11th Aarhus Workshop in Breast Surgery

May 24-25, 2023

Generelle biopsykosociale senfølger efter kræft – relevante behandlinger

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DBCG DCCL
Danish Breast Cancer Group
Center & Clinic for Late Effects

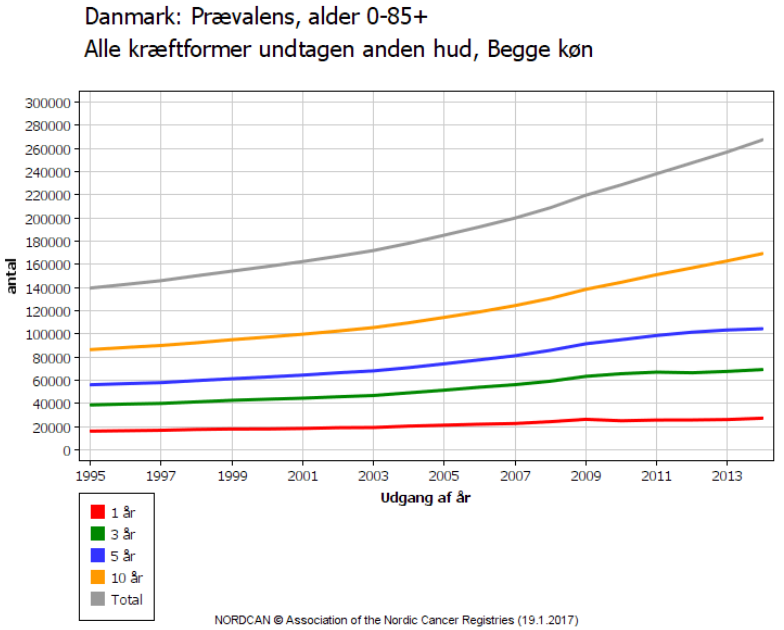
Dansk Center for Brystkræftsenfølger

Bedre Viden Om Senfølger

Danish Comprehensive Cancer Center

- Hver tredje dansker diagnosticeres med kræft
- Flere kræfttilfælde og forbedret behandling fører til, at stadig flere mennesker lever med kræft
- Danmark: 374.286 lever med kræftdiagnose

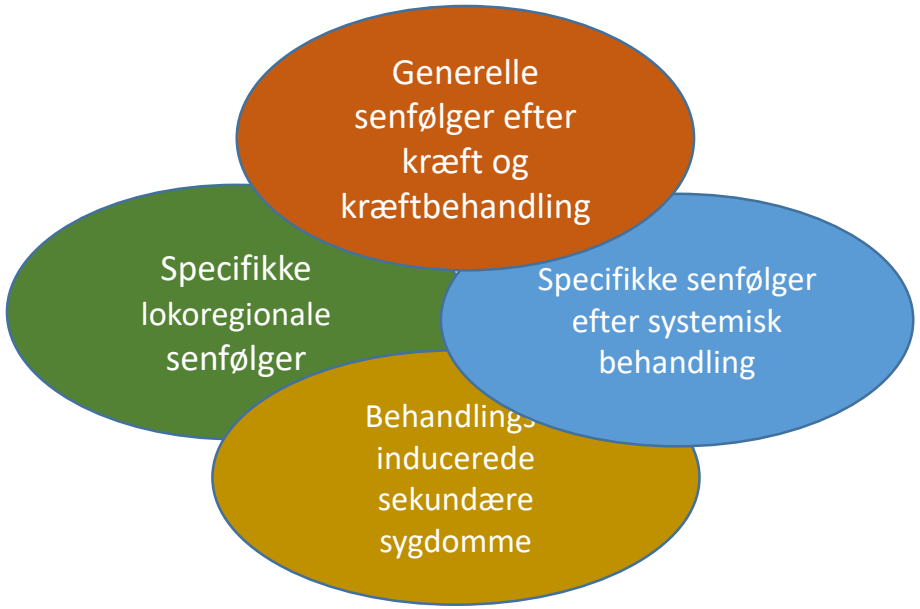
  (Nordic Cancer Registries, 2021)
- Ca. 50% vil opleve en eller flere senfølger efter kræftbehandling



- Forbedret behandling og overlevelse betyder, at kræftoverleveres **livskvalitet** bliver et stadigt vigtigere tema

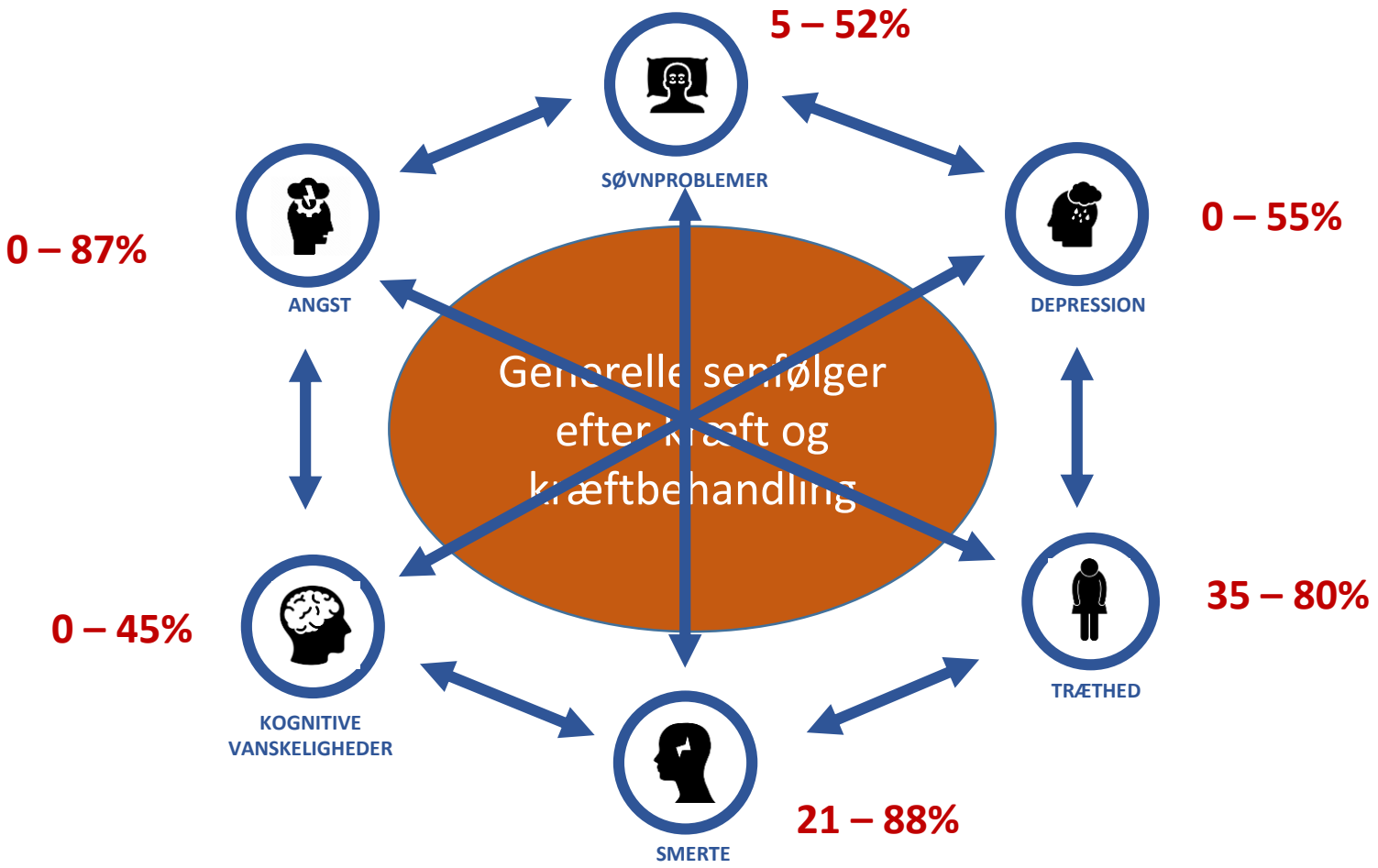
- Livskvalitet og helbred trues af fysiske og psykiske **senfølger** efter kræft og kræftbehandling

Fokus: de generelle, tværgående senfølger



- Generelle, tværgående senfølger:
  - De **hyppigst forekommende** senfølger
  - Senfølger og symptomer, som opstår på tværs af kræfttyper og deres behandling
    - **Depression**
    - **Frygt for tilbagefald**
    - **Søvnproblemer**
    - **Træthed (fatigue)**
    - **Smerter**
    - **Kognitive vanskeligheder**
  - De senfølger **som flest ønsker hjælp** til (unmet needs)
  - Der **savnes effektive medicinske** behandlinger

Generelle senfølger på tværs af kræfttype og behandling

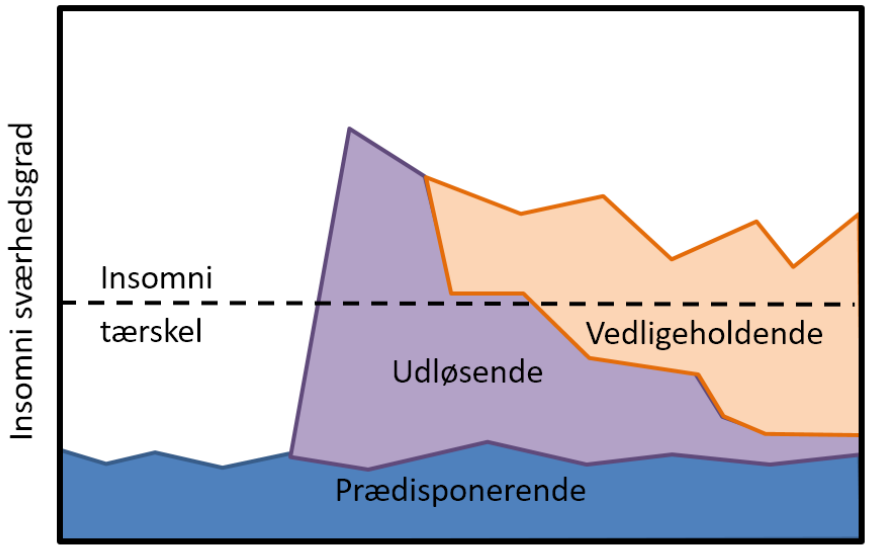


Optræder i klynger af symptomer der vedligeholder og forstærker hinanden!

Brandao et al. 2016; Horneber et al. 2012; Saligan et al. 2015; Otte et al. 2016; van den Beuken-van Everdingen et al. 2007; Simard et al. 2013; Zachariae & Mehlsen, 2011; Moore et al. 2014.

Principper i behandling af vedvarende symptomer

- Prædisponerende
- Udløsende
- Vedligeholdende



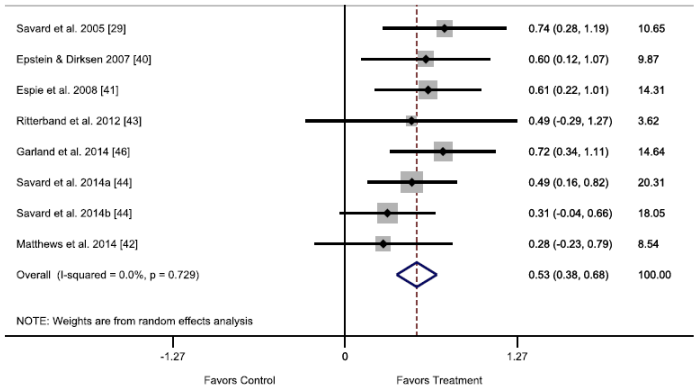
Efter Spielman et al. 1987

- Prædisponerende
  - Genetiske, fysiologiske, psykologiske, adfærd
- Udløsende
  - Kræftsygdom og behandling
- Vedligeholdende
  - Tanker
  - Emotioner
  - Adfærd

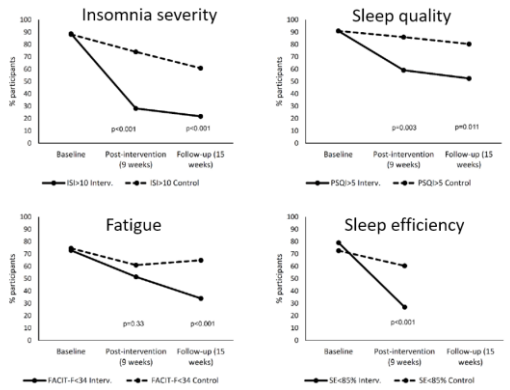
Behandling

Søvnproblemer

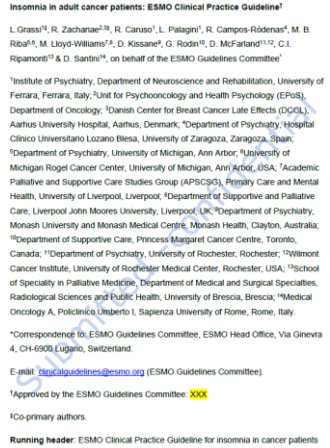
Vedligeholdende faktorer	Terapeutisk tilgang	Specifik komponent
Ændre søvnmønster	Kognitiv adfærdsterapi for insomni	Søvnrestriktion
Betinget arousal (seng, sovevær.)	Kognitiv adfærdsterapi for insomni	Stimulus-kontrol-terapi
Fysisk hyperarousal	Mind-body-terapi	Afspænding, geare ned
Inaktivitet, social isolation	Adfærdsaktivering/ACT	Værdiorienterede aktiviteter
Bekymring, rumination	Mindfulness-baseret terapi	Decentrering
Adfærd (f.eks. sover om dagen)	Søvnhygiejneundervisning	Adfærds- og livsstilsændringer



Johnson et al. 2016



Zachariae et al. 2016



Insomnia in adult cancer patients: ESMO Clinical Practice Guideline†

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†Approved by the ESMO Guidelines Committee: XXX

‡Co-primary authors.

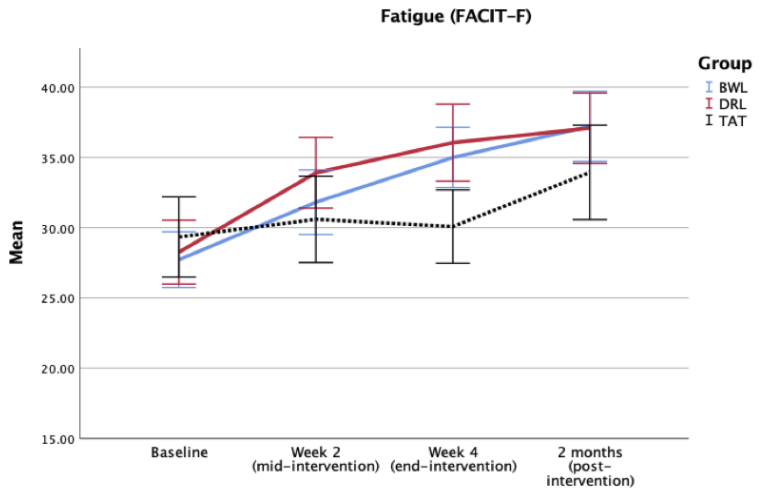
Running header: ESMO Clinical Practice Guideline for insomnia in cancer patients

- **American Academy of Sleep Medicine**: Kognitiv adfærdsterapi førstelinje-behandling for insomni
- **ESMO guidelines**: Kognitiv adfærdsterapi for insomni første-linjevalg til behandling af insomni blandt kræftpatienter og overlevere
- Fysisk aktivitet, melatonin er mulige valg, hvis KAT ikke er tilgængeligt

Træthed (fatigue)

Vedligeholdende faktorer	Terapeutisk tilgang	Specifikke komponenter
Søvnforstyrrelser	Kognitiv adfærdsterapi for insomni	(Se søvnproblemer)
Døgnrytmeforstyrrelse	Kronoterapi	Lysbehandling/aktivering
Adfærd (inaktivitet)	Fysisk aktivitet	Fysisk træning
Social isolation (inaktivitet)	Adfærdsaktivering/ACT	Værdiorienterede aktiviteter

Behandling	Antal studier	Effekt (SMD)	Sign.
EPO	14	0.52	*
Stimulanser (methylphenidate, modafinil)	9	0.16	n.s.
Kortikosteroider	3	0.43	n.s.
Fysisk træning	69	0.30	*
Psykologisk behandling	34	0.27	*
Fysisk + psykologisk	10	0.26	*
Farmakologisk	14	0.09	n.s.



De mest robuste effekter er fundet af **fysisk træning**, **psykologisk behandling** og **kombinationen** af de to

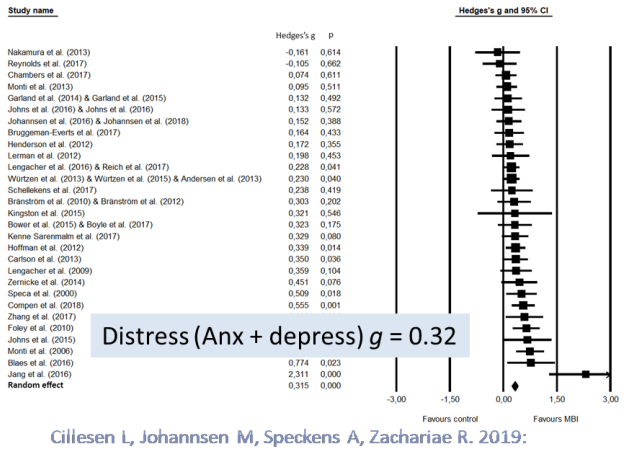
Tomlinson et al. 2018; Mustian et al. 2017; Ancoli-Israel et al. 2012; Redd et al. 2014; Amidi et al. (in preparation)

Depression

Vedligeholdende faktorer	Terapeutisk tilgang	Specifikke komponenter
Passivitet/tilbagetrækning	Adfærdsaktivering/ACT	Værdiorienterede aktiviteter
Rumination/opmærksomhed	MBT	Decentrering/opmærksomhedstræning

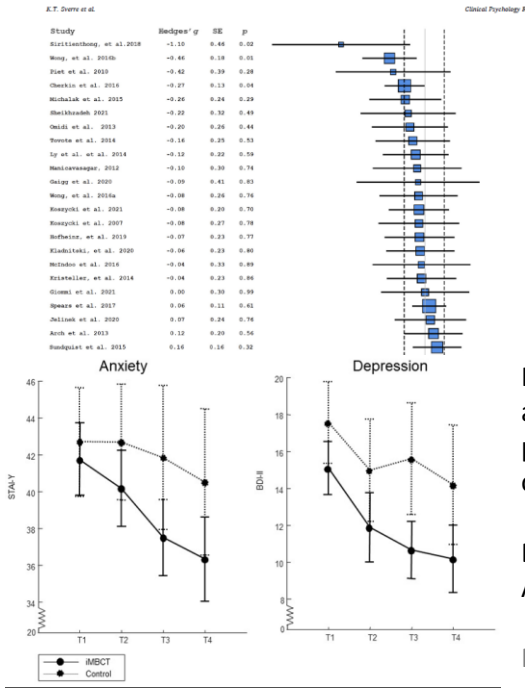
Psykologiske interventioner (Cohen's d)

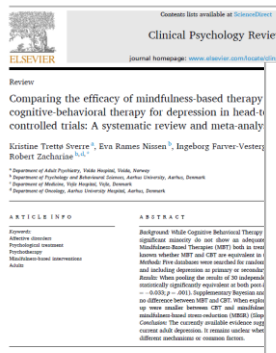
- Psykoterapier: 0.58 – 0.83 (**psykiatriske pt**)
- Mindfulness-baserede: 0.95 (**psykiatriske pt.**)
- Psykoterapier: 0.21 – 0.37 (**kræft**)
- Mindfulness-baserede: 0.32 (**kræft**)



Cillesen L, Johannsen M, Speckens A, Zachariae R. 2019:

Cuijpers et al. 2017; Hofmann et al. 2010; Piet et al. 2012; Sanjida et al. 2018; Cillesen et al. 2019

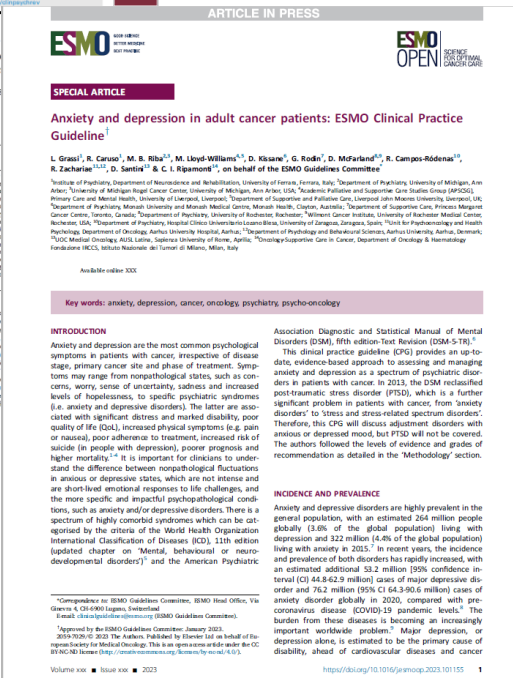




Internet-leveret MBCT for angst og depression blandt personer behandlet for bryst og prostatakræft:

Depression: Cohen's d = 0.42
Angst: Cohen's d = 0.45

Nissen et al. 2020

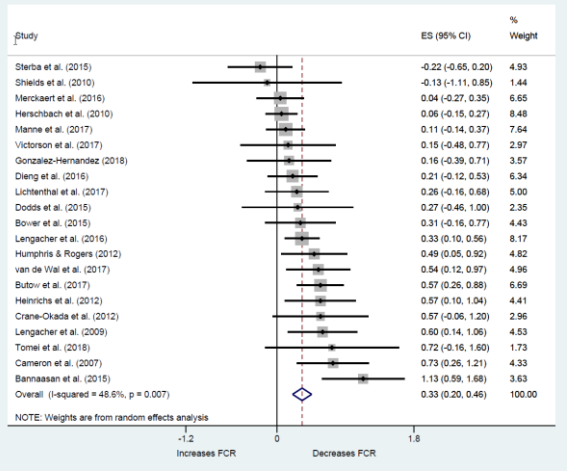


Frygt for tilbagefald

Vedligeholdende faktorer	Terapeutisk tilgang	Specifikke komponenter
Passivitet/tilbagetrækning	Adfærdsaktivering/ACT	Værdiorienterede aktiviteter
Rumination/opmærksomhed	MBT	Decentrering/opmærksomhedstræning

For 23 RCT-er af psykologiske behandlinger af frygt for tilbagefald er der fundet effekter såvel umiddelbart efter interventionen (Hedges's g = 0.33) og ved follow-up (g=0.30)

Effekten af nyere kognitive-adfærds-terapeutiske metoder (f.eks. ACT, Mindfulness-baserede) er større (g=0.42) end effekten af klassiske kognitive adfærdsterapier (g=0.24)



Effect of Psychological Intervention on Fear of Cancer Recurrence: A Systematic Review and Meta-Analysis

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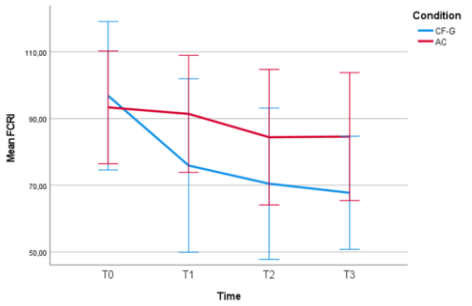
PURPOSE Fear of cancer recurrence (FCR) is a significantly distressing problem that affects a substantial number of patients with and survivors of cancer; however, the overall efficacy of available psychological interventions on FCR remains unknown. We therefore evaluated this in the present systematic review and meta-analysis.

METHODS We searched key electronic databases to identify trials that evaluated the effect of psychological interventions on FCR among patients with and survivors of cancer. Controlled trials were subjected to meta-analysis, and the moderating influence of study characteristics on the effect were examined. Overall quality of evidence was evaluated using the GRADE system. Open trials were narratively reviewed to explore ongoing developments in the field (PROSPERO registration no.: CRD42017076514).

RESULTS A total of 23 controlled trials (21 randomized controlled trials) and nine open trials were included. Small effects (Hedges's *g*) were found both at postintervention ($g = 0.33$; 95% CI, 0.20 to 0.46; $P < .001$) and at follow-up ($g = 0.28$; 95% CI, 0.17 to 0.40; $P < .001$). Effects at postintervention of contemporary cognitive behavioral therapies (CBTs; $g = 0.42$) were larger than those of traditional CBTs ($g = 0.24$; $\beta = .22$; 95% CI, .04 to .41; $P = .018$). At follow-up, larger effects were associated with shorter time to follow-up ($\beta = -.01$; 95% CI, −.01 to −.00; $P = .027$) and group-based formats ($\beta = .18$; 95% CI, .01 to .36; $P = .041$). A GRADE evaluation indicated evidence of moderate strength for effects of psychological intervention for FCR.

CONCLUSION Psychological interventions for FCR revealed a small but robust effect at postintervention, which was largely maintained at follow-up. Larger postintervention effects were found for contemporary CBTs that were focused on processes of cognition—for example, worry, rumination, and attentional bias—rather than the content, and aimed to change the way in which the individual relates to his or her inner experiences. Future trials could investigate how to further optimize and tailor interventions to individual patients' FCR presentation.

J Clin Oncol 37:2899-2915. © 2019 by American Society of Clinical Oncology



Tauber et al. 2021

Lovende effekter af en ny gruppe-baseret udgave af en targeteret behandling for frygt for tilbagefald (ConquerFear-Group).

ARTICLE IN PRESS

ESMO OPEN

SPECIAL ARTICLE

Anxiety and depression in adult cancer patients: ESMO Clinical Practice Guideline

L. Grassi, R. Caruso, M. B. Riba, M. Lloyd-Williams, D. Kissane, G. Rodin, D. McFarland, R. Campos-Ródenas, R. Zachariae, D. Santini & C. I. Ripamonti, on behalf of the ESMO Guidelines Committee

Key words: anxiety, depression, cancer, oncology, psychiatry, psycho-oncology

INTRODUCTION

Anxiety and depression are the most common psychological symptoms in patients with cancer, irrespective of disease stage, primary cancer site and phase of treatment. Symptoms may range from nonpathological states, such as concerns, worry, sense of uncertainty, sadness and increased levels of hopelessness, to specific psychiatric syndromes (i.e. anxiety and depressive disorders). The latter are associated with significant distress and marked disability, poor quality of life (QoL), increased physical symptoms (e.g. pain or nausea), poor adherence to treatment, increased risk of suicide (in people with depression), poorer prognosis and higher mortality.[1-4] It is important for clinicians to understand the difference between nonpathological fluctuations in anxious or depressive states, which are not intense and are short-lived emotional responses to life challenges, and the more specific and impactful psychopathological conditions, such as anxiety and/or depressive disorders. There is a spectrum of highly comorbid syndromes which can be categorised by the criteria of the World Health Organization International Classification of Diseases (ICD), 11th edition (updated chapter on 'Mental, behavioural or neurodevelopmental disorders')[5] and the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM), fifth edition-Text Revision (DSM-5-TR).[6]

This clinical practice guideline (CPG) provides an up-to-date, evidence-based approach to assessing and managing anxiety and depression as a spectrum of psychiatric disorders in patients with cancer. In 2013, the DSM reclassified post-traumatic stress disorder (PTSD), which is a further significant problem in patients with cancer, from 'anxiety disorders' to 'stress and stress-related spectrum disorders'. Therefore, this CPG will discuss adjustment disorders with anxious or depressed mood, but PTSD will not be covered. The authors followed the levels of evidence and grades of recommendation as detailed in the 'Methodology' section.

INCIDENCE AND PREVALENCE

Anxiety and depressive disorders are highly prevalent in the general population, with an estimated 264 million people globally (3.6% of the global population) living with depression and 322 million (4.4% of the global population) living with anxiety in 2015.[7] In recent years, the incidence and prevalence of both disorders has rapidly increased, with an estimated additional 53.2 million [95% confidence interval (CI) 44.8-62.9 million] cases of major depressive disorder and 76.2 million (95% CI 64.3-90.6 million) cases of anxiety disorder globally in 2020, compared with pre-coronavirus disease (COVID)-19 pandemic levels.[8] The burden from these diseases is becoming an increasingly important worldwide problem.[7] Major depression, or depression alone, is estimated to be the primary cause of disability, ahead of cardiovascular diseases and cancer

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†Approved by the ESMO Guidelines Committee: January 2023.

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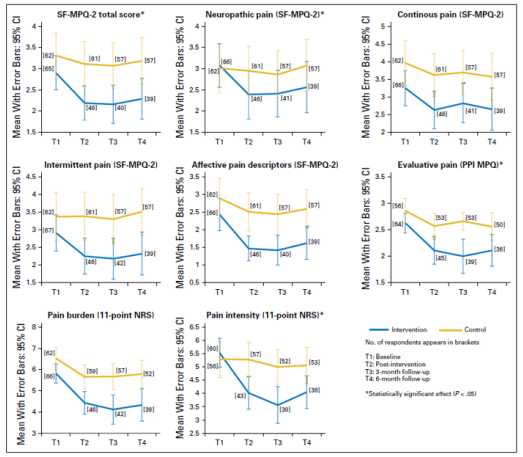
Smerter

Vedligeholdende faktorer	Terapeutisk tilgang	Specifikke komponent
Fear-avoidance modellen (catastrophizing, hypervigilance, avoidance)	MBT	Decentrering
	Adfærdsaktivering/ACT	Værdiorienterede aktiviteter
	Mind-body-terapi	Afspænding/visualisering

Klinisk relevante effekter på smerte blandt kvinder behandlet for brystkræft af **mindfulness-baseret kognitiv terapi.**
Behandlingen blev endvidere vist at være omkostnings-effektiv.

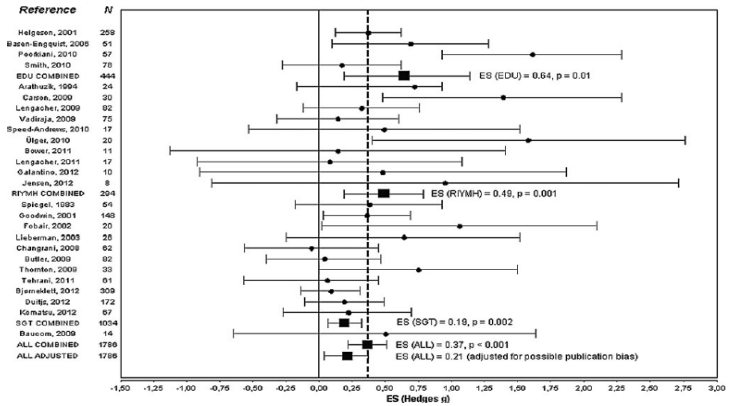


Johannsen et al. JCO, 2016

Farmakologiske behandlinger: blandede effekter. Afhænger af smertetype (f.eks. tricykliske antidepressiva ved neuropatiske smerter)

Fysiske og kirurgiske behandlinger ved specifikke, lokoregionale smerter, f.eks. Lymfødem.

Psykologiske behandlinger. Metaanalyse: Effekter af (kognitiv adfærdsterapi, hypnose, afspænding, mindfulness-baseret intervention, visualisering: Hedges's *g* = **0.37**



Hollen et al. 2015; Kwon et al. 2014; Sullivan et al. 2009; Johannsen et al., 2013, 2016, 2018

Kognitive vanskeligheder

Vedligeholdende faktorer	Terapeutisk tilgang	Specifik komponent
Selektiv opmærksomhed	Psykoedukation	Kortlægning af styrker/udfordringer
Kognitiv funktionsnedsættelse	Psykoedukation	Kompensatoriske strategier
	Træning	Kognitiv træning
Inaktivitet	Aktivering (fysisk, social)	Værdiorienterede aktiviteter
Søvnproblemer	Kognitiv adfærdsterapi for insomni	Søvnrestriktion m.m.

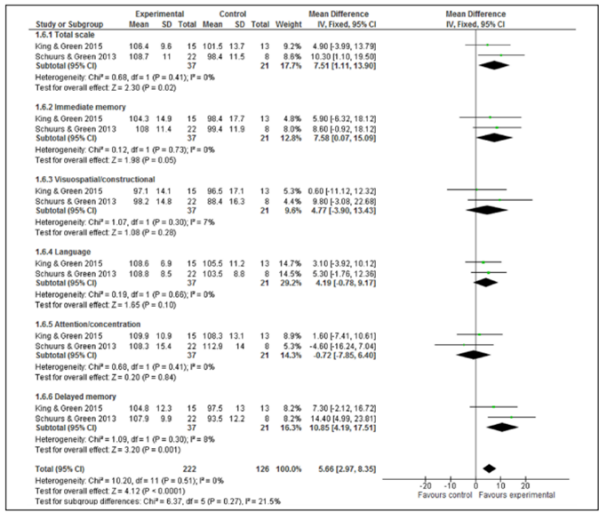
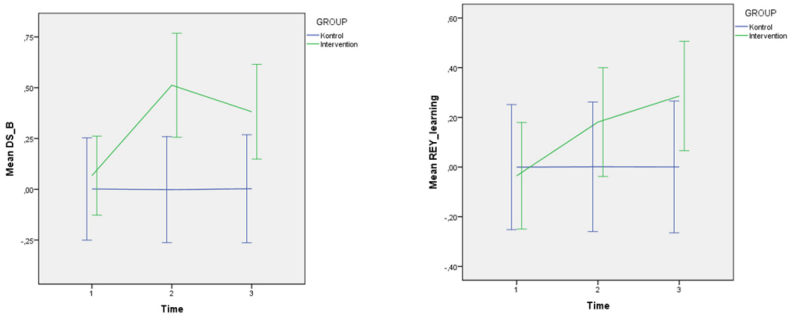


Figure 4. Repeatable Battery for Neuropsychological Status (RBANS) test at postintervention.

De primære behandlinger er kognitiv træning og kompensatoriske strategier. En metaanalyse af 11 studier har fundet effekter på hukommelse (d=**0.21**), generel kognitiv funktion (**0.41**). Andre metaanalyser har inkluderet få studier og er ikke specielt informative.

Oh et al. 2016; Zeng et al. 2016; Damholdt et al. 2016



En undersøgelse af et internet-leveret kognitivt træningsprogram med kvinder behandlet for brystkræft med kognitive problemer viste enkelte, men begrænsede effekter. Deltagerne var meget tilfredse.

MDT-konference: udredning og valg af behandling

- Deltagere
  - Screening: Søvnvanskeligheder, træthed, depression, frygt for tilbagefald, angst, kognitiv funktion, smerte, har du brug for hjælp? DCCL-PRO
  - Patienten selv, henvisende læge, psykologer med relevante specialer, som forestår eller superviserer den psykologiske behandling
- Varighed:
  - 15-45 min
- Formål
  - Identificere de mest belastende symptomer
  - Identificere de mest grundliggende problemstillinger (adfærd, kognition)
  - Identificere de mest centrale vedligeholdende mekanismer
  - Foreslå et *individuelt tilpasset* behandlingsforløb (6 sessioner)
  - Forklare behandlingens formål: her-og-nu fokuseret, at træne færdigheder
  - Undersøge patientens motivation – kræver indsats, kan patienten se sig selv i det?
  - Indhente patientens accept
- Effekter
  - Optimerer/effektiviserer behandlingen
  - Har afledte psykoedukative effekter for patienten
  - Bidrager til at etablere en fælles forståelsesramme for deltagende personalegrupper

- Vedvarende smerter efter kræftbehandling
- Kræftrelateret træthed
- Søvnproblemer efter kræft og kræftbehandling
- Kognitive forandringer efter kræft og kræftbehandling
- Psykologiske reaktioner blandt personer behandlet for kræft
- Seksualitet og fertilitet
- Mennesket efter kræftsygdom
- Arbejdslivet efter kræft
- Pårørende

Hvis man vide mere …

www.brystkræftsenfølger.dk