
4
5 533 linear mixed models will be conducted comparing the DAHLIA treatment to TAU. Analysis
6
7 534 will be performed using group as a fixed between-person factor (two levels: DAHLIA
8
9 535 treatment and TAU), and time as a fixed within-person variable (four levels: baseline, post-
10
11 536 treatment, 3-month FU, 6-month FU). The linear mixed model will estimate fixed effects
12
13 537 (regression slopes) for change in the intervals during (baseline to post-treatment assessment),
14
15 538 and after (post-treatment to 3- and 6-month FU) the treatment period. The intervals will be
16
17 539 entered as a categorical dummy variable (three levels). Potential confounders will be added to
18
19 540 the model as covariates (i.e., age, gender, pain diagnosis, pain duration). Data will be analysed
20
21 541 with the support of a statistician and using the latest version of SPSS. Mean change will be
22
23 542 reported and test of significance will be two-sided with a set alpha level of 0.05.

23 543 **Health economic evaluation**

24
25 544 A short-term health economic evaluation will compare the DAHLIA treatment and the TAU at
26
27 545 the primary endpoint (post-treatment). Additionally, an equivalent long-term evaluation will
28
29 546 be performed at the end of the FU period using cumulative data collected up to that assessment
30
31 547 point. Costs in both trial arms will be estimated from a societal perspective for each participant
32
33 548 in the trial based on resource items and associated relevant unit costs. The use of societal
34
35 549 resources comprises information on the use of resources related to healthcare contacts and
36
37 550 medication (medical records and register data), and productivity losses related to absence from
38
39 551 work (the LISA database). Costs to deliver the digital intervention will be estimated based on,
40
41 552 for instance, HCPs' time spent on treatment. Total costs will be aggregated by trial arm.

42 553 The self-report tool EQ5D⁸⁴ will be completed by the participants at pre-, post-
43
44 554 treatment and FUs and used to measure changes in health-related quality of life (HRQoL), to
45
46 555 calculate quality adjusted life years (QALYs). Total QALY gains for participants over the trial
47
48 556 will be estimated using the area under the curve method⁸⁹. Cost data and QALYs will be
49
50 557 analysed using generalized linear models to account for non-normal distributions⁹⁰. Data will
51
52 558 be analysed controlling for the influence of covariates, and by adjusting for baseline data. Cost-
53
54 559 utility analysis (CUA) will be conducted with QALYs gained as primary outcome, comparing
55
56 560 incremental costs with incremental changes in QALYs for digital treatment and TAU. Results
57
58 561 will be presented as an incremental cost-effectiveness ratio (ICER), representing the ratio
59
60 562 between the difference in costs and the difference in QALY gained between the digital
563
564 treatment and TAU. Incremental cost-effectiveness ratio will be expressed as cost per
additional QALY, which is the most common approach in health economics⁹¹. Uncertainty

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2
3 565 around the cost and outcome data will be explored and presented on cost-effectiveness plans,
4 566 representing the distribution of the cost and outcome differences between both conditions. The
5 567 probability of digital treatment being cost-effective compared to TAU will be presented across
6 568 a range of price values a decision-maker would be willing to pay, represented by a cost-
7 569 effectiveness acceptability curve⁹².

12 570 **Phase 4: Post-market surveillance (Study 5)**

13 571 Similar to the development phase (Study 2), interviews with stakeholders will be conducted,
14 572 recorded, and transcribed. The stakeholders participating in study 2 will be approached, along
15 573 with additional key stakeholders identified during the implementation process. Appendix 4
16 574 provides the full overview of the interview questions. Questions reflect on the process so far
17 575 (e.g., *‘What kind and how many resources were needed to bring this intervention into*
18 576 *practice?’*), on the current status (e.g., *‘What issues are you currently facing?’*), and
19 577 prospective adjustments (e.g., *‘What will the prospective maintenance and upkeep look like?’*).
20 578 These questions are preliminary and may be adjusted based on findings of Phase 1-3. Even
21 579 though the 1177.se website is free for the end users (i.e., patients and HCPs), special attention
22 580 may also be paid to financing, as a lack thereof can be a barrier for long-term implementation
23 581 of eHealth interventions⁹³.

24 582 The qualitative data will be analysed following the same process as that used in Phase
25 583 1. Specifically, an inductive analysis to identify and summarise themes will be performed, and
26 584 information will be mapped onto the domains of the CFIR⁴⁴. The implementation strategy and
27 585 plan will be reviewed, and lessons-learned will be presented to inform prospective
28 586 implementation studies.

33 587 **Patient and public involvement**

34 588 This is a study protocol and due to ethical and practical reasons, no patients were directly
35 589 involved in the project yet. However, the Personas originated from interviews with patients, as
36 590 described above, and patients and other stakeholders will be involved in all planned phases of
37 591 the DAHLIA project. Dissemination to patients and the public is described in more detail the
38 592 section ‘Ethics and Dissemination’.

593 DISCUSSION

594 Chronic pain is a huge public health problem, in suffering, disability, and costs for individuals
595 and society. Widely accessible and sustainable behavioural treatment options could help to
596 address this problem. An agile and user-centred development integrating a data-driven
597 decision-making process and scientific evaluation of effects is essential to produce an
598 evidence-based intervention of this type for individuals with CP. To our knowledge, this is the
599 first project utilizing the mHealth agile development framework²⁶ to systematically build a
600 digital behavioural treatment within a nationally used health care hub. The purpose of this
601 project is to improve the standard of care for individuals with CP by applying the innovative
602 development framework, thus providing an accessible, user-friendly, and empirically
603 supported behavioural treatment to maintain or improve resilience, functioning, and well-being
604 in this population.

605 Strengths include (i) the execution of the project by a multi-disciplinary, inter-sectorial,
606 and international research team, (ii) the overall agile, iterative, and data-driven process, and
607 (iii) the involvement of patients and different stakeholders early and throughout the
608 development. Furthermore, (iv) the richness of methodologies using mixed methods,
609 combining a traditional clinical trial evaluation on the population level (RCT), fine-graded data
610 collection (SCED) on the level of the individual, and (v) an explicit focus on cost-effectiveness
611 and determinants of implementation will be highlighted. The project is (vi) based on innovative
612 strategies in the field of eHealth and digital treatments, and (vii) key gatekeepers such as
613 regional leaders support the initiative.

614 Due to the ambitious and multifaceted nature of the project, several inherent challenges
615 and risks should also be acknowledged. In case a sub-study should be delayed, e.g., due to
616 recruitment difficulties or technical development issues, this delay could affect the whole
617 project. Subsequently, adjustments following the agile approach could be discussed to balance
618 the practical feasibility of executing the study and limiting the impact on its robustness.

619 Furthermore, the multidisciplinary, inter-sectorial approach is certainly a strength of
620 the DAHLIA project, however, it might also have inherent challenges. For example, interests
621 of stakeholders might differ, which needs to be considered and addressed. Here,
622 communication is key, but compromises might be needed to ascertain satisfactory benefits for
623 all parties involved.

624 Regarding the DAHLIA treatment itself, a high level of patient engagement (e.g., four
625 micro-session per week combined with frequent diary assessments) will be required. These

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3 626 demands might be perceived as burdensome by some individual. However, contact with HCPs
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5 627 will support participants' motivation and engagement. Furthermore, the focus groups and
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7 628 optimisation studies will provide insight into the perceived intensity, thus feasibility of the
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9 629 intervention set-up, and the agile process allows to adjust it accordingly. Specially, tailoring of
10
11 630 the length of the micro-sessions and frequency of diary prompts will be explored.

12 631 Furthermore, the DAHLIA treatment may not be suitable for all people with CP and
13
14 632 the question of "what fits for whom" will be continuously discussed. The website
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16 633 (www.1177.se) is a national health care hub in Sweden, but research shows that older adults,
17
18 634 people with cognitive problems, or disabilities are less likely to use technologies⁹⁴, which could
19
20 635 result in a bias in recruitment and usability. To improve inclusivity, the possibility to provide
21
22 636 additional training for certain populations, such as older adults⁹⁵, will be explored. An
23
24 637 additional issue is that the project is currently executed in Swedish, which excludes people with
25
26 638 limited proficiency in Swedish. Therefore, translation into other languages and further cultural
27
28 639 adaptations will be considered.

29 640 The DALHIA treatment may have the potential to become a widely implemented first
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31 641 line of treatment. However, some CP groups will likely benefit from an alternative treatment
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33 642 format (e.g., face-to-face), or complementary interventions. Thus, additional studies may
34
35 643 explore if and how physiotherapists, general practitioners, or occupational therapists can
36
37 644 deliver the DAHLIA treatment.

38 645 Finally, the treatment could prospectively be scaled and adjusted for other groups of
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40 646 patients with CP, e.g., children and adolescents, people with disabilities, and/or other medical
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42 647 conditions such as individuals with severe mental or physical co-morbidities. In addition,
43
44 648 support offered as part of the DAHLIA treatment can be extended to significant others and
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46 649 family members of people living with CP. Thus, by using an agile development approach, the
47
48 650 DAHLIA project might grow to support the heterogeneous group of individuals with CP and
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50 651 their complex health needs.
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652 **Ethics and Dissemination**

653 The study received approval from Swedish ethical review authorities (Dnr 2021-02437). All
654 participants will receive a detailed patient information sheet, have one week time to consider
655 participation, and sign informed consent prior to participation. Each study participant will
656 receive a unique study code to ensure anonymity and confidentiality. Data will be stored
657 confirm Swedish privacy regulations on secure servers at Karolinska Institutet.

658 The project is announced on the Karolinska Institutet website (Rikard Wicksell's
659 research group), and on social media, primarily twitter. The general outline of the project has
660 been presented at online conferences. Next to the study protocol paper, the intention is to
661 publish a number of peer-reviewed manuscripts, in which any protocol modifications will also
662 be communicated. The results will be presented at (inter-)national conferences and networking
663 events. Popular science articles, podcasts, radio interviews, and animated videos are
664 additionally planned to disseminate the results to the wider public.

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3 666 **Author's contribution**
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5 667 SB, SJ, KB, LMcC, IFI, SP, and RW were involved in the conception and design of this project.
6
7 668 RW acquired the funding. RW received the funding. HC provided specific input on the topic
8
9 669 of implementation, IFe contributed with her expertise on health economy, and LS, PO, and JV
10
11 670 added valuable knowledge on the single-case experimental design aspects of the project. SB
12
13 671 drafted the manuscript, and all authors revised the manuscript and checked the intellectual
14
15 672 content. All authors gave final approval and agree to be accountable for all aspects of the work.

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17

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21
22 676 feedback. All icons presented in Figure 4, 5, and 7 are from www.freepik.com.

23
24 677 **Completing interests**
25

26 678 None declared.
27

28 679 **Access to data and protocol details**
29

30 680 Only the research team will have access to the raw data and participant code. Anonymised data
31
32 681 will be made available as part of publications, whenever possible. Researchers from other
33
34 682 universities may request to receive access to other information (e.g., informed consent sheets,
35
36 683 data management plan).

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38

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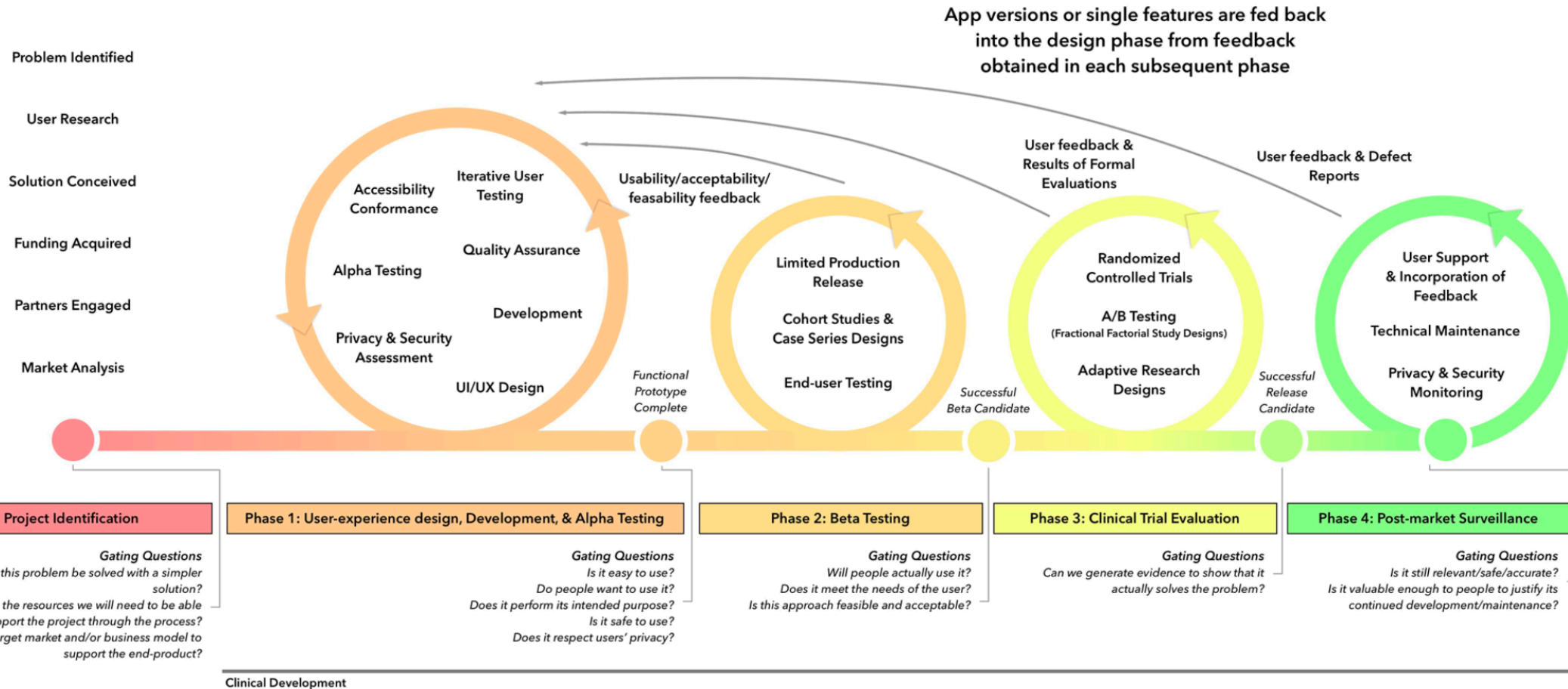
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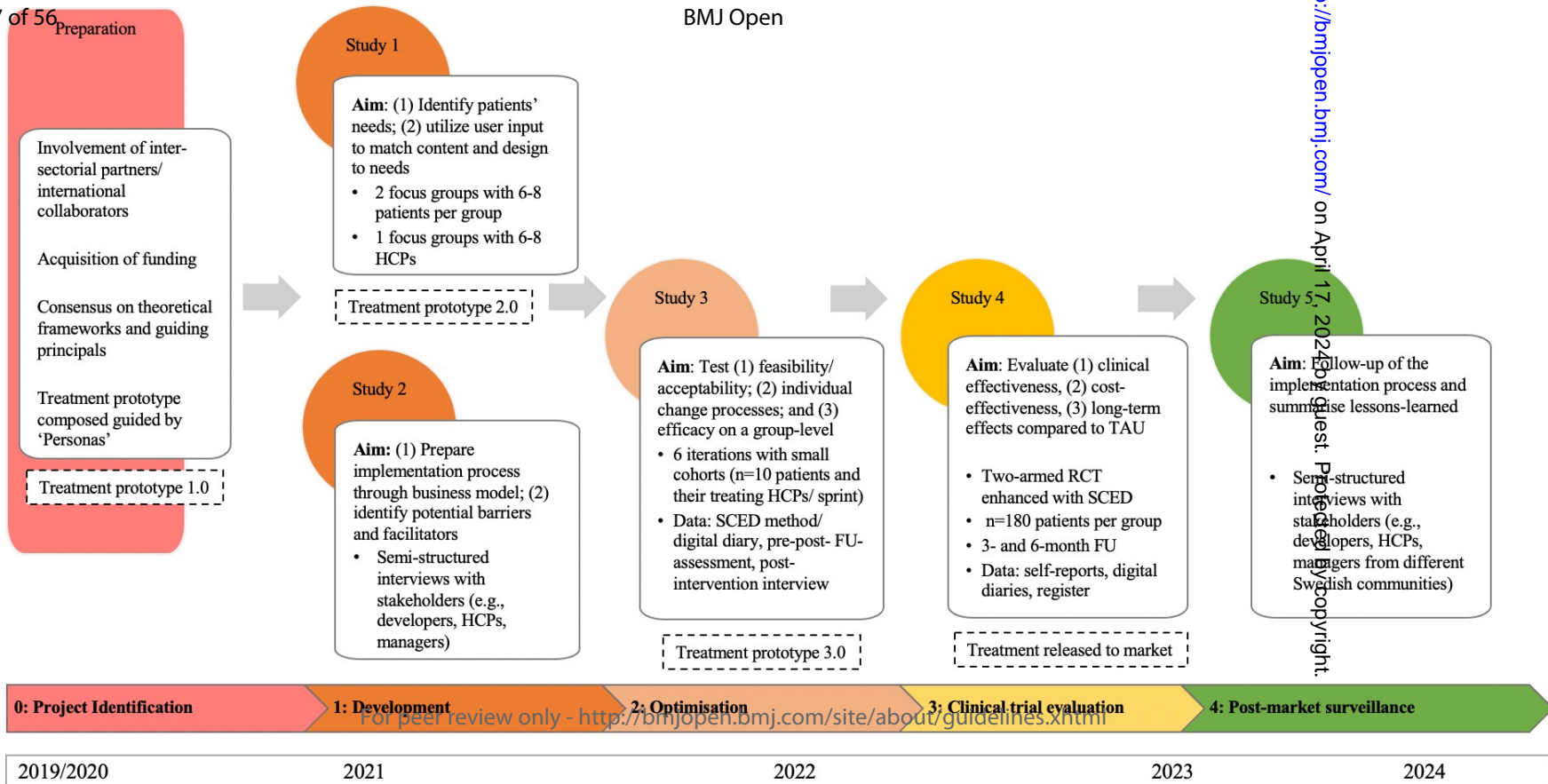
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3 957 **Figure legend**
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- 5 958 • Figure 1. mHealth Agile Development & Evaluation Lifecycle (Wilson et al., 2018).
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7 959 • Figure 2. DAHLIA project overview including highlights of each study and time plan.
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9 960 HCP= health care professional; SCED= single case experimental design; TAU=
10 961 treatment as usual; RCT= randomised controlled trial; FU= follow-up.
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12 962 • Figure 3. Example of a DAHLIA Persona with chronic pain.
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14 963 • Figure 4. DAHLIA treatment micro-session elements. HCP= health care professional.
15 964 Note: The name “DAHLIA treatment” is mainly for academic settings; in the 1177
16 965 web-platform, a more intuitive treatment name will be chosen.
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18 966 • Figure 5. The DAHLIA treatment components.
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20 967 • Figure 6. Template of business model canvas (based on Osterwald & Pigneur, 2010).
21 968 Grey boxes: Example aspects of the DAHLIA business model; the final model will be
22 969 a result of the stakeholder interviews.
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24 970 • Figure 7. General overview of the optimisation studies and specific procedure in each
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26 971 iteration. SCED= Single-case experimental design. FU= Follow-up. HCP= Health care
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mHealth Agile Development & Evaluation Lifecycle



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HEALTH CARE & TREATMENT

Contact with health care:

- Checked vision and has gone through a variety of investigations for the recurrent headaches.
- Visited dentist focusing on temporomandibular joints (jaw region).
- Sought care due to various somatic disorders (head, neck, stomach).

Comorbidities:

- Stress
- Anxiety
- Sleeping problems

Medicine:

- Pain killers

PERSONAL NEEDS & GOALS

Treatment needs:

- Wants to be independent and take an active part in her treatment. Needs to feel that she can influence her situation.
- Wants to follow/have an overview of own progress.

Goals:

- To live an active and productive life without pain.
- To learn how to maintain a balanced lifestyle without guilt when resting.

PATIENT PAIN PROFILE

Pain problems:

- No clinical diagnosis.
- Recurrent headaches.
- Tensions in shoulders and neck.
- Stomach ache.

Consequences:

- Difficult to concentrate when in pain.
- Although Aida really wants to go to school, she is increasingly staying at home as she cannot manage.
- "Jojo behavior" – some days she keeps active and works out, while other days she is completely exhausted.

Pain behavior:

- Wants a "quick fix" and prefers to continue pushing rather than taking a step back and think.
- Exercises to get in better shape to handle the pain.
- Keeps on going to alleviate anxiety despite feeling the need to rest.

Attitude to treatment:

- Wants to be a "good patient" and do everything she is told (and then some).
- Happy to visit doctors but does not see herself as someone who needs mental health support or treatment.

Employment:

N/A, high school student.

Education:

Primary school
Ongoing high school education.

Family:

Mother and father with foreign background, four younger siblings.

Background and social context:

Born in Pakistan, moved to Sweden when she was four years old. Leads an active life with hobbies and after-school activities. Frequently works out at the gym, pushing herself.

Aida has many friends and it is important for her to be popular. She is ambitious in school with high demands from her home-environment. She often feels stressed and does not think she is performing as expected. Aida carries a lot of responsibility at home. She has a high level of technological literacy and uses her smartphone for everything.

Social support (related to pain): Despite her family and many friends, Aida feels lonely in her pain. She feels that no one understands or takes it seriously. Her parents are constantly nagging, stressing that the health services should be able to help. Aida finds it strange that she is in so much pain even though she works out a lot and does everything she is "supposed to". Despite her efforts, there are days when she is paralyzed by pain and the feeling of being under pressure.

City/countryside: Apartment in large city.

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

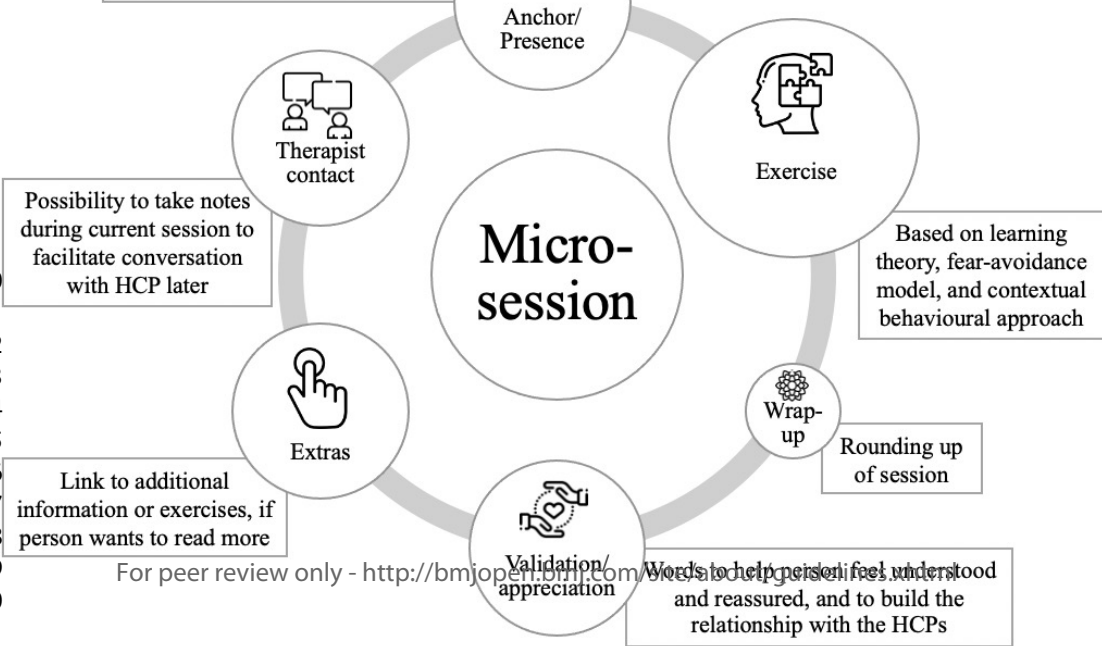


AIDA
18 yrs. old

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A question/ sentence to connect to the person's current situation, needs, wishes, or issues; supporting relevance and reliability of session

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4 self-guided **micro-sessions** per week inspired by process-based therapy approaches



Aware

Chat function to contact health care professional



Digital diary twice daily to promote self-monitoring



Living well with chronic pain

After 6-week intervention period, **booster-sessions** after 2 and 4 months for long-term support



Accepting/ Open



Active





Key Partners
(8) Describes the network of suppliers and partners that make the business model work, e.g.:

- Optimization and economy of scale
- Reduction of risks and uncertainty
- Acquisition of particular resources and activities

➤ *Soft ware partners*
➤ *Health care*

Key Activities

(7) Describes the most important things a company must do to make its business model work, e.g.:

- Production
- Problem solving
- Platform/ Network

➤ *Developing content*
➤ *IT support and development*

Key Resources

(6) Describes the most important assets required to make a business model work, e.g.:

- Physical
- Intellectual
- Human
- Financial

➤ *IT upkeep*

Value Propositions

(2) Describes the bundle of products and services that create value for a specific customer segment, e.g.:

- Newness
- Performance
- Customisation
- "Getting the job done" Design
- Brand/Status
- Price
- Cost reduction
- Risk reduction
- Accessibility
- Convenience/Usability

➤ *Usable, effective, evidence-based treatment*
➤ *Accessible and free for patients*

Customer Relationships

(4) Describes the types of relationships a company establishes with specific customer segments, e.g.:

- Personal assistance
- Self-service
- Automated services
- Communities
- Co-creation

➤ *Personal assistance*
➤ *Co-creation*

Channels

(3) Describes how a company communicates with and reaches its customer segments to deliver a value proposition (direct/indirect), e.g.:

- Sales Force
- Web sale
- Own stores
- Partner stores
- Wholesaler

➤ *Information on 1177*

Customer Segments

(1) Defines the different groups of people or organizations an enterprise aims to reach and serve. e.g.:

- Mass market
- Niche market
- Segmented
- Diversified
- Multi-sided platforms (multi-sided markets)

➤ *Patients with chronic pain*
➤ *Health care organisations*

Cost Structure

(9) Describes all costs incurred to operate a business model, e.g.:

- Cost-driven
- Value-driven
- Fixed costs
- Variable costs
- Economies of scale
- Economies of scope

➤ *Platform and content development/upkeep*

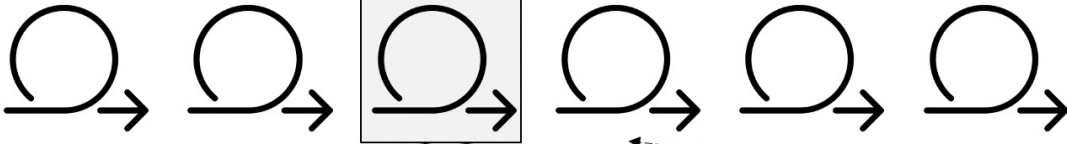
Revenue Streams

(5) Represents the cash a company generates from each customer segment (costs must be subtracted from revenues to create earnings), e.g.:

- Asset sale
- Usage fee
- Subscription fees
- Licensing/ renting/ leasing
- Brokers fees
- Advertising

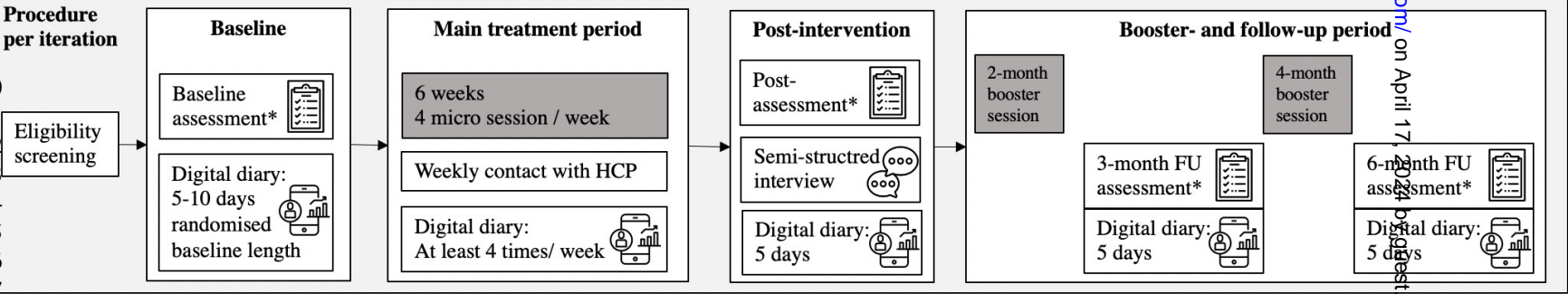
➤ *Free for patients*
➤ *Licensing for regions*

4-6 iterations with each n=10 patients and their treating HCP

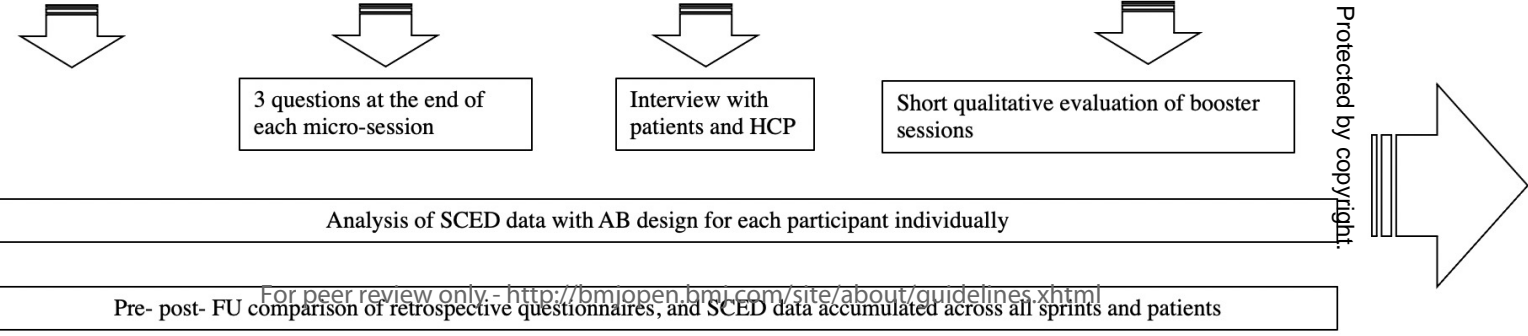


Overall outcome: Prototype 2.0

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- Objectives**
- Feasibility/ acceptability
 - Individual change processes
 - Efficacy



*Retrospective self-reports including process-, primary- and secondary outcome measures

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Appendix 1:

Semi-structured focus group guide

6-8 participants per focus group

FOR PATIENTS (2 focus groups; heterogenic in terms of age, gender, pain condition, pain history, etc.):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Living with chronic pain** (30min.)

It would be amazing to have a magic pill to just take all the pain away, so you could live without it. But unfortunately, we don't have that magic pill. Instead, we want to help you and other people with chronic pain to find a way to live well with the pain. (*Presentation on definition of health (Huber et al., 2011): ability to adapt and self-manage physical, mental and social aspects of health, and examples*).

 - a. Based on this definition of health, can you describe your own health needs? Which (aspects of your) needs are currently unmet?
 - b. In which moments of your life do you feel happiest/ most engaged/ most satisfied?
 - c. What helps you to engage in these 'happy moments'?
 - d. What are barriers to engage in these 'happy moments'?
 - e. What would you need to engage in these moments more often?

BREAK 10 Min.

4. Core question 2: **The DAHLIA treatment**

Presentation of the proposed treatment, aim, design, theoretical background, and examples of exercises (10min); following a discussion (30min)

 - a. What do you think of this treatment? What do you like, what do you dislike? (Please reflect on (1) design, (2) set-up, (3) content, (4) other (e.g., terminology: treatment, intervention, program; patient vs. person))
 - b. How feasible would it be to do this treatment?
 - c. Do you think this treatment meets you needs?
 - d. Is there anything else you would like to add?

FOR HEALTH CARE PROFESSIONALS (1 focus group, psychologists/ psychotherapists trained in cognitive-behavioural therapy; heterogenic in terms of age, gender, cultural background):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Supporting people with chronic pain** (30min)

People with chronic pain have complex needs and treatment has to meet these needs. We are interested in your experiences in what works well to improve

1
2
3 the overall health and well-being of patients with chronic pain. (*Presentation*
4 *on definition of health (Huber et al., 2011): ability to adapt and self-manage*
5 *physical, mental and social aspects of health, and examples*).

- 6
7 a. Which (aspects of) your patient's health needs are unmet? What is
8 needed to support chronic pain patients in the best way?
9
10 b. What barriers and facilitators to deliver support to chronic pain patients
11 do you face? Please reflect on elements related to the patient, treatment
12 options, and the health care in general.

13
14 BREAK 10 Min.

15
16 4. Core question 2: **The DAHLIA treatment**

17 Presentation of the proposed treatment, aim, design, theoretical background,
18 and examples of exercises (10min); following a discussion (30min)

- 19 a. What do you think of this treatment? What do you like, what do you
20 not like? (Please reflect on (1) design, (2) set-up, (3) content, (4) other
21 (e.g., terminology: treatment, intervention, program; patient vs.
22 person))
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24 b. How feasible would it be for you to deliver this treatment?
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26 c. Does the treatment meet the needs of the patients with chronic pain?
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28 d. Is there anything else you would like to add?
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Appendix 2. Baseline interviews with stakeholders

Various stakeholders will be approached, including developers, health care professionals, and managers. Through snow-ball sampling, other potential stakeholders will be identified and approached (e.g., individuals from policy making or municipality representatives).

Stakeholder: developers

I. General

Theme: Experience and development of digital interventions within the 1177 web-platform

1. What is your job description and what are your responsibilities?
2. How is the 1177 web-platform structured, in the region of Kalmar and Sweden?
3. How many digital interventions are available within 1177 in your region?
4. Who developed these interventions; who integrated them in the platform?
5. How are these interventions financed?
6. Who is responsible/ involved in the maintenance of the interventions?
7. If/ how is the interventions' content updated?
8. If/ how are the interventions used and promoted in health care?
9. If/how is user satisfaction with interventions evaluated?
10. If/how do collaborations with other regions look like?

II. Specifics (focus about DAHLIA project)

1. How would you describe the anticipated implementation process of this intervention?
2. What is needed to support the implementation process?
3. What could facilitate the implementation process?
4. What could hinder the implementation process?
5. What are benefits for you/ the 1177 web-platform when developing this intervention?
6. Are you enthusiastic about this intervention, if so, why?
7. Do you think this intervention has the potential to be successful in your region, and Sweden?
8. Where would you like to see this intervention in 5 years?

Stakeholder: health care professionals

I. General

Theme: Experience and use of digital interventions with patients

1. What is your job description and what are your responsibilities?
2. What is your experience in delivering interventions via the 1177 web-platform?
3. If/when there is a new intervention available in the 1177 web-platform, how do you usually hear about it?
4. What makes it attractive to deliver such an intervention?
5. What resources are needed for you to deliver these interventions (e.g., time, knowledge, managerial support)?
6. What hinders you to deliver these interventions?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What benefits for yourself/your work do you anticipate through this intervention?
3. What benefits for your patients do you anticipate?
4. What disadvantages or problems do you anticipate when delivering this intervention?

5. What disadvantages or problems for your patients when receiving the intervention do you anticipate?
6. What would hinder you to deliver this intervention?
7. What would facilitate you to deliver this intervention?
8. Are you enthusiastic about this intervention, if so, why?
9. Do you think this intervention has the potential to be successful in your care facility?
10. Where would you like to see this intervention in 5 years?

Stakeholder: health care managers

Theme: Experience and promotion of digital interventions in care facility

1. What is your job description and what are your responsibilities?
2. How many digital interventions are currently offered by the 1177 web-platform (and used) in your care facility?
3. What is needed to implement an intervention from the 1177 web-platform in your care facility?
4. How do digital interventions get financed in your care facility?
5. What is your involvement in digital interventions in your care facility? How do you support the use of digital interventions?
6. What hinders the implementation of these interventions, in your eyes?
7. If/ how does your care facility collaborate with other regions regarding digital interventions from the 1177 web-platform?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What kind of benefits do you anticipate for employees through this intervention?
3. What kind of benefits do you anticipate for patients through this intervention?
4. What kind of disadvantages or problems for employees do you anticipate through this intervention?
5. What kind of disadvantages or problems for patients do you anticipate through this intervention?
6. Are you enthusiastic about this intervention, and if so, why?
7. How will you promote this intervention in your care facility?
8. Do you think this intervention has the potential to be successful in your care facility?
9. Where would you like to see this intervention in 5 years?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Appendix 3. Feasibility/ acceptability; questionnaire.

Table 1. Semi-structured interview guide to evaluate the general feasibility and acceptability of the treatment.

Topics	Questions	Answering scores	Open question
You recently completed the 6-week treatment. For us, it is very important to hear how you experienced it so that we can improve the content, design, and other aspects further. Thank you for taking the time to provide us with your input. First, we would like to ask you to reflect on and rate the past weeks and treatment in general.			
General	Were the past 6 weeks usual weeks for you?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did special events occur?		
	Were you able to read the text in the treatment well?		
	Was the text understandable?		
	Did the intervention hinder your daily occupations?		
	Did technical issues occur?		
Would you recommend this treatment to a friend?			
Secondly, we would like to ask you to reflect on and rate the four short sessions that were offered each week.			
Micro-sessions	Did you like doing the sessions?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Were the sessions difficult or unclear?		
	Did you experience the sessions as helpful?		
	Have the sessions influenced your behavior?		
	Have the sessions influenced your emotions?		
	Have the sessions influenced your thoughts?		
	Did you experience the sessions as time consuming?		
Did you experience the sessions as boring?			
Third, we would like to ask you to reflect and rate the messenger function with which you could communicate with your health care professional.			
Messenger function/ health care professional	Was the messenger function overall helpful?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did you experience the weekly messages sent by your health care professional as motivating?		
	Did you feel supported by your health care professional?		
Fourth, we would like to ask you to reflect on and rate the daily diary .			
Digital diary	Did you experience the daily diaries as burdensome?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Was it enjoyable to complete the digital diary?		
	Did you become more aware of your thoughts using the digital diary?		
	Did you become more aware of your behavior using the digital diary?		
	Did you become more aware of your emotions using the digital diary?		
Is there anything else you would like to add?			Free text

Appendix 4: Follow-up interviews with stakeholders

The stakeholders from the baseline assessment will be approached again. Furthermore, through snow-ball sampling, potential new stakeholders will be identified and also approached.

Stakeholder: developers

Process so far:

1. When reflecting on the overall development, evaluation, and implementation process, what went well?
2. When reflecting on the overall development, evaluation, and implementation process, what did not go well?
3. What factors supported the process of bringing this intervention into practice?
4. What factors hindered the process of bringing this intervention into practice?
5. What kind and how much resources were needed?
6. Did the process go as anticipated? If not, what was surprising?
7. How satisfied are you with the process so far?
8. What was most challenging during the implementation process?

Current use:

1. What are you currently doing to keep the intervention implemented?
2. Do you have sufficient resources? Please elaborate.
3. What issues are you currently facing? What solutions for these issues do you have?

Prospective adjustments:

1. What will the prospective maintenance and upkeep look like?
2. Who is responsible for that?
3. If there should be a change in employment, who ensures that the intervention remains updated?

Stakeholder: health care professionals

Process so far:

1. How often did you deliver the digital intervention?
2. What kind of benefits for yourself, your work, and/or your patients did you experience?
3. What kind of disadvantages for yourself, your work, and/or your patients did you experience?
4. What kind of support for delivering the intervention (e.g., training, technical guidance when issues arose) did you receive?
5. What hindered you in delivering the intervention?
6. What facilitated you to deliver the intervention?

Current use:

1. How satisfied are you with the intervention overall?
2. Which elements of the intervention need improvement?

Prospective adjustments:

1. Do you plan on delivering the intervention in the future? If not, please elaborate.
2. Would you recommend the intervention to a colleague?
3. What kind of problems do you anticipate in the future; and do you have potential solutions for them?

Stakeholder: health care managers

Process so far:

1. How would you describe your involvement in implementing the intervention?
2. How many resources were needed for the implementation?
3. Did the implementation process go as expected? If not, what was surprising?
4. How did you support your employees to deliver the intervention?

Current use:

1. How satisfied are you currently with the intervention (e.g., reflecting on use, content, promotion, required resources, (technical) issues)?
2. What aspects of the current implementation/ practical use need improvements?

Prospective adjustments:

1. Do you plan to offer the intervention in your region in the future? Please elaborate.
2. Would you recommend this intervention to another region/ other health care organizations? Please elaborate.
3. What kind of problems do you anticipate in the future?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,3
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	28
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1,28
Roles and	#5b	Name and contact information for the trial sponsor	1

responsibilities:

1 sponsor contact
2 information

3 Roles and

4 responsibilities:

5 sponsor and funder

[#5c](#)

6 Role of study sponsor and funders, if any, in study design;
7 collection, management, analysis, and interpretation of data;
8 writing of the report; and the decision to submit the report for
9 publication, including whether they will have ultimate
10 authority over any of these activities

n/a

11 Roles and

12 responsibilities:

13 committees

[#5d](#)

14 Composition, roles, and responsibilities of the coordinating
15 centre, steering committee, endpoint adjudication committee,
16 data management team, and other individuals or groups
17 overseeing the trial, if applicable (see Item 21a for data
18 monitoring committee)

8

21 Introduction

22 Background and

23 rationale

[#6a](#)

24 Description of research question and justification for
25 undertaking the trial, including summary of relevant studies
26 (published and unpublished) examining benefits and harms for
27 each intervention

5-7

28 Background and

29 rationale: choice of

30 comparators

[#6b](#)

31 Explanation for choice of comparators

n/a

32 Objectives

[#7](#)

33 Specific objectives or hypotheses

6-8

34 Trial design

[#8](#)

35 Description of trial design including type of trial (eg, parallel
36 group, crossover, factorial, single group), allocation ratio, and
37 framework (eg, superiority, equivalence, non-inferiority,
38 exploratory)

8, Fig. 2

39 Methods:

40 **Participants,**

41 **interventions, and**

42 **outcomes**

43 Study setting

[#9](#)

44 Description of study settings (eg, community clinic, academic
45 hospital) and list of countries where data will be collected.
46 Reference to where list of study sites can be obtained

11,12

47 Eligibility criteria

[#10](#)

48 Inclusion and exclusion criteria for participants. If applicable,

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		eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	
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4	Interventions:	#11a Interventions for each group with sufficient detail to allow	9-11, Fig 4,
5	description	replication, including how and when they will be administered	Fig 5
6			
7			
8	Interventions:	#11b Criteria for discontinuing or modifying allocated interventions	12, 14,15
9	modifications	for a given trial participant (eg, drug dose change in response	
10		to harms, participant request, or improving / worsening	
11		disease)	
12			
13			
14	Interventions:	#11c Strategies to improve adherence to intervention protocols, and	15
15	adherence	any procedures for monitoring adherence (eg, drug tablet	
16		return; laboratory tests)	
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19			
20	Interventions:	#11d Relevant concomitant care and interventions that are permitted	11
21	concomitant care	or prohibited during the trial	
22			
23			
24	Outcomes	#12 Primary, secondary, and other outcomes, including the specific	Fig 7, Tab 2,
25		measurement variable (eg, systolic blood pressure), analysis	Tab 3, and
26		metric (eg, change from baseline, final value, time to event),	related
27		method of aggregation (eg, median, proportion), and time	sections
28		point for each outcome. Explanation of the clinical relevance	
29		of chosen efficacy and harm outcomes is strongly	
30		recommended	
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34			
35	Participant timeline	#13 Time schedule of enrolment, interventions (including any run-	14, Fig 7
36		ins and washouts), assessments, and visits for participants. A	
37		schematic diagram is highly recommended (see Figure)	
38			
39			
40	Sample size	#14 Estimated number of participants needed to achieve study	12, 13, 14, 21
41		objectives and how it was determined, including clinical and	
42		statistical assumptions supporting any sample size calculations	
43			
44			
45			
46	Recruitment	#15 Strategies for achieving adequate participant enrolment to	11,12
47		reach target sample size	
48			
49			
50	Methods:		
51	Assignment of		
52	interventions (for		
53	controlled trials)		
54			
55			
56	Allocation: sequence	#16a Method of generating the allocation sequence (eg, computer-	21, Tabl. 1
57	generation	generated random numbers), and list of any factors for	
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stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions

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7	Allocation	#16b	Mechanism of implementing the allocation sequence (eg, 21, Fig 7
8	concealment		central telephone; sequentially numbered, opaque, sealed
9	mechanism		envelopes), describing any steps to conceal the sequence until
10			interventions are assigned
11			
12			
13			
14	Allocation:	#16c	Who will generate the allocation sequence, who will enrol 14, 21
15	implementation		participants, and who will assign participants to interventions
16			
17	Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial n/a (Tab 1)
18			participants, care providers, outcome assessors, data analysts),
19			and how
20			
21			
22			
23	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is n/a
24	emergency unblinding		permissible, and procedure for revealing a participant's
25			allocated intervention during the trial
26			
27			
28	Methods: Data		
29	collection,		
30	management, and		
31	analysis		
32			
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35	Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and Described for
36			other trial data, including any related processes to promote each sub-
37			data quality (eg, duplicate measurements, training of study
38			assessors) and a description of study instruments (eg,
39			questionnaires, laboratory tests) along with their reliability and
40			validity, if known. Reference to where data collection forms
41			can be found, if not in the protocol
42			
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46	Data collection plan:	#18b	Plans to promote participant retention and complete follow-up, n/a
47	retention		including list of any outcome data to be collected for
48			participants who discontinue or deviate from intervention
49			protocols
50			
51			
52			
53	Data management	#19	Plans for data entry, coding, security, and storage, including 26, 28
54			any related processes to promote data quality (eg, double data
55			entry; range checks for data values). Reference to where
56			details of data management procedures can be found, if not in
57			
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		the protocol	
1			
2	Statistics: outcomes	#20a Statistical methods for analysing primary and secondary	Tab 1, 19-21
3		outcomes. Reference to where other details of the statistical	
4		analysis plan can be found, if not in the protocol	
5			
6			
7			
8	Statistics: additional	#20b Methods for any additional analyses (eg, subgroup and	12-14, 21, 22,
9	analyses	adjusted analyses)	
10			
11	Statistics: analysis	#20c Definition of analysis population relating to protocol non-	19, 20
12	population and	adherence (eg, as randomised analysis), and any statistical	
13	missing data	methods to handle missing data (eg, multiple imputation)	
14			
15			
16			
17	Methods: Monitoring		
18			
19	Data monitoring:	#21a Composition of data monitoring committee (DMC); summary	28
20	formal committee	of its role and reporting structure; statement of whether it is	
21		independent from the sponsor and competing interests; and	
22		reference to where further details about its charter can be	
23		found, if not in the protocol. Alternatively, an explanation of	
24		why a DMC is not needed	
25			
26			
27			
28			
29	Data monitoring:	#21b Description of any interim analyses and stopping guidelines,	n/a
30	interim analysis	including who will have access to these interim results and	
31		make the final decision to terminate the trial	
32			
33			
34	Harms	#22 Plans for collecting, assessing, reporting, and managing	20-21 (NEQ)
35		solicited and spontaneously reported adverse events and other	
36		unintended effects of trial interventions or trial conduct	
37			
38			
39			
40	Auditing	#23 Frequency and procedures for auditing trial conduct, if any,	n/a
41		and whether the process will be independent from	
42		investigators and the sponsor	
43			
44			
45	Ethics and		
46	dissemination		
47			
48			
49	Research ethics	#24 Plans for seeking research ethics committee / institutional	3, 27
50	approval	review board (REC / IRB) approval	
51			
52			
53	Protocol amendments	#25 Plans for communicating important protocol modifications	27
54		(eg, changes to eligibility criteria, outcomes, analyses) to	
55		relevant parties (eg, investigators, REC / IRBs, trial	
56		participants, trial registries, journals, regulators)	
57			
58			
59			

1	Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11-12, 27
2				
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4				
5				
6	Consent or assent:	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7	ancillary studies			
8				
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10				
11	Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	27, 28
12				
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16				
17	Declaration of	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	28
18	interests			
19				
20				
21	Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
22				
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24				
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26	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
27	trial care			
28				
29				
30	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	27
31	trial results			
32				
33				
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37				
38	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
39	authorship			
40				
41				
42	Dissemination policy:	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	28
43	reproducible research			
44				
45				
46	Appendices			
47				
48	Informed consent	#32	Model consent form and other related documentation given to participants and authorised surrogates	28
49	materials			
50				
51				
52	Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
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2 Attribution License CC-BY-NC. This checklist can be completed online using <https://www.goodreports.org/>, a
3 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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BMJ Open

Development, evaluation, and implementation of a digital behavioural health treatment for chronic pain: Study protocol of the multi-phase DAHLIA project

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1 **Title: Development, evaluation, and implementation of a digital behavioural**
2 **health treatment for chronic pain: Study protocol of the multi-phase**
3 **DAHLIA project**

4
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37 Institutet Protocol Record Dnr 2021-02437.

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39 **Version of Protocol:** 2 (07.03.2022)

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4 40 Development, evaluation, and implementation of a digital behavioural health
5 41 treatment for chronic pain: Study protocol of the multi-phase DAHLIA project
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7 42

8
9 43 **ABSTRACT**

10 44 **Introduction:** Chronic pain affects about 20-40% of the population and is linked to mental
11 45 health outcomes and impaired daily functioning. Pharmacological interventions are commonly
12 46 insufficient for producing relief and recovery of functioning. Behavioural health treatment is
13 47 key to generate lasting benefits across outcome domains. However, most people with chronic
14 48 pain cannot easily access evidence-based behavioural interventions. The overall aim of the
15 49 DAHLIA project is to develop, evaluate, and implement a widely accessible digital behavioural
16 50 health treatment to improve well-being in individuals with chronic pain.

17 51 **Methods and analysis:** The project follows the four phases of the mHealth Agile Development
18 52 and Evaluation Lifecycle: (i) *development and pre-implementation surveillance* using focus
19 53 groups, stakeholder interviews, and a business model; (ii) iterative *optimisation studies*
20 54 applying single case experimental design (SCED) method in 4-6 iterations with n=10 patients
21 55 and their health care professionals per iteration; (iii) a two-armed *clinical randomized*
22 56 *controlled trial* enhanced with SCED (n=180 patients per arm); (iv) and interview-based *post-*
23 57 *market surveillance*. Data analyses include multilevel modelling, cost-utility, and indicative
24 58 analyses.

25 59 In October 2021, inter-sectorial partners are engaged and funding is secured for four years. The
26 60 treatment content is compiled and the first treatment prototype is in preparation. Clinical sites
27 61 in three Swedish regions are informed and recruitment for phase one will start in autumn 2021.
28 62 To facilitate long-term impact and accessibility, the treatment will be integrated into a Swedish
29 63 health platform (www.1177.se), which is used on a national level as a hub for advice,
30 64 information, guidance, and e-services for health and healthcare.

31 65 **Ethics and dissemination:** The study plan has been reviewed and approved by Swedish
32 66 Ethical Review Authorities. Findings will be actively disseminated through peer-reviewed
33 67 journals, conference presentations, social media, and outreach activities for the wider public.

34 68 **Trial Registration number:** ClinicalTrials.gov Identifier: NCT05066087; Karolinska
35 69 Institutet Protocol Record Dnr 2021-02437.

36 70 **Keywords:** chronic pain; digital; behavioral health; protocol; intervention; single case
37 71 experimental design; diary; implementation; randomized controlled trial
38 72

73 **Strength and limitations of the study**

- 74 • An agile, iterative, and data-driven process is ideally suited to navigate the complex
75 challenges faced during the development, evaluation, and implementation of a digital
76 behavioural treatment.
- 77 • Executing the project with a multi-disciplinary, inter-sectorial, and international team
78 brings expertise and insights from complementary views together.
- 79 • Patients and different stakeholders, such as health care professionals, managers and
80 digital developers, are involved in the project from the start, thus ensuring that
81 individual needs to use and/ or promote the treatment can be met.
- 82 • The richness of methodologies combining traditional clinical trial evaluations on the
83 population level, fine-graded momentary data collection on the individual level, explicit
84 focus on cost-effectiveness, and determinants of implementation allows for a treatment
85 evaluation from all angles.
- 86 • Due to the complexity and step-wise approach of this project, problems (e.g., delays in
87 recruitment) in earlier phases might negatively affect the execution of later phases, thus
88 calling for mitigation strategies to address potential delays.

89 INTRODUCTION

90 Chronic pain (CP) affects 20 to 40 % of the adult population¹. Due to the COVID-19 pandemic,
91 prevalence rates may increase further since CP can develop as a post-viral syndrome, from
92 insufficient risk factor management during lockdown (e.g., inactivity, stress), or from
93 accumulated unmet rehabilitation needs in overburdened rehab services^{2 3}. Chronic pain
94 impacts not only individuals' daily activities and overall quality of life, but also social and
95 working contexts⁴. Thus, considerable direct and indirect health-related costs are associated
96 with CP⁵ and it represents a major issue for health care services and society at large.

97 A consensus exists regarding the importance of a holistic perspective integrating social,
98 psychological, and biological factors of CP to accommodate this condition and its implications,
99 and to guide interventions aimed at providing support⁶. Considering the typical complexity of
100 CP, pharmacological treatment alone is usually insufficient in producing sustained relief and
101 recovery of functioning⁷. Instead, management plans should target key behavioural, emotional,
102 cognitive, and social factors in everyday functioning and quality of life⁸.

103 To generate general and lasting benefits across outcome domains, person-centred,
104 behavioural health interventions are critical. The necessity to match the pain treatment with
105 specific needs of each patient has been the focus of discussion for the past decades⁹. Existing
106 evidence supports methods that stem from cognitive behavioural frameworks¹⁰, including the
107 fear-avoidance model of pain and disability¹¹ and the psychological flexibility model, the
108 model underlying acceptance and commitment therapy (ACT)^{12 13}. In this type of treatment,
109 the objective is to optimize effects by individualising treatment through evidence-based
110 therapeutic procedures¹⁴. In clinical practice, face-to-face therapy dominates in effectively
111 promoting well-being in patients with CP^{7 15}. Modes of treatment delivery are evolving,
112 however, as new models of care emerge.

113 Until now and despite the empirical support, interdisciplinary treatment, including
114 behavioural interventions, are commonly not available or difficult to access for most
115 individuals with CP^{16 17}. Digital solutions aiming at promoting health, also known as eHealth,
116 appear promising to bridge this gap as they appear cost-effective, can be tailored to individual
117 needs, applied in everyday life, and used at the patients' convenience¹⁸. Particularly in light of
118 the COVID-19 pandemic, distance approaches are gaining more attention in the management
119 of CP¹⁹. However, the development and implementation of evidence-based digital
120 interventions face challenges.

1
2
3 121 Innovative digital treatments require an accurate scientific evaluation to ensure clinical
4
5 122 effectiveness. As it is still seen as the “gold standard”, digital interventions for CP are often
6
7 123 assessed through research-led randomized controlled trials (RCTs)^{18 20 21}. However, a call for
8
9 124 real-world and n-of-1 evaluations of efficacy and safety of individual assessment and treatment
10
11 125 approaches is also being heard²². Compared to RCTs, n-of-1 study designs utilise repeated
12
13 126 measurements to provide a more fine-graded, time- and context-sensitive picture of individual
14
15 127 trajectories and pattern, thus allowing to evaluate effects at the within-person level²³.

16
17 128 Moreover, it has been shown that eHealth innovations purely originated from an
18
19 129 academic context are rarely sustainably implemented into health care practice due to a lack of
20
21 130 infrastructure, funding, and time²⁴. To avoid research waste when creating new eHealth
22
23 131 solutions, a strong user-centred design and focus on implementation is suggested^{25 26}. A
24
25 132 framework that combines the scientific rigor of traditional research methods with a rapid and
26
27 133 iterative digital product development approach is needed. Then, the development of an
28
29 134 evidence-based and user-friendly digital behavioural treatment is facilitated that is
30
31 135 implementation-ready for applied health care.

32
33 136 The ‘mHealth agile development and evaluation lifecycle’ (Figure 1) is a framework
34
35 137 created to promote the development of evidence-based, effective, and sustainable digital
36
37 138 solutions²⁷. This framework emphasises practicality, flexibility, rapid evaluation, and the
38
39 139 possibility to adjust protocols to meet technological changes and insights that emerge as part
40
41 140 of the process. Therefore, Wilson, et al. ²⁷’s framework will guide the present project.
42
43 141 Additionally, the Medical Research Council guidance for developing and evaluating complex
44
45 142 interventions will inform the processes^{26 28}. By applying these perspectives, the ultimate goal
46
47 143 to develop, evaluate, and implement an effective and accessible behavioural treatment will be
48
49 144 reached, thus improving health in individuals with CP across Sweden.

50
51 145 --- FIGURE 1 NEAR HERE---

52 146 **Research objectives**

53
54 147 The overall aim of this project is to develop, evaluate, and implement a digital behavioural
55
56 148 health treatment to improve well-being in individuals with CP. The treatment will be integrated
57
58 149 into a nationally available health care web-platform, which facilitates large scale evaluations,
59
60 150 further development, dissemination, and long-term use in clinical practice across Sweden.
151
152 151 Within the project, we will (i) develop a prototype of the digital treatment matching the needs
153
154 152 of individuals with CP, using focus groups to assess user demands, and discuss possible
155
156 153 treatment structures and content, (ii) pilot the treatment in several iterations to evaluate its

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3 154 feasibility and acceptability, efficacy, and individual change processes by combining intensive
4
5 155 (Single case experimental design (SCED)) and extensive methods; (iii) conduct a two-armed
6
7 156 RCT enhanced with SCED to assess the clinical effectiveness, cost-effectiveness, and long-
8
9 157 term effects compared to treatment as usual (TAU) on a between- and within-person level; and
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11 158 (iv) identify barriers and facilitators, and monitor the implementation process of the treatment,
12
13 159 through a business model and stakeholder interviews.
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160 **METHODS AND ANALYSIS**

161 Following the mHealth agile lifecycle²⁷, the DAHLIA (Acronym: Digital behaviourAI HeaLth
162 for chronIc pAin) project consists of an identification phase 0 and four main phases:
163 Development, optimisation, clinical trial evaluation, and post-market surveillance (See
164 overview of the DAHLIA project in Figure 2). Phase 1 includes two studies: focus groups with
165 patients and health care professionals (HCPs) to develop the treatment prototype (Study 1), and
166 stakeholder interviews to prepare for the implementation process by creating a business model
167 and identifying of barriers and facilitators (Study 2). Phase 2 (Optimisation) aims at optimising
168 the treatment and entails 4-6 iterations to test and gradually improve the prototype in a data-
169 driven manner (Study 3). Phase 3 consists of a large-scale clinical trial to evaluate the digital
170 treatment in comparison to TAU in a two-armed RCT enhanced with SCED (Study 4). Finally
171 in phase 4, a post-market surveillance is conducted using interviews with stakeholders from
172 different Swedish regions, also presenting lessons-learned (Study 5). Each phase may inform
173 and alter subsequent phases, in line with the agile approach. Details of the studies are described
174 in the following paragraphs.

175 --- FIGURE 2 NEAR HERE ---

176 **Project Identification**

177 **Involvement of inter-sectorial partners and international collaborators**

178 This project is a collaboration between academia, health care, and industry. The academic
179 partners come from seven universities in four countries (Sweden, Belgium, the Netherlands,
180 and the U.S.). The researchers contribute to the project with their scientific and clinical
181 experience in developing and evaluating digital treatments, implementation sciences, cost-
182 utilisation analysis, CP and related health issues, and the SCED method. The DAHLIA
183 treatment will be designed within the www.1177.se platform in collaboration with health care
184 developers and digital designers in Region Kalmar and supported by the industry partner Inera,
185 who is responsible for the maintenance of the platform. The health care partners currently
186 represent three of the 21 regions in Sweden, and include primary care centres in Region
187 Kalmar, the Pain Clinic at Capio St. Göran Hospital, Region Stockholm, and the Rehabilitation
188 centre in Region Örebro.

189 **Personas as early user research**

190 Personas are typical patient- or user-profiles illustrating the target group of a treatment or
191 product and can be useful in the development of digital interventions to communicate user

1
2
3 192 needs to the development team^{29 30}. By giving a narrative and name, personas facilitate a more
4
5 193 concrete discussion of patient needs, and to what extent the treatment might match those
6
7 194 needs³¹. In the DAHLIA project, three distinct patient personas evolved in an online workshop
8
9 195 and were edited over several months until the project partners were developed in a stepwise
10
11 196 manner. The personas originated from patient interviews in a previous study²⁹, and discussed
12
13 197 in an online workshop to assess the relevance for the DAHLIA project. The personas were then
14
15 198 adjusted based on factors identified in research³²⁻³⁴, other personas used in digital development
16
17 199 projects region Kalmar, and input from the clinical researchers (RW, IF, KB, LMcC, SP). The
18
19 200 personas were continuously edited over several months until the project partners agreed on the
20
21 201 final versions. The categories for each persona are: (i) *personal information*, including
22
23 202 employment, education, family, background and social context, social support, and living area;
24
25 203 (ii) *patient pain profile*, including pain problem, consequences, pain behaviour, and attitude to
26
27 204 treatment; (iii) *health care and treatment*, including contact with health care, comorbidities,
28
29 205 and medicine; and (iv) *personal needs and goals*, specifically related to the treatment. Figure
30
31 206 3 illustrates one of the personas used in the DAHLIA project.

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--- FIGURE 3 NEAR HERE ---

208 During the early development of the DAHLIA treatment prototype (version 1.0), and
209 prior to patient involvement, personas were used to ensure that relevant characteristics and
210 contextual factors were considered³⁵. The personas were presented at the start of treatment
211 workshops to discuss, for instance, if and how the treatment content and structure fit the
212 personas' characteristics and met their needs. Potential problems for a persona in relation to
213 treatment elements were identified, resulting in further discussions and consensus-based
214 adjustments.

215 **Guiding principles in the development process of the DAHLIA treatment**

216 When developing and evaluating complex interventions, one might either rely on already
217 existing treatments or adapt these to the context, or chose to build a new treatment based on
218 research evidence and theory of the problem²⁶. In the present project, the latter was chosen for
219 the following reasons. Firstly, the initiative for this project originated from the Swedish Region
220 Kalmar identifying the need for a digital treatment for chronic pain patients, which resulted in
221 a collaboration with the research team. Furthermore, contextual factors such as organisational
222 aspects, technical systems, and licencing agreements define the conditions for in this project.
223 Finally, by creating a new treatment together with stakeholders (i.e., managers, regional

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3 224 developers, therapists, patients) and building on an existing digital structure (www.1177.se),
4 225 the digital treatment can accommodate all identified requirements.

6 226 The following process was therefore followed to create the new treatment: Four three-
7
8 227 hour online workshops took place between June 2020 and June 2021 to discuss the theoretical
9
10 228 framework, conceptual model, and treatment components. Project partners presented their
11
12 229 previous work related to behavioural treatment approaches and conferred on the guiding
13
14 230 principles for the prototype development. The group reached consensus on using learning
15
16 231 theory³⁶ as the theoretical framework for assessment and treatment. Furthermore, it was agreed
17
18 232 that the fear-avoidance model¹¹ and psychological flexibility model^{10 14 37} should be used as
19
20 233 conceptual models for the DAHLIA treatment. Conclusively, the primary objective of the
21
22 234 treatment is to increase resilience to pain and distress by promoting and training behavioural
23
24 235 skills of relevance to the individual's functioning and well-being. Furthermore, a self-guided
25
26 236 micro-learning format³⁸ was chosen, including brief and frequent sessions (micro-sessions),
27
28 237 delivered digitally and accessible via a smartphone or desktop computer (www.1177.se; details
29
30 238 see 'Stakeholder interviews (Study 2)').

31 239 Based on the theoretical framework and conceptual models, values-oriented exposure
32
33 240 is considered to be the core procedure. Exposure implies the use of systematic contact with
34
35 241 negative experience such as pain and feelings of emotional distress that promotes avoidance,
36
37 242 in a way that reduces their adverse influence and produces more flexible, varied, and engaged
38
39 243 patterns of behaviour. Essentially, the function of exposure is to reduce negatively reinforced
40
41 244 behaviour focused on alleviating unwanted experiences, in favour of positively reinforced
42
43 245 behaviour focused on approaching goals in daily life. Exposure is enabled by several
44
45 246 behavioural processes, such as identifying life values and noticing own thoughts and emotions,
46
47 247 known as defusion (OPEN), flexible attention to the present (AWARE), and the building of
48
49 248 extended habits of engagement (ACTIVE)¹⁰.

50 249 At the end of Phase 0, the following is envisioned: The DAHLIA treatment will run
51
52 250 over six weeks and includes four self-guided micro-sessions per week. Each session will
53
54 251 include a set of key elements (see Figure 4). The extent to which each of these elements will
55
56 252 be included in the session can vary. It should be noted that due to the agile process, data-driven
57
58 253 decisions might result in changes to this suggested structure.

59 254 --- FIGURE 4 NEAR HERE---

60 255 A chat function will enable patients to connect with their health care professionals
61
62 256 (HCPs, see details section 'participants and recruitment') for additional guidance,
63
64 257 asynchronous feedback, and further instructions. The role of the HCP is to encourage and

1
2
3 258 motivate patients to remain in the program and intervene in case the individual situation
4
5 259 worsens. At the start of the treatment, a specific weekday will be agreed on, during which the
6
7 260 HCP replies to the patient's message. Potentially, the reply could also be a chat message, a
8
9 261 phone call, or a video call. The contact with the HCP will take place once a week, with a
10
11 262 minimum of six individual interactions between the HCP and patient. HCPs will receive
12
13 263 training, a manual, and supervision to provide the treatment.

14 264 Furthermore, patients will be prompted to fill in a pre-scheduled digital diary twice a
15
16 265 day. The digital diary has the purpose to enable self-monitoring for increased self-awareness
17
18 266 of own behaviours, emotions, and routines, and thus enhanced orientation towards values and
19
20 267 goals³⁹, and data collection to gain insight into the individual change processes and effects of
21
22 268 the treatment in the context of the SCED. The full list of the daily diary items can be found in
23
24 269 the 'Individual change processes' section.

25 270 After the main six-week intervention period, the treatment also entails booster-sessions
26
27 271 delivered through the www.1177.se web-platform after two and four months. The participants
28
29 272 get invited via SMS or emails to revisit the web-platform where they can engage in short
30
31 273 behavioural exercises. Booster sessions are suggested in other contexts to support long-term
32
33 274 behavioural changes⁴⁰ and reinforce patients learned coping strategies. Figure 5 summarises
34
35 275 the DAHLIA treatment components.

36
37 276 --- FIGURE 5 NEAR HERE ---

38 277 **Participants and recruitment**

39 278 In the DAHLIA project, participants will be people who either use or deliver the digital
40
41 279 treatment, or who facilitate the treatment implementation. Thus, study participants are (i)
42
43 280 patients with CP, (ii) HCPs treating patients with CP, (iii) health care managers, (iv) developers
44
45 281 of the www.1177.se web platform, (v) other stakeholders identified in the process (e.g., policy
46
47 282 makers, representatives from patient organisations). Health care professionals will be licensed
48
49 283 psychologists or psychotherapists trained in cognitive behavioural therapy. Health care
50
51 284 managers, developers, and other stakeholders need to be directly or indirectly connected with
52
53 285 the treatment (e.g., decision-making on an organisational level; technical support etc.), but no
54
55 286 other requirements apply.

56 287 Patients are eligible for inclusion if they: are older than 18 years of age; report a pain
57
58 288 duration of ≥ 3 months; are able to communicate in Swedish; and have access to a computer,
59
60 289 smartphone, and internet in their home environment. The exclusion criteria are: injury or illness
290 290 that require immediate assessment and treatment, or is expected to progress significantly during

1
2
3 291 the next 6 months; unstable medication (based on self-report: changes in medication during the
4
5 292 past 3 months or expected within the next 3 months that could influence well-being and
6
7 293 functioning substantially, such as opioids, anti-epileptic drugs, antidepressants); previous CBT
8
9 294 treatment (including ACT) during the past 6 months; severe psychiatric co-morbidity (for
10
11 295 instance, high risk of suicide). For study 1 (focus groups), only the exclusion criteria “severe
12
13 296 psychiatric co-morbidity (for instance, high risk of suicide) will be applied as long-term health
14
15 297 aspects are not expected to cause practical or ethical issues.

15 298 Information regarding the DAHLIA project and specific sub-studies will be provided
16
17 299 to the clinics, including detailed instructions for eligibility. Regions recruiting patients are
18
19 300 Kalmar, Stockholm, and Örebro. Additional regions have expressed interest in participating
20
21 301 and recruitment might be extended. Patients will be approached via their health care centres
22
23 302 and once patients have expressed interest in study participation, a formal eligibility check will
24
25 303 be conducted. Potential participants will be screened at their respective clinic via a face-to-face
26
27 304 or online meeting by their treating care professionals, including psychologist and pain
28
29 305 physicians. A short interview will be conducted to confirm eligibility and ensure that none of
30
31 306 the exclusion criteria are met. Informed consent is then obtained from all participants prior to
32
33 307 enrolment in the study. Sociodemographic and pain-descriptive information will be collected
34
35 308 from all participants including age, sex, level of education, occupation, location, level, and
36
37 309 duration of pain, pain diagnosis (if applicable), and approaches to relief pain (e.g., medication,
38
39 310 heat, physiotherapy).

311 **Phase 1: Development**

312 **Focus groups (Study 1)**

313 The aim of this study is to (i) identify the needs of patients and HCPs and (ii) match the
314 treatment content to their needs. At least three focus groups will be conducted in autumn 2021,
315 one with HCPs (i.e., psychologists/ psychotherapists trained in CBT) and two with patients.
316 Per focus group, 6-8 participants will join⁴¹. An attempt will be made to recruit a heterogeneous
317 group of patients in terms of such characteristics as pain condition, sex, and socio-economic
318 background. The focus groups will be held online and take 90-120 minutes. A semi-structured
319 guide inspired by Gruters, et al.⁴² will be followed. In addition to a general discussion around
320 health and individual needs at the start, the focus group leader (i.e., research assistant and
321 clinical coordinator) will ask participants to reflect on the design, set-up, content, and
322 prospective feasibility of the DAHLIA treatment (details see Appendix 1). The group

1
2
3 323 conversations will be audio- and video-taped. Field notes will provide further insight into
4
5 324 relevant cues and observations.

6 325 The recordings will be transcribed verbatim and the data analysis will be performed by
7
8 326 two independent researchers. The information for the patient groups and HCP group will be
9
10 327 analysed separately. A combination of inductive and deductive content analysis will be used.
11
12 328 First, the deductive approach will determine the themes emerging from the semi-structured
13
14 329 guide: (i) health needs and determinants to live well with CP, and (ii) feedback on the DAHLIA
15
16 330 treatment. Then, an indicative analysis will be performed to identify categories within the
17
18 331 themes. The transcript will be read carefully and open coding will be used. A consensus
19
20 332 meeting with a third researcher will be conducted as a final step. This approach has been
21
22 333 described previously and appears valid to answer the research question^{42 43}. The results from
23
24 334 the focus groups will be integrated into the treatment prototype (version 2.0).

25 335 **Stakeholder interviews (Study 2)**

26 336 The aim of this study is to develop a preliminary business model for the digital behavioural
27
28 337 treatment and identify barriers and facilitators of the prospective implementation process. An
29
30 338 explicit focus on implementation and economic aspects early during treatment development
31
32 339 has been recommended^{44 45}. Particularly, business modelling in the context of eHealth
33
34 340 technologies can help to create a set of success factors that will influence uptake, sustainability,
35
36 341 and effectiveness⁴⁶. A business model is part of the implementation strategy and also presented
37
38 342 a foundation for conversations with users and stakeholders regarding the value and purpose of
39
40 343 an eHealth technology⁴⁶. Moreover, to build the knowledge base across the multiple studies
41
42 344 and settings, the consolidated framework for implementation research (CFIR)⁴⁷ will be used.
43
44 345 The CFIR has five major domains: intervention characteristics, outer setting, inner setting,
45
46 346 characteristics of the individuals involved, and the process of implementation. It is utilized as
47
48 347 part of the analysis, as explained below.

49 348 As a first step, a preliminary version of the business model canvas was filled in by the
50
51 349 research team (SB, SJ, RW, HC). As suggested by Osterwalder and Pigneur⁴⁸ ‘a business
52
53 350 model describes the rationale of how an organization creates, delivers, and captures value’
54
55 351 (p.14) and demonstrates the logic of how a company or organisation intends to generate profit
56
57 352 for a service or product. The nine blocks of the business model cover four areas of a business:
58
59 353 customers, offers, infrastructure, and financial viability. Figure 6 presents the template of the
60
354 business model canvas and short definitions for each segment, including example aspects
355 relevant for the DAHLIA project.

1
2
3 356 --- FIGURE 6 NEAR HERE---

4
5 357 In the present study, the treatment will be integrated into the national public health care
6 website (www.1177.se), using the digital platform for behavioural health ('Stöd och
7 358 Behandling'). This digital platform is free from commercial interests, maintained by Inera,
8 359 which is owned by the county councils and regions. The general aim of this national website is
9 360 to increase access to healthcare, strengthen the position of the patient, and contribute to
10 361 improved public health. The website (www.1177.se) contains health care information,
11 362 inspiration, and e-services. Each of the 21 regions in Sweden is responsible for coordinating
12 363 activities and services provided on www.1177.se, which are conducted by own staff or
13 364 contracted providers. Through a national network, providers and regions can cooperate and
14 365 share licenses for services.
15 366

16 367 The business model will be discussed and refined as part of the stakeholder interviews.
17 368 Currently identified stakeholders are software developers, HCPs, and health care managers. A
18 369 semi-structured guide inspired by a previous study on eHealth implementation⁴⁹ will structure
19 370 the interviews and gather information on gatekeepers, barriers, and facilitators for prospective
20 371 dissemination and use. Questions are tailored to the different stakeholders and include, for
21 372 example, '*If/how is the interventions' content updated?*', '*Who is responsible/ involved in the*
22 373 *maintenance of the intervention?*', '*What could facilitate/ hinder the implementation process?*',
23 374 and '*Do you think this intervention has the potential to become successful in your care*
24 375 *facility?*'. The full guide can be seen in Appendix 2. As part of the agile process, the guide may
25 376 be adjusted based on information collected during the interviews and tailored to additional
26 377 stakeholders including policy makers or representatives from patient organisations.

27 378 A minimum of eight interviews will be conducted and snow-ball sampling will identify
28 379 additional participants that can inform the process. Interviews will be conducted until data
29 380 saturation is achieved and no new topics seem to emerge. The interviews will be executed
30 381 online, take 60-90 min, and the conversation will be recorded. The qualitative data will be
31 382 transcribed. Then, a qualitative thematic analysis will be performed⁵⁰ with statements related
32 383 to potential barriers and facilitators. An inductive approach to group the information will
33 384 applied in order to best scope the replies and map categories onto the CFIR domains⁴⁷ as
34 385 previously described.

35 386 Finally, implementation strategies matching the emerging topics will be formulated⁵¹.
36 387 Together with the business model, these two elements represent the implementation plan for
37 388 the DAHLIA project. Findings from this study may furthermore influence the post- market
38 389 surveillance (Study 5, see details below).

390 **Phase 2: Optimisation (Study 3)**

391 The aim of the optimisation phase is to pilot the treatment and improve it through an iterative
392 data-driven process using small patient cohorts. The primary objective is to determine the
393 treatment feasibility and acceptability, and the secondary objectives are to examine individual
394 change processes, and efficacy across iterations on a group-level. The general procedures
395 include the eligibility check, and four assessment periods: baseline, main treatment period,
396 post-intervention, and 3- and 6-months follow-ups. Results from each iteration will be
397 integrated into the subsequent iteration, then tested again, until satisfaction is reached and no
398 new major issues seem to emerge. In the optimisation studies, different methodologies will be
399 combined namely momentary data collection using digital diaries, retrospective questionnaires,
400 and semi-structured interviews. The latter will be conducted by a research assistant, while the
401 diaries and questionnaires will be completed online. Figure 7 provides an overview of the
402 procedure in relation to the research objectives.

403 --- FIGURE 7 NEAR HERE ----

404 In total, 40 to 60 patients and their treating HCPs will be included, with n=10 patient-
405 HCP dyads each iteration. Four iterations have been seen as sufficient in a previous study to
406 optimise a digital treatment⁵², therefore, a minimum of four iterations will be conducted in the
407 DAHLIA project. In accordance with the agile approach, additional iterations may be
408 performed if deemed necessary. The rationales for the approaches and methodological details
409 are described below.

410 **Feasibility and acceptability**

411 The mixed-method procedure to evaluate the feasibility and acceptability of the treatment
412 includes self-reports, interviews, and technical data. Short self-reports will be collected after
413 each micro- and booster-session. Specifically, patients will be asked to rate the micro-session
414 on its usefulness, enjoyment, and comprehension (*'I experienced today's session as helpful/
415 enjoyable/ understandable.'*, rated on a 7-point numerical scale from 1=not at all, to 7=very
416 much).

417 Furthermore, at the end of the main intervention period, interviews will be conducted
418 following a semi-structured guide to assess the participants' general experience and different
419 treatment components, specifically the diary, micro-sessions, and chat function. Questions are
420 first rated on a 7-point numeric scale and participants are then encouraged to elaborate on their
421 response with further details, if possible. Examples of questions are *'Did the intervention
422 hinder your daily occupation?'*, *'Were the micro-sessions difficult or unclear?'*, *'Did you*

1
2
3 423 *experience the digital diary as burdensome?*, or *‘Would you recommend the treatment to a*
4 *friend?’* (details see Appendix 3). This guide is based on other feasibility studies^{52 53} and
5 424 tailored to the DAHLIA treatment components. The HCPs will also be interviewed using a
6 425 guide that follows the same structure (i.e., numeric scale and open elaborations), but the
7 426 specific questions will be informed by the focus groups (study 1).
8
9 427

10 428 Additionally, technical data generated from the www.1177.se website will be collected.
11 429 These data include time and frequency of log-ins, duration of engagement with the treatment,
12 430 and use of components. Technical data will be used to describe the overall use and adherence,
13 431 and allows mediation analyses to determine the influence of engagement rates on treatment
14 432 outcomes.

15 433 Data from the feasibility assessments will be analysed using descriptive statistics and
16 434 qualitative synthesis to identify trends. The results will be presented reflecting the two core
17 435 variables from the Technology Acceptance Model (TAM): ‘Perceived Usefulness’ and
18 436 ‘Perceived Ease of Use’⁵⁴. After each iteration, the insight gathered will be fed back to the
19 437 developers and integrated to gradually improve the feasibility and acceptability through data-
20 438 driven adjustments of the treatment. Next to the qualitative self-report, quantitative ratings of
21 439 the treatment components, and technical usage data, outcome measure to determine the
22 440 feasibility and acceptability also include flow of participant recruitment and retention (i.e.,
23 441 number of participants that were approached, signed informed consent, and started/ completed
24 442 the treatment), treatment-fidelity rates (i.e., post-treatment therapist self-report *“Was the*
25 443 *treatment delivered as planned?”*), treatment compliance (i.e., indicated through log-in data,
26 444 self-report from patients and therapists), and (reasons for) dropouts in each iteration.

445 **Individual change processes**

446 The optimisation studies implement a sequential replicated and randomized single case
447 experimental design (SCED) to gain detailed insight into within-person behavioural changes,
448 and to develop and test the DAHLIA intervention, which has been recommended in the context
449 of CP⁵⁵. In SCEDs, each case functions as their own control and changes are evaluated
450 comparing levels of the outcome variables across different phases (e.g., baseline phase ‘A’ and
451 treatment phase ‘B’)⁵⁶. The methodology aims to demonstrate cause-effect relationships
452 between the treatment (independent variable) and the target behaviour (dependent variable)⁵⁷.

453 When planning a SCED study, the Risk of Bias in N-of-1 Trials (RoBiNT) Scale, a
454 critical appraisal tool that evaluates the methodological quality of intervention studies using
455 single-case methodology, can be followed as guidance^{57 58}. The design decision made in the

456 present study were based on this appraisal tool to ensure a scientifically robust approach. Table
457 1 provides details on the design elements.

458

459 Table 1. Methodological SCED approach of the DAHLIA study based on the RoBiNT Scale.

Item	RoBiNT Scale	SCED details, per optimisation iteration (<i>anticipated points</i>)
INTERNAL VALIDITY SUBSCALE		
1	Design	A replicated randomised AB-design with 10 x A-B (total of 20 phases), providing the opportunity to observe the experimental effect 10 times. (2 points)
2	Randomisation	The start of the treatment phase and therefore length of baseline phase will be determined randomly for each participant, with the baseline phase lasting between 5 to 10 days. This means that the treatment phase will start on any day between the 6 th and 11 th assignment. (2 points)
3	Sampling behaviour during all phases	The baseline phase will last at least 5 days, with twice daily sampling, resulting in 10 data points or more (phase A) (assuming 100% compliance to diary). The treatment phase will run over 6 weeks, with twice daily sampling on at least 4 days per week (6 weeks x 4 days x twice daily sampling), resulting in 48 data points or more (phase B) (assuming 100% compliance to diary). Even if the compliance rate should be lower, the amount of data points will lie >5 data points. (2 points)
4	Blinding of participants and HCP delivering the treatment	Blinding of the participant and practitioner is not feasible in the DAHLIA project. The behavioural treatment is delivered through a web-platform independently of the HCP; however, the HCP provides weekly, tailored support in addition to the online treatment. Neither the participant nor the HCP are blinded. (0 points).
5	Blinding (masking) of assessors	Patients complete self-report diaries and are not blinded to treatment phase, therefore, not independent of the therapy process. (0 point)
6	Inter-rater agreement	The measure of the target behaviour is a subject measure relying on self-reports from the digital diaries. (0 points)
7	Treatment adherence	The treatment is delivered through a web-platform following a standardized approach. Adherence to treatment (%) is calculated using digital log-in data . (2 points)
EXTERNAL VALIDITY AND INTERPRETATION SUBSCALE		
8	Baseline characteristics	A short interview by an HCP as part of the eligibility check will be conducted. Furthermore, a case formulation including information on age, sex, aetiology of CP, and severity of CP will be presented when presenting the results; this information will be based on a baseline assessment (online self-report). (2 points)
9	Setting	Information on the general location (Swedish region, hospital/ pain clinic) will be provided; however, the participant will engage with the online treatment in their everyday life, and therefore, it will not be possible to include details about the specific environment. (1 point)
10	Dependent variable (target behaviour)	Table 2 provides an overview of all diary items, which are scores on a 7-point Likert-Scale, except from the pain level item (0-100). Process outcome measures: 5 items on psychological (in)flexibility (see Table 2), 2 items on pain self-efficacy, 1 item on pain avoidance. Primary outcome measures: 1 item on pain level, 1 item on pain interference, 1 item on pain catastrophizing. Secondary outcome measures: 3 items on sleep, 2 items on affect, 1 item on stress, 1 item on fatigue. (2 points)
11	Independent variable (treatment)	A detailed description of the DAHLIA treatment is given above, including the treatment content, and number, duration, and frequency of sessions . (2 points)
12	Raw data record	Ten cases will be recorded (4-6 iteration with n=10 participants per iteration). Raw data will be presented with a data point for each diary entry. (2 points)
13	Data analysis	Data will be analysed and reported for each participant individually. Structured visual analysis, effect size measures and a randomization test wrapper for multilevel models will be applied. (2 points).

14	Replication	Ten participants will be included (per optimisation iteration). Across all iterations, data from n=40-60 participants will be available. (2 points)
15	Generalization	Patients will be heterogeneous in their characteristics. Furthermore, retrospective self-reports will be completed by each participant pre-post treatment , including two FUs (details see Table 3). (1 point)

460

461 Under the condition that all choices can be executed as intended, the internal validity
 462 of this SCED study will reach 8/14 points, and the external validity will reach 14/16 points.
 463 The total interpretation score will be 22/30 points. This score indicates a moderate
 464 methodological rigour⁵⁹.

465 Target behaviours will be assessed via self-reports collected through a digital diary.
 466 This diary will be prompted through the SMS function of REDCap, or a smartphone application
 467 (e.g., www.mpath.io). Both data collection methods will be piloted with participants to ensure
 468 that the diary works reliably. Participants will be prompted to complete the diary twice daily
 469 (for details see Table 2). Proposed diary items are based on traditional questionnaires and diary
 470 studies⁶⁰, and were chosen as they assess relevant aspects in the context of CP. More
 471 specifically, sleep items are based on the Insomnia Severity Index⁶¹, mood, stress, and fatigue
 472 items are adapted from previous digital diaries studies⁶⁰, psychological (in-) flexibility items
 473 (experiential avoidance/ acceptance; lack of contact with present moment/ present moment
 474 awareness; self as context/ context; (de-)fusion; (lack of contact with) values); inaction/
 475 committed action) are based on Multidimensional psychological flexibility inventory⁶², the
 476 pain level item is based on a Pain Rating Scale⁶³, pain catastrophizing item are based on the
 477 Pain Catastrophizing Scale⁶⁴, the pain avoidance item is based on the Psychological
 478 Inflexibility in Pain Scale⁶⁵, pain interference categories are based on the Brief Pain Inventory
 479 Scale⁶⁶, and pain self-efficacy items are is based on the Pain Self-Efficacy Questionnaire⁶⁷.

480 Generally, items should be short and easily to answer quickly⁶⁰. The order of the items
 481 will be the same in each prompt to allow participants to get used to the questions, minimise
 482 time to complete the diary, and thus limit interference with their daily flow. The reliability,
 483 validity, and sensitivity of the items will be explored through pilot studies and as part of the
 484 optimisation studies using suggested statistics (e.g., P-technique factor analysis). Idiosyncratic
 485 items might also be discussed with patients, in line with the agile approach, to improve validity
 486 and potentially patient engagement and ownership. Based on user-input, scientific evidence,
 487 and insight gained, diary items might be optimised and adjusted, and any adjustments made
 488 will be reported in prospective publications.

489

490 Table 2. Proposed daily diary items.

LUNCH/ EVENING DIARY		
Instructions (Availability to fill out: Lunch diary 12-14h, evening diary 18-20h)	<p>LUNCH: Hello & welcome to your digital diary! Please reflect on last night and this morning, and rate the following statements. Self-reflections can help to understand your daily routines and needs better. Let's get started.</p> <p>EVENING: Welcome back to your daily diary. Please take 2-3 minutes to reflect on this afternoon.</p>	
Construct	Item	Answering scale
Last night, ...		
1 Sleep ¹	... I had problems falling asleep.	7-point numeric scale
2 Sleep ¹	... I had problems sleeping.	7-point numeric scale
3 Sleep ¹	... I woke up too early.	7-point numeric scale
During the morning/ During the afternoon...		
4 Positive affect	... I felt happy, energetic, at ease, or enthusiastic.	7-point numeric scale
5 Negative affect	... I felt down, irritated, depressed, or hopeless.	7-point numeric scale
6 Stress	... I felt stressed.	7-point numeric scale
7 Fatigue	... I felt tired.	7-point numeric scale
8 Experiential avoidance/ Acceptance ²	... I tried to distract myself when I felt unpleasant emotions. ... I opened myself to all my feelings, the good and the bad.	7-point numeric scale
9 Lack of contact with present moment/ Present moment awareness ²	... I did most things on "automatic" with little awareness of what I was doing. ... I was attentive and aware of my emotions.	7-point numeric scale
10 Self as content/ Self as context ²	... I criticized myself for having irrational or inappropriate emotions. ... I tried to see the larger picture, even when I was down, depressed, or hopeless.	7-point numeric scale
11 Fusion/ Defusion ²	... distressing thoughts tended to spin around in my mind like a broken record. ... I was able to notice my thoughts and feelings without getting overwhelmed by them.	7-point numeric scale
12 Lack of contact with values/ Values ²	... I didn't have time to focus on things that are important to me. ... I tried to connect with what is truly important to me.	7-point numeric scale
13 Inaction / Committed action ²	... negative feelings trapped me in inaction. ... I didn't quit working towards what is important even if it was though.	7-point numeric scale
14 Pain level	... my overall pain level was:	0 (no pain) to 10 (worst pain imaginable)
15 Pain interference	... my pain interfered with my...	7-point numeric scale <ul style="list-style-type: none"> ○ General activities ○ Mood ○ Walking abilities

			<ul style="list-style-type: none"> ○ Normal work (including housework) ○ Relations with others ○ Enjoyment of life
16	Pain catastrophizing (rumination)	... I kept thinking about how much I hurt.	7-point numeric scale
17	Pain catastrophizing (magnification)	... I felt my pain overwhelmed me.	7-point numeric scale
18	Pain catastrophizing (Helplessness)	... I was afraid that my pain would get worse.	7-point numeric scale
19	Pain avoidance	... I avoided planning activities because of my pain.	7-point numeric scale
20	Pain self-efficacy	... I could do some form of housework/ paid/ unpaid work, despite the pain.	7-point numeric scale
21	Pain self-efficacy	... I could live a normal lifestyle, despite the pain.	7-point numeric scale
22	Open question	I would also like to share this about my morning/ afternoon:	Free text
23	Treatment interaction ³	Today, I completed a treatment module.	<ul style="list-style-type: none"> ○ Yes. ○ No, because it was a 'module free day'. ○ No, but I will do it tonight. No, because: <i>free text</i>
	Instructions	LUNCH: Thank you & have a nice afternoon! EVENING: Thank you very much for taking the time to fill in your diary. Have a nice evening!	

491 7-point numerical scale ranges from 1: not at all, to 7: very much; alternatively, based on user input,
 492 a visual analogue slider scale from 0: not at all, to 100: very much might be used. Note: ¹Sleep items
 493 only as part of the morning questionnaire; ²Both psychological flexibility and inflexibility items will be
 494 tested to determine with are more feasible and suitable to use; ³Treatment interaction item only as part
 495 of the evening questionnaire.

497 In addition to the information in Table 1, the analysis will be executed as follows. Diary
 498 data have a multilevel structure because repeated measurements (level 1) are nested within
 499 individuals (level 2). First, structured visual analysis will be conducted for each individual
 500 separately following the four steps described in Kratochwill, et al. ⁵⁶ to examine the within-
 501 and between-phase patterns in respect to the effects on level, trend, variability, immediacy,
 502 overlap, and consistency. Additionally, effect size measures will be calculated at the individual

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3 503 level using standardized mean difference and Tau-U, and at a group level using the between-
4 case standardised mean difference⁶⁸. Finally, to avoid making distributional and random
5 504 sampling assumptions, the randomization test wrapper for multilevel models will be used to
6 505 synthesise the data from the whole group of cases and evaluate treatment effects⁶⁹. Scientific
7 506 advisors of this project will provide expertise and support in the SCED analyses. Results will
8 507 be presented following the RoBiNT scale and SCRIBE guideline⁷⁰.
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15 509 **Efficacy across iterations**

16 510 In the optimization studies, efficacy will be determined using both intensive (SCED) as well
17 511 as extensive methods (retrospective self-reports from baseline, post-intervention and FUs; see
18 512 Figure 7). The diary and questionnaire data will be aggregated across all iterations, thus include
19 513 data from 40-60 participants. This approach allows to investigate the generalisability of results
20 514 of the SCED and evaluate treatment effects in applied research⁷¹. MultiSCED will be used for
21 515 the SCED data⁷².
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31 516 The proposed retrospective questionnaires used can be separated into process, primary,
32 517 and secondary outcome measures (see Table 3). Additionally, negative treatment effects may
33 518 occur in the context of internet interventions, and therefore, need to be acknowledged and
34 519 systematically assessed⁷³. Negative treatment effects are here assessed post-treatment using the
35 520 negative effects questionnaire (NEQ), a tool with reliable and valid psychometrics⁷⁴.
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40 521 Descriptive statistics of the retrospective questionnaires will summarize demographics
41 522 and pre-treatment clinical characteristics of the sample. To evaluate changes in treatment
42 523 outcomes over time, linear multilevel modelling (MLM) will also be used. MLM accounts for
43 524 repeated measures within subjects and can handle missing data, which will be addressed per
44 525 variable. Using a random intercept model, time will be treated as a categorical variable and pre-
45 526 treatment values will be specified as the reference point. Therefore, results will be interpreted
46 527 as a change from pre-treatment to post-treatment and, from pre-treatment to follow-up
47 528 assessments. Anchor-based methods will be applied to determine clinical significance of
48 529 changes in outcome measures⁷⁵. Separate linear growth models⁷⁶ will be computed for each
49 530 variable, while controlling for multiple testing. Significance level is set at Alpha (α)=0.05.
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60 532 Table 3. Proposed outcome variables and tools used to assess efficacy using extensive methods.

Focus	Variables	Instrument	Supported psychometrics
Process outcome measures	Open/ Acceptance	Chronic Pain Acceptance Questionnaire (CPAQ)	Internal consistency and criterion validity (Swedish version) ⁷⁷
	Aware	5 items on, 'acting with awareness' from the Five Facets Mindfulness Questionnaire (FFMQ)	Internal consistency, reliability, and construct validity (Swedish version) ⁷⁸
	Engaged/ committed actions	(i) Valuing questionnaire; (ii) Committed action questionnaire	(i) Internal consistency and construct validity (Swedish version) ⁷⁹ ; (ii) Proven validity and reliability (Swedish version) ⁸⁰
	Psychological flexibility	Swedish translation of the Multidimensional psychological flexibility inventory (MPFI)	Convergent and discriminant validities (English version) ⁶²
	Self-efficacy	General self-efficacy scale (S-GSE)	Reliable with high internal consistency (Swedish version) ⁸¹
	Pain self-efficacy	Pain self-efficacy questionnaires (PSEQ-2)	Evidence for reliability and validity (English version) ⁶⁷ , translated into Swedish ⁸²
	Avoidance	Avoidance subscale of Psychological Inflexibility in Pain Scale (PIPS)	Internal validity and construct validity (Swedish version) ⁶⁵
Primary outcome measure	Catastrophizing	3-Item Daily Pain Catastrophizing Scale (PCS)	Recommended instrument to understand mechanisms ⁶⁴
	(Dis)ability/ pain screening	Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ)	Clinically reliable and valid (Swedish version) ⁸³
	Work ability	Work ability index (WAI)	Validated (Swedish version) ⁸⁴
	Functioning	Brief pain inventory (BPI-SF)	Reliable and valid in multiple languages (including Swedish version) ⁶⁶
Secondary outcome measure	Well-being/ depression	Patient Health Questionnaire (PHQ-9)	Satisfactory content validity and sufficient reliability (Swedish version) ⁸⁵
	Perceived stress	Perceived Stress Scale (PSS)	Internal reliability and construct validity (Swedish version) ⁸⁶
	Sleep problems	Insomnia Severity Index (ISI)	Satisfactory factor structure, internal reliability, and concurrent validity (Swedish version) ⁶¹
	Health-related quality of life	EQ-5D	Standardised measure of health-related quality of life developed by the EuroQol Group ⁸⁷

533 Phase 3: Clinical evaluation (Study 4)

534 Randomized controlled trial enhanced by SCED

535 To determine the clinical effectiveness of the DAHLIA treatment, a RCT enhanced with SCED
 536 will be conducted. While RCTs provide estimates of between-subject treatment responses,

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3 537 differences in average scores between groups, they are unable to indicate specific within-
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5 538 subject responses. Simons, et al. ⁸⁸ apply a similar design and argue that SCED is a valuable
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7 539 addition to a traditional RCT design. One reason for this combined approach is that RCTs
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9 540 provide information on the population level, whereas SCEDs focus on the individual level.
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11 541 Furthermore, heterogeneity of treatment effects might remain undetected in a traditional RCT
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13 542 design⁸⁹. Additionally, the need for large cohorts of patients for adequate sub-group analysis⁹⁰,
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15 543 and a lack of feasibility to reach certain patient groups⁹¹ limits the insights from a traditional
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17 544 RCT. Applying SCED and multilevel modelling, even group results from small and distinct
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19 545 cohorts can be performed on a meta-analysis level⁸⁸.

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21 546 Outcome measures will be the same as in the optimisation studies, including the diary
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23 547 items for the SCED (see Table 2), and retrospective questionnaires (see details Table 3;
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25 548 including NEQ post-treatment⁷⁴). A priori computations based on a power of .95, four
26
27 549 questionnaire assessment points and a medium effect size shows that 360 participants (180 in
28
29 550 each arm) are sufficient to generate stable findings in the analyses of treatment effects. With
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31 551 an estimated attrition rate of 18%, this implies that 295 participants will provide post-treatment
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33 552 data, which is considered adequate also for moderator/ predictor and cost-effectiveness
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35 553 evaluations. However, outcome measures and calculated sample size will be updated and might
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37 554 be modified based on iterations in the prior phase.

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39 555 Treatment arm randomization is conducted by a research assistant following the
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41 556 decision on study inclusion by the HCP and after the baseline assessment (sociodemographic
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43 557 information, questionnaires, A-phase of SCED) is completed. Participants are randomized to
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45 558 the treatment arm or treatment as usual (TAU) using a block randomization strategy to ascertain
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47 559 equal distributions across the arms. Randomization is conducted by a local project manager
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49 560 who is not involved in the screening or intervention. Next, participants undergo treatment; then
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51 561 all participants complete the post-intervention assessment (questionnaires and 5-day digital
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53 562 diary). Booster-sessions will be sent to the participants in the intervention group at 2- and 4-
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55 563 months. Finally, at the 3- and 6-month follow-ups (FUs), all participants complete the
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57 564 questionnaires and 5-day digital diary period. In case participants decide to discontinue the
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59 565 study at any point in time, they might choose to provide a reason.

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566 To examine changes in process, primary and secondary outcome measures (Table 3),
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568 linear mixed models will be conducted comparing the DAHLIA treatment to TAU. Analysis
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570 will be performed using group as a fixed between-person factor (two levels: DAHLIA
treatment and TAU), and time as a fixed within-person variable (four levels: baseline, post-
treatment, 3-month FU, 6-month FU). The linear mixed model will estimate fixed effects

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3 571 (regression slopes) for change in the intervals during (baseline to post-treatment assessment),
4 572 and after (post-treatment to 3- and 6-month FU) the treatment period. The intervals will be
5 573 entered as a categorical dummy variable (three levels). Potential confounders will be added to
6 574 the model as covariates (i.e., age, gender, pain diagnosis, pain duration). Data will be analysed
7 575 with the support of a statistician and using the latest version of SPSS. Mean change will be
8 576 reported and test of significance will be two-sided with a set alpha level of 0.05.

14 577 **Health economic evaluation**

16 578 A short-term health economic evaluation will compare the DAHLIA treatment and the TAU at
17 579 the primary endpoint (post-treatment). Additionally, an equivalent long-term evaluation will
18 580 be performed at the end of the FU period using cumulative data collected up to that assessment
19 581 point. Costs in both trial arms will be estimated from a societal perspective for each participant
20 582 in the trial based on resource items and associated relevant unit costs. The use of societal
21 583 resources comprises information on the use of resources related to healthcare contacts and
22 584 medication (medical records and register data), and productivity losses related to absence from
23 585 work (the LISA database). Costs to deliver the digital intervention will be estimated based on,
24 586 for instance, HCPs' time spent on treatment. Total costs will be aggregated by trial arm.

25 587 The self-report tool EQ5D⁸⁷ will be completed by the participants at pre-, post-
26 588 treatment and FUs and used to measure changes in health-related quality of life (HRQoL), to
27 589 calculate quality adjusted life years (QALYs). Total QALY gains for participants over the trial
28 590 will be estimated using the area under the curve method⁹². Cost data and QALYs will be
29 591 analysed using generalized linear models to account for non-normal distributions⁹³. Data will
30 592 be analysed controlling for the influence of covariates, and by adjusting for baseline data. Cost-
31 593 utility analysis (CUA) will be conducted with QALYs gained as primary outcome, comparing
32 594 incremental costs with incremental changes in QALYs for digital treatment and TAU. Results
33 595 will be presented as an incremental cost-effectiveness ratio (ICER), representing the ratio
34 596 between the difference in costs and the difference in QALY gained between the digital
35 597 treatment and TAU. Incremental cost-effectiveness ratio will be expressed as cost per
36 598 additional QALY, which is the most common approach in health economics⁹⁴. Uncertainty
37 599 around the cost and outcome data will be explored and presented on cost-effectiveness plans,
38 600 representing the distribution of the cost and outcome differences between both conditions. The
39 601 probability of digital treatment being cost-effective compared to TAU will be presented across
40 602 a range of price values a decision-maker would be willing to pay, represented by a cost-
41 603 effectiveness acceptability curve⁹⁵.

604 **Phase 4: Post-market surveillance (Study 5)**

605 Similar to the development phase (Study 2), interviews with stakeholders will be conducted,
606 recorded, and transcribed. The stakeholders participating in study 2 will be approached, along
607 with additional key stakeholders identified during the implementation process. Appendix 4
608 provides the full overview of the interview questions. Questions reflect on the process so far
609 (e.g., *‘What kind and how many resources were needed to bring this intervention into*
610 *practice?’*), on the current status (e.g., *‘What issues are you currently facing?’*), and
611 prospective adjustments (e.g., *‘What will the prospective maintenance and upkeep look like?’*).
612 These questions are preliminary and may be adjusted based on findings of Phase 1-3. Even
613 though the www.1177.se website is free for the end users (i.e., patients and HCPs), special
614 attention may also be paid to financing, as a lack thereof can be a barrier for long-term
615 implementation of eHealth interventions⁹⁶.

616 The qualitative data will be analysed following the same process as that used in Phase
617 1. Specifically, an inductive analysis to identify and summarise themes will be performed, and
618 information will be mapped onto the domains of the CFIR⁴⁷. The implementation strategy and
619 plan will be reviewed, and lessons-learned will be presented to inform prospective
620 implementation studies.

621 **Patient and public involvement**

622 This is a study protocol and due to ethical and practical reasons, no patients were directly
623 involved in the project yet. However, the Personas originated from interviews with patients, as
624 described above, and patients and other stakeholders will be involved in all planned phases of
625 the DAHLIA project. Dissemination to patients and the public is described in more detail the
626 section ‘Ethics and Dissemination’.

627 **DISCUSSION**

628 Chronic pain is a huge public health problem, in suffering, disability, and costs for individuals
629 and society. Widely accessible and sustainable behavioural treatment options could help to
630 address this problem. An agile and user-centred development integrating a data-driven
631 decision-making process and scientific evaluation of effects is essential to produce an
632 evidence-based intervention of this type for individuals with CP. To our knowledge, this is the
633 first project utilizing the mHealth agile development framework²⁷ to systematically build a
634 digital behavioural treatment within a nationally used health care hub. The purpose of this
635 project is to improve the standard of care for individuals with CP by applying the innovative
636 development framework, thus providing an accessible, user-friendly, and empirically
637 supported behavioural treatment to maintain or improve resilience, functioning, and well-being
638 in this population.

639 Strengths include (i) the execution of the project by a multi-disciplinary, inter-sectorial,
640 and international research team, (ii) the overall agile, iterative, and data-driven process, and
641 (iii) the involvement of patients and different stakeholders early and throughout the
642 development. Furthermore, (iv) the richness of methodologies using mixed methods,
643 combining a traditional clinical trial evaluation on the population level (RCT), fine-graded data
644 collection (SCED) on the level of the individual, and (v) an explicit focus on cost-effectiveness
645 and determinants of implementation will be highlighted. The project is (vi) based on innovative
646 strategies in the field of eHealth and digital treatments, and (vii) key gatekeepers such as
647 regional leaders support the initiative. The DAHLIA approach is also in line with the widely
648 used MRC framework by considering contextual and economical aspects, building on theory,
649 involving stakeholders, and refining the intervention⁴⁵.

650 Due to the ambitious and multifaceted nature of the project, several inherent challenges
651 and risks should also be acknowledged. In case a sub-study should be delayed, e.g., due to
652 recruitment difficulties or technical development issues, this delay could affect the whole
653 project. Subsequently, adjustments following the agile approach could be discussed to balance
654 the practical feasibility of executing the study and limiting the impact on its robustness.

655 Furthermore, the multidisciplinary, inter-sectorial approach is certainly a strength of
656 the DAHLIA project, however, it might also have inherent challenges. For example, interests
657 of stakeholders might differ, which needs to be considered and addressed. Here,
658 communication is key, but compromises might be needed to ascertain satisfactory benefits for
659 all parties involved.

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3 660 Regarding the DAHLIA treatment itself, a high level of patient engagement (e.g., four
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5 661 micro-session per week combined with frequent diary assessments) will be required. These
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7 662 demands might be perceived as burdensome by some individual. However, contact with HCPs
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9 663 will support participants' motivation and engagement. Furthermore, the focus groups and
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11 664 optimisation studies will provide insight into the perceived intensity, thus feasibility of the
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13 665 intervention set-up, and the agile process allows to adjust it accordingly. Specially, tailoring of
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15 666 the length of the micro-sessions and frequency of diary prompts will be explored.

15 667 Furthermore, the DAHLIA treatment may not be suitable for all people with CP and
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17 668 the question of “what fits for whom” will be continuously discussed. The website
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19 669 (www.1177.se) is a national health care hub in Sweden, but research shows that older adults,
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21 670 people with cognitive problems, or disabilities are less likely to use technologies⁹⁷, which could
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23 671 result in a bias in recruitment and usability. To improve inclusivity, the possibility to provide
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25 672 additional training for certain populations, such as older adults⁹⁸, will be explored. An
26
27 673 additional issue is that the project is currently executed in Swedish, which excludes people with
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29 674 limited proficiency in Swedish. Therefore, translation into other languages and further cultural
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31 675 adaptations will be considered.

31 676 The DALHIA treatment may have the potential to become a widely implemented first
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33 677 line of treatment. However, some CP groups will likely benefit from an alternative treatment
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35 678 format (e.g., face-to-face), or complementary interventions. Thus, additional studies may
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37 679 explore if and how physiotherapists, general practitioners, or occupational therapists can
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39 680 deliver the DAHLIA treatment.

39 681 Finally, the treatment could prospectively be scaled and adjusted for other groups of
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41 682 patients with CP, e.g., children and adolescents, people with disabilities, and/or other medical
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43 683 conditions such as individuals with severe mental or physical co-morbidities. In addition,
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45 684 support offered as part of the DAHLIA treatment can be extended to significant others and
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47 685 family members of people living with CP. Thus, by using an agile development approach, the
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49 686 DAHLIA project might grow to support the heterogeneous group of individuals with CP and
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51 687 their complex health needs.

688 **Ethics and Dissemination**

689 The study received approval from Swedish ethical review authorities (Dnr 2021-02437). All
690 participants will receive a detailed patient information sheet, have one week time to consider
691 participation, and sign informed consent prior to participation. Each study participant will
692 receive a unique study code to ensure anonymity and confidentiality. Data will be stored in
693 accordance with Swedish regulations on secure servers at Karolinska Institutet.

694 The project is announced on the Karolinska Institutet website (Rikard Wicksell's
695 research group), and on social media, primarily twitter. The general outline of the project has
696 been presented at online conferences. Next to the study protocol paper, the intention is to
697 publish a number of peer-reviewed manuscripts, in which any protocol modifications will also
698 be communicated. The results will be presented at (inter-)national conferences and networking
699 events. Popular science articles, podcasts, radio interviews, and animated videos are
700 additionally planned to disseminate the results to the wider public.

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3 701 **Author's contribution**
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5 702 SB, SJ, KB, LMcC, IFI, SP, and RW were involved in the conception and design of this project.
6 703 RW acquired and received the funding. HC provided specific input on the topic of
7 704 implementation, IFe contributed with her expertise on health economy, and LS, PO, and JV
8 705 added valuable knowledge on the single-case experimental design aspects of the project. SB
9 706 drafted the manuscript, and all authors revised the manuscript and checked the intellectual
10 707 content. All authors gave final approval and agree to be accountable for all aspects of the work.
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23

24 712 **Completing interests**
25

26 713 None declared.
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28 714 **Access to data and protocol details**
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30 715 Only the research team will have access to the raw data and participant code. Anonymised data
31 716 will be made available as part of publications, whenever possible. Researchers from other
32 717 universities may request to receive access to other information (e.g., informed consent sheets,
33 718 data management plan).
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38

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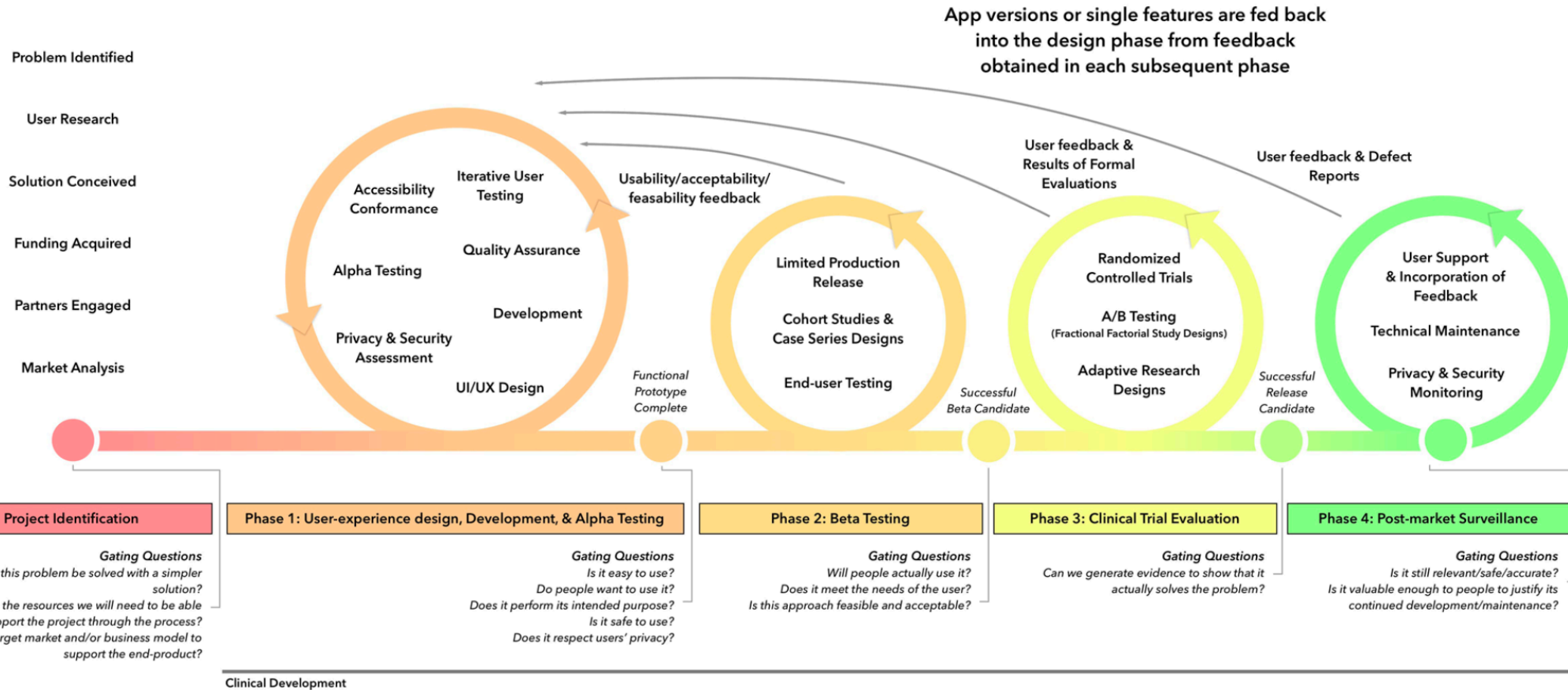
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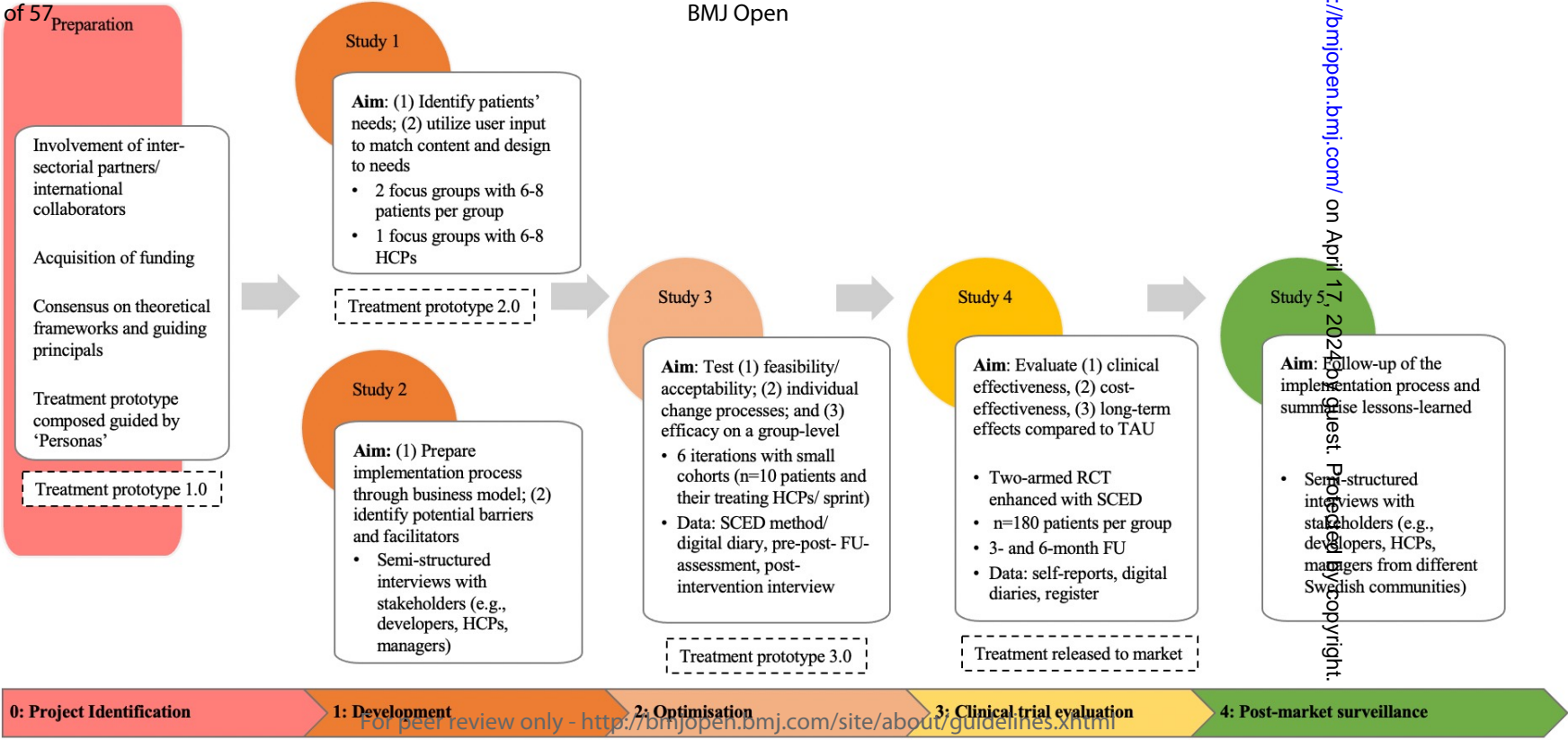
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- 5 1001 • Figure 1. mHealth Agile Development & Evaluation Lifecycle (Wilson et al., 2018).
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7 1002 • Figure 2. DAHLIA project overview including highlights of each study and time plan.
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9 1003 HCP= health care professional; SCED= single case experimental design; TAU=
10 treatment as usual; RCT= randomised controlled trial; FU= follow-up.
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12 1005 • Figure 3. Example of a DAHLIA Persona with chronic pain.
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14 1006 • Figure 4. DAHLIA treatment micro-session elements. HCP= health care professional.
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16 1007 Note: The name “DAHLIA treatment” is mainly for academic settings; in the
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18 1008 www.1177.se web-platform, a more intuitive treatment name will be chosen.
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20 1009 • Figure 5. The DAHLIA treatment components.
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22 1010 • Figure 6. Template of business model canvas (based on Osterwald & Pigneur, 2010).
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24 1011 Grey boxes: Example aspects of the DAHLIA business model; the final model will be
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26 1012 a result of the stakeholder interviews.
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28 1013 • Figure 7. General overview of the optimisation studies and specific procedure in each
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30 1014 iteration. SCED= Single-case experimental design. FU= Follow-up. HCP= Health care
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mHealth Agile Development & Evaluation Lifecycle



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2019/2020	2021	2022	2023	2024
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AIDA
18 yrs. old

Employment:
N/A, high school student.

Education:
Primary school
Upper secondary school (ongoing).

Family:
Mother and father with foreign background, four younger siblings.

Background and social context:
Born in Pakistan, moved to Sweden when she was four years old. Leads an active life with hobbies and after-school activities. Frequently works out at the gym, pushing herself.
Aida has many friends and it is important for her to be popular. She is ambitious in school with high demands from her home-environment. She often feels stressed and does not think she is performing as expected. Aida carries a lot of responsibility at home. She has a high level of technological literacy and uses her smartphone for everything.

Social support (related to pain): Despite her family and many friends, Aida feels lonely with her pain. She feels that no one understands or takes it seriously. Her parents are constantly nagging, stressing that the health services should be able to help. Aida finds it strange that she is in so much pain even though she works out a lot and does everything she is "supposed to". Despite her efforts, there are days when she is paralyzed by pain and the feeling of being under pressure.

City/ countryside: Apartment in large city.

PATIENT PAIN PROFILE

Pain problems:

- No clinical diagnosis.
- Recurrent headaches.
- Tensions in shoulders and neck.
- Stomach ache.

Consequences:

- Difficult to concentrate when in pain.
- Although Aida really wants to go to school, she is increasingly staying at home as she cannot manage.
- "Yoyo behaviour" – some days she keeps active and works out, while other days she is completely exhausted.

Pain behaviour:

- Wants a "quick fix" and prefers to continue pushing rather than taking a step back and think.
- Exercises to get in better shape to handle the pain.
- Keeps on going to alleviate anxiety despite feeling the need to rest.

Attitude to treatment:

- Wants to be a "good patient" and do everything she is told (and then some).
- Happy to visit doctors but does not see herself as someone who needs mental health support or treatment.

HEALTH CARE & TREATMENT

Contact with health care:

- Undertaken eye test and has gone through various investigations for the recurrent headaches.
- Visited dentist focusing on temporomandibular joints (jaw region).
- Sought care due to various somatic disorders (head, neck, stomach).

Comorbidities:

- Stress
- Anxiety
- Sleeping difficulties

Medicine:

- Pain killers

PERSONAL NEEDS & GOALS

Treatment needs:

- Wants to be independent and take an active part in her treatment. Needs to feel that she can influence her situation.
- Wants to follow/have an overview of own progress.

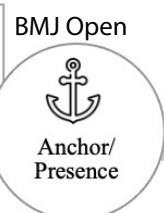
Goals:

- To live an active and productive life without pain.
- To learn how to maintain a balanced lifestyle without guilt when resting.

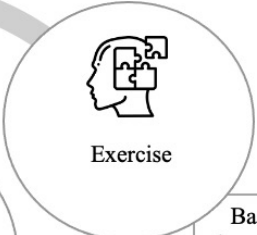
Figure 3. Example of a DAHLIA Persona with chronic pain.

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A question/ sentence to connect to the person's current situation, needs, wishes, or issues; supporting relevance and reliability of session



Anchor/
Presence



Exercise

Based on learning theory, fear-avoidance model, and contextual behavioural approach

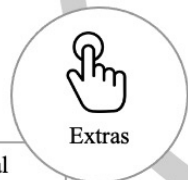


Micro-
session



Therapist
contact

Possibility to take notes during current session to facilitate conversation with HCP later



Extras

Link to additional information or exercises, if person wants to read more



Wrap-
up

Rounding up of session



Validation/
appreciation

Words to help person feel understood and reassured, and to build the relationship with the HCPs

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4 self-guided **micro-sessions** per week inspired by process-based therapy approaches



Aware

Chat function to contact health care professional



Digital diary twice daily to promote self-monitoring



Living well with chronic pain

After 6-week intervention period, **booster-sessions** after 2 and 4 months for long-term support



Accepting/ Open



Active



Key Partners 

(8) Describes the network of suppliers and partners that make the business model work, e.g.:

- Optimization and economy of scale
- Reduction of risks and uncertainty
- Acquisition of particular resources and activities

➤ *Soft ware partners*

➤ *Health care*


Key Activities 

(7) Describes the most important things a company must do to make its business model work, e.g.:

- Production
- Problem solving
- Platform/ Network

➤ *Developing content*


➤ *IT support and development*

Key Resources 

(6) Describes the most important assets required to make a business model work, e.g.:

- Physical
- Intellectual
- Human
- Financial

➤ *IT upkeep*


Value Propositions 

(2) Describes the bundle of products and services that create value for a specific customer segment, e.g.:

- Newness
- Performance
- Customisation
- "Getting the job done" Design
- Brand/Status
- Price
- Cost reduction
- Risk reduction
- Accessibility
- Convenience/Usability

➤ *Usable, effective, evidence-based treatment*

➤ *Accessible and free for patients*


Customer Relationships 

(4) Describes the types of relationships a company establishes with specific customer segments, e.g.:

- Personal assistance
- Self-service
- Automated services
- Communities
- Co-creation

➤ *Personal assistance*


➤ *Co-creation*

Channels 

(3) Describes how a company communicates with and reaches its customer segments to deliver a value proposition (direct/indirect), e.g.:

- Sales Force
- Web sale
- Own stores
- Partner stores
- Wholesaler

➤ *Information on 1177*


Customer Segments 

(1) Defines the different groups of people or organizations an enterprise aims to reach and serve. e.g.:

- Mass market
- Niche market
- Segmented
- Diversified
- Multi-sided platforms (multi-sided markets)

➤ *Patients with chronic pain*


➤ *Health care organisations*

Cost Structure 

(9) Describes all costs incurred to operate a business model, e.g.:

- Cost-driven
- Value-driven
- Fixed costs
- Variable costs
- Economies of scale
- Economies of scope

➤ *Platform and content development/upkeep*

Revenue Streams 

(5) Represents the cash a company generates from each customer segment (costs must be subtracted from revenues to create earnings), e.g.:

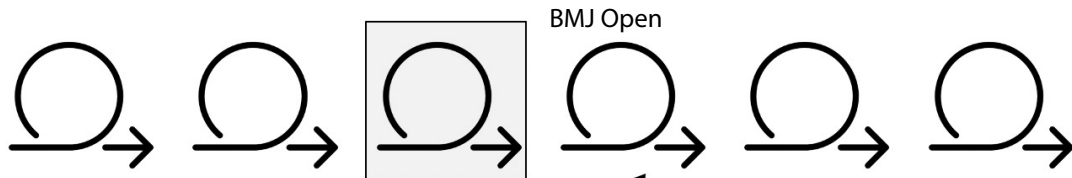
- Asset sale
- Usage fee
- Subscription fees
- Lending/ renting/ leasing
- Licensing
- Brokerage fees
- Advertising

➤ *Free for patients*

➤ *Licensing for regions*

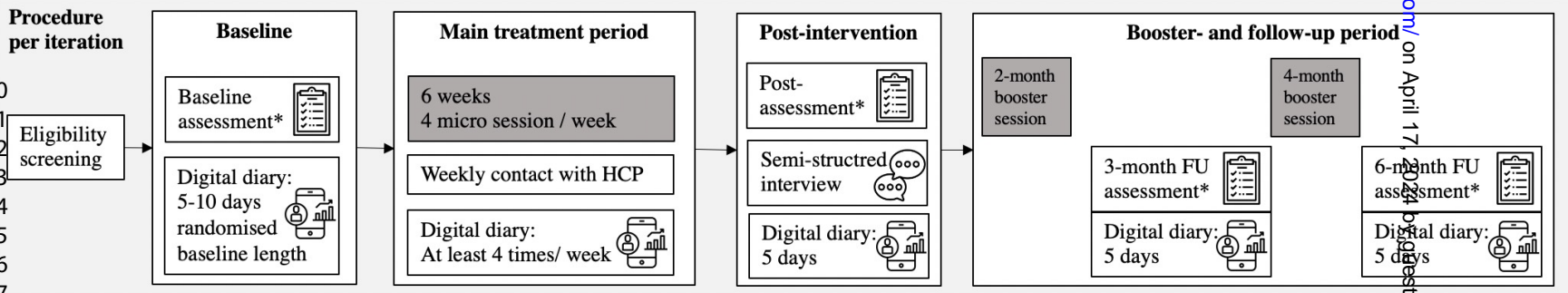
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4-6 iterations with each n=10 patients and their treating HCP

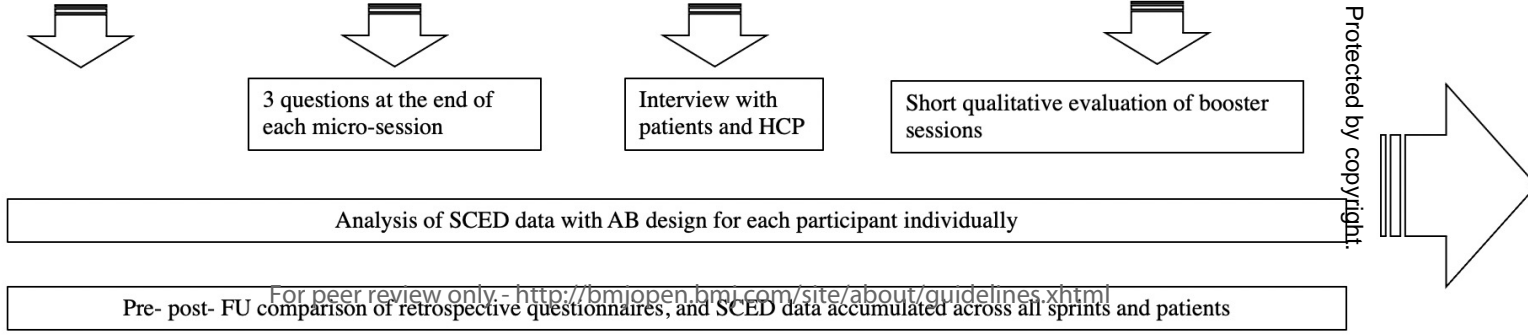


Overall outcome:
Prototype 2.0

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- Objectives**
- Feasibility/ acceptability
 - Individual change processes
 - Efficacy



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*Retrospective self-reports including process-, primary- and secondary outcome measures

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Appendix 1:

Semi-structured focus group guide

6-8 participants per focus group

FOR PATIENTS (2 focus groups; heterogenic in terms of age, gender, pain condition, pain history, etc.):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Living with chronic pain** (30min.)

It would be amazing to have a magic pill to just take all the pain away, so you could live without it. But unfortunately, we don't have that magic pill. Instead, we want to help you and other people with chronic pain to find a way to live well with the pain. (*Presentation on definition of health (Huber et al., 2011): ability to adapt and self-manage physical, mental and social aspects of health, and examples*).

 - a. Based on this definition of health, can you describe your own health needs? Which (aspects of your) needs are currently unmet?
 - b. In which moments of your life do you feel happiest/ most engaged/ most satisfied?
 - c. What helps you to engage in these 'happy moments'?
 - d. What are barriers to engage in these 'happy moments'?
 - e. What would you need to engage in these moments more often?

BREAK 10 Min.

4. Core question 2: **The DAHLIA treatment**

Presentation of the proposed treatment, aim, design, theoretical background, and examples of exercises (10min); following a discussion (30min)

 - a. What do you think of this treatment? What do you like, what do you dislike? (Please reflect on (1) design, (2) set-up, (3) content, (4) other (e.g., terminology: treatment, intervention, program; patient vs. person))
 - b. How feasible would it be to do this treatment?
 - c. Do you think this treatment meets you needs?
 - d. Is there anything else you would like to add?

FOR HEALTH CARE PROFESSIONALS (1 focus group, psychologists/ psychotherapists trained in cognitive-behavioural therapy; heterogenic in terms of age, gender, cultural background):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Supporting people with chronic pain** (30min)

People with chronic pain have complex needs and treatment has to meet these needs. We are interested in your experiences in what works well to improve

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3 the overall health and well-being of patients with chronic pain. (*Presentation*
4 *on definition of health (Huber et al., 2011): ability to adapt and self-manage*
5 *physical, mental and social aspects of health, and examples*).

- 6
7 a. Which (aspects of) your patient's health needs are unmet? What is
8 needed to support chronic pain patients in the best way?
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10 b. What barriers and facilitators to deliver support to chronic pain patients
11 do you face? Please reflect on elements related to the patient, treatment
12 options, and the health care in general.

13
14 BREAK 10 Min.

15
16 4. Core question 2: **The DAHLIA treatment**

17 Presentation of the proposed treatment, aim, design, theoretical background,
18 and examples of exercises (10min); following a discussion (30min)

- 19 a. What do you think of this treatment? What do you like, what do you
20 not like? (Please reflect on (1) design, (2) set-up, (3) content, (4) other
21 (e.g., terminology: treatment, intervention, program; patient vs.
22 person))
23
24 b. How feasible would it be for you to deliver this treatment?
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26 c. Does the treatment meet the needs of the patients with chronic pain?
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28 d. Is there anything else you would like to add?
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Appendix 2. Baseline interviews with stakeholders

Various stakeholders will be approached, including developers, health care professionals, and managers. Through snow-ball sampling, other potential stakeholders will be identified and approached (e.g., individuals from policy making or municipality representatives).

Stakeholder: developers

I. General

Theme: Experience and development of digital interventions within the 1177 web-platform

1. What is your job description and what are your responsibilities?
2. How is the 1177 web-platform structured, in the region of Kalmar and Sweden?
3. How many digital interventions are available within 1177 in your region?
4. Who developed these interventions; who integrated them in the platform?
5. How are these interventions financed?
6. Who is responsible/ involved in the maintenance of the interventions?
7. If/ how is the interventions' content updated?
8. If/ how are the interventions used and promoted in health care?
9. If/how is user satisfaction with interventions evaluated?
10. If/how do collaborations with other regions look like?

II. Specifics (focus about DAHLIA project)

1. How would you describe the anticipated implementation process of this intervention?
2. What is needed to support the implementation process?
3. What could facilitate the implementation process?
4. What could hinder the implementation process?
5. What are benefits for you/ the 1177 web-platform when developing this intervention?
6. Are you enthusiastic about this intervention, if so, why?
7. Do you think this intervention has the potential to be successful in your region, and Sweden?
8. Where would you like to see this intervention in 5 years?

Stakeholder: health care professionals

I. General

Theme: Experience and use of digital interventions with patients

1. What is your job description and what are your responsibilities?
2. What is your experience in delivering interventions via the 1177 web-platform?
3. If/when there is a new intervention available in the 1177 web-platform, how do you usually hear about it?
4. What makes it attractive to deliver such an intervention?
5. What resources are needed for you to deliver these interventions (e.g., time, knowledge, managerial support)?
6. What hinders you to deliver these interventions?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What benefits for yourself/your work do you anticipate through this intervention?
3. What benefits for your patients do you anticipate?
4. What disadvantages or problems do you anticipate when delivering this intervention?

5. What disadvantages or problems for your patients when receiving the intervention do you anticipate?
6. What would hinder you to deliver this intervention?
7. What would facilitate you to deliver this intervention?
8. Are you enthusiastic about this intervention, if so, why?
9. Do you think this intervention has the potential to be successful in your care facility?
10. Where would you like to see this intervention in 5 years?

Stakeholder: health care managers

Theme: Experience and promotion of digital interventions in care facility

1. What is your job description and what are your responsibilities?
2. How many digital interventions are currently offered by the 1177 web-platform (and used) in your care facility?
3. What is needed to implement an intervention from the 1177 web-platform in your care facility?
4. How do digital interventions get financed in your care facility?
5. What is your involvement in digital interventions in your care facility? How do you support the use of digital interventions?
6. What hinders the implementation of these interventions, in your eyes?
7. If/ how does your care facility collaborate with other regions regarding digital interventions from the 1177 web-platform?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What kind of benefits do you anticipate for employees through this intervention?
3. What kind of benefits do you anticipate for patients through this intervention?
4. What kind of disadvantages or problems for employees do you anticipate through this intervention?
5. What kind of disadvantages or problems for patients do you anticipate through this intervention?
6. Are you enthusiastic about this intervention, and if so, why?
7. How will you promote this intervention in your care facility?
8. Do you think this intervention has the potential to be successful in your care facility?
9. Where would you like to see this intervention in 5 years?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Appendix 3. Feasibility/ acceptability; questionnaire.

Table 1. Semi-structured interview guide to evaluate the general feasibility and acceptability of the treatment.

Topics	Questions	Answering scores	Open question
You recently completed the 6-week treatment. For us, it is very important to hear how you experienced it so that we can improve the content, design, and other aspects further. Thank you for taking the time to provide us with your input. First, we would like to ask you to reflect on and rate the past weeks and treatment in general.			
General	Were the past 6 weeks usual weeks for you?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did special events occur?		
	Were you able to read the text in the treatment well?		
	Was the text understandable?		
	Did the intervention hinder your daily occupations?		
	Did technical issues occur?		
Would you recommend this treatment to a friend?			
Secondly, we would like to ask you to reflect on and rate the four short sessions that were offered each week.			
Micro-sessions	Did you like doing the sessions?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Were the sessions difficult or unclear?		
	Did you experience the sessions as helpful?		
	Have the sessions influenced your behavior?		
	Have the sessions influenced your emotions?		
	Have the sessions influenced your thoughts?		
	Did you experience the sessions as time consuming?		
Did you experience the sessions as boring?			
Third, we would like to ask you to reflect and rate the messenger function with which you could communicate with your health care professional.			
Messenger function/ health care professional	Was the messenger function overall helpful?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did you experience the weekly messages sent by your health care professional as motivating?		
	Did you feel supported by your health care professional?		
Fourth, we would like to ask you to reflect on and rate the daily diary .			
Digital diary	Did you experience the daily diaries as burdensome?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Was it enjoyable to complete the digital diary?		
	Did you become more aware of your thoughts using the digital diary?		
	Did you become more aware of your behavior using the digital diary?		
	Did you become more aware of your emotions using the digital diary?		
Is there anything else you would like to add?			Free text

Appendix 4: Follow-up interviews with stakeholders

The stakeholders from the baseline assessment will be approached again. Furthermore, through snow-ball sampling, potential new stakeholders will be identified and also approached.

Stakeholder: developers

Process so far:

1. When reflecting on the overall development, evaluation, and implementation process, what went well?
2. When reflecting on the overall development, evaluation, and implementation process, what did not go well?
3. What factors supported the process of bringing this intervention into practice?
4. What factors hindered the process of bringing this intervention into practice?
5. What kind and how much resources were needed?
6. Did the process go as anticipated? If not, what was surprising?
7. How satisfied are you with the process so far?
8. What was most challenging during the implementation process?

Current use:

1. What are you currently doing to keep the intervention implemented?
2. Do you have sufficient resources? Please elaborate.
3. What issues are you currently facing? What solutions for these issues do you have?

Prospective adjustments:

1. What will the prospective maintenance and upkeep look like?
2. Who is responsible for that?
3. If there should be a change in employment, who ensures that the intervention remains updated?

Stakeholder: health care professionals

Process so far:

1. How often did you deliver the digital intervention?
2. What kind of benefits for yourself, your work, and/or your patients did you experience?
3. What kind of disadvantages for yourself, your work, and/or your patients did you experience?
4. What kind of support for delivering the intervention (e.g., training, technical guidance when issues arose) did you receive?
5. What hindered you in delivering the intervention?
6. What facilitated you to deliver the intervention?

Current use:

1. How satisfied are you with the intervention overall?
2. Which elements of the intervention need improvement?

Prospective adjustments:

1. Do you plan on delivering the intervention in the future? If not, please elaborate.
2. Would you recommend the intervention to a colleague?
3. What kind of problems do you anticipate in the future; and do you have potential solutions for them?

Stakeholder: health care managers

Process so far:

1. How would you describe your involvement in implementing the intervention?
2. How many resources were needed for the implementation?
3. Did the implementation process go as expected? If not, what was surprising?
4. How did you support your employees to deliver the intervention?

Current use:

1. How satisfied are you currently with the intervention (e.g., reflecting on use, content, promotion, required resources, (technical) issues)?
2. What aspects of the current implementation/ practical use need improvements?

Prospective adjustments:

1. Do you plan to offer the intervention in your region in the future? Please elaborate.
2. Would you recommend this intervention to another region/ other health care organizations? Please elaborate.
3. What kind of problems do you anticipate in the future?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,3
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	28
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1,28
Roles and	#5b	Name and contact information for the trial sponsor	1

responsibilities:

sponsor contact
information

Roles and

responsibilities:

sponsor and funder

[#5c](#)

Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities

n/a

Roles and

responsibilities:

committees

[#5d](#)

Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

8

Introduction

Background and

rationale

[#6a](#)

Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

5-7

Background and

rationale: choice of

comparators

[#6b](#)

Explanation for choice of comparators

n/a

Objectives

[#7](#)

Specific objectives or hypotheses

6-8

Trial design

[#8](#)

Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)

8, Fig. 2

Methods:

Participants,

interventions, and

outcomes

Study setting

[#9](#)

Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained

11,12

Eligibility criteria

[#10](#)

Inclusion and exclusion criteria for participants. If applicable,

11

		eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	9-11, Fig 4, Fig 5
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12, 14,15
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Fig 7, Tab 2, Tab 3, and related sections
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14, Fig 7
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12, 13, 14, 21
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	11,12
Methods:			
Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for	21, Tabl. 1

stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions

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7	Allocation	#16b	Mechanism of implementing the allocation sequence (eg, 21, Fig 7
8	concealment		central telephone; sequentially numbered, opaque, sealed
9	mechanism		envelopes), describing any steps to conceal the sequence until
10			interventions are assigned
11			
12			
13			
14	Allocation:	#16c	Who will generate the allocation sequence, who will enrol 14, 21
15	implementation		participants, and who will assign participants to interventions
16			
17	Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial n/a (Tab 1)
18			participants, care providers, outcome assessors, data analysts),
19			and how
20			
21			
22			
23	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is n/a
24	emergency unblinding		permissible, and procedure for revealing a participant's
25			allocated intervention during the trial
26			
27			
28	Methods: Data		
29	collection,		
30	management, and		
31	analysis		
32			
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35	Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and Described for
36			other trial data, including any related processes to promote each sub-
37			data quality (eg, duplicate measurements, training of study
38			assessors) and a description of study instruments (eg,
39			questionnaires, laboratory tests) along with their reliability and
40			validity, if known. Reference to where data collection forms
41			can be found, if not in the protocol
42			
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46	Data collection plan:	#18b	Plans to promote participant retention and complete follow-up, n/a
47	retention		including list of any outcome data to be collected for
48			participants who discontinue or deviate from intervention
49			protocols
50			
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52			
53	Data management	#19	Plans for data entry, coding, security, and storage, including 26, 28
54			any related processes to promote data quality (eg, double data
55			entry; range checks for data values). Reference to where
56			details of data management procedures can be found, if not in
57			
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		the protocol	
1			
2	Statistics: outcomes	#20a Statistical methods for analysing primary and secondary	Tab 1, 19-21
3		outcomes. Reference to where other details of the statistical	
4		analysis plan can be found, if not in the protocol	
5			
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7			
8	Statistics: additional	#20b Methods for any additional analyses (eg, subgroup and	12-14, 21, 22,
9	analyses	adjusted analyses)	
10			
11	Statistics: analysis	#20c Definition of analysis population relating to protocol non-	19, 20
12	population and	adherence (eg, as randomised analysis), and any statistical	
13	missing data	methods to handle missing data (eg, multiple imputation)	
14			
15			
16			
17	Methods: Monitoring		
18			
19	Data monitoring:	#21a Composition of data monitoring committee (DMC); summary	28
20	formal committee	of its role and reporting structure; statement of whether it is	
21		independent from the sponsor and competing interests; and	
22		reference to where further details about its charter can be	
23		found, if not in the protocol. Alternatively, an explanation of	
24		why a DMC is not needed	
25			
26			
27			
28			
29	Data monitoring:	#21b Description of any interim analyses and stopping guidelines,	n/a
30	interim analysis	including who will have access to these interim results and	
31		make the final decision to terminate the trial	
32			
33			
34	Harms	#22 Plans for collecting, assessing, reporting, and managing	20-21 (NEQ)
35		solicited and spontaneously reported adverse events and other	
36		unintended effects of trial interventions or trial conduct	
37			
38			
39			
40	Auditing	#23 Frequency and procedures for auditing trial conduct, if any,	n/a
41		and whether the process will be independent from	
42		investigators and the sponsor	
43			
44			
45	Ethics and		
46	dissemination		
47			
48			
49	Research ethics	#24 Plans for seeking research ethics committee / institutional	3, 27
50	approval	review board (REC / IRB) approval	
51			
52			
53	Protocol amendments	#25 Plans for communicating important protocol modifications	27
54		(eg, changes to eligibility criteria, outcomes, analyses) to	
55		relevant parties (eg, investigators, REC / IRBs, trial	
56		participants, trial registries, journals, regulators)	
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1	Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11-12, 27
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6	Consent or assent:	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7	ancillary studies			
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11	Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	27, 28
12				
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17	Declaration of	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	28
18	interests			
19				
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21	Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
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26	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
27	trial care			
28				
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30	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	27
31	trial results			
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38	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
39	authorship			
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42	Dissemination policy:	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	28
43	reproducible research			
44				
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46	Appendices			
47				
48	Informed consent	#32	Model consent form and other related documentation given to participants and authorised surrogates	28
49	materials			
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52	Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
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2 Attribution License CC-BY-NC. This checklist can be completed online using <https://www.goodreports.org/>, a
3 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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BMJ Open

Development, evaluation, and implementation of a digital behavioural health treatment for chronic pain: Study protocol of the multi-phase DAHLIA project

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Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Mental health
Keywords:	PAIN MANAGEMENT, MENTAL HEALTH, PUBLIC HEALTH

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Manuscripts

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4 1 **Title: Development, evaluation, and implementation of a digital behavioural**
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6 2 **health treatment for chronic pain: Study protocol of the multi-phase**
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8 3 **DAHLIA project**
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11
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34 **Word count:** 7443 (excluding title page, abstract, tables, figures, and references)

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36 **Trial Registration number:** ClinicalTrials.gov Identifier: NCT05066087; Karolinska
37 Institutet Protocol Record Dnr 2021-02437.

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39 **Version of Protocol:** 3 (28.03.2022)

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4 40 Development, evaluation, and implementation of a digital behavioural health
5 41 treatment for chronic pain: Study protocol of the multi-phase DAHLIA project
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8
9 43 **ABSTRACT**

10 44 **Introduction:** Chronic pain affects about 20-40% of the population and is linked to mental
11 45 health outcomes and impaired daily functioning. Pharmacological interventions are commonly
12 46 insufficient for producing relief and recovery of functioning. Behavioural health treatment is
13 47 key to generate lasting benefits across outcome domains. However, most people with chronic
14 48 pain cannot easily access evidence-based behavioural interventions. The overall aim of the
15 49 DAHLIA project is to develop, evaluate, and implement a widely accessible digital behavioural
16 50 health treatment to improve well-being in individuals with chronic pain.

17 51 **Methods and analysis:** The project follows the four phases of the mHealth Agile Development
18 52 and Evaluation Lifecycle: (i) *development and pre-implementation surveillance* using focus
19 53 groups, stakeholder interviews, and a business model; (ii) iterative *optimisation studies*
20 54 applying single case experimental design (SCED) method in 4-6 iterations with n=10 patients
21 55 and their health care professionals per iteration; (iii) a two-armed *clinical randomized*
22 56 *controlled trial* enhanced with SCED (n=180 patients per arm); (iv) and interview-based *post-*
23 57 *market surveillance*. Data analyses include multilevel modelling, cost-utility, and indicative
24 58 analyses.

25 59 In October 2021, inter-sectorial partners are engaged and funding is secured for four years. The
26 60 treatment content is compiled and the first treatment prototype is in preparation. Clinical sites
27 61 in three Swedish regions are informed and recruitment for phase one will start in autumn 2021.
28 62 To facilitate long-term impact and accessibility, the treatment will be integrated into a Swedish
29 63 health platform (www.1177.se), which is used on a national level as a hub for advice,
30 64 information, guidance, and e-services for health and healthcare.

31 65 **Ethics and dissemination:** The study plan has been reviewed and approved by Swedish
32 66 Ethical Review Authorities. Findings will be actively disseminated through peer-reviewed
33 67 journals, conference presentations, social media, and outreach activities for the wider public.

34 68 **Trial Registration number:** ClinicalTrials.gov Identifier: NCT05066087; Karolinska
35 69 Institutet Protocol Record Dnr 2021-02437.

36 70 **Keywords:** chronic pain; digital; behavioral health; protocol; intervention; single case
37 71 experimental design; diary; implementation; randomized controlled trial
38 72

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3 73 **Strength and limitations of the study**
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- 5 74 • An agile, iterative, and data-driven process is ideally suited to navigate the complex
6 75 challenges faced during the development, evaluation, and implementation of a digital
7 76 behavioural treatment.
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10 77 • Executing the project with a multi-disciplinary, inter-sectorial, and international team
11 78 brings expertise and insights from complementary views together.
12
13 79 • Patients and different stakeholders, such as health care professionals, managers and
14 80 digital developers, are involved in the project from the start, thus ensuring that
15 81 individual needs to use and/ or promote the treatment can be met.
16
17 82 • The richness of methodologies combining traditional clinical trial evaluations on the
18 83 population level, fine-graded momentary data collection on the individual level, explicit
19 84 focus on cost-effectiveness, and determinants of implementation allows for a treatment
20 85 evaluation from all angles.
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22 86 • Due to the complexity and step-wise approach of this project, problems (e.g., delays in
23 87 recruitment) in earlier phases might negatively affect the execution of later phases, thus
24 88 calling for mitigation strategies to address potential delays.
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89 INTRODUCTION

90 Chronic pain (CP) affects 20 to 40 % of the adult population¹. Due to the COVID-19 pandemic,
91 prevalence rates may increase further since CP can develop as a post-viral syndrome, from
92 insufficient risk factor management during lockdown (e.g., inactivity, stress), or from
93 accumulated unmet rehabilitation needs in overburdened rehab services^{2 3}. Chronic pain
94 impacts not only individuals' daily activities and overall quality of life, but also social and
95 working contexts⁴. Thus, considerable direct and indirect health-related costs are associated
96 with CP⁵ and it represents a major issue for health care services and society at large.

97 A consensus exists regarding the importance of a holistic perspective integrating social,
98 psychological, and biological factors of CP to accommodate this condition and its implications,
99 and to guide interventions aimed at providing support⁶. Considering the typical complexity of
100 CP, pharmacological treatment alone is usually insufficient in producing sustained relief and
101 recovery of functioning⁷. Instead, management plans should target key behavioural, emotional,
102 cognitive, and social factors in everyday functioning and quality of life⁸.

103 To generate general and lasting benefits across outcome domains, person-centred,
104 behavioural health interventions are critical. The necessity to match the pain treatment with
105 specific needs of each patient has been the focus of discussion for the past decades⁹. Existing
106 evidence supports methods that stem from cognitive behavioural frameworks¹⁰, including the
107 fear-avoidance model of pain and disability¹¹ and the psychological flexibility model, the
108 model underlying acceptance and commitment therapy (ACT)^{12 13}. In this type of treatment,
109 the objective is to optimize effects by individualising treatment through evidence-based
110 therapeutic procedures¹⁴. In clinical practice, face-to-face therapy dominates in effectively
111 promoting well-being in patients with CP^{7 15}. Modes of treatment delivery are evolving,
112 however, as new models of care emerge.

113 Until now and despite the empirical support, interdisciplinary treatment, including
114 behavioural interventions, are commonly not available or difficult to access for most
115 individuals with CP^{16 17}. Digital solutions aiming at promoting health, also known as eHealth,
116 appear promising to bridge this gap as they appear cost-effective, can be tailored to individual
117 needs, applied in everyday life, and used at the patients' convenience¹⁸. Particularly in light of
118 the COVID-19 pandemic, distance approaches are gaining more attention in the management
119 of CP¹⁹. However, the development and implementation of evidence-based digital
120 interventions face challenges.

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3 121 Innovative digital treatments require an accurate scientific evaluation to ensure clinical
4
5 122 effectiveness. As it is still seen as the “gold standard”, digital interventions for CP are often
6
7 123 assessed through research-led randomized controlled trials (RCTs)^{18 20 21}. However, a call for
8
9 124 real-world and n-of-1 evaluations of efficacy and safety of individual assessment and treatment
10
11 125 approaches is also being heard²². Compared to RCTs, n-of-1 study designs utilise repeated
12
13 126 measurements to provide a more fine-graded, time- and context-sensitive picture of individual
14
15 127 trajectories and pattern, thus allowing to evaluate effects at the within-person level²³.

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17 128 Moreover, it has been shown that eHealth innovations purely originated from an
18
19 129 academic context are rarely sustainably implemented into health care practice due to a lack of
20
21 130 infrastructure, funding, and time²⁴. To avoid research waste when creating new eHealth
22
23 131 solutions, a strong user-centred design and focus on implementation is suggested^{25 26}. A
24
25 132 framework that combines the scientific rigor of traditional research methods with a rapid and
26
27 133 iterative digital product development approach is needed. Then, the development of an
28
29 134 evidence-based and user-friendly digital behavioural treatment is facilitated that is
30
31 135 implementation-ready for applied health care.

32
33 136 The ‘mHealth agile development and evaluation lifecycle’ (Figure 1) is a framework
34
35 137 created to promote the development of evidence-based, effective, and sustainable digital
36
37 138 solutions²⁷. This framework emphasises practicality, flexibility, rapid evaluation, and the
38
39 139 possibility to adjust protocols to meet technological changes and insights that emerge as part
40
41 140 of the process. Therefore, Wilson, et al. ²⁷’s framework will guide the present project.
42
43 141 Additionally, the framework commissioned by the Medical Research Council and National
44
45 142 Institute for Health Research for developing and evaluating complex interventions will inform
46
47 143 the processes^{26 28}. By applying these perspectives, the ultimate goal to develop, evaluate, and
48
49 144 implement an effective and accessible behavioural treatment will be reached, thus improving
50
51 145 health in individuals with CP across Sweden.

52
53 146 --- FIGURE 1 NEAR HERE---

54 55 147 **Research objectives**

56
57 148 The overall aim of this project is to develop, evaluate, and implement a digital behavioural
58
59 149 health treatment to improve well-being in individuals with CP. The treatment will be integrated
60
150 into a nationally available health care web-platform, which facilitates large scale evaluations,
151 further development, dissemination, and long-term use in clinical practice across Sweden.
152 Within the project, we will (i) develop a prototype of the digital treatment matching the needs
153 of individuals with CP, using focus groups to assess user demands, and discuss possible

1
2
3 154 treatment structures and content, (ii) pilot the treatment in several iterations to evaluate its
4
5 155 feasibility and acceptability, efficacy, and individual change processes by combining intensive
6
7 156 (Single case experimental design (SCED)) and extensive methods; (iii) conduct a two-armed
8
9 157 RCT enhanced with SCED to assess the clinical effectiveness, cost-effectiveness, and long-
10
11 158 term effects compared to treatment as usual (TAU) on a between- and within-person level; and
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13 159 (iv) identify barriers and facilitators, and monitor the implementation process of the treatment,
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15 160 through a business model and stakeholder interviews.
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For peer review only

161 **METHODS AND ANALYSIS**

162 Following the mHealth agile lifecycle²⁷, the DAHLIA (Acronym: Digital behaviourAI HeaLth
163 for chronIc pAin) project consists of an identification phase 0 and four main phases:
164 Development, optimisation, clinical trial evaluation, and post-market surveillance (See
165 overview of the DAHLIA project in Figure 2). Phase 1 includes two studies: focus groups with
166 patients and health care professionals (HCPs) to develop the treatment prototype (Study 1), and
167 stakeholder interviews to prepare for the implementation process by creating a business model
168 and identifying of barriers and facilitators (Study 2). Phase 2 (Optimisation) aims at optimising
169 the treatment and entails 4-6 iterations to test and gradually improve the prototype in a data-
170 driven manner (Study 3). Phase 3 consists of a large-scale clinical trial to evaluate the digital
171 treatment in comparison to TAU in a two-armed RCT enhanced with SCED (Study 4). Finally
172 in phase 4, a post-market surveillance is conducted using interviews with stakeholders from
173 different Swedish regions, also presenting lessons-learned (Study 5). Each phase may inform
174 and alter subsequent phases, in line with the agile approach. Project planning started in January
175 2020, data collection takes place since end of 2021, and the anticipated completion of the
176 project is 2025. Details of the studies are described in the following paragraphs.

177 --- FIGURE 2 NEAR HERE ---

178 **Project Identification**

179 **Involvement of inter-sectorial partners and international collaborators**

180 This project is a collaboration between academia, health care, and industry. The academic
181 partners come from seven universities in four countries (Sweden, Belgium, the Netherlands,
182 and the U.S.). The researchers contribute to the project with their scientific and clinical
183 experience in developing and evaluating digital treatments, implementation sciences, cost-
184 utilisation analysis, CP and related health issues, and the SCED method. The DAHLIA
185 treatment will be designed within the www.1177.se platform in collaboration with health care
186 developers and digital designers in Region Kalmar and supported by the industry partner Inera,
187 who is responsible for the maintenance of the platform. The health care partners currently
188 represent three of the 21 regions in Sweden, and include primary care centres in Region
189 Kalmar, the Pain Clinic at Capio St. Göran Hospital, Region Stockholm, and the Rehabilitation
190 centre in Region Örebro.

191 **Personas as early user research**

192 Personas are typical patient- or user-profiles illustrating the target group of a treatment or
193 product and can be useful in the development of digital interventions to communicate user
194 needs to the development team^{29 30}. By giving a narrative and name, personas facilitate a more
195 concrete discussion of patient needs, and to what extent the treatment might match those
196 needs³¹. In the DAHLIA project, three distinct patient personas evolved in an online workshop
197 and were edited over several months until the project partners were developed in a stepwise
198 manner. The personas originated from patient interviews in a previous study²⁹, and discussed
199 in an online workshop to assess the relevance for the DAHLIA project. The personas were then
200 adjusted based on factors identified in research³²⁻³⁴, other personas used in digital development
201 projects region Kalmar, and input from the clinical researchers (RW, IF, KB, LMcC, SP). The
202 personas were continuously edited over several months until the project partners agreed on the
203 final versions. The categories for each persona are: (i) *personal information*, including
204 employment, education, family, background and social context, social support, and living area;
205 (ii) *patient pain profile*, including pain problem, consequences, pain behaviour, and attitude to
206 treatment; (iii) *health care and treatment*, including contact with health care, comorbidities,
207 and medicine; and (iv) *personal needs and goals*, specifically related to the treatment. Figure
208 3 illustrates one of the personas used in the DAHLIA project.

209 --- FIGURE 3 NEAR HERE ---

210 During the early development of the DAHLIA treatment prototype (version 1.0), and
211 prior to patient involvement, personas were used to ensure that relevant characteristics and
212 contextual factors were considered³⁵. The personas were presented at the start of treatment
213 workshops to discuss, for instance, if and how the treatment content and structure fit the
214 personas' characteristics and met their needs. Potential problems for a persona in relation to
215 treatment elements were identified, resulting in further discussions and consensus-based
216 adjustments.

217 **Guiding principles in the development process of the DAHLIA treatment**

218 When developing and evaluating complex interventions, one might either rely on already
219 existing treatments or adapt these to the context, or chose to build a new treatment based on
220 research evidence and theory of the problem²⁶. In the present project, the latter was chosen for
221 the following reasons. Firstly, the initiative for this project originated from the Swedish Region
222 Kalmar identifying the need for a digital treatment for chronic pain patients, which resulted in
223 a collaboration with the research team. Furthermore, contextual factors such as organisational

1
2
3 224 aspects, technical systems, and licencing agreements define the conditions for in this project.
4
5 225 Finally, by creating a new treatment together with stakeholders (i.e., managers, regional
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7 226 developers, therapists, patients) and building on an existing digital structure (www.1177.se),
8
9 227 the digital treatment can accommodate all identified requirements.

10 228 The following process was therefore followed to create the new treatment: Four three-
11
12 229 hour online workshops took place between June 2020 and June 2021 to discuss the theoretical
13
14 230 framework, conceptual model, and treatment components. Project partners presented their
15
16 231 previous work related to behavioural treatment approaches and conferred on the guiding
17
18 232 principles for the prototype development. The group reached consensus on using learning
19
20 233 theory³⁶ as the theoretical framework for assessment and treatment. Furthermore, it was agreed
21
22 234 that the fear-avoidance model¹¹ and psychological flexibility model^{10 14 37} should be used as
23
24 235 conceptual models for the DAHLIA treatment. Conclusively, the primary objective of the
25
26 236 treatment is to increase resilience to pain and distress by promoting and training behavioural
27
28 237 skills of relevance to the individual's functioning and well-being. Furthermore, a self-guided
29
30 238 micro-learning format³⁸ was chosen, including brief and frequent sessions (micro-sessions),
31
32 239 delivered digitally and accessible via a smartphone or desktop computer (www.1177.se; details
33
34 240 see 'Stakeholder interviews (Study 2)).

35 241 Based on the theoretical framework and conceptual models, values-oriented exposure
36
37 242 is considered to be the core procedure. Exposure implies the use of systematic contact with
38
39 243 negative experience such as pain and feelings of emotional distress that promotes avoidance,
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41 244 in a way that reduces their adverse influence and produces more flexible, varied, and engaged
42
43 245 patterns of behaviour. Essentially, the function of exposure is to reduce negatively reinforced
44
45 246 behaviour focused on alleviating unwanted experiences, in favour of positively reinforced
46
47 247 behaviour focused on approaching goals in daily life. Exposure is enabled by several
48
49 248 behavioural processes, such as identifying life values and noticing own thoughts and emotions,
50
51 249 known as defusion (OPEN), flexible attention to the present (AWARE), and the building of
52
53 250 extended habits of engagement (ACTIVE)¹⁰.

54 251 At the end of Phase 0, the following is envisioned: The DAHLIA treatment will run
55
56 252 over six weeks and includes four self-guided micro-sessions per week. Each session will
57
58 253 include a set of key elements (see Figure 4). The extent to which each of these elements will
59
60 254 be included in the session can vary. It should be noted that due to the agile process, data-driven
255 decisions might result in changes to this suggested structure.

256 --- FIGURE 4 NEAR HERE---

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3 257 A chat function will enable patients to connect with their health care professionals
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5 258 (HCPs, see details section ‘participants and recruitment’) for additional guidance,
6
7 259 asynchronous feedback, and further instructions. The role of the HCP is to encourage and
8
9 260 motivate patients to remain in the program and intervene in case the individual situation
10
11 261 worsens. At the start of the treatment, a specific weekday will be agreed on, during which the
12
13 262 HCP replies to the patient’s message. Potentially, the reply could also be a chat message, a
14
15 263 phone call, or a video call. The contact with the HCP will take place once a week, with a
16
17 264 minimum of six individual interactions between the HCP and patient. HCPs will receive
18
19 265 training, a manual, and supervision to provide the treatment.

20
21 266 Furthermore, patients will be prompted to fill in a pre-scheduled digital diary twice a
22
23 267 day. The digital diary has the purpose to enable self-monitoring for increased self-awareness
24
25 268 of own behaviours, emotions, and routines, and thus enhanced orientation towards values and
26
27 269 goals³⁹, and data collection to gain insight into the individual change processes and effects of
28
29 270 the treatment in the context of the SCED. The full list of the daily diary items can be found in
30
31 271 the ‘Individual change processes’ section.

32
33 272 After the main six-week intervention period, the treatment also entails booster-sessions
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35 273 delivered through the www.1177.se web-platform after two and four months. The participants
36
37 274 get invited via SMS or emails to revisit the web-platform where they can engage in short
38
39 275 behavioural exercises. Booster sessions are suggested in other contexts to support long-term
40
41 276 behavioural changes⁴⁰ and reinforce patients learned coping strategies. Figure 5 summarises
42
43 277 the DAHLIA treatment components.

44
45 278 --- FIGURE 5 NEAR HERE ---

46 279 **Participants and recruitment**

47
48 280 In the DAHLIA project, participants will be people who either use or deliver the digital
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50 281 treatment, or who facilitate the treatment implementation. Thus, study participants are (i)
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52 282 patients with CP, (ii) HCPs treating patients with CP, (iii) health care managers, (iv) developers
53
54 283 of the www.1177.se web platform, (v) other stakeholders identified in the process (e.g., policy
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56 284 makers, representatives from patient organisations). Health care professionals will be licensed
57
58 285 psychologists or psychotherapists trained in cognitive behavioural therapy. Health care
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60 286 managers, developers, and other stakeholders need to be directly or indirectly connected with
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288 the treatment (e.g., decision-making on an organisational level; technical support etc.), but no
other requirements apply.

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2
3 289 Patients are eligible for inclusion if they: are older than 18 years of age; report a pain
4 290 duration of ≥ 3 months; are able to communicate in Swedish; and have access to a computer,
5 291 smartphone, and internet in their home environment. The exclusion criteria are: injury or illness
6 292 that require immediate assessment and treatment, or is expected to progress significantly during
7 293 the next 6 months; unstable medication (based on self-report: changes in medication during the
8 294 past 3 months or expected within the next 3 months that could influence well-being and
9 295 functioning substantially, such as opioids, anti-epileptic drugs, antidepressants); previous CBT
10 296 treatment (including ACT) during the past 6 months; severe psychiatric co-morbidity (for
11 297 instance, high risk of suicide). For study 1 (focus groups), only the exclusion criteria “severe
12 298 psychiatric co-morbidity (for instance, high risk of suicide) will be applied as long-term health
13 299 aspects are not expected to cause practical or ethical issues.

22 300 Information regarding the DAHLIA project and specific sub-studies will be provided
23 301 to the clinics, including detailed instructions for eligibility. Regions recruiting patients are
24 302 Kalmar, Stockholm, and Örebro. Additional regions have expressed interest in participating
25 303 and recruitment might be extended. Patients will be approached via their health care centres
26 304 and once patients have expressed interest in study participation, a formal eligibility check will
27 305 be conducted. Potential participants will be screened at their respective clinic via a face-to-face
28 306 or online meeting by their treating care professionals, including psychologist and pain
29 307 physicians. A short interview will be conducted to confirm eligibility and ensure that none of
30 308 the exclusion criteria are met. Informed consent is then obtained from all participants prior to
31 309 enrolment in the study. Sociodemographic and pain-descriptive information will be collected
32 310 from all participants including age, sex, level of education, occupation, location, level, and
33 311 duration of pain, pain diagnosis (if applicable), and approaches to relief pain (e.g., medication,
34 312 heat, physiotherapy).

313 **Phase 1: Development**

314 **Focus groups (Study 1)**

315 The aim of this study is to (i) identify the needs of patients and HCPs and (ii) match the
316 treatment content to their needs. At least three focus groups will be conducted in autumn 2021,
317 one with HCPs (i.e., psychologists/ psychotherapists trained in CBT) and two with patients.
318 Per focus group, 6-8 participants will join⁴¹. An attempt will be made to recruit a heterogeneous
319 group of patients in terms of such characteristics as pain condition, sex, and socio-economic
320 background. The focus groups will be held online and take 90-120 minutes. A semi-structured

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2
3 321 guide inspired by Gruters, et al.⁴² will be followed. In addition to a general discussion around
4
5 322 health and individual needs at the start, the focus group leader (i.e., research assistant and
6
7 323 clinical coordinator) will ask participants to reflect on the design, set-up, content, and
8
9 324 prospective feasibility of the DAHLIA treatment (details see Appendix 1). The group
10
11 325 conversations will be audio- and video-taped. Field notes will provide further insight into
12
13 326 relevant cues and observations.

14 327 The recordings will be transcribed verbatim and the data analysis will be performed by
15
16 328 two independent researchers. The information for the patient groups and HCP group will be
17
18 329 analysed separately. A combination of inductive and deductive content analysis will be used.
19
20 330 First, the deductive approach will determine the themes emerging from the semi-structured
21
22 331 guide: (i) health needs and determinants to live well with CP, and (ii) feedback on the DAHLIA
23
24 332 treatment. Then, an indicative analysis will be performed to identify categories within the
25
26 333 themes. The transcript will be read carefully and open coding will be used. A consensus
27
28 334 meeting with a third researcher will be conducted as a final step. This approach has been
29
30 335 described previously and appears valid to answer the research question^{42 43}. The results from
31
32 336 the focus groups will be integrated into the treatment prototype (version 2.0).

337 **Stakeholder interviews (Study 2)**

338 The aim of this study is to develop a preliminary business model for the digital behavioural
339
340 treatment and identify barriers and facilitators of the prospective implementation process. An
341
342 explicit focus on implementation and economic aspects early during treatment development
343
344 has been recommended^{44 45}. Particularly, business modelling in the context of eHealth
345
346 technologies can help to create a set of success factors that will influence uptake, sustainability,
347
348 and effectiveness⁴⁶. A business model is part of the implementation strategy and also presented
349
350 a foundation for conversations with users and stakeholders regarding the value and purpose of
351
352 an eHealth technology⁴⁶. Moreover, to build the knowledge base across the multiple studies
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354 and settings, the consolidated framework for implementation research (CFIR)⁴⁷ will be used.
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356 The CFIR has five major domains: intervention characteristics, outer setting, inner setting,
357
358 characteristics of the individuals involved, and the process of implementation. It is utilized as
359
360 part of the analysis, as explained below.

361 As a first step, a preliminary version of the business model canvas was filled in by the
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363 research team (SB, SJ, RW, HC). As suggested by Osterwalder and Pigneur⁴⁸ ‘a business
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365 model describes the rationale of how an organization creates, delivers, and captures value’
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367 (p.14) and demonstrates the logic of how a company or organisation intends to generate profit

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2
3 354 for a service or product. The nine blocks of the business model cover four areas of a business:
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5 355 customers, offers, infrastructure, and financial viability. Figure 6 presents the template of the
6
7 356 business model canvas and short definitions for each segment, including example aspects
8
9 357 relevant for the DAHLIA project.

10 358 --- FIGURE 6 NEAR HERE---

11
12 359 In the present study, the treatment will be integrated into the national public health care
13
14 360 website (www.1177.se), using the digital platform for behavioural health ('Stöd och
15
16 361 Behandling'). This digital platform is free from commercial interests, maintained by Inera,
17
18 362 which is owned by the county councils and regions. The general aim of this national website is
19
20 363 to increase access to healthcare, strengthen the position of the patient, and contribute to
21
22 364 improved public health. The website (www.1177.se) contains health care information,
23
24 365 inspiration, and e-services. Each of the 21 regions in Sweden is responsible for coordinating
25
26 366 activities and services provided on www.1177.se, which are conducted by own staff or
27
28 367 contracted providers. Through a national network, providers and regions can cooperate and
29
30 368 share licenses for services.

31
32 369 The business model will be discussed and refined as part of the stakeholder interviews.
33
34 370 Currently identified stakeholders are software developers, HCPs, and health care managers. A
35
36 371 semi-structured guide inspired by a previous study on eHealth implementation⁴⁹ will structure
37
38 372 the interviews and gather information on gatekeepers, barriers, and facilitators for prospective
39
40 373 dissemination and use. Questions are tailored to the different stakeholders and include, for
41
42 374 example, '*If/how is the interventions' content updated?*', '*Who is responsible/ involved in the*
43
44 375 *maintenance of the intervention?*', '*What could facilitate/ hinder the implementation process?*',
45
46 376 and '*Do you think this intervention has the potential to become successful in your care*
47
48 377 *facility?*'. The full guide can be seen in Appendix 2. As part of the agile process, the guide may
49
50 378 be adjusted based on information collected during the interviews and tailored to additional
51
52 379 stakeholders including policy makers or representatives from patient organisations.

53
54 380 A minimum of eight interviews will be conducted and snow-ball sampling will identify
55
56 381 additional participants that can inform the process. Interviews will be conducted until data
57
58 382 saturation is achieved and no new topics seem to emerge. The interviews will be executed
59
60 383 online, take 60-90 min, and the conversation will be recorded. The qualitative data will be
384
385 transcribed. Then, a qualitative thematic analysis will be performed⁵⁰ with statements related
386
387 to potential barriers and facilitators. An inductive approach to group the information will
applied in order to best scope the replies and map categories onto the CFIR domains⁴⁷ as
previously described.

1
2
3 388 Finally, implementation strategies matching the emerging topics will be formulated⁵¹.
4
5 389 Together with the business model, these two elements represent the implementation plan for
6
7 390 the DAHLIA project. Findings from this study may furthermore influence the post- market
8
9 391 surveillance (Study 5, see details below).

10 11 392 **Phase 2: Optimisation (Study 3)**

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13 393 The aim of the optimisation phase is to pilot the treatment and improve it through an iterative
14
15 394 data-driven process using small patient cohorts. The primary objective is to determine the
16
17 395 treatment feasibility and acceptability, and the secondary objectives are to examine individual
18
19 396 change processes, and efficacy across iterations on a group-level. The general procedures
20
21 397 include the eligibility check, and four assessment periods: baseline, main treatment period,
22
23 398 post-intervention, and 3- and 6-months follow-ups. Results from each iteration will be
24
25 399 integrated into the subsequent iteration, then tested again, until satisfaction is reached and no
26
27 400 new major issues seem to emerge. In the optimisation studies, different methodologies will be
28
29 401 combined namely momentary data collection using digital diaries, retrospective questionnaires,
30
31 402 and semi-structured interviews. The latter will be conducted by a research assistant, while the
32
33 403 diaries and questionnaires will be completed online. Figure 7 provides an overview of the
34
35 404 procedure in relation to the research objectives.

36
37 405 --- FIGURE 7 NEAR HERE ---

38
39 406 In total, 40 to 60 patients and their treating HCPs will be included, with n=10 patient-
40
41 407 HCP dyads each iteration. Four iterations have been seen as sufficient in a previous study to
42
43 408 optimise a digital treatment⁵², therefore, a minimum of four iterations will be conducted in the
44
45 409 DAHLIA project. In accordance with the agile approach, additional iterations may be
46
47 410 performed if deemed necessary. The rationales for the approaches and methodological details
48
49 411 are described below.

50 51 412 **Feasibility and acceptability**

52
53 413 The mixed-method procedure to evaluate the feasibility and acceptability of the treatment
54
55 414 includes self-reports, interviews, and technical data. Short self-reports will be collected after
56
57 415 each micro- and booster-session. Specifically, patients will be asked to rate the micro-session
58
59 416 on its usefulness, enjoyment, and comprehension (*'I experienced today's session as helpful/
60
61 417 enjoyable/ understandable.'*, rated on a 7-point numerical scale from 1=not at all, to 7=very
62
63 418 much).

1
2
3 419 Furthermore, at the end of the main intervention period, interviews will be conducted
4
5 420 following a semi-structured guide to assess the participants' general experience and different
6
7 421 treatment components, specifically the diary, micro-sessions, and chat function. Questions are
8
9 422 first rated on a 7-point numeric scale and participants are then encouraged to elaborate on their
10
11 423 response with further details, if possible. Examples of questions are '*Did the intervention*
12 424 *hinder your daily occupation?*', '*Were the micro-sessions difficult or unclear?*', '*Did you*
13 425 *experience the digital diary as burdensome?*', or '*Would you recommend the treatment to a*
14 426 *friend?*' (details see Appendix 3). This guide is based on other feasibility studies^{52 53} and
15
16 427 tailored to the DAHLIA treatment components. The HCPs will also be interviewed using a
17
18 428 guide that follows the same structure (i.e., numeric scale and open elaborations), but the
19
20 429 specific questions will be informed by the focus groups (study 1).

22 430 Additionally, technical data generated from the www.1177.se website will be collected.
23
24 431 These data include time and frequency of log-ins, duration of engagement with the treatment,
25
26 432 and use of components. Technical data will be used to describe the overall use and adherence,
27
28 433 and allows mediation analyses to determine the influence of engagement rates on treatment
29
30 434 outcomes.

31 435 Data from the feasibility assessments will be analysed using descriptive statistics and
32
33 436 qualitative synthesis to identify trends. The results will be presented reflecting the two core
34
35 437 variables from the Technology Acceptance Model (TAM): 'Perceived Usefulness' and
36
37 438 'Perceived Ease of Use'⁵⁴. After each iteration, the insight gathered will be fed back to the
38
39 439 developers and integrated to gradually improve the feasibility and acceptability through data-
40
41 440 driven adjustments of the treatment. Next to the qualitative self-report, quantitative ratings of
42
43 441 the treatment components, and technical usage data, outcome measure to determine the
44
45 442 feasibility and acceptability also include flow of participant recruitment and retention (i.e.,
46
47 443 number of participants that were approached, signed informed consent, and started/ completed
48
49 444 the treatment), treatment-fidelity rates (i.e., post-treatment therapist self-report "*Was the*
50
51 445 *treatment delivered as planned?*"), treatment compliance (i.e., indicated through log-in data,
52
53 446 self-report from patients and therapists), and (reasons for) dropouts in each iteration.

52 447 **Individual change processes**

54 448 The optimisation studies implement a sequential replicated and randomized single case
55
56 449 experimental design (SCED) to gain detailed insight into within-person behavioural changes,
57
58 450 and to develop and test the DAHLIA intervention, which has been recommended in the context
59
60 451 of CP⁵⁵. In SCEDs, each case functions as their own control and changes are evaluated

452 comparing levels of the outcome variables across different phases (e.g., baseline phase ‘A’ and
 453 treatment phase ‘B’)⁵⁶. The methodology aims to demonstrate cause-effect relationships
 454 between the treatment (independent variable) and the target behaviour (dependent variable)⁵⁷.

455 When planning a SCED study, the Risk of Bias in N-of-1 Trials (RoBiNT) Scale, a
 456 critical appraisal tool that evaluates the methodological quality of intervention studies using
 457 single-case methodology, can be followed as guidance^{57 58}. The design decision made in the
 458 present study were based on this appraisal tool to ensure a scientifically robust approach. Table
 459 1 provides details on the design elements.

460

461 Table 1. Methodological SCED approach of the DAHLIA study based on the RoBiNT Scale.

Item	RoBiNT Scale	SCED details, per optimisation iteration (<i>anticipated points</i>)
INTERNAL VALIDITY SUBSCALE		
1	Design	A replicated randomised AB-design with 10 x A-B (total of 20 phases), providing the opportunity to observe the experimental effect 10 times. (2 points)
2	Randomisation	The start of the treatment phase and therefore length of baseline phase will be determined randomly for each participant, with the baseline phase lasting between 5 to 10 days. This means that the treatment phase will start on any day between the 6 th and 11 th assignment. (2 points)
3	Sampling behaviour during all phases	The baseline phase will last at least 5 days, with twice daily sampling, resulting in 10 data points or more (phase A) (assuming 100% compliance to diary). The treatment phase will run over 6 weeks, with twice daily sampling on at least 4 days per week (6 weeks x 4 days x twice daily sampling), resulting in 48 data points or more (phase B) (assuming 100% compliance to diary). Even if the compliance rate should be lower, the amount of data points will lie >5 data points. (2 points)
4	Blinding of participants and HCP delivering the treatment	Blinding of the participant and practitioner is not feasible in the DAHLIA project. The behavioural treatment is delivered through a web-platform independently of the HCP; however, the HCP provides weekly, tailored support in addition to the online treatment. Neither the participant nor the HCP are blinded. (0 points).
5	Blinding (masking) of assessors	Patients complete self-report diaries and are not blinded to treatment phase, therefore, not independent of the therapy process. (0 point)
6	Inter-rater agreement	The measure of the target behaviour is a subject measure relying on self-reports from the digital diaries. (0 points)
7	Treatment adherence	The treatment is delivered through a web-platform following a standardized approach. Adherence to treatment (%) is calculated using digital log-in data . (2 points)
EXTERNAL VALIDITY AND INTERPRETATION SUBSCALE		
8	Baseline characteristics	A short interview by an HCP as part of the eligibility check will be conducted. Furthermore, a case formulation including information on age, sex, aetiology of CP, and severity of CP will be presented when presenting the results; this information will be based on a baseline assessment (online self-report). (2 points)
9	Setting	Information on the general location (Swedish region, hospital/ pain clinic) will be provided; however, the participant will engage with the online treatment in their everyday life, and therefore, it will not be possible to include details about the specific environment. (1 point)
10	Dependent variable (target behaviour)	Table 2 provides an overview of all diary items, which are scores on a 7-point Likert-Scale, except from the pain level item (0-100). Process outcome measures: 5 items on psychological (in)flexibility (see Table 2), 2 items on pain self-efficacy, 1 item on pain avoidance. Primary outcome measures: 1 item on pain level, 1 item on pain interference, 1 item on pain catastrophizing. Secondary outcome

		measures: 3 items on sleep, 2 items on affect, 1 item on stress, 1 item on fatigue. (2 points)
11	Independent variable (treatment)	A detailed description of the DAHLIA treatment is given above, including the treatment content , and number, duration, and frequency of sessions . (2 points)
12	Raw data record	Ten cases will be recorded (4-6 iteration with n=10 participants per iteration). Raw data will be presented with a data point for each diary entry. (2 points)
13	Data analysis	Data will be analysed and reported for each participant individually. Structured visual analysis, effect size measures and a randomization test wrapper for multilevel models will be applied. (2 points).
14	Replication	Ten participants will be included (per optimisation iteration). Across all iterations, data from n=40-60 participants will be available. (2 points)
15	Generalization	Patients will be heterogeneous in their characteristics. Furthermore, retrospective self-reports will be completed by each participant pre-post treatment , including two FUs (details see Table 3). (1 point)

462

463 Under the condition that all choices can be executed as intended, the internal validity
 464 of this SCED study will reach 8/14 points, and the external validity will reach 14/16 points.
 465 The total interpretation score will be 22/30 points. This score indicates a moderate
 466 methodological rigour⁵⁹.

467 Target behaviours will be assessed via self-reports collected through a digital diary.
 468 This diary will be prompted through the SMS function of REDCap, or a smartphone application
 469 (e.g., www.mpath.io). Both data collection methods will be piloted with participants to ensure
 470 that the diary works reliably. Participants will be prompted to complete the diary twice daily
 471 (for details see Table 2). Proposed diary items are based on traditional questionnaires and diary
 472 studies⁶⁰, and were chosen as they assess relevant aspects in the context of CP. More
 473 specifically, sleep items are based on the Insomnia Severity Index⁶¹, mood, stress, and fatigue
 474 items are adapted from previous digital diaries studies⁶⁰, psychological (in-) flexibility items
 475 (experiential avoidance/ acceptance; lack of contact with present moment/ present moment
 476 awareness; self as context/ context; (de-)fusion; (lack of contact with) values); inaction/
 477 committed action) are based on Multidimensional psychological flexibility inventory⁶², the
 478 pain level item is based on a Pain Rating Scale⁶³, pain catastrophizing item are based on the
 479 Pain Catastrophizing Scale⁶⁴, the pain avoidance item is based on the Psychological
 480 Inflexibility in Pain Scale⁶⁵, pain interference categories are based on the Brief Pain Inventory
 481 Scale⁶⁶, and pain self-efficacy items are based on the Pain Self-Efficacy Questionnaire⁶⁷.

482 Generally, items should be short and easily to answer quickly⁶⁰. The order of the items
 483 will be the same in each prompt to allow participants to get used to the questions, minimise
 484 time to complete the diary, and thus limit interference with their daily flow. The reliability,
 485 validity, and sensitivity of the items will be explored through pilot studies and as part of the
 486 optimisation studies using suggested statistics (e.g., P-technique factor analysis). Idiosyncratic

487 items might also be discussed with patients, in line with the agile approach, to improve validity
 488 and potentially patient engagement and ownership. Based on user-input, scientific evidence,
 489 and insight gained, diary items might be optimised and adjusted, and any adjustments made
 490 will be reported in prospective publications.

491

492 Table 2. Proposed daily diary items.

LUNCH/ EVENING DIARY		
Instructions (Availability to fill out: Lunch diary 12-14h, evening diary 18-20h)	LUNCH: Hello & welcome to your digital diary! Please reflect on last night and this morning, and rate the following statements. Self-reflections can help to understand your daily routines and needs better. Let's get started. EVENING: Welcome back to your daily diary. Please take 2-3 minutes to reflect on this afternoon.	
Construct	Item	Answering scale
Last night, ...		
1 Sleep ¹	... I had problems falling asleep.	7-point numeric scale
2 Sleep ¹	... I had problems sleeping.	7-point numeric scale
3 Sleep ¹	... I woke up too early.	7-point numeric scale
During the morning/ During the afternoon...		
4 Positive affect	... I felt happy, energetic, at ease, or enthusiastic.	7-point numeric scale
5 Negative affect	... I felt down, irritated, depressed, or hopeless.	7-point numeric scale
6 Stress	... I felt stressed.	7-point numeric scale
7 Fatigue	... I felt tired.	7-point numeric scale
8 Experiential avoidance/ Acceptance ²	... I tried to distract myself when I felt unpleasant emotions. ... I opened myself to all my feelings, the good and the bad.	7-point numeric scale
9 Lack of contact with present moment/ Present moment awareness ²	... I did most things on "automatic" with little awareness of what I was doing. ... I was attentive and aware of my emotions.	7-point numeric scale
10 Self as content/ Self as context ²	... I criticized myself for having irrational or inappropriate emotions. ... I tried to see the larger picture, even when I was down, depressed, or hopeless.	7-point numeric scale
11 Fusion/ Defusion ²	... distressing thoughts tended to spin around in my mind like a broken record. ... I was able to notice my thoughts and feelings without getting overwhelmed by them.	7-point numeric scale
12 Lack of contact with values/ Values ²	... I didn't have time to focus on things that are important to me. ... I tried to connect with what is truly important to me.	7-point numeric scale

13	Inaction / Committed action ²	... negative feelings trapped me in inaction. ... I didn't quit working towards what is important even if it was though.	7-point numeric scale
14	Pain level	... my overall pain level was:	0 (no pain) to 10 (worst pain imaginable)
15	Pain interference	... my pain interfered with my...	7-point numeric scale <ul style="list-style-type: none"> ○ General activities ○ Mood ○ Walking abilities ○ Normal work (including housework) ○ Relations with others ○ Enjoyment of life
16	Pain catastrophizing (rumination)	... I kept thinking about how much I hurt.	7-point numeric scale
17	Pain catastrophizing (magnification)	... I felt my pain overwhelmed me.	7-point numeric scale
18	Pain catastrophizing (Helplessness)	... I was afraid that my pain would get worse.	7-point numeric scale
19	Pain avoidance	... I avoided planning activities because of my pain.	7-point numeric scale
20	Pain self-efficacy	... I could do some form of housework/ paid/ unpaid work, despite the pain.	7-point numeric scale
21	Pain self-efficacy	... I could live a normal lifestyle, despite the pain.	7-point numeric scale
22	Open question	I would also like to share this about my morning/ afternoon:	Free text
23	Treatment interaction ³	Today, I completed a treatment module.	<ul style="list-style-type: none"> ○ Yes. ○ No, because it was a 'module free day'. ○ No, but I will do it tonight. No, because: <i>free text</i>
	Instructions	LUNCH: Thank you & have a nice afternoon! EVENING: Thank you very much for taking the time to fill in your diary. Have a nice evening!	

493 7-point numerical scale ranges from 1: not at all, to 7: very much; alternatively, based on user input,
 494 a visual analogue slider scale from 0: not at all, to 100: very much might be used. Note: ¹Sleep items
 495 only as part of the morning questionnaire; ²Both psychological flexibility and inflexibility items will be
 496 tested to determine which are more feasible and suitable to use; ³Treatment interaction item only as part
 497 of the evening questionnaire.

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499 In addition to the information in Table 1, the analysis will be executed as follows. Diary
500 data have a multilevel structure because repeated measurements (level 1) are nested within
501 individuals (level 2). First, structured visual analysis will be conducted for each individual
502 separately following the four steps described in Kratochwill, et al.⁵⁶ to examine the within-
503 and between-phase patterns in respect to the effects on level, trend, variability, immediacy,
504 overlap, and consistency. Additionally, effect size measures will be calculated at the individual
505 level using standardized mean difference and Tau-U, and at a group level using the between-
506 case standardised mean difference⁶⁸. Finally, to avoid making distributional and random
507 sampling assumptions, the randomization test wrapper for multilevel models will be used to
508 synthesise the data from the whole group of cases and evaluate treatment effects⁶⁹. Scientific
509 advisors of this project will provide expertise and support in the SCED analyses. Results will
510 be presented following the RoBiNT scale and SCRIBE guideline⁷⁰.

511 **Efficacy across iterations**

512 In the optimization studies, efficacy will be determined using both intensive (SCED) as well
513 as extensive methods (retrospective self-reports from baseline, post-intervention and FUs; see
514 Figure 7). The diary and questionnaire data will be aggregated across all iterations, thus include
515 data from 40-60 participants. This approach allows to investigate the generalisability of results
516 of the SCED and evaluate treatment effects in applied research⁷¹. MultiSCED will be used for
517 the SCED data⁷².

518 The proposed retrospective questionnaires used can be separated into process, primary,
519 and secondary outcome measures (see Table 3). Additionally, negative treatment effects may
520 occur in the context of internet interventions, and therefore, need to be acknowledged and
521 systematically assessed⁷³. Negative treatment effects are here assessed post-treatment using the
522 negative effects questionnaire (NEQ), a tool with reliable and valid psychometrics⁷⁴.

523 Descriptive statistics of the retrospective questionnaires will summarize demographics
524 and pre-treatment clinical characteristics of the sample. To evaluate changes in treatment
525 outcomes over time, linear multilevel modelling (MLM) will also be used. MLM accounts for
526 repeated measures within subjects and can handle missing data, which will be addressed per
527 variable. Using a random intercept model, time will be treated as a categorical variable and pre-

528 treatment values will be specified as the reference point. Therefore, results will be interpreted
 529 as a change from pre-treatment to post-treatment and, from pre-treatment to follow-up
 530 assessments. Anchor-based methods will be applied to determine clinical significance of
 531 changes in outcome measures⁷⁵. Separate linear growth models⁷⁶ will be computed for each
 532 variable, while controlling for multiple testing. Significance level is set at Alpha (α)=0.05.

533

534 Table 3. Proposed outcome variables and tools used to assess efficacy using extensive methods.

Focus	Variables	Instrument	Supported psychometrics
Process outcome measures	Open/ Acceptance	Chronic Pain Acceptance Questionnaire (CPAQ)	Internal consistency and criterion validity (Swedish version) ⁷⁷
	Aware	5 items on, 'acting with awareness' from the Five Facets Mindfulness Questionnaire (FFMQ)	Internal consistency, reliability, and construct validity (Swedish version) ⁷⁸
	Engaged/ committed actions	(i) Valuing questionnaire; (ii) Committed action questionnaire	(i) Internal consistency and construct validity (Swedish version) ⁷⁹ ; (ii) Proven validity and reliability (Swedish version) ⁸⁰
	Psychological flexibility	Swedish translation of the Multidimensional psychological flexibility inventory (MPFI)	Convergent and discriminant validities (English version) ⁶²
	Self-efficacy	General self-efficacy scale (S-GSE)	Reliable with high internal consistency (Swedish version) ⁸¹
	Pain self-efficacy	Pain self-efficacy questionnaires (PSEQ-2)	Evidence for reliability and validity (English version) ⁶⁷ , translated into Swedish ⁸²
	Avoidance	Avoidance subscale of Psychological Inflexibility in Pain Scale (PIPS)	Internal validity and construct validity (Swedish version) ⁶⁵
Primary outcome measure	Catastrophizing	3-Item Daily Pain Catastrophizing Scale (PCS)	Recommended instrument to understand mechanisms ⁶⁴
	(Dis)ability/ pain screening	Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ)	Clinically reliable and valid (Swedish version) ⁸³
	Work ability	Work ability index (WAI)	Validated (Swedish version) ⁸⁴
	Functioning	Brief pain inventory (BPI-SF)	Reliable and valid in multiple languages (including Swedish version) ⁶⁶
Secondary outcome measure	Well-being/ depression	Patient Health Questionnaire (PHQ-9)	Satisfactory content validity and sufficient reliability (Swedish version) ⁸⁵
	Perceived stress	Perceived Stress Scale (PSS)	Internal reliability and construct validity (Swedish version) ⁸⁶
	Sleep problems	Insomnia Severity Index (ISI)	Satisfactory factor structure, internal reliability, and concurrent validity (Swedish version) ⁶¹

	Health-related quality of life	EQ-5D	Standardised measure of health-related quality of life developed by the EuroQol Group ⁸⁷
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535 **Phase 3: Clinical evaluation (Study 4)**

536 **Randomized controlled trial enhanced by SCED**

537 To determine the clinical effectiveness of the DAHLIA treatment, a RCT enhanced with SCED
 538 will be conducted. While RCTs provide estimates of between-subject treatment responses,
 539 differences in average scores between groups, they are unable to indicate specific within-
 540 subject responses. Simons, et al. ⁸⁸ apply a similar design and argue that SCED is a valuable
 541 addition to a traditional RCT design. One reason for this combined approach is that RCTs
 542 provide information on the population level, whereas SCEDs focus on the individual level.
 543 Furthermore, heterogeneity of treatment effects might remain undetected in a traditional RCT
 544 design⁸⁹. Additionally, the need for large cohorts of patients for adequate sub-group analysis⁹⁰,
 545 and a lack of feasibility to reach certain patient groups⁹¹ limits the insights from a traditional
 546 RCT. Applying SCED and multilevel modelling, even group results from small and distinct
 547 cohorts can be performed on a meta-analysis level⁸⁸.

548 Outcome measures will be the same as in the optimisation studies, including the diary
 549 items for the SCED (see Table 2), and retrospective questionnaires (see details Table 3;
 550 including NEQ post-treatment⁷⁴). A priori computations based on a power of .95, four
 551 questionnaire assessment points and a medium effect size shows that 360 participants (180 in
 552 each arm) are sufficient to generate stable findings in the analyses of treatment effects. With
 553 an estimated attrition rate of 18%, this implies that 295 participants will provide post-treatment
 554 data, which is considered adequate also for moderator/ predictor and cost-effectiveness
 555 evaluations. However, outcome measures and calculated sample size will be updated and might
 556 be modified based on iterations in the prior phase.

557 Treatment arm randomization is conducted by a research assistant following the
 558 decision on study inclusion by the HCP and after the baseline assessment (sociodemographic
 559 information, questionnaires, A-phase of SCED) is completed. Participants are randomized to
 560 the treatment arm or treatment as usual (TAU) using a block randomization strategy to ascertain
 561 equal distributions across the arms. Randomization is conducted by a local project manager
 562 who is not involved in the screening or intervention. Next, participants undergo treatment; then
 563 all participants complete the post-intervention assessment (questionnaires and 5-day digital
 564 diary). Booster-sessions will be sent to the participants in the intervention group at 2- and 4-

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3 565 months. Finally, at the 3- and 6-month follow-ups (FUs), all participants complete the
4 566 questionnaires and 5-day digital diary period. In case participants decide to discontinue the
5 567 study at any point in time, they might choose to provide a reason.

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8 568 To examine changes in process, primary and secondary outcome measures (Table 3),
9 569 linear mixed models will be conducted comparing the DAHLIA treatment to TAU. Analysis
10 570 will be performed using group as a fixed between-person factor (two levels: DAHLIA
11 571 treatment and TAU), and time as a fixed within-person variable (four levels: baseline, post-
12 572 treatment, 3-month FU, 6-month FU). The linear mixed model will estimate fixed effects
13 573 (regression slopes) for change in the intervals during (baseline to post-treatment assessment),
14 574 and after (post-treatment to 3- and 6-month FU) the treatment period. The intervals will be
15 575 entered as a categorical dummy variable (three levels). Potential confounders will be added to
16 576 the model as covariates (i.e., age, gender, pain diagnosis, pain duration). Data will be analysed
17 577 with the support of a statistician and using the latest version of SPSS. Mean change will be
18 578 reported and test of significance will be two-sided with a set alpha level of 0.05.

28 579 **Health economic evaluation**

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30 580 A short-term health economic evaluation will compare the DAHLIA treatment and the TAU at
31 581 the primary endpoint (post-treatment). Additionally, an equivalent long-term evaluation will
32 582 be performed at the end of the FU period using cumulative data collected up to that assessment
33 583 point. Costs in both trial arms will be estimated from a societal perspective for each participant
34 584 in the trial based on resource items and associated relevant unit costs. The use of societal
35 585 resources comprises information on the use of resources related to healthcare contacts and
36 586 medication (medical records and register data), and productivity losses related to absence from
37 587 work (the LISA database). Costs to deliver the digital intervention will be estimated based on,
38 588 for instance, HCPs' time spent on treatment. Total costs will be aggregated by trial arm.

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45 589 The self-report tool EQ5D⁸⁷ will be completed by the participants at pre-, post-
46 590 treatment and FUs and used to measure changes in health-related quality of life (HRQoL), to
47 591 calculate quality adjusted life years (QALYs). Total QALY gains for participants over the trial
48 592 will be estimated using the area under the curve method⁹². Cost data and QALYs will be
49 593 analysed using generalized linear models to account for non-normal distributions⁹³. Data will
50 594 be analysed controlling for the influence of covariates, and by adjusting for baseline data. Cost-
51 595 utility analysis (CUA) will be conducted with QALYs gained as primary outcome, comparing
52 596 incremental costs with incremental changes in QALYs for digital treatment and TAU. Results
53 597 will be presented as an incremental cost-effectiveness ratio (ICER), representing the ratio
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3 598 between the difference in costs and the difference in QALY gained between the digital
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5 599 treatment and TAU. Incremental cost-effectiveness ratio will be expressed as cost per
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7 600 additional QALY, which is the most common approach in health economics⁹⁴. Uncertainty
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9 601 around the cost and outcome data will be explored and presented on cost-effectiveness plans,
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11 602 representing the distribution of the cost and outcome differences between both conditions. The
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13 603 probability of digital treatment being cost-effective compared to TAU will be presented across
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15 604 a range of price values a decision-maker would be willing to pay, represented by a cost-
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17 605 effectiveness acceptability curve⁹⁵.

18 606 **Phase 4: Post-market surveillance (Study 5)**

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20 607 Similar to the development phase (Study 2), interviews with stakeholders will be conducted,
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22 608 recorded, and transcribed. The stakeholders participating in study 2 will be approached, along
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24 609 with additional key stakeholders identified during the implementation process. Appendix 4
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26 610 provides the full overview of the interview questions. Questions reflect on the process so far
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28 611 (e.g., ‘*What kind and how many resources were needed to bring this intervention into*
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30 612 *practice?*’), on the current status (e.g., ‘*What issues are you currently facing?*’), and
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32 613 prospective adjustments (e.g., ‘*What will the prospective maintenance and upkeep look like?*’).
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34 614 These questions are preliminary and may be adjusted based on findings of Phase 1-3. Even
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36 615 though the www.1177.se website is free for the end users (i.e., patients and HCPs), special
37
38 616 attention may also be paid to financing, as a lack thereof can be a barrier for long-term
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40 617 implementation of eHealth interventions⁹⁶.

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42 618 The qualitative data will be analysed following the same process as that used in Phase
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44 619 1. Specifically, an inductive analysis to identify and summarise themes will be performed, and
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46 620 information will be mapped onto the domains of the CFIR⁴⁷. The implementation strategy and
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48 621 plan will be reviewed, and lessons-learned will be presented to inform prospective
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50 622 implementation studies.

51 623 **Patient and public involvement**

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53 624 This is a study protocol and due to ethical and practical reasons, no patients were directly
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55 625 involved in the project yet. However, the Personas originated from interviews with patients, as
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57 626 described above, and patients and other stakeholders will be involved in all planned phases of
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59 627 the DAHLIA project. Dissemination to patients and the public is described in more detail the
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628 section ‘Ethics and Dissemination’.

629 DISCUSSION

630 Chronic pain is a huge public health problem, in suffering, disability, and costs for individuals
631 and society. Widely accessible and sustainable behavioural treatment options could help to
632 address this problem. An agile and user-centred development integrating a data-driven
633 decision-making process and scientific evaluation of effects is essential to produce an
634 evidence-based intervention of this type for individuals with CP. To our knowledge, this is the
635 first project utilizing the mHealth agile development framework²⁷ to systematically build a
636 digital behavioural treatment within a nationally used health care hub. The purpose of this
637 project is to improve the standard of care for individuals with CP by applying the innovative
638 development framework, thus providing an accessible, user-friendly, and empirically
639 supported behavioural treatment to maintain or improve resilience, functioning, and well-being
640 in this population.

641 Strengths include (i) the execution of the project by a multi-disciplinary, inter-sectorial,
642 and international research team, (ii) the overall agile, iterative, and data-driven process, and
643 (iii) the involvement of patients and different stakeholders early and throughout the
644 development. Furthermore, (iv) the richness of methodologies using mixed methods,
645 combining a traditional clinical trial evaluation on the population level (RCT), fine-graded data
646 collection (SCED) on the level of the individual, and (v) an explicit focus on cost-effectiveness
647 and determinants of implementation will be highlighted. The project is (vi) based on innovative
648 strategies in the field of eHealth and digital treatments, and (vii) key gatekeepers such as
649 regional leaders support the initiative. The DAHLIA approach is also in line with the widely
650 used MRC/NIHR framework by considering contextual and economical aspects, building on
651 theory, involving stakeholders, and refining the intervention^{26 45}.

652 Due to the ambitious and multifaceted nature of the project, several inherent challenges
653 and risks should also be acknowledged. In case a sub-study should be delayed, e.g., due to
654 recruitment difficulties or technical development issues, this delay could affect the whole
655 project. Subsequently, adjustments following the agile approach could be discussed to balance
656 the practical feasibility of executing the study and limiting the impact on its robustness.

657 Furthermore, the multidisciplinary, inter-sectorial approach is certainly a strength of
658 the DAHLIA project, however, it might also have inherent challenges. For example, interests
659 of stakeholders might differ, which needs to be considered and addressed. Here,
660 communication is key, but compromises might be needed to ascertain satisfactory benefits for
661 all parties involved.

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3 662 Regarding the DAHLIA treatment itself, a high level of patient engagement (e.g., four
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5 663 micro-session per week combined with frequent diary assessments) will be required. These
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7 664 demands might be perceived as burdensome by some individual. However, contact with HCPs
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9 665 will support participants' motivation and engagement. Furthermore, the focus groups and
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11 666 optimisation studies will provide insight into the perceived intensity, thus feasibility of the
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13 667 intervention set-up, and the agile process allows to adjust it accordingly. Specially, tailoring of
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15 668 the length of the micro-sessions and frequency of diary prompts will be explored.

15 669 Furthermore, the DAHLIA treatment may not be suitable for all people with CP and
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17 670 the question of "what fits for whom" will be continuously discussed. The website
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19 671 (www.1177.se) is a national health care hub in Sweden, but research shows that older adults,
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21 672 people with cognitive problems, or disabilities are less likely to use technologies⁹⁷, which could
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23 673 result in a bias in recruitment and usability. To improve inclusivity, the possibility to provide
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25 674 additional training for certain populations, such as older adults⁹⁸, will be explored. An
26
27 675 additional issue is that the project is currently executed in Swedish, which excludes people with
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29 676 limited proficiency in Swedish. Therefore, translation into other languages and further cultural
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31 677 adaptations will be considered.

31 678 The DALHIA treatment may have the potential to become a widely implemented first
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33 679 line of treatment. However, some CP groups will likely benefit from an alternative treatment
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35 680 format (e.g., face-to-face), or complementary interventions. Thus, additional studies may
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37 681 explore if and how physiotherapists, general practitioners, or occupational therapists can
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39 682 deliver the DAHLIA treatment.

39 683 Finally, the treatment could prospectively be scaled and adjusted for other groups of
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41 684 patients with CP, e.g., children and adolescents, people with disabilities, and/or other medical
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43 685 conditions such as individuals with severe mental or physical co-morbidities. In addition,
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45 686 support offered as part of the DAHLIA treatment can be extended to significant others and
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47 687 family members of people living with CP. Thus, by using an agile development approach, the
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49 688 DAHLIA project might grow to support the heterogeneous group of individuals with CP and
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51 689 their complex health needs.

690 **Ethics and Dissemination**

691 The study received approval from Swedish ethical review authorities (Dnr 2021-02437). All
692 participants will receive a detailed patient information sheet, have one week time to consider
693 participation, and sign informed consent prior to participation. Each study participant will
694 receive a unique study code to ensure anonymity and confidentiality. Data will be stored in
695 accordance with Swedish regulations on secure servers at Karolinska Institutet.

696 The project is announced on the Karolinska Institutet website (Rikard Wicksell's
697 research group), and on social media, primarily twitter. The general outline of the project has
698 been presented at online conferences. Next to the study protocol paper, the intention is to
699 publish a number of peer-reviewed manuscripts, in which any protocol modifications will also
700 be communicated. The results will be presented at (inter-)national conferences and networking
701 events. Popular science articles, podcasts, radio interviews, and animated videos are
702 additionally planned to disseminate the results to the wider public.

703 **Author's contribution**

704 SB, SJ, KB, LMcC, IFI, SP, and RW were involved in the conception and design of this project.
705 RW acquired and received the funding. HC provided specific input on the topic of
706 implementation, IFe contributed with her expertise on health economy, and LS, PO, and JV
707 added valuable knowledge on the single-case experimental design aspects of the project. SB
708 drafted the manuscript, and all authors revised the manuscript and checked the intellectual
709 content. All authors gave final approval and agree to be accountable for all aspects of the work.

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714 **Completing interests**

715 None declared.

716 **Access to data and protocol details**

717 Only the research team will have access to the raw data and participant code. Anonymised data
718 will be made available as part of publications, whenever possible. Researchers from other
719 universities may request to receive access to other information (e.g., informed consent sheets,
720 data management plan).

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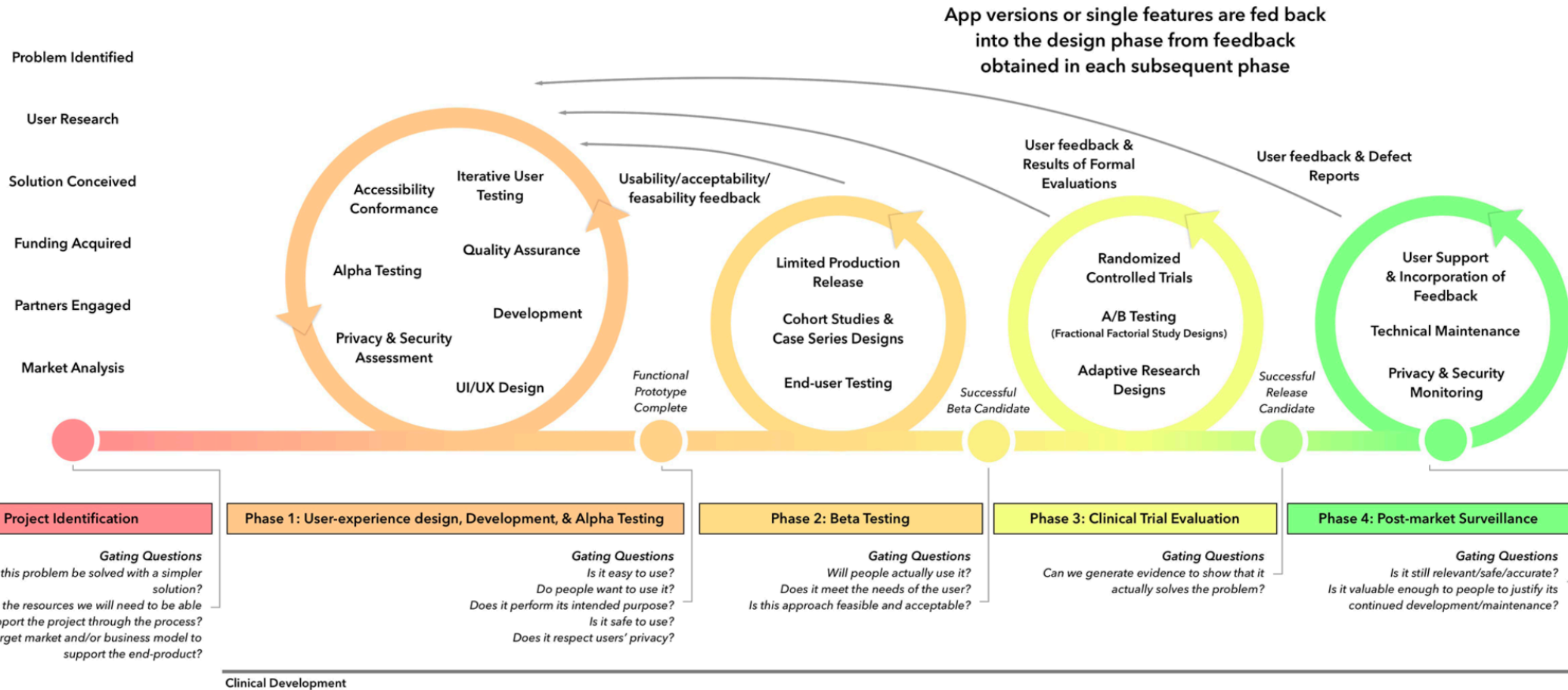
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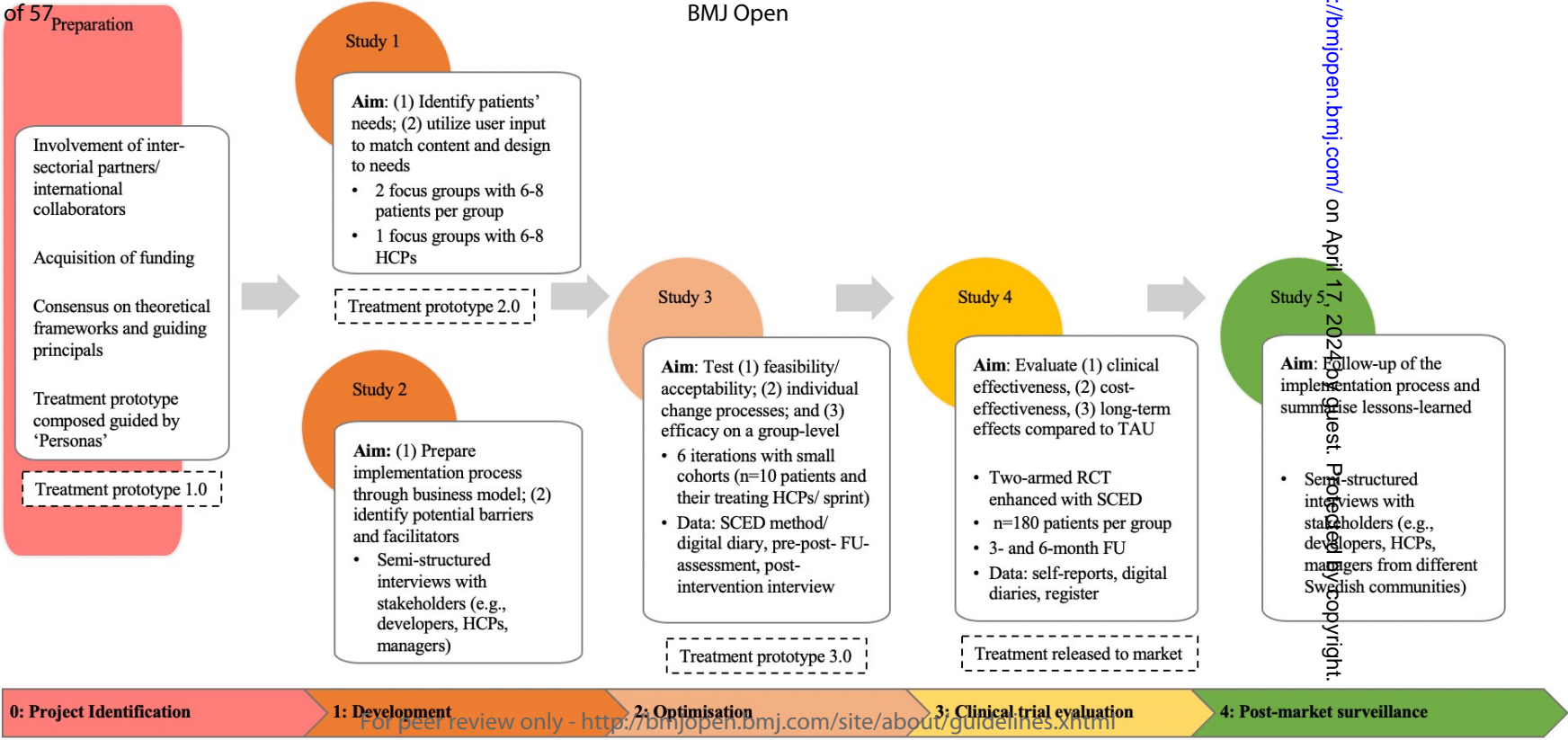
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3 1002 **Figure legend**
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- 5 1003 • Figure 1. mHealth Agile Development & Evaluation Lifecycle (Wilson et al., 2018).
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7 1004 • Figure 2. DAHLIA project overview including highlights of each study and time plan.
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9 1005 HCP= health care professional; SCED= single case experimental design; TAU=
10 treatment as usual; RCT= randomised controlled trial; FU= follow-up.
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12 1007 • Figure 3. Example of a DAHLIA Persona with chronic pain.
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14 1008 • Figure 4. DAHLIA treatment micro-session elements. HCP= health care professional.
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16 1009 Note: The name “DAHLIA treatment” is mainly for academic settings; in the
17 1010 www.1177.se web-platform, a more intuitive treatment name will be chosen.
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19 1011 • Figure 5. The DAHLIA treatment components.
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21 1012 • Figure 6. Template of business model canvas (based on Osterwald & Pigneur, 2010).
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23 1013 Grey boxes: Example aspects of the DAHLIA business model; the final model will be
24 1014 a result of the stakeholder interviews.
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26 1015 • Figure 7. General overview of the optimisation studies and specific procedure in each
27 1016 iteration. SCED= Single-case experimental design. FU= Follow-up. HCP= Health care
28 1017 professional.
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mHealth Agile Development & Evaluation Lifecycle



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2019/2020	2021	2022	2023	2024
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AIDA
18 yrs. old

Employment:
N/A, high school student.

Education:
Primary school
Upper secondary school (ongoing).

Family:
Mother and father with foreign background, four younger siblings.

Background and social context:
Born in Pakistan, moved to Sweden when she was four years old. Leads an active life with hobbies and after-school activities. Frequently works out at the gym, pushing herself.
Aida has many friends and it is important for her to be popular. She is ambitious in school with high demands from her home-environment. She often feels stressed and does not think she is performing as expected. Aida carries a lot of responsibility at home. She has a high level of technological literacy and uses her smartphone for everything.

Social support (related to pain): Despite her family and many friends, Aida feels lonely with her pain. She feels that no one understands or takes it seriously. Her parents are constantly nagging, stressing that the health services should be able to help. Aida finds it strange that she is in so much pain even though she works out a lot and does everything she is "supposed to". Despite her efforts, there are days when she is paralyzed by pain and the feeling of being under pressure.

City/ countryside: Apartment in large city.

PATIENT PAIN PROFILE

Pain problems:

- No clinical diagnosis.
- Recurrent headaches.
- Tensions in shoulders and neck.
- Stomach ache.

Consequences:

- Difficult to concentrate when in pain.
- Although Aida really wants to go to school, she is increasingly staying at home as she cannot manage.
- "Yoyo behaviour" – some days she keeps active and works out, while other days she is completely exhausted.

Pain behaviour:

- Wants a "quick fix" and prefers to continue pushing rather than taking a step back and think.
- Exercises to get in better shape to handle the pain.
- Keeps on going to alleviate anxiety despite feeling the need to rest.

Attitude to treatment:

- Wants to be a "good patient" and do everything she is told (and then some).
- Happy to visit doctors but does not see herself as someone who needs mental health support or treatment.

HEALTH CARE & TREATMENT

Contact with health care:

- Undertaken eye test and has gone through various investigations for the recurrent headaches.
- Visited dentist focusing on temporomandibular joints (jaw region).
- Sought care due to various somatic disorders (head, neck, stomach).

Comorbidities:

- Stress
- Anxiety
- Sleeping difficulties

Medicine:

- Pain killers

PERSONAL NEEDS & GOALS

Treatment needs:

- Wants to be independent and take an active part in her treatment. Needs to feel that she can influence her situation.
- Wants to follow/have an overview of own progress.

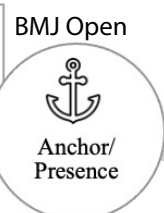
Goals:

- To live an active and productive life without pain.
- To learn how to maintain a balanced lifestyle without guilt when resting.

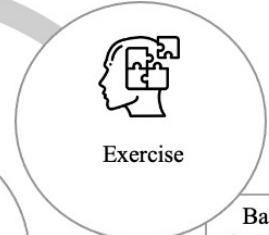
Figure 3. Example of a DAHLIA Persona with chronic pain.

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A question/ sentence to connect to the person's current situation, needs, wishes, or issues; supporting relevance and reliability of session



Anchor/
Presence



Exercise

Based on learning theory, fear-avoidance model, and contextual behavioural approach

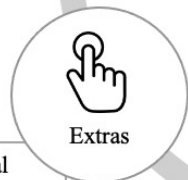


Micro-
session



Therapist
contact

Possibility to take notes during current session to facilitate conversation with HCP later



Extras

Link to additional information or exercises, if person wants to read more



Wrap-
up

Rounding up of session



Validation/
appreciation

Words to help person feel understood and reassured, and to build the relationship with the HCPs

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4 self-guided **micro-sessions** per week inspired by process-based therapy approaches



Aware

Chat function to contact health care professional



Digital diary twice daily to promote self-monitoring



Living well with chronic pain

After 6-week intervention period, **booster-sessions** after 2 and 4 months for long-term support



Accepting/ Open



Active



Key Partners 

(8) Describes the network of suppliers and partners that make the business model work, e.g.:

- Optimization and economy of scale
- Reduction of risks and uncertainty
- Acquisition of particular resources and activities

➤ *Soft ware partners*

➤ *Health care*


Key Activities 

(7) Describes the most important things a company must do to make its business model work, e.g.:

- Production
- Problem solving
- Platform/ Network

➤ *Developing content*


➤ *IT support and development*

Key Resources 

(6) Describes the most important assets required to make a business model work, e.g.:

- Physical
- Intellectual
- Human
- Financial

➤ *IT upkeep*


Value Propositions 

(2) Describes the bundle of products and services that create value for a specific customer segment, e.g.:

- Newness
- Performance
- Customisation
- "Getting the job done" Design
- Brand/Status
- Price
- Cost reduction
- Risk reduction
- Accessibility
- Convenience/Usability

➤ *Usable, effective, evidence-based treatment*

➤ *Accessible and free for patients*


Customer Relationships 

(4) Describes the types of relationships a company establishes with specific customer segments, e.g.:

- Personal assistance
- Self-service
- Automated services
- Communities
- Co-creation

➤ *Personal assistance*


➤ *Co-creation*

Channels 

(3) Describes how a company communicates with and reaches its customer segments to deliver a value proposition (direct/indirect), e.g.:

- Sales Force
- Web sale
- Own stores
- Partner stores
- Wholesaler

➤ *Information on 1177*


Customer Segments 

(1) Defines the different groups of people or organizations an enterprise aims to reach and serve. e.g.:

- Mass market
- Niche market
- Segmented
- Diversified
- Multi-sided platforms (multi-sided markets)

➤ *Patients with chronic pain*


➤ *Health care organisations*

Cost Structure 

(9) Describes all costs incurred to operate a business model, e.g.:

- Cost-driven
- Value-driven
- Fixed costs
- Variable costs
- Economies of scale
- Economies of scope

➤ *Platform and content development/upkeep*

Revenue Streams 

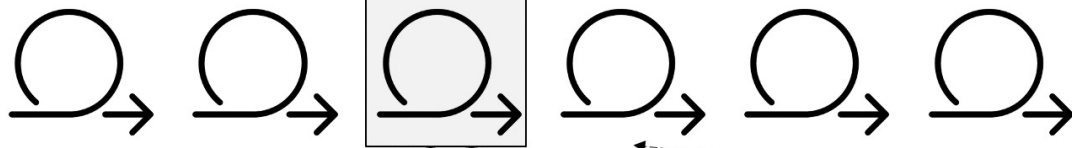
(5) Represents the cash a company generates from each customer segment (costs must be subtracted from revenues to create earnings), e.g.:

- Asset sale
- Usage fee
- Subscription fees
- Lending/ renting/ leasing
- Licensing
- Brokerage fees
- Advertising

➤ *Free for patients*

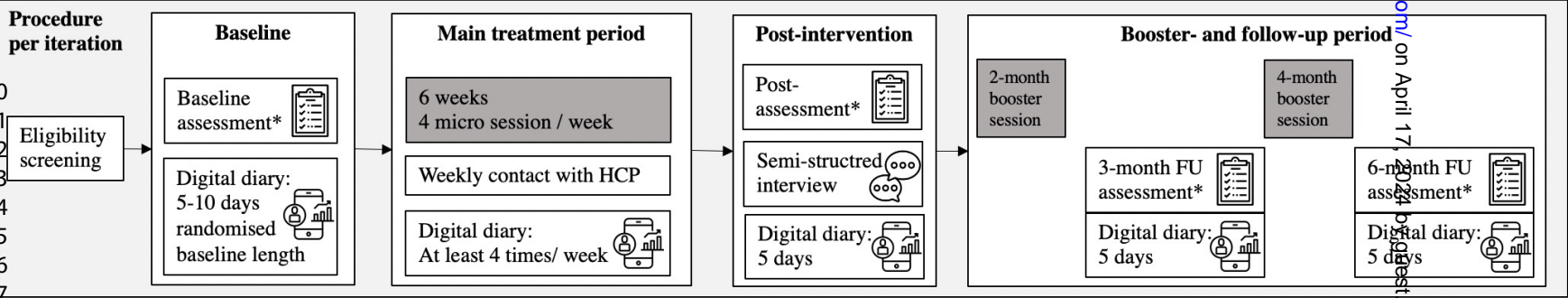
➤ *Licensing for regions*

4-6 iterations with each n=10 patients and their treating HCP

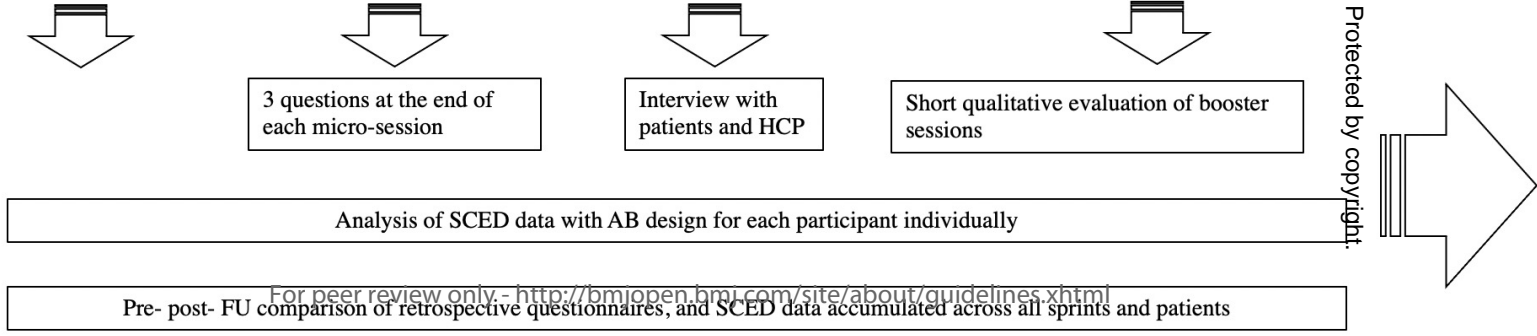


Overall outcome:
Prototype 2.0

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- Objectives**
- Feasibility/ acceptability
 - Individual change processes
 - Efficacy



For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

*Retrospective self-reports including process-, primary- and secondary outcome measures

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Appendix 1:

Semi-structured focus group guide

6-8 participants per focus group

FOR PATIENTS (2 focus groups; heterogenic in terms of age, gender, pain condition, pain history, etc.):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Living with chronic pain** (30min.)

It would be amazing to have a magic pill to just take all the pain away, so you could live without it. But unfortunately, we don't have that magic pill. Instead, we want to help you and other people with chronic pain to find a way to live well with the pain. (*Presentation on definition of health (Huber et al., 2011): ability to adapt and self-manage physical, mental and social aspects of health, and examples*).

 - a. Based on this definition of health, can you describe your own health needs? Which (aspects of your) needs are currently unmet?
 - b. In which moments of your life do you feel happiest/ most engaged/ most satisfied?
 - c. What helps you to engage in these 'happy moments'?
 - d. What are barriers to engage in these 'happy moments'?
 - e. What would you need to engage in these moments more often?

BREAK 10 Min.

4. Core question 2: **The DAHLIA treatment**

Presentation of the proposed treatment, aim, design, theoretical background, and examples of exercises (10min); following a discussion (30min)

 - a. What do you think of this treatment? What do you like, what do you dislike? (Please reflect on (1) design, (2) set-up, (3) content, (4) other (e.g., terminology: treatment, intervention, program; patient vs. person))
 - b. How feasible would it be to do this treatment?
 - c. Do you think this treatment meets you needs?
 - d. Is there anything else you would like to add?

FOR HEALTH CARE PROFESSIONALS (1 focus group, psychologists/ psychotherapists trained in cognitive-behavioural therapy; heterogenic in terms of age, gender, cultural background):

1. General introduction, informed consent, collect sociodemographic details (10min.)
2. Short introduction round (10min.)
3. Core question 1: **Supporting people with chronic pain** (30min)

People with chronic pain have complex needs and treatment has to meet these needs. We are interested in your experiences in what works well to improve

1
2
3 the overall health and well-being of patients with chronic pain. (*Presentation*
4 *on definition of health (Huber et al., 2011): ability to adapt and self-manage*
5 *physical, mental and social aspects of health, and examples*).

- 6
7 a. Which (aspects of) your patient's health needs are unmet? What is
8 needed to support chronic pain patients in the best way?
9
10 b. What barriers and facilitators to deliver support to chronic pain patients
11 do you face? Please reflect on elements related to the patient, treatment
12 options, and the health care in general.

13
14 BREAK 10 Min.

15
16 4. Core question 2: **The DAHLIA treatment**

17 Presentation of the proposed treatment, aim, design, theoretical background,
18 and examples of exercises (10min); following a discussion (30min)

- 19
20 a. What do you think of this treatment? What do you like, what do you
21 not like? (Please reflect on (1) design, (2) set-up, (3) content, (4) other
22 (e.g., terminology: treatment, intervention, program; patient vs.
23 person))
24
25 b. How feasible would it be for you to deliver this treatment?
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27 c. Does the treatment meet the needs of the patients with chronic pain?
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29 d. Is there anything else you would like to add?
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Appendix 2. Baseline interviews with stakeholders

Various stakeholders will be approached, including developers, health care professionals, and managers. Through snow-ball sampling, other potential stakeholders will be identified and approached (e.g., individuals from policy making or municipality representatives).

Stakeholder: developers

I. General

Theme: Experience and development of digital interventions within the 1177 web-platform

1. What is your job description and what are your responsibilities?
2. How is the 1177 web-platform structured, in the region of Kalmar and Sweden?
3. How many digital interventions are available within 1177 in your region?
4. Who developed these interventions; who integrated them in the platform?
5. How are these interventions financed?
6. Who is responsible/ involved in the maintenance of the interventions?
7. If/ how is the interventions' content updated?
8. If/ how are the interventions used and promoted in health care?
9. If/how is user satisfaction with interventions evaluated?
10. If/how do collaborations with other regions look like?

II. Specifics (focus about DAHLIA project)

1. How would you describe the anticipated implementation process of this intervention?
2. What is needed to support the implementation process?
3. What could facilitate the implementation process?
4. What could hinder the implementation process?
5. What are benefits for you/ the 1177 web-platform when developing this intervention?
6. Are you enthusiastic about this intervention, if so, why?
7. Do you think this intervention has the potential to be successful in your region, and Sweden?
8. Where would you like to see this intervention in 5 years?

Stakeholder: health care professionals

I. General

Theme: Experience and use of digital interventions with patients

1. What is your job description and what are your responsibilities?
2. What is your experience in delivering interventions via the 1177 web-platform?
3. If/when there is a new intervention available in the 1177 web-platform, how do you usually hear about it?
4. What makes it attractive to deliver such an intervention?
5. What resources are needed for you to deliver these interventions (e.g., time, knowledge, managerial support)?
6. What hinders you to deliver these interventions?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What benefits for yourself/your work do you anticipate through this intervention?
3. What benefits for your patients do you anticipate?
4. What disadvantages or problems do you anticipate when delivering this intervention?

5. What disadvantages or problems for your patients when receiving the intervention do you anticipate?
6. What would hinder you to deliver this intervention?
7. What would facilitate you to deliver this intervention?
8. Are you enthusiastic about this intervention, if so, why?
9. Do you think this intervention has the potential to be successful in your care facility?
10. Where would you like to see this intervention in 5 years?

Stakeholder: health care managers

Theme: Experience and promotion of digital interventions in care facility

1. What is your job description and what are your responsibilities?
2. How many digital interventions are currently offered by the 1177 web-platform (and used) in your care facility?
3. What is needed to implement an intervention from the 1177 web-platform in your care facility?
4. How do digital interventions get financed in your care facility?
5. What is your involvement in digital interventions in your care facility? How do you support the use of digital interventions?
6. What hinders the implementation of these interventions, in your eyes?
7. If/ how does your care facility collaborate with other regions regarding digital interventions from the 1177 web-platform?

II. Specifics (short introduction of DAHLIA project and details of digital behavioral health treatment for people with chronic pain)

1. Do you think there is a need for this intervention? Please elaborate.
2. What kind of benefits do you anticipate for employees through this intervention?
3. What kind of benefits do you anticipate for patients through this intervention?
4. What kind of disadvantages or problems for employees do you anticipate through this intervention?
5. What kind of disadvantages or problems for patients do you anticipate through this intervention?
6. Are you enthusiastic about this intervention, and if so, why?
7. How will you promote this intervention in your care facility?
8. Do you think this intervention has the potential to be successful in your care facility?
9. Where would you like to see this intervention in 5 years?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Appendix 3. Feasibility/ acceptability; questionnaire.

Table 1. Semi-structured interview guide to evaluate the general feasibility and acceptability of the treatment.

Topics	Questions	Answering scores	Open question
You recently completed the 6-week treatment. For us, it is very important to hear how you experienced it so that we can improve the content, design, and other aspects further. Thank you for taking the time to provide us with your input. First, we would like to ask you to reflect on and rate the past weeks and treatment in general.			
General	Were the past 6 weeks usual weeks for you?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did special events occur?		
	Were you able to read the text in the treatment well?		
	Was the text understandable?		
	Did the intervention hinder your daily occupations?		
	Did technical issues occur?		
Would you recommend this treatment to a friend?			
Secondly, we would like to ask you to reflect on and rate the four short sessions that were offered each week.			
Micro-sessions	Did you like doing the sessions?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Were the sessions difficult or unclear?		
	Did you experience the sessions as helpful?		
	Have the sessions influenced your behavior?		
	Have the sessions influenced your emotions?		
	Have the sessions influenced your thoughts?		
	Did you experience the sessions as time consuming?		
Did you experience the sessions as boring?			
Third, we would like to ask you to reflect and rate the messenger function with which you could communicate with your health care professional.			
Messenger function/ health care professional	Was the messenger function overall helpful?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Did you experience the weekly messages sent by your health care professional as motivating?		
	Did you feel supported by your health care professional?		
Fourth, we would like to ask you to reflect on and rate the daily diary .			
Digital diary	Did you experience the daily diaries as burdensome?	7-points Likert-scale: from 1='not at all' to 7= 'very much'	Please elaborate if possible
	Was it enjoyable to complete the digital diary?		
	Did you become more aware of your thoughts using the digital diary?		
	Did you become more aware of your behavior using the digital diary?		
	Did you become more aware of your emotions using the digital diary?		
Is there anything else you would like to add?			Free text

Appendix 4: Follow-up interviews with stakeholders

The stakeholders from the baseline assessment will be approached again. Furthermore, through snow-ball sampling, potential new stakeholders will be identified and also approached.

Stakeholder: developers

Process so far:

1. When reflecting on the overall development, evaluation, and implementation process, what went well?
2. When reflecting on the overall development, evaluation, and implementation process, what did not go well?
3. What factors supported the process of bringing this intervention into practice?
4. What factors hindered the process of bringing this intervention into practice?
5. What kind and how much resources were needed?
6. Did the process go as anticipated? If not, what was surprising?
7. How satisfied are you with the process so far?
8. What was most challenging during the implementation process?

Current use:

1. What are you currently doing to keep the intervention implemented?
2. Do you have sufficient resources? Please elaborate.
3. What issues are you currently facing? What solutions for these issues do you have?

Prospective adjustments:

1. What will the prospective maintenance and upkeep look like?
2. Who is responsible for that?
3. If there should be a change in employment, who ensures that the intervention remains updated?

Stakeholder: health care professionals

Process so far:

1. How often did you deliver the digital intervention?
2. What kind of benefits for yourself, your work, and/or your patients did you experience?
3. What kind of disadvantages for yourself, your work, and/or your patients did you experience?
4. What kind of support for delivering the intervention (e.g., training, technical guidance when issues arose) did you receive?
5. What hindered you in delivering the intervention?
6. What facilitated you to deliver the intervention?

Current use:

1. How satisfied are you with the intervention overall?
2. Which elements of the intervention need improvement?

Prospective adjustments:

1. Do you plan on delivering the intervention in the future? If not, please elaborate.
2. Would you recommend the intervention to a colleague?
3. What kind of problems do you anticipate in the future; and do you have potential solutions for them?

Stakeholder: health care managers

Process so far:

1. How would you describe your involvement in implementing the intervention?
2. How many resources were needed for the implementation?
3. Did the implementation process go as expected? If not, what was surprising?
4. How did you support your employees to deliver the intervention?

Current use:

1. How satisfied are you currently with the intervention (e.g., reflecting on use, content, promotion, required resources, (technical) issues)?
2. What aspects of the current implementation/ practical use need improvements?

Prospective adjustments:

1. Do you plan to offer the intervention in your region in the future? Please elaborate.
2. Would you recommend this intervention to another region/ other health care organizations? Please elaborate.
3. What kind of problems do you anticipate in the future?

Final question for all participants:

The main points I take away from this interview are [summary]. I appreciate the time you took for this interview. Who else should we talk about regarding the implementation of this intervention? Is there anything else you think would be helpful for me to know?

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1,3
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2,3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	28
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1,28
Roles and	#5b	Name and contact information for the trial sponsor	1

responsibilities:

sponsor contact
information

Roles and

responsibilities:

sponsor and funder

[#5c](#)

Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities

n/a

Roles and

responsibilities:

committees

[#5d](#)

Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

8

Introduction

Background and

rationale

[#6a](#)

Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

5-7

Background and

rationale: choice of

comparators

[#6b](#)

Explanation for choice of comparators

n/a

Objectives

[#7](#)

Specific objectives or hypotheses

6-8

Trial design

[#8](#)

Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)

8, Fig. 2

Methods:

Participants,

interventions, and

outcomes

Study setting

[#9](#)

Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained

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Eligibility criteria

[#10](#)

Inclusion and exclusion criteria for participants. If applicable,

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		eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	
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4	Interventions:	#11a Interventions for each group with sufficient detail to allow	9-11, Fig 4,
5	description	replication, including how and when they will be administered	Fig 5
6			
7			
8	Interventions:	#11b Criteria for discontinuing or modifying allocated interventions	12, 14,15
9	modifications	for a given trial participant (eg, drug dose change in response	
10		to harms, participant request, or improving / worsening	
11		disease)	
12			
13			
14	Interventions:	#11c Strategies to improve adherence to intervention protocols, and	15
15	adherence	any procedures for monitoring adherence (eg, drug tablet	
16		return; laboratory tests)	
17			
18			
19			
20	Interventions:	#11d Relevant concomitant care and interventions that are permitted	11
21	concomitant care	or prohibited during the trial	
22			
23			
24	Outcomes	#12 Primary, secondary, and other outcomes, including the specific	Fig 7, Tab 2,
25		measurement variable (eg, systolic blood pressure), analysis	Tab 3, and
26		metric (eg, change from baseline, final value, time to event),	related
27		method of aggregation (eg, median, proportion), and time	sections
28		point for each outcome. Explanation of the clinical relevance	
29		of chosen efficacy and harm outcomes is strongly	
30		recommended	
31			
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34			
35	Participant timeline	#13 Time schedule of enrolment, interventions (including any run-	14, Fig 7
36		ins and washouts), assessments, and visits for participants. A	
37		schematic diagram is highly recommended (see Figure)	
38			
39			
40	Sample size	#14 Estimated number of participants needed to achieve study	12, 13, 14, 21
41		objectives and how it was determined, including clinical and	
42		statistical assumptions supporting any sample size calculations	
43			
44			
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46	Recruitment	#15 Strategies for achieving adequate participant enrolment to	11,12
47		reach target sample size	
48			
49			
50	Methods:		
51	Assignment of		
52	interventions (for		
53	controlled trials)		
54			
55			
56	Allocation: sequence	#16a Method of generating the allocation sequence (eg, computer-	21, Tabl. 1
57	generation	generated random numbers), and list of any factors for	
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stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions

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7	Allocation	#16b	Mechanism of implementing the allocation sequence (eg, 21, Fig 7
8	concealment		central telephone; sequentially numbered, opaque, sealed
9	mechanism		envelopes), describing any steps to conceal the sequence until
10			interventions are assigned
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14	Allocation:	#16c	Who will generate the allocation sequence, who will enrol 14, 21
15	implementation		participants, and who will assign participants to interventions
16			
17	Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial n/a (Tab 1)
18			participants, care providers, outcome assessors, data analysts),
19			and how
20			
21			
22			
23	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is n/a
24	emergency unblinding		permissible, and procedure for revealing a participant's
25			allocated intervention during the trial
26			
27			
28	Methods: Data		
29	collection,		
30	management, and		
31	analysis		
32			
33			
34			
35	Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and Described for
36			other trial data, including any related processes to promote each sub-
37			data quality (eg, duplicate measurements, training of study
38			assessors) and a description of study instruments (eg,
39			questionnaires, laboratory tests) along with their reliability and
40			validity, if known. Reference to where data collection forms
41			can be found, if not in the protocol
42			
43			
44			
45			
46	Data collection plan:	#18b	Plans to promote participant retention and complete follow-up, n/a
47	retention		including list of any outcome data to be collected for
48			participants who discontinue or deviate from intervention
49			protocols
50			
51			
52			
53	Data management	#19	Plans for data entry, coding, security, and storage, including 26, 28
54			any related processes to promote data quality (eg, double data
55			entry; range checks for data values). Reference to where
56			details of data management procedures can be found, if not in
57			
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		the protocol	
1			
2	Statistics: outcomes	#20a Statistical methods for analysing primary and secondary	Tab 1, 19-21
3		outcomes. Reference to where other details of the statistical	
4		analysis plan can be found, if not in the protocol	
5			
6			
7	Statistics: additional	#20b Methods for any additional analyses (eg, subgroup and	12-14, 21, 22,
8	analyses	adjusted analyses)	
9			
10			
11	Statistics: analysis	#20c Definition of analysis population relating to protocol non-	19, 20
12	population and	adherence (eg, as randomised analysis), and any statistical	
13	missing data	methods to handle missing data (eg, multiple imputation)	
14			
15			
16	Methods: Monitoring		
17			
18			
19	Data monitoring:	#21a Composition of data monitoring committee (DMC); summary	28
20	formal committee	of its role and reporting structure; statement of whether it is	
21		independent from the sponsor and competing interests; and	
22		reference to where further details about its charter can be	
23		found, if not in the protocol. Alternatively, an explanation of	
24		why a DMC is not needed	
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29	Data monitoring:	#21b Description of any interim analyses and stopping guidelines,	n/a
30	interim analysis	including who will have access to these interim results and	
31		make the final decision to terminate the trial	
32			
33			
34	Harms	#22 Plans for collecting, assessing, reporting, and managing	20-21 (NEQ)
35		solicited and spontaneously reported adverse events and other	
36		unintended effects of trial interventions or trial conduct	
37			
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39	Auditing	#23 Frequency and procedures for auditing trial conduct, if any,	n/a
40		and whether the process will be independent from	
41		investigators and the sponsor	
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45	Ethics and		
46	dissemination		
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49	Research ethics	#24 Plans for seeking research ethics committee / institutional	3, 27
50	approval	review board (REC / IRB) approval	
51			
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53	Protocol amendments	#25 Plans for communicating important protocol modifications	27
54		(eg, changes to eligibility criteria, outcomes, analyses) to	
55		relevant parties (eg, investigators, REC / IRBs, trial	
56		participants, trial registries, journals, regulators)	
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1	Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11-12, 27
2				
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6	Consent or assent:	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7	ancillary studies			
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11	Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	27, 28
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17	Declaration of	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	28
18	interests			
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21	Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
22				
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26	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
27	trial care			
28				
29				
30	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	27
31	trial results			
32				
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38	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a
39	authorship			
40				
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42	Dissemination policy:	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	28
43	reproducible research			
44				
45				
46	Appendices			
47				
48	Informed consent	#32	Model consent form and other related documentation given to participants and authorised surrogates	28
49	materials			
50				
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52	Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a
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2 Attribution License CC-BY-NC. This checklist can be completed online using <https://www.goodreports.org/>, a
3 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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