Evaluating the effectiveness of innovative psychological intervention tools in optimizing health outcomes: A multimethod approach

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General introduction

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Psychological interventions entail therapeutic strategies to improve physical and/or psychological well-being by means of modifying emotions, cognitions and/or behaviors (1, 2). One of the most well-researched psychological interventions is Cognitive Behavioral Therapy (CBT) (3), which is based on challenging dysfunctional beliefs and cognitive distortions by various cognitive and behavioral strategies (3, 4). CBT has been demonstrated to be effective in optimizing physical and psychological health in various populations, including patients with type 2 diabetes (5), cancer (6), chronic fatigue (7), and chronic pain (8). Despite the generally positive effects of CBT for those patient populations, there are a number of barriers for traditional face-to-face CBT, including limitations concerning accessibility, such as mobility, treatment costs, and the limited number of qualified therapists, resulting in longer waiting lists (9, 10). Second, a substantial number of participants in treatment programs drop out during the treatment program, primarily due to a lack of motivation and engagement with the intervention (11). Finally, not only the actual experience of success of an intervention is of importance, also the expectancies people have concerning the outcomes of the intervention prior to starting the intervention predict the actual effectiveness of psychological interventions (12). From the placebo literature, positive outcome expectancies are already known to be an important component to maximize treatment outcomes, for example by means of verbal suggestions (13). Therefore, there is a need for innovative tools that can optimize accessibility, engagement, and positive outcome expectancies in psychological interventions.

Innovative tools to optimize psychological interventions

Optimizing accessibility: delivering interventions via the internet

Web-based tools offer great potential for enhancing the accessibility of psychological interventions. Electronic interventions aiming to optimize health, i.e., e-health interventions, are always and anywhere accessible from a networked device, and can thereby overcome the barrier of accessibility (14). Furthermore, they can reduce intervention costs and as more patients can be treated simultaneously, they can also reduce waiting lists (14, 15). However, the drop-out rates in internet-based interventions can be even higher as compared to those of face-to-face interventions; non-familiarity with use of a computer and/or internet is considered to be an important reason (16, 17). Adherence to e-health interventions seems to increase when they are tailored to the specific needs of an individual, and it is well known that therapeutically guided e-health interventions are more effective than non-guided interventions (17, 18). Although internet-based interventions offer fewer key features for developing and maintaining a therapeutic relationship as compared to traditional face-to-face interventions, they are

better able to strengthen independent problem-solving skills, as well as self-determination and empowerment (19, 20). Another strength of guided e-health interventions compared to face-to-face interventions is that the former optimizes accessibility not only for the patient, but also for the therapist, as it costs less time for the therapist to carry out an internet-based intervention compared to a face-to-face intervention (17). A meta-analytic review already provided support for the effectiveness of guided e-health-based CBT in improving psychological and somatic outcomes in patients with chronic somatic conditions (10). Additionally, a systematic review provided support for guided e-health interventions outperforming unguided internet-based interventions in optimizing treatment outcomes (21). Therefore, guided e-health interventions can optimize the accessibility of psychological interventions.

Optimizing engagement: implementing serious gaming elements

Engagement with the e-health interventions, i.e., the process of involving users in health education in such a way that it enhances users' motivation and leads to behavioral changes, is a key factor in enhancing the effectiveness of psychological interventions (22, 23). Engagement therefore can reduce drop-out rates. An innovative e-health method that can be applied to enhance engagement is serious gaming. Serious games are interventions that at least partially exist of gaming elements as a way to accomplish a serious goal, i.e., health optimization (24). It is a rather promising tool to enhance engagement as serious games are entertaining, rewarding and reinforcing, resulting in intrinsic motivation (24-26). Previous studies have provided support for the potential effectiveness of serious gaming in reducing symptoms of mental health disorders (25, 27). Additionally, serious games can promote health behaviors (28, 29) and are therefore a promising tool to provide added value to internet-based CBT interventions.

Optimizing positive outcome expectancies: providing verbal suggestions

In addition to innovative e-health tools, enhancing positive outcome expectancies concerning an intervention have the potential to maximize treatment effects (30, 31). The effectiveness of inducing positive outcome expectancies has already been demonstrated by a large body of placebo studies, showing that providing people with verbal suggestions can optimize perceived treatment credibility and health outcomes (32). For instance, interventions based on expectations have shown to be effective in relieving itch in healthy participants (33), and to effectively relieve pain in various patient populations (34). Concerning psychological interventions, a study on the effectiveness of a smoking cessation intervention found that the efficacy of tailored messages in this intervention was higher when positive outcome expectancies were raised for this intervention (30). Additionally,

a meta-analytic review on the effectiveness of outcomes expectancies in altering the effectiveness of psychotherapy provided evidence for the effects of positive outcome expectancies in optimizing treatment outcomes (35). Positive outcome expectancies do not only increase adherence to the therapy, but can also improve outcomes by increasing feelings of hope and alleviation of symptoms (36). As positive outcome expectancies have shown promising results in optimizing treatment outcomes in various somatic conditions, it would be interesting to explore whether those outcome expectancies are also effective in maximizing the effectiveness of psychological interventions directed at optimizing health outcomes.

Evaluating the effects of psychological interventions on health outcomes

Evaluating basal health outcomes

Health can be defined as a dynamic state of well-being, consisting of physical and psychological potential that can handle challenging demands, such as physical stress (e.g., a wound) or psychological stress (e.g., daily hassles) (37, 38). There are numerous ways to evaluate health. Most studies so far that evaluated health outcomes are based on observing basal levels of health outcomes by including self-reporting outcome measures concerning mental and physical well-being. Those self-reporting outcomes can provide valuable information concerning the participants' view on his/her health status. Although self-reporting outcomes are often well validated and reliable, there are discrepancies between self-reported outcomes and actual health outcomes. Therefore, in order to acquire more insights in actual health outcomes, these outcomes should be evaluated next to self-report measures whenever possible and preferably using multiple independent methods. Self-reporting outcomes, for example, could be supplemented with observations of behavioral outcomes and psychophysiological measures to gather a more complete view on the effectiveness of psychological interventions. Behavioral outcomes can be assessed, e.g., by exposing people to a choice between healthy and unhealthy food products and subsequently observing their actual choice. Besides behavioral outcomes, psychophysiological outcomes could also complement knowledge on self-reported outcomes, including evaluations of the HPA-axis (e.g., measuring cortisol in saliva), Sympathetic Adrenal Medullary (SAM)-axis (e.g., measuring heart rate) and immunological outcomes (e.g., measuring various cytokines in blood serum) in order to acquire a multi parameter view of health-related determinants. Besides, measuring these outcomes in the presence of circumstances that challenge the health status could provide meaningful additional insights on whether individuals can handle such situations adequately.

Evaluating health outcomes in the context of a challenge

A factor that significantly challenges individuals' health status in everyday life is stress, which is determined by the interaction between characteristics of the individual such as appraisal (i.e., interpretations of the situation, event and/or behavior), the environment in which the event occurs, and the internal and external resources a person encompasses (37, 39). Due to unsuccessful cognitive appraisal and coping strategies, stress can have adverse effects on health, including adverse effects on the immune system (40, 41). Chronic stress, for instance, can suppress protective immune responses and promote pathological inflammatory immune responses (42-44). These immune alterations can result in slower wound healing processes (43, 44), impaired responses to vaccines (45), and progression of infectious and immune-mediated diseases (42, 46). Stress does not only have direct detrimental health consequences but can also indirectly affect health. For example, stress can increase health-risk behaviors, including unhealthy eating behaviors, cigarette smoking, and alcohol use (47-50). Those health-risk behaviors, in turn, can have physiological consequences, such as weight gain and even chronic somatic conditions. As psychological interventions are mainly aimed at optimizing health, it would be interesting to investigate the effects of a psychological intervention in the context of a challenge that directly targets the factors that can negatively affect health.

To evaluate the effectiveness of a psychological intervention, participants can be exposed to a situation that simulates the target of the interventions, such as psychophysiological or physical challenges. In the case of psychological interventions that aim to optimize coping with stress, it is, for example, possible to provide participants with challenges that are known to increase stress, in order to observe participants' self-reported as well as psychophysiological responses to the controlled stressful situation. A well-known test to induce psychological stress is the Trier Social Stress Test, which involves a mental arithmetic test and a job interview in front of jury members who do not give any personal feedback (51). This test reliably affects self-reported state anxiety, the HPA-axis, the SAM-axis as well as the immune system (52). Additionally, physical challenges can also result in insightful evaluations of health outcomes, including providing participants with experimentally created wounds and subsequently observing the wound healing process (53). By incorporating those challenges into the study design, more information can be acquired on the effectiveness of psychological interventions in adequately handling with stress and subsequently on optimizing health outcomes. In summary, a model that can be proposed is shown in Figure 1.

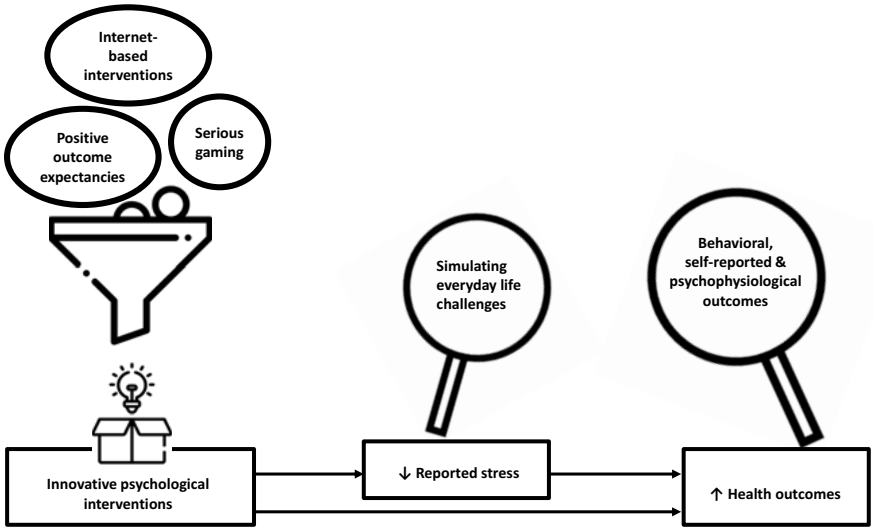


Figure 1. Hypothetical model of how to develop innovative psychological interventions and subsequently assess their effectiveness in optimizing health outcomes.

Aims and outline of the thesis

The main aim of this thesis is to examine the effectiveness of innovative psychological interventions on health optimization by (1) evaluating the effectiveness of innovative psychological tools, i.e., serious gaming, verbal suggestions, and internet-based interventions, to optimize various health behaviors and psychophysiological outcomes; (2) providing a concise overview of the currently existing evidence of psychological interventions in optimizing immune function in response to *in vitro* or *in vivo* immunological as well as psychophysiological challenges; and (3) incorporating various self-reporting, behavioral and psychophysiological outcome measures, but also physical and psychophysiological challenges, including psychophysiological, physical and/or cognitive stressors, to evaluate the effectiveness of psychological interventions on health outcomes. In Figure 2, a visual overview of the content of the present thesis is displayed.

Chapters 2 – 4 describe the results of innovative psychological intervention tools to optimize health outcomes. **Chapter 2** describes the results of a study on the effectiveness of serious gaming in optimizing health behaviors. In this study, health behaviors were evaluated through self-reporting, and by behavioral observations of participants' choices between unhealthy and healthy food products, as well as choosing between using stairs or elevator. Subsequently, **Chapter 3 and 4** report on the possible independent or additional role of innovative intervention tools. Specifically, **Chapter 3** reports on the effectiveness

of serious gaming and verbal suggestions in optimizing self-reported and actual food outcomes, and **Chapter 4** shows the results of a relaxation intervention accompanied or not with verbal suggestions in optimizing self-reported (e.g., state anxiety), as well as psychophysiological stress outcomes (e.g., heart rate and cortisol). **Chapter 5** provides a thorough meta-analytic review on the effectiveness of psychological interventions in optimizing immune function. This review summarized studies that incorporated an *in vitro* immunological, *in vivo* immunological or psychophysiological challenge into the study design and studied the effectiveness of psychological interventions in optimizing immune function. **Chapters 6** and **7** provide the design and results for a study on the effectiveness of a psychological intervention, based on a combination of multiple evidence-based innovative tools, on optimizing self-reported (e.g., vitality) and psychophysiological (e.g., immune outcomes, heart rate, cortisol) health outcomes. The effectiveness of psychological interventions on various health outcomes was evaluated by including *in vitro* and *in vivo* immunological as well as psychophysiological challenges into the study design. **Chapter 6** provides the rationale and design for this psychological intervention study and **Chapter 7** reports on the results of this study. Finally, **Chapter 8** provides an overarching overview and discussion of the findings from the present thesis by focusing on the scientific and clinical implications.

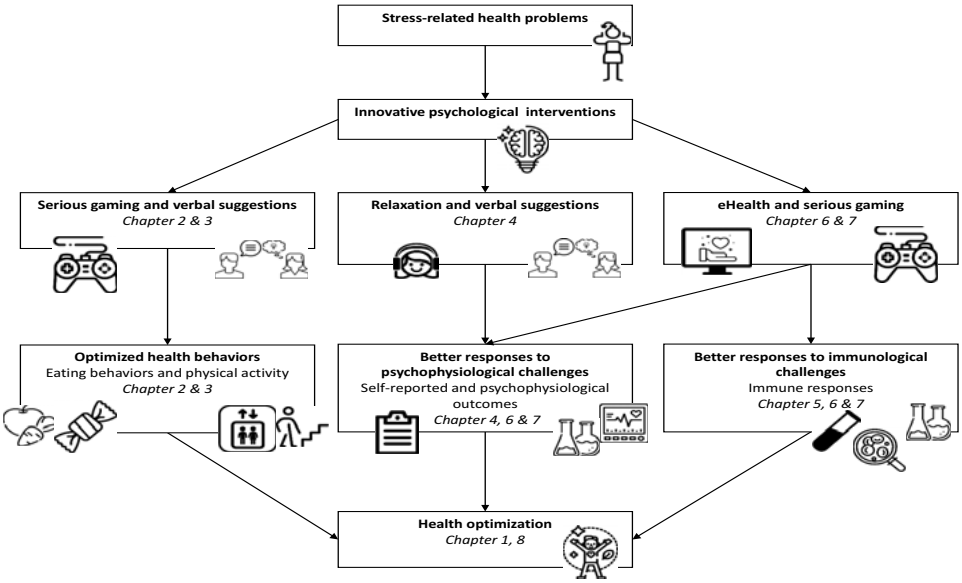
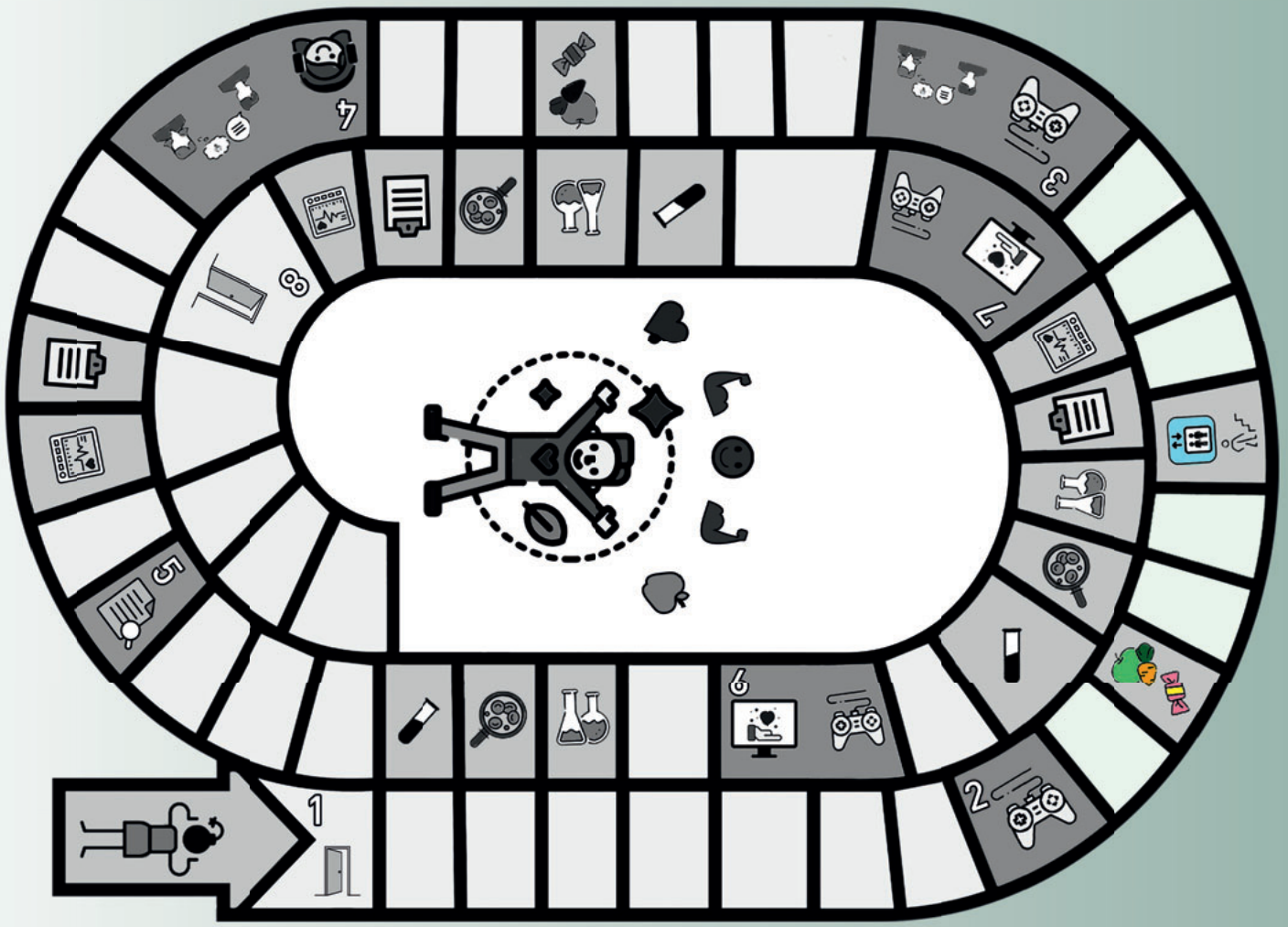


Figure 2. Visual overview of the thesis.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