

# CANCER-RELATED FATIGUE INTERVENTION



DISSERTATION

For a Doctoral Degree (Dr. rer. nat.)

At Faculty of Human Sciences

Julius-Maximilians-Universität Würzburg

Section Psychological Intervention, Behavior Analysis and

Regulation of Behavior

Submitted by

TERESA MARGARETE ZETZL

Born in Weiden i.d. Opf.

Würzburg, 2021



Members of the Committee:

Chairperson: PD Dr. Stefan Schulz  
Primary Supervisor: Prof. Dr. Andrea Kübler  
Supervisor (Second): PD Dr. Andre Pittig  
Supervisor (Third): Prof. Dr. Birgitt van Oorschot

Date of Public Defense: \_\_\_\_\_

Date of Receipt of Certificates: \_\_\_\_\_

Submitted on: \_\_\_\_\_  
Office stamp

---

## ACKNOWLEDGEMENTS

This dissertation would not have been possible without the guidance and support of several people who contributed in one way or another to the preparation and completion of this dissertation.

First of all, I would like to thank my PhD supervisor, Prof. Dr. A. Kübler, who willingly offered her support and mentored and encouraged me during my PhD, gave me new ideas and perspectives, and inspired me to participate in the scientia-program. Thank you very much for your feedback and time!

Furthermore, I would like to thank my supervisor, Dr. A. Pittig, who always supported me with patience and constructive feedback. Thank you very much for the support with the papers. I am very grateful for your appreciative and helpful support.

I would also like to thank Prof. Dr. van Oorschot, who gave me the opportunity to do research in this interesting field, supported me and also gave me enough freedom to be independent and creative. Many thanks!

Special thanks also go to my best friend, Theresa Fehn, who was always there to give me advice and support, who encouraged me when self-doubt was at its greatest, who was always ready to give feedback and sacrificed much of her valuable time. Thank you for the preparatory conversations, reading through documents, weighing decisions, and for always having an open ear and heart. Without her, the many stumbling blocks on the way to my doctorate would have been much greater.

A special thanks also goes to my fiancé, who cared about my well-being, created free times for me to be busy with the PhD, and reminded me what really counts.

Last but not least, I would like to thank everyone who participated in this research project and whose commitment and willingness made a valuable contribution to improving the care of oncology patients.

---

Financial support:

This work was supported by German Cancer Aid (Nr: 70112812) Buschstr. 32, 53113 Bonn. Funding covers costs for personal, materials and traveling expenses. As a sponsor, German Cancer Aid plays no role in the study design, collection, analysis, interpretation or writing of the manuscript.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 declaration of Helsinki. The study protocol was approved by the Ethics Committee of the University Würzburg on 15/05/2018 (Nr. 59/18 sc). The study has been registered with the German Clinical Trials Register DRKS00016034

Conflict of interest:

The author declares no competing interests.

TABLE OF CONTENTS

Figures ..... VI

Tables ..... VIII

Abbreviations ..... X

**Summary ..... 1**

**Zusammenfassung ..... 4**

**1. Introduction ..... 7**

    1.1. Cancer and its side-effects..... 7

    1.2. Cancer-related fatigue ..... 9

        1.2.1. Definition and prevalence of cancer-related fatigue ..... 9

        1.2.2. Assessment of cancer-related fatigue ..... 10

        1.2.3. Etiology of cancer-related fatigue ..... 11

        1.2.4. Consequences of cancer-related fatigue on life and therapy ..... 12

        1.2.5. Therapy of cancer-related fatigue ..... 14

    1.3. Yoga ..... 17

        1.3.1. Definition of yoga and mindfulness ..... 17

        1.3.2. General effects of yoga ..... 18

        1.3.3. Efficacy of yoga in oncological patients ..... 20

        1.3.4. Yoga and cancer-related fatigue ..... 21

    1.4. Objective ..... 23

**2. Publications ..... 24**

    Yoga intervention and reminder e-mails for reducing cancer-related fatigue - a study  
 protocol of a randomized controlled trial ..... 25

    Abstract ..... 26

---

Background .....	27
Methods .....	29
Discussion .....	39
Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer.....	41
Abstract .....	42
Background .....	43
Methods .....	45
Results .....	49
Discussion .....	57
Yoga therapy to reduce fatigue in cancer: effects of reminder e-mails and long-term efficacy .....	61
Abstract .....	62
Introduction .....	63
Methods .....	66
Results .....	70
Discussion .....	80
<b>3. General Discussion .....</b>	<b>84</b>
3.1. Overall Summary and integration of the study results.....	85
3.1.1. Cancer-related fatigue .....	87
3.1.2. Influence of yoga practice on efficacy of yoga .....	89
3.1.3. Cancer type.....	91
3.1.4. Recruitment .....	94
3.1.5. Evaluation of yoga therapy and reminder e-mails by participants.....	95
3.2. Limitations .....	96

---

3.2.1.	Sample .....	96
3.2.2.	Study Design .....	97
3.2.3.	Measures.....	98
3.2.4.	Analytic procedure .....	100
3.2.5.	Differentiation between fatigue and depression.....	101
3.3.	Theoretical and practical implications .....	102
3.3.1.	Cancer-related fatigue .....	102
3.3.2.	Influence of yoga practice on efficacy of yoga .....	104
3.3.3.	Cancer type.....	106
3.3.4.	Recruitment .....	107
3.3.5.	Adaptions of yoga therapy and reminder e-mails .....	108
3.4.	Conclusion.....	110
<b>4.</b>	<b>References .....</b>	<b>111</b>
<b>5.</b>	<b>Appendix.....</b>	<b>144</b>
	Figures .....	144
	Tables .....	149
	Statement of individual author contributions .....	150
	Eidesstattliche Erklärungen.....	152

**Figures**

Figure 1 shows the study design of the research project; Abbreviations: IOT= interdisciplinary oncological therapy outpatient clinic; RAD= radiation therapy ambulance; R= randomization; IG = intervention group; CG = control group; TAU= treatment as usual..... 32

Figure 2 CONSORT diagram showing screening, allocation, and participant flow by group. 46

Figure 3 Mean changes in (A) EORTC QLQ FA 12- General Fatigue, (B) EORTC QLQ FA12 – Physical Fatigue, (C) PHQ-9 Depression Score, and (D) EORTC QLQ C15 PAL – Quality between T0 und T1 in IG (completers) and CG. Results show mean and 95% CI..... 56

Figure 4 CONSORT diagram showing screening, allocation, and participant flow by group 70

Figure 5 Mean changes in (A) EORTC QLQ FA-12 General Fatigue (B) EORTC QLQ FA-12 Emotional Fatigue between T1 and T2 in e-mail group and no-e-mail group. Results show means and 95% CI..... 76

Figure 6 Mean changes in (A) EORTC QLQ FA 12- General Fatigue, (B) PHQ-9 Depression Score and (C) EORTC QLQ C15 PAL – Quality of life between T0,T1 and T2 in all participants. Results show means and 95% CI..... 79

Figure A7 Scatterplots: Difference of fatigue and subscores between pre and post and attended classes..... 145



Figure A8 Scatterplots: Difference in fatigue and subscores between post and follow-up and practice frequency (min) ..... 146

Figure A9 Descriptive analysis of mean fatigue in pre, post and follow-up measurement for patients who participated in yoga therapy. Different colors indicate different types of cancer ..... 147

**Tables**

Table 1 Description of yoga class: poses, Sanskrit names and duration of the single poses ... 47

Table 2 Demographic and clinical characteristics of study population by group (IG= intervention group, CG = control group, SD = Standard deviation, CNS= Central nervous system) ..... 50

Table 3 Adherence and evaluation of yoga sessions (SD=Standard deviation, NA= not applicable) ..... 52

Table 4 Means (m), standard deviation (SD) & p-values of ANOVA analyses of time and group effects, and time\*group-interaction between IG and CG, for per-protocol with completers and intent-to-treat-analyses for primary outcome (fatigue and subscales) and secondary outcomes (depression and quality of life)..... 54

Table 5 Demographic and clinical characteristics of study population by group (SD = Standard deviation, CNS= Central nervous system) ..... 71

Table 6 Practice frequency, subjective benefits of yoga and reasons not to practice (higher values represent higher agreement range 1-4) (SD=Standard deviation, NA= not applicable)73

Table 7 Means (m), standard deviation (SD) & p-values of ANOVA analyses of time and group effects, and time\*group-interaction between reminder and no-reminder group for fatigue and subscales..... 77

---

Table 8 Description of the eight limbed path (Patanyali) ..... 149

---

**Abbreviations**

ACT	Acceptance and commitment therapy
ANOVA	Analysis of variances
BC	Breast cancer
CAM	Complementary and alternative medicine
CG	Control group
CI	Confidence interval
CNS	Central nervous system
CRF	Cancer-related fatigue
EORTC QLQ C15 PAL	European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Palliative
EORTC QLQ FA	European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Fatigue
ESAS	Edmonton Symptom Assessment Scale
IG	Intervention group
IOT	Interdisciplinary oncological therapy outpatient clinic
M	Mean
MBSR	Mindfulness-based stress reduction
NA	Not applicable
NBC	Non breast cancer
NCCN	National comprehensive cancer network
PHQ-9	Patient health questionnaire
QoL	Quality of life

r	Pearson's product-moment correlation coefficient
RAD	Radiotherapy outpatient clinic
RCT	Randomized controlled trial
RGS	Residual gain score
SOC	Sense of coherence
SD	Standard deviation
TAU	Treatment as usual

## SYNOPSIS

### Summary

The incidence of cancer cases is rising steadily, while improved early detection and new cancer-specific therapies are reducing the mortality rate. In addition to curing cancer or prolonging life, increasing the quality of life is thus an important goal of oncology, which is why the burdens of cancer and treatment are becoming more important. A common side effect of cancer and its therapy is cancer-related fatigue, a tiredness that manifests itself on physical, emotional and cognitive levels and is not in proportion to previous physical efforts. Since the etiology of fatigue has not yet been fully clarified, symptom-oriented therapy is preferable to cause-specific therapy. In addition to activity management, sleep hygiene, and cognitive behavioral therapy, mind-body interventions such as yoga are recommended for reducing fatigue.

Previous studies with small sample sizes were able to examine the efficacy of yoga regarding fatigue predominantly in patients with breast cancer. Long-term effects of yoga have rarely been studied and there have been no attempts to increase long-term effects through interventions such as reminder e-mails. This dissertation takes a closer look at these mentioned aspects of the study sample and long-term effects. An 8-week randomized controlled yoga intervention was conducted, including patients with different cancer types reporting mild to severe fatigue. Following the 8-week yoga therapy, a randomized group of participants received weekly reminder e-mails for 6 months for regular yoga practice, whereas the control group did not receive reminder e-mails.

The first paper is a protocol article, which addresses the design and planned implementation of the research project this dissertation is based upon. This serves to ensure better replicability and comparability with other yoga studies. Due to a very low consent rate of patients in the pilot phase, it was necessary to deviate from the protocol article in the actual implementation and the planned inclusion criterion of fatigue  $>5$  was reduced to fatigue  $>1$ .

## SYNOPSIS

The second paper examines the efficacy of the eight-week yoga intervention. Patients in the intervention group who participated in the yoga classes seven times or more showed a significantly greater reduction in general and physical fatigue than those who participated less often. The efficacy of yoga was related to the number of attended yoga sessions. Women with breast cancer who participated in yoga reported greater reductions in fatigue than women with other cancer types. There was also an improvement for depression and quality of life after eight weeks of yoga therapy compared to no yoga therapy. These results imply that yoga is helpful in reducing depression and cancer-related fatigue, especially in terms of physical aspects and improving quality of life.

The third paper focuses on the efficacy of reminder e-mails in terms of fatigue and practice frequency. Patients who received reminder e-mails reported greater reductions in general and emotional fatigue, as well as significant increases in practice frequency, compared to patients who did not receive reminder e-mails. Compared to fatigue scores before yoga, significantly lower fatigue and depression scores and higher quality of life were reported after yoga therapy and at follow-up six months later. Weekly e-mail reminders after yoga therapy may have positive effects on general and emotional fatigue and help cancer patients with fatigue establish a regular yoga practice at home. However, higher practice frequency did not lead to higher improvement in physical fatigue as found in Paper 2. This may indicate other factors that influence the efficacy of yoga practice on physical fatigue, such as mindfulness or side effects of therapy.

This research project provides insight into the efficacy of yoga therapy for oncology patients with fatigue. It is important that such interventions be offered early, while fatigue symptoms are not too severe. Regular guided yoga practice can reduce physical fatigue, but subsequent yoga practice at home does not further reduce physical fatigue. Reminder emails after completed yoga therapy could only reduce patients' emotional fatigue. It may be that physical fatigue was reduced as much as possible by the previous yoga therapy and that there was a floor

## SYNOPSIS

effect, or it may be that reminder emails are not suitable as an intervention to reduce physical fatigue at all. Further research is needed to examine the mechanisms of the different interventions in more detail and to find appropriate interventions that reduce all levels of fatigue equally.



## SYNOPSIS

### **Zusammenfassung**

Die Anzahl der Krebs-Neuerkrankungen steigt stetig, während durch verbesserte Früherkennung und neue krebspezifische Therapien die Sterberate sinkt. Neben der Heilung von Krebs oder Verlängerung der Lebenszeit ist somit eine Erhöhung der Lebensqualität wichtige Aufgabe der Onkologie, weshalb Nebenwirkungen der Krebsbehandlung näher betrachtet werden müssen. Eine häufige Folge von Krebserkrankungen und deren Therapie ist die krebsbedingte Fatigue, eine Müdigkeit, die sich auf physischer, emotionaler und kognitiver Ebene zeigt und nicht im Verhältnis zu vorhergehenden Anstrengungen steht. Da die Ätiologie der Fatigue bisher nicht vollständig geklärt ist, ist eine symptomorientierte Therapie der ursachenspezifischen Therapie vorzuziehen. Neben Aktivitätsmanagement, Schlafhygiene und kognitiver Umstrukturierung werden Mind-Body-Interventionen wie Yoga zur Reduktion von krebsbedingter Fatigue empfohlen.

Bisherige Studien mit geringer Stichprobengröße konnten die Wirksamkeit von Yoga hinsichtlich Fatigue überwiegend bei Brustkrebspatientinnen überprüfen. Langfristige Effekte von Yoga wurden nur selten überprüft. Es gibt bisher keine Interventionen, wie beispielsweise Erinnerungs-E-Mails, die darauf zielen, derartige langfristige Effekte zu erhöhen. In dieser Dissertation werden auf die Aspekte Stichprobe und langfristige Effekte, näher eingegangen. Es wurde eine achtwöchige randomisierte, kontrollierte Yoga-Intervention durchgeführt, die in die Stichprobe alle PatientInnen mit onkologischen Erkrankungen einschloss, die leichte bis schwere Fatigue berichteten. Im Anschluss an die achtwöchige Yogatherapie erhielt eine randomisierte Gruppe der Teilnehmenden für sechs Monate wöchentliche Erinnerungs-E-Mails für die regelmäßige Yogapraxis, die die Kontrollgruppe nicht erhielt.

Das erste Paper befasst sich als Protokollartikel genauer mit dem Aufbau und der geplanten Durchführung des gesamten Forschungsprojekts. Dies dient der Sicherung einer besseren Replizierbarkeit und Vergleichbarkeit mit anderen Yogastudien. Aufgrund einer sehr geringen Zustimmungsrates der PatientInnen in der Pilotphase musste vom Protokollartikel

## SYNOPSIS

abgewichen werden und das geplante Einschlusskriterium der Fatigue  $>5$  auf Fatigue  $>1$  gesetzt werden.

Das zweite Paper beschäftigt sich mit der Wirksamkeit der achtwöchigen Yoga-Intervention. PatientInnen in der Interventionsgruppe, die sieben Mal oder häufiger an der Yogaintervention teilgenommen haben, zeigten eine signifikant stärkere Reduktion der allgemeinen und physischen Fatigue als die PatientInnen der Kontrollgruppe. Die Wirksamkeit der Yoga-Intervention stand im Zusammenhang mit der Anzahl der teilgenommenen Yogastunden. Frauen mit Brustkrebs, die am Yoga teilnahmen, berichteten eine stärkere Reduktion der Fatigue als Frauen mit anderen Krebsarten. Auch für Depression und Lebensqualität konnte durch die achtwöchige Yogatherapie eine Verbesserung erzielt werden. Diese Ergebnisse implizieren, dass Yoga hilfreich ist, krebsbedingte Fatigue zu reduzieren, vor allem hinsichtlich physischer Aspekte.

Das dritte Paper beschäftigt sich mit der Wirksamkeit von Erinnerungs-E-Mails hinsichtlich der Fatigue und Übungshäufigkeit. PatientInnen, die Erinnerungs-E-Mails erhielten, berichteten von einer stärkeren Reduktion der allgemeinen und emotionalen Fatigue, sowie einer signifikanten Erhöhung der Übungshäufigkeit. Im Vergleich zu den Werten vor der Yogatherapie wurden nach Yogatherapie und im Follow-Up sechs Monate später signifikant geringere Fatigue und Depressionswerte sowie eine höhere Lebensqualität berichtet. Wöchentliche Erinnerungs-E-Mails nach einer Yogatherapie können positive Effekte auf die allgemeine und emotionale Fatigue haben und KrebspatientInnen mit Fatigue helfen, eine regelmäßige Yogapraxis zu Hause zu etablieren. Eine höhere Übungshäufigkeit führte jedoch nicht zu einer höheren Verbesserung der physischen Fatigue, wie es in Paper 2 zu finden war. Dies kann auf andere Faktoren hindeuten, die die Wirksamkeit der Yogapraxis auf die physische Fatigue beeinflussen, wie Achtsamkeit oder Nebenwirkungen der Therapie.

## SYNOPSIS

Dieses Forschungsprojekt gibt Aufschluss über die Wirksamkeit der Yogatherapie bei onkologischen PatientInnen mit Fatigue. Wichtig ist, dass derartige Interventionen früh angeboten werden, solange die Fatigue-Symptomatik nicht stark ausgeprägt ist. Regelmäßige geleitete Yogapraxis kann die physische Fatigue verringern, anschließend mehr Yogapraxis zu Hause reduzierte jedoch die physische Fatigue in diesem Forschungsprojekt nicht mehr weiter. Erinnerungs-E-Mails nach abgeschlossener Yogatherapie wirkten sich nur positiv auf die emotionale Fatigue der PatientInnen aus. Dies kann daran liegen, dass physische Fatigue durch die vorhergehende Yogatherapie bereits so stark wie möglich reduziert wurde und ein Boden-Effekt vorlag oder auch daran, dass die Erinnerungs-E-Mails als Intervention zur Reduktion von physischer Fatigue nicht ausreichend geeignet sind. Weitere Forschung ist notwendig, um die Mechanismen der verschiedenen Interventionen genauer zu überprüfen und geeignete Interventionen zu entwickeln, die alle Ebenen der Müdigkeit gleichermaßen reduzieren.

---

## 1. Introduction

### 1.1. Cancer and its side-effects

Every year, about 500,000 people in Germany get cancer, and about 230,000 die of it, making cancer the second most frequent cause of death in Germany after cardiovascular diseases (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019). One quarter of all deaths in Germany can be attributed to cancer. The most common types of cancer are breast, prostate, colon, and lung cancer (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019). The risk of developing cancer in the course of life is 51% for men and 43% for women (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019). It is therefore very likely that probably everyone will have contact with cancer in the course of his or her life due to his or her illness or that of relatives or acquaintances. Due to improved early detection and better treatment options, cancer mortality is declining overall but not without side-effects (Allemani et al., 2018). As a result, physical and psychological stress associated with the disease or treatment are becoming more prominent.

Depending on the cancer-specific treatment, the side effects are very diverse. Whereas radiation therapy as a local treatment can cause various early damages (such as reddening of the skin, disturbances of the sensory organs, dry mouth, feeling of fullness, nausea and, in the case of whole-body radiation, also the so-called "radiation hangover") depending on the irradiated area, frequent late effects include loss of taste, lack of concentration and fatigue. During chemotherapy, patients suffer damage to the mucous membranes, bone marrow, internal organs, and gonads, which can lead to nausea, vomiting, anemia, fatigue, polyneuropathy, and limited brain performance. Antihormone therapy causes symptoms similar to those of menopause, such as sweating, sleep disorders, or mood swings. Immunotherapy, on the other hand, tends to cause flu-like symptoms and depressed mood and fatigue.

---

In summary, in addition to pain and nausea in all treatments, profound fatigue, the so-called cancer-related fatigue (CRF) is a common side effect. This term will be discussed in more detail in the following.

---

## 1.2. Cancer-related fatigue

In the following, the definition and prevalence of cancer-related fatigue will be discussed in more detail. The assessment and etiology of fatigue will be presented. Subsequently, the consequences of cancer-related fatigue on everyday life will be discussed closer. The chapter concludes with the treatment options for cancer-related fatigue.

### 1.2.1. Definition and prevalence of cancer-related fatigue

According to the National Comprehensive Cancer Network (NCCN), cancer-related fatigue is “*a distressing, persistent, subjective sense of physical, emotional, and cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning*” (Berger et al., 2015). Cancer-related fatigue is a frequently occurring symptom in cancer patients (Berger et al., 2015; Bower, 2014). The prevalence rates for cancer-related fatigue are 27-97% (Banipal et al., 2017; Miller et al., 2008; Weis et al., 2013), depending on the time of onset of the disease, type of cancer, and therapy as well as diagnostic tools (Karthikeyan et al., 2012). The affected patients report severe physical exhaustion and persistent weakness and lack of strength, emotional loss of drive and sadness, and cognitive problems with concentration, attention and short-term memory (Bower, 2014; Scott et al., 2011; Shi et al., 2011). Patients mostly report symptoms on the physical level (Fischer et al., 2017; Schmidt et al., 2020). Considering the factors gender, age, body-mass-index and cancer therapy, patients with stomach, lung, kidney, pancreas and endometrial cancer report higher physical fatigue than patients with breast cancer (Schmidt et al., 2020). During the treatment phase with radiation, fatigue complaints are among the most common and most stressful symptoms of a patient (Muszalik et al., 2016) and significantly impair the quality of life (Scott et al., 2011; Shi et al., 2011). Whereas in some cases, symptoms decrease after treatment is terminated, fatigue often becomes chronic and symptoms persist months or even years after the end of therapy (Servaes et al., 2002). About 20% of patients suffer severe fatigue

---

even 10 years after treatment (Joly et al., 2019; Miller et al., 2008). For patients with breast cancer, this relationship is very well evaluated (Abrahams et al., 2016; Kuhnt et al., 2019). On average, they suffer three and a half years of fatigue after end of therapy (Kuhnt et al., 2019).

### *1.2.2. Assessment of cancer-related fatigue*

Almost three-quarters of those affected believe that fatigue is part of the cancer and should be tolerated; half of patients are convinced that nothing can be done about it (Curt et al., 2000). As a result, patients rarely mention their fatigue symptoms to their physicians and nurses (Pearson et al., 2015), leading to physicians and oncology nurses significantly underestimating the frequency, intensity and impact of fatigue (Williams et al., 2016). Regular screening, as performed by one third of the oncology nurses, is therefore essential to better recognize and treat patients with fatigue symptoms (Pearson et al., 2015). Individual screening questions have proven to be economical and helpful, e.g. "Have you often felt tired and exhausted lately? (fatigue intensity) and "Do you feel impaired because of this tiredness or exhaustion? (fatigue impairment) (Berger et al., 2015; Fischer et al., 2017). On an 11-point Likert scale, people can assess the intensity and impairment caused by fatigue in the last week. From an intensity of 4 and an impairment of 5, the fatigue should be clarified more precisely in a medical anamnesis (Berger et al., 2015; Fischer et al., 2017). In the palliative situation, the differential diagnosis of somatic and psychological alternatives is particularly important in order to offer a possible causal therapy with rapid efficacy (Fischer et al., 2017).

Fatigue is usually measured by the subjective symptoms, less by biological markers or parameters, therefore questionnaires are frequently used. Owing to the multidimensional nature of cancer-related fatigue, appropriate questionnaires should include physical, emotional and cognitive aspects of fatigue. The EORTC QLQ Fatigue Module F13 (Weis et al., 2013; Weis et al., 2017), Cancer Fatigue Scale (Kröz et al., 2008) and Fatigue Assessment Questionnaire (Glaus & Müller, 2001) are particularly common in the German-speaking region. The EORTC

---

QLQ-Fatigue Module-FA13 questionnaire is especially characterized by the fact that it can be used in all stages and phases of disease and treatment and care (Weis et al., 2013).

### *1.2.3. Etiology of cancer-related fatigue*

There is no consistent etiology model for cancer-related fatigue, whereby a multidimensional explanatory approach is assumed, based on physiological, psychological and psychosocial conditions. Concerning physiological factors, proinflammatory cytokines (Bower, 2007; Miller et al., 2008; Schubert et al., 2007), hypothalamic-pituitary-adrenal axis dysregulation (Bower, 2007) and skeletal muscle wasting (al-Majid & McCarthy, 2001) might play a role. The influence of the tumor type has not yet been sufficiently investigated. Patients with breast or colorectal cancer report a higher burden of fatigue than prostate cancer patients (Jones et al., 2016). Psychological amplifying conditions can be depression, anxiety and somatization (Kuhnt et al., 2019; Servaes et al., 2002). Previous fatigue and depression can be seen as risk factors (Kuhnt et al., 2019). An existing partnership can serve as a protective factor for fatigue (Kuhnt et al., 2019; van Muijen et al., 2017). There seems to be no correlation with age (Schwarz et al., 2003).

Miller et al. (2008) and Olson et al. (2008) developed a multidimensional concept of the development of fatigue, emphasizing the relevance of inflammation markers (Miller et al., 2008; Olson et al., 2008). During cancer disease and treatment, cytokine secretion and activation of the hypothalamic-pituitary-adrenal-axis is increased and sustained to such an extent that the body can no longer achieve homeostasis. This mechanism results in loss of muscle strength, sleep disturbances, declines in cognitive capacity and nutritional status. The interplay of these four areas then leads to further deterioration of fatigue in the long term (Olson et al., 2008). In summary, the development of cancer-related fatigue is a complex interaction of changes and consequences of the disease and treatment. First and foremost is an increase in the inflammatory parameters and the associated consequences described above. Nevertheless, since



---

most of these results come from correlation studies, which means that no causal relationships can be deduced, the study situation is generally unsatisfactory.

#### *1.2.4. Consequences of cancer-related fatigue on life and therapy*

The consequences of cancer-related fatigue on everyday life and therapy are numerous. Fatigue can affect all areas of social life: Partnership, family, sexuality, social participation, professional activity, and health behavior (Bower, 2014; Curt et al., 2000). Many of those affected by fatigue have to make fundamental changes to their daily routines and can no longer lead their "normal" lives (Curt et al., 2000; Díaz et al., 2008). The quality of life decreases significantly with higher fatigue scores (Alcântara-Silva et al., 2013; Rodríguez Antolín et al., 2019). In the private sphere, those affected engage in fewer entertainment activities, care less about themselves, and withdraw more from relationships (Díaz et al., 2008). The distribution of roles within the family changes (Curt et al., 2000; Curt & Johnston, 2003). Family members take on many additional tasks, which lowers the self-efficacy expectations of cancer patients, makes them question their meaning, and can lead to frustration, anger, and irritability (Joly et al., 2019).

High levels of fatigue are also associated with high levels of depression, although the mechanism of action has not yet been sufficiently verified (Ahlberg et al., 2004; Berger et al., 2015; Brown & Kroenke, 2009; Rodrigues et al., 2015). On the one hand, increased fatigue and lack of drive can be one of the main symptoms of depression; on the other hand, depressive symptoms can also result from existing fatigue and the associated physical, emotional and cognitive limitations. Depression can be a direct or indirect consequence of fatigue and can be caused by the functional impairment, the perceived helplessness, loss of performance or also by the depressive processing of the illness (Beck et al., 2005). At the same time, it is obvious that fatigue and the associated loss of performance significantly reduce the quality of life (Ahlberg et al., 2004).

---

Moreover, despite the high relevance of fatigue in the everyday context, only very few patients actively report fatigue in doctor's consultations (Díaz et al., 2008; Joly et al., 2019), which can have a negative impact on the doctor-patient relationship and compliance for therapy. Fatigue is also associated with reduced treatment success and overall survival rate in diverse cancer types (Efficace et al., 2015; Hofer et al., 2018; Lacourt et al., 2018; Trajkovic-Vidakovic et al., 2012).

In the professional context, fatigue and associated concentration difficulties severely impair the ability to work of those affected. As a result, they reduce their working hours, take on less responsibility, and take more additional sick leave (Curt & Johnston, 2003).

---

### *1.2.5. Therapy of cancer-related fatigue*

The following procedure is recommended for the treatment of fatigue symptoms according to the NCCN guidelines (Berger et al., 2017). As a first step after comprehensive diagnostics, possible causal factors, such as anemia, nutritional deficits, or infections should be treated by blood transfusions, nutritional counseling or dietary supplementation, or anti-infectives. For patients on active treatment and post treatment further specific non-pharmacologic interventions are recommended.

As a second step, psychoeducational interventions should explain general strategies for management of fatigue, such as self-monitoring fatigue or energy conservation through pacing and delegating. Patients should use distraction such as games or music and should try to find meaning in their current situation. Psychoeducation has proven to be very helpful both in video-based (Stanton et al., 2005), telephone-based (Barsevick et al., 2004) and group therapy (Fillion et al., 2008; Reif et al., 2013) especially after cancer treatment and if the interventions are specifically focused on fatigue (Goedendorp et al., 2009). Furthermore, cognitive behavioral therapy is recommended to help patients find meaning in their current situation, to individualize behavioral interventions and to improve stress management. Small to moderate effects of cognitive behavioral therapy on cancer-related fatigue can be found in systematic reviews (Bower, 2014; Jacobsen et al., 2007; Kangas et al., 2008; Wang & Woodruff, 2015). Third wave behavioral interventions such as Acceptance and Commitment Therapy (ACT) can also be helpful in reducing symptoms of fatigue and subjective cognitive impairment in people who survived cancer (Kuba et al., 2019). A further important part of the behavior therapy for fatigue is improving sleep, as sleep disorders are a common side effect of cancer and treatment and can further promote fatigue. Sleep hygiene can improve daytime functioning and sleep parameters (Simeit et al., 2004) and there is evidence that this has a positive impact on fatigue (Berger et al., 2002; Zengin & Aylaz, 2019).

---

NCCN guidelines recommend specific non-pharmacologic interventions as a third step, such as starting an exercise program, physical-based therapy or yoga as a mind-body intervention. Physical activity adapted to individual strength and limitations should be maintained. Physical exercise interventions are effective in reducing fatigue with mean effect sizes of 0.27 – 0.38 (Bower, 2014; Cramp & Byron-Daniel, 2012; Mohandas et al., 2017). Regular physical exercise increases strength and functional capacity, thus reducing the amount of effort required for daily activities (Kangas et al., 2008; Lucía et al., 2003; Mohandas et al., 2017). Exercise programs such as aerobics are very well evaluated (Courneya et al., 2009; Pinto et al., 2005). With regard to resistance to exercise, there are less clear findings (Brown & Kroenke, 2009; Cramp & Byron-Daniel, 2012; Strasser et al., 2013). Although physical activity is safe and well tolerated by cancer survivors (Mustian et al., 2007), it must be considered that fatigue can be an important barrier to physical activity. However, to intrinsically motivate patients, it is useful to give them the opportunity to choose their own type of training (Schwartz et al., 2001; Segal et al., 2001). Pedometers (Vallance et al., 2007) can also be motivating for increased physical activity because of the constant feedback. According to NCCN guidelines (Berger et al., 2015) physical based therapy like massage should be also implemented. Massage therapy as a popular therapy of complementary and alternative medicine (CAM) can be helpful in reducing fatigue (Kinkead et al., 2018; Listing et al., 2009).

Mind-body interventions are also often named as a part of CAM. The term "mind-body intervention" refers to interventions that aim to strengthen self-care through active and health-promoting strategies. With regard to fatigue, the focus here is mostly on mindfulness-based procedures, meditation as well as yoga or Qigong. A meta-analysis reports a moderate effect of mind-body interventions on fatigue symptoms (Buffart et al., 2012). Yoga as a special form of mind-body interventions is explicitly recommended by the NCCN guidelines for reducing fatigue (Berger et al., 2017) and has small to medium effects on reducing fatigue (Lin et al.,

---

2018). Yoga also seems to be superior to a purely psychoeducative therapy (Bower et al., 2012). According to a meta-analysis by Hilfiker et al. (2018), yoga is the non-pharmacologic intervention with the strongest effect on fatigue compared to cognitive behavior therapy, exercises and other CAM therapies for cancer patients after treatment. The effects of yoga in general and specifically on oncological patients are discussed further in the next section.

Even if non-pharmacological interventions appear clearly superior to pharmacological therapies in terms of efficacy and side effect profile (Mustian et al., 2017), psychostimulants are recommended in NCCN guidelines as a fourth step (Berger et al., 2015). Neurobiologically, psychostimulants increase the release of norepinephrine and dopamine in the presynapses, which is helpful against fatigue. However, common side effects of psychostimulants are agitation and insomnia. In some studies, psychostimulants like methylphenidate seems to be more effective than placebos in reducing fatigue (Bruera et al., 2003; Minton et al., 2011). In other studies, the efficacy of methylphenidate is limited to patients with severe fatigue and advanced cancer (Bruera et al., 2013; Moraska et al., 2010) or not higher than placebo therapy (Bruera et al., 2006).

For patients at the end of life, the recommended general strategies are mostly the same as for patients on active treatment and post treatment as mentioned above. Non-pharmacologic specific interventions focus on optimizing the level on activity on physical limitations. Exercise programs or yoga are not specifically recommended by NCCN.

---

### 1.3. Yoga

In the following chapter, yoga is described as more specific. The chapter begins with a more detailed definition of yoga and mindfulness. Then, the general effects of yoga on physical and mental health in the general population and subsequently in people with cancer are discussed. Finally, yoga is discussed with regard to cancer-related fatigue.

#### 1.3.1. *Definition of yoga and mindfulness*

Yoga, as a very original form of mind-body practice, evolved over 5000 years ago in ancient India. The term yoga comes from the Sanskrit word "yuj," which translated means approximately "to join" and is supposed to illustrate the unity of the body with breath and consciousness (Falkenberg et al., 2019; Mohammad et al., 2019). The eight-limbed path (Patanjali) of yoga is supposed to strengthen this unity between body, breath and consciousness and to help the fluctuation of the mind to come to rest (Bryant, 2009; Mohammad et al., 2019; Pal & Gupta, 2019). For a detailed description of the eight-limbed path, see Table 8, p.149.

Through various styles of yoga, the eight-limbed path is to be followed and is supposed to lead to a higher state of ethics, spirit, and healing (Pal & Gupta, 2019). Among the most popular yoga styles are Hatha, Ashtanga, Iyengar, Sivananda, Yin, Vinyasa, and Bikram Yoga (Broad, 2013). In the western world, the practice of asanas plays the most central role within the eight-limbed path. Regardless of the yoga style, mindfulness is the essential basis for the yoga practice. According to John Kabat-Zinn, biologist and founder of the mindfulness-based stress reduction (MBSR), mindfulness is a specific form of attention that deliberately refers to the present moment and is not judgmental (Kabat-Zinn, 2015). In yoga practice, this is reflected in a gentle and mindful execution of yoga postures, which are performed without violence against the own body. The focus is on the non-judgmental perception of body sensations, thoughts, feelings, and breath. For people with health problems, this implies patiently accepting their current condition, experiencing and dealing with their own physical and psychological limits to

---

create a balance between overstraining and avoidance through protective behavior (Kabat-Zinn, 2015).

### *1.3.2. General effects of yoga*

Overall, yoga can affect the body in very different ways. Between the various styles of yoga mentioned above, no differences in odds of reaching positive results have been found so far (Cramer et al., 2016). However, no distinction was made between specific outcomes in this study by Cramer et al. (2016). The positive results of yoga are often based on a reduction of stress markers. Yoga influences the immune system by reducing pro-inflammatory markers, such as interleukins, especially IL-1beta and cell-mediated immunity like IFN-gamma (Falkenberg et al., 2019; Schoenborn & Wilson, 2007). Yoga can also help to lower the plasma level of adrenaline and, at the same time, promote the plasma level of serotonin (Lim & Cheong, 2015) and increase the level of glutathione, total antioxidants status and activity of glutathione S-transferase (Mohammad et al., 2019).

This reduction of various stress markers, in turn, has a positive effect on cardiovascular symptoms, such as reduction of heart rate and blood pressure (Bhutkar et al., 2008; Haider et al., 2017; Mooventhan & Nivethitha, 2017) and improvement of lung function (Abel et al., 2012). Moreover, regular yoga practice also positively influences the consequences of stroke, Parkinson's disease, multiple sclerosis, epilepsy, migraine, and Alzheimer's disease (Mooventhan & Nivethitha, 2017) and is effective in reducing musculoskeletal and spinal pain (Crow et al., 2015; Monson et al., 2017). Yoga also has beneficial effects on metabolic conditions such as type 2 diabetes and obesity (Bijlani et al., 2005).

In the long term, yoga can also lead to an increase in gray matter with increases in frontal cortex activation and improvement in frequency and amplitude in alpha, beta, and theta brain waves (Desai et al., 2015), which leads to higher perception of calmness, higher task performance and reduction of anxiety. Therefore, yoga therapy can lead to better working

---

memory and attention switching ability (Gothe et al., 2014), a higher spatial and verbal memory (Naveen et al., 1997), and reduced reaction time (Sharma et al., 2014). Yoga also has positive effects on the limbic brain system, especially in decreasing the activation of the amygdala and the insula cortex (Desai et al., 2015). This influences the perception of pain (Villemure et al., 2014) and can have a positive impact on mental diseases, as described below (Cramer et al., 2016; Hofmann et al., 2010; Saeed et al., 2019; Smith et al., 2007).

In addition to the positive biophysiological and neuronal effects, yoga also has positive effects on mental diseases. There is strong evidence that yoga can reduce symptoms of depression (Bridges & Sharma, 2017; Cramer et al., 2013; Saeed et al., 2019). There are also some significant findings for anxiety disorders, but these are inconclusive (Cramer et al., 2018; Li & Goldsmith, 2012; Saeed et al., 2019). Yoga is also helpful in patients with PTSD (Gallegos et al., 2017), for treating and preventing addictive behaviors (Khanna & Greeson, 2013) and eating disorders (Borden & Cook-Cottone, 2020). Yoga can also be helpful in the acceptance of bipolar disorders (Uebelacker et al., 2014).

Despite the many positive effects of yoga, the type of yoga must always be individually adapted to the needs and limits of the participants since an incorrect application can have negative consequences, such as vertebral compression fracture (Sfeir et al., 2018). Yoga can be recommended but must be carefully considered especially with patients of bone metastasis (Guo & Molinares, 2020).



---

### *1.3.3. Efficacy of yoga in oncological patients*

Since 2010, yoga in oncological patients has increasingly become the focus of scientific research. Both cancer patients during chemotherapy and radiation therapy and cancer survivors after completion of surgery, chemotherapy and radiation therapy can safely participate in yoga (Lin et al. 2018). In oncological patients, yoga can have strong positive effects on anxiety, depression and distress (Amritanshu et al., 2017; Buffart et al., 2012; Danhauer et al., 2017; Tolia et al., 2018), medium effects on emotional functionality, social functionality and quality of life (Agarwal & Maroko-Afek, 2018; Danhauer et al., 2017; Tolia et al., 2018) and small effects on sleep disorders (Chaoul et al., 2018; Rao et al., 2017; Tolia et al., 2018). Markers of immunity can also be improved by yoga therapy (Agarwal & Maroko-Afek, 2018), e.g., by a reduction of cytokines (Kiecolt-Glaser et al., 2014). However, according to current studies, yoga therapy cannot improve nausea and vomiting during chemotherapy (Anestin et al., 2017).

---

### *1.3.4. Yoga and cancer-related fatigue*

Regarding fatigue, a review suggests that Iyengar yoga and gentle Hatha in 60 to 120-minute sessions, one to three times per week over a period of four up to 12 weeks in the treatment of fatigue in cancer patients and survivors can be effective (Lin et al. 2018). Yoga seems to be more effective after cancer therapy than during cancer therapy (Danahauer et al., 2019; Hilfiker et al., 2018) and compared to other non-pharmaceutical interventions, yoga showed the highest effect after cancer treatment on cancer-related fatigue (Hilfiker et al., 2018). Most of the previous studies were conducted only with patients with breast cancer, only a few included other cancer types like lymphoma (Cohen et al., 2004). Therefore, in the research project this dissertation is based upon, we included patients of all cancer types in the yoga therapy.

Although yoga is helpful in reducing fatigue both before and after treatment (Hilfiker et al., 2018; Lin et al., 2018) and practice frequency has an important impact on efficacy (Kiecolt-Glaser et al., 2014), lack of time, competing priorities (McCall, Thorne, et al., 2015) and fatigue (Frikkel et al., 2020; Mackenzie et al., 2016) are often reported as barriers to regular yoga practice. To motivate patients to practice independently at home, exercise books or CDs are often provided (Bower et al., 2015; Chandwani et al., 2010; Moadel et al., 2007; Vadiraja et al., 2017). In some cases, the independent documentation of the daily practice time seems also to be motivating (Kiecolt-Glaser et al., 2014). Outside the oncological area, daily reminder e-mails were used to increase drug compliance (Fox et al., 2003; Haramiova et al., 2017) or to remind patients of a healthy lifestyle (Cicolini et al., 2014). However, there are no randomized controlled trials to test the efficacy of reminder e-mails in oncology patients for fatigue and practice frequency.

In summary, fatigue is a non-negligible side effect of cancer and its therapy, the etiology of which is not yet well understood. Inflammation markers play a very important role (Miller et

---

al. 2008) (see 1.2.3). Yoga as a mind-body practice reduces pro-inflammatory markers (see 1.3.2) (Falkenberg et al., 2019; Schoenborn & Wilson, 2007), which may also contribute to the reduction of cancer-related fatigue, as shown in several studies with breast cancer patients (see 1.3.3 and 1.3.4). As innovations, this research project included other types of cancer in addition to breast cancer, and subsequently intervened to increase the long-term effects of yoga therapy through reminder e-mails.

#### **1.4. Objective**

The general aim of the research project presented in this dissertation was to gain insight into the efficacy of yoga therapy in reducing fatigue in patients with various types of cancer, as well as to examine the efficacy of reminder e-mails in improving practice frequency and thus improving fatigue.

Chapter 2 contains the published papers. The first paper describes the rationale, methods and design of the research project. The second paper deals with the results of the yoga therapy regarding fatigue, depression and quality of life in comparison to the control group without yoga. The third paper describes the influence of the reminder e-mails on practice frequency and fatigue and the long-term changes six months after the end of yoga therapy. Finally, in chapter 3, all results are summarized and discussed.

---

## 2. Publications

This dissertation is based on three articles which have either been submitted, accepted or published in different high-ranked journals prior to this dissertation and which are embedded in the text. The content of the studies corresponds to the submitted or published form in the respective research journals, merely the format and the figure and table captions were edited to suit this dissertation.

The studies will be presented in the following order:

**Publication 1 - Zetzl, T.,** Schuler, M., Renner, A., Jentschke, E., & van Oorschot, B. (2019). Yoga intervention and reminder e-mails for reducing cancer-related fatigue - a study protocol of a randomized controlled trial. *BMC psychology*, 7(1), 64. <https://doi.org/10.1186/s40359-019-0339-3>

**Publication 2 - Zetzl, T.,** Renner, A., Pittig, A., Jentschke, E., Roch, C., & van Oorschot, B. (2020). Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 29(6), 2973–2982. <https://doi.org/10.1007/s00520-020-05794-2>

**Publication 3 - Zetzl, T.,** Pittig, A., Renner A., van Oorschot, B., Jentschke, E. (resubmitted). Yoga therapy to reduce fatigue in cancer: Effects of reminder e-mails and long-term efficacy. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*

Yoga intervention and reminder e-mails for reducing cancer-related fatigue - a study protocol  
of a randomized controlled trial

Zetzl, Teresa<sup>1</sup>, Schuler, Michael<sup>2</sup>, Renner, Agnes<sup>1</sup>, Jentschke, Elisabeth<sup>1</sup>, van Oorschot,  
Birgitt<sup>1</sup>

<sup>1</sup> Interdisciplinary Center, Palliative Medicine, Universitätsklinikum Würzburg

<sup>2</sup> Institute of Clinical Epidemiology, University of Würzburg

Corresponding author: Zetzl, T., Interdisciplinary Center, Palliative Medicine,  
Universitätsklinikum Würzburg, Josef-Schneider-Str. 2, 97080 Würzburg Germany. E-Mail:

Zetzl\_T@ukw.de

Published 2019 in BMC Psychology 19(7): 64

---

***Abstract***

**Background:** Almost 90% of cancer patients suffer from symptoms of fatigue during treatment. Supporting treatments are increasingly used to alleviate the burden of fatigue. This study examines the short-term and long-term effects of yoga on fatigue and the effect of weekly reminder e-mails on exercise frequency and fatigue symptoms.

**Methods:** The aim of the first part of the study will evaluate the effectiveness of yoga for cancer patients with mixed diagnoses reporting fatigue. We will randomly allocate 124 patients to an intervention group (N=62) receiving yoga and a wait-list control group (N=62) receiving yoga 9 weeks later. The yoga therapy will be performed in weekly sessions of 60 minutes each for 8 weeks. The primary outcome will be self-reported fatigue symptoms. In the second part of the study, the effectiveness of reminder e-mails with regard to the exercise frequency and self-reported fatigue symptoms will be evaluated. A randomized allocated group of the participants (“e-mail”) receives weekly reminder e-mails, the other group does not. Data will be assessed using questionnaires the beginning and after yoga therapy as well as after 6 months.

**Discussion:** Support of patients suffering from fatigue is an important goal in cancer patients care. If yoga therapy will reduce fatigue, this type of therapy may be introduced into routine practice. If the reminder e-mails prove to be helpful, new offers for patients may also develop from this.

**Trial Registration:** German Clinical Trials Register (DRKS00016034, 12/2018), retrospectively registered

**Keywords:** Cancer – Fatigue – Yoga- reminder e-mails- supportive therapy – randomized controlled trial

---

### *1. Background*

Cancer-related fatigue (CRF) is the most common symptom of cancer treatment. Up to 90 % of oncological patients suffer from fatigue during treatment (Berger et al., 2015; Körner et al., 2017). Both physiological and psychosocial factors play an important role in the development of fatigue. Often, however, no specific cause can be identified and therefore no specific treatment can be offered. In these cases, additional support services should be provided to help patients to cope with symptoms of fatigue. These range from drug treatment approaches psychosocial counseling, psychoeducation, exercise training to so-called mind-body interventions (Berger et al., 2015).

CRF is characterized by an intense and chronic sense of tiredness and exhaustion that is not associated with previous stress and cannot completely be relieved by rest. This tiredness can be found on three levels: physical, emotional and cognitive. In order to manage the fatigue symptoms on all three levels, results of meta-analyses support a multimodal approach of cognitive, physical and emotional aspects to symptom relief (Kangas et al., 2008) for example consisting of psychoeducation and mind-body intervention. Few findings on the efficacy of psychoeducative interventions covering cognitive and emotional aspects and behavioral techniques on fatigue symptoms in cancer patients exist (Duijts et al., 2011; Gielissen et al., 2006; Reif et al., 2013). With regard to mind-body interventions (physical and emotional aspects), there are predominantly findings that speak for their efficacy in fatigue. The term "mind-body intervention" refers to interventions that aim to strengthen self-care through active and health-promoting strategies. With regard to fatigue, the focus here is mostly on mindfulness-based procedures, meditations as well as Yoga or QiGong. A meta-analysis reports a moderate effect of mind-body interventions on fatigue symptoms (Buffart et al., 2012). Both the 'mindfulness-based Stress reduction program' (MBSR) by John Kabat-Zinn (Kabat-Zinn, 2015; Ledesma & Kumano, 2009; Rahmani & Talepasand, 2015) and yoga interventions



---

(Banasik et al., 2011; Bower et al., 2014; Carson et al., 2009; Cramer et al., 2015) or Pranayama (Chakrabarty et al., 2015) help reducing fatigue. Even compared to a supportive or psychoeducative group of patients with fatigue, yoga therapy showed significant effects (Vadiraja et al., 2017). However, there are also contradictory findings that do not support significant differences in fatigue symptoms through yoga intervention compared to a control group (Chandwani et al., 2010; Culos-Reed et al., 2006; Moadel et al., 2007).

Follow-up findings for mind-body interventions dealing with fatigue vary widely. While some randomized controlled trials (RCT) show significant effects in fatigue following a mind-body intervention, but no longer after three months (Bower et al., 2015; Cramer et al., 2015), others found no effects immediately after an intervention, but three months later (Kiecolt-Glaser et al., 2014). Lengacher et al. (2016) showed significant reduction of fatigue compared to a CG after the intervention and also in a catamnesis six weeks later. An observational study showed significant long-term effects of mind-body intervention regarding depression and general mood after one year, but no long term effects regarding fatigue (Kieviet-Stijnen et al., 2008).

The yoga therapy intervention we used in our study was already evaluated in previous studies. Using a randomized controlled design, Lundt et al. (2019) showed that this kind of yoga therapy significantly reduce anxiety in cancer patients with mean to high effect size ( $d=0.75$ ). However, no effects significant effects were found for fatigue and depression (Hardoerfer & Jentschke, 2018). In an observational, catamnestic study without control group based on the study above, 6 months after yoga intervention significant changes in fatigue ( $d=0.32$ ), anxiety ( $d=0.33$ ) and depression ( $d=0.40$ ) were observed compared to baseline measurement (Lundt & Jentschke, 2019).

An important moderator of the effect on fatigue is frequency in exercising of the patients during and after the intervention (Kiecolt-Glaser et al., 2014; Moadel et al., 2007). To improve exercise frequencies, participants often receive exercise CDs and/or exercise books at the end

---

of yoga intervention (Bower et al., 2015; Carson et al., 2009; Chandwani et al., 2010; Moadel et al., 2007; Vadiraja et al., 2017). Documentation of their daily exercise duration in addition to the exercise CD has also shown to be helpful for the sustainability of the effects (Kiecolt-Glaser et al., 2014). In the area of oncological complementary therapy, supporting participants via phone calls at weekends within an ongoing mind-body intervention helps to maintain the continuity of the exercises (Banerjee et al., 2007). In the medical context, daily reminder e-mails increased adherence to medication (Fox et al., 2003; Haramiova et al., 2017). However, there are no comparable studies on mind-body procedures to improve fatigue symptoms that use weekly reminder e-mails to promote sustainable effects.

In this study, the following research questions will be examined:

Primary research question:

1. Does an 8-week yoga intervention (IG) reduce self-reported fatigue symptoms directly after the intervention compared to a waiting-list control group (CG)? We expect an effect of  $d=0.50$  in favor of the IG.

Secondary research questions

2. Do gender, age, cancer, baseline fatigue, depression and period since first diagnosis moderate the effects of the yoga intervention on self-reported fatigue?
3. Do reminder-e-mails after the yoga intervention reduce self-reported fatigue symptoms and improve exercise frequency compared to participants of the yoga-intervention receiving no reminder e-mails?
4. Is exercise frequency associated with lower self-reported fatigue symptoms?

## **2. Methods**

The study will take place in the premises of the University Hospital Würzburg Radiotherapy/Palliative Care Unit. Written informed consent will be obtained from all

---

participants. To answer the research questions, a combination of two RCTs will be implemented (see Figure 1). In the first part, eligible patients will be randomized to the IG (8-week yoga intervention) or CG. The CG will also receive the yoga intervention, but nine weeks later than the IG. At the end of the yoga intervention, the second RCT will be implemented: all patients will be again randomized to get reminder-e-mails (e-mail group) or no reminder e-mails after the yoga-interventions. The e-mail group will receive a weekly e-mail over 24 weeks a week, in which one asana out of the yoga intervention is repeated and described in detail. In addition, through the reminder-e-mail participants will be encouraged to practice by themselves regularly. The first RCT is described in 2.1 and will be used to answer research questions 1 and 2, the second RCT is described in 2.2 and will be used to answer research questions 3 and 4.

### 2.1. First RCT (Yoga intervention)

#### Study-Setting and eligibility criteria

The participants will be at least 18 years old, will have a previous oncological disease and will undergo treatment at the radiotherapy outpatient clinic or the interdisciplinary oncological therapy outpatient clinic (IOT) at the time of screening and they report fatigue in Fischer screening (intensity  $\geq 4$ , impairment  $\geq 5$ ). Exclusion criteria will be insufficient knowledge of German and severe emotional or physical impairment as well as more than 50km distance to the university hospital, which would require travelling.

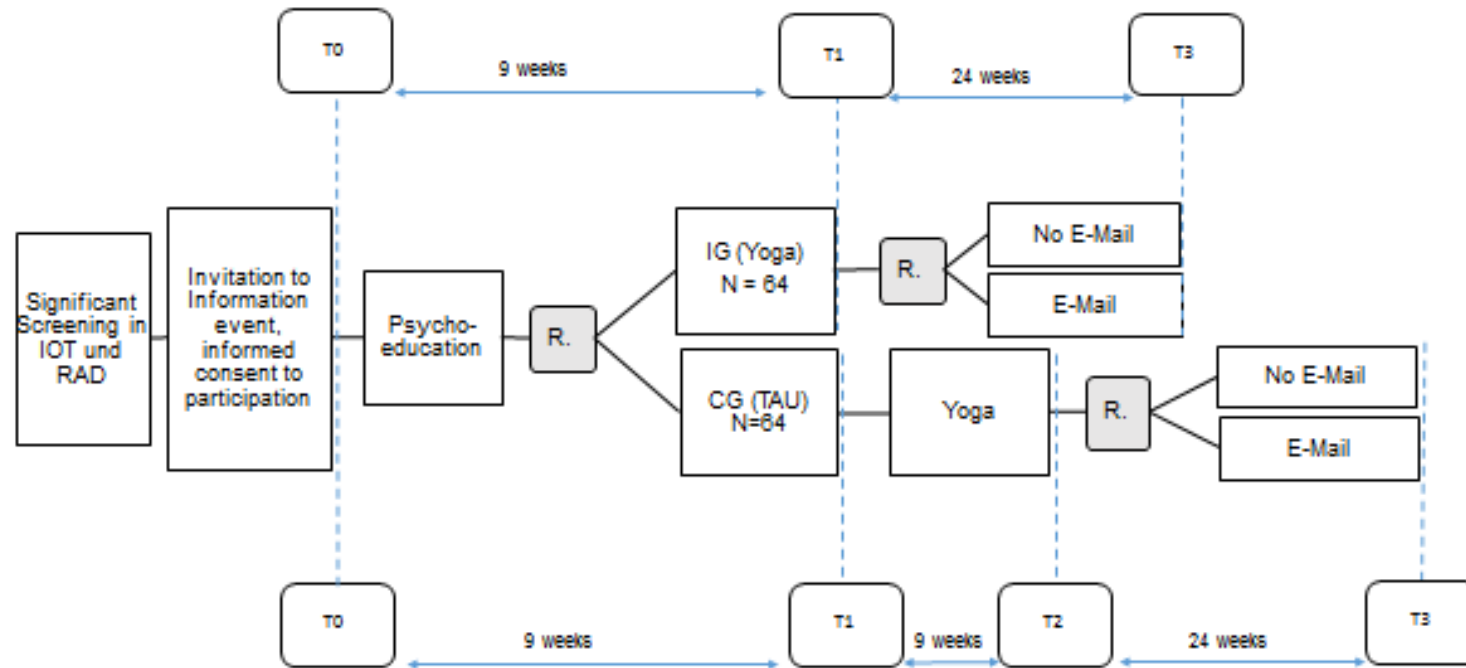
#### Study design and measurement occasions

Eligible patients will receive the first set of questionnaires as a baseline assessment (T0). All participants will receive psychoeducation intervention (coping with fatigue). Subsequently, they will be randomized to IG or CG. The IG starts with the yoga intervention one week after T0, the CG starts ten weeks after T0. The yoga intervention will be conducted for 8 weeks plus an additional lesson in the ninth week to give the participants the opportunity to catch up on a missed session. Primary and secondary outcomes will be assessed ten weeks after the start of

---

yoga intervention (T1) via questionnaires. Participants of the CG will also answer a questionnaire at the begin of the yoga intervention (T1) and at the end of the yoga intervention (T2) this will be used in the second RCT).

Figure 1 shows the study design of the research project; Abbreviations: IOT= interdisciplinary oncological therapy outpatient clinic; RAD= radiation therapy ambulance; R= Randomization; IG = Intervention group; CG = Control group; TAU= treatment as usual



---

### Yoga-Intervention

Certified yoga teachers will carry out yoga intervention. The sequence of exercises will remain constant from beginning to end. The asanas (physical exercises from yoga) were inspired by John-Kabat Zinn and adopted for cancer patients by Dr. Jentschke (psychooncologist, physiotherapist and yoga teacher). One yoga session will last one hour. It consists of physical exercises (asanas), conscious breathing (Pranayama) and deep relaxation (Savasana). Nonviolence (ahimsa) as an important basic principle of yoga is to be repeated every hour and helps to encourage the participants to deal gently with their bodies. Participants should not perform any physical exercises that cause pain. The subsequent body exercises are structured from lying to sitting to standing. The following sequence of exercises will be repeated in each yoga unit: 1) Relaxation: conscious breathing, body scan, mindfulness 2) Vein pump 3) Pelvis and back rotation (adapted variation of the "nakrasana") 4) Pelvis opening (adapted variation of the "supta baddha konasana") 5) Shoulder bridge ("setu bandha sarvangasana) 6) Forward folds (Paschimottanasana and variations with Pranayama) 7) Backbend: intense east stretch (Purvottasana) 8) Diagonal static yoga cat (Majariasana 1 and resting pose) 9) Standing exercise 10) Upward Salute (Urdhva Hastasana) 11) Warrior 1 (Virabhadrasana 1) 12) Warrior 3 (Virabhadrasana 3) 13) Tree (Vrkasana variation) 14) Relaxation (Savasana). In all exercises, participants are reminded to breathe slowly, deeply and consciously. Adverse events and complications during yoga therapy are recorded by yoga teachers on a standardized basis.

### Sample Size Calculation

Two randomized intervention studies investigating yoga therapies in cancer patients of comparable type and duration using an intervention condition and a waiting-list control group condition produced intergroup effect size in fatigue self-assessment scales of  $d=0.66$  (Danhauer et al., 2009) and  $d=0.51$  (Chandwani et al., 2010). Based on the lower effect size of  $d=0.50$

---

alpha=0.05 and Power=0.80 result in a case number of n=62 per group, i.e. 124 patients in total, for a t-test for independent samples with two-sided testing.

### Recruitment

Oncological patients from the radiotherapy outpatient clinic and the interdisciplinary oncological therapy outpatient clinic who score high in fatigue screening will be invited to a non-binding event via mail where they will receive further information on the study. If no response is received within a week of the invitations being sent, patients will be contacted again by telephone to clarify any ambiguities. Through this recruitment, we hope to maximize participation rate in the first information event. At the first event, the patients will be explained the purpose and procedure of the study and asked to participate in the study.

### Randomization

The information events will take place every 4 weeks. The participants of the study will be recruited on each information event. All patients who met inclusion criteria will be asked to participate. Participants who will have signed the consent form and completed the first questionnaire set will be randomly assigned to the IG or CG. To ensure that enough patients will be randomized to the intervention group to perform the intervention, a block randomization procedure will be used. Patients meeting the same information event will form a block. The randomization list with computer-generated numbers will be created by the Institute of Clinical Epidemiology of the university of Würzburg.

## 2.2. Second RCT (Reminder e-mails)

### Study design and measurement occasions

After the yoga intervention, all participants are randomly assigned to group “E-mail” who will get weekly reminder e-mail or to group “NoE-mail” who will receive no reminder e-mails. Participants of both groups will receive a practice book and a practice CD. Outcomes will be assessed six months after the end of the yoga therapy (T3).

---

### Reminder e-mail

Reminder e-mails are used for the second question. The e-mails in the first 12 weeks contain descriptions of the twelve asanas - one asana each week - and an encouragement to practice yoga during this week. The asanas are described analogously to the order of the yoga classes. In the following 12 weeks, the 12 reminder e-mails will be repeated in the same order.

### Randomization

All participants of the Yoga study will be randomly assigned to the group "E-mail" or "NoE-mail". A block randomization procedure will be used. Patients assigned to a group (IG or CG) after the information event form a block. The randomization list with computer-generated numbers is compiled by staff members of the interdisciplinary Palliative Medicine Centre.

Outcomes, ethics, data management and statistics

### Outcomes and other measures

Outcomes will be assessed using patient questionnaires or will be extracted from the patient-documentation system. Unless otherwise specified, all outcomes are recorded at all measurement times (T0, T1, T2, T3).

### Primary Outcome: Self-reported fatigue

Self-reported fatigue will be assessed using the German version of EORTC QLQ-FA13 13 Items (European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Fatigue) (Weis et al., 2017). This questionnaire can be used in all tumor diseases in all stages and phases of the disease and in all areas of treatment (chemotherapy, radiation, surgery) or care (acute care, rehabilitation, aftercare or palliative care) (Weis et al., 2017). Fatigue is measured using 13 items. Response categories of all items are 'not at all', 'a little', 'quite a bit', and 'very much', coded with scores from 1 to 4. All Items are summed up to one fatigue score. The scores range from 0 to 100. Higher values indicate a higher level of



---

fatigue symptoms. The internal consistency for the German version was good with Cronbach's alpha values ranging from .79 -.90 (Fuhrmann et al., 2015; Weis et al., 2017).

### Secondary Outcomes

#### Depression

The Patient Health Questionnaire (PHQ-9) will be used to assess depression. The 9 items assess depression symptoms according to DSM-IV/DSM-V and are scored on a 4-point Likert scale (0 = not at all, 1 = several days; 2 = more than half of the days; 3 = nearly all days). All items are summed up to one sum score, ranging from (0-27). Higher values indicate higher depression. The internal consistency for the PHQ-9 proved to be good with Cronbach's  $\alpha = 0.79$  for cancer patients (Hartung et al., 2017).

#### Quality of life (QoL)

The EORTC QLQ-C15-PAL is a short form (Groenvold, et al., 2006) of the QLQ-C30 for palliative care settings. The 15 items of the questionnaire assess nine categories: physical function, emotional function, global QoL, pain, fatigue, appetite, dyspnea, constipation, and sleep. The four response categories are coded with scores from 1 to 4 (1: not at all; 2: a little; 3: quite a bit; 4: very much) and are transformed to a 0- 100 scale range. As an exception, global QoL is scored from 1 (very poor) to 7 (excellent). A higher score represents better function and QoL, while for symptom scale, it indicates greater symptom burden.

#### Symptom Assessment

The German version of the Edmonton Symptom Assessment Scale (ESAS) (Stiel et al., 2010) will be used to assess symptom severity. The nine symptoms pain, fatigue, nausea, sadness, anxiety, drowsiness, appetite, general condition and shortness of breath are assessed on a numerical rating scale from 0 = none to 10 = worst possible. Higher values in the summed scale score indicate high symptom burden. The internal consistency according to Cronbach's alpha range between 0.67 - 0.73 (Stiel et al., 2010).

---

### Distress Thermometer

The distress thermometer is used to measure psychosocial stress. It uses a numeric rating scale ranging from 0 (no distress) to 10 (extreme distress) and is widely used in clinical practice (Mehnert et al., 2006). A cut-off value of  $\geq 5$  is referred to as high distress. Both the dichotomous classification and the sum score of the distress thermometer are to be recorded in the study. As a short screening instrument, the Distress Thermometer is well suitable for identifying high loads recorded by Hospital Anxiety and Depression Scale  $>11$  (AUC values 0.71 - 0.76) (Mehnert et al., 2006).

### Sense of coherence SOC L9

The German version of the short form of Sense of Coherence Scale (SOC L9) (Schumacher et al., 2000) will be used to record the sense of coherence. This is a reliable, valid and economic alternative short form of the SOC developed by Antonovsky (1983). The 9 items are scored on an 8-point Likert scale. Response formats vary between items. Higher values indicate a high degree of coherence, whereby age- and gender-dependent norms must be applied. The internal consistency of the SOC L9 can be rated as good (Cronbach's alpha = .87) (Schumacher et al., 2000).

### Sociodemographic and health data

The following socio-demographic data will be assessed at T0: age, gender, marital status, number of children, level of education, professional status. Individual coping with the tumor disease, treatment status and use of analgesics and psychopharmaceuticals will be assessed at each measurement occasion. In addition, previous experience with yoga and expectations of the participants on yoga will be asked at T0.

### Program evaluation and training time

At the end of the intervention (IG: T1; CG: T2), participants' comprehensibility and applicability of the yoga theory and psychoeducation as well as subjective benefit will be

---

assessed on a scale from 0 (not at all) to 3 (very). Furthermore, the current scope of the exercise duration (yoga) and the application frequency of the recommendations for handling fatigue will be measured at T1(IG)/T2(CG) and T3(IG and CG). Reasons for continuing or ending yoga practice are documented.

#### Data management and confidentiality

In order to guarantee the confidentiality of data, the data will be pseudonymized using an allocation list. A research code will be assigned to each study participant so that only the code and no personal data will be used on all questionnaires. All questionnaires will be kept in locked cabinets and/or password protected computers. The allocation list will be only accessible to the data manager of the University Hospital Würzburg responsible for allocating medical data. The allocation list is deleted after the end of the study. It will contain the name, address, date of birth, SAP research number and contact data of the patients. During the period of this assignment, the research data will be considered "personal data" and the data protection laws are to be complied. The questionnaires will be scanned by the software EvaSys. The data will be exported to statistical programs for further statistical analysis. The data manager will compare the transferred data of the questionnaires item by item with the original questionnaires. Additional data, such as treatment duration and intensity, will be taken from the electronic patient file. The data manager will also advise on storage, back up and archiving of data to ensure databases are regularly backed up to ensure data is safeguarded from accidental loss. The study master file and all study documentation will be archived for at least 10 years.

#### Statistical analysis

To answer the first research question, analyses of covariance (ANCOVA) will be performed, using fatigue score T1 (primary outcome) as dependent variable, type of treatment (IG vs. CG) as independent variable and fatigue at baseline as covariate. The second research

---

question will be analyzed by including the moderator (e.g. gender, age) and the interaction terms (for example group X gender) in the model.

The third research question will be tested again by using ANCOVA, with fatigue T3 as dependent variable, fatigue after the intervention (IG: T1, CG: T2) as covariate and type of reminder (e-mail vs. no e-mail) as independent variable. The fourth research question will be tested by computing a mediation model using structural equation modeling framework (MacKinnon et al., 2004; Preacher & Hayes, 2004)

### Ethics, consent and permission

The investigation will conform to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the University Würzburg on 15/05/2018 (Nr. 59/18 sc). If interested, all potential participants will receive detailed written information on all relevant aspects of the study. Participants will be informed that they could withdraw from the study at any given time and without reason and that participation in the study is voluntary. Participants will be assured that any future treatment will not be affected in any way should they choose to withdraw. The patients will consent to the study after detailed information. The study is registered on German Clinical Trials Register (DRKS00016034, 12/2018). This paper contains the original study protocol. Material changes to the study protocol will be submitted to the Ethics Committee of the University of Würzburg for approval. These changes are documented in detail in the German Register of Clinical Trials and described transparently in study reports.

### **3. Discussion**

Many cancer patients report fatigue as a very negative stressful side effect at the simultaneous time strong perceived helplessness. In this study, we will offer demand-oriented psychoeducation and Yoga therapy to patients of all tumor entities who suffer from fatigue. The effect of psychoeducation with yoga is compared to psychoeducation without yoga. To our

---

knowledge, the combination of psychoeducation and yoga therapy is an innovation that follows the multidimensional approach for overcoming fatigue. Exploratively, the results of this study (yoga plus psychoeducation) can be compared with other studies (yoga only) at the Interdisciplinary Center for Palliative Medicine. By including different tumor entities, this study can provide indications as to which patients with which tumor entities can benefit most from yoga therapy. So other hypotheses can be generated, such as the degree of fatigue that patients benefit most from the intervention, whether there are differences between the different tumor types in terms of the benefit and feasibility of the intervention, or to what extent tumor therapy has an influence on the intervention.

At the same time, it is to be examined to what degree reminder e-mails are helpful for the sustainability of the practice time for yoga exercises six months after yoga therapy. In addition, the relationship between exercise frequency and the extent of fatigue symptoms will be examined.

If yoga therapy proves to be supportive for oncological patients and reduces fatigue, this type of therapy should continue to be introduced into routine practice. If differences in the effectiveness of yoga therapy are found in different patient groups, it should be considered whether yoga therapy needs to be adapted to specific patient needs. Further studies should also be conducted to determine the barriers to participation in yoga therapy. The aim is to develop a supportive program for oncological patients that is as adapted as possible to their needs.

If the reminder e-mails prove to be helpful with regard to exercise frequency and fatigue symptoms, new offers for patients may also develop from this. For example, the focus is on internet-based training sessions or independent yoga exercises at home.

The findings of this study will be published in peer-reviewed journals and will be presented in conferences.

---

Yoga effectively reduces fatigue and symptoms of depression in patients with different types  
of cancer

Teresa Zetzl <sup>1</sup>; Agnes Renner <sup>1</sup>; Andre Pittig <sup>2,3</sup>; Elisabeth Jentschke<sup>1</sup>; Carmen Roch<sup>1</sup>; Birgitt  
van Oorschot<sup>1</sup>

<sup>1</sup> Interdisciplinary Center, Palliative Medicine, University Hospital Würzburg, Würzburg,  
Germany

<sup>2</sup> Department of Psychology (Biological Psychology, Clinical Psychology, and  
Psychotherapy), University of Würzburg

<sup>3</sup> Center of Mental Health, University of Würzburg

Corresponding author: Teresa Zetzl; University Hospital Würzburg, Josef-Schneider-Str. 11,  
B1, 97080 Würzburg; mail: Zetzl\_T@ukw.de

Published Oktober 2020 in Supportive Care in Cancer

---

***Abstract***

**Purpose:** Examine the effects of an 8-week yoga therapy on fatigue in patients with different types of cancer.

**Methods:** 173 cancer patients suffering from mild to severe fatigue were randomly allocated to yoga intervention (n=84) (IG) versus waitlist control group (CG) (n=88). Yoga therapy consisted of eight weekly sessions à 60 minutes. The primary outcome was self-reported fatigue symptoms. Secondary outcomes were symptoms of depression and quality of life (QoL). Data were assessed using questionnaires before (T0) and after yoga therapy for IG versus waiting-period for CG (T1).

**Results:** A stronger reduction of general fatigue ( $p=.033$ ) physical fatigue ( $p=.048$ ), and depression ( $p<.001$ ) as well as a stronger increase in QoL ( $p=.002$ ) was found for patients who attended 7 or 8 sessions compared to controls. Within the yoga group, both higher attendance rate and lower T0-fatigue were significant predictors of lower T1-fatigue ( $p\leq.001$ ). Exploratory results revealed that women with breast cancer report a higher reduction of fatigue than women with other types of cancer ( $p=.016$ ) after yoga therapy.

**Conclusion:** The findings support the assumption that yoga therapy is useful to reduce cancer-related fatigue, especially for the physical aspects of fatigue. Women with breast cancer seem to benefit most, and higher attendance rate results in greater reduction of fatigue.

**Keywords:** yoga – complementary alternative medicine – Mind body intervention – fatigue - depression - quality of life

---

***Background***

The overall survival rate in cancer is rising steadily due to better early detection and treatment options (Allemani et al., 2018). Therefore, not only the treatment itself but also side effects of cancer and its treatment are gaining more and more attention. Cancer-related fatigue is one of the most common side effects of cancer, which is perceived by patients as even more distressing than pain (Berger et al., 2015). Fatigue is characterized by an intense and chronic sense of tiredness that is not associated with previous stress and cannot completely be eliminated by rest. On the physical level, fatigue expresses as tiredness and lack of bodily strength, on the emotional level as demotivation and depressed mood, and on the cognitive level as difficulty concentrating. It considerably reduces the quality of life (Ahlberg et al., 2004) and prevents patients from living a normal life (Curt et al., 2000). Fatigue poses a high risk for the development of clinical depression and anxiety (Brown & Kroenke, 2009) due to the loss of positive experience and increasing avoidance behavior. Prevalence and subjective evaluation of fatigue differ between different types of cancer: Patients with breast or colorectal cancer report a higher burden of fatigue than prostate cancer patients (Jones et al., 2016).

Despite the high prevalence and impairments, the underlying mechanisms are not fully understood. A multimodal etiology including physical and psychosocial factors is assumed. On the physical level, pro-inflammatory cytokines (Bower, 2007; Miller et al., 2008; Schubert et al., 2007), hypothalamic-pituitary-adrenal (HPA) axis dysregulation (Bower, 2007), and skeletal muscle dystrophy (al-Majid & McCarthy, 2001) might play a role. On the psychosocial level, low social and emotional support, low income, and high catastrophizing thoughts can be risk factors for fatigue (Bower et al., 2000; Donovan et al., 2007). As the etiology of fatigue comprises multiple levels, a multimodal approach to reduce fatigue is recommended in various meta-analyses (Kangas et al., 2008). According to NCCN guidelines, non-pharmacological interventions, such as physical activation management, cognitive behavioral therapy, or mind-body-interventions, should be applied before pharmacological ones (Berger et al., 2015).



---

Moderate effects of mind-body-interventions such as yoga on fatigue are reported in meta-analyses (Buffart et al., 2012; Xunlin et al., 2020). Yoga combines both psychological (“Mind”) and physical (“Body”) aspects and is becoming increasingly important in supportive cancer research (Cramer et al., 2013). Even compared to a supportive or psychoeducative group of patients with fatigue, yoga therapy showed significant effects in reducing fatigue symptoms (Vadiraja et al., 2017). Besides direct effects on the self-reported fatigue symptoms, yoga also showed positive effects on the assumed physical background by reducing pro-inflammatory cytokines (Bower, 2014; Chen et al., 2016; Kiecolt-Glaser et al., 2014), decreasing salivary cortisol level, and restoring HPA-balance (Banasik et al., 2011; Göthe et al., 2016; Vadiraja et al., 2009). It also helped to increase muscle strength and to reduce musculoskeletal symptoms such as muscle pain (Peppone et al., 2015).

Since patients with breast cancer in particular are highly motivated for mind-body interventions, especially yoga, (Cramer et al., 2016) previous studies have examined the effect of yoga therapy on physical and psychosocial aspects predominantly in breast cancer patients with a low sample size (Banasik et al., 2011; Bower, 2014; Carson et al., 2017; Chandwani et al., 2010; Vadiraja et al., 2017). Although other types of cancer suffer just as much from fatigue as patients with breast cancer (Jones et al., 2016) no study has compared the effect of yoga on different types of cancer using the same protocol. As recommended by Lin et al. (2018), we included other types of cancer, which enabled us to compare the efficacy of yoga-therapy in the well-evaluated group of women with breast cancer versus women with other types of cancer.

This led to the following research questions:

1. The primary aim of this study was to assess the changes in self-reported fatigue after an 8-week yoga intervention compared to a CG with no intervention for patients with different types of cancer. We expected a higher reduction of fatigue following the yoga intervention compared to CG.

2. For IG, we hypothesized that reduction of fatigue score is higher for patients with a higher attendance rate.
3. In this present study, we examined the difference in efficacy between women with breast (BC) vs. no-breast cancer patients (NBC).

## ***Methods***

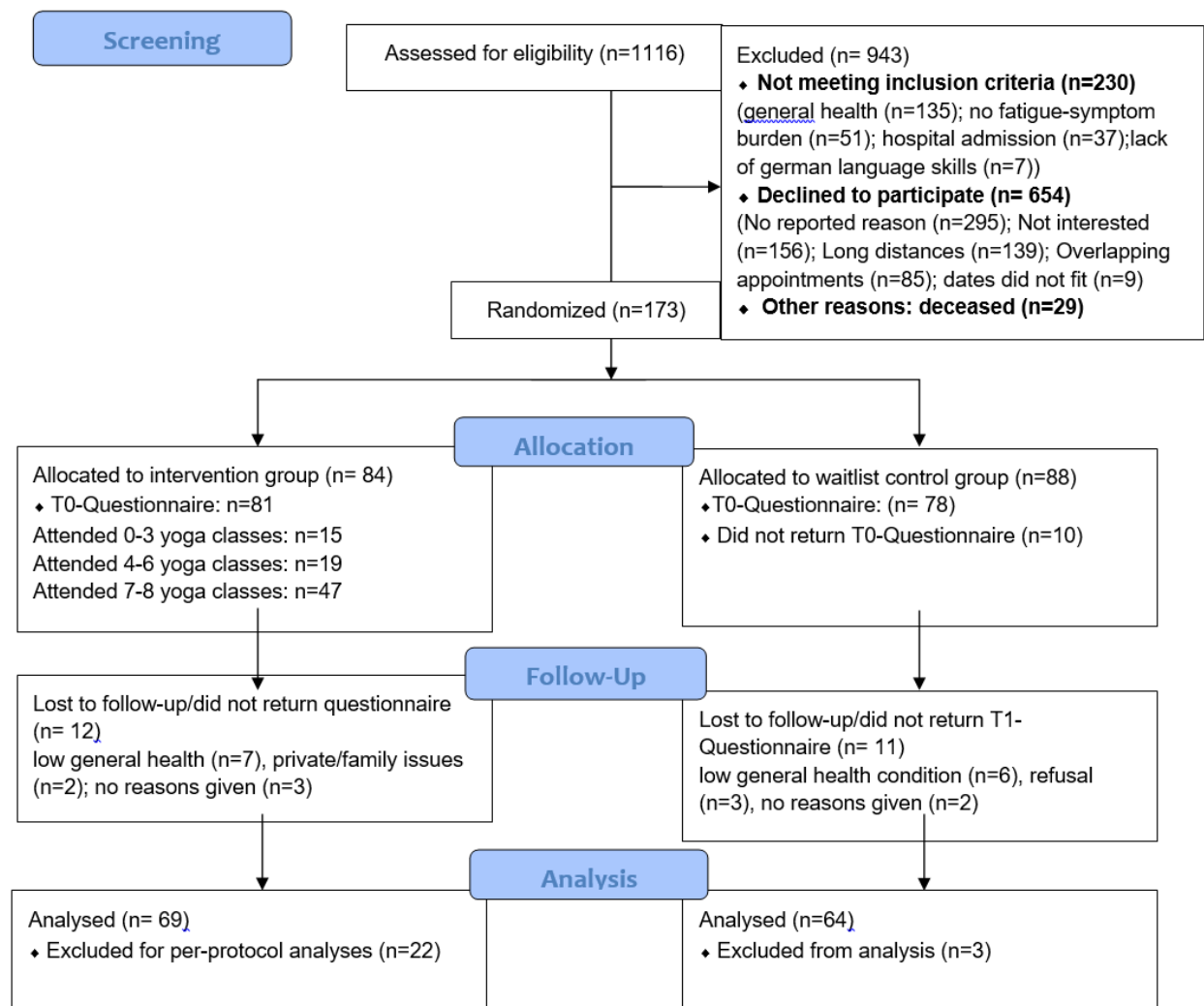
### **Trial design**

A randomized controlled trial examining the efficacy of yoga compared to a control group for decreasing fatigue symptoms in oncological patients was conducted at radiotherapy outpatient clinic (RAD) and the interdisciplinary oncological therapy outpatient clinic (IOT) of the University Hospital Würzburg. Oncological patients with fatigue scores  $\geq 1$  on a scale from 0 – 10 (Fischer et al., 2017) were recruited for a non-binding information event. The information events took place every four weeks. Participants, who had signed the consent form and completed the first questionnaire set (T0) were randomly assigned to IG or CG. To ensure that enough patients were randomized to the IG to perform the intervention, a block randomization procedure with an allocation ratio of 1:1 was used. Patients attending the same information event formed one block. The randomization lists with computer-generated numbers were created by the Institute of Clinical Epidemiology of the University of Würzburg. All participants of the study received information after the first event on how to deal with fatigue, e.g. management of energy and activities. The IG started with the yoga intervention one week after T0; the CG started ten weeks after T0. The yoga intervention was conducted for eight weeks plus an additional class in the ninth week to allow the participants to catch up on a missed session. Primary (fatigue) and secondary outcomes (depression and quality of life) were assessed ten weeks after the start of yoga intervention (T1) via questionnaires.

## Participants

The participants had to be at least 18 years old, had an oncological disease, were planning to undergo treatment at the time of screening, and had to report at least mild fatigue symptoms (intensity  $\geq 1$ , impairment  $\geq 1$ ). Exclusion criteria were insufficient knowledge of German and severe emotional (e.g. severe depressive episode, psychosis) or physical impairment (e.g. unstable metastatic bone disease, acute fractures) as well as more than 50km distance to the university hospital (due to a high risk of drop-out). Patients were recruited between November 2018 – December 2019. 173 of 1116 eligible patients volunteered to participate (recruitment rate 15.5%), 157 from RAD and 16 from IOT. Reasons – if given - for non-participation were documented. For more information, see figure 2.

Figure 2 CONSORT diagram showing screening, allocation, and participant flow by group.



## Intervention

The yoga therapy consisted of eight one-hour yoga sessions once a week over eight weeks, which was carried out by certified yoga teachers and was already evaluated in a previous study (Lundt & Jentschke, 2019). Nonviolence (ahimsa) as an essential basic principle of yoga was repeated every class to encourage the participants to be gentle with themselves and accept personal physical limitations. A yoga session consisted of physical postures with awareness (asanas), small series of conscious breathing and deep relaxation (savasana) at the beginning and end of the class (see Table 1). The sequence remained constant for all sessions. In all exercises, participants were reminded to breathe slowly, and consciously. Personal assistance and instructions to adjust the postures and practices were given verbally throughout the class. Participants were encouraged to use tools like rolls or pillows to adapt to individual requirements. The CG received no specific treatment and was asked to complete the questionnaires at the same intervals as IG. After the waiting period, the CG was given the same yoga therapy for eight weeks.

*Table 1 Description of yoga class: poses, Sanskrit names and duration of the single poses*

	<b>Exercise and description</b>	<b>Sanskrit</b>	<b>Duration (min)</b>
1	Relaxation: conscious breathing, body scan, mindfulness	Savasana	10
2	Vein pump		3
3	Pelvis and back rotation	Nakrasana	3
4	Pelvis opening und strengthening of the abs	Supta Baddha Konasana	4
5	Shoulder bridge Strengthening of back and gluteal muscles	Setu Bandhasana	2

6	Seated forward bend pose and variations:	Paschimottanasana and variations with conscious breathing, shoulderstretch	6
7	Backbend: Strengthening the muscles in shoulders, arms and hands	Purvottasana	1
8	Diagonal static yoga cat	Majariasana	4
9	Resting pose	Balāsana	2
10	Standing exercise/ Balance exercise		2
11	Upward Salute: Strengthening of the upper body, training of the balance	Chandrasana	2
12	Warrior 1	Virabhadrasana	4
13	Warrior 3: Balance exercise	Virabhadrasana	3
14	Tree: Balance Exercise	Vrksasana	4
15	Relaxation	Savasana	10

### Sample Size Calculation

Two randomized clinical studies investigated similar yoga therapies in cancer patients produced intergroup effect size in fatigue self-assessment scales of  $d=0.66$  (Danhauer et al., 2009) and  $d=0.51$  (Chandwani et al., 2010). Based on the smaller effect size of  $d=0.50$   $\alpha=0.05$  and  $\text{Power}=0.80$ , a case number of  $n=64$  per group, 128 patients in total was chosen, to conduct a t-test for independent samples with two-sided testing.

### Measures

Outcomes were assessed using self-report questionnaires at baseline and ten weeks later after yoga therapy. Sociodemographic data (age, gender, marital status, level of education) and treatment status were assessed at T0. Previous experience with and expectations of yoga were

---

asked at T0. The primary outcome was fatigue. Therefore, German version of EORTC QLQ-FA12 (European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Fatigue) (Weis et al., 2017) were used. This questionnaire can be used for all cancer diseases in all stages and phases of the disease and all areas of treatment (chemotherapy, radiation, surgery) or care (acute care, rehabilitation, aftercare or palliative care). All items were summed up to one fatigue score and subscores (physical, emotional and cognitive). Higher scores reflected more fatigue burden. Symptoms of depression, according to DSM-V, were assessed with the Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001), a higher score reflected higher burden of depression. EORTC QLQ-C15-PAL (Groenvold et al., 2006) was used to measure Quality of Life (QoL) for cancer patients and palliative care settings, higher score reflects a higher QoL. For the IG, satisfaction with yoga sessions on different subscales was assessed on a scale 1 (not at all satisfied) to 6 = (very satisfied) at the end of the intervention.

### Statistical analysis

For the first research question, repeated measure analyses of variance (ANOVAs) were performed on per-protocol-basis with completers (at least 7 sessions) and intent-to-treat-basis using time (T0 vs. T1) as within-factor and type of treatment (IG vs. CG) as between-factor for fatigue and each subscale (physical, emotional and cognitive), respectively. The second research question was analyzed by linear regression, including attendance rate and T0-fatigue score as independent variable and T1-fatigue score as dependent variable. The third explorative research question was examined by repeated measure ANOVA in women of IG using cancer type (Breast vs. No Breast) as between factor.

## **Results**

### Sample description and baseline data

There were no significant differences between IG and CG in demographic or health-related characteristics. Participants' age ranges from 24 to 84 ( $M=60.4$ ,  $SD=11.6$ ), 69.8 % were

female, 66% were married or partnered. The participants were predominantly diagnosed with breast cancer (49.1%), followed by prostate cancer (11.9%) and gastrointestinal cancer (10.1%). 76% were under cancer-related treatment at T0 (see Table 2). There was no significant difference in T0-fatigue between patients still in treatment and those who had currently no treatment.

*Table 2 Demographic and clinical characteristics of study population by group (IG= intervention group, CG = control group, SD = Standard deviation, CNS= Central nervous system)*

<b>Characteristics</b>	<b>All (N=159)</b>	<b>IG (N=81)</b>	<b>CG (N=78)</b>
<b>Age [M(SD)]</b>	60.4 (11.6)	59.9 (11.7)	60.9 (10.9)
range	24-84	36-82	24-84
	<b>% (N)</b>	<b>% (N)</b>	<b>% (N)</b>
<b>Female</b>	69.8 (111)	67.9 (55)	71.8 (56)
<b>Marital Status</b>			
Married/Partnered	66.0 (105)	71.6 (58)	60.3 (47)
Never Married/single	13.8 (22)	14.8 (12)	12.8 (10)
Divorced/separated	10.7 (17)	7.4 (6)	14.1 (11)
Widowed	6.9 (11)	4.9 (4)	8.9 (7)
<b>Education level</b>			
Primary education	29.6 (47)	25.6 (21)	33.3 (26)
Secondary education	30.2 (48)	30.9 (25)	29.5 (23)
Tertiary education	37.1 (59)	40.7 (33)	33.3 (26)
others	3.1 (5)	2.5 (2)	3.8 (3)
<b>Tumor diagnosis</b>			

Breast cancer	49.1 (78)	44.4 (36)	53.8 (42)
Prostate cancer	11.9 (19)	16.0 (13)	7.7 (6)
Gastrointestinal cancer	10.1 (16)	12.3 (10)	7.7 (6)
Lung cancer	8.2 (13)	8.6 (7)	7.7 (6)
Lymphoma	8.2 (13)	6.2 (5)	10.3 (8)
Gynecological cancer	4.4 (7)	6.2 (5)	2.6 (2)
Head and neck cancer	3.1 (5)	2.5 (2)	3.8 (3)
Cancer of CNS	2.5 (4)	2.5 (2)	2.6 (2)
Skin cancer	1.3 (2)	1.2 (1)	1.3 (1)
Other cancer	1.2 (2)	0	2.6 (2)
<b>Therapy during study</b>	<b>T0/T1</b>	<b>T0/T1</b>	<b>T0/T1</b>
Had a cancer-related therapy	76.1 (121)/ 50.1 (81)	79.0 (64)/ 48.1 (39)	73.1 (57)/ 53.8 (42)
Chemotherapy	15.1 (24)/ 10.1 (16)	19.8 (16)/ 11.1 (9)	10.3 (8)/ 9.0 (7)
Radiation therapy	53.2 (8)/ 7.6 (12)	53.1 (43)/ 6.2 (5)	51.3 (40)/ 9.0 (7)
Hormone therapy	22.6 (36)/ 26.5 (42)	22.2 (18)/ 22.2 (18)	23.1 (18)/ 30.8 (24)
Antibody therapy	10.1 (16)/ 12.7 (20)	8.6 (7)/ 9.9 (8)	11.5 (9)/ 15.4 (12)
other	8.2 (13)/ 13.2 (21)	6.2 (5)/ 13.6 (11)	10.3 (8)/ 12.8 (10)
<b>Treatment intention</b>	<b>% (N)</b>	<b>% (N)</b>	<b>% (N)</b>
curative	48.4 (77)	53.1 (43)	43.6 (34)
palliative	31.4 (50)	28.4 (23)	34.6 (27)
unknown	20.1 (32)	18.5 (15)	21.8 (17)



### Intervention adherence and evaluation

55.8% of the IG and 50.7% of the CG had no yoga experience at all. Eight participants of the IG and five participants of the CG were practicing yoga before the study. On average, the participants of the IG attended yoga sessions 6.1 ( $SD=2.3$ ) times. 58% of participants attended 7-8 sessions. There were no significant differences at baseline between participants who attended 0-6 sessions vs.  $\geq 7$  sessions (completer) in fatigue, depression or quality of life.

Participants of the IG were very satisfied with the yoga sessions. Mean ratings on the different subscales (possible range from 1="not at all satisfied" to 6="very satisfied") were very high from 4.69 -5.75. 95% would recommend yoga sessions to other patients and 94.9% would (very) certainly participate in yoga sessions again. No adverse events were reported. See Table 3.

*Table 3 Adherence and evaluation of yoga sessions (SD=Standard deviation, NA= not applicable)*

	Intervention group	Control group
<b>Experience of yoga</b>		
No experience	55.8 (43)	50.7 (35)
Little to moderate experience	39.0 (30)	39.7 (31)
(very) much experience	5.2 (4)	4.3 (3)
practicing yoga before the study	9.8 (8)	6.4 (5)
<b>Mean (SD) number of yoga classes attended</b>	6.1 (2.3)	NA
$\leq 3$ yoga classes	18.5 (15)	NA
4-6 yoga classes	23.5 (19)	NA
$\geq 7$ yoga classes	58.0 (47)	NA
<b>Evaluation</b>	Mean(SD)	

---

...the selection and combination of exercises?	5.58 (0.66)	NA
...the overall structure of a yoga class?	5.75 (0.47)	NA
...the length/duration of a therapy session?	5.58 (0.82)	NA
...the length of the whole therapy (8 weeks)?	4.71 (1.35)	NA
...the instruction by the yoga-teachers?	5.86 (0.35)	NA
...the group size?	5.56 (0.71)	NA
...the possibility to exchange experiences?	4.69 (1.21)	NA
...the atmosphere / well-being in the group?	5.48 (0.73)	NA
...the breathing exercises/pranayama?	5.38 (0.84)	NA
...the meditation part?	5.57 (0.79)	NA
Recommendation of yoga classes to other patients	5.94 (0.30)	NA
Further participation in yoga classes	5.73 (0.55)	NA

#### Primary outcome: General, physical, emotional, and cognitive fatigue

Per-protocol-analyses with completers compared to controls (IG: n=64, CG: n=47) showed a larger reduction of general fatigue ( $F(109;1)=4.66$ ,  $p=.033$ ,  $d=0.42$ ) as well as physical fatigue ( $F(109;1)=4.06$ ,  $p=.048$ ,  $d=0.39$ ) (see Table 2.4). In intent-to-treat-analyses, less general, physical, and emotional, and cognitive fatigue was reported at T1 compared to T0 (main-effects time ( $F(131;1)>5.35$ ,  $p's<0.022$ ,  $d>0.40$ ). On general, physical and emotional fatigue, IG compared to CG yielded significantly lower scores ( $F(131;1)>5.60$ ,  $p's<0.02$ ,  $d>0.41$ ). Although reduction of fatigue did not differ significantly, this effect was explained by attendance rate. For mean scores and significance statistics for fatigue and subscores, see Table 4 and Figure 3

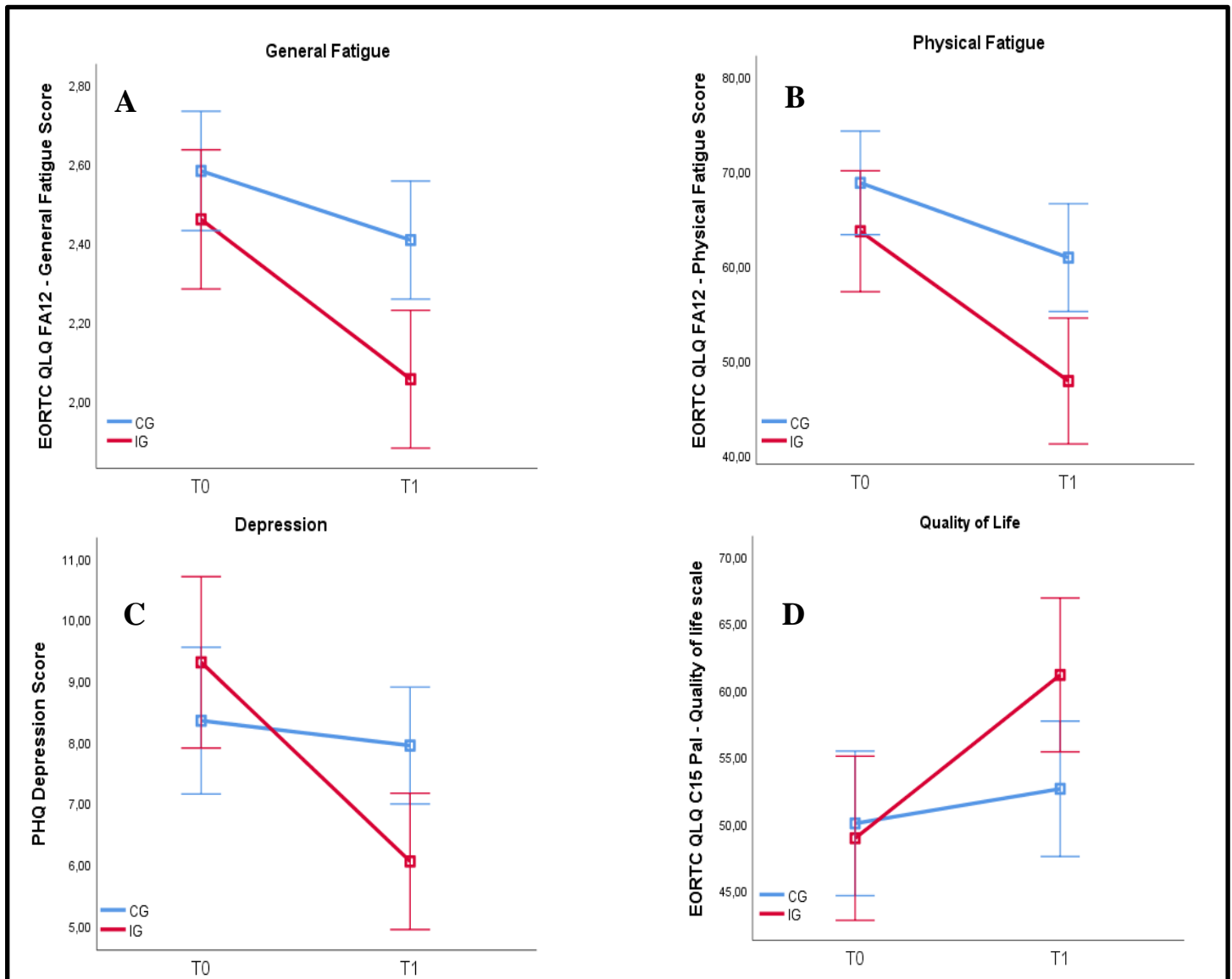
Table 4 Means (m), standard deviation (SD) & p-values of ANOVA analyses of time and group effects, and time\*group-interaction between IG and CG, for per-protocol with completers and intent-to-treat-analyses for primary outcome (fatigue and subscales) and secondary outcomes (depression and quality of life)

Per Protocol-Analyses	Yoga group		Control group		time	group	time*group
	T0 m (SD)	T1 m (SD)	T0 m (SD)	T1 m (SD)	p-value	p-value	p-value
	N=47	N=47	N=75	N=67			
<b>Fatigue</b>	2.5 (0.7)	2.0 (0.5)	2.5 (0.6)	2.4 (0.7)	<.001*	.024*	.033*
<b>Physical Fatigue</b>	63.6 (25.5)	47.8 (21.9)	67.5 (19.7)	60.1 (24.0)	<.001*	.048*	.020*
<b>Emotional Fatigue</b>	35.6 (28.4)	27.1 (25.1)	42.1 (24.9)	38.1 (27.1)	.010*	.030*	.530
<b>Cognitive Fatigue</b>	30.9 (23.9)	18.8 (16.1)	31.8 (22.9)	28.6 (24.6)	<.001*	.089	.110
<b>Depression</b>	9.3 (5.2)	6.0 (3.5)	8.0 (4.6)	7.9 (4.1)	<.001*	.540	<.001*
<b>Quality of life</b>	48.9 (20.3)	60.9 (18.2)	51.6 (20.9)	53.0 (19.7)	.001*	.275	.026*
ITT-Analyses	Yoga group		Control-group		time	group	time*group
	T0 m (SD)	T1 m (SD)	T0 m (SD)	T1 m (SD)	p-value	p-value	p-value
	N=81	N=69	N=75	N=67			
<b>Fatigue</b>	2.5 (0.7)	2.1 (0.6)	2.5 (0.6)	2.4 (0.7)	.001*	.013*	.166

---

<b>Physical Fatigue</b>	65.1 (24.8)	49.6 (23.2)	67.5 (19.7)	60.1 (24.0)	.001*	.020*	.124
<b>Emotional Fatigue</b>	36.6 (29.4)	28.3 (26.0)	42.1 (24.9)	38.1 (27.1)	.022*	.016*	.877
<b>Cognitive Fatigue</b>	29.8 (23.4)	21.0 (19.1)	31.8 (22.9)	28.6 (24.6)	.001*	.086	.341
<b>Depression</b>	8.8 (5.0)	6.1 (3.9)	8.0 (4.6)	7.9 (4.1)	<.001*	.271	.001*
<b>Quality of life</b>	50.6 (21.3)	59.5 (19.9)	51.6 (20.9)	53.0 (19.7)	.002*	.081	.256

Figure 3 Mean changes in (A) EORTC QLQ FA 12- General Fatigue, (B) EORTC QLQ FA12 – Physical Fatigue, (C) PHQ-9 Depression Score, and (D) EORTC QLQ C15 PAL – Quality between T0 und T1 in IG(Completers) and CG. Results show mean and 95% CI



Attendance: Within IG, multiple linear regression with T1-fatigue as dependent variable and T0-fatigue and attendance rate as independent variable had a significant regression equation ( $F(66;2)=18.3$   $p<.001$ ) with  $R^2=.36$ . T1-fatigue decreased .11 for each attended class. Both T0-fatigue ( $r=.491$ ) and attendance rate ( $r=-.273$ ) were significant predictors of T1-fatigue ( $p\leq.001$ ).

---

Within IG, ANOVA with attendance rate as categorical dependent variable (0-3 vs. 4-6 vs. 7-8 attended sessions) showed a significant time\*attendance-rate interaction ( $F(66; 2)=6.513, p=.003$ ). Participants who attended three or fewer sessions had higher general fatigue scores at T1 compared to participants who attended 4-6 sessions respectively 7-8 sessions.

Cancer diagnosis: Within females of IG, there was no significant group effect ( $p=.813$ ) when comparing BC (N=26) vs. NBC (N=20), but significant time-effect ( $F(44;1)=21.0; p<.001$ ) and time\*group-interaction ( $F(44;1)=7.0; p=.011$ ). BC-patients reported a higher reduction in fatigue between T0 and T1 than NBC-patients did.

#### Secondary Outcomes: Depression and QoL

Depression: In per-protocol-analysis a significant time\*group-interaction with high effect size was found ( $F(109;1)=16.83; p<.001; d=.79$ ). Participants in the IG had significant lower depression scores after participating in yoga sessions compared to the CG with medium effect size. Intent-to-treat-analysis also revealed a significant time\*group-interaction ( $F(131;1)=10.71; p=.001; d=.57$ ).

Quality of life: In per-protocol-analysis significant group\*time-interaction with medium effect size was found ( $F(101;1)=5.08; p=.026; d=.45$ ). The IG had a higher QoL after 8 weeks than the CG after this time. Intent-to-treat-analysis revealed a significant time-effect ( $F(122;1)=9.65; p=.002; d=.56$ ). Participants in the IG had higher QoL with medium size effect.

See more in Figure 3 and Table 4.

#### ***Discussion***

This randomized controlled trial examined the efficacy of an 8-week yoga intervention on fatigue in a group of oncological patients with different cancer types. Only few studies have investigated the efficacy of yoga with such a large sample size (Derry et al., 2015; Garland et al., 2013). In addition to patients diagnosed with breast cancer, this study also included other types of cancers (Cramer et al., 2016; Speca et al., 2000).

---

In per-protocol-analyses with completers, significant time\*group-interactions with a small effect size (0.39 - 0.42) were found in general fatigue and physical fatigue. However, these effects crucially depend on attendance, intent-to-treat-analyses revealed a general decrease, but no significant interaction has been found. More importantly, higher frequency of attended sessions was associated with a more pronounced decrease of fatigue, which supports the findings in previous studies (Kiecolt-Glaser et al., 2014). Significant difference in efficacy has been found between patients who attended 0-3 sessions vs. more (4-6 or 7-8). So at least four participations seem to be useful for decreasing fatigue.

Overall, the results of the study are predominantly in line with the results of more recent meta-analyses, which could only find small to medium effect sizes through yoga therapy regarding fatigue (Lin et al. 2018). At this point, it is important to note that a yoga therapy with only 8 one-hour sessions is a rather short and small intervention. It can be supposed that a yoga therapy with higher intensity in length, regularity and frequency of practice would result in bigger effects (Chandwani et al., 2010; Danhauer et al., 2009; Kiecolt-Glaser et al., 2014; Littman et al., 2012; Moadel et al., 2007).

In addition, the differences in efficacy concerning different types of cancer must be considered. To the best of our knowledge, there is currently no study comparing different types of cancer in a yoga therapy (Banasik et al., 2011; Bower, 2014; Carson et al., 2017; Chandwani et al., 2010; Vadiraja et al., 2017). In this study, women with BC compared to women with other cancer showed a stronger reduction of fatigue. Patients with BC experience a higher reduction of fatigue through yoga, and thus benefit the BC-patients, however, report descriptive higher levels of fatigue at all subscales. Therefore, the lower efficacy in NBC-women might also be a possible bottom effect, as they already suffer little or less from fatigue. It must also be taken into account that BC-patients, as middle-aged women, belong to the group that is very much addressed by yoga (Cramer et al., 2016). Therefore, it might be possible that expectation

---

effects might contribute to higher benefits in patients with breast cancer. In this study, there was no significant difference in self-reported expectation regarding yoga therapy between BC and NBC women ( $p=.460$ ). Nevertheless, this can only be seen explorative since the group of NBC-patients is very diverse.

This study differs from other studies by the diversity of the sample. In this study, patients with other types of cancer were included in addition to BC patients, including mainly prostate and gastrointestinal cancer, which also reflects the general cancer prevalence in the general population (Barnes et al., 2016). Furthermore, this study may benefit from a higher relative number of recruited men of 30% compared to other studies of about 5% (Hardoerfer & Jentschke, 2018; Mustian, 2013), which contributes to a better generalizability of the results. Nevertheless, a balanced gender ratio could not be achieved and a selection bias has to be assumed. Women are more interested in complementary alternative medicine, such as yoga or acupuncture than men (Adams & Jewell, 2007; Bahall, 2017), which can lead to a higher participation and attendance rate and thus to a better efficacy (Kiecolt-Glaser et al., 2014). Nevertheless, the low consent rate of 15.5 % must be taken into account for very broad inclusion criteria (fatigue  $\geq 1$ ). However, the inclusion criterion of fatigue was deliberately chosen to be so broad, as 90% of cancer patients undergoing therapy suffer from fatigue during the course of treatment (Bower, 2014). Therefore, it seems to be appropriate to offer yoga therapy at the earliest possible point in treatment, if there is no contradiction against yoga for each single patient, so that patients can learn helpful techniques for the prophylactic management of fatigue.

The diversity of the sample must also be viewed critically. Cancer subgroups cannot be validly compared with each other due to the very different sample sizes. Further research with same sample sizes in the different types of cancer is certainly necessary. The treatment status has also to be considered. Some of the participants were still under treatment at the beginning of the study ( $N=121$ ), others had already completed treatment ( $N=34$ ). A worsening of the



---

fatigue symptoms during the study can also be due to the presence of treatment or an improvement in the symptoms due to the absence of treatment (Danhauer et al., 2019). Studies involving both patients during and after treatment had less consistent and significant findings regarding fatigue (Danhauer et al., 2019; Littman et al., 2012). In this sample, there was no significant association between treatment status and baseline fatigue. Thus, in this study, the influence of treatment status on T0 in terms of fatigue can be considered negligible. Furthermore, due to the lack of an active waiting control group, it cannot be excluded that the effects found are due to unspecific factors, such as the influence of the group or the mere activation by a regular weekly appointment. Thus, only an efficacy of the yoga therapy can be investigated, but not an efficiency compared to other interventions (Bower et al., 2012).

The study shows that yoga therapy is feasible and accepted in and very well evaluated by patients with breast - and other types of cancer. It has positive effects on physical and general fatigue if the attendance rate is sufficient. The influence of the type of cancer on the effectiveness of the yoga therapy cannot be clarified due to the very small subgroups. In addition, studies with an active control group such as walking or psychoeducation would be helpful to shed light on the effectiveness of yoga.

Yoga therapy should continue to be offered, evaluated, and expanded as supportive therapy. Further investigation is needed to explore factors, which might possibly hinder or help in practicing yoga. As attendance rate plays an important role for the effectiveness of yoga, new ways as online or video supported yoga sessions, combined with regular reminders could be promising and should be explored in future studies, as they could help to overcome barriers to a regular self-practice.

---

Yoga therapy to reduce fatigue in cancer: effects of reminder e-mails and long-term efficacy

Teresa Zetzl<sup>1</sup>; Andre Pittig<sup>2,3</sup>; Agnes Renner<sup>1</sup>; Birgitt van Oorschot<sup>1</sup>; Elisabeth Jentschke<sup>1,4</sup>

<sup>1</sup> Interdisciplinary Center, Palliative Medicine, University Hospital Würzburg

<sup>2</sup> Department of Psychology (Biological Psychology, Clinical Psychology, and  
Psychotherapy), University of Würzburg

<sup>3</sup> Center of Mental Health, University of Würzburg

<sup>4</sup> Comprehensive Cancer Center Mainfranken, University Hospital Würzburg

Corresponding author: Teresa Zetzl; University Hospital Würzburg, Josef-Schneider-Str. 11,  
B1, 97080 Würzburg, mail: Zetzl\_T@ukw.de

Submitted December 2020 in Supportive Care in Cancer

---

**Abstract**

**Objective:** Examine the efficacy of reminder e-mails for continuation of yoga therapy on practice frequency and fatigue in cancer patients and long-term effects of yoga on fatigue, depression, and quality of life.

**Methodology:** 102 cancer patients who completed an 8-week yoga therapy were randomly allocated to two groups: reminder (N=51) vs. no-reminder group (N=51). After completion of yoga therapy, the reminder group received weekly e-mail for 24 weeks, which reminded them of practicing yoga, whereas the no-reminder group did not. Primary outcomes were self-reported fatigue and practice frequency. Data were assessed using questionnaires after yoga therapy (T1) and six months after completing yoga therapy (T2). As long-term outcomes we measured fatigue, depression and quality of life.

**Result:** A significantly stronger reduction of general ( $p=.038$ ,  $d=0.42$ ) and emotional fatigue ( $p=.004$ ,  $d=0.59$ ) between T1 and T2 was found for the reminder group compared to the no-reminder group. Patients in the reminder group reported a higher increase of practice frequency than in the no-reminder group ( $p=.015$ ,  $d=0.52$ ). In the mediation model, practice frequency as a mediator did not significantly explain the changes in fatigue. Long-term effects of yoga therapy regarding fatigue, depression and quality of life were found ( $F>7.46$ ,  $p<.001$ ,  $d>.54$ ).

**Conclusion:** Weekly reminder e-mails after yoga therapy can have positive effects on general and emotional fatigue and help cancer patients with fatigue to establish a regular yoga practice at home. However, higher practice frequency did not lead to higher improvement in physical or cognitive fatigue, suggesting other factors that mediate efficacy on physical or cognitive fatigue, such as mindfulness or side effects of therapy.

**Keywords:** Mind-Body-Intervention –complementary alternative medicine – long-term effects – Yoga – fatigue- reminder e-mails

---

***Introduction***

Detection and treatment of cancer have significantly improved, leading to increased survival time in cancer patients. However, contemporary treatment methods are not without side effects (Allemani et al., 2018). As a result, side effects of cancer and their treatment gain more and more attention. Fatigue, one of the most common side effects of cancer and cancer-related treatment, is described as an intense and chronic tiredness on a physical, emotional and cognitive level, which is not related to previous activities and cannot be completely reduced by sleep (Bower, 2007). 20-80% of cancer patients suffer from fatigue during therapy (Miller et al., 2008; Weis et al., 2013) and fatigue can persist even 5 years after therapy-completion (Servaes et al., 2002). Increased interleukins (Bower, 2007; Miller et al., 2008), anemia and psychological stress (Kuhnt et al., 2019; Servaes et al., 2002) might play a major causal role in the etiology of fatigue, but the complexity of this interaction is not yet fully understood. Therefore, symptom-oriented treatment of fatigue is usually preferred to cause-specific treatment. The National Comprehensive Care Network recommends yoga as a category 1/grade A non-pharmacologic intervention for cancer patients during and after cancer-related therapy. Yoga interventions of different styles and duration were found to be effective in reducing fatigue in cancer patients (Banasik et al., 2011; Bower et al., 2014; Carson et al., 2017; Cramer et al., 2016; Zetzl et al., 2020). Meta-analyses of yoga with cancer patients report small to moderate effects on fatigue (Buffart et al., 2012; Cramer et al., 2011; Danhauer et al., 2019; Dong et al., 2019).

Findings on long-term effects of yoga in cancer patients are less coherent than those for short-time effects. Some randomized controlled trials report a significant reduction in fatigue after yoga therapy, but no effect after three months compared to control groups without interventions (Bower et al., 2015; Cramer et al., 2015). Another randomized controlled trial finds no significant improvement in fatigue directly after yoga compared to a control group, but

---

three months later (Kiecolt-Glaser et al., 2014). In an observational study without a control group and with pre-post measurements, yoga intervention also showed significant long-term effects on fatigue as well as on depression and anxiety months after the completion of the yoga intervention (Lundt & Jentschke, 2019).

The sustainability of such positive effects of yoga interventions is related to patients' individual practice frequency during and after the intervention (Amritanshu et al., 2017; Kiecolt-Glaser et al., 2014; Moadel et al., 2007). Patients suffering from fatigue are physically, emotionally and cognitively exhausted. Therefore, it is quite comprehensible that patients affected by fatigue have difficulties motivating themselves to practice independently outside of regular classes (Frikkel et al., 2020). Knowledge about physical activity and its impact on quality of life, physical activity prior to diagnosis (Frikkel et al., 2020), social support as well as a given structure and appointed times for sports classes (Mikkelsen et al., 2019) have a positive influence on the patients' motivation for physical activity. Clinical depression in contrast keeps patients from physical activity (Frikkel et al., 2020). To facilitate patients' independent practice, it is an established method to provide them with an exercise CD and exercise book at the end of a yoga intervention (Bower et al., 2015; Chandwani et al., 2010; Moadel et al., 2007; Vadiraja et al., 2017). An individual documentation of the daily exercise duration in addition to the exercise CD was also proven to be helpful with respect to the sustainability of positive effects (Kiecolt-Glaser et al., 2014). Although these methods aim to establish regular yoga exercises, they are usually offered only once at the end of the yoga therapy and due to a lack of regularity and frequency they do not represent a reminder of the yoga practice.

In the medical context, daily reminder e-mails proved to be helpful in increasing adherence to medication (Fox et al., 2003; Haramiova et al., 2017). Cicolini et al. (2014) also used weekly reminder e-mails to remind patients with cardiovascular risk factors to adopt a

---

healthy lifestyle. This led to significantly lower cardiovascular risk factors compared to a group that did not receive reminder e-mails. However, there are no comparable studies on yoga for improving fatigue symptoms that use weekly reminder e-mails to promote lasting effects.

In a previous paper, we described the efficacy of yoga therapy regarding fatigue, depression and quality of life. Patients who participated in an eight-week yoga therapy reported significantly lower general and physical fatigue and depression and higher quality of life compared to patients in a waiting-list control group. Higher attendance rate was associated with more reduction in fatigue (Zetzl et al., 2020). This paper builds on the results of the previous paper and examines the stabilization of the efficacy of yoga therapy through reminder e-mails as described above and long-term effects of yoga therapy as an additional research question.

Thus, the first research question of this study should examine the efficacy of reminder e-mails on fatigue and its subscores compared to patients who do not receive reminder e-mails (Berger et al., 2010). We hypothesized that patients who receive reminder e-mails would report lower fatigue scores. Our second research question aimed at examining the efficacy of reminder-e-mails on increasing practice frequency compared to patients without reminder e-mails. The hypothesis was that patients with reminder e-mails practice more frequently than patients without reminder e-mails. The third hypothesis was that the effect of reminder e-mails on fatigue and its subscores would be mediated by practice frequency. The fourth research question addressed the long-term changes in self-reported fatigue, depression and quality of life after an 8-week yoga intervention for patients with different types of cancer after six months. We hypothesized that fatigue would be significantly lower immediately after yoga therapy and at the follow-up six months later compared to the baseline.

---

## *Methods*

### Design and Procedure

This randomized controlled trial took part in the premises of the University Hospital Würzburg from November 2018 – September 2020. After informed consent, patients participated in eight-week yoga classes, for one hour a week. At the end of the yoga therapy, participants received a booklet and a CD with instructions of the asanas they learnt in class. Afterwards, participants were randomly assigned to “reminder” or “no-reminder” group. A block randomization procedure was used. Patients assigned to a yoga group form a block. The randomization list with computer generated numbers was compiled by staff members of the Palliative Medicine Centre. The reminder group received a weekly reminder e-mail over 24 weeks. Primary (fatigue, practice frequency) and secondary outcomes (depression, quality of life) were assessed before and after yoga therapy and 24 weeks after the end of yoga therapy via self-report questionnaires. The Ethics Commission of the University of Würzburg has approved the study in advance (59/18-sc). The study design can be found in the protocol article (Zetzl et al., 2019).

### Participants

Participants of this randomized controlled trial were adult cancer patients, at least 18 years old, that were planning to undergo cancer treatment in University Hospital Würzburg at the time of screening. In order to be included, patients had to report at least mild self-reported fatigue symptoms in the Fischer screening (intensity  $\geq 1$ , impairment  $\geq 1$ ) (Fischer et al., 2017). Exclusion criteria were insufficient knowledge of the German language, severe emotional or physical impairment as well as more than 50km distance to the university hospital.

### Yoga Intervention

The yoga intervention ran for eight weeks. Patients took part in one session of one hour per week. The yoga intervention consisted of different asanas (physical postures with

---

awareness), small series of conscious breathing (pranayama) and deep relaxation (savasana) at the beginning and at the end of each class, inspired by mindfulness based stress reduction program (MBSR) (Kabat-Zinn, 2015). The sequence of exercises was structured from lying to sitting to standing and was kept constant for all sessions. In all exercises, participants were reminded to breathe slowly, deeply and consciously. Nonviolence (ahimsa) as an important basic principle of yoga was repeated in every session and helped to encourage the participants to be gentle with their bodies and personal limitations.

#### E-mail reminder

After completion of yoga-therapy, personal e-mails were sent on the same day every week, for 24 weeks altogether. E-mails in the first twelve weeks contained descriptions of twelve yoga exercises - one exercise each week - and a personal encouragement to practice yoga independently during this week. The yoga exercises, known to the participants from the yoga classes, were described analogously to the description in the group yoga classes. In the following twelve weeks, the twelve reminder e-mails with these exercises were repeated in the same order.

#### Questionnaires

Outcomes were assessed directly before and after yoga-therapy (T0 and T1) and 6 months later (T2).

#### Primary Outcomes

##### Self-reported fatigue

Self-reported fatigue was assessed using the German version of EORTC QLQ-FA13 - 13 Items (European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Fatigue) (Weis et al., 2017). This questionnaire can be used in all tumor diseases in all stages and phases of the disease and in all areas of treatment (chemotherapy, radiation, surgery) or care (acute care, rehabilitation, aftercare or palliative care) (Weis, 2013).



---

The EORTC QLQ-FA 13 measures general fatigue using 13 items overall. Physical fatigue assessed with five items (e.g., *have you felt exhausted?*), emotional fatigue with three items (e.g., *did you feel discouraged?*) and cognitive fatigue with two items (e.g., *did you have trouble thinking clearly?*). Response categories of all items are 'not at all', 'a little', 'quite a bit', and 'very much', coded with scores from 1 to 4. Mean scores are calculated for each subscale and for the overall scale and then linear transformed to symptom scales ranging from 0 to 100. Higher values indicate a higher level of fatigue symptoms. The internal consistency for the German version was good with Cronbach's alpha values ranging from .79 -.90 (Fuhrmann et al., 2015; Weis et al., 2017).

#### Practice Frequency

The practice frequency was assessed after yoga therapy and 6 months later with open responses. Patients indicated on how many days they had practiced in an average week and how many minutes they practiced on average per practice day. The variable was calculated by multiplication of average days and average minutes.

#### Secondary Outcomes

##### Depression and Quality of life

Depression was assessed by using the Patient Health Questionnaire (PHQ-9) which assesses symptoms of depression according to the DSM-V (Kroenke et al., 2001; Löwe et al., 2004). Higher values indicate higher depression. The internal consistency for the PHQ-9 proved to be good with Cronbach's  $\alpha = 0.79$  for cancer patients (Hartung et al., 2017).

Quality of life was assessed with the function scale of EORTC QLQ-C15-PAL (Groenvold et al., 2006). This scale consists of the item "*How would you rate your overall quality of life during the past week?*", scaled from 1 (very poor) to 7 (excellent). Higher scores represent higher quality of life.

---

### Sociodemographic and Health Data

The following socio-demographic data was assessed at T0: age, gender, marital status, number of children, educational level, professional status, tumor diagnosis. In addition, subjective benefits of yoga and reasons not to practice (anymore) were assessed at T2 on a four-point Likert scale (does not apply at all – applies completely).

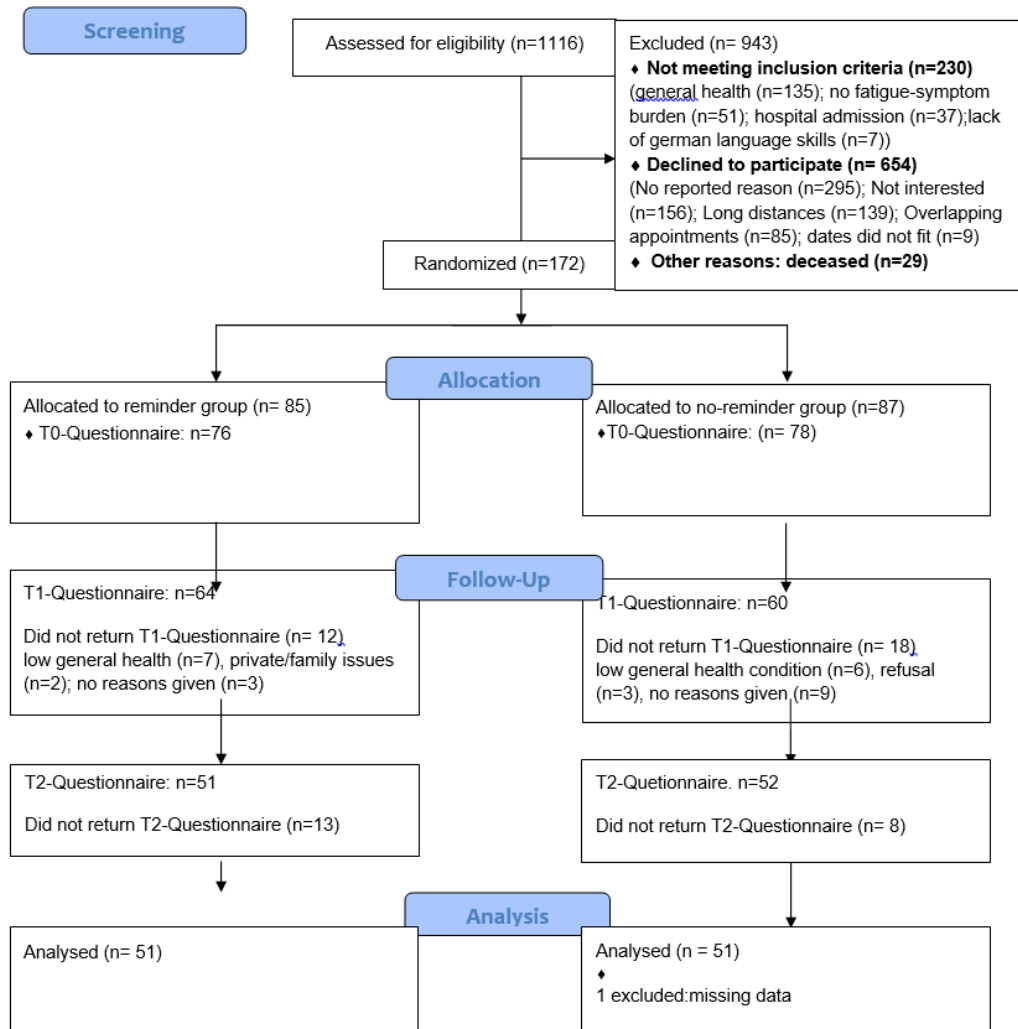
### Statistical Analyses

All analyses were performed on intention-to-treat-basis on significance level of  $\alpha=.05$ . Data analysis was carried out using IBM SPSS Statistics version 26. For the first hypothesis analyses of variance (ANOVA) for fatigue and each subscale (physical, emotional and cognitive) using time (T1 vs. T2) as within-factor, type of reminder (reminder vs. no-reminder) as between-subject factor were performed. For the second hypothesis, we calculated a t-test for independent samples (reminder vs. no-reminder) with residual gain scores (RGS) of practice frequency (Steketee & Chambless, 1992) as the outcome variable. RGS were calculated by subtracting the standardized z-values of the practice frequency at T1 multiplied with the correlation of T1 and T2 from the standardized z-values of the practice frequency at T2. RGS control baseline differences and measurement errors occurring in the use of repeated measures on the same instrument (Steketee & Chambless, 1992). The third research question was tested using a mediation model with group (reminder vs. no-reminder) as predictor, RGS of practice frequency as mediator and fatigue and subscore as dependent variable. For the mediation model, the causal steps method for linear regression models was used (Baron & Kenny, 1986; Müller, 2009). The fourth research question was tested with an ANOVA and paired t- tests with adjusted  $\alpha=.016$  to analyze long-term changes in fatigue, depression and quality of life between baseline, after yoga and follow-up.

## Results

### Participant Flow and Assignment

Figure 4 CONSORT diagram showing screening, allocation, and participant flow by group



Patients were recruited between November 2018 and December 2019. 172 patients agreed to participate and were randomly assigned to a reminder (n=85) or no-reminder group (n=87). Due to drop-outs and non-returned questionnaires, a total of 102 patients (reminder n=51, no-reminder n=51) were finally included in the analyses. For a detailed description of participant flow see Figure 4.

### Demographics and clinical characteristics

Participants' age ranged from 24 to 82 ( $M=59.2$ ,  $SD=11.5$ ), 72.5 % were female, 68.8% were married or in a long-term relationship. The participants were predominantly diagnosed

with breast cancer (52.5%), followed by prostate cancer (13.1%) and lymphoma (9.1%). 86% were under cancer-specific treatment at T0 (see Table 5). There were no significant differences between reminder and no-reminder group in demographic (age, gender, marital status) or health-related (cancer, treatment state) characteristics.

*Table 5 Demographic and clinical characteristics of study population by group, SD = Standard deviation, CNS= Central nervous system)*

<b>Characteristics</b>	<b>All (N=102)</b>	<b>Reminder (N=51)</b>	<b>No-reminder (N=51)</b>
<b>Age [M(SD)]</b>	59.2 (11.5)	56.6 (10.7)	61.7 (11.7)
range	24-82	34-81	36-82
	<b>% (N)</b>	<b>% (N)</b>	<b>% (N)</b>
<b>Female</b>	72.5 (74)	78.4 (40)	66.7 (34)
<b>Marital Status</b>			
Married/Partnered	68.8 (70)	70.6 (36)	66.7 (34)
Never Married/single	11.8 (12)	7.8 (4)	15.7 (8)
Divorced/separated	12.7 (13)	17.6 (9)	7.8 (4)
Widowed	4.9 (5)	2.0 (1)	7.8 (4)
<b>Education level</b>			
Primary education	29.4 (30)	25.5 (13)	33.3 (17)
Secondary education	27.5 (28)	25.5 (13)	29.4 (15)
Tertiary education	40.2 (41)	47.0 (24)	33.3 (17)
others	1,0 (1)	0.0 (0)	2.0 (1)
<b>Tumor diagnosis</b>			
Breast cancer	52.5 (52)	60.4 (29)	45.1 (23)

---

Prostate cancer	13.1 (13)	10.4 (5)	15.7 (8)
Gastrointestinal cancer	7.1 (7)	10.4 (5)	3.9 (2)
Lung cancer	5.1 (5)	0.0 (0)	9.8 (5)
Lymphoma	9.1 (9)	8.3 (4)	9.8 (5)
Gynecological cancer	6.1 (6)	6.3 (3)	5.9 (3)
Head and neck cancer	3.0 (3)	0.0 (0)	5.9 (3)
Cancer of CNS	2.0 (2)	2.0 (1)	2.0 (1)
Other cancer	2.0 (2)	2.0 (1)	2.0 (1)
<b>Metastases</b>			
Present	18.6 (19)	15.7 (8)	21.6 (11)
<b>Therapystatus 6 month after yoga therapy</b>			
Had a cancer-related therapy	44.1 (45)	58.8 (30)	29.4 (15)
Chemotherapy	5.9 (6)	5.9 (3)	5.9 (3)
Radiation therapy	1.0 (1)	2.0 (1)	0.0 (0)
Hormone therapy	28.4 (29)	37.3 (19)	19.6 (10)
Antibody therapy	7.8 (8)	5.9 (3)	9.8 (5)
other	10.8 (11)	17.6 (9)	3.9 (2)

#### Practice frequency and evaluation of reminder e-mails

74.5% of the reminder group and 62.0% of the no-reminder group reported six months after the end of yoga-therapy that they were currently practicing yoga. Patients in the reminder group reported an average practice of 39.7 minutes per week at T1 ( $SD=44.7$ ) and 68.5 minutes ( $SD=57.0$ ) at T2. In the no-reminder group, the self-reported average practice time was 36.3

minutes at T1 ( $SD=43.1$ ) and 39.9 minutes ( $SD=39.1$ ) at T2. The main reason for not practicing yoga anymore in both groups was lacking motivation without professional instruction (reminder: 55.6%, no-reminder: 58.6%). For more perceived benefits of yoga and reasons not to practice (anymore) see Table 6.

In the reminder group, 74.0% reported to have read the e-mails always or frequently, only 8.0% indicated they never or almost never read them. 67.3% reported that they were strongly or very strongly reminded of yoga therapy by the e-mails and 54% found the e-mails (very) helpful to keep up their independent yoga practice. 86% of the patients felt that the e-mails were not at all or very little annoying.

*Table 6 Practice frequency, subjective benefits of yoga and reasons not to practice (higher values represent higher agreement range 1-4) ( $SD=$ Standard deviation,  $NA=$  not applicable)*

	Reminder Group	No Reminder Group
<b>Yoga practice frequency</b>	<b>N=51</b>	<b>N=51</b>
Practiced yoga in the last 6 month (%(N))	88.2 (45)	72.5 (37)
Practiced yoga currently at the moment (%(N))	74.5 (38)	62.0 (31)
Average amount of yoga practice a week in minutes (m( $SD$ ))	68.5 (56.9)	39.9 (39.0)
<b>Subjective benefits of yoga (m(<math>SD</math>))</b>	<b>N=47</b>	<b>N=44</b>
..better concentration	2.72 (.90)	2.57 (.87)
..less tired	2.77 (.84)	2.65 (.84)
..feeling more fit	3.47 (.78)	3.27 (.79)
.. better dealing with cancer disease	2.98 (.87)	3.02 (.92)
..better dealing with anxiety concerning my cancer disease	2.94 (.90)	2.73 (.90)

---

.. less worried about my future	2.89 (.91)	2.81 (.88)
.. less sad/depressed	3.11 (.84)	3.05 (.82)
<b>Reasons to stop practicing yoga (m(SD))</b>	<b>N=18</b>	<b>N=29</b>
..not motivated without professional instruction	2.11 (1.4)	2.66 (1.0)
..physically not able to do yoga	1.68 (1.25)	1.90 (1.0)
..no need for yoga due to good state of health	1.24 (0.75)	1.82 (0.77)
.. no benefit of yoga therapy	1.44 (1.11)	1.30 (0.61)
...subjective experienced harm through yoga	1.12 (0.93)	1.21 (0.49)
...no time for yoga in everyday life	2.06 (1.56)	1.89 (0.89)

#### Primary Outcome: Efficacy of reminder e-mails on fatigue and yoga practice

Fatigue: The reminder group reported a significant reduction from T1 to T2 compared to the no-reminder group in general fatigue ( $F(100;1)=4.420$ ;  $p=.038$ ;  $d=0.42$ ) as well as in emotional fatigue ( $F(99;1)=8.538$ ;  $p=.004$ ;  $d=0.59$ ). No significant effects were found for physical and cognitive fatigue (See Table 7 and Figure 5). Controlling for baseline differences with ANCOVA, group (reminder vs. no reminder) differed significantly in emotional fatigue ( $F(98;1)=6.43$ ;  $p=.013$ ;  $d=0.51$ ), but not in general fatigue ( $F(99;1)=3.611$ ;  $p=.06$ ).

Practice frequency: The mean of RGS of practice frequency score differed significantly between the reminder group ( $M=0.28$   $SD=1.14$ ) and the no-reminder group ( $M=-0.24$ ,  $SD=.79$ ) ( $t(86)=2.47$ ,  $p=.015$ , 95%  $CI [-.94; -.10]$ ) with a medium effect size  $d=.52$ .

Influence of practice frequency on fatigue: To test whether practice frequency mediated the effect of reminder e-mails on fatigue and its subscores, a mediation analysis was conducted (Baron & Kenny, 1986; Müller, 2009). Significant correlations between reminder e-mails, practice frequency and fatigue could only be found for emotional fatigue ( $r [0.28;0.51]$ ;  $p<.02$ ),

---

so the mediation model was tested only for emotional fatigue. First, reminder e-mails were positively associated with RGS of emotional fatigue ( $b = -0.42$ , 95% CI [-0.75; -0.09],  $p = .013$ ). Second, there was a significant relation between reminder e-mails and the mediator RGS of practice frequency ( $b = 0.52$ , 95% CI [0.10; 0.94],  $p = .015$ ). In a third step the coefficient from practice frequency to emotional fatigue was not significant ( $b = -0.18$ , 95% CI [-0.36; 0.01],  $p > .05$ ). The effect of e-mail to emotional fatigue mediated by practice frequency was lower ( $b = -0.32$ , 95% CI [-0.69; 0.05],  $p = .09$ ) than the direct effect without mediation ( $b = -.042$ ).



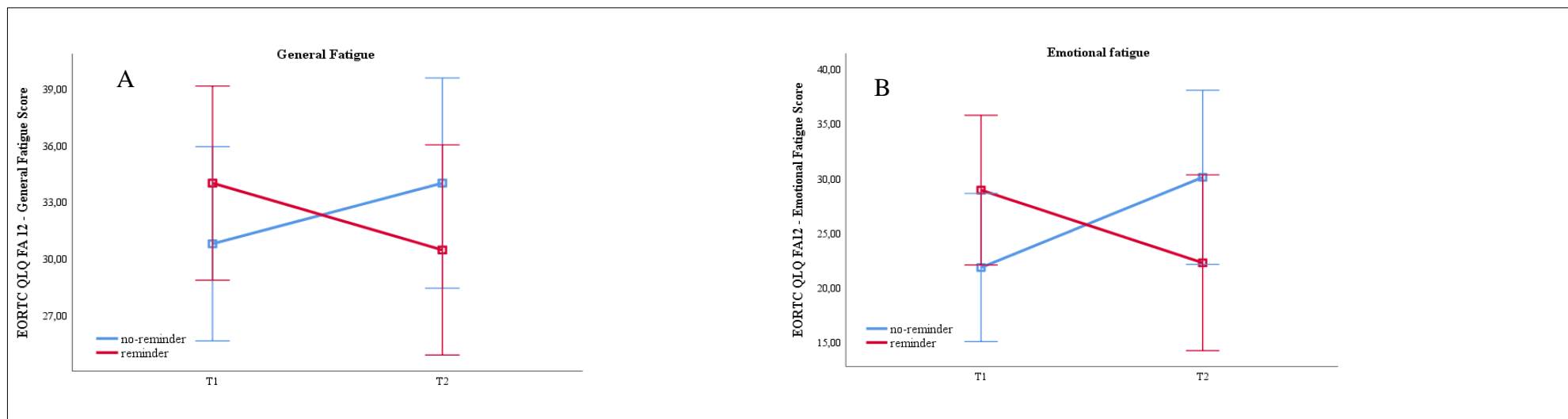


Figure 5 Mean changes in (A) EORTC QLQ FA-12 General Fatigue (B) EORTC QLQ FA-12 Emotional Fatigue between T1 and T2 in e-mail group and no-e-mail group. Results show means and 95% CI

*Table 7 Means (m), standard deviation (SD) & p-values of ANOVA analyses of time and group effects, and time\*group-interaction between reminder and no-reminder group for fatigue and subscales*

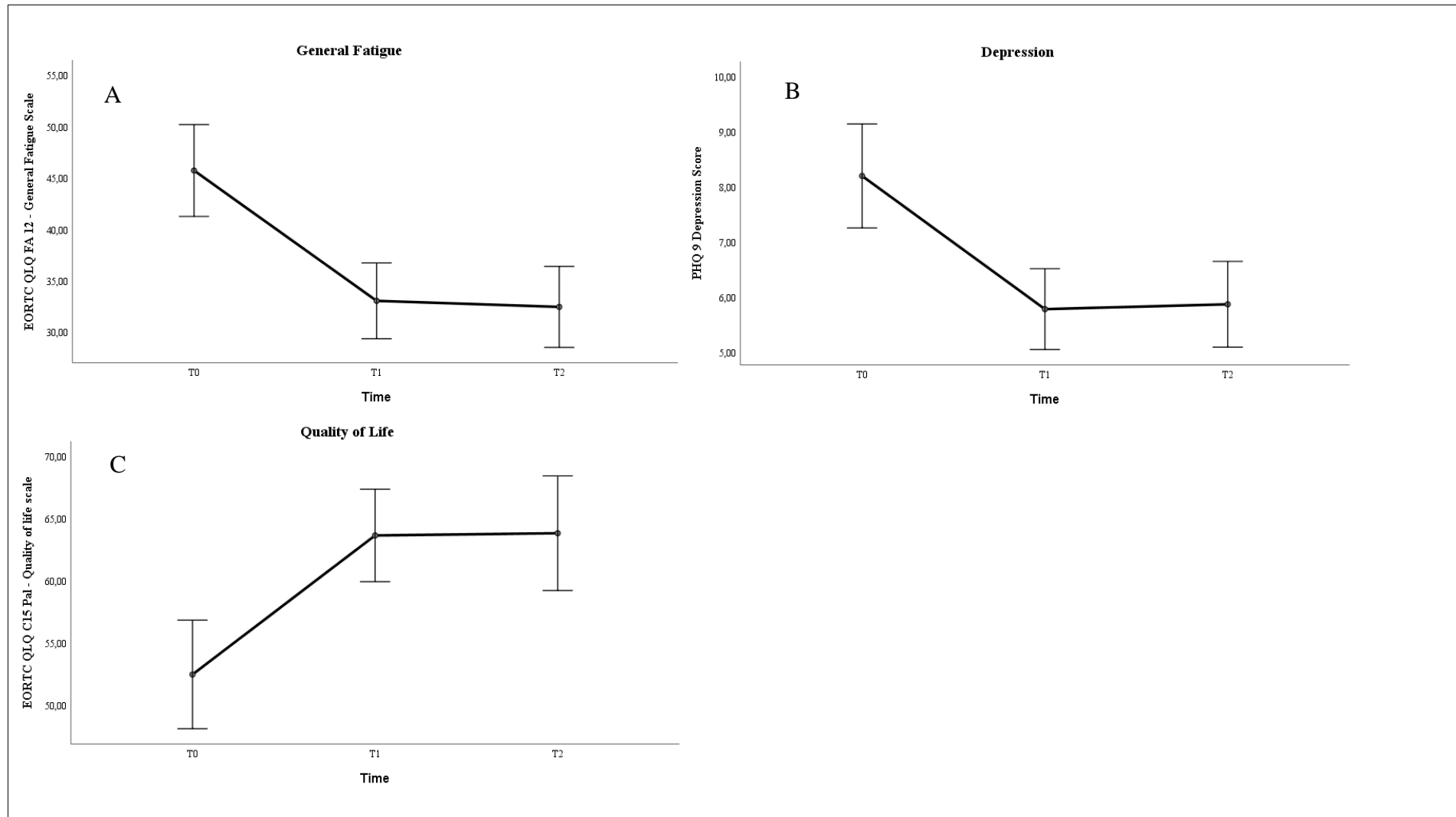
	reminder		no-reminder		time	group	time*group
	T1 m (SD) N=51	T2 m (SD) N=51	T1 m (SD) N=51	T2 m (SD) N=51	p-value	p-value	p-value
<b>Fatigue</b>	33.97 (20.7)	30.45 (21.49)	30.78 (16.02)	33.98 (18.47)	.919	.962	.038*
<b>Physical Fatigue</b>	45.23 (24.30)	42.48 (25.12)	42.80 (20.21)	44.40 (20.98)	.779	.825	.289
<b>Emotional Fatigue</b>	28.89 (26.47)	22.22 (29.09)	21.78 (22.32)	30.06 (28.40)	.753	.937	.004*
<b>Cognitive Fatigue</b>	18.62 (21.25)	16.01 (16.65)	20.26 (13.46)	20.92 (20.51)	.610	.288	.396

---

### Secondary Outcome: Long-term effects

The assumption of sphericity was not met, therefore all following ANOVAs were adjusted according to Greenhouse Geiser. Regarding general, as well as physical, emotional and cognitive fatigue, there were significant time effects ( $F > 7.46$ ,  $p < .001$ ,  $d > .54$ ). In the subsequent paired t-tests with alpha adjustment, significant effects between T0 and T1 ( $t > 3.11$ ,  $p < .002$ ) were found for fatigue and its subscores. This significant difference was also evident between baseline (T0) and six months after completion of yoga therapy (T2) ( $t > 3.10$ ,  $p < .002$ ). Similar significant results were found for depression ( $F(202;1.80) = 24.95$ ;  $p < .001$ ) and quality of life ( $F(186;1.86) = 15.58$ ,  $p < .001$ ). Regarding the paired t-test, there were also significant differences between T0 and T1 ( $t > 4.76$ ,  $p < .001$ ) and T0 and T2 ( $t > 4.48$ ,  $p < .001$ ). In none of the scales were significant differences between T1 and T2 ( $p > .35$ ) (See Figure 6).

Figure 6 Mean changes in (A) EORTC QLQ FA 12- General Fatigue, (B) PHQ-9 Depression Score and (C) EORTC QLQ C15 PAL – Quality of life between T0,T1 and T2 in all participants. Results show means and 95% CI



---

### *Discussion*

This randomized controlled trial examined the efficacy of reminder e-mails on yoga practice and fatigue in oncological patients with different types of cancer. Yoga for reducing fatigue is well-evaluated in cancer patients but findings on long-term effects of yoga are rare (Bower et al., 2012; Cramer et al., 2015; Kiecolt-Glaser et al., 2014; Lundt & Jentschke, 2019). Even less studies considered practice frequency as a potential mediator (Kiecolt-Glaser et al., 2014).

To the best of our knowledge, there has not yet been any study that actively tried to enhance the efficacy of yoga therapy by sending reminder e-mails. Reminder e-mails have been used predominantly in the medical context to improve compliance and adherence to appointments (Fox et al., 2003; Haramiova et al., 2017; Liu et al., 2014), but not yet in regard to such a complex construct with physical, emotional and cognitive aspects as fatigue. We found that patients who received reminder e-mails had significantly lower scores in general and emotional fatigue six months after the end of yoga-therapy with small to medium effect sizes ( $d=0.42-0.59$ ) compared to the group who did not receive reminder e-mails. However, we did not find significant effects regarding physical and cognitive fatigue. Furthermore, the reminder group reported a significant higher increase of practice frequency than the no-reminder group. The mediation analysis also showed a significant relation between reminder e-mails and increase in practice frequency. However, the reduction in emotional fatigue observed in this study as a result of reminder e-mails was not mediated by practice frequency.

In several studies, higher attendance rates in yoga classes or higher practice frequency during and after yoga therapy were shown to significantly reduce fatigue (Buffart et al., 2014; Kiecolt-Glaser et al., 2014; Zetzel et al., 2020). In the current study, this could be confirmed only for emotional fatigue and general fatigue. Although reminder e-mails lead to a significantly higher practice frequency and patients in the reminder group reported lower general and

---

emotional fatigue, a higher practice frequency was not associated with lower physical fatigue symptoms, as it was in other studies (Kiecolt-Glaser et al., 2014; Zetzl et al., 2020). Patients in the reminder group received weekly specific yoga instructions. Therefore, they may have felt more supported and less alone by the personal e-mails compared to the group without reminder e-mails. This may, for example, have increased their self-efficacy (Buffart et al., 2014) and motivation to do yoga, which might reflect in the increased practice frequency. By actively working to improve symptoms while receiving support through reminder e-mails, they might have felt less discouraged, helpless and frustrated than the no reminder group, leading to an improvement of emotional fatigue.

The independent yoga exercise at home was only recorded quantitatively but not qualitatively. For a successful yoga practice, a mindful practice of the exercises is an important basis (Kabat-Zinn, 2015). In the classes of the study, the focus was set on mindful practice through the instructions of the yoga teacher and higher attendance rate led to more improvement in fatigue (Zetzl et al., 2020). However, this level of mindfulness in yoga practice cannot be assumed during the practice at home due to a potentially higher prevalence of disturbance factors and patients' comparatively little expertise in mindfulness. A lack of mindfulness in performing the exercises at home could be a reason why there was no improvement in physical fatigue. To test the influence of mindfulness on the efficacy of home-based yoga, further research is needed. In addition, it must also be critically mentioned that the exercise time during the last six months was asked retrospectively. This might have led to a strong retrospective bias or social desirability issues. The tendency to answer in a socially desirable way might be higher for those participants who received personal e-mails for 24 weeks. Thus, future research may follow up on the present results by repeatedly assessing the quality and quantity of yoga exercises during the follow-up period instead of only once at the end.

---

Although yoga is helpful in the beginning to reduce fatigue, it does not result in complete remission of fatigue symptoms. This is also reflected in the long-term results of this study. We found long-term improvements of fatigue, depression and quality of life for all patients compared to baseline. Yoga can help reducing fatigue, depression and improving quality of life. These positive effects remained 6 months after the end of yoga therapy. However, there was no significant improvement between T1 and T2 after the end of yoga therapy. Yoga is helpful especially during active cancer treatment (Lin et al., 2018) to a limited extent to reduce fatigue. 44.4% of the study population were still in therapy six month after yoga therapy. Only 40% of the participants reported a stable state of health at T2. It is therefore reasonable that both health status and continued therapy have a strong influence on the fatigue symptoms and that yoga can prevent a further deterioration of the symptoms.

However, it must be critically considered that we did not include a control group that did not take part in yoga classes, thus the long-term improvement might not be solely due to yoga. Other factors, such as spontaneous remission, tumor treatment and disease, alternative supportive offers or social support may have contributed to the improvement. Since most yoga studies observe very short follow-up periods from six to 12 weeks (Bower et al., 2012; Bower et al., 2015; Cramer et al., 2016), we decided to use a comparatively long follow-up period of six months. As a result, because of cancer patients' short life expectancy, it would not have been ethically justifiable to place these patients on a six-month waiting list. In addition to ethical reasons, the risk of low compliance with a very long waiting period also spoke against a waiting control group. Despite a high drop out between T0 and T2, of a total of 40% of the patients who agreed to the study at the beginning, the response rate for the long follow-up of six months was very high at 83% compared to other studies.

In summary, previous studies supported that yoga is helpful in reducing fatigue and that more participation in yoga leads to higher reduction of symptoms (Zetzl et al., 2020). However,

---

our results suggest that after the end of yoga therapy, more frequent practice does not lead to further reduction of fatigue but might help to prevent the fatigue symptoms from increasing again despite active cancer treatment. Furthermore, we have found positive effects of reminder e-mails on general and emotional fatigue after yoga therapy compared to a group without reminder e-mails. Reminder e-mails are feasible, very well accepted and positively evaluated by cancer patients. In long-term, yoga can also help to reduce fatigue and depression and improve the quality of life. A home-based yoga therapy with weekly reminder e-mails and explicit instructions for a mindful practice could be a combination that reduces the barrier of long journeys to join a yoga class in a yoga-studio and increases personal motivation to individual practice.



---

### 3. General Discussion

Fatigue is one of the most common side effects of cancer, which places a heavy burden on cancer patients. To reduce fatigue, the National Comprehensive Cancer Network (NCCN) recommends yoga, among other interventions (Berger et al., 2015), which has been very well evaluated in patients with breast cancer (Bower et al., 2012; Kiecolt-Glaser et al., 2014; Vadiraja et al., 2017). In broadening the perspective of previous studies, this dissertation aimed at extending the existing research on yoga by including patients with different types of cancer and putting an additional focus on the possibility to ensure long-term effects through the use of reminder e-mails.

This dissertation was based on three papers, all published as part of the same research project. Publication 1 was a method paper dealing with the detailed objectives, inclusion and exclusion criteria, measurement instruments and above all the design of the interventions. Publishing study protocols should help to improve the standard of research. Previous yoga studies with oncological patients have been very diverse regarding aspects of the yoga intervention (duration, intensity, frequency) and main outcomes. In addition, the structure and sequence of the yoga sessions is often reported in insufficient detail, which makes replicating individual studies difficult. For this reason, a method paper/study protocol was prepared. Publication 2 covered the efficacy of yoga therapy in terms of fatigue, depression and quality of life, taking into account attendance rate at yoga therapy. Publication 3 examined the efficacy of reminder e-mails for long-term effects on fatigue and practice frequency.

In the following sections, I will summarize the findings of the studies and integrate them regarding the aspects of cancer-related fatigue, yoga practice, cancer-type, recruitment, yoga therapy and reminder e-mails. Moreover, I will discuss the limitations of this dissertation and its implications for research and practice. This chapter will end with a general conclusion.

---

### 3.1. Overall Summary and integration of the study results

The general aim of the research project presented in this dissertation was to examine the efficacy of yoga therapy in reducing fatigue in patients with various types of cancer. Overall, there was a significant reduction of fatigue after an eight-week yoga therapy as well as six months after completion of the yoga therapy compared to baseline. Compared to a waitlist control group, the eight-week yoga therapy reduced general and physical fatigue for cancer patients who participated seven times or more. Emotional and cognitive fatigue was not significantly reduced in yoga participants compared to those who did not participate in yoga. Participants with higher attendance rate reported higher reduction of fatigue. Women with breast cancer who participated in yoga therapy had a higher reduction of fatigue than women with other cancer types.

The second aim of this research project was to examine the efficacy of reminder e-mails after yoga therapy in improving practice frequency and thus reducing fatigue. Patients who received reminder e-mails after yoga therapy reported a significantly higher reduction of general and emotional fatigue compared to patients without reminder e-mail. Also, patients with reminder e-mails reported a higher increase in practice frequency than patients without reminder e-mails. Practice frequency did not mediate the relationship between reminder e-mails and emotional fatigue significantly.

Furthermore, there was a significant reduction of depression and an increase in quality of life after an eight-week yoga therapy as well as six months after the completion of yoga therapy compared to baseline. Compared to the waitlist control group, the eight-week yoga therapy reduced depression and increased quality of life for cancer patients who participated seven times or more.

---

In the following sections, I will discuss the results summarized above in more detail according to the main themes of cancer-related fatigue, influence of yoga practice on efficacy of yoga, cancer type, recruitment, yoga therapy, and reminder e-mails.

---

### *3.1.1. Cancer-related fatigue*

The main outcome variable of this research project was fatigue with the subscores physical, emotional, and cognitive fatigue. Fatigue symptoms decreased significantly during the eight-week yoga therapy and remained at approximately the same level six months after the end of yoga therapy. Patients who participated in yoga seven or eight times (completers) had significantly lower general and physical fatigue scores after participation compared to the waiting control group without yoga. In intent-to-treat analyses, no such significant reductions were found. This result was consistent with results from comparable yoga studies with patients with breast cancer, which found an effect of yoga therapy dependent on the frequency of participation (Kiecolt-Glaser et al., 2014; Moadel et al., 2007). Overall, the effect sizes found in publication 2 ( $d=.039-0.42$ ) were consistent with results from meta-analyses, which also found only small to medium effect sizes with regard to fatigue (Lin et al. 2018). Patients who received reminder e-mails for six months reported a stronger reduction of overall and emotional fatigue compared to the control group with a small to medium effect size ( $d=0.42-0.59$ ). To date, there are no studies that actively influenced fatigue after yoga therapy through intervention.

The subscores of fatigue (physical, emotional, and cognitive) were examined individually to understand the complex construct of fatigue in greater detail (Lin et al. 2018). This represents an important innovation and can contribute to a better understanding of the mechanisms of fatigue. Although some other studies have used multidimensional questionnaires (Kiecolt-Glaser et al., 2014; Lötze et al., 2016), subscores of fatigue are hardly reported. In most studies, fatigue is even only measured one-dimensionally (Banasik et al., 2011; Cohen et al., 2004; Danhauer et al., 2009; Littman et al., 2012; Moadel et al., 2007). In a review of yoga therapy in patients with breast cancer, yoga was expected to have a beneficial effect on physical fatigue, a medium effect on cognitive fatigue and no impact on emotional

---

fatigue (Dong et al., 2019). This could be confirmed in the current research project regarding physical and emotional fatigue, but no significant changes in cognitive fatigue were found in our study.

As the results from publication 2 and 3 show, various interventions (yoga and reminder e-mails) reduce fatigue in general. The eight-week yoga therapy initially reduced mainly physical fatigue, while the subsequent reminder e-mails reduced emotional fatigue. In multi-step interventions, such as in this research project, attention should be paid to which fatigue subscore is reduced first. It might be the case that emotional fatigue is only reduced as a result of a previous reduction in physical fatigue, implying that e-mail reminders were not the only cause for reduced emotional fatigue.

---

### *3.1.2. Influence of yoga practice on efficacy of yoga*

An important factor influencing the efficacy of yoga therapy is the amount of yoga practice, i.e. participation in yoga classes or the frequency of practice at home. This aspect will be discussed in the following.

In the linear regression reported in publication 2, the amount of yoga practice during yoga therapy, represented by attendance rate, was a significant predictor that reduced fatigue after yoga therapy by .11 points for each attended class. The influence of the yoga practice on reducing fatigue was also apparent when comparing the results of the intent-to-treat and per-protocol analyses with the completers of the yoga study. There were no significant changes in fatigue in the intent-to-treat analyses, but there were significant changes with the completers in the per-protocol analyses. Regarding yoga practice after the study, the mediation analysis in publication 3 showed that reminder e-mails led to more independent practice time in follow-up, but that this did not contribute to a significant improvement in fatigue. Scatterplots with difference in fatigue after yoga therapy and follow-up and reported practice time at the time of follow-up also show a linear relationship (see Figure A8, p. 146). In this research project, the independent practice time after yoga therapy did not result in a higher reduction of fatigue. Practical and theoretical implications of these results are discussed in paragraph 3.3.2 (pp. 104104).

Interventions in yoga studies differ considerably in length and intensity and thus in the total duration of the yoga practice. Lin et al. (2018) recommended 60 to 120-minute sessions to improve fatigue, one to three times per week over a period of four to twelve weeks, i.e. a total of 240 - 4320 minutes of yoga practice. With 480 minutes, this research project was rather in the lower range of the recommended duration for yoga practice. The question arises whether fatigue is reduced linearly to the practice time. In scatterplots with attendance rate and the change in fatigue before and after the yoga study, a linear relationship ( $R^2=.145$ ) became

---

apparent, which is also shown in the subscores ( $R^2=.081$ -.098) (see Figure A7, p.145). Several studies also found a linear dose-response relationship between practice frequency and cancer-related outcomes. Carson et al. (2007) found greater invigoration and acceptance on the same day of exercise, and less pain and fatigue the next day. Dhruva et al. (2012) found a dose-response relationship between pranayama use and improvements in chemotherapy-associated symptoms and quality of life. In comparable yoga studies with higher duration and exercise frequency (Kiecolt-Glaser et al., 2014) a linear relationship was also assumed. Ten minutes more exercise time per day reduced the values of fatigue in the MFSI (Multidimensional Fatigue Symptom Inventory Source) by 1.7 points (Smets et al., 1995).

In summary, the results of this research project confirmed that there is a linear relationship between yoga practice and a reduction in fatigue. After the eight weeks of yoga therapy, fatigue could no longer be significantly reduced only by independent practice. The efficacy of yoga practice depends not only on the amount of yoga practice, but also on the way it is done. A lack of mindfulness during yoga practice might be an issue here and will be discussed further in the implications.

---

### *3.1.3. Cancer type*

An important new aspect of this study was the inclusion of different cancer types, which allows for a better generalization of the results to oncological patients in general (Lin et al. 2018). However, due to the different sample sizes of the cancer-type-subgroups, a comparison of the cancer types was not possible. About half of the sample consisted of patients with breast cancer. Therefore, the sample of women with breast cancer, which was well evaluated in other yoga studies, was compared with the heterogeneous group of women with other cancers. Among the heterogeneous group of women with other cancers, 25% had lymphoma, 22% had gynecological cancer, 19% had gastrointestinal cancer, 17% had lung cancer and 11% had cancer of the central nervous system. In publication 2, women with breast cancer who participated in yoga reported a greater reduction in general fatigue symptoms than women without breast cancer who participated in yoga. This partly contradicts the results of a review (Boehm et al., 2012), which reported lower effects in yoga studies in patients with breast cancer than with other conditions. Under the other conditions, healthy individuals were also included, which may explain the contradictory results. Due to the very small subgroups regarding cancer type, the main cancers (breast, prostate, lung, gastrointestinal, lymphoma) could not be included in the analysis as an additional between-group independent variable. In future studies, the sample should ensure an equal distribution of the subgroup with respect to cancer type

Regarding the efficacy of reminder e-mails, no subgroup analyses could be performed for different types of cancer. When comparing the efficacy of reminder e-mails between women with breast cancer (N=29) and women without breast cancer (N=22) there were no significant differences. The reminder e-mails had no different effect on patients with breast cancer than on non-breast cancer patients.

The long-term results reported in publication 3 could be exploratively screened for the five main cancers types (breast, prostate, gastrointestinal, lung, lymphoma) (see Figure A9,



---

p.147). The profile showed a reduction in general fatigue for breast cancer, prostate and lymphoma patients between pre- and post-treatment which was also maintained during the follow-up period. In patients with gastrointestinal cancer, a reduction in fatigue was also seen between post-treatment and follow-up. The profile for lung cancer patients also showed a reduction between pre- and post-treatment, but there was a stronger increase in fatigue in follow-up measurement than in other cancer types. These differences in the profile could be influenced by characteristics of the cancer disease and therapy. 90% of lung cancer patients in this study reported metastases and thus far more than the other types of cancer (27-41%). Among lung cancer patients, there was a drop-out of 65% during the study. Among patients with breast and prostate cancer, the drop-out was only 21%, and 23%, respectively. Patients with lung cancer were thus more affected by cancer in this sample, similar to the cancer population. With a low relative 5-year survival rate of about 21% in women and 15% in men, lung cancer is one of the prognostically unfavorable tumor types (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019). Possible positive effects of yoga therapy can be reduced by the severity of the disease and further therapies in the follow-up, which could be a reason for a stronger increase in fatigue seen in the long-term results.

Only a few studies included other types of cancer than breast cancer. A comparable RCT examined the efficacy of a 7-week yoga therapy in patients with lymphoma. Yoga could improve sleep related outcomes, but not fatigue (Cohen et al., 2004). Similar results were reported by Mustian (2013) with a mixed sample of cancer survivors, 75% of whom were breast cancer survivors. In patients with colorectal cancer, ten weeks of yoga therapy only improved anxiety and depression, but not fatigue or quality of life (Cramer et al., 2016). Due to a high drop-out and low intervention adherence, these results must be interpreted very cautiously. In a non-controlled pilot study, a sample of women with ovarian cancer showed positive changes in depression, negative affect, state anxiety, mental health, and overall quality of life after ten

---

weeks of yoga therapy (Danhauer et al., 2009). In feasibility studies, it was found that yoga is also well accepted and positively evaluated by patients with prostate and lung cancer (McCall et al., 2015; Milbury et al., 2015). Nevertheless, exercise training studies are more likely to be conducted with patients with prostate cancer and have also been shown to be very effective with regard to fatigue (Horgan & O'Donovan, 2018). In summary, further research is needed to evaluate the efficacy of yoga in patients with cancers other than breast cancer. In addition, in patients with prostate cancer, it might be interesting to evaluate other interventions besides exercise training.

The prevalence and severity of fatigue depends on the type of cancer. Very high levels of fatigue are found particularly in patients with pancreas, gall bladder, lung and stomach cancer (Schmidt et al., 2020; Singer et al., 2011; Wang & Woodruff, 2015). Less pronounced fatigue is particularly prevalent in prostate and breast cancer (Schmidt et al., 2020; Singer et al., 2011; Wang & Woodruff, 2015), with patients with breast cancer reporting less fatigue than lung cancer patients, but for a longer time (Wang & Woodruff, 2015). Emotional fatigue is most commonly reported by bladder and rectal cancer patients (Schmidt et al., 2020). Of the five most common tumor types in this research project (breast, prostate, gastrointestinal, lung, lymphoma), lung cancer patients descriptively reported the highest fatigue values, while gastrointestinal and prostate patients reported the lowest fatigue values. This was largely consistent with the results of other studies.

In summary, with the background of the different prevalence, it is becoming clear that patients who, according to studies, suffer heavily from fatigue, such as lung cancer patients, may benefit less from yoga therapy in the long term. Patients who are less affected by fatigue, such as patients with breast cancer, seem to respond well to yoga therapy. However, further studies need to investigate differences in the efficacy of yoga in different types of cancer.

---

### ***3.1.4. Recruitment***

Many yoga studies included only “cancer survivors” in their sample, patients who had already successfully completed cancer therapy (Banasik et al., 2011; Culos-Reed et al., 2006; Kiecolt-Glaser et al., 2014; Littman et al., 2012; Mustian, 2013; Peppone et al., 2015). Fatigue was not even considered as an inclusion criterion and the yoga therapies were thus not specifically designed for patients with fatigue. The research project underlying this dissertation was designed to include patients affected by fatigue. In publication 1, regarding the recruitment of patients, the inclusion criterion "fatigue" was planned to be at least 5 or higher (range 0-10). With an inclusion criterion of fatigue >5, almost 90% of those invited refused to participate in the study (consent rate of 11.3%). The most frequent reasons for refusal were long journey to the study and fatigue (Zetzl et al. 2020). The fatigue was often already too pronounced and was in itself a barrier to starting physical activity despite the knowledge of positive consequences (Moadel et al., 2007). Considering that fatigue affects 25-97% of cancer patients during their treatment (Banipal et al., 2017; Miller et al., 2008; Weis et al., 2013) and fatigue is a common barrier to physical activity (McCall et al., 2015), it is reasonable to offer interventions before fatigue symptomatology is too pronounced. Therefore, we decided to reduce the inclusion criterion of fatigue from 5 to 1 for this research project. This allowed patients to have access to an intervention recommended for reducing fatigue, at a time before the fatigue becomes too severe and leads to a reduction in motivation (Moadel et al., 2007). The expansion of the inclusion criterion had a positive effect on the size of the total sample and led to an increased consent rate of 15.5%. Overall, it is hardly feasible to recruit patients with high fatigue scores for yoga studies.

---

### *3.1.5. Evaluation of yoga therapy and reminder e-mails by participants*

As described in publication 2, yoga therapy was rated very well by the participants. Especially the instruction by the yoga-teachers (86.2%), the overall structure of yoga class (76.6%), meditation parts (69.8%) and group size (67.2%) were rated "very good". Less frequently rated "very good" were the length of the whole therapy with 8 weeks (33.9%) and the possibilities for exchange of experiences (34.4%). Patients wished for a rather longer yoga therapy than 8 weeks and more opportunities for exchange.

In the long term, patients report that they felt fitter (30.8%) and less depressed (30.1%) as a result of yoga therapy. They also worried less (23.7%) and were better able to cope with their cancer (22.3%). In addition, "Relaxation" was often mentioned in the questionnaire as a benefit of yoga therapy. With regard to concentration and fatigue, only 7.7% each reported "very good" improvements. The most common reason for lack of yoga practice after yoga therapy was lack of motivation (19.2%).

As described in publication 3, almost three-quarters of the people read their e-mails at least regularly; only one person never read the e-mails. Almost 50% felt very strongly supported in recall of yoga therapy and 30% found the e-mails very motivating for their own yoga practice. Nobody described the e-mails as very or a little annoying.

In summary, the e-mails were rated very good and not annoying at all. Through the e-mails the patients were reminded of the yoga practice, but there is still need for improvement regarding motivation, which will be discussed in the implications.

---

### **3.2. Limitations**

There were several limitations to this dissertation that need to be closely considered in order to properly interpret its findings.

#### **3.2.1. Sample**

Regarding the sample, the heterogeneity must be viewed critically. The sample of the research project represented a random sample with a high sample size, which, due to its heterogeneity, increased external validity. However, the very high diversity concerning cancer type did not allow for comparisons among the subgroups due to the large number of too small subgroups. Therefore, factors potentially influencing the efficacy of yoga and reminder mail, such as the type of cancer, could not be examined in detail.

The prevalence of cancer in men and women is approximately the same (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019). Nevertheless, 70% of the sample consisted of women, 65% of whom suffered from breast cancer. Although in this research project, the proportion of men was considerably higher (30%) than in comparable yoga therapies (Hardoerfer & Jentschke, 2018; Mustian, 2013), a selection bias must be assumed here. Overall, the group of women and even more the group of patients with breast cancer, which makes up about 30% of women on average in Germany, was strongly overrepresented. White women aged 41-50 years are most interested in complementary alternative medicine including yoga (Adams & Jewell, 2007; Bahall, 2017). Women under 50 are the high-risk group for patients with breast cancer (Robert Koch-Institute & Society of epidemiological cancer registries in Germany, 2019), which is why it is understandable that the group of patients with breast cancer was most frequently represented in the sample of the research project. In further studies, possibilities to increase the motivation of men to use complementary alternative medicine should be further investigated.

---

### *3.2.2. Study Design*

The first RCT had a waiting control group design, but no active control group. It can not be excluded that belonging to a group or increased attention through others also had an effect on fatigue and depression. A 3-armed study including an active control group, like physical exercise (Lötzke et al., 2016) or psychoeducation (Bower et al., 2012) would have been preferable to identify specific effects of yoga. The same applies to the second RCT. Due to the lack of an active control group, the effects on emotional fatigue and exercise frequency could not be attributed exclusively to the reminder e-mails. Again, an active control group seems to be useful, such as filling up exercise protocols (Kiecolt-Glaser et al., 2014; Lengacher et al., 2016) to evaluate alternative ways to increase practice frequency. In addition, six months after yoga therapy there was no control group in the follow-up that had not received yoga therapy up to this point. Therefore, the long-term improvements could not be attributed solely to yoga. A 6-month waiting period was ethically not justifiable due to the partly severe illness of the study participants and the strong life time limitation.

---

### 3.2.3. *Measures*

In the entire research project, only self-reports were collected by questionnaires, but no objective parameters. However, especially with regards to fatigue, the inclusion of objective health measures such as interleukins (Bower et al., 2014; Kiecolt-Glaser et al., 2014) may be a useful complement to the findings of this research project. Due to the lack of objective parameters, it was not possible to accurately distinguish whether improvements were due to an actual reduction in symptoms, improved symptom management, or a socially desirable response tendencies among participants. However, fatigue is mainly a subjective experience of impairment described as severely and extensively limiting. Subjective limitations and extent of fatigue are usually higher than objectifiable parameters as interleukins (Pullens et al., 2010). Therefore, we decided to use only self-assessment questionnaires to assess cancer-related fatigue.

Furthermore, the assessment of the practice time must be viewed critically. Patients reported their average exercise time once after the yoga therapy and in the follow-up, which could have led to a strong retrospective bias due to the long period of time. Changes in the practice time during the last six months were therefore not noticeable. It is possible that the reminder e-mails had an even greater influence on the frequency of practice in the first three months, but this intervention lost its efficacy after a few months, i.e. the efficacy of the e-mails did not increase linearly with the number of reminder e-mails (Zhang et al., 2017). Moreover, the documentation of the practice frequency could be biased due to social desirability. In addition, the practice time was only recorded quantitatively, but the information provided by the participants could not be used to determine how the yoga exercises were performed. Since 82% of the participants practiced less than 60 minutes per exercise unit, it can be assumed that less than 20% of the participants have performed yoga analogous to the 60-minute yoga class in the study. However, it could not be deduced whether the patients performed fewer of the learned asanas or whether

---

the learned asanas were performed faster and thus with less mindfulness. The yoga CD and yoga book provided at the end of the study were evaluated as very helpful and understandable, but the CD did not seem to be used in its full extent.



---

#### *3.2.4. Analytic procedure*

The per-protocol analyses in the second paper systematically overestimated the benefits of yoga therapy, since a systematic drop-out of patients who had participated in yoga less than seven times could not be excluded. However, the per-protocol analyses underlined the importance of regular participation, which could also be strengthened by the results of the regression analysis.

In the third publication, the residual gain scores were used to determine the frequency of exercise. Difference scores between post and follow-up can be interpreted more intuitively due to the linear relationship. However, the residual gain scores were used since they control for both initial differences and for measurement error inherent in the use of repeated measures on the same instrument (Beutler & Hamblin, 1986; Steketee & Chambless, 1992).

With regard to the mediation analysis, the procedure according to Baron and Kenny (1986) must be viewed critically. Although this is widely used, it is controversial due to its lower statistical significance and lack of consideration of relevant variables (Müller, 2009). However, the method of Barron and Kenny has a low type-1 error rate. In the future, other methods like difference-in-coefficients-method or product-of-coefficients-methods (MacKinnon et al., 2004) should be considered (Hayes, 2009).

---

### 3.2.5. *Differentiation between fatigue and depression*

Another important limitation concerns the difficult distinction between fatigue and depression. Fatigue and depression overlap in many aspects, especially with regard to loss of energy, lack of motivation and decreased concentration. However, depression differs from fatigue in terms of cognitions, especially in terms of suicidal thoughts and feelings of guilt (Fischer et al., 2017). In comparison, all symptoms of fatigue are also symptoms of depression (Reuter & Härter, 2004). In the sample of the research project, there were significant correlations between depression and fatigue as well as all subscales, which is in line with the literature (Jacobsen et al., 2003). In the present research project, yoga therapy reduced depression with a greater effect ( $d=.79$ ) than fatigue symptoms ( $d=.42$ ). In summary, depression seems to improve more through yoga than fatigue, which can also be found in reviews (Amritanshu et al., 2017; Buffart et al., 2012; Danhauer et al., 2017; Tolia et al., 2018).

Publication 2 reported a linear regression in which fatigue before yoga therapy and attended yoga classes significantly predicted fatigue after yoga therapy. Adding depression as another predictor in the linear regression model did not explain significantly more variance. However, this is not conclusive due to the high correlation between fatigue and depression and resulting issues regarding multicollinearity.

It remains difficult to statistically distinguish fatigue from depression. In the current study, patients affected by both fatigue and depression reported noticing a marked difference between fatigue and depression that was not be adequately represented in the questionnaires. Whereas patients in depressive episodes lack motivation to do something ("I don't want to"), patients in episodes of severe fatigue appear to lack more ability ("I want to, but I can't").

This distinction needs to be further verified. In addition, questionnaires should be evaluated, which can address this difference between motivation and ability.

---

### **3.3. Theoretical and practical implications**

In the following, I will illustrate the theoretical and practical implications of this dissertation.

The implications are summarized and structured analogous to the summary.

#### ***3.3.1. Cancer-related fatigue***

The primary aim of this research project was to investigate the efficacy of yoga in cancer patients. The eight-week yoga therapy significantly reduced fatigue in a sample with mixed cancers. Especially with regard to physical fatigue, yoga was initially helpful. After an initial reduction of physical fatigue, the reminder e-mails could further reduce emotional fatigue. The differentiation of fatigue into the three subscales seemed very useful with regard to these results and must be further evaluated in future yoga studies. For this reason, following studies should preferably use questionnaires that measure fatigue in several dimensions, such as the EORTC QLQ Fatigue Module F13 (Weis et al., 2013; Weis et al., 2017), the Cancer Fatigue Scale (Kröz et al., 2008) or the Fatigue Assessment Questionnaire (Glaus & Müller, 2001). At the same time, further questionnaires with a high discriminative validity between depression and fatigue should be evaluated.

The construct of cognitive fatigue also needs to be better examined in terms of possible interventions. Cognitive fatigue is often associated with difficulties in maintaining attention and information processing, as well as memory and executive functions (Irestorm et al., 2020). It is therefore not essentially different from "Chemo Brain" or Cognitive Impairment (Joly et al., 2019), from which many patients suffer under chemotherapy. This includes limitations in the cognitive domains of memory, attention, processing speed, and executive function (Kovalchuk & Kolb, 2017). In general, yoga practitioners are found to have better cognitive performance and there is a positive correlation between gray matter volume and yoga experience (Desai et al., 2015; Froeliger et al., 2012). The hippocampus enlarges through yoga therapy (Hariprasad et al., 2013). In summary, there is evidence for a positive effect of yoga on cognitive functions.

---

In patients with breast cancer yoga seems to have a medium effect on cognitive fatigue (Dong et al., 2019). A twelve-week twice-weekly hatha yoga intervention reduced cognitive fatigue in patients with breast cancer three months after the end of yoga therapy compared to a waiting control group (Derry et al., 2015). In this research project, it appeared that only physical fatigue can be reduced by yoga therapy, while limitations in cognitive fatigue could hardly be changed. In the study by Derry et al. (2015), participants received a longer and more intensive yoga therapy compared to this research project. The improvement regarding cognitive fatigue was not evident immediately after yoga therapy, but only at follow-up 3 months after the end of yoga therapy. Together with the greater success in patients who practice a lot, this suggests that more yoga practice is needed to improve cognitive fatigue. Further studies are needed to determine how yoga therapy should be designed (length, intensity) to reduce cognitive fatigue. In addition, it needs to be examined, whether only patients with breast cancer can benefit from yoga in terms of cognitive fatigue, as described by Dong et al. (2019).

### *3.3.2. Influence of yoga practice on efficacy of yoga*

The attendance rate in the yoga classes had a linear influence on the reduction of fatigue, so continuous yoga practice is desirable. Therefore, reasons for lack of participation and physical activity must be investigated. Studies show that those who participated more in yoga classes indicated less fatigue at the beginning of therapy (Danhauer et al., 2009; Moadel et al., 2007). In this study, however, there was no significant correlation between baseline fatigue and participation in yoga classes ( $p = .292$ ). Motivation and expectations regarding yoga are the only variables in this research project that differed significantly between patients who practiced a lot and a little. Other studies stress the importance of motivation as a predictor for physical activity (Frikkel et al., 2020). According to Frikkel et al. (2020), motivation for physical activity is significantly influenced by clinically relevant fatigue, depression, knowledge about the influence of physical activity on quality of life, physical activity prior to cancer diagnosis and interest in exercise programs. Depression and fatigue are the outcome variables to be modified by yoga, and physical activity before cancer diagnosis is no longer modifiable at the time of intervention. Therefore, for similar yoga studies in the future, it is important to increase the knowledge of physical activity on quality of life and interest in physical activity programs through psychoeducation and motivational interviewing prior to the intervention to increase motivation for physical activity and thus be able to reduce fatigue and depression.

An increase in the quality of life through yoga is well established by various studies (Agarwal & Maroko-Afek, 2018; Danhauer et al., 2017; Tolia et al., 2018). Patients who have already participated in yoga reported feelings of solidarity and safety in yoga classes (Mackenzie et al., 2016). They also reported various benefits from participation, such as a feeling of having control over their life, an increased ability to relax and focus, more physical strength and more confidence for activities. Participants believed yoga practice benefits were derived from heightened awareness of the mind-body connection, breath regulation, better self-

---

regulation, and improved self-confidence (Mackenzie et al., 2016). In this research project, patients mentioned less feelings of fatigue and depression, less fear of recurrence and the future, and a better management of cancer as frequent reasons for them to continue to practice yoga.

Regular information events, brochures or video sequences from former participants, in which these positive effects of yoga therapy with cancer-specific instructions are illustrated, could increase the knowledge about the positive influence of physical activity on the quality of life, thus increase motivation to be active and participate in yoga therapy and consequently also reduce fatigue.

The reminder e-mails increased the practice frequency, but in this research project, this increase in practice frequency had no significant effect on the reduction of fatigue. It is possible that the previous yoga intervention already reduced (physical) fatigue as much as possible and that there was a floor effect. It must be examined to what extent fatigue can be reduced by yoga practice as a whole or whether floor effects are present. In addition to quantity, the quality of practice frequency should also be considered. Mindfulness as a state during the yoga practice should be measured, for example, by the State Mindfulness Scale (Tanay & Bernstein, 2013). In order to reduce retrospective bias in the reporting of practice time, exercise diaries are suitable, which record both the duration of the yoga practice and the mindfulness during the practice. Questionnaires that record mindfulness as a trait, such as the Five Facet Mindfulness Questionnaire (Danielson & Jones, 2017) or the Mindful Attention Awareness Scale (Carlson & Brown, 2005), also appear useful for examining the efficacy of yoga therapy in relation to the general mindfulness of the patients. Thus, mediator analyses could be used to test whether a yoga intervention is more effective in those with higher levels of mindfulness in daily life.

---

### 3.3.3. *Cancer type*

Overall, the influence of the type of cancer on the efficacy of yoga therapy must be researched with larger samples. Patients with breast cancer seemed to benefit more from yoga therapy in this research project. However, other studies imply that this group is more motivated and more devoted to yoga than patients with other cancer types (Cramer et al., 2016). In addition, patients with breast cancer are three times more likely to be physically active than patients with other tumor types (Frikkel et al., 2020). No causal relationship can be deduced from this. It is possible that patients with breast cancer experience yoga therapy as more beneficial than other cancer patients and are therefore more motivated. It might also be the case that patients with breast cancer are more interested in yoga per se and therefore have higher placebo and expectation effects. In further studies, the sample should be drawn with a stratified random sampling strategy, to better compare less represented cancers, such as lung cancer with the main cancers, breast and prostate cancer. The differences in the prevalence of fatigue, motivation to do yoga, yoga practice and efficacy on fatigue should be taken into account.

---

#### **3.3.4. Recruitment**

As is shown by the recruitment difficulties at the beginning of the study, fatigue was often cited as a reason for refusing yoga therapy (Zetzl et al., 2020) and is thus an important obstacle to physical activity (McCall et al., 2015). Therefore, yoga should be offered as early as possible, preferably before the start of cancer-specific therapy, to enable patients to experience the positive effects of yoga therapy before the fatigue caused by therapy and illness is too pronounced. Transport difficulties, scheduling conflicts, feeling weakened due to tumor therapy and other physical symptoms like insomnia or weakness are main barriers for participation and hinder physical activity (Frikkel et al., 2020; McCall et al., 2015) and must be further considered. Online offers using recordings of yoga sessions could circumvent both transport difficulties and scheduling conflicts. However, physically active and inactive patients report the same barriers (Frikkel et al., 2020). This indicates that patients who are physically active are more likely to have found better, individualized solutions to the barriers for themselves, rather than changing the environment or the offerings. Motivational interviewing (Miller & Rollnick, 2012) could help patients to build up a higher intrinsic motivation to change their behavior and thus find better, individualized solutions to the barriers to physical activity.



### *3.3.5. Adaptions of yoga therapy and reminder e-mails*

In total, the participants wished for a longer yoga program than eight weeks, which also seems reasonable regarding the comparatively short intervention (Lin et al. 2018). The yoga therapy should only be accessible to oncological patients so that they feel safe and understood (Mackenzie et al., 2016) and a safe exchange with the other participants is possible. The yoga teachers should be trained in cancer specific instructions (Mackenzie et al., 2016). Since in this research project, women were also predominantly interested in yoga intervention, the program must be designed in such a way that it is more interesting for men as well. Therefore, in the information events or brochures, besides mindfulness, a focus should also be placed on the athletic aspects of yoga, as this is more likely to address to men (Horgan & O'Donovan, 2018). It can also be useful to encourage patients to practice yoga regularly during yoga therapy and to reward independent training intermittently by small non-material reinforcements. Already during the yoga therapy, this can help to build up the new behavior and thus compensate for the lack of motivation that is often reported. At the same time, it seems useful to repeat the relevance of mindful practice and dwelling in the asanas and savasana (Daukantaitė et al., 2018) during yoga therapy in small psychoeducative elements.

The reminder e-mails seemed to be an inexpensive and well feasible intervention to increase practice frequency and reduce emotional fatigue. The 24 reminder e-mails in total were evaluated as very positive and not annoying despite the high number. Other studies find no difference in the efficacy of two or 14 reminder e-mails (Woods, 2002). From this point of view, a review of a both sufficient and effective number and frequency of reminder e-mails is still necessary.

In addition to the number of reminder e-mails, the type of reminders must also be discussed. Even if reminder e-mails are inexpensive and feasible, it must be considered whether this is the most effective reminder method. Older patients do not read their e-mails as regularly

---

(Gatto & Tak, 2008; Kiel, 2005), which can distort the efficacy. In other studies, e-mail or SMS had equally good effects, but the effects were even higher for personal calls (Ghadieh et al., 2015). Therefore, in further studies other access methods, such as e-mail, SMS or phone calls, must be compared.

Although the patients in this research project read the reminder e-mails frequently and thus felt reminded of the yoga therapy, the motivation through the reminder e-mails is in need of improvement. Other e-mail formats need to be evaluated. For example, patients may be asked to provide active feedback on their practice frequency during the past week. This could lead to more practice time through an increased control mechanism. At the same time, as a reward for regular yoga practice, booster sessions could be offered to stabilize behavioral change (Fleig et al., 2013; Whisman, 1990). Furthermore, it seems to be reasonable to address other channels besides the visual channel in the reminder e-mails. Single asanas or relaxation exercises could also be offered in audio files in addition to a written description to give patients the opportunity to practice while listening. With well-formulated instructions, this could also lead to an overall increase in mindfulness during performance.

### **3.4. Conclusion**

Oncological patients are heavily burdened by the disease and tumor-specific treatment. Yoga as a supportive therapy can help to reduce self-reported fatigue and depression and to improve quality of life. Reminder e-mails are helpful to increase practice frequency and reduce emotional fatigue. Yoga should continue to be offered, as is also stated in the NCCN guidelines. The yoga exercises (asanas) are easy to learn and can be continued by patients at home. Mindful practice should be ensured to take full advantage of yoga. To increase the motivation to participate in yoga, it should be offered as early as possible and there should be regular information events where the positive effects of yoga are highlighted. With regard to the current world political situation or a further pandemic, an online program can be helpful, and it can also lead to a reduction of barriers to participate. In further studies, the efficacy of yoga regarding differences in patients with different types of cancer should be examined in more detail.

---

#### 4. References

- Abel, A. N., Lloyd, L. K. & Williams, J. S. (2012). The Effects of Regular Yoga Practice on Pulmonary Function in Healthy Individuals: A Literature Review. *The Journal of Alternative and Complementary Medicine*, 19(3), 185–190. <https://doi.org/10.1089/acm.2011.0516>
- Abrahams, H. J. G., Gielissen, M. F. M., Schmits, I. C., Verhagen, C. A. H. H. V. M., Rovers, M. M. & Knoop, H. (2016). Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. *Annals of oncology : official journal of the European Society for Medical Oncology*, 27(6), 965–974. <https://doi.org/10.1093/annonc/mdw099>
- Adams, M. & Jewell, A. P. (2007) The use of complementary and alternative medicine by cancer patients. In *International Seminars in Surgical Oncology* (S. 1–7). BioMed Central.
- Agarwal, R. P. & Maroko-Afek, A. (2018). Yoga into Cancer Care: A Review of the Evidence-based Research. *International journal of yoga*, 11(1), 3–29. [https://doi.org/10.4103/ijoy.IJOY\\_42\\_17](https://doi.org/10.4103/ijoy.IJOY_42_17)
- Ahlberg, K., Ekman, T., Wallgren, A. & Gaston-Johansson, F. (2004). Fatigue, psychological distress, coping and quality of life in patients with uterine cancer. *Journal of advanced nursing*, 45(2), 205–213. <https://doi.org/10.1046/j.1365-2648.2003.02882.x>
- Alcântara-Silva, T. R., Freitas-Junior, R., Freitas, N. M. A. & Machado, G. D. P. (2013). Fatigue related to radiotherapy for breast and/or gynaecological cancer: a systematic review. *Journal of clinical nursing*, 22(19-20), 2679–2686.
- Allemani, C., Matsuda, T., Di Carlo, V., Harewood, R., Matz, M., Niksic, M., Bonaventure, A., Valkov, M., Johnson, C. J., Esteve, J., Ogunbiyi, O. J., Azevedo E Silva, G., Chen, W.-Q., Eser, S., Engholm, G., Stiller, C. A., Monnereau, A., Woods, R. R., Visser, O., . . . Coleman, M. P. (2018). Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): Analysis of individual records for 37 513 025 patients diagnosed

- 
- with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet (London, England)*, 391(10125), 1023–1075. [https://doi.org/10.1016/S0140-6736\(17\)33326-3](https://doi.org/10.1016/S0140-6736(17)33326-3)
- al-Majid, S. & McCarthy, D. O. (2001). Cancer-Induced Fatigue and Skeletal Muscle Wasting: The Role of Exercise. *Biol Res Nurs*, 2(3), 186–197. <https://doi.org/10.1177/109980040100200304>
- Amritanshu, R. R., Rao, R. M., Nagaratna, R., Veldore, V. H., Usha Rani, U., Gopinath, K. S & Ajaikumar, B. S. (2017). Effect of Long-term Yoga Practice on Psychological outcomes in Breast Cancer Survivors. *Indian journal of palliative care*, 23(3), 231–236. [https://doi.org/10.4103/IJPC.IJPC\\_93\\_17](https://doi.org/10.4103/IJPC.IJPC_93_17)
- Anestin, A. S., Dupuis, G., Lanctôt, D. & Bali, M. (2017). The Effects of the Bali Yoga Program for Breast Cancer Patients on Chemotherapy-Induced Nausea and Vomiting: Results of a Partially Randomized and Blinded Controlled Trial. *Journal of evidence-based complementary & alternative medicine*, 22(4), 721–730. <https://doi.org/10.1177/2156587217706617>
- Barnes, B., Kraywinkel, K., Nowossadeck, E., Schönfeld, I., Starker, A., Wienecke, A. & Wolf, U. (2016). Bericht zum Krebsgeschehen in Deutschland 2016. 38960627.
- Bahall, M. (2017). Prevalence, patterns, and perceived value of complementary and alternative medicine among cancer patients: a cross-sectional, descriptive study. *BMC complementary and alternative medicine*, 17(1), 345.
- Banasik, J., Williams, H., Haberman, M., Blank, S. E. & Bendel, R. (2011). Effect of Iyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors. *Journal of the American Academy of Nurse Practitioners*, 23(3), 135–142. <https://doi.org/10.1111/j.1745-7599.2010.00573.x>
- Banerjee, B., Vadiraj, H. S., Ram, A., Rao, R., Jayapal, M., Gopinath, K. S, Ramesh, B. S, Rao, N., Kumar, A., Raghuram, N., Hegde, S., Nagendra, H. R. & Prakash Hande, M.

- 
- (2007). Effects of an integrated yoga program in modulating psychological stress and radiation-induced genotoxic stress in breast cancer patients undergoing radiotherapy. *Integr Cancer Ther*, 6(3), 242–250.
- Banipal, R. P. S., Singh, H. & Singh, B. (2017). Assessment of Cancer-related Fatigue among Cancer Patients Receiving Various Therapies: A Cross-sectional Observational Study. *Indian journal of palliative care*, 23(2), 207–211. [https://doi.org/10.4103/IJPC.IJPC\\_135\\_16](https://doi.org/10.4103/IJPC.IJPC_135_16)
- Baron, R. M. & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of personality and social psychology*, 51(6), 1173.
- Barsevick, A. M., Dudley, W., Beck, S., Sweeney, C., Whitmer, K. & Nail, L. (2004). A randomized clinical trial of energy conservation for patients with cancer-related fatigue. *Cancer*, 100(6), 1302–1310. <https://doi.org/10.1002/cncr.20111>
- Beck, S. L., Dudley, W. N. & Barsevick, A. (2005). Pain, sleep disturbance, and fatigue in patients with cancer: using a mediation model to test a symptom cluster. *Oncology nursing forum*, 32(3), 542. <https://doi.org/10.1188/04.ONF.E48-E55>
- Berger, A. M., Mooney, K., Alvarez-Perez, A., Breitbart, W. S., Carpenter, K. M., Cella, D, Cleeland, C., Dotan, E., Eisenberger, M. A., Escalante, C. P., Jacobsen, P. B., Jankowski, C., LeBlanc, T., Ligibel, J. A., Loggers, E. T., Mandrell, B., Murphy, B. A., Palesh, O., Pirl, W. F., . . . Smith, C (2015). Cancer-Related Fatigue, Version 2.2015. *Journal of the National Comprehensive Cancer Network : JNCCN*, 13(8), 1012–1039. <https://doi.org/10.6004/jnccn.2015.0122>
- Berger, A. M., Mooney, K., Banerjee, C., Breitbart, W., Carpenter, K. M., Cella, D, Chang, Y., Cleeland, C., Dotan, E., DuBenske, L. & et al. (2017). NCCN Clinical Practice Guidelines in Oncology - Cancer related Fatigue: Version 1.2017.

- 
- Berger, A. M., VonEssen, S., Khun, B. R., Piper, B. F., Farr, L., Agrawal, S., Lynch, J. C. & Higginbotham, P. (2002). Feasibility of a sleep intervention during adjuvant breast cancer chemotherapy. *Oncology nursing forum*, 29(10), 1431–1441. <https://doi.org/10.1188/02.ONF.1431-1441>
- Berger, A. M., Wielgus, K., Hertzog, M., Fischer, P. & Farr, L. (2010). Patterns of circadian activity rhythms and their relationships with fatigue and anxiety/depression in women treated with breast cancer adjuvant chemotherapy. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 18(1), 105–114. <https://doi.org/10.1007/s00520-009-0636-0>
- Beutler, L. E. & Hamblin, D. L. (1986). Individualized outcome measures of internal change: Methodological considerations. *Journal of consulting and clinical psychology*, 54(1), 48.
- Bhutkar, P. M., Bhutkar, M. V., Taware, G. B., Doijad V. & Doddamani, B. R. (2008). Effect of Suryanamaskar Practice on Cardio-respiratory Fitness Parameters: A Pilot Study. *Al Ameen J Med Sci*(1(2)), 126–129.
- Bijlani, R. L., Vempati, R. P., Yadav, R. K., Ray, R. B., Gupta, V., Sharma, R., Mehta, N. & Mahapatra, S. C. (2005). A Brief but Comprehensive Lifestyle Education Program Based on Yoga Reduces Risk Factors for Cardiovascular Disease and Diabetes Mellitus. *The Journal of Alternative and Complementary Medicine*, 11(2), 267–274. <https://doi.org/10.1089/acm.2005.11.267>
- Boehm, K., Ostermann, T., Milazzo, S. & Büssing, A (2012). Effects of yoga interventions on fatigue: a meta-analysis. *Evidence-based complementary and alternative medicine : eCAM*, 2012.
- Borden, A. & Cook-Cottone, C. (2020). Yoga and eating disorder prevention and treatment: A comprehensive review and meta-analysis. *Eating Disorders*, 28(4), 400–437.

- 
- Bower, J. E., Ganz, P. A., Desmond, K. A., Rowland, J. H., Meyerowitz, B. E. & Belin, T. R. (2000). Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. *Journal of Clinical Oncology*, *18*(4), 743–753. <https://doi.org/10.1089/acm.2005.11.267>
- Bower, J. E. (2007). Cancer-related fatigue: Links with inflammation in cancer patients and survivors. *Brain, behavior, and immunity*, *21*(7), 863–871. <https://doi.org/10.1016/j.bbi.2007.03.013>
- Bower, J. E. (2014). Cancer-related fatigue—mechanisms, risk factors, and treatments. *Nature reviews. Clinical oncology*, *11*(10), 597–609. <https://doi.org/10.1038/nrclinonc.2014.127>
- Bower, J. E., Crosswell, A. D., Stanton, A. L., Crespi, C. M., Winston, D., Arevalo, J., Ma, J., Cole, S. W. & Ganz, P. A. (2015). Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. *Cancer*, *121*(8), 1231–1240. <https://doi.org/10.1002/cncr.29194>
- Bower, J. E., Garet, D., Sternlieb, B., Ganz, P. A. [Patricia A.], Irwin, M. R., Olmstead, R. & Greendale, G. (2012). Yoga for persistent fatigue in breast cancer survivors: a randomized controlled trial. *Cancer*, *118*(15), 3766–3775. <https://doi.org/10.1002/cncr.26702>
- Bower, J. E., Greendale, G., Crosswell, A. D., Garet, D., Sternlieb, B., Ganz, P. A., Irwin, M. R., Olmstead, R., Arevalo, J. & Cole, S. W. (2014). Yoga reduces inflammatory signaling in fatigued breast cancer survivors: A randomized controlled trial. *Psychoneuroendocrinology*, *43*, 20–29. <https://doi.org/10.1016/j.psyneuen.2014.01.019>
- Bridges, L. & Sharma, M. (2017). The efficacy of yoga as a form of treatment for depression. *Journal of evidence-based complementary & alternative medicine*, *22*(4), 1017–1028.
- Broad, W. J. (2013). *The Science of Yoga: Was es verspricht ; und was es kann*. Herder GmbHreasrac.



- 
- Brown, L. F. & Kroenke, K (2009). Cancer-Related Fatigue and Its Associations With Depression and Anxiety: A Systematic Review. *Psychosomatics*, 50(5), 440–447. [https://doi.org/10.1016/S0033-3182\(09\)70835-7](https://doi.org/10.1016/S0033-3182(09)70835-7)
- Bruera, E., Driver, L., Barnes, E. A., Willey, J., Shen, L., Palmer, J. L. & Escalante, C. (2003). Patient-Controlled Methylphenidate for the Management of Fatigue in Patients With Advanced Cancer: A Preliminary Report. *Journal of Clinical Oncology*, 21(23), 4439–4443. <https://doi.org/10.1200/JCO.2003.06.156>
- Bruera, E., Valero, V., Driver, L., Shen, L., Willey, J., Zhang, T. & Palmer, J. L. (2006). Patient-controlled methylphenidate for cancer fatigue: a double-blind, randomized, placebo-controlled trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 24(13), 2073–2078. <https://doi.org/10.1200/JCO.2005.02.8506>
- Bruera, E., Yennurajalingam, S., Palmer, J. L., Perez-Cruz, P. E., Frisbee-Hume, S., Allo, J. A., Williams, J. L. & Cohen, M. Z. (2013). Methylphenidate and/or a nursing telephone intervention for fatigue in patients with advanced cancer: a randomized, placebo-controlled, phase II trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 31(19), 2421–2427. <https://doi.org/10.1200/JCO.2012.45.3696>
- Bryant, E. F. (2009). *The Yoga sūtras of Patañjali: A new edition, translation, and commentary; with insights from the traditional commentators*. Noth Point Press.
- Buffart, L. M., Ros, W. J. G., Chinapaw, M. J. M., Brug, J., Knol, D. L., Korstjens, I., van Weert, E., Mesters, I., van den Borne, B., Hoekstra-Weebers, J. E. H. M. & May, A. M. (2014). Mediators of physical exercise for improvement in cancer survivors' quality of life. *Psycho-oncology*, 23(3), 330–338. <https://doi.org/10.1002/pon.3428>
- Buffart, L. M., van Uffelen, J. G. Z., Riphagen, I. I., Brug, J., van Mechelen, W., Brown, W. J. & Chinapaw, M. J. M [Mai J. M.] (2012). Physical and psychosocial benefits of yoga in

- 
- cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. *BMC Cancer*, 12(1), 559. <https://doi.org/10.1186/1471-2407-12-559>
- Carlson, L. E. & Brown, K. W. (2005). Validation of the Mindful Attention Awareness Scale in a cancer population. *Journal of psychosomatic research*, 58(1), 29–33.
- Carson, J. W., Carson, K. M., Olsen, M. K., Sanders, L. & Porter, L. S. (2017). Mindful Yoga for women with metastatic breast cancer: Design of a randomized controlled trial. *BMC complementary and alternative medicine*, 17(1), 153. <https://doi.org/10.1186/s12906-017-1672-9>
- Carson, J. W., Carson, K. M., Porter, L. S., Keefe, F. J. & Seewaldt, V. L. (2009). Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, 17(10), 1301–1309.
- Carson, J. W., Carson, K. M., Porter, L. S., Keefe, F. J., Shaw, H. & Miller, J. M. (2007). Yoga for women with metastatic breast cancer: results from a pilot study. *Journal of pain and symptom management*, 33(3), 331–341.
- Chakrabarty, J., Vidyasagar, M. S., Fernandes, D., Joisa, G., Varghese, P. & Mayya, S. (2015). Effectiveness of pranayama on cancer-related fatigue in breast cancer patients undergoing radiation therapy: a randomized controlled trial. *International journal of yoga*, 8(1), 47.
- Chandwani, K. D., Thornton, B., Perkins, G. H., Arun, B., Raghuram, N. V., Nagendra, H. R., Wei, Q. & Cohen, L. (2010). Yoga improves quality of life and benefit finding in women undergoing radiotherapy for breast cancer. *Journal of the Society for Integrative Oncology*, 8(2), 43–55.
- Chaoul, A., Milbury, K., Spelman, A., Basen-Engquist, K., Hall, M. H., Wei, Q., Shih, Y.-C. T., Arun, B., Valero, V., Perkins, G. H., Babiera, G. V., Wangyal, T., Engle, R., Harrison, C. A., Li, Y. & Cohen, L. (2018). Randomized trial of Tibetan yoga in patients

- 
- with breast cancer undergoing chemotherapy. *Cancer*, 124(1), 36–45.  
<https://doi.org/10.1002/cncr.30938>
- Chen, N., Xia, X., Qin, L., Luo, L., Han, S., Wang, G., Zhang, R. & Wan, Z. (2016). Effects of 8-Week Hatha Yoga Training on Metabolic and Inflammatory Markers in Healthy, Female Chinese Subjects: A Randomized Clinical Trial. *BioMed research international*, 2016, 5387258. <https://doi.org/10.1155/2016/5387258>
- Cicolini, G., Simonetti, V., Comparcini, D., Celiberti, I., Di Nicola, M., Capasso, L. M., Flacco, M. E., Bucci, M., Mezzetti, A. & Manzoli, L. (2014). Efficacy of a nurse-led e-mail reminder program for cardiovascular prevention risk reduction in hypertensive patients: a randomized controlled trial. *International journal of nursing studies*, 51(6), 833–843.  
<https://doi.org/10.1016/j.ijnurstu.2013.10.010>
- Cohen, L., Warneke, C., Fouladi, R. T., Rodriguez, M. A. & Chaoul-Reich, A. (2004). Psychological adjustment and sleep quality in a randomized trial of the effects of a Tibetan yoga intervention in patients with lymphoma. *Cancer*, 100(10), 2253–2260.
- Courneya, K. S., Sellar, C. M., Stevinson, C., McNeely, M. L., Peddle, C. J., Friedenreich, C. M., Tankel, K., Basi, S., Chua, N., Mazurek, A. & Reiman, T. (2009). Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 27(27), 4605–4612.  
<https://doi.org/10.1200/JCO.2008.20.0634>
- Cramer, Lauche, R, Langhorst, J & Dobos, G (2016). Is one yoga style better than another? A systematic review of associations of yoga style and conclusions in randomized yoga trials. *Complementary Therapies in Medicine*, 25, 178–187.  
<https://doi.org/10.1016/j.ctim.2016.02.015>

- 
- Cramer, H, Lauche, R, Langhorst, J, Paul, A, Michalsen, A & Dobos, G (2013). Predictors of yoga use among internal medicine patients. *BMC Complementary Alternative Medicine*, *13*(1), 172.
- Cramer, H, Lange, S., Klose, P., Paul, A & Dobos, G (2011). Can yoga improve fatigue in breast cancer patients? A systematic review. *Acta oncologica (Stockholm, Sweden)*, *51*, 559–560.
- Cramer, H, Lauche, R, Anheyer, D., Pilkington, K., Manincor, M. de, Dobos, G & Ward, L. (2018). Yoga for anxiety: A systematic review and meta-analysis of randomized controlled trials. *Depression and anxiety*, *35*(9), 830–843.
- Cramer, H, Lauche, R, Langhorst, J & Dobos, G (2013). Yoga for depression: A systematic review and meta-analysis. *Depression and anxiety*, *30*(11), 1068–1083.
- Cramer, H, Pokhrel, B., Fester, C., Meier, B., Gass, F., Lauche, R, Eggleston, B., Walz, M., Michalsen, A & Kunz, R. (2016). A randomized controlled bicenter trial of yoga for patients with colorectal cancer. *Psycho-oncology*, *25*(4), 412–420.
- Cramer, H, Rabsilber, S., Lauche, R, Kummel, S. & Dobos, G [Gustav] (2015). Yoga and meditation for menopausal symptoms in breast cancer survivors-A randomized controlled trial. *Cancer*, *121*(13), 2175–2184. <https://doi.org/10.1002/cncr.29330>
- Cramer, H, Ward, L., Steel, A., Lauche, R [Romy], Dobos, G [Gustav] & Zhang, Y. (2016). Prevalence, Patterns, and Predictors of Yoga Use: Results of a U.S. Nationally Representative Survey. *American journal of preventive medicine*, *50*(2), 230–235. <https://doi.org/10.1016/j.amepre.2015.07.037>
- Cramp, F. & Byron-Daniel, J. (2012). Exercise for the management of cancer-related fatigue in adults. *The Cochrane database of systematic reviews*, *11*, CD006145. <https://doi.org/10.1002/14651858.CD006145.pub3>

- 
- Crow, E. M., Jeannot, E. & Trehwela, A. (2015). Effectiveness of Iyengar yoga in treating spinal (back and neck) pain: A systematic review. *International journal of yoga*, 8(1), 3–14. <https://doi.org/10.4103/0973-6131.146046>
- Culos-Reed, S., Carlson, L. E., Daroux, L. M. & Hatley-Aldous, S. (2006). A pilot study of yoga for breast cancer survivors: physical and psychological benefits. *Psycho-oncology*, 15(10), 891–897.
- Curt, G. A., Breitbart, W., Cella, D. [D.], Groopman, J. E., Horning, S. J., Itri, L. M., Johnson, D. H., Miaskowski, C. [C.], Scherr, S. L., Portenoy, R. K. & Vogelzang, N. J. (2000). Impact of cancer-related fatigue on the lives of patients: New findings from the Fatigue Coalition. *The oncologist*, 5(5), 353–360. <https://doi.org/10.1634/theoncologist.5-5-353>
- Curt, G. & Johnston, P. G. (2003). Cancer fatigue: the way forward. *The oncologist*, 8 Suppl 1, 27–30. [https://doi.org/10.1634/theoncologist.8-suppl\\_1-27](https://doi.org/10.1634/theoncologist.8-suppl_1-27)
- Danhauer, S. C., Addington, E. L., Cohen, L., Sohl, S. J., van Puymbroeck, M., Albinati, N. K. & Culos-Reed, S. N. (2019a). Yoga for symptom management in oncology: A review of the evidence base and future directions for research. *Cancer*, 125(12), 1979–1989. <https://doi.org/10.1002/cncr.31979>
- Danhauer, S. C., Addington, E. L., Sohl, S. J., Chaoul, A. & Cohen, L. (2017). Review of yoga therapy during cancer treatment. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, 25(4), 1357–1372. <https://doi.org/10.1007/s00520-016-3556-9>
- Danhauer, S. C., Mihalko, S. L., Russell, G. B., Campbell, C. R., Felder, L., Daley, K. & Levine, E. A. (2009). Restorative yoga for women with breast cancer: Findings from a randomized pilot study. *Psycho-oncology*, 18(4), 360–368. <https://doi.org/10.1002/pon.1503>

- 
- Danielson, C. M. & Jones, S. M. (2017). Five Facet Mindfulness Questionnaire (FFMQ) (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006). *The Sourcebook of Listening Research: Methodology and Measures*, 281–289.
- Daukantaitė, D., Tellhed, U., Maddux, R. E., Svensson, T. & Melander, O. (2018). Five-week yin yoga-based interventions decreased plasma adrenomedullin and increased psychological health in stressed adults: A randomized controlled trial. *PloS one*, 13(7), e0200518.
- Derry, H. M., Jaremka, L. M., Bennett, J. M., Peng, J., Andridge, R., Shapiro, C., Malarkey, W. B., Emery, C. F., Layman, R., Mrozek, E., Glaser, R. & Kiecolt-Glaser, J. K. (2015). Yoga and self-reported cognitive problems in breast cancer survivors: A randomized controlled trial. *Psycho-oncology*, 24(8), 958–966. <https://doi.org/10.1002/pon.3707>
- Desai, R., Tailor, A. & Bhatt, T. (2015). Effects of yoga on brain waves and structural activation: A review. *Complementary therapies in clinical practice*, 21(2), 112–118. <https://doi.org/10.1016/j.ctcp.2015.02.002>
- Dhruva, A., Miaskowski, C, Abrams, D., Acree, M., Cooper, B., Goodman, S. & Hecht, F. M. (2012). Yoga breathing for cancer chemotherapy–associated symptoms and quality of life: results of a pilot randomized controlled trial. *The Journal of Alternative and Complementary Medicine*, 18(5), 473–479.
- Díaz, N., Menjón, S., Rolfo, C., García-Alonso, P., Carulla, J., Magro, A., Miramón, J., Rodríguez, C. A., Castellar, R. de & Gasquet, J. A. (2008). Patients’ perception of cancer-related fatigue: results of a survey to assess the impact on their everyday life. *Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico*, 10(11), 753–757. <https://doi.org/10.1007/s12094-008-0282-x>

- 
- Dong, B., Xie, C., Jing, X., Lin, L. & Tian, L. (2019). Yoga has a solid effect on cancer-related fatigue in patients with breast cancer: a meta-analysis. *Breast cancer research and treatment*, *177*(1), 5–16. <https://doi.org/10.1007/s10549-019-05278-w>
- Donovan, K. A., Small, B. J., Andrykowski, M. A., Munster, P. & Jacobsen, P. B. (2007). Utility of a cognitive-behavioral model to predict fatigue following breast cancer treatment. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association*, *26*(4), 464–472. <https://doi.org/10.1037/0278-6133.26.4.464>
- Duijts, S. F. A., Faber, M. M., Oldenburg, H. S. A., van Beurden, M. & Aaronson, N. K. (2011). Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors—a meta-analysis. *Psycho-oncology*, *20*(2), 115–126.
- Efficace, F., Gaidano, G., Breccia, M., Voso, M. T., Cottone, F., Angelucci, E., Caocci, G., Stauder, R., Selleslag, D., Sprangers, M., Platzbecker, U., Ricco, A., Sanpaolo, G., Beyne-Rauzy, O., Buccisano, F., Palumbo, G. A., Bowen, D., Nguyen, K., Niscola, P., . . . Mandelli, F. (2015). Prognostic value of self-reported fatigue on overall survival in patients with myelodysplastic syndromes: a multicentre, prospective, observational, cohort study. *The Lancet. Oncology*, *16*(15), 1506–1514. [https://doi.org/10.1016/S1470-2045\(15\)00206-5](https://doi.org/10.1016/S1470-2045(15)00206-5)
- Falkenberg, R. I., Eising, C. & Peters, M. L. (2019). Yoga and immune system functioning: a systematic review of randomized controlled trials. *Journal of Behavioral Medicine* (41), 467–482. <https://doi.org/10.1007/s10865-018-9914-y>
- Fillion, L., Gagnon, P., Leblond, F., Gélinas, C., Savard, J., Dupuis, R., Duval, K. & Larochelle, M. (2008). A brief intervention for fatigue management in breast cancer survivors. *Cancer nursing*, *31*(2), 145–159. <https://doi.org/10.1097/01.NCC.0000305698.97625.95>

- 
- Fischer, I., Weis, J., Ruffer, U., Heim, M., Bojko, P. & Ostgathe, C. (2017). Cancer-Related Fatigue in the Palliative Situation: Basics, Diagnosis and Evidence-Based Treatment. *Z Palliativmed*(18), 97–110.
- Fleig, L., Pomp, S., Schwarzer, R. & Lippke, S. (2013). Promoting exercise maintenance: How interventions with booster sessions improve long-term rehabilitation outcomes. *Rehabilitation psychology*, 58(4), 323.
- Fox, M. C., Creinin, M. D., Murthy, A. S., Harwood, B. & Reid, L. M. (2003). Feasibility study of the use of a daily electronic mail reminder to improve oral contraceptive compliance. *Contraception*, 68(5), 365–371.  
<https://doi.org/10.1016/j.contraception.2003.08.01>
- Frikkel, J., Götte, M., Beckmann, M., Kasper, S., Hense, J., Teufel, M., Schuler, M [M.] & Tewes, M. (2020). Fatigue, barriers to physical activity and predictors for motivation to exercise in advanced Cancer patients. *BMC Palliative Care*, 19(1), 43.  
<https://doi.org/10.1186/s12904-020-00542-z>
- Froeliger, B., Garland, E. L., Modlin, L. A. & McClernon, F. J. (2012). Neurocognitive correlates of the effects of yoga meditation practice on emotion and cognition: a pilot study. *Frontiers in integrative neuroscience*, 6, 48.
- Fuhrmann, K., Mehnert, A., Geue, K. & Hinz, A (2015). Fatigue in breast cancer patients: Psychometric evaluation of the fatigue questionnaire EORTC QLQ-FA13. *Breast Cancer*, 22(6), 608–614.
- Gallegos, A. M., Crean, H. F., Pigeon, W. R. & Heffner, K. L. (2017). Meditation and yoga for posttraumatic stress disorder: A meta-analytic review of randomized controlled trials. *Clinical Psychology Review*, 58, 115–124.
- Garland, S. N., Tamagawa, R., Todd, S. C., Specia, M. & Carlson, L. E. (2013). Increased mindfulness is related to improved stress and mood following participation in a mindfulness-



- 
- based stress reduction program in individuals with cancer. *Integrative cancer therapies*, 12(1), 31–40.
- Gatto, S. L. & Tak, S. H. (2008). Computer, Internet, and E-mail Use Among Older Adults: Benefits and Barriers. *Educational Gerontology*, 34(9), 800–811. <https://doi.org/10.1080/03601270802243697>
- Ghadieh, A. S., Hamadeh, G. N., Mahmassani, D. M. & Lakkis, N. A. (2015). The effect of various types of patients' reminders on the uptake of pneumococcal vaccine in adults: A randomized controlled trial. *Vaccine*, 33(43), 5868–5872. <https://doi.org/10.1016/j.vaccine.2015.07.050>
- Gielissen, M. F. M., S., Witjes, F. & Bleijenberg, G (2006). Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. *Journal of Clinical Oncology*, 24(30), 4882–4887.
- Glaus, A. & Müller, S. (2001). Measuring fatigue of cancer patients in the German-speaking region: development of the Fatigue Assessment Questionnaire [Messung der Müdigkeit bei Krebskranken im Deutschen Sprachraum: Die Entwicklung des Fatigue Assessment Questionnaires]. *Pflege*, 14(3), 161–170. <https://doi.org/10.1024/1012-5302.14.3.161>
- Goedendorp, M. M., Gielissen, M. F. M., Verhagen, C. A. & Bleijenberg, G (2009). Psychosocial interventions for reducing fatigue during cancer treatment in adults. *Cochrane database of systematic reviews*.
- Göthe, N. P., Keswani, R. K. & McAuley, E. (2016). Yoga practice improves executive function by attenuating stress levels. *Biological psychology*, 121(Pt A), 109–116. <https://doi.org/10.1016/j.biopsycho.2016.10.010>

- 
- Göthe, N. P., Kramer, A. F. & McAuley, E. (2014). The effects of an 8-week Hatha yoga intervention on executive function in older adults. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, 69(9), 1109–1116.
- Groenvold, M., Petersen, M. A., Aaronson, N. K., Arraras, J. I [Juan I.], Blazeby, J. M., Bottomley, A., Fayers, P. M., Graeff, A. de, Hammerlid, E., Kaasa, S., Sprangers, M. A. G. & Bjorner, J. B. (2006). The development of the EORTC QLQ-C15-PAL: A shortened questionnaire for cancer patients in palliative care. *Eur J Cancer*, 42(1), 55–64.
- Guo, Y. & Molinares, D. (2020). Precautions for yoga practice are necessary in cancer patients. *Supportive Care in Cancer*, 28(9), 3981–3982. <https://doi.org/10.1007/s00520-019-05154-9>
- Haider, T., Sharma, M. & Branscum, P. (2017). Yoga as an Alternative and Complimentary Therapy for Cardiovascular Disease: A Systematic Review. *Journal of evidence-based complementary & alternative medicine*, 22(2), 310–316. <https://doi.org/10.1177/2156587215627390>
- Haramiova, Z., Stasko, M., Hulin, M., Tesar, T., Kuzelova, M. & Morisky, D. M. (2017). The effectiveness of daily SMS reminders in pharmaceutical care of older adults on improving patients' adherence to antihypertensive medication (SPPA): study protocol for a randomized controlled trial. *Trials*, 18(1), 334. <https://doi.org/10.1186/s13063-017-2063-8>
- Hardoerfer, K. & Jentschke, E. (2018). Effect of Yoga Therapy on Symptoms of Anxiety in Cancer Patients. *Oncology research and treatment*, 41(9), 526–532. <https://doi.org/10.1159/000488989>
- Hariprasad, V. R., Varambally, S., Shivakumar, V., Kalmady, S. V., Venkatasubramanian, G. & Gangadhar, B. N. (2013). Yoga increases the volume of the hippocampus in elderly subjects. *Indian journal of psychiatry*, 55(Suppl 3), S394.

- 
- Hartung, T. J., Friedrich, M., Johansen, C., Wittchen, H.-U., Faller, H., Koch, U., Brahler, E., Harter, M., Keller, M., Schulz, H., Wegscheider, K., Weis, J. & Mehnert, A. (2017). The Hospital Anxiety and Depression Scale (HADS) and the 9-item Patient Health Questionnaire (PHQ-9) as screening instruments for depression in patients with cancer. *Cancer*, *123*(21), 4236–4243.
- Hartung, T. J., Friedrich, M., Johansen, C., Wittchen, H.-U., Faller, H., Koch, U., Brähler, E., Härter, M., Keller, M. & Schulz, H. (2017). The Hospital Anxiety and Depression Scale (HADS) and the 9-item Patient Health Questionnaire (PHQ-9) as screening instruments for depression in patients with cancer. *Cancer*, *123*(21), 4236–4243.
- Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical Mediation Analysis in the New Millennium. *Communication Monographs*, *76*(4), 408–420. <https://doi.org/10.1080/03637750903310360>
- Hilfiker, R., Meichtry, A., Eicher, M., Balfe, L. N., Knols, R. H., Verra, M. L. & Taeymans, J. (2018). Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: a systematic review incorporating an indirect-comparisons meta-analysis. *British journal of sports medicine*, *52*(10), 651–658.
- Hofer, F., Koinig, K. A., Nagl, L., Borjan, B. & Stauder, R. (2018). Fatigue at baseline is associated with geriatric impairments and represents an adverse prognostic factor in older patients with a hematological malignancy. *Annals of hematology*, *97*(11), 2235–2243. <https://doi.org/10.1007/s00277-018-3420-8>
- Hofmann, S. G., Sawyer, A. T., Witt, A. A. & Oh, D. (2010). The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *Journal of consulting and clinical psychology*, *78*(2), 169–183. <https://doi.org/10.1037/a0018555>

- 
- Horgan, S. & O'Donovan, A. (2018). The impact of exercise during radiation therapy for prostate cancer on fatigue and quality of life: A systematic review and meta-analysis. *Journal of Medical Imaging and Radiation Sciences*, 49(2), 207–219.
- Irestorm, E., Tonning Olsson, I., Johansson, B. & Øra, I. (2020). Cognitive fatigue in relation to depressive symptoms after treatment for childhood cancer. *BMC psychology*, 8, 1–9.
- Jacobsen, P. B., Donovan, K. A., Vadaparampil, S. T. & Small, B. J. (2007). Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association*, 26(6), 660–667.
- Jacobsen, P. B., Donovan, K. A. & Weitzner, M. A. (2003). Distinguishing Fatigue and Depression in Patients with cancer. *Seminars in clinical neuropsychiatry*, 8(4), 229–240. <https://doi.org/10.1037/0278-6133.26.6.660>
- Joly, F., Lange, M., Dos Santos, M., Vaz-Luis, I. & Di Meglio, A. (2019). Long-Term Fatigue and Cognitive Disorders in Breast Cancer Survivors. *Cancers*, 11(12). <https://doi.org/10.3390/cancers11121896>
- Jones, J. M., Olson, K., Catton, P., Catton, C. N., Fleshner, N. E., Krzyzanowska, M. K., McCready, D. R., Wong, R. K. S., Jiang, H. & Howell, D. (2016). Cancer-related fatigue and associated disability in post-treatment cancer survivors. *J Cancer Surviv*, 10(1), 51–61.
- Kabat-Zinn, J. (2015). *Die MBSR Yogäübungen: Stressbewältigung durch Achtsamkeit*. (4. Aufl.). Arbor Verlag.
- Kangas, M., Bovberg & Monthomery, G. (2008). Cancer -Related Fatigue: A Systematic and Meta-Analytic Review of Non-Pharmacological Therapies of Cancer Patients. *Psychological Bulletin*, 134.

- 
- Kangas, M., Bovbjerg, D. H. & Montgomery, G. H. (2008). *Cancer-related fatigue: A systematic and meta-analytic review of non-pharmacological therapies for cancer patients*. United States.
- Karthikeyan, G., Jumrani, D., Prabhu, R., Manoor, U. K. & Supe, S. S. (2012). Prevalence of fatigue among cancer patients receiving various anticancer therapies and its impact on quality of life: a cross-sectional study. *Indian journal of palliative care*, 18(3), 165–175. <https://doi.org/10.4103/0973-1075.105686>
- Khanna, S. & Greeson, J. M. (2013). A narrative review of yoga and mindfulness as complementary therapies for addiction. *Complementary Therapies in Medicine*, 21(3), 244–252.
- Kiecolt-Glaser, J. K., Bennett, J. M., Andridge, R., Peng, J., Shapiro, C. L., Malarkey, W. B., Emery, C. F., Layman, R., Mrozek, E. E. & Glaser, R. (2014). Yoga's impact on inflammation, mood, and fatigue in breast cancer survivors: A randomized controlled trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 32(10), 1040–1049. <https://doi.org/10.1200/JCO.2013.51.8860>
- Kiel, J. M. (2005). The digital divide: Internet and e-mail use by the elderly. *Medical Informatics and the Internet in Medicine*, 30(1), 19–23. <https://doi.org/10.1080/14639230500066900>
- Kieviet-Stijnen, A., Visser, A., Garssen, B. & Hudig, W. (2008). Mindfulness-based stress reduction training for oncology patients: Patients' appraisal and changes in well-being. *Patient education and counseling*, 72(3), 436–442.
- Kinkead, B., Schettler, P. J., Larson, E. R., Carroll, D., Sharenko, M., Nettles, J., Edwards, S. A., Miller, A. H., Torres, M. A., Dunlop, B. W., Rakofsky, J. J. & Rapaport, M. H. (2018). Massage therapy decreases cancer-related fatigue: Results from a randomized early phase trial. *Cancer*, 124(3), 546–554. <https://doi.org/10.1002/cncr.31064>

- 
- Körner, P., Ehrmann, K., Hartmannsgruber, J., Metz, M., Steigerwald, S., Flentje, M. & van Oorschot, B. (2017). Patient-reported symptoms during radiotherapy. *Strahlentherapie und Onkologie*, *193*(7), 570–577.
- Kovalchuk, A. & Kolb, B. (2017). Chemo brain: from discerning mechanisms to lifting the brain fog—an aging connection. *Cell Cycle*, *16*(14), 1345–1349.
- Kroenke, K., Spitzer, R. L. & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*, *16*(9), 606–613. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
- Kröz, M., Zerm, R., Reif, M., Laue, H. B. von, Schad, F., Büssing, A., Bartsch, C., Feder, G. & Girke, M. (2008). Validation of the German version of the Cancer Fatigue Scale (CFS-D). *European journal of cancer care*, *17*(1), 33–41. <https://doi.org/10.1111/j.1365-2354.2007.00799.x>
- Kuba, K., Weißflog, G., Götze, H., García-Torres, F., Mehnert, A. & Esser, P. (2019). The relationship between acceptance, fatigue, and subjective cognitive impairment in hematologic cancer survivors. *International Journal of Clinical and Health Psychology*, *19*(2), 97–106.
- Kuhnt, S., Friedrich, M., Schulte, T., Esser, P. & Hinz, A. (2019). Predictors of fatigue in cancer patients: a longitudinal study. *Supportive Care in Cancer*, *27*(9), 3463–3471. <https://doi.org/10.1007/s00520-019-4660-4>
- Lacourt, T. E., Kavelaars, A., Ohanian, M., Shah, N. D., Shelburne, S. A., Futreal, A., Kontoyiannis, D. P. & Heijnen, C. J. (2018). Patient-reported fatigue prior to treatment is prognostic of survival in patients with acute myeloid leukemia. *Oncotarget*, *9*(58), 31244–31252. <https://doi.org/10.18632/oncotarget.25787>
- Ledesma, D. & Kumano, H. (2009). Mindfulness-based stress reduction and cancer: a meta-analysis. *Psycho-oncology*, *18*(6), 571–579.

- 
- Lengacher, C. A., Reich, R. R., Paterson, C. L., Ramesar, S., Park, J. Y., Alinat, C., Johnson-Mallard, V., Moscoso, M., Budhrani-Shani, P., Miladinovic, B., Jacobsen, P. B., Cox, C. E., Goodman, M. & Kip, K. E. (2016). Examination of Broad Symptom Improvement Resulting From Mindfulness-Based Stress Reduction in Breast Cancer Survivors: A Randomized Controlled Trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *34*(24), 2827–2834. <https://doi.org/10.1200/JCO.2015.65.7874>
- Li, A. W. & Goldsmith, C.-A. W. (2012). The effects of yoga on anxiety and stress. *Alternative Medicine Review*, *17*(1).
- Lim, S.-A. & Cheong, K.-J. (2015). Regular Yoga Practice Improves Antioxidant Status, Immune Function, and Stress Hormone Releases in Young Healthy People: A Randomized, Double-Blind, Controlled Pilot Study. *The Journal of Alternative and Complementary Medicine*, *21*(9), 530–538. <https://doi.org/10.1089/acm.2014.0044>
- Lin, P.-J, Peppone, L. J, Janelins, M. C, Mohile, S. G, Kamen, C. S, Kleckner, I. R, Fung, C, Asare, M, Cole, C. L & Culakova, E (2018). Yoga for the management of cancer treatment-related toxicities. *Curr Oncol*, *20*(1), 5. <https://doi.org/10.1007/s11912-018-0657-2>
- Listing, M., Reissauer, A., Krohn, M., Voigt, B., Tjahono, G., Becker, J., Klapp, B. F. & Rauchfuss, M. (2009). Massage therapy reduces physical discomfort and improves mood disturbances in women with breast cancer. *Psycho-oncology*, *18*(12), 1290–1299. <https://doi.org/10.1002/pon.1508>
- Littman, A. J., Bertram, L. C., Ceballos, R., Ulrich, C. M., Ramaprasad, J., McGregor, B. & McTiernan, A. (2012). Randomized controlled pilot trial of yoga in overweight and obese breast cancer survivors: effects on quality of life and anthropometric measures. *Supportive Care in Cancer*, *20*(2), 267–277. <https://doi.org/10.1007/s00520-010-1066-8>
- Liu, Q., Abba, K., Alejandria, M. M., Sinclair, D., Balanag, V. M. & Lansang, M. A. D. (2014). Reminder systems to improve patient adherence to tuberculosis clinic appointments

- 
- for diagnosis and treatment. *The Cochrane database of systematic reviews*, 2014(11), CD006594-CD006594. <https://doi.org/10.1002/14651858.CD006594.pub3>
- Lötzke, D., Wiedemann, F., Rodrigues Recchia, D., Ostermann, T., Sattler, D., Ettl, J., Kiechle, M., Büssing, A. & Manuel, A.-M. (2016). Iyengar-Yoga Compared to Exercise as a Therapeutic Intervention during (Neo)adjuvant Therapy in Women with Stage I–III Breast Cancer: Health-Related Quality of Life, Mindfulness, Spirituality, Life Satisfaction, and Cancer-Related Fatigue. *Evidence-based complementary and alternative medicine : eCAM*, 2016, 5931816. <https://doi.org/10.1155/2016/5931816>
- Löwe, B., Kroenke, K, Herzog, W. & Gräfe, K. (2004). Measuring depression outcome with a brief self-report instrument: sensitivity to change of the Patient Health Questionnaire (PHQ-9). *Journal of Affective Disorders*, 81(1), 61–66. [https://doi.org/10.1016/S0165-0327\(03\)00198-8](https://doi.org/10.1016/S0165-0327(03)00198-8)
- Lucía, A., Earnest, C. & Pérez, M. (2003). Cancer-related fatigue: can exercise physiology assist oncologists? *The Lancet. Oncology*, 4(10), 616–625. [https://doi.org/10.1016/s1470-2045\(03\)01221-x](https://doi.org/10.1016/s1470-2045(03)01221-x)
- Lundt, A. & Jentschke, E. (2019). Long-Term Changes of Symptoms of Anxiety, Depression, and Fatigue in Cancer Patients 6 Months After the End of Yoga Therapy. *Integrative cancer therapies*, 18, 1534735418822096. <https://doi.org/10.1177/1534735418822096>
- Mackenzie, M. J., Wurz, A. J., Yamauchi, Y., Pires, L. A. & Culos-Reed, S. N. (2016). Yoga Helps Put the Pieces Back Together: A Qualitative Exploration of a Community-Based Yoga Program for Cancer Survivors. *Evidence-based complementary and alternative medicine : eCAM*, 2016, 1832515. <https://doi.org/10.1155/2016/1832515>
- MacKinnon, D. P., Lockwood, C. M. & Williams, J. (2004). Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate behavioral research*, 39(1), 99–128.



- 
- McCall, M., McDonald, M., Thorne, S., Ward, A. & Heneghan, C. (2015). Yoga for health-related quality of life in adult cancer: a randomized controlled feasibility study. *Evidence-based complementary and alternative medicine : eCAM*, 2015.
- McCall, M., Thorne, S., Ward, A. & Heneghan, C. (2015). Yoga in adult cancer: an exploratory, qualitative analysis of the patient experience. *BMC complementary and alternative medicine*, 15, 245. <https://doi.org/10.1186/s12906-015-0738-9>
- Mehnert, A., Müller, D, Lehmann, C. & Koch, U. (2006). Die deutsche version des NCCN distress-thermometers: empirische Prüfung eines screening-instruments zur erfassung psychosozialer belastung bei krebspatienten. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie*, 54(3), 213–223.
- Mikkelsen, M. K., Nielsen, D. L., Vinther, A., Lund, C. M. & Jarden, M. (2019). Attitudes towards physical activity and exercise in older patients with advanced cancer during oncological treatment - A qualitative interview study. *European journal of oncology nursing : the official journal of European Oncology Nursing Society*, 41, 16–23. <https://doi.org/10.1016/j.ejon.2019.04.005>
- Milbury, K., Chaoul, A., Engle, R., Liao, Z., Yang, C., Carmack, C., Shannon, V., Spelman, A., Wangyal, T. & Cohen, L. (2015). Couple-based Tibetan yoga program for lung cancer patients and their caregivers. *Psycho-oncology*, 24(1), 117.
- Miller, A. H., Ancoli-Israel, S., Bower, J. E., Capuron, L. & Irwin, M. R. (2008). Neuroendocrine-immune mechanisms of behavioral comorbidities in patients with cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 26(6), 971–982.
- Miller, W. R. & Rollnick, S. (2012). *Motivational interviewing: Helping people change*. Guilford press. <https://doi.org/10.1200/JCO.2007.10.7805>

- 
- Minton, O., Richardson, A., Sharpe, M., Hotopf, M. & Stone, P. C. (2011). Psychostimulants for the management of cancer-related fatigue: a systematic review and meta-analysis. *Journal of pain and symptom management*, 41(4), 761–767. <https://doi.org/10.1016/j.jpainsymman.2010.06.020>
- Moadel, A. B., Shah, C., Wylie-Rosett, J., Harris, M. S., Patel, S. R., Hall, C. B. & Sparano, J. A. (2007). Randomized Controlled Trial of Yoga Among a Multiethnic Sample of Breast Cancer Patients: Effects on Quality of Life. *Journal of Clinical Oncology*, 25(28), 4387–4395. <https://doi.org/10.1200/JCO.2006.06.6027>
- Mohammad, A., Thakur, P., Kumar, R., Kaur, S., Saini, R. V. & Saini, A. K. (2019). Biological markers for the effects of yoga as a complementary and alternative medicine. *Journal of complementary & integrative medicine*, 16(1). <https://doi.org/10.1200/JCO.2006.06.6027>
- Mohandas, H., Jaganathan, S., Mani, M., Ayyar, M. & Rohini Thevi, G. (2017). Cancer-related fatigue treatment: An overview. *Journal of Cancer Research and Therapeutics*, 13(6), 916–929. [https://doi.org/10.4103/jcrt.JCRT\\_50\\_17](https://doi.org/10.4103/jcrt.JCRT_50_17)
- Monson, A. L., Chismark, A. M., Cooper, B. R. & Krenik-Matejcek, T. M. (2017). Effects of Yoga on Musculoskeletal Pain. *American Dental Hygienists Association*, 91(2), 15.
- Mooventhan, A. & Nivethitha, L. (2017). Evidence based effects of yoga in neurological disorders. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*, 43, 61–67. <https://doi.org/10.1016/j.jocn.2017.05.012>
- Moraska, A. R., Sood, A., Dakhil, S. R., Sloan, J. A., Barton, D., Atherton, P. J., Suh, J. J., Griffin, P. C., Johnson, D. B., Ali, A., Silberstein, P. T., Duane, S. F. & Loprinzi, C. L. (2010). Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Long-Acting Methylphenidate for Cancer-Related Fatigue: North Central Cancer Treatment Group

- 
- NCCTG-N05C7 Trial. *Journal of Clinical Oncology*, 28(23), 3673–3679.  
<https://doi.org/10.1200/JCO.2010.28.1444>
- Müller, D. (2009). Moderatoren und Mediatoren in Regressionen. In S. Albers, D. Klapper, U. Konradt, A. Walter & J. Wolf (Hg.), *Methodik der empirischen Forschung* (S. 237–252). Gabler Verlag. [https://doi.org/10.1007/978-3-322-96406-9\\_16](https://doi.org/10.1007/978-3-322-96406-9_16)
- Mustian, K. M. (2013). Yoga as treatment for insomnia among cancer patients and survivors: a systematic review. *European medical journal. Oncology*, 1, 106.
- Mustian, K. M., Alfano, C. M., Heckler, C., Kleckner, A. S., Kleckner, I. R. [Ian R.], Leach, C. R., Mohr, D., Palesh, O. G., Peppone, L. J. & Piper, B. F. (2017). Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: a meta-analysis. *JAMA oncology*, 3(7), 961–968.
- Mustian, K. M., Morrow, G. R., Carroll, J. K., Figueroa-Moseley, C. D., Jean-Pierre, P. & Williams, G. C. (2007). Integrative nonpharmacologic behavioral interventions for the management of cancer-related fatigue. *The oncologist*, 12(1), 52.
- Muszalik, M., Kołucka-Pluta, M., Kędziora-Kornatowska, K. & Robaczewska, J. (2016). Quality of life of women with breast cancer undergoing radiotherapy using the Functional Assessment of Chronic Illness Therapy-Fatigue questionnaire. *Clinical interventions in aging*, 11, 1489–1494. <https://doi.org/10.2147/CIA.S113530>
- Naveen, K. V., Nagendra, R. N. H. & Telles, S. (1997). Yoga breathing through a particular nostril increases spatial memory scores without lateralized effects. *Psychological reports*, 81(2), 555–561.
- Olson, K [Karin], Turner, A. R., Courneya, K. S., Field, C., Man, G., Cree, M. & Hanson, J. (2008). Possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion in advanced cancer. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, 16(3), 241–249.

- 
- Pal, R. & Gupta, N. (2019). Yogic practices on oxidative stress and of antioxidant level: a systematic review of randomized controlled trials. *Journal of Complementary and Integrative Medicine*, 16(4), 20170079. <https://doi.org/10.1515/jcim-2017-0079>
- Pearson, E. J. M., Morris, M. E. & McKinstry, C. E. (2015). Cancer-related fatigue: a survey of health practitioner knowledge and practice. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, 23(12), 3521–3529. <https://doi.org/10.1007/s00520-015-2723-8>
- Peppone, L. J., Janelsins, M. C. [Michelle C.], Kamen, C., Mohile, S. G. [Supriya G.], Sprod, L. K., Gewandter, J. S., Kirshner, J. J., Gaur, R., Ruzich, J., Esparaz, B. T. & Mustian, K. M. (2015). The effect of YOCAS® yoga for musculoskeletal symptoms among breast cancer survivors on hormonal therapy. *Breast cancer research and treatment*, 150(3), 597–604. <https://doi.org/10.1007/s10549-015-3351-1>
- Pinto, B. M., Frierson, G. M., Rabin, C., Trunzo, J. J. & Marcus, B. H. (2005). Home-based physical activity intervention for breast cancer patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 23(15), 3577–3587. <https://doi.org/10.1200/JCO.2005.03.080>
- Preacher, K. J. & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior research methods, instruments, & computers*, 36(4), 717–731.
- Pullens, M. J. J., Vries, J. de & Roukema, J. A. (2010). Subjective cognitive dysfunction in breast cancer patients: a systematic review. *Psycho-oncology*, 19(11), 1127–1138.
- Rahmani, S. & Talepasand, S. (2015). The effect of group mindfulness-based stress reduction program and conscious yoga on the fatigue severity and global and specific life quality in women with breast cancer. *Medical journal of the Islamic Republic of Iran*, 29, 175.

- 
- Rao, R. M., Vadiraja, H. S., Nagaratna, R., Gopinath, K. S., Patil, S., Diwakar, R. B., Shahsidhara, H. P., Ajaikumar, B. S. & Nagendra, H. R. (2017). Effect of Yoga on Sleep Quality and Neuroendocrine Immune Response in Metastatic Breast Cancer Patients. *Indian journal of palliative care*, 23(3), 253–260. [https://doi.org/10.4103/IJPC.IJPC\\_102\\_17](https://doi.org/10.4103/IJPC.IJPC_102_17)
- Reif, K., Vries, U. de, Petermann, F. & Görres, S. (2013). A patient education program is effective in reducing cancer-related fatigue: a multi-centre randomised two-group waiting-list controlled intervention trial. *European journal of oncology nursing : the official journal of European Oncology Nursing Society*, 17(2), 204–213. <https://doi.org/10.1016/j.ejon.2012.07.002>
- Reuter, K. & Härter, M. (2004). The concepts of fatigue and depression in cancer. *European journal of cancer care*, 13(2), 127–134. <https://doi.org/10.1111/j.1365-2354.2003.00464.x>
- Robert Koch-Institute & Society of epidemiological cancer registries in Germany. (2019). *Krebs in Deutschland 2015/2016: 12. Ausgabe*.
- Rodrigues, A. R., Trufelli, D. C., Fonseca, F., Paula, L. C. de & Giglio, A. d. (2015). Fatigue in Patients With Advanced Terminal Cancer Correlates With Inflammation, Poor Quality of Life and Sleep, and Anxiety/Depression. *American Journal of Hospice and Palliative Medicine®*, 33(10), 942–947. <https://doi.org/10.1177/1049909115603055>
- Rodríguez Antolín, A., Martínez-Piñeiro, L., Jiménez Romero, M. E., García Ramos, J. B., López Bellido, D., Muñoz Del Toro, J., García García-Porrero, A. & Gómez Veiga, F. (2019). Prevalence of fatigue and impact on quality of life in castration-resistant prostate cancer patients: the VITAL study. *BMC urology*, 19(1), 92. <https://doi.org/10.1186/s12894-019-0527-8>
- Saeed, S. A., Cunningham, K. & Bloch, R. M. (2019). Depression and Anxiety Disorders: Benefits of Exercise, Yoga, and Meditation. *American family physician*, 99(10), 620–627.

- 
- Schmidt, M. E., Hermann, S., Arndt, V. & Steindorf, K. (2020). Prevalence and severity of long-term physical, emotional, and cognitive fatigue across 15 different cancer entities. *Cancer medicine*, 9(21), 8053–8061. <https://doi.org/10.1002/cam4.3413>
- Schoenborn, J. R. & Wilson, C. B. (2007). Regulation of interferon-gamma during innate and adaptive immune responses. *Advances in immunology*, 96, 41–101. [https://doi.org/10.1016/S0065-2776\(07\)96002-2](https://doi.org/10.1016/S0065-2776(07)96002-2)
- Schubert, C., Hong, S., Natarajan, L., Mills, P. J. & Dimsdale, J. E. (2007). The association between fatigue and inflammatory marker levels in cancer patients: A quantitative review. *Brain, behavior, and immunity*, 21(4), 413–427. <https://doi.org/10.1016/j.bbi.2006.11.004>
- Schumacher, J., Wilz, G., Gunzelmann, T. & Brähler, E [E.] (2000). The Antonovsky Sense of Coherence Scale. Test statistical evaluation of a representative population sample and construction of a brief scale. *Psychotherapie, Psychosomatik, Medizinische Psychologie*, 50(12), 472–482.
- Schwartz, A. L., Mori, M., Gao, R., Nail, L. M. & King, M. E. (2001). Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. *Medicine and science in sports and exercise*, 33(5), 718–723. <https://doi.org/10.1097/00005768-200105000-00006>
- Schwarz, R., Krauss, O. & Hinz, A (2003). Fatigue in the General Population. *Oncology research and treatment*, 26(2), 140–144. <https://doi.org/10.1159/000069834>
- Scott, J., Lasch, K., Barsevick, A. & Piault-Louis, E. (2011). Patients' Experiences With Cancer-Related Fatigue: A Review and Synthesis of Qualitative Research. *Oncology nursing forum*, 38, E191-203. <https://doi.org/10.1188/11.ONF.E191-E203>
- Segal, R., Evans, W., Johnson, D., Smith, J., Colletta, S., Gayton, J., Woodard, S., Wells, G. & Reid, R. (2001). Structured exercise improves physical functioning in women with stages I and II breast cancer: results of a randomized controlled trial. *Journal of clinical oncology* :

- 
- official journal of the American Society of Clinical Oncology*, 19(3), 657–665.  
<https://doi.org/10.1200/JCO.2001.19.3.657>
- Servaes, P., Verhagen, C. & Bleijenberg, G (2002). Fatigue in cancer patients during and after treatment: Prevalence, correlates and interventions. *European journal of cancer (Oxford, England : 1990)*, 38(1), 27–43. [https://doi.org/10.1016/s0959-8049\(01\)00332-x](https://doi.org/10.1016/s0959-8049(01)00332-x)
- Sfeir, J. G., Drake, M. T., Sonawane, V. J. & Sinaki, M. (2018). Vertebral compression fractures associated with yoga: a case series. *European journal of physical and rehabilitation medicine*, 54(6), 947–951. <https://doi.org/10.23736/S1973-9087.18.05034-7>
- Sharma, V. K., Rajajeyakumar, M., Velkumary, S., Subramanian, S. K., Bhavanani, A. B., Madanmohan, A. S. & Thangavel, D. (2014). Effect of fast and slow pranayama practice on cognitive functions in healthy volunteers. *Journal of clinical and diagnostic research: JCDR*, 8(1), 10.
- Shi, Q., Smith, T. G., Michonski, J. D., Stein, K. D., Kaw, C. & Cleeland, C. S. (2011). Symptom burden in cancer survivors 1 year after diagnosis: a report from the American Cancer Society's Studies of Cancer Survivors. *Cancer*, 117(12), 2779–2790. <https://doi.org/10.1002/cncr.26146>
- Simeit, R., Deck, R. & Conta-Marx, B. (2004). Sleep management training for cancer patients with insomnia. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, 12(3), 176–183. <https://doi.org/10.1007/s00520-004-0594-5>
- Singer, S., Kuhnt, S., Zwerenz, R., Eckert, K, Hofmeister, D., Dietz, A., Giesinger, J., Hauss, J., Papsdorf, K. & Briest, S. (2011). Age- and sex-standardised prevalence rates of fatigue in a large hospital-based sample of cancer patients. *British journal of cancer*, 105(3), 445–451.

- 
- Smets, E. M., Garssen, B., Bonke, B. de & Haes, J. de (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of psychosomatic research*, 39(3), 315–325.
- Smith, C., Hancock, H., Blake-Mortimer, J. & Eckert, K. (2007). A randomised comparative trial of yoga and relaxation to reduce stress and anxiety. *Complementary Therapies in Medicine*, 15(2), 77–83.
- Specia, M., Carlson, L. E., Goodey, E. & Angen, M. (2000). A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosomatic medicine*, 62(5), 613–622.
- Stanton, A. L., Ganz, P. A., Kwan, L., Meyerowitz, B. E., Bower, J. E., Krupnick, J. L., Rowland, J. H., Leedham, B. & Belin, T. R (2005). Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 23(25), 6009–6018. <https://doi.org/10.1200/JCO.2005.09.101>
- Steketee, G. & Chambless, D. L (1992). Methodological issues in prediction of treatment outcome. *Clinical Psychology Review*, 12(4), 387–400. [https://doi.org/10.1016/0272-7358\(92\)90123-P](https://doi.org/10.1016/0272-7358(92)90123-P)
- Stiel, S., Matthes, M. E., Bertram, L., Ostgathe, C., Elsner, F. & Radbruch, L. (2010). Validation of the new version of the minimal documentation system (MIDOS) for patients in palliative care: the German version of the edmonton symptom assessment scale (ESAS). *Schmerz (Berlin, Germany)*, 24(6), 596–604.
- Strasser, B., Steindorf, K., Wiskemann, J. & Ulrich, C. M. (2013). Impact of resistance training in cancer survivors: a meta-analysis. *Medicine and science in sports and exercise*, 45(11), 2080–2090. <https://doi.org/10.1249/MSS.0b013e31829a3b63>



- 
- Tanay, G. & Bernstein, A. (2013). State Mindfulness Scale (SMS): development and initial validation. *Psychological assessment*, 25(4), 1286.
- Tolia, M., Tsoukalas, N., Nikolaou, M., Mosa, E., Nazos, I., Poultside, A., Hajioannou, J., Tsanadis, K., Spyropoulou, D., Charalampakis, N., Kardamakis, D., Kouloulis, V., Pistevou-Gombaki, K. & Kyrgias, G. (2018). Utilizing Yoga in Oncologic Patients Treated with Radiotherapy: Review. *Indian journal of palliative care*, 24(3), 355–358. [https://doi.org/10.4103/IJPC.IJPC\\_112\\_17](https://doi.org/10.4103/IJPC.IJPC_112_17)
- Trajkovic-Vidakovic, M., Graeff, A. de, Voest, E. E. & Teunissen, Saskia C C M (2012). Symptoms tell it all: a systematic review of the value of symptom assessment to predict survival in advanced cancer patients. *Critical reviews in oncology/hematology*, 84(1), 130–148. <https://doi.org/10.1016/j.critrevonc.2012.02.011>
- Uebelacker, L. A., Weinstock, L. M. & Kraines, M. A. (2014). Self-reported benefits and risks of yoga in individuals with bipolar disorder. *Journal of psychiatric practice*, 20(5), 345–352. <https://doi.org/10.1097/01.pra.0000454779.59859.f8>
- Vadiraja, H. S., Raghavendra, R. M., Nagarathna, R., Nagendra, H. R., Rekha, M., Vanitha, N., Gopinath, K. S., Srinath, B. S., Vishweshwara, M. S., Madhavi, Y. S., Ajaikumar, B. S., Ramesh, B. S., Nalini, R. & Kumar, V. (2009). Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: A randomized controlled trial. *Integrative cancer therapies*, 8(1), 37–46. <https://doi.org/10.1177/1534735409331456>
- Vadiraja, H. S., Raghavendra, RM, Nagarathna, R., Nagendra, H. R., Patil, S., Diwakar, R. B., Shashidhara, H. P., Gopinath, K. S. & Ajaikumar, B. S. (2017). Effects of yoga in managing fatigue in breast cancer patients: a randomized controlled trial. *Indian J Pall care*, 23(3), 247.

- 
- Vadiraja, H. S., Rao, R. M., Nagarathna, R., Nagendra, H. R., Patil, S., Diwakar, R. B., Shashidhara, H. P., Gopinath, K. S. & Ajaikumar, B. S. (2017). Effects of Yoga in Managing Fatigue in Breast Cancer Patients: A Randomized Controlled Trial. *Indian journal of palliative care*, 23(3), 247–252. [https://doi.org/10.4103/IJPC.IJPC\\_95\\_17](https://doi.org/10.4103/IJPC.IJPC_95_17)
- Vallance, J. K. H., Courneya, K. S., Plotnikoff, R. C., Yasui, Y. & Mackey, J. R. (2007). Randomized controlled trial of the effects of print materials and step pedometers on physical activity and quality of life in breast cancer survivors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, 25(17), 2352–2359. <https://doi.org/10.1200/JCO.2006.07.9988>
- van Muijen, P., Duijts, S. F. A., Bonefaas-Groenewoud, K., van der Beek, A. J. & Anema, J. R. (2017). Predictors of fatigue and work ability in cancer survivors. *Occupational Medicine*, 67(9), 703–711. <https://doi.org/10.1093/occmed/kqx165>
- Villemure, C., Ceko, M., Cotton, V. A. & Bushnell M. C. (2014). Insular Cortex Mediates Increased Pain Tolerance in Yoga Practitioners. *Cerebral Cortex*(24(10)), 2732–2740.
- Wang, X. S. & Woodruff, J. F. (2015). Cancer-related and treatment-related fatigue. *Gynecologic oncology*, 136(3), 446–452. <https://doi.org/10.1016/j.ygyno.2014.10.013>
- Weis, J. (2013). Diagnostik und Erfassung der tumorassozierten Fatigue. *Forum*, 28(1), 39–42.
- Weis, J., Arraras, J. I., Conroy, T., Efficace, F., Fleissner, C., Görög, A., Hammerlid, E., Holzner, B., Jones, L. & Lanceley, A. (2013). Development of an EORTC quality of life phase III module measuring cancer-related fatigue (EORTC QLQ-FA13). *Psycho-oncology*, 22(5), 1002–1007.
- Weis, J., Tomaszewski, K. A., Hammerlid, E., Ignacio Arraras, J., Conroy, T., Lanceley, A., Schmidt, H., Wirtz, M., Singer, S [Susanne], Pinto, M., Alm El-Din, M., Compter, I., Holzner, B., Hofmeister, D [Dirk], Chie, W.-C., Czeladzki, M., Harle, A., Jones, L.,

- 
- Ritter, S., . . . Bottomley, A. (2017). International Psychometric Validation of an EORTC Quality of Life Module Measuring Cancer Related Fatigue (EORTC QLQ-FA12). *Journal of the National Cancer Institute, 109*(5). <https://doi.org/10.1093/jnci/djw273>
- Whisman, M. A. (1990). The efficacy of booster maintenance sessions in behavior therapy: Review and methodological critique. *Clinical Psychology Review, 10*(2), 155–170.
- Williams, L. A., Bohac, C., Hunter, S. & Cella, D. (2016). Patient and health care provider perceptions of cancer-related fatigue and pain. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer, 24*(10), 4357–4363. <https://doi.org/10.1007/s00520-016-3275-2>
- Woods, R. H. (2002). How much communication is enough in online courses?--exploring the relationship between frequency of instructor-initiated personal e-mail and learners' perceptions of and participation in online learning. *International Journal of Instructional Media, 29*(4), 377.
- Xunlin, N. G., Lau, Y. & Klainin-Yobas, P. (2020). The effectiveness of mindfulness-based interventions among cancer patients and survivors: a systematic review and meta-analysis. *Supportive Care in Cancer, 28*(4), 1563–1578. <https://doi.org/10.1007/s00520-019-05219-9>
- Zengin, L. & Aylaz, R. (2019). The effects of sleep hygiene education and reflexology on sleep quality and fatigue in patients receiving chemotherapy. *European journal of cancer care, 28*(3), e13020.
- Zetzl, T., Overbeck, L. & van Oorschot, B. (2020). „Gesagt ist nicht gehört, gehört ist nicht verstanden “–Therapiezieleinschätzung aus Sicht von PatientInnen in der Radiologie. *Der Onkologe, 26*(10), 951–956.

- 
- Zetzl, T., Renner, A., Pittig, A., Jentschke, E., Roch, C. & van Oorschot, B. (2020). Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. *Supportive Care in Cancer*. <https://doi.org/10.1007/s00520-020-05794-2>
- Zetzl, T., Schuler, M., Renner, A., Jentschke, E. & van Oorschot, B. (2019). Yoga intervention and reminder e-mails for reducing cancer-related fatigue - a study protocol of a randomized controlled trial. *BMC psychology*, 7(1), 64. <https://doi.org/10.1186/s40359-019-0339-3>
- Zhang, X., Kumar, V. & Cosguner, K. (2017). Dynamically managing a profitable e-mail marketing program. *Journal of marketing research*, 54(6), 851–866.

---

## 5. Appendix

### Figures

Figure A7 Scatterplots: Difference of Fatigue and Subscores between Pre and Post and Attended Classes

,092

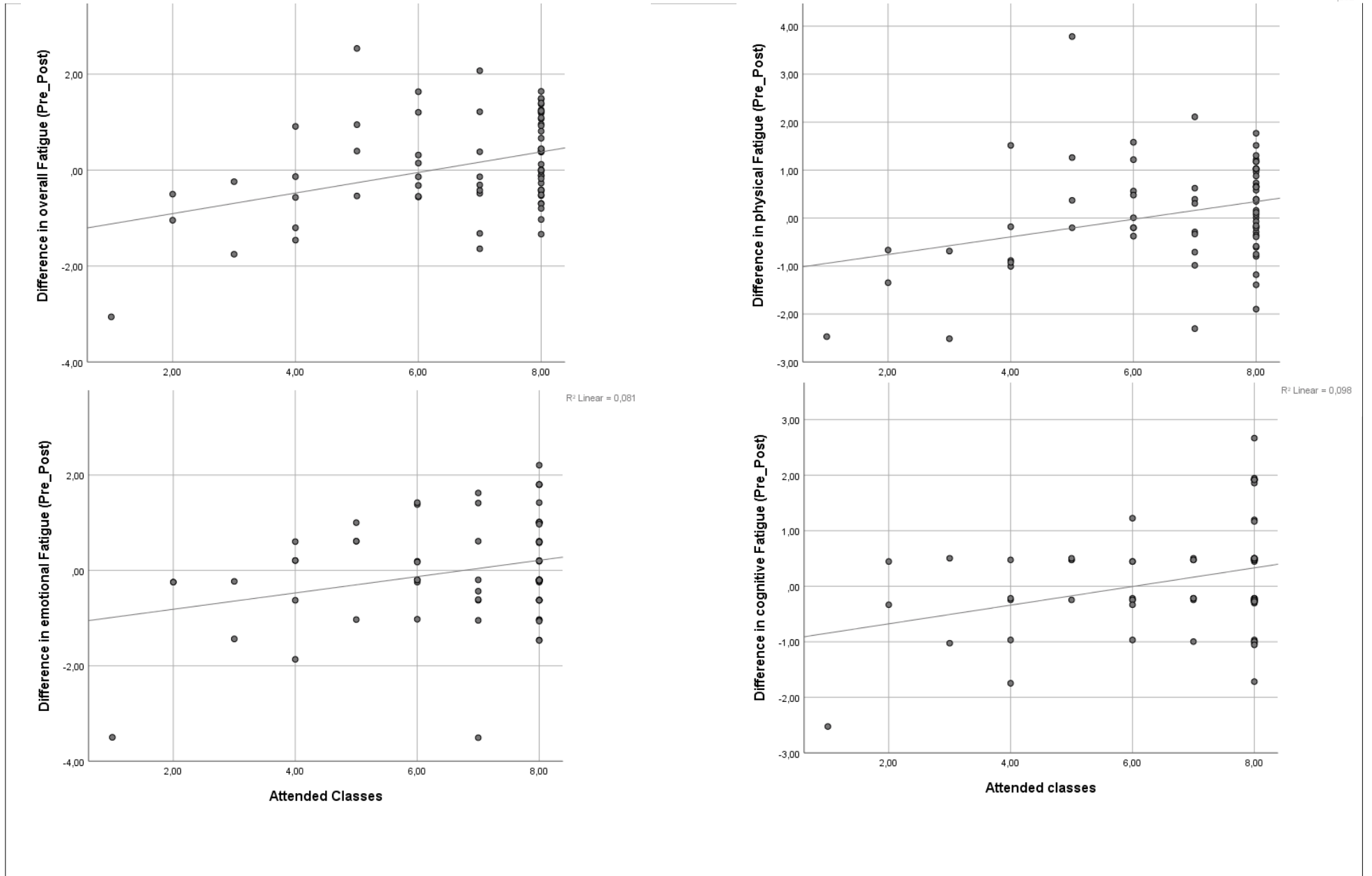


Figure A8 Scatterplots: Difference in Fatigue and Subscores between Post and Follow-Up and Practice frequency (min)

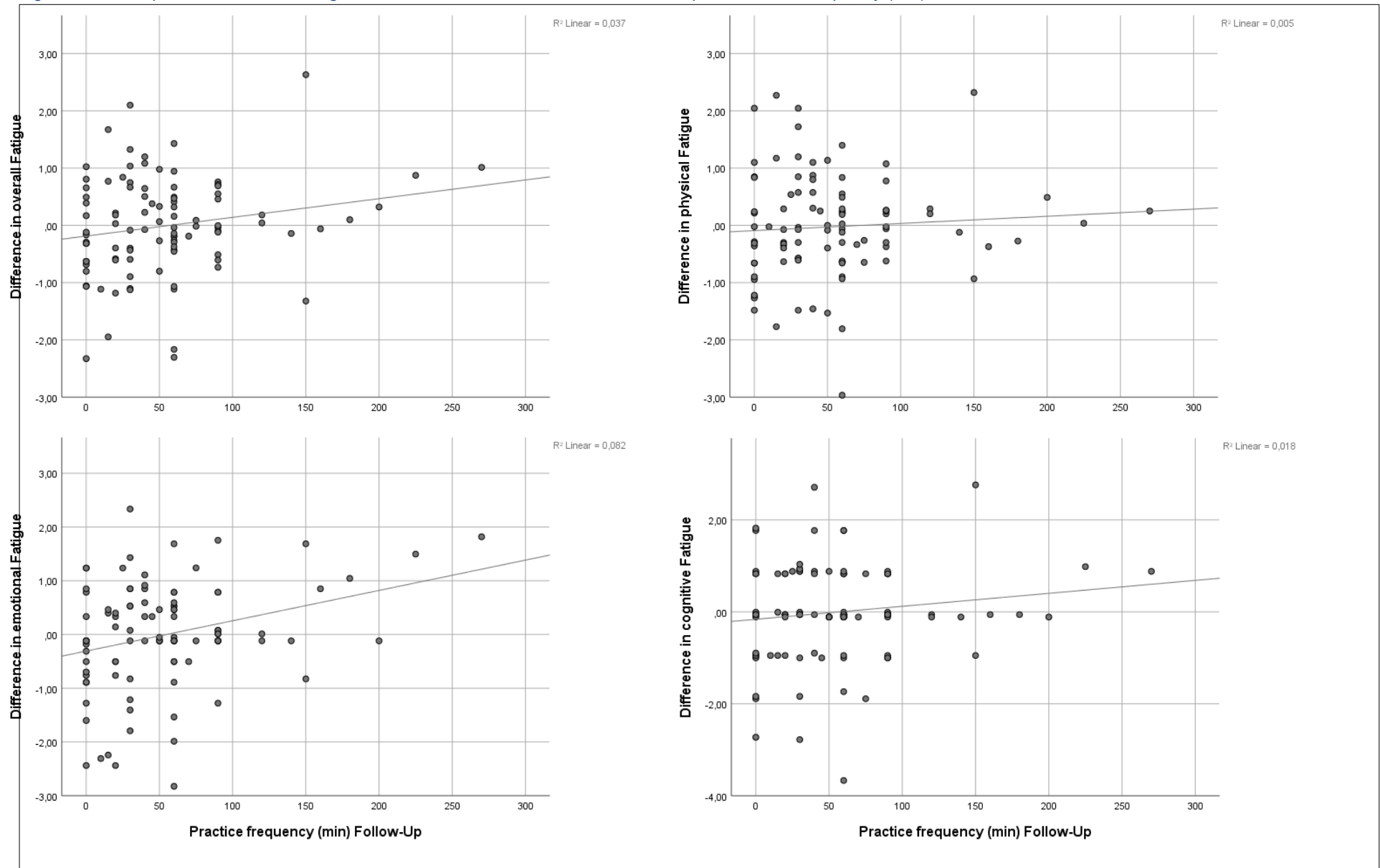
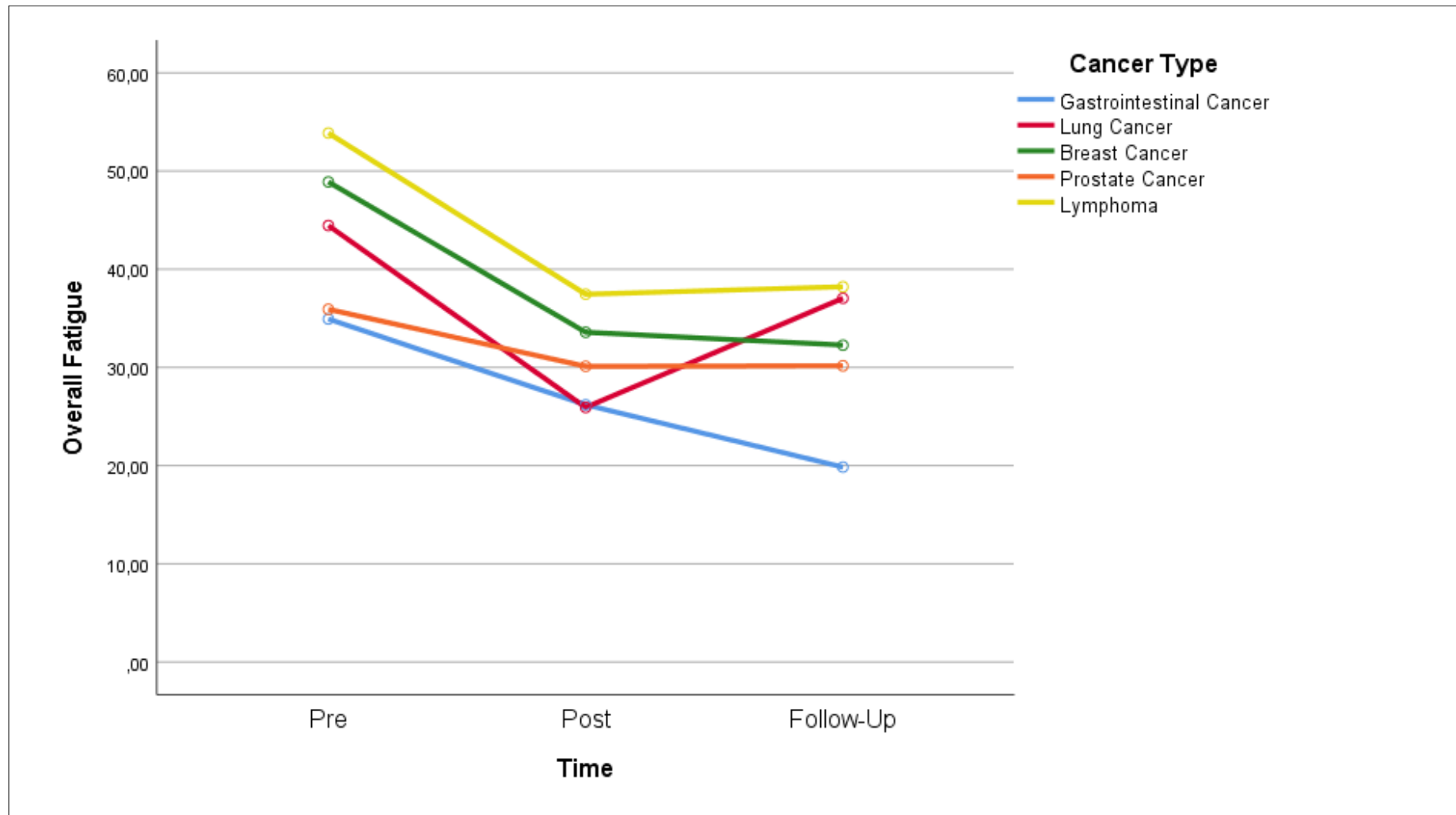


Figure A9 Descriptive analysis of mean fatigue in pre, post and follow up measurement for patients who participated in yoga therapy. Different colors indicate different types of cancer







---

**Tables**
*Table 8: Description of the eight limbed path (Patanyali)*

Practical yoga (Kriya Yoga)	
1. Yama	<u>dealing with the environment:</u> non-violence truthfulness righteousness chastity/wisdom or purity of thought, word and deed non-avarice/simplicity and moderation
2. Niyama	<u>dealing with oneself</u> purity contentment persistence self-study contemplation
3. Asana:	dealing with the body
4. Pranayama	dealing with breath and breathing techniques
5. Pratyahara	dealing with the senses, separation of the connection of the mind and the senses
Royal yoga (Raja Yoga)	
6. Dharana	concentration
7. Dhyana	meditation
8. Samadhi	the highest: inner freedom and state of bliss

---

### Statement of individual author contributions

Publication (complete reference): Zetzl, T., Schuler, M., Renner, A., Jentschke, E., van Oorschot, B. (2019). Yoga intervention and reminder e-mails for reducing cancer-related fatigue - a study protocol of a randomized controlled trial. <i>BMC Psychology</i> . 7. 10.1186/s40359-019-0339-3					
Participated in	Author Initials, Responsibility decreasing from left to right				
Study Design Methods	TZ	EJ	vBO	MS	AR
Development	TZ	EJ	vBO	MS	AR
Data collection	TZ	AR	EJ	vOB	MS
Manuscript Writing	TZ	AR	MS	vOB	EJ

T. Zetzl: Conceptualization, supervising study and data collection, writing original draft as well as writing review and editing

M. Schuler: conceptualization, funding acquisition, conducting study and statistical analysis plan, editing first draft

A. Renner: Editing first draft

E. Jentschke: conceptualization, supervision

B.v. Oorschot: supervision, funding acquisition, editing first draft

Publication (complete reference): Zetzl, T., Renner, A., Pittig, A., Jentschke E., Roch C., van Oorschot B. Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. <i>Support Care Cancer</i> (2020). <a href="https://doi.org/10.1007/s00520-020-05794-2">https://doi.org/10.1007/s00520-020-05794-2</a>					
Participated in	Author Initials, Responsibility decreasing from left to right				
Study Design Methods	TZ	AR	EJ	vBO	AP
Study Design Development	TZ	EJ	AR	vBO	AP
Data analysis and interpretation	TZ	AP	AR	vBO EJ	
Data collection	TZ	AR	EJ	vOB	AP
Manuscript Writing	TZ	AR	AP	vOB	EJ

T. Zetzl: conceptualization, supervising study and data collection, formal analysis, visualization, writing original draft as well as writing review and editing

A.Renner: participation in Data collection, data interpretation, editing first draft

A.Pittig: conducting statistical analysis plan, editing first draft

E. Jentschke: conceptualization, supervision

B.v. Oorschot: supervision, funding acquisition, editing first draft

Publication (complete reference): Zetzl, T., Pittig, A., Renner A., van Oorschot, B., Jentschke, E. (submitted). Yoga therapy to reduce fatigue in cancer: Effects of reminder e-mails and long-term efficacy. <i>Support Care Cancer</i>					
Participated in	Author Initials, Responsibility decreasing from left to right				
Study Design Methods	TZ	AR	EJ	vBO	AP
Study Design Development	TZ	EJ	AR	vBO	AP
Data analysis and interpretation	TZ	AP	AR	vBO EJ	
Data collection	TZ	AR	EJ	vOB	AP
Manuscript Writing	TZ	AR	AP	vOB	EJ

T.Zetzl: conceptualization, supervising study and data collection, formal analysis, visualization, writing original draft as well as writing review and editing

A.Pittig: conducting statistical analysis plan, editing first draft

A.Renner: participation in data collection, data interpretation, editing first draft

B.v. Oorschot: supervision, funding acquisition, editing first draft

E. Jentschke: conceptualization, supervision

The doctoral researcher confirms that she/he has obtained permission from both the publishers and the co-authors for legal second publication.

The doctoral researcher and the primary supervisor confirm the correctness of the above mentioned assessment.

---

**Eidesstattliche Erklärungen**Erklärungen gemäß §6 Promotionsordnung 2014 der Fakultäten für Humanwissenschaften

§ 6 Abs. 2 Nr. 5: Hiermit versichere ich an Eides statt,

- dass ich die Dissertation selbständig angefertigt und keine anderen als die von mir angegebenen Quellen und Hilfsmittel benutzt habe,
- dass ich die Gelegenheit zum Promotionsvorhaben nicht kommerziell vermittelt bekommen und keine Person oder Organisation eingeschaltet habe, die gegen Entgelt Betreuer bzw. Betreuerinnen für die Anfertigung von Dissertationen sucht.

§ 6 Abs. 2 Nr. 6: Hiermit erkläre ich, dass ich die Regeln der Universität Würzburg über gute wissenschaftliche Praxis eingehalten wurde.

§ 6 Abs. 2 Nr. 8: Die vorgelegte Dissertation wurde bisher bei keinem Prüfungsverfahren eingereicht; sie ist nicht identisch mit einer früher abgefassten wissenschaftlichen Arbeit, z. B. einer Magister-, Diplom-, Master, Bachelor- oder Zulassungsarbeit.

Die Dissertation basiert nicht auf bereits eingereichte veröffentlichte Artikel bzw. es handelt sich um keine publikationsbasierte Dissertation.\*

Publikationsbasierte Dissertation:

Sofern es sich um eine publikationsbasierte Dissertation handelt, sind die entsprechenden Kriterien der Fakultät für Humanwissenschaften zu berücksichtigen.\*

\* Zutreffendes bitte ankreuzen

---

Würzburg, den 17.12.2021

Teresa Zetzl