Beating cancer-related fatigue with the Untire app

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Chapter 7

General discussion
Chapter 7

Principal findings

Millions of cancer patients and survivors all around the globe suffer from cancer-related fatigue and experience a reduced quality of life due to their cancer and cancer treatment. With our large-scale international waiting-list RCT, including participants from four English-speaking countries (i.e., Australia, Canada, the United Kingdom, and the United States), we demonstrated that fatigue could be reduced and QoL improved by means of a self-management mHealth app (chapter 5). From March till October 2018, we recruited via 76 Facebook Ads and included 755 participants, of which 355 completed the follow-up measure 12 weeks later, at the expense of €22.42 and €47.69 per participant, respectively (chapter 4). We saw that the most interested participants were female, middle-aged, and came from the UK. We think that reaching participants for international mHealth studies via Facebook Ads has potential but can be very costly, especially when more balanced sub-samples are desired. However, we believe that constant optimization and testing of ads can make an essential difference in reducing recruitment costs. Regarding the app’s effectiveness, we learned that participants do not need to engage excessively with the intervention since medium app use (3-8 days) was already significantly associated with fatigue reduction (chapter 5). Our findings on fatigue reduction were statistically significant and clinically relevant since more people recovered in the intervention group than the control group. We explored whether the effect of the intervention was related to specific age groups and saw that the intervention effect was significant across all age groups but even more pronounced in younger individuals (<56 years). Individuals with different education levels and both cancer patients and survivors seemed to benefit significantly from the app. We do not have enough data to compare outcomes between gender, cancer types, and treatment types and must acknowledge that our study sample is limited in its representativeness to Facebook users. We also explored several processes targeted by the app and their effect on fatigue reduction (chapter 6). We found that app access was significantly associated with reduced fatigue severity and interference via the mechanism of reduced fatigue catastrophizing, depression, sleep disruption, and increased mindfulness and physical activity. Besides, we described the experiences we had with applying for ethical approval in different countries (chapter 3). We believe that research guidelines could support scientists aiming to conduct international internet-based studies regarding whether these should be considered single or multi-center trials. We describe where researchers can apply for ethical approval across different countries.
Interpretation of findings

We learned that the Untire app could reduce fatigue with small-to-moderate effect sizes. Hence, we believe that our findings deliver some preliminary understanding of what self-management mHealth interventions can provide for (ex-) cancer patients and their clinical symptomatology. One crucial advantage of self-management is that no direct contact with a therapist or healthcare practitioner is required. For that reason, the question remains about how people engage with such a form of standalone intervention. We observed that not everybody who had access to the intervention also used it eventually. Specifically, we saw that 30% of the intervention group did not download and activate their app. This issue raises questions upon barriers to accessing a potentially low-threshold mHealth app.

Did participants experience technical difficulties with registering in the app? Or did they lose motivation or interest due to their disabling fatigue or other demands? We cannot know for sure. However, we did collect some information on baseline motivation. Participants reported high expectation and motivation levels to manage their fatigue and work with an app (responses to both questions scored an average of 8 out of 10). Initial expectation and motivation levels of those who did not activate the app as compared to those who activated it did not differ statistically significantly (expectations of regaining energy with this app \( p = .30 \); motivated to work with this app \( p = .07 \)). We are not surprised by this finding since expectations and intentions (i.e., motivations) do not always match implementations (i.e., working actively with an app). Also, we assume that the onboarding process (i.e., downloading and activating the app) might have been a barrier for some participants. Further, we found that participants who activated the app also had slightly higher education levels \( p < .02 \) than those who did not. Our participants’ education levels (high = 43%, moderate = 38%, low = 19%) also match with current research in the field of online Facebook-based mHealth recruitment. An online survey study indicated that more people with moderate and higher education levels tend to engage in (m)health research in general, possibly due to greater health literacy and digital mobile phone literacy. We believe that easing the registration process could make the app more accessible to eligible patients with levels of e-health literacy.

The small-to-moderate intervention effects for fatigue severity and interference reductions are somewhat larger than the effects of many self-management eHealth interventions but somewhat smaller than therapist-guided online interventions and face-to-face therapy targeted at CRF. We imagine that due to
the self-management, dropout in both intervention and control groups is more likely to occur since many patients might feel less adherent without any personal contact provided. The lack of personal contact in self-management eHealth or mHealth intervention studies could also explain the overall higher dropout rates than those in face-to-face intervention studies. Specifically, we saw that in total, 56% of the 755 randomized baseline participants were lost to follow-up, but this percentage was larger in the intervention (68%) than in the control group (36%). Differential dropout in eHealth/mHealth interventions is a relatively common phenomenon and has already been described as ‘the law of attrition’. We can imagine that calling participants once at the start of the study and during the app's registration process could make a meaningful difference due to a minimum of personal contact. Further, we could imagine that due to a minimum of personal contact provided, ‘low users’ (i.e., the lower one-third of all app users) who only engaged in 1-3 days of app use might use the app more often.

Moreover, the Untire app has been developed to reduce fatigue and its underlying clinical symptoms via several mechanisms. Previous research indicated that several factors (e.g., female sex, chemo-radiotherapy, sleep disruption, rumination, pain, and depression) could all impact outcomes of CRF. Our study findings showed that treatment outcomes in the intervention group were associated with reduced catastrophizing, sleep disruption, and depression. It is good to see that app access also improves these aspects since, if left untreated, many symptoms associated with these factors can easily manifest. Specifically, CRF can lead to a vicious circle of impaired physical performance, avoidance of exertion, inactivity, inadequate physical recovery, helplessness, and depressed mood. However, since we cannot disentangle the causal chain of clinical symptomatology, more research on the clinical symptom dynamics is needed (e.g., whether fatigue should be considered an outcome or mediator?). For now, we can imagine that one of the best ways to break the vicious circle seems to start intervening as early as possible. It might be essential to provide psycho-education about fatigue and give patients the tools (i.e., different app components) to manage their fatigue and underlying symptoms right away (i.e., from diagnosis moment onwards). The early-on approach could be especially beneficial since it could also help patients prepare for their (invasive) treatment. In this way, patients could be supported to manage their expectations realistically. A current survey finds that 1 in 3 patients wished to have had more information on cancer treatment side effects (e.g., CRF) before the treatment started. We can imagine that multi-component mHealth interventions are advantageous for that purpose. mHealth interventions can easily target different factors and could be easily prescribed directly as low-threshold support from the diagnosis moment onwards.
Furthermore, it is essential to realize that the findings on fatigue reduction were statistically significant and clinically relevant due to significant differences in recovery rates. Specifically, for fatigue severity, 14% of the intervention group recovered fully versus 6% in the control group, and for fatigue interference, 30% of the intervention group recovered fully versus 19% in the control group. Nevertheless, the supportive findings on the app’s effectiveness regarding fatigue severity and interference, we know that mHealth apps need to be further examined by additional RCTs and picked up by systematic reviews and meta-analyses RCT’s for the most substantial evidence.

As the number one side effect of cancer and cancer treatment, CRF can disrupt QoL and might even be a risk factor of reduced survival. We asked participants about their QoL experience “of the past week” as well as their “overall QoL” experience. Interestingly, we found differences between these two outcomes. Specifically, the outcome of “QoL of the past week” did not significantly differ between groups over 12-weeks. In contrast, we saw that the “overall QoL” levels were indeed significantly improved compared to the control group over 12-weeks, with a small-to-medium effect size. However, which of the outcomes gives us a robust understanding of whether the app improves QoL? We cannot answer this question directly. However, when we zoom into the data, we can see that “QoL of the past week” tends to improve significantly over time (p<.01) regardless of whether participants are in the intervention group or the control group (time by group difference: p=.24). One explanation for the finding could be that control participants also experienced significant improvements of “QoL of the past week” due to any care as usual. We could also imagine that taking part in our study might have motivated a fraction of control participants to reach out for other support options, which indeed could have had a significant impact on the “QoL of the past week” assessment. Another explanation could be regression towards the mean, leading to improvements in both groups towards their true mean given more extreme baseline scores. Further, we can imagine that the 12-week outcome of QoL of the past week might be more of a momentary assessment, influenceable by many other personal events or experiences beyond the ones included in our study. Apart from the two different QoL outcomes, we can also consider fatigue interference as a QoL indicator. Fatigue interference describes to what extend patients’ fatigue interferes with their daily activities. Since we found improvements in ‘QoL of the past week’ in both intervention and control groups and small-to-moderate effect sizes for ‘overall QoL’ and ‘fatigue interference,’ we would assume potential benefits of the mHealth intervention on QoL levels in general. However, more research is needed to elucidate the effectiveness of mHealth interventions on QoL in cancer patients and survivors.
While we encountered mixed findings on QoL outcomes, we are aware that large-scale RCTs will be needed to explore the effectiveness in individuals with other cancer types than breast cancer and men. A single RCT can only provide limited results, and therefore systematic reviews and meta-analyses of several RCTs will be needed for a higher evaluation. Recently, a meta-analysis investigated whether eHealth interventions (i.e., including mHealth apps) can alleviate cancer survivors’ QoL and concluded overall effectiveness, although substantial differences were found. The meta-analysis describes that mHealth apps were among the most effective interventions compared to web-based vs. telephone-based. However, the review does not consider whether these interventions were self-management-based or therapist-guided. For instance, out of six reviewed apps, the two most effective ones were guided interventions, whereas the remainders were self-management-based. Unavoidably, studies brought together in a systematic review will differ. Therefore, when considering systematic reviews, we have to be aware of the heterogeneity of studies, recognize possible confounders (e.g., whether therapist guidance or self-management is provided), and have to take limitations to generalizability into account (e.g., most of the apps were examined in a sample of female breast cancer survivors).

Another interesting point to consider is the length of a mHealth self-management intervention. How many weeks will patients need to use the app to experience a robust improvement in fatigue and QoL, and how sustainable would these improvements be? While our controlled study is limited to 12-weeks, the aforementioned systematic review and meta-analysis on eHealth interventions and mHealth apps for cancer survivors’ QoL also derive to an own conclusion. According to the systematic review, short-term interventions are deemed most effective (<3 months). This is good news since the app was also built to give patients the tools to manage their fatigue as self-help for some limited time. The goal has been to empower the patient and not to make them dependent for the long run. Therefore, although we cannot extrapolate our study findings, we can imagine that using an app for fatigue for 12-weeks seems like an adequate time for potentially robust effects.

**Recruitment**

We recruited our study participants via Facebook/Instagram Ads and discovered that the most interested group were middle-aged female breast cancer patients from the UK. Our participants reported being highly fatigued and had barely received any support to manage their fatigue before the study start. Thus, we learned that we were indeed reaching out to people in need. Still, we believe that
we missed relevant data on other patient groups. Considering world incidence rates of different cancer types, we can determine exactly which patient groups are still missing (Figure 1). We see a scarcity of male participants and other cancer types like lung or prostate cancer in our study, despite high global incidence rates.

![FIGURE 1. Age-standardized (world) incidence rates (ASR) per sex, top 10 cancers. Slightly adapted from WHO, GLOBOCAN 2021](image)

Looking at the discrepancy between global incidence rates and our study sample brings up many questions. For instance, we wondered whether lung cancer and prostate cancer patients and survivors might be more reluctant to access care in general? For both lung and prostate cancer patients, fatigue has been described as the most frequently reported symptom throughout the disease pathway. The most common cause of cancer death worldwide remains lung cancer, with tobacco dependence as one of the most significant predictors. Many of these patients struggle with smoking cessation, and despite substantial progress in diagnostic and therapeutic areas, only 11% live five years or more. As a result, lung cancer patients might perceive further unique barriers to seek support to manage their fatigue (e.g., issues of self-blame, stigma, anticipated short survival time, and increased symptom burden and distress). In turn, prostate cancer is more likely to develop in older men (above 65 years of age). Therefore, age could also be a barrier to accessing care on several levels. For example, we know that fewer people above 65 use social media. Also, app-literacy might be lower with older age, despite a largely unmet need for psychological care and psycho-education.

Further, we wondered whether men are generally harder to recruit than women or whether men are perhaps less inclined to seek help via social media or use an app? While we assume that the effectiveness of the Untire app does not differ principally between men and women, we cannot be sure since the
sample reached included so few men (8%). Research shows that gender can be an essential predictor of health behavior in general. For example, men are often more risk-taking, engage in poorer lifestyle choices (eating, smoking, and drinking habits), and are less likely to perform health-protective behaviors than women. Further, we see that samples in health behavior research are heavily biased towards females in general, showing us that unequal division might be more of a general issue. A review suggested that the socialization of men and the following masculine ideologies may be a significant factor in men’s decision-making to seek help when confronted with illness. We can imagine that gender differences in health-seeking behavior might also lead to the gender imbalance observed in our study. There might be further complex barriers hindering male participant recruitment to health behaviors studies that may require systemic strategies, including other channels than social media (e.g., recruitment via healthcare staff, family, and friends).

Moreover, we believe that evidence-based approaches could improve Facebook recruitment outcomes further. In our study, Facebook Ads with images of male participants were slightly associated with improved uptake among men. In line with that, also a recent study demonstrated that using male-specific ads can indeed result in a significantly higher proportion of men completing a survey than gender-neutral ads (38% male vs. 25% gender-neutral; \( P < .001 \)). However, we also believe that using various versions of Facebook Ads can lead to selection bias regarding demographic and health characteristics. For instance, depending on the content (i.e., combinations of texts and images), ads might be differently perceived by men and women or younger and older individuals. Another explanation for our predominantly female sample might be part of the recruitment strategy. We targeted cancer patients and survivors and then created lookalike audience based on individuals with similar characteristics. Since we saw that the cost per click (CPC) was significantly higher for men than for women, we also spent more money recruiting female participants. By recruiting based on lookalike audiences of participants who showed initial interest, we have indirectly contributed to a majorly female sample. By spending more money to recruit the same lookalike audiences, we would have probably reached a similar group. Besides our study, in-app data collected from May 2020 until May 2021 from the app developer showed that 74% of regular app users are female. While we imagine that women might be somewhat more accessible or interested in such a form of intervention, we are also aware that our recruitment strategy with lookalike audiences could have reinforced this issue. Therefore, we believe there is a need for large-scale RCTs, including substantial numbers of other more challenging to recruit cancer groups.
with high incidence rates to confirm the effects of mHealth interventions in (ex-) cancer patients. Researchers should carefully consider the content of social media ads to match their target population. Further, researchers should consider sharing their advertisement strategies and decide whether multi-center recruitment should be carried out. The respective application could then be recommended and guided by a healthcare provider, allowing recruiters to control patient characteristics while adding a minimum amount of personal contact.

**Strengths and limitations**

Our waiting-list RCT entails both strengths and limitations. On the one hand, an RCT design can be considered as the gold standard for causal effectiveness research\(^1\)\(^9\). On the other hand, the methodology is also rigid in terms of new developments and slow-paced since it takes considerable time to receive ethical approval, especially if carried across several countries. While recent developments and content-related updates of the app were in planning by the app developers, we decided to stick to the basic version of the app and did not alter it during the study to comply with the version presented for ethical review. We also did not want to change the app’s content to avoid participant confusion during the study. While rigidity is needed for RCT designs, it can also present a challenge and potential harm to scientific innovation and developer creativity. This can be an issue for (technical) mHealth intervention development, which tends to be fast-paced as it is quickly outdated if not updated regularly. In addition to RCT designs, we can imagine that observational within-app (log-) data could be potentially beneficial for app developers aiming to improve the intervention further.

Another shortcoming of our study concerns the low recruitment Facebook conversion rates (i.e., 8.2% of participants who clicked on the ad clicks started with the baseline survey), adding substantial recruitment costs. While Facebook ads generated significant interest in the study (i.e., Facebook clicks = 37,376), only a tiny proportion (3%) of those potential participants went on to complete the online consent process (eligibility check & signed consent = 1,137). Why did so many people click on our Ads but do not proceed? Did they not proceed because they were not interested, or were the ads just irrelevant to them (e.g., never had cancer, or not fatigued)? Is this only an issue in our study or rather a general problem? A recent study indicated that this seems to be more of a common issue since participants who became aware of the study via social media were less likely to be eligible and enrolled in the study than those recruited through
traditional methods\textsuperscript{20}. We believe that this finding could be partially explained due to minimal clinical targeting opportunities in social media. While it is possible to target male or female participants, it is impossible to target cancer patients or survivors directly. Therefore, future research should explore further recruitment options with clinical targeting opportunities to maximize conversion rates and reduce recruitment costs.

A methodological issue we have to acknowledge is the significantly higher loss to follow-up rate in the intervention group than the control group, portraying potential threats to the generalizability. Why did more persons quit assessments in the intervention group than in the control group? Dropout in RCTs is typical and can threaten the validity of results, as completers may differ from people who drop out. Low retention rates prohibit any inferences about participants who dropped out and might introduce selection bias, usually minimized by the randomization procedure. It is essential to realize that differential dropout rates in intervention and control groups (i.e., attrition) do not necessarily imply that effect estimates are biased\textsuperscript{21}. Our data analysis did not find any substantial differences when comparing the characteristics of participants who started with those who completed the study. One explanation might be that participants had less motivation to complete further study assessments in the intervention group after receiving their app access incentive. Further, we can imagine that technical obstacles with the app onboarding process were experienced (e.g., failed logins, forgotten passwords, no internet, etc.), resulting in motivation decline. Technical issues can threaten the adoption of mHealth and are not encountered in traditional face-to-face psycho-oncology care. In addition to technical difficulties, we can imagine that a considerable part of participants must have felt too fatigued to carry out assessments despite initial high self-reported motivation levels. However, we suspect that this would have affected more the control group, which had to wait for app access. We highlight the relevance for future research studies to involve RCT designs that are pilot and extensively usability tested to offer participants a smooth experience.

Concerning the app’s effectiveness, we compared app access with a waiting list control condition. However, it might also be interesting to compare the app with another active control group where participants receive some time and attention. With an active control condition, it would be possible to blind participants. Not blinding participants can entail performance bias since knowledge of group assignment (i.e., intervention vs. control) may affect participants’ behavior in the trial and their responses to self-reported outcome measures. We could imagine
that one way to blind participants with an active control condition would be to provide a simple symptom tracker app without any further psycho-education, feedback, or actual content. Additionally, we must acknowledge that we cannot extrapolate and make claims about long-term outcomes (beyond the 12-weeks). Specifically, we cannot be sure whether fatigue symptom reduction or QoL improvements persist beyond 12-weeks, meaning that our study has relatively short-term implications. However, this might not be an issue since short-term (<3 months) telemedicine interventions for QoL of cancer survivors were found to have considerable long-term evidence so far\(^9\).

**Implications**

**Dissemination and implementation**

The focus on managing late and long-term physical, cognitive, psychological, and social effects of cancer and cancer treatment have emerged more and more in the last decade. We are glad to see that our study also fits the scope of February 2021 published ‘Europe’s Beating Cancer Plan’ (see figure 2). The plan aims to tackle the complete disease path by focusing on prevention, early detection, diagnosis and treatment, and QoL of cancer patients and survivors. By 2030, 90% of eligible patients should have access to Comprehensive Cancer Centers (CCCs) linked through a new EU Network. Additionally, a new ‘Cancer Diagnostic and Treatment for All’ initiative will be launched by the end of 2021 to help improve the QoL of many cancer patients and survivors and support social integration and re-integration in the workplace.

We believe that all efforts are needed to implement these plans and imagine that a self-management app could ideally contribute to these goals. A mHealth app would be potentially beneficial since it can reach numerous people simultaneously, and costs could be saved due to self-management. Even if occasionally contact with a practitioner is favored, a hybrid blended care version could be offered, referring to a combination of face-to-face contact and mHealth. On the one hand, we already know that face-to-face therapy for cancer patients and survivors works but is resource-intensive. On the other hand, we have demonstrated support for the effectiveness of the Untire self-management app. However, difficulties with registering the app and dropout might be relevant matters to look into. Future research could investigate the (cost)-effectiveness of a blended care version, for instance, embedded in the clinical practice of European CCCs. Specifically, the app could be recommended and introduced by a healthcare practitioner or therapist,
and contact could be provided occasionally. While the Untire app has its potential as a standalone intervention, we believe that the best of both sides could be supplied in blended care. CCCs could take a key role in targeting patients in need.

FIGURE 2. Europe’s beating cancer plan, the current care gap, and why we need to act now. From the European Commission.\(^{22,23}\)

**Health by technology**

Attitudes about digital healthcare have changed over the years. An indirect consequence of COVID-19 might be the mass adoption of technology by healthcare and society. For instance, a study found a patient shift from 11% to 76% of being interested in using eHealth, and 72% of eHealth users reported high levels of satisfaction.\(^{24}\) While smartphone use is highly endorsed nowadays, it remains essential to embed the technology sustainably. Ideally, the technology should be used by a growing patient network and is preferably reimbursed by public health insurance. Further, during the pandemic, we had to experience the convenience of virtual communication by technology, also giving patients the tools to access healthcare from home. For the current time, but especially also for the time after COVID-19, healthcare providers may already consider nowadays actions that integrate mHealth further into healthcare. Long-term expected prospects are enriched convenience and low-threshold access to care, improved
patient outcomes and satisfaction, and a more (cost-) efficient healthcare system, which aims to reach patients over various channels.

**Future research**

Future research could extend our knowledge by focusing on different aspects. One issue of self-management mHealth interventions concerns maintaining user engagement and prohibiting dropout. We believe that the key for successful mHealth interventions is provided by delivering both first-rate treatment-specific and common therapeutic factors. Specific factors include the content of the intervention. Treatment manuals and insights from traditional face-to-face clinical practice were re-written and adapted to the themes of the Untire app. While the Untire app already provides several themes, we can imagine that newly added content could also be of added value. For instance, many cancer patients and survivors may struggle to get back to their working life due to disabling fatigue. Thus, a theme regarding their cognitive functioning addressing the question “how to return to work?” could be beneficial. By adding new relevant content to an app, patients can be further supported, overpassing the apparent limitations of a static self-help book. However, we know that specific therapeutic factors are just one side of the medal from traditional face-to-face therapy.

Apart from specific factors, we also know that common therapeutic factors such as working alliance / therapeutic alliance are highly relevant for effective treatments and often cited as excellent predictors for treatment adherence and treatment outcomes in face-to-face therapy independent of various psychotherapy approaches and outcome measures\(^\text{25}\). However, how does this translate to mHealth? Traditionally, the therapeutic alliance is commonly defined as patient and healthcare provider agreement on tasks, goals, and establishing a personalized bond\(^\text{26}\). While this seems reasonable for face-to-face healthcare, the question arises of how the working alliance could be established and maintained between a patient and a digital standalone self-management app. For example, we can imagine that an agreement on tasks could be pushed via reminder notifications, and goals could be measured with motivation or milestones reached within an app. On the other hand, the “bond” factor might be a bit harder to target within mHealth, and an absence of a “bond” might account for current issues on disengagement and dropout among mHealth interventions. A mobile version of the well-known Agnew Relationship Measure (mARM) Questionnaire has recently been developed to assess the digital working alliance among app users. One
example statement of the mARM questionnaire would be, for instance, whether a patient feels that “the app is like having a member of their care team in their pocket.” Apart from the mARM, a digital version of the working alliance inventory (DWAI) has been developed and validated for its predictive value. For example, a validation study of two smartphone meditation apps assessed digital working alliance. Results indicated that at weeks 3 or 4 of the intervention, but not earlier, DWAI scores predicted pre-post reductions in psychological distress outcomes, showing us that working alliance might not be limited to face-to-face interventions but could also be very important for mHealth interventions. However, how can a person be guided to establish a positive bond and relationship with an app?

We believe that the key lies in personalization. Via personalized content and personalized feedback, the digital “bond” factor could be potentially improved. We can imagine that this could add remarkably to improved adherence and improved treatment outcomes. For instance, in addition to newly updated content, the themes addressed by the app could also be tailored to patients’ needs, preferences, and interests. Personalized content and feedback could be provided via artificial intelligence (AI) technology. AI is already on the rise, and machine-learning algorithms could be directly applied to mHealth. Quantitative assessments could be used with item-response theory (IRT), but also qualitative assessments could be used via computerized text analysis (text mining), using log-data collected from the app. For instance, for the Untire app, the patient input provided for the “Vase of energy” could be screened, and relevant, personalized content could be provided on that base. Also, based on the gathered data, the fill-in options within the app where the patient can provide text could be enhanced by predefined answer options (i.e., similar to Google’s auto-fill in function). We can see that the Untire app aims to build a bond by welcoming the patients with their names on the home screen and welcoming notifications. However, we imagine that further efforts for personalization could improve user experience and prolong engagement via improved working alliance, which is not limited to face-to-face interventions. Possible further ideas could include a chatbot mimicking personalized content or gamification elements to reward users for adherence. We believe that assessing and optimizing the digital working alliance holds the potential to make mHealth apps more effective and improve adherence to their use. However, more research about its integration and predictive value for mHealth apps is needed.

In addition to specific and common therapeutic factors, there might also be technical factors to consider, which can be barriers to the effectiveness of
mHealth interventions. We believe that in-depth usability testing research among barriers to accessing and using the intervention effect is needed to improve uptake, retention, and engagement significantly. For instance, in our study, we noticed that some people had issues with the app registration process. We believe that extensive usability testing can help to prevent those issues while easing the onboarding process further. Apart from focus groups, one idea could also be to consider the Facebook community and query them which aspects we still miss, which barriers they experience, and which concerns remain. Eventually, research findings need to be communicated from scientists to the app developers, and strategies need to be implemented. We can imagine that many of these insights might be specific to the intervention at hand. We invite mHealth researchers and app developers to publish their UX research outcomes, improving the understanding of barriers and facilitators to this type of intervention.

Future research regarding the effectiveness of an app should also focus on the interplay of several mechanisms by which the mHealth intervention aims to achieve its effects. Further, more research upon the generalizability of findings is needed. For example, while female breast cancer patients were among the most prevalent participant group in our study, we need large-scale RCTs to determine the interest of cancer survivors and the effectiveness for other cancer and treatment types and men to support the generalization of current findings. In addition to relatively rigid RCT designs, other additional research methods could be retained. For instance, collecting ongoing observational data (i.e., symptom severity, functioning, well-being, and preferences) of patients using the app could be an additional strategy for researchers to consider. Specifically, routine outcome monitoring (ROM) allows researchers to access big data and give feedback to patients and practitioners (ROM Feedback)\(^3\). Coming back to the example of the CCCs, and the immense psycho-oncological and psychosocial care need, we could imagine that ROM assessments could be embedded into routine (clinical) practice while being easily implemented within app-log-data. Insights from these observational data could show us associations among different variables of interest and could be valuable for theoretical understanding and used for automatized personalized feedback. Eventually, scientists and developers could decide to modify or add components to the intervention and carefully explore the impact on different outcome metrics over time.

While we have already discussed the benefits of a self-management app and the opportunities for increased personalization due to AI, we could also imagine promising results in a blended care setting when healthcare providers
introduce the app to the patient. We know that face-to-face therapist-guided interventions convey decent results. Therefore, one arising question would be to what extent the app’s effectiveness could be increased in a blended care setting. What amount of therapist/caregiver contact should be provided at a minimum? These are important research questions to consider for the future, also in the context of cost-effectiveness. We should also bear in mind that there might not be a one-size-fits-all solution. A self-management app might not be ideal for everyone, while others might prefer an app over face-to-face healthcare visits. Therefore, it seems crucial that the intervention modality (self-management, blended care, face-to-face) is tailored to patients’ needs and preferences. However, more research is needed on that matter.

Conclusions

Our study suggests that besides existing face-to-face therapy or therapist-guided eHealth interventions, low-threshold apps could be an effective and exciting treatment solution for different individuals. Using the Untire app for 12-weeks could reduce CRF among many cancer patients and survivors. The reductions in fatigue experienced were significantly associated with several mechanisms targeted by the multi-component app (i.e., reduced fatigue catastrophizing, depression, sleep disruption, and increased mindfulness and physical activity). Overall, app users also experienced improvements in QoL. We understand that a standalone self-management app might not be the ideal healthcare solution for everyone. However, via mHealth, we could bridge parts of the current healthcare burden and lack of access to healthcare, even though many challenges like dropout and engagement remain. Future research could explore how the effects of mHealth interventions and adherence can be further improved. We wonder to what extent the effectiveness could be enhanced if a healthcare provider introduced the app in a blended care setting. Further, we can imagine that combing mHealth with AI methods could add new exciting opportunities for automatized personalization of content and feedback. In sum, we believe that the Untire app could present a scalable opportunity to support many people worldwide experiencing disabling fatigue.
References


Chapter 7


General discussion