National Institute for Health and Care Excellence

Draft for consultation

Menopause

[A] Cognitive behavioural therapy

NICE guideline number tbc

Evidence review underpinning recommendations 1.4.4, 1.4.9, 1.4.16, 1.4.35, 1.4.36 and 1.4.37 in the NICE guideline

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This evidence review was developed by NICE

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Cognitive behavioural therapy

Review question

What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Introduction

Some women who experience symptoms associated with the menopause do not wish to take hormone therapy, or it may be contraindicated. The effectiveness of alternative options available to women who wish to manage their symptoms are currently not well known. This review will look at the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women, non-binary and trans people with symptoms associated with menopause.
Intervention	• Cognitive behavioural therapy

Comparison	• Treatment as usual
	  ○ Hormone replacement therapy
	  ○ Non-hormone replacement therapy
	• No treatment (including waiting list)
	• Attention control (sham cognitive behavioural therapy)

Outcome	**Critical**
	• Quality of life (any validated scale e.g., SF-36, all subscales)
	• Vasomotor symptoms:
	  ○ Frequency of vasomotor symptoms
	  ○ Severity of vasomotor symptoms
	  ○ Distress or bother caused by vasomotor symptoms
	• Difficulties with sleep (any)
	Important
	• Patient satisfaction
	• Discontinuation of treatment
	• Musculoskeletal symptoms
	• Altered sexual function
	• Psychological symptoms
	  ○ Anxiety
	  ○ Low mood (not clinical depression)
	  ○ Stress

SF-36: 36-item short form health survey

For further details see the review protocol in Appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document (Supplement 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

Fourteen randomised controlled trials (RCTs), reported across 17 publications, were included for this review (RCTs: Abdelazis 2021, Atema 2019, Ayers 2012, Cheng 2020, Drake 2019, Duijts 2012, Fenlon 2020, Green 2019, Green 2020, Hardy 2018, Hummel 2017, Kalmbach 2019, Keefer 2005, Mann 2012, McCurry 2016, Moradi Farsani 2021, Soori 2019).

The Kalmbach 2019 trial was also reported in Cheng 2020 and Drake 2019, the Green 2019 trial was also reported in Green 2020.

Five trials (7 publications) compared cognitive behavioural therapy (CBT) to treatment as usual (Cheng 2020, Drake 2019, Fenlon 2020, Kalmbach 2019, Mann 2012, McCurry 2016, Moradi Farsani 2021). Nine trials (10 publications) compared CBT to no treatment (or waiting list) (Abdelazis 2021, Atema 2019, Ayers 2012, Duijts 2012, Green 2019, Green 2020, Hardy 2018, Hummel 2017, Keefer 2005, Soori 2019).

The trials were from Iran, Saudi Arabia, the Netherlands, United Kingdom and United States.

The included studies are summarised in Table 2.

See the literature search strategy in Appendix B and study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in Appendix J.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Abdelaziz 2021 RCT Saudi Arabia	N=98 menopausal women, mean age (SD): 53.06 (4.28) years Experienced poor sleep quality and insomnia associated with menopause	CBT – internet based therapy targeting menopausal insomnia • Internet CBT • 6 weekly modules • Supported by researchers	No treatment • Concerns and needs were answered without intervention • Limited interaction between researchers and participants	• Difficulties with sleep (any) • Discontinuation of treatment
Atema 2019	N=254 women	CBT – internet based	No treatment	• Quality of life

Study	Population	Intervention	Comparison	Outcomes
RCT Netherlands	experiencing cancer treatment induced menopausal symptoms, mean age (SD): 47.4 (5.45) years Experienced cancer treatment induced problematic hot flushes and night sweats	<u>guided therapy targeting menopausal hot flushes and night sweats as well as other topics such as stress management and sleep problems</u> • Internet CBT • 6 weekly modules • Information presented by experts and breast cancer survivors with similar menopausal symptoms, and feedback provided by trained medical social workers and psychologists <u>CBT – internet based self-managed therapy targeting menopausal hot flushes and night sweats as well as other topics such as stress management and sleep problems</u> • Internet CBT • 6 weekly sessions • Information presented by experts and breast cancer survivors with similar menopausal symptoms	• Waiting list • No specific programs or clinical pathways for dealing with menopausal symptoms	• Vasomotor symptoms: frequency, severity, distress or bother • Difficulties with sleep (any) • Discontinuation of treatment • Altered sexual function • Psychological symptoms: anxiety
Ayers 2012 RCT UK	N=140 women experiencing menopausal symptoms, mean age (SD): 53.09 (5.4) years Experienced problematic hot flushes and night sweats	<u>CBT – group therapy targeting menopausal hot flushes and night sweats</u> • Group CBT • 4 weekly sessions (2 hours each) • Delivered by a clinical psychologist <u>CBT – Self-help targeting hot flushes and night sweats</u> • Self-help CBT	<u>No treatment</u> • Access to GP and other healthcare options	• Quality of life • Vasomotor symptoms: frequency, severity, distress or bother • Difficulties with sleep (any) • Discontinuation of treatment • Psychological symptoms: anxiety, low mood

Study	Population	Intervention	Comparison	Outcomes
		• Completed during a 4 week period • Two contacts with a clinical psychologist (introductory session and telephone call)		
Cheng 2020 (Secondary analysis of Kalmbach 2019) RCT US	N=100 postmenopausal women, mean age (SD): 56.44 (5.65) years Met DSM-5 criteria for insomnia disorder	<u>CBT – targeting menopausal insomnia</u> • Face to face individual CBT • 6 weekly sessions • Delivered by registered nurse specialised in behavioural sleep medicine	<u>Treatment as usual</u> Sleep education consisting of 6 weekly psychoeducation emails that include sleep hygiene	• Difficulties with sleep (any)
Drake 2019 (Secondary analysis of Kalmbach 2019) RCT US	N=100 postmenopausal women, mean age (SD): 56.44 (5.64) years Met DSM-5 criteria for insomnia disorder that onset or was exacerbated during the perimenopausal or postmenopausal period Unclear history of breast cancer	<u>CBT – targeting menopausal insomnia</u> • Face to face individual CBT • 6 weekly sessions • Delivered by registered nurse specialised in behavioural sleep medicine	<u>Treatment as usual</u> Sleep hygiene education consisting of 6 weekly psychoeducation emails that include sleep hygiene	• Difficulties with sleep (any)
Duijts 2012 RCT Netherlands	N=212 premenopausal women with breast cancer treatment induced menopausal symptoms, mean age (SD): 48.2 (5.6) years Experienced at least two of the following cancer treatment induced symptoms sometimes, or one symptom often: hot flushes, night sweats, and/or vaginal dryness	<u>CBT – Group therapy primarily targeting hot flushes and night sweats as well as other menopausal symptoms</u> • Group CBT • 6 weekly sessions (90 minutes each) • Delivered by clinical psychologist and clinical social workers	<u>No treatment</u> • Waiting list	• Quality of life • Vasomotor symptoms: distress or bother • Discontinuation of treatment • Altered sexual function

Study	Population	Intervention	Comparison	Outcomes
Fenlon 2020 RCT United Kingdom	N=130 women with primary breast cancer, mean age NR: mean age (SD) per group; CBT: 53.5 (9.78), TAU: 55.2 (10.19) Experienced treatment related hot flushes or night sweats	CBT – Group therapy targeting treatment induced hot flushes and night sweats • Face to face group CBT • 6 weekly sessions (90 minutes each) • Delivered by breast care nurse who was trained by a clinical psychologist	Treatment as usual • Standard NHS care at the site • Generally, women given advice about hot flushes and night sweats	• Vasomotor symptoms: frequency; distress or bother • Difficulties with sleep (any) • Psychological symptoms: anxiety
Green 2019 RCT US	N=72 perimenopausal or postmenopausal women, mean age (SD): 53.08 (4.02) years Experienced various menopausal symptoms and mild depressive symptoms	CBT – Group therapy targeting menopausal symptoms • Group CBT • 12 weekly sessions (2 hours each) • Delivered by clinical psychologist and graduate-level psychology trainee	No treatment • Waiting list	• Vasomotor symptoms: severity • Difficulties with sleep (any) • Discontinuation of treatment • Altered sexual function • Psychological symptoms: anxiety
Green 2020 (Secondary analysis from Green 2019) RCT US	N=36 perimenopausal or postmenopausal women, mean age (SD): 53.56 (4.14) years Experienced various menopausal symptoms and mild depressive symptoms	CBT – Group therapy targeting menopausal symptoms • Group CBT • 12 weekly sessions (2 hours each) • Delivered by clinical psychologist and graduate-level psychology trainee	No treatment • Waiting list	• Vasomotor symptoms: frequency, distress or bother
Hardy 2018 RCT UK	N=124 menopausal women, mean age (SD): 54.09 (3.4) years Experienced problematic hot flushes and night sweats	CBT – Self-help targeting menopausal hot flushes and night sweats • CBT Self-help booklet and CD • Completed over 4 weeks	No treatment • Waiting list • Access to their general practitioner and other health care options	• Quality of life • Vasomotor symptoms: frequency, distress or bother • Difficulties with sleep (any) • Discontinuation of treatment • Psychological symptoms: anxiety

Study	Population	Intervention	Comparison	Outcomes
Hummel 2017 RCT Netherlands	N=169 women pre or post menopause (>80% post-menopausal) with a history of breast cancer, mean age (SD): 51.1 (7.2) years Met DSM-4 criteria for sexual dysfunction	CBT – Internet therapy targeting sexual dysfunction • Internet CBT • 20 weekly sessions • Guided by personal psychologist or sexologist	No treatment • Waiting list • Booklet provided addressing sexuality issues after breast cancer treatment • Telephone call from psychologist or sexologist at 6 weeks to discuss questions arisen after reading the booklet	• Quality of life • Vasomotor symptoms: severity • Discontinuation of treatment • Altered sexual function • Psychological symptoms: anxiety
Kalmbach 2019 RCT US	N=100 postmenopausal women, mean age (SD): 56.44 (5.64) years Met DSM-5 criteria for insomnia disorder that onset or worsened during the perimenopausal or postmenopausal period	CBT – targeting menopausal insomnia • Face to face individual CBT • 6 weekly sessions • Delivered by nurse specialised in behavioural sleep medicine	Treatment as usual Sleep hygiene consisting of 6 weekly emails on sleep hygiene	• Quality of life • Vasomotor symptoms: frequency • Difficulties with sleep (any)
Keefer 2005 RCT US	N=19 menopausal and postmenopausal women who had never used hormone replacement therapy, mean age (SD): 51.0 (4.7) years Experienced various menopausal symptoms	CBT – Group therapy targeting menopausal hot flushes • Group CBT • 8 weekly sessions (90 minutes each) • Delivered by a doctoral candidate in clinical psychology	No treatment • Waiting list • Symptom monitoring only	• Vasomotor symptoms: frequency, distress or bother
Mann 2012 RCT United Kingdom	N=96 women, with treatment related menopause symptoms, mean age NR: mean age (SD) per group; CBT: 53.16 (8.10), TAU: 54.05 (7.76)	CBT – Group therapy targeting menopausal hot flushes and night sweats • Face to face group CBT • 6 weekly sessions	Treatment as usual Women followed up by an oncologist or clinical nurse specialist every 6 months	• Quality of life • Vasomotor symptoms: frequency; distress or bother • Difficulties with sleep (any)

Study	Population	Intervention	Comparison	Outcomes
	Experienced problematic hot flush or night sweats	(90 minutes each) • Delivered by a clinical psychologist		• Psychological symptoms: anxiety; low mood
McCurry 2016 RCT US	N=106 perimenopausal and menopausal women, mean age (SD): 54.8 (4.2) years Experienced significant insomnia symptoms and hot flushes	CBT – Telephone based therapy targeting menopausal insomnia • 6 telephone sessions over 8 weeks (20 to 30 minutes each) • First session in person • Individual CBT • Delivered by a social worker and psychologist	Treatment as usual Menopause education. 6 telephone sessions, first session in person	• Vasomotor symptoms: distress or bother • Difficulties with sleep (any)
Moradi Farsani 2021 RCT Iran	N=46 menopausal and postmenopausal women, mean age NR: mean age (SD) per group; CBT: 51.41 (3.00), TAU: 52.35 (3.48) Met DSM-5 or ICSD criteria for insomnia disorder	CBT – Group therapy targeting menopausal insomnia • Face to face group CBT • 6 weekly sessions (60 minutes each) • Delivered by researcher trained in CBT – insomnia	Treatment as usual General information on sleep hygiene and controlling menopause. Some received herbal medicine	• Difficulties with sleep (any)
Soori 2019 RCT Iran	N=90 women with normal menopause, mean age (SD): 53.0 (2.76) years Experienced various menopausal symptoms	CBT – Group therapy targeting menopausal symptoms • Group CBT • 6 weekly sessions (30 minutes each) • Unclear who delivered the intervention	No treatment • One session of educational counselling after the assessments were done	• Vasomotor symptoms: severity • Discontinuation of treatment • Altered sexual function • Psychological symptoms: anxiety

Note, The spelling 'hot flush' is used throughout this table for consistency with current UK convention. This may differ to the evidence tables where the terminology of the study is used.
Abbreviations: CBT: Cognitive Behavioural Therapy; CD: compact disc; DSM-4: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; GP: general practitioner; ICSD: International Classification of Sleep Disorders; NHS: national health service; RCT: randomised controlled trial; TAU: treatment as usual; UK: United Kingdom; US: United States of America.

See the full evidence tables in Appendix D and the forest plots in Appendix E.

Summary of the evidence

Comparison 1: Cognitive Behavioural Therapy (CBT) versus treatment as usual (TAU)

There was no evidence for the primary outcome severity of vasomotor symptoms, and the secondary outcomes patient satisfaction, discontinuation of treatment, musculoskeletal symptoms, altered sexual function and psychological symptoms: stress.

Personal history of breast cancer

Most of the evidence showed no important difference between CBT and TAU for the outcome quality of life. However low quality evidence from 1 study suggested an important benefit in quality of life (measured with the SF-36 vitality subscale) with CBT in people with no personal history of breast cancer, and low quality evidence from 1 study suggested an important benefit in quality of life (measured with the SF-36 social functioning subscale) with CBT in people with a personal history of breast cancer.

The evidence showed no important differences between CBT and TAU in the frequency of vasomotor symptoms with the exception of very low quality evidence from 1 study showing an important benefit for CBT in the distress or bother caused by vasomotor symptoms in people with a personal history of breast cancer.

There was an important benefit for CBT compared to TAU in difficulties with sleep for both people with and without a personal history of breast cancer as shown by very low quality evidence from 3 studies (endpoint) and 2 studies (follow-up) respectively. Low quality evidence from 1 study also showed an important benefit of for CBT compared to TAU in psychological symptoms: low mood for people with a personal history of breast cancer, but evidence showed no important difference in psychological symptoms: anxiety.

Group or individual CBT

Most of the evidence showed no important difference for either group or individual CBT, compared to TAU for the outcome quality of life. However, there was low quality evidence from 2 studies which showed an important benefit in quality of life. One study showed a benefit with group CBT (measured with the SF-36 subscale social functioning) and 1 study showed a benefit with individual CBT (measured with the SF-36 subscale vitality). There was moderate quality evidence from 1 study which showed an important benefit in difficulties with sleep with group CBT, and very low quality evidence from 2 studies which showed an important benefit in difficulties with sleep with individual CBT compared to TAU at endpoint. While at 6 months follow-up there was very low quality evidence from 2 studies which showed an important benefit in difficulties with sleep with group CBT, and moderate quality evidence from 1 study which showed an important benefit in difficulties with sleep with individual CBT compared to TAU.

Evidence showed no important difference in the frequency of vasomotor symptoms with either group or individual CBT with the exception of very low quality evidence from 1 study demonstrating an important benefit in the distress or bother caused by vasomotor symptoms with Group CBT, compared to TAU.

Group and individual CBT were not compared separately to TAU (with stratification) for any reported important outcomes (psychological symptoms: anxiety and low mood).

Face-to-face or online CBT and duration of CBT (number of sessions: <6 sessions versus ≥ 6 sessions)

All the evidence comparing CBT to TAU was face-to-face with a duration of ≥ 6 sessions.

Comparison 2: Cognitive Behavioural Therapy (CBT) versus no treatment

There was no evidence for the secondary outcomes of patient satisfaction, musculoskeletal symptoms, and psychological symptoms: stress.

Personal history of breast cancer

Most of the evidence showed no important difference in the outcome quality of life with CBT compared to no treatment in people with or without a personal history of breast cancer. However low quality evidence from 1 study suggested an important benefit in quality of life (measured with the SF-36 subscales, physical functioning, bodily pain, and mental health) in people with no personal history of breast cancer who underwent CBT compared to no treatment.

Very low quality evidence from 1 study suggested a reduction in the frequency of vasomotor symptoms (night sweats) in people with a personal history of breast cancer who underwent CBT compared to no treatment. However, an important benefit showing a reduction in the severity as well as distress or bother caused by vasomotor symptoms was also seen in very low quality and moderate quality evidence respectively from 2 studies in people with no personal history of breast cancer who underwent CBT compared to no treatment.

Low quality evidence from up 4 studies showed an important benefit in the outcome difficulties with sleep in people with no personal history of breast cancer who underwent CBT, and very low quality evidence from 2 studies showed an important benefit in the outcome altered sexual function in people with no personal history of breast cancer who underwent CBT, compared to no treatment. However, very low quality evidence from 8 studies showed an increase in discontinuation in both people with and without a personal history of breast cancer who underwent CBT, compared to no treatment. There was no important difference in the psychological symptom anxiety with CBT compared to no treatment in people with and with no personal history of breast cancer.

Group or individual CBT

The evidence showed no important differences in quality of life and the distress or bother caused by vasomotor symptoms with group or individual CBT, compared to no treatment. Low quality evidence from 1 study showed a reduction in the frequency of vasomotor symptoms with group CBT and very low quality evidence from 2 studies showed a reduction in the severity of vasomotor symptoms with group CBT compared to no treatment. In comparison, very low quality evidence from 4 studies showed a reduction in difficulties with sleep with individual CBT compared to no treatment. Group and individual CBT were not compared separately to no treatment (with stratification) for any reported important outcomes (patient satisfaction, discontinuation of treatment, musculoskeletal symptoms, altered sexual function, and the psychological symptoms anxiety, low mood, and stress).

Face-to-face or online CBT

Most of the evidence for quality of life showed no important differences in either face-to-face or online CBT with the exception of a single low quality study showing benefit for face-to-face CBT (measured with the SF-36 mental health subscale) when compared to no treatment. Very low and moderate quality evidence from 2 studies also showed a reduction in the severity and distress or bother caused by vasomotor symptoms with face-to-face CBT, respectively, when compared to no treatment. In comparison, very low quality evidence from 1 study showed a reduction in the frequency of vasomotor symptoms (night sweats) with online CBT, compared to no treatment. Both face-to-face and online CBT showed a reduction in difficulties with sleep, from very low quality evidence from 2 and 3 studies respectively, compared to no treatment. Face-to-face and online CBT were not compared separately to no treatment with stratification) for any reported important outcomes (patient

satisfaction, discontinuation of treatment, musculoskeletal symptoms, altered sexual function, and the psychological symptoms anxiety, low mood, and stress).

Self-help or guided CBT

The evidence showed no important differences in quality of life with self-help or guided CBT, compared to no treatment. Very low and moderate quality evidence from 2 studies showed a reduction in the frequency, severity and distress or bother caused by vasomotor symptoms with guided CBT, and very low quality evidence from 4 studies showed a reduction in difficulties with sleep with guided CBT, compared to no treatment. Very low quality evidence from 1 study also showed a reduction in the severity of vasomotor symptoms with self-help CBT compared to no treatment. Self-help and guided CBT were not compared separately to no treatment for any reported important outcomes (patient satisfaction, discontinuation of treatment, musculoskeletal symptoms, altered sexual function, and the psychological symptoms anxiety, low mood, and stress).

Duration of CBT (number of sessions: <6 sessions versus ≥ 6 sessions)

Most of the evidence showed reduction in the frequency, severity and distress or bother caused by vasomotor symptoms and difficulties with sleep with CBT with a duration of ≥ 6 sessions. The evidence was considered very low to moderate quality and was derived from 1 to 3 studies. However, for quality of life the evidence showed an important benefit for CBT with a duration of <6 sessions (measured with the SF-36 subscales physical functioning, bodily pain and mental health). The duration of CBT was not compared to no treatment for any reported important outcomes (patient satisfaction, discontinuation of treatment, musculoskeletal symptoms, altered sexual function, and the psychological symptoms anxiety, low mood, and stress).

See the evidence profiles in Appendix D.

Economic evidence

Included studies

Two economic studies were identified which were relevant to this question (Verbeek 2019, Mewes 2015). Both studies compared a form of CBT to waiting list control in women with 254 breast cancer survivors with treatment induced menopausal symptoms.

A single economic search was undertaken for all topics included in the scope of this guideline. See Supplement 2 for details.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided in Supplement 2.

Summary of included economic evidence

Table 3: Economic evidence profile for cognitive behavioural therapy versus waiting list control in people with a previous diagnosis of breast cancer

Study	Limitations	Applicability	Other comments	Incremental Costs[3]	Incremental QALYs	Incremental Cost per QALY[3]	Uncertainty
Verbeek 2019 (Netherlands) **1**) Guided internet based cognitive behavioural therapy (iCBT) **2**) Self-managed iCBT Vs **3**) Waiting list control (WLC)	Minor limitations[1]	Partially applicable[2]	Largely based on Atema 2019 discussed in the accompanying clinical evidence review. 5-year time horizon increased to 7 years during sensitivity analysis.	**1 vs 3** €322 (£284) **1 vs 2** €198 (£175) **2 vs 3** €124 (£109)	**1 vs 3** 0.0138 **1 vs 2** 0.0028 **2 vs 3** 0.0110	**1 vs 3** €23,331 (£20,530) **1 vs 2** €70,714 (£62,229) **2 vs 3** €11,278 (£10,329)	Self-managed iCBT (2) has a 68.9% probability of being the preferred option at a threshold of €30k per additional QALY.
Mewes 2015 (Netherlands) Group cognitive behavioural therapy (CBT) Vs Waiting list control (WLC)	Minor limitations[1]	Partially applicable[2]	Largely based on Duijt 2012 discussed in the accompanying clinical evidence review. Study also considered physical exercise which is outside the scope of this review question and has been excluded from this summary 5-year time horizon	€184 (£162)	0.0079	€22,502 (£19,817)	CBT has a 49% probability of being cost effective compared to WLC and PE at a threshold of €30k per additional QALY. Not reported excluding PE

CBT: Cognitive Behavioural Therapy; iCBT: Internet Based Cognitive Behavioural Therapy; QALY: Quality Adjusted Life Year; Vs: Versus; WLC: Waiting List Control

[1] Based on randomised controlled trial evidence, includes all relevant costs, time-horizon sufficient to capture all important differences.

[2] The models took a Dutch Health Care payer perspective and discounted costs and QALYs at 4% and 1.5% per annum respectively

[3] *Costs converted to UK sterling using CCEMG - EPPI-Centre Cost Converter tool available at CCEMG - EPPI-Centre Cost Converter v.1.4 (ioe.ac.uk) using International Monetary Fund Purchasing Power Parity values for 2023 €1=£0.88*

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Economic evidence statements

Verbeek 2019 and Mewes 2015 were cost utility analyses which reported outcomes in terms of cost per QALY gained in a population of breast cancer survivors with treatment related symptoms of the menopause. Verbeek compared both guided internet-based CBT and self-led CBT and Mewes compared group based CBT compared to waiting list control (WLC). Both studies took a Dutch healthcare payer perspective.

Both studies found CBT to be cost effective compared to WLC when a €30,000 per QALY gained threshold was assumed. Verbeek 2019 found self-led internet-based CBT to be the preferred option to more costly guided internet-based CBT even though guided was associated with a very small extra gain in QALYs. The conclusions of both studies were robust to sensitivity analysis.

Both previous studies were deemed to be partially applicable to the decision problem with minor methodological limitations.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Vasomotor symptoms and difficulties with sleep associated with menopause were prioritised as critical outcomes by the committee as they can negatively affect quality of life. The committee discussed how it is important to consider how frequent, bothersome and severe the vasomotor symptoms are since people prioritise each of these outcomes and their impact differently. Quality of life was considered a critical outcome to measure the overall impact CBT may have on people's lives. The committee also chose patient satisfaction and discontinuation of treatment as important outcomes to determine how women viewed the suitability of the intervention. The committee selected musculoskeletal symptoms, altered sexual function and psychological symptoms as important outcomes as they are common in women of menopausal age but recognised that it is uncertain whether they are due to menopause.

The quality of the evidence

The quality of the evidence was rated from very low to moderate, with most of the evidence of very low and low quality.

Most of the evidence was downgraded for imprecision around the effect estimate. There were also concerns about bias for some of the evidence mainly due to lack of blinding in the studies, although blinding is difficult to achieve with psychological treatments. Some of the evidence was also downgraded for inconsistency due to high heterogeneity which was not resolved by subgroup analysis. There was no publication bias detected in the evidence.

For comparison 1, (CBT versus TAU), there were also concerns around indirectness for some outcomes that did not directly measure difficulties with sleep, but rather sleepiness which may or may not be because of sleep difficulties.

For comparison 2, (CBT versus no treatment), the stratified analysis for most of the primary outcomes were either single or two-study analyses, and most of the evidence was

considered low or very low quality. The evidence included pilot studies and secondary analyses of studies which lowered confidence in the findings.

Benefits and harms

The committee discussed the evidence on cognitive behavioural therapy (CBT) compared to treatment as usual and no treatment. They noted that CBT showed an important benefit for some of the symptoms associated with the menopause, although there was variation where not all the evidence showed a benefit in outcomes.

Quality of life

The committee discussed the evidence on quality of life (measured with the 36-item short form survey: SF-36) and highlighted that whilst there was evidence to suggest an important benefit for CBT, this was only seen in the social functioning, physical functioning, bodily pain, vitality, and mental health subscales when the evidence was stratified according to personal history of breast cancer, and type and duration of CBT. The committee concluded that there was too much uncertainty in the evidence to make a recommendation for CBT based on quality of life outcomes. However, they also noted that as CBT can effectively treat other symptoms it may also indirectly positively affect quality of life.

Vasomotor symptoms

The committee discussed the evidence on vasomotor symptoms (VMS) and noted that CBT appeared beneficial in reducing the frequency, severity and distress or bother caused by symptoms. They highlighted that not all the evidence on VMS showed a benefit for CBT and this variation depended on the type of outcome measurement used. However, the committee agreed that the hot flush rating scale (HFRS) and hot flash related daily interference scale (HFRDIS) were valid and reliable measures and both showed an important benefit for CBT in reducing the frequency and distress or bother caused by VMS. The committee also discussed the variation in clinically important differences for VMS depending on which statistical measurement (minimally important difference) was used. They agreed this reflected the variation amongst women in how they experienced VMS. The committee agreed that there was sufficient evidence to support the use of CBT in reducing vasomotor symptoms associated with menopause. However, given that there was variability in the evidence as to whether CBT was beneficial, and the strength of the evidence ranged from moderate to very low quality, they agreed that CBT should not be offered routinely, but rather considered as a treatment option for troublesome VSM associated with the menopause.

Difficulties with sleep

The committee discussed the evidence on difficulties with sleep and noted that most of the evidence showed a benefit for CBT. The evidence was variable depending on the type of outcome measurement used and the committee agreed that it was difficult to clearly define difficulties with sleep. The committee discussed that despite showing a clear benefit on various aspects of sleep using validated measures, the evidence for CBT was mainly low to very low quality. Therefore, the committee agreed that a strong recommendation offering CBT was not supported by the evidence, but CBT should be considered as a treatment option for people with menopause experiencing difficulties with sleep.

Psychological symptoms

The committee discussed the evidence on the psychological symptoms low mood and anxiety. There was an improvement in the depressed mood subscale of the Women's Health Questionnaire (WHQ) in people receiving CBT compared to treatment as usual although the evidence was low quality. However, the evidence showed no important difference in the

depressed mood subscale of the WHQ in people receiving CBT when compared to no treatment. The committee included a reference to the NICE guidance for depression in adults in this section of the guideline to ensure that people with depression receive the diagnosis and clinical care needed and agreed that CBT should be considered as a treatment option as it may have a benefit in terms of improving low mood (or depressive symptoms) with people experiencing these symptoms associated with the menopause as supported by the evidence. Since the evidence did not show any important difference between CBT and treatment as usual or no treatment, on the psychological symptom anxiety, the committee did not make a recommendation on this.

Personal history of breast cancer

The committee considered whether a history of breast cancer would have an impact on the treatment effects of CBT. Since the evidence showed a benefit for CBT in both people with and without a history of breast cancer, the committee agreed that specific recommendations based on a person's history of breast cancer cannot be made from the evidence base.

Number of sessions

The committee discussed the evidence by duration of sessions and noted that when CBT was compared to treatment as usual or no treatment, the duration was 6 or more sessions for all or most of the evidence respectively. Subsequently the committee agreed there was not enough available evidence to draw conclusions on how effective CBT was if it lasted less than 6 sessions and therefore did not specify the most appropriate or effective length of CBT in the recommendation.

Mode of delivery

The committee discussed how the evidence on CBT varied between face-to-face, online, guided and self-help, and whether it was delivered in groups or as individual therapy and noted that it was difficult to determine whether a particular mode of CBT delivery was more beneficial than the other. The evidence suggested a benefit for most CBT delivery methods for VMS (frequency, severity and distress or bother caused by VMS) and difficulties with sleep. The committee agreed that the various available options should be discussed with the person when considering CBT as a treatment option for symptoms associated with menopause.

CBT for trans-men and non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past

This discussed that no evidence related to trans-men or non-binary people registered female at birth. However, given that CBT is not a risky intervention, they agreed that their recommendation in favour of CBT for vasomotor, difficulties with sleep and depressive symptoms associated with the menopause should extend to trans-men and non-binary people registered female at birth, irrespective of whether or not they have taken gender-affirming hormone therapy in the past. The committee recognised the need for an equitable approach to ensure access to CBT services for managing menopause symptoms. In light of this, the committee decided to advocate for a specific recommendation for trans-men and non-binary people registered female at birth regardless of whether or not they have previously taken gender-affirming hormone therapy. They agreed that this would promote equality in access to CBT services for managing menopausal symptoms within this particular group, acknowledging their unique experiences and needs. By making this a separate recommendation, the committee aimed to enhance inclusivity and ensure that individuals within this group receive targeted support, aligning with the principle of providing equitable healthcare tailored to diverse gender identities.

Cost effectiveness and resource use

Two economic evaluations were identified for this review question. Both studies found CBT, in the 3 forms considered (guided internet-based CBT, self-led internet-based CBT and group CBT) to be cost effective compared to waiting list control/standard care from a Dutch healthcare payer perspective. All types of interventions led to an overall increase in costs even when downstream and foregone costs (i.e., avoided clinical appointments) were considered.

The committee acknowledged that the studies were from outside a UK NHS setting and that it was based on quality-of-life evidence that was identified in the accompanying evidence review. The committee had expressed their uncertainty at that evidence given the reasons discussed under the 'Quality of life' heading in the 'Benefits and harms' section above especially in regards to uncertainty and benefit only being identified on certain subscales. The committee also thought whilst the studies showed certain modes of CBT to be cost effective over waiting list it was difficult to compare across the studies and therefore it was difficult to highlight any mode of delivery as more effective or cost effective than any other. Every area in the country has a 'NHS Talking Therapies' service which offers group and individual CBT for mild to moderate mental health problems. Whilst it is unlikely there would be menopause specific groups in these services, the same CBT principles apply and practitioners could tailor current CBT treatment to the individual's symptoms. Given this, the committee made a recommendation for CBT but emphasised that the particular mode of delivery would likely be based on local factors such as availability.

The committee noted that a recommendation in favour of considering CBT for people who have taken gender-affirming hormone therapy in the past may increase referrals. However, the committee felt that access to CBT is a matter of equality and inclusivity.

Other factors the committee took into account

The committee ensured that the section related to psychological symptoms included a cross reference to the NICE guideline depression in adults: treatment and management so that for people experiencing menopause who are suspected to have, or are diagnosed with depression recommendations on both menopause and depression are taken into account to achieve an optimal treatment plan.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.4, 1.4.9, 1.4.16, 1.4.35, 1.4.36 and 1.4.37 in the NICE guideline.

References – included studies

Effectiveness

Abdelaziz 2021

Abdelaziz, Enas M; Elsharkawy, Nadia B; Mohamed, Sayeda M (2021) Efficacy of Internet-based cognitive behavioral therapy on sleeping difficulties in menopausal women: A randomized controlled trial. Perspectives in psychiatric care

Atema 2019

Atema, Vera, van Leeuwen, Marieke, Kieffer, Jacobien M et al. (2019) Efficacy of Internet-Based Cognitive Behavioral Therapy for Treatment-Induced Menopausal Symptoms in Breast Cancer Survivors: Results of a Randomized Controlled Trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 37(10): 809-822

Ayers 2012

Ayers B, Smith M, Hellier J et al. (2012) Effectiveness of group and self-help cognitive behavior therapy in reducing problematic menopausal hot flushes and night sweats (MENOS 2): a randomized controlled trial. Menopause (New York, N.Y.) 19(7): 749-759

Cheng 2020

Cheng, Philip, Kalmbach, David, Fellman-Couture, Cynthia et al. (2020) Risk of excessive sleepiness in sleep restriction therapy and cognitive behavioral therapy for insomnia: a randomized controlled trial. Journal of clinical sleep medicine: JCSM : official publication of the American Academy of Sleep Medicine 16(2): 193-198

Drake 2019

Drake, Christopher L, Kalmbach, David A, Arnedt, J Todd et al. (2019) Treating chronic insomnia in postmenopausal women: a randomized clinical trial comparing cognitive-behavioral therapy for insomnia, sleep restriction therapy, and sleep hygiene education. Sleep 42(2)

Duijts 2012

Duijts, Saskia F.A., van Beurden, Marc, Oldenburg, Hester S.A. et al. (2012) Efficacy of Cognitive Behavioral Therapy and Physical Exercise in Alleviating Treatment-Induced Menopausal Symptoms in Patients With Breast Cancer: Results of a Randomized, Controlled, Multicenter Trial. Journal of Clinical Oncology 30(33): 4124-4133

Fenlon 2020

Fenlon D, Maishman T, Day L et al. (2020) Effectiveness of nurse-led group CBT for hot flushes and night sweats in women with breast cancer: Results of the MENOS4 randomised controlled trial. Psycho-oncology 29(10): 1514-1523

Green 2019

Green, Sheryl M, Donegan, Eleanor, Frey, Benicio N et al. (2019) Cognitive behavior therapy for menopausal symptoms (CBT-Meno): a randomized controlled trial. Menopause (New York, N.Y.) 26(9): 972-980

Green 2020

Green, S M, Donegan, E, McCabe, R E et al. (2020) Objective and subjective vasomotor symptom outcomes in the CBT-Meno randomized controlled trial. Climacteric: the journal of the International Menopause Society 23(5): 482-488

Hardy 2018

Hardy, Claire, Griffiths, Amanda, Norton, Sam et al. (2018) Self-help cognitive behavior therapy for working women with problematic hot flushes and night sweats (MENOS@Work): a multicenter randomized controlled trial. Menopause (New York, N.Y.) 25(5): 508-519

Hummel 2017

Hummel, Susanna B, van Lankveld, Jacques J D M, Oldenburg, Hester S A et al. (2017) Efficacy of Internet-Based Cognitive Behavioral Therapy in Improving Sexual Functioning of Breast Cancer Survivors: Results of a Randomized Controlled Trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 35(12): 1328-1340

Kalmbach 2019

Kalmbach, David A, Cheng, Philip, Arnedt, J Todd et al. (2019) Improving Daytime Functioning, Work Performance, and Quality of Life in Postmenopausal Women With Insomnia: Comparing Cognitive Behavioral Therapy for Insomnia, Sleep Restriction Therapy, and Sleep Hygiene Education. Journal of clinical sleep medicine: JCSM : official publication of the American Academy of Sleep Medicine 15(7): 999-1010

Keefer 2005

Keefer, Laurie and Blanchard, Edward B (2005) A behavioral group treatment program for menopausal hot flashes: results of a pilot study. Applied psychophysiology and biofeedback 30(1): 21-30

Mann 2012

Mann E, Smith MJ, Hellier J et al. (2012) Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial. The Lancet. Oncology 13(3): 309-318

McCurry 2016

McCurry, Susan M, Guthrie, Katherine A, Morin, Charles M et al. (2016) Telephone-Based Cognitive Behavioral Therapy for Insomnia in Perimenopausal and Postmenopausal Women With Vasomotor Symptoms: A MsFLASH Randomized Clinical Trial. JAMA internal medicine 176(7): 913-20

Moradi Farsani 2021

Moradi Farsani, Hadis, Afshari, Poorandokht, Sadeghniiat Haghighi, Khosro et al. (2021) The effect of group cognitive behavioural therapy for insomnia in postmenopausal women. Journal of sleep research 30(5): e13345

Soori 2019

Soori, M., Kolivand, M., Abolfathi Momtaz, Y. et al. (2019) The effect of cognitive-behavioral group therapy on menopausal symptoms. Journal of Babol University of Medical Sciences 21(1): 215-222

Economic

Mewes 2015

Mewes JC, Steuten LM, Duijts SF et al (2015) Cost-effectiveness of cognitive behavioral therapy and physical exercise for alleviating treatment-induced menopausal symptoms in breast cancer patients. Journal of cancer survivorship.126-35.

Verbeek 2019

Verbeek JG, Atema V, Mewes JC et al (2019) Cost-utility, cost-effectiveness, and budget impact of Internet-based cognitive behavioural therapy for breast cancer survivors with treatment-induced menopausal symptoms. Breast cancer research and treatment.178:573-85.

Appendices

Appendix A Review protocols

Review protocol for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Table 4: Review protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42022347304
1.	Review title	Cognitive behavioural therapy (CBT) for managing symptoms associated with the menopause.
2.	Review question	What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?
3.	Objective	To determine if CBT is effective for managing symptoms associated with the menopause.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE, MEDLINE ePub Ahead-of-Print and MEDLINE-in-Process • Epistemonikos • HTA via CRD • INAHTA • PsycInfo Searches will be restricted by: • English language • Human studies

ID	Field	Content
		• RCTs and Systematic Reviews The full search strategies will be published in the final review.
5.	Condition or domain being studied	Symptoms associated with the menopause
6.	Population	Women, non-binary and trans people with symptoms associated with menopause.
7.	Intervention	• CBT

8.	Comparator/Reference standard/Confounding factors	• Treatment as usual
		  ○ HRT
		  ○ Non-HRT
		• No treatment (including waiting list)
		• Attention control (sham CBT)

9.	Types of study to be included	Include published English language, full-text papers: • Systematic reviews of RCTs • RCTs
10.	Other exclusion criteria	Conference abstracts will be excluded
11.	Context	This review partially updates review question D4 from NICE guideline NG23: What is the most clinical and cost effective treatment for the relief of individual menopause-related symptoms for women in menopause?

12.	Primary outcomes (critical outcomes)	• Quality of life (any validated scale e.g., SF-36, all subscales)
		• Vasomotor symptoms (VMS):
		  ○ Frequency of VMS
		  ○ Severity of VMS
		  ○ Distress or bother caused by VMS
		• Difficulties with sleep (any)

13.	Secondary outcomes (important outcomes)	• Patient satisfaction • Discontinuation of treatment • Musculoskeletal symptoms

ID	Field	Content

		• Altered sexual function
		• Psychological symptoms
		  ○ Anxiety
		  ○ Low mood (not clinical depression)
		  ○ Stress

14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
15.	Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
16.	Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted, and data will be presented as risk ratios if possible or

ID	Field	Content
		odds ratios when required (for example, if only available in this form in included studies) for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I^2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis, then a random effects model will be used for meta-analysis, or the data will not be pooled. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • All-cause mortality: statistical significance • Serious intervention-related adverse effects: statistical significance • Validated scales/continuous outcomes: published MIDs where available • All other outcomes & where published MIDs are not available: 0.8 and 1.25 for all relative dichotomous outcomes; +/- 0.5x control group SD for continuous outcomes **How the evidence included in NG23 will be incorporated with the new evidence:** Studies meeting the current protocol criteria and previously included in the NG23 will be included in this update. The methods for quantitative analysis (data extraction, risk of bias, strategy for data synthesis, and analysis of subgroups) will be the same as for the new evidence and as outlined in this protocol.
17.	Analysis of sub-groups	Evidence will be stratified by: • Personal history of breast cancer • High risk of breast cancer

ID	Field	Content	
		• Contra-indication to HRT vs not choosing HRT • Group vs individual CBT • Face-to-face vs online CBT • Self-help vs guided CBT • Duration of CBT (number of sessions: <6 sessions versus ≥ 6 sessions) Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: • Therapist experience of menopause • Who is delivering CBT e.g., which healthcare professional • Modification of CBT • Groups identified in the equality considerations section of the scope: ○ Age ○ Disability ○ Ethnicity ○ Socioeconomic status ○ non-binary and trans-masculine people. Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative

ID	Field	Content		
		☐	Epidemiologic	
		☐	Service Delivery	
		☐	Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	11 July 2022		
22.	Anticipated completion date	23 August 2023		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☑	☑
		Piloting of the study selection process	☑	☑
		Formal screening of search results against eligibility criteria	☑	☑
		Data extraction	☑	☑
		Risk of bias (quality) assessment	☑	☑
		Data analysis	☑	☑
24.	Named contact	**5a. Named contact** Guideline development team NGA **5b Named contact e-mail** menopause@nice.org.uk		

ID	Field	Content
		5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE)
25.	Review team members	Senior Systematic Reviewer, Guideline Development Team NGA, National Institute for Health and Care Excellence Systematic Reviewer, Guideline Development Team NGA, National Institute for Health and Care Excellence
26.	Funding sources/sponsor	This systematic review is being completed by the [Insert Development centre] which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/ng23
29.	Other registration details	Cognitive Behavioural Therapy; Female; Humans; Menopause
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=347304
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

ID	Field	Content	
		[Add in any additional agree dissemination plans.]	
32.	Keywords	[Give words or phrases that best describe the review.]	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

CBT: cognitive behavioural therapy; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HRT: hormone replacement therapy; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; ROBIS: risk of bias in systematic reviews; SD: standard deviation; VMS: vasomotor symptoms

Appendix B Literature search strategies

Literature search strategies for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Clinical searches

Database: Ovid MEDLINE(R) ALL <1946 to July 26, 2022>
Date of last search: 27/07/2022

#	Searches	
1	Climacteric/	4935
2	Menopause/ or Perimenopause/ or Postmenopause/	56064
3	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	102495
4	("change of life" or life change?).tw.	3149
5	or/1-4	116647
6	exp Cognitive Behavioral Therapy/	34671
7	problem solving/ or metacognition/ or biofeedback, psychology/ or dialectical behavior therapy/ or psychotherapy, rational-emotive/ or schema therapy/ or role playing/	38301
8	(cogniti* adj4 (behavio* or therap* or refram* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)).tw.	92558
9	((behavio* or autogenic) adj4 (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*)).tw.	154563
10	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP).tw.	14887
11	(biofeedback or contingency management or covert conditioning or covert sensiti?ation or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive).tw.	41421
12	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) adj4 (intervention* or therap* or treatment* or training)).tw.	27292
13	(acceptance adj2 commitment).tw.	1446
14	(REBT or RET or DBT or CFT or ACT or MCT).tw.	331776
15	(mindfulness* or MBCT* or mind training or role play*).tw.	33680
16	psychosocial support systems/	917
17	(psychosocial* or psycho-social* or "psycho social*").tw.	115142
18	(psychoeducat* or psycho-educat* or "psycho educat*").tw.	7921
19	Therapy, Computer-Assisted/	6961
20	((computer* or online or internet or digital*) adj4 (intervention* or program* or therap* or treatment*)).tw.	43936
21	Psychotherapy, Group/	14412
22	(group adj2 (intervention* or therap* or treatment* or support* or program*)).tw.	150623
23	Self Care/ or Self Efficacy/ or Self-Help Groups/	66073
24	bibliotherapy/	431
25	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*).tw.	63689
26	(self-direct* adj4 therap*).tw.	91
27	or/6-26	1044638
28	5 and 27	5624
29	letter/	1189892
30	editorial/	614142
31	news/	213629
32	exp historical article/	408694
33	Anecdotes as Topic/	4746
34	comment/	973673
35	case report/	2284248
36	(letter or comment*).ti.	179310

#	Searches	
37	or/29-36	4786879
38	randomized controlled trial/ or random*.ti,ab	1471297
39	37 not 38	4756154
40	animals/ not humans/	5006719
41	exp Animals, Laboratory/	942971
42	exp Animal Experimentation/	10214
43	exp Models, Animal/	632237
44	exp Rodentia/	3479223
45	(rat or rats or mouse or mice).ti.	1408951
46	or/39-45	10635575
47	28 not 46	5129
48	limit 47 to english language	4736
49	Meta-Analysis/	165981
50	Meta-Analysis as Topic/	21683
51	(meta analy* or metanaly* or metaanaly*).ti,ab	243004
52	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab	301741
53	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	51420
54	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	73892
55	(search* adj4 literature).ab.	87926
56	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	322707
57	cochrane.jw.	16095
58	or/49-57	606449
59	randomized controlled trial.pt.	575650
60	controlled clinical trial.pt.	94990
61	pragmatic clinical trial.pt.	2137
62	randomi#ed.ab.	684060
63	placebo.ab.	230983
64	drug therapy.fs.	2522803
65	randomly.ab.	389231
66	trial.ab.	613386
67	groups.ab.	2393527
68	or/59-67	5455391
69	Clinical Trials as topic.sh.	200305
70	trial.ti.	268774
71	or/59-63	65
72	58 or 71	1971481
73	48 and 72	1894

Database: Embase <1974 to 2022 July 29>
Date of last search: 01/08/2022

#	Searches	
1	climacterium/ or "menopause and climacterium"/	8930
2	menopause/ or early menopause/ or postmenopause/ or exp menopause related disorder/	133601
3	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	147803
4	("change of life" or life change?).tw.	4239
5	or/1-4	183218
6	exp Cognitive Behavioral Therapy/	21876
7	mindfulness/ or "acceptance and commitment therapy"/ or rational emotive behavior therapy/ or problem solving/ or metacognition/ or biofeedback/ or schema therapy/ or cognitive reappraisal/ or role playing/	74261
8	(cogniti* adj4 (behavio* or therap* or refram* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)).tw.	128019
9	((behavio* or autogenic) adj4 (activation or analys* or cathar* or condition* or intervention*	194447

#	Searches	
	or modification* or therap* or training or treatment* or program* or strateg* or technique*)).tw.	
10	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP).tw.	22096
11	(biofeedback or contingency management or covert conditioning or covert sensiti?ation or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive).tw.	53759
12	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) adj4 (intervention* or therap* or treatment* or training)).tw.	38779
13	(acceptance adj2 commitment).tw.	1960
14	(REBT or RET or DBT or CFT or ACT or MCT).tw.	406391
15	(mindfulness* or MBCT* or mind training or role play*).tw.	41046
16	Psychosocial Care/ or Psychoeducation/	30987
17	(psychosocial* or psycho-social* or "psycho social*").tw.	156623
18	(psychoeducat* or psycho-educat* or "psycho educat*").tw.	11840
19	Computer Assisted Therapy/	4819
20	((computer* or online or internet or digital*) adj4 (intervention* or program* or therap* or treatment*)).tw.	56491
21	group therapy/	20032
22	(group adj2 (intervention* or therap* or treatment* or support* or program*)).tw.	222236
23	Self Care/ or Self Help/ or Self Concept/	178583
24	bibliotherapy/	294
25	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*).tw.	83255
26	(self-direct* adj4 therap*).tw.	138
27	or/6-26	1426688
28	5 and 27	9713
29	letter.pt. or letter/	1241876
30	note.pt.	901797
31	editorial.pt.	733613
32	case report/ or case study/	2836641
33	(letter or comment*).ti.	224206
34	or/29-33	5462442
35	randomized controlled trial/ or random*.ti,ab.	1928915
36	34 not 35	5407726
37	animal/ not human/	1159758
38	nonhuman/	6983755
39	exp Animal Experiment/	2874637
40	exp Experimental Animal/	770091
41	animal model/	1570755
42	exp Rodent/	3850325
43	(rat or rats or mouse or mice).ti.	1557060
44	or/36-43	14181910
45	28 not 44	8342
46	limit 45 to english language	7605
47	(conference abstract or conference paper or conference proceeding or "conference review").pt.	5261008
48	46 not 47	5360
49	systematic review/	363203
50	meta-analysis/	253203
51	(meta analy* or metanaly* or metaanaly*).ti,ab.	310546
52	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	355433
53	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	62595
54	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	88284
55	(search* adj4 literature).ab.	110483

#	Searches	
56	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	392983
57	((pool* or combined) adj2 (data or trials or studies or results)).ab.	85092
58	cochrane.jw.	23650
59	or/49-58	855389
60	random*.ti,ab.	1819404
61	factorial*.ti,ab.	44407
62	(crossover* or cross over*).ti,ab.	119260
63	((doubl* or singl*) adj blind*).ti,ab.	259738
64	(assign* or allocat* or volunteer* or placebo*).ti,ab.	1185067
65	crossover procedure/	71128
66	single blind procedure/	47122
67	randomized controlled trial/	721669
68	double blind procedure/	197421
69	or/60-68	2708925
70	59 or 69	3307021
71	48 and 70	2084

Database: APA PsycInfo 1806 to July Week 3 2022
Date of last search: 28/07/2022

#	Searches	
1	menopause/ or life changes/	9131
2	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	7265
3	("change of life" or life change?).tw.	3336
4	or/1-3	15316
5	exp cognitive behavior therapy/	25122
6	problem solving/ or metacognition/ or biofeedback training/ or dialectical behavior therapy/ or rational emotive behavior therapy/ or schema therapy/ or role playing/ or cognitive restructuring/ or solution focused therapy/ or mindfulness/ or mindfulness-based interventions/ or behavior modification/ or covert sensitization/	71632
7	(cogniti* adj4 (behavio* or therap* or refram* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)).tw.	121238
8	((behavio* or autogenic) adj4 (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*)).tw.	174316
9	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP).tw.	17363
10	(biofeedback or contingency management or covert conditioning or covert sensiti?ation or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive).tw.	76881
11	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) adj4 (intervention* or therap* or treatment* or training)).tw.	16369
12	(acceptance adj2 commitment).tw.	3057
13	(REBT or RET or DBT or CFT or ACT or MCT).tw.	86589
14	(mindfulness* or MBCT* or mind training or role play*).tw.	31807
15	Social Support/ or Psychoeducation/	46085
16	(psychosocial* or psycho-social* or "psycho social*").tw.	99497
17	(psychoeducat* or psycho-educat* or "psycho educat*").tw.	13243
18	computer assisted therapy/ or exp Online Therapy/	4797
19	((computer* or online or internet or digital*) adj4 (intervention* or program* or therap* or treatment*)).tw.	22509
20	Group Psychotherapy/ or support groups/	25066
21	(group adj2 (intervention* or therap* or treatment* or support* or program*)).tw.	62504
22	exp self-help techniques/ or self-care/ or self-evaluation/ or self-monitoring/ or self-regulation/ or self-efficacy/	64154
23	bibliotherapy/	802

#	Searches	
24	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*).tw.	91955
25	(self-direct* adj4 therap*).tw.	119
26	or/5-25	744975
27	4 and 26	3022
28	(letter or editorial or comment reply).dt. or case report/	226237
29	(letter or comment*).ti.	43125
30	28 or 29	236049
31	exp randomized controlled trial/	1237
32	random*.ti,ab.	226591
33	31 or 32	226649
34	30 not 33	229677
35	animal.po.	430281
36	(rat or rats or mouse or mice).ti.	123199
37	or/34-36	657312
38	27 not 37	2869
39	limit 38 to english language	2713
40	(meta analysis or "systematic review").md.	56917
41	META ANALYSIS/	5243
42	SYSTEMATIC REVIEW/	708
43	(meta analy* or metanaly* or metaanaly*).ti,ab.	45868
44	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.	57143
45	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	21798
46	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	9225
47	(search* adj4 literature).ab.	13324
48	cochrane.jx.	0
49	((pool* or combined) adj2 (data or trials or studies or results)).ab.	8507
50	(medline or pubmed or cochrane or embase or psychlit or psyclit or cinahl or science citation index or bids or cancerlit).ab.	33005
51	or/40-50	135183
52	clinical trial.md.	34113
53	Clinical trials/	12081
54	Randomized controlled trials/	886
55	Randomized clinical trials/	359
56	assign*.ti,ab.	106009
57	allocat*.ti,ab.	34679
58	crossover*.ti,ab.	8304
59	cross over*.ti,ab.	3219
60	((doubl* or singl*) adj blind*).ti,ab.	27928
61	factorial*.ti,ab.	21688
62	placebo*.ti,ab.	42762
63	random*.ti,ab.	226591
64	volunteer*.ti,ab.	41427
65	trial?.ti,ab.	201625
66	or/52-65	507543
67	51 or 66	613930
68	39 and 67	473

1
2 Database: Cochrane Database of Systematic Reviews (CDSR) Issue 7 of 12, July 2022
3 Date of last search: 27/07/2022

#	Searches	
1	MeSH descriptor: [Climacteric] this term only	335

#	Searches	
2	MeSH descriptor: [Menopause] this term only	1621
3	MeSH descriptor: [Perimenopause] this term only	168
4	MeSH descriptor: [Postmenopause] this term only	4982
5	(menopau* or postmenopau* or perimenopau* or climacteri*):ti,ab,kw	29327
6	("change of life" or "life change" or "life changes"):ti,ab,kw	887
7	{or #1-#6}	30200
8	MeSH descriptor: [Cognitive Behavioral Therapy] explode all trees	10432
9	MeSH descriptor: [Problem Solving] this term only	1562
10	MeSH descriptor: [Metacognition] this term only	99
11	MeSH descriptor: [Biofeedback Psychology] this term only	1081
12	MeSH descriptor: [Dialectical Behavior Therapy] this term only	47
13	MeSH descriptor: [Psychotherapy Rational-Emotive] this term only	29
14	MeSH descriptor: [Schema Therapy] this term only	3
15	MeSH descriptor: [Role Playing] this term only	166
16	(cogniti* near/2 (behavio* or therap* or refram* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)):ti,ab,kw	36056
17	((behavio* or autogenic) near/2 (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*)):ti,ab,kw	44563
18	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP):ti	1708
19	(biofeedback or contingency management or covert conditioning or covert sensitisation or sensitization or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive):ti,ab,kw	20065
20	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) near/2 (intervention* or therap* or treatment* or training)):ti,ab,kw	16977
21	(acceptance near/2 commitment):ti	1483
22	(REBT or RET or DBT or CFT or ACT or MCT):ti	1591
23	(mindfulness* or MBCT* or mind training or role play*):ti,ab,kw	32668
24	MeSH descriptor: [Psychosocial Support Systems] this term only	65
25	(psychosocial* or psycho-social* or "psycho social*"):ti,ab,kw	18175
26	(psychoeducat* or psycho-educat* or "psycho educat*"):ti,ab,kw	5500
27	MeSH descriptor: [Therapy Computer-Assisted] this term only	1372
28	((computer* or online or internet or digital*) near/2 (intervention* or program* or therap* or treatment*)):ti,ab,kw	13099
29	MeSH descriptor: [Psychotherapy, Group] this term only	2298
30	(group near/2 (intervention* or therap* or treatment* or support* or program*)):ti,ab,kw	169154
31	MeSH descriptor: [Self Care] this term only	4370
32	MeSH descriptor: [Self Efficacy] this term only	3473
33	MeSH descriptor: [Self-Help Groups] this term only	741
34	MeSH descriptor: [Bibliotherapy] this term only	131
35	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*):ti,ab,kw	21861
36	(self-direct* near/4 therap*):ti	76
37	{or #8-#36}	294862
38	#7 AND #37	4271
39	#7 AND #37 in Cochrane Reviews	33

Database: Cochrane Central Register of Controlled Trials (CENTRAL) Issue 7 of 12, July 2022

Date of last search: 01/08/2022

#	Searches	
1	MeSH descriptor: [Climacteric] this term only	335
2	MeSH descriptor: [Menopause] this term only	1622
3	MeSH descriptor: [Perimenopause] this term only	168

#	Searches	
4	MeSH descriptor: [Postmenopause] this term only	4982
5	(menopau* or postmenopau* or perimenopau* or climacteri*):ti,ab	27681
6	("change of life" or "life change" or "life changes"):ti,ab	444
7	{or #1-#6}	28529
8	MeSH descriptor: [Cognitive Behavioral Therapy] explode all trees	10433
9	MeSH descriptor: [Problem Solving] this term only	1562
10	MeSH descriptor: [Metacognition] this term only	99
11	MeSH descriptor: [Biofeedback, Psychology] this term only	1081
12	MeSH descriptor: [Dialectical Behavior Therapy] this term only	47
13	MeSH descriptor: [Psychotherapy, Rational-Emotive] this term only	29
14	MeSH descriptor: [Schema Therapy] this term only	3
15	MeSH descriptor: [Role Playing] this term only	166
16	(cogniti* near/2 (behavio* or therap* or refram* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)):ti,ab	32030
17	((behavio* or autogenic) near/2 (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*)):ti,ab	35413
18	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP):ti	1708
19	(biofeedback or contingency management or covert conditioning or covert sensitisation or sensitization or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive):ti,ab	18189
20	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) near/2 (intervention* or therap* or treatment* or training)):ti,ab	14795
21	(acceptance near/2 commitment):ti,ab	1382
22	(REBT or RET or DBT or CFT or ACT or MCT):ti	1591
23	(mindfulness* or MBCT* or mind training or role play*):ti,ab	32124
24	MeSH descriptor: [Psychosocial Support Systems] this term only	65
25	(psychosocial* or psycho-social* or "psycho social*"):ti,ab	15540
26	(psychoeducat* or psycho-educat* or "psycho educat*"):ti,ab	5059
27	MeSH descriptor: [Therapy, Computer-Assisted] this term only	1372
28	((computer* or online or internet or digital*) near/2 (intervention* or program* or therap* or treatment*)):ti,ab	9992
29	MeSH descriptor: [Psychotherapy, Group] this term only	2298
30	(group near/2 (intervention* or therap* or treatment* or support* or program*)):ti,ab	167764
31	MeSH descriptor: [Self Care] this term only	4370
32	MeSH descriptor: [Self Efficacy] this term only	3473
33	MeSH descriptor: [Self-Help Groups] this term only	741
34	MeSH descriptor: [Bibliotherapy] this term only	131
35	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*):ti,ab	14158
36	(self-direct* near/4 therap*):ti,ab	74
37	{or #8-#36}	281591
38	#7 AND #37 in Trials	3790
39	"conference":pt or (clinicaltrials or trialsearch):so	608941
40	#38 not #39	2068

Database: Epistemonikos
Date of last search: 27/07/2022

#	Searches	
1	(title:((title:((menopau* OR postmenopau* OR perimenopau* OR climacteri*)) OR abstract:((menopau* OR postmenopau* OR perimenopau* OR climacteri*))) OR (title:(("change of life" OR "life change" OR "life changes")) OR abstract:(("change of life" OR "life change" OR "life changes")))	
2	(title:((cogniti* AND (behavio* OR therap* OR refram* OR re-fram* OR restructur* OR re-structur* OR intervention* OR program* OR treatment* OR strateg* OR training* OR	

#	Searches	
	technique*))) OR abstract:((cogniti* AND (behavio* OR therap* OR reframe* OR re-fram* OR restructur* OR re-structur* OR intervention* OR program* OR treatment* OR strateg* OR training* OR technique*)))) OR (title:(((behavio* OR autogenic) AND (activation OR analys* OR cathar* OR condition* OR intervention* OR modification* OR therap* OR training OR treatment* OR program* OR strateg* OR technique*))) OR abstract:(((behavio* OR autogenic) AND (activation OR analys* OR cathar* OR condition* OR intervention* OR modification* OR therap* OR training OR treatment* OR program* OR strateg* OR technique*)))) OR (title:((CBT* OR iCBT OR eCBT OR dCBT OR cCBT OR CTBT OR CCBT OR CBASP)) OR abstract:((CBT* OR iCBT OR eCBT OR dCBT OR cCBT OR CTBT OR CCBT OR CBASP))) OR (title:((biofeedback OR contingency management OR covert conditioning OR covert sensitisation OR covert sensitization OR defusion OR neurofeedback OR problem focus* OR problem solving OR schema OR solution focus* OR rational emotive)) OR abstract:((biofeedback OR contingency management OR covert conditioning OR covert sensitisation OR covert sensitization OR defusion OR neurofeedback OR problem focus* OR problem solving OR schema OR solution focus* OR rational emotive))) OR (title:(((third wave OR 3rd wave OR compassion* OR time-limited OR goal orientated OR exposure OR successive approximation OR guided discovery OR metacognitive OR dialectic*) AND (intervention* OR therap* OR treatment* OR training))) OR abstract:(((third wave OR 3rd wave OR compassion* OR time-limited OR goal orientated OR exposure OR successive approximation OR guided discovery OR metacognitive OR dialectic*) AND (intervention* OR therap* OR treatment* OR training)))) OR (title:((acceptance AND commitment)) OR abstract:((acceptance AND commitment))) OR (title:((REBT OR RET OR DBT OR CFT OR ACT OR MCT)) OR abstract:((REBT OR RET OR DBT OR CFT OR ACT OR MCT))) OR (title:((mindfulness* OR MBCT* OR mind training OR role play*)) OR abstract:((mindfulness* OR MBCT* OR mind training OR role play*))) OR (title:((psychosocial* OR psycho-social* OR "psycho social*")) OR abstract:((psychosocial* OR psycho-social* OR "psycho social*"))) OR (title:((psychoeducat* OR psycho-educat* OR "psycho educat*")) OR abstract:((psychoeducat* OR psycho-educat* OR "psycho educat*"))) OR (title:(((computer* OR online OR internet OR digital*) AND (intervention* OR program* OR therap* OR treatment*))) OR abstract:(((computer* OR online OR internet OR digital*) AND (intervention* OR program* OR therap* OR treatment*)))) OR (title:((group AND (intervention* OR therap* OR treatment* OR support* OR program*))) OR abstract:((group AND (intervention* OR therap* OR treatment* OR support* OR program*)))) OR (title:((self-help OR self-care OR self-therap* OR self-analy* OR self-esteem OR self-control OR self-imag* OR self-validat* OR bibliotherap*)) OR abstract:((self-help OR self-care OR self-therap* OR self-analy* OR self-esteem OR self-control OR self-imag* OR self-validat* OR bibliotherap*))) OR (title:((self-direct* AND therap*))	
3	1 AND 2	394

1
2 Database: HTA via CRD
3 Date of last search: 27/07/2022

#	Searches	
1	MeSH DESCRIPTOR Climacteric	9
2	MeSH DESCRIPTOR Menopause	117
3	MeSH DESCRIPTOR Perimenopause	7
4	MeSH DESCRIPTOR Postmenopause	209
5	((menopau* or postmenopau* or perimenopau* or climacteri*))	957
6	(("change of life" or "life change" or "life changes"))	38
7	MeSH DESCRIPTOR Cognitive Behavioral Therapy EXPLODE ALL TREES	28
8	MeSH DESCRIPTOR problem solving	48
9	MeSH DESCRIPTOR metacognition	0
10	MeSH DESCRIPTOR Biofeedback, Psychology	75
11	MeSH DESCRIPTOR dialectical behavior therapy	0
12	MeSH DESCRIPTOR psychotherapy, rational-emotive	2
13	MeSH DESCRIPTOR Schema Therapy	0
14	MeSH DESCRIPTOR role playing	3
15	((cogniti* NEAR4 (behavio* or therap* or reframe* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*)))	1692
16	(((behavio* or autogenic) NEAR4 (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*)))	2425
17	((CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP))	396
18	((biofeedback or contingency management or covert conditioning or covert sensitisation or sensitization or defusion or neurofeedback or problem focus* or problem solving or schema	520

#	Searches	
	or solution focus* or rational emotive))	
19	(((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or successive approximation or guided discovery or metacognitive or dialectic*) NEAR4 (intervention* or therap* or treatment* or training)))	209
20	((acceptance NEAR2 commitment))	15
21	((REBT or RET or DBT or CFT or ACT or MCT))	382
22	((mindfulness* or MBCT* or mind training or role play*))	173
23	MeSH DESCRIPTOR psychosocial support systems	0
24	((psychosocial* or psycho-social* or "psycho social*"))	957
25	((psychoeducat* or psycho-educat* or "psycho educat*"))	217
26	MeSH DESCRIPTOR Therapy, Computer-Assisted	111
27	(((computer* or online or internet or digital*) NEAR4 (intervention* or program* or therap* or treatment*)))	542
28	MeSH DESCRIPTOR Psychotherapy, Group	129
29	((group NEAR2 (intervention* or therap* or treatment* or support* or program*)))	1110
30	MeSH DESCRIPTOR Self Care	479
31	MeSH DESCRIPTOR Self Efficacy	61
32	MeSH DESCRIPTOR Self-Help Groups	89
33	MeSH DESCRIPTOR bibliotherapy	12
34	((self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*))	1104
35	((self-direct* NEAR4 therap*))	4
36	#1 OR #2 OR #3 OR #4 OR #5 OR #6	994
37	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35	6106
38	#36 AND #37	58
39	(#36 AND #37) IN HTA	3

Database: INAHTA

Date of last search: 27/07/2022

#	Searches	
1	"Climacteric"[mh]	2
2	"Menopause"[mh]	28
3	"Perimenopause"[mh]	1
4	"Postmenopause"[mh]	31
5	(menopau* or postmenopau* or perimenopau* or climacteri*)	159
6	("change of life" or "life change" or "life changes")	1
7	#6 OR #5 OR #4 OR #3 OR #2 OR #1	163
8	"Cognitive Behavioral Therapy"[mhe]	43
9	"Problem Solving"[mh]	5
10	"Metacognition"[mh]	0
11	"Biofeedback, Psychology"[mh]	5
12	"Dialectical Behavior Therapy"[mh]	0
13	"Psychotherapy, Rational-Emotive"[mh]	0
14	"Schema Therapy"[mh]	0
15	"Role Playing"[mh]	0
16	(cogniti* AND (behavio* or therap* or reframe* or re-fram* or restructur* or re-structur* or intervention* or program* or treatment* or strateg* or training* or technique*))	329
17	((behavio* or autogenic) AND (activation or analys* or cathar* or condition* or intervention* or modification* or therap* or training or treatment* or program* or strateg* or technique*))	590
18	(CBT* or iCBT or eCBT or dCBT or cCBT or CTBT or CCBT or CBASP)	81
19	(biofeedback or contingency management or covert conditioning or covert sensitisation or sensitization or defusion or neurofeedback or problem focus* or problem solving or schema or solution focus* or rational emotive)	3063
20	((third wave or 3rd wave or compassion* or time-limited or goal orientated or exposure or	2672

#	Searches	
	successive approximation or guided discovery or metacognitive or dialectic*) AND (intervention* or therap* or treatment* or training)))	
21	(acceptance AND commitment)	1
22	(REBT or RET or DBT or CFT or ACT or MCT)	158
23	(mindfulness* or MBCT* or mind training or role play*)	1197
24	"Psychosocial Support Systems"[mh]	2
25	(psychosocial* or psycho-social* or "psycho social*")	1384
26	(psychoeducat* or psycho-educat* or "psycho educat*")	437
27	"Therapy, Computer-Assisted"[mh]	25
28	((computer* or online or internet or digital*) AND (intervention* or program* or therap* or treatment*))	303
29	"Psychotherapy, Group"[mh]	11
30	(group AND (intervention* or therap* or treatment* or support* or program*))	1506
31	"Self Care"[mh]	65
32	"Self Efficacy"[mh]	3
33	"Self-Help Groups"[mh]	3
34	"Bibliotherapy"[mh]	0
35	(self-help or self-care or self-therap* or self-analy* or self-esteem or self-control or self-imag* or self-validat* or bibliotherap*)	10251
36	(self-direct* AND therap*)	481
37	#36 OR #35 OR #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8	12079
38	#37 AND #7	125

Economic searches

Database: Ovid MEDLINE(R) ALL <1946 to July 27, 2022>
Date of last search: 28/07/2022

#	Searches	
1	Climacteric/	4935
2	Menopause/ or Perimenopause/ or Postmenopause/	55972
3	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	102310
4	("change of life" or life change?).tw.	3141
5	or/1-4	116452
6	limit 5 to english language	103660
7	limit 6 to yr="2012 -Current"	41579
8	letter/	1188475
9	editorial/	613156
10	news/	213557
11	exp historical article/	408665
12	Anecdotes as Topic/	4746
13	comment/	973045
14	case report/	2282504
15	(letter or comment*).ti.	179095
16	or/8-15	4782431
17	randomized controlled trial/ or random*.ti,ab.	1466248
18	16 not 17	4751747
19	animals/ not humans/	4997958
20	exp Animals, Laboratory/	942090
21	exp Animal Experimentation/	10205
22	exp Models, Animal/	631246
23	exp Rodentia/	3472512
24	(rat or rats or mouse or mice).ti.	1407073
25	or/18-24	10620565

#	Searches	
26	7 not 25	34368
27	Economics/	27455
28	Value of life/	5793
29	exp "Costs and Cost Analysis"/	259348
30	exp Economics, Hospital/	25612
31	exp Economics, Medical/	14359
32	Economics, Nursing/	4013
33	Economics, Pharmaceutical/	3074
34	exp "Fees and Charges"/	31172
35	exp Budgets/	14034
36	budget*.ti,ab.	33535
37	cost*.ti.	136425
38	(economic* or pharmaco?economic*).ti.	56592
39	(price* or pricing*).ti,ab.	48567
40	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	191586
41	(financ* or fee or fees).ti,ab.	145674
42	(value adj2 (money or monetary)).ti,ab.	2817
43	or/27-42	689907
44	exp models, economic/	16130
45	*Models, Theoretical/	64214
46	*Models, Organizational/	6490
47	markov chains/	15758
48	monte carlo method/	31445
49	exp Decision Theory/	12940
50	(markov* or monte carlo).ti,ab.	79077
51	econom* model*.ti,ab.	4760
52	(decision* adj2 (tree* or analy* or model*)).ti,ab.	31806
53	or/44-52	210296
54	43 or 53	865352
55	26 and 54	849

Database: Embase <1974 to 2022 July 27>
Date of last search: 28/07/2022

#	Searches	
1	climacterium/ or "menopause and climacterium"/	8930
2	menopause/ or early menopause/ or postmenopause/ or exp menopause related disorder/	133601
3	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	147803
4	("change of life" or life change?).tw.	4239
5	or/1-4	183218
6	limit 5 to english language	163179
7	limit 6 to yr="2012 -Current"	81270
8	letter.pt. or letter/	1241876
9	note.pt.	901797
10	editorial.pt.	733613
11	case report/ or case study/	2836641
12	(letter or comment*).ti.	224206
13	or/8-12	5462442
14	randomized controlled trial/ or random*.ti,ab.	1928915
15	13 not 14	5407726
16	animal/ not human/	1159758
17	nonhuman/	6983755
18	exp Animal Experiment/	2874637
19	exp Experimental Animal/	770091

#	Searches	
20	animal model/	1570755
21	exp Rodent/	3850325
22	(rat or rats or mouse or mice).ti.	1557060
23	or/15-22	14181910
24	7 not 23	61890
25	health economics/	34559
26	exp economic evaluation/	337213
27	exp health care cost/	322230
28	exp fee/	42496
29	budget/	32003
30	funding/	67739
31	budget*.ti,ab.	44183
32	cost*.ti.	181970
33	(economic* or pharmaco?economic*).ti.	70774
34	(price* or pricing*).ti,ab.	67140
35	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	264737
36	(financ* or fee or fees).ti,ab.	200470
37	(value adj2 (money or monetary)).ti,ab.	3792
38	or/25-37	1085390
39	statistical model/	171255
40	exp economic aspect/	2251504
41	39 and 40	27469
42	*theoretical model/	30994
43	*nonbiological model/	5065
44	stochastic model/	19388
45	decision theory/	1802
46	decision tree/	18095
47	monte carlo method/	46995
48	(markov* or monte carlo).ti,ab.	87061
49	econom* model*.ti,ab.	7134
50	(decision* adj2 (tree* or analy* or model*)).ti,ab.	43807
51	or/41-50	225433
52	38 or 51	1266430
53	24 and 52	2248

Database: Cochrane Database of Systematic Reviews (CDSR) Issue 7 of 12, July 2022
Date of last search: 01/08/2022

#	Searches	
1	MeSH descriptor: [Climacteric] this term only	335
2	MeSH descriptor: [Menopause] this term only	1622
3	MeSH descriptor: [Perimenopause] this term only	168
4	MeSH descriptor: [Postmenopause] this term only	4982
5	(menopau* or postmenopau* or perimenopau* or climacteri*):ti,ab	27681
6	("change of life" or "life change" or "life changes"):ti,ab	444
7	{or #1-#6}	28529
8	MeSH descriptor: [Economics] this term only	45
9	MeSH descriptor: [Value of Life] this term only	32
10	MeSH descriptor: [Costs and Cost Analysis] explode all trees	11515
11	MeSH descriptor: [Economics, Hospital] explode all trees	736
12	MeSH descriptor: [Economics, Medical] explode all trees	62
13	MeSH descriptor: [Economics, Nursing] explode all trees	13
14	MeSH descriptor: [Economics, Pharmaceutical] explode all trees	65
15	MeSH descriptor: [Fees and Charges] explode all trees	259

#	Searches	
16	MeSH descriptor: [Budgets] explode all trees	32
17	budget*:ti,ab	1284
18	cost*:ti,ab	75603
19	(economic* or pharmaco?economic*):ti,ab	21792
20	(price* or pricing*):ti,ab	2632
21	(financ* or fee or fees or expenditure* or saving*):ti,ab	22897
22	(value near/2 (money or monetary)):ti,ab	347
23	resourc* allocat*:ti,ab	4633
24	(fund or funds or funding* or funded):ti,ab	20420
25	(ration or rations or rationing* or rationed):ti,ab	713
26	{or #8-#25}	120278
27	MeSH descriptor: [Models, Economic] explode all trees	371
28	MeSH descriptor: [Models, Theoretical] this term only	744
29	MeSH descriptor: [Models, Organizational] this term only	180
30	MeSH descriptor: [Markov Chains] this term only	288
31	MeSH descriptor: [Monte Carlo Method] this term only	203
32	MeSH descriptor: [Decision Theory] explode all trees	174
33	(markov* or monte carlo):ti,ab	2214
34	econom* model*:ti,ab	7061
35	(decision* near/2 (tree* or analy* or model*)):ti,ab	2140
36	{or #27-#35}	11044
37	#26 or #36	123649
38	#7 and #37	1179
39	#7 and #37 with Cochrane Library publication date Between Jan 2012 and Aug 2022, in Cochrane Reviews	37

Database: Cochrane Central Register of Controlled Trials (CENTRAL) Issue 7 of 12, July 2022

Date of last search: 01/08/2022

#	Searches	
1	MeSH descriptor: [Climacteric] this term only	335
2	MeSH descriptor: [Menopause] this term only	1622
3	MeSH descriptor: [Perimenopause] this term only	168
4	MeSH descriptor: [Postmenopause] this term only	4982
5	(menopau* or postmenopau* or perimenopau* or climacteri*):ti,ab	27681
6	("change of life" or "life change" or "life changes"):ti,ab	444
7	{or #1-#6}	28529
8	MeSH descriptor: [Economics] this term only	45
9	MeSH descriptor: [Value of Life] this term only	32
10	MeSH descriptor: [Costs and Cost Analysis] explode all trees	11515
11	MeSH descriptor: [Economics, Hospital] explode all trees	736
12	MeSH descriptor: [Economics, Medical] explode all trees	62
13	MeSH descriptor: [Economics, Nursing] explode all trees	13
14	MeSH descriptor: [Economics, Pharmaceutical] explode all trees	65
15	MeSH descriptor: [Fees and Charges] explode all trees	259
16	MeSH descriptor: [Budgets] explode all trees	32
17	budget*:ti,ab	1284
18	cost*:ti,ab	75603
19	(economic* or pharmaco?economic*):ti,ab	21792
20	(price* or pricing*):ti,ab	2632
21	(financ* or fee or fees or expenditure* or saving*):ti,ab	22897
22	(value near/2 (money or monetary)):ti,ab	347
23	resourc* allocat*:ti,ab	4633

#	Searches	
24	(fund or funds or funding* or funded):ti,ab	20420
25	(ration or rations or rationing* or rationed):ti,ab	713
26	{or #8-#25}	120278
27	MeSH descriptor: [Models, Economic] explode all trees	371
28	MeSH descriptor: [Models, Theoretical] this term only	744
29	MeSH descriptor: [Models, Organizational] this term only	180
30	MeSH descriptor: [Markov Chains] this term only	288
31	MeSH descriptor: [Monte Carlo Method] this term only	203
32	MeSH descriptor: [Decision Theory] explode all trees	174
33	(markov* or monte carlo):ti,ab	2214
34	econom* model*:ti,ab	7061
35	(decision* near/2 (tree* or analy* or model*)):ti,ab	2140
36	{or #27-#35}	11044
37	#26 or #36	123649
38	#7 and #37	1179
39	"conference":pt or (clinicaltrials or trialsearch):so	608941
40	#38 not #39 with Publication Year from 2012 to 2022, in Trials	326

Database: EconLit <1886 to July 21, 2022>
Date of last search: 28/07/2022

#	Searches	
1	Climacteric/	0
2	Menopause/ or Perimenopause/ or Postmenopause/ or exp Menopause Related Disorder/	0
3	(menopau* or postmenopau* or perimenopau* or climacteri*).tw.	70
4	("change of life" or life change?).tw.	92
5	or/1-4	162
6	limit 5 to yr="2012 -Current"	69

Database: CRD HTA
Date of last search: 28/07/2022

#	Searches	
1	MeSH DESCRIPTOR Climacteric	9
2	MeSH DESCRIPTOR Menopause	117
3	MeSH DESCRIPTOR Perimenopause	7
4	MeSH DESCRIPTOR postmenopause	209
5	(((menopau* or postmenopau* or perimenopau* or climacteri*)))	957
6	((("change of life" or "life change" or "life changes")))	38
7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6) IN HTA FROM 2012 TO 2022	42

Database: INAHTA
Date of last search: 28/07/2022

#	Searches	
1	"Climacteric"[mh]	2
2	"Menopause"[mh]	28
3	"Perimenopause"[mh]	1
4	"Postmenopause"[mh]	31
5	(menopau* or postmenopau* or perimenopau* or climacteri*)	159
6	("change of life" or "life change" or "life changes")	1
7	#6 OR #5 OR #4 OR #3 OR #2 OR #1	163
8	Limit to English Language	134

1 Database: EED
2 Date of last search: 28/07/2022

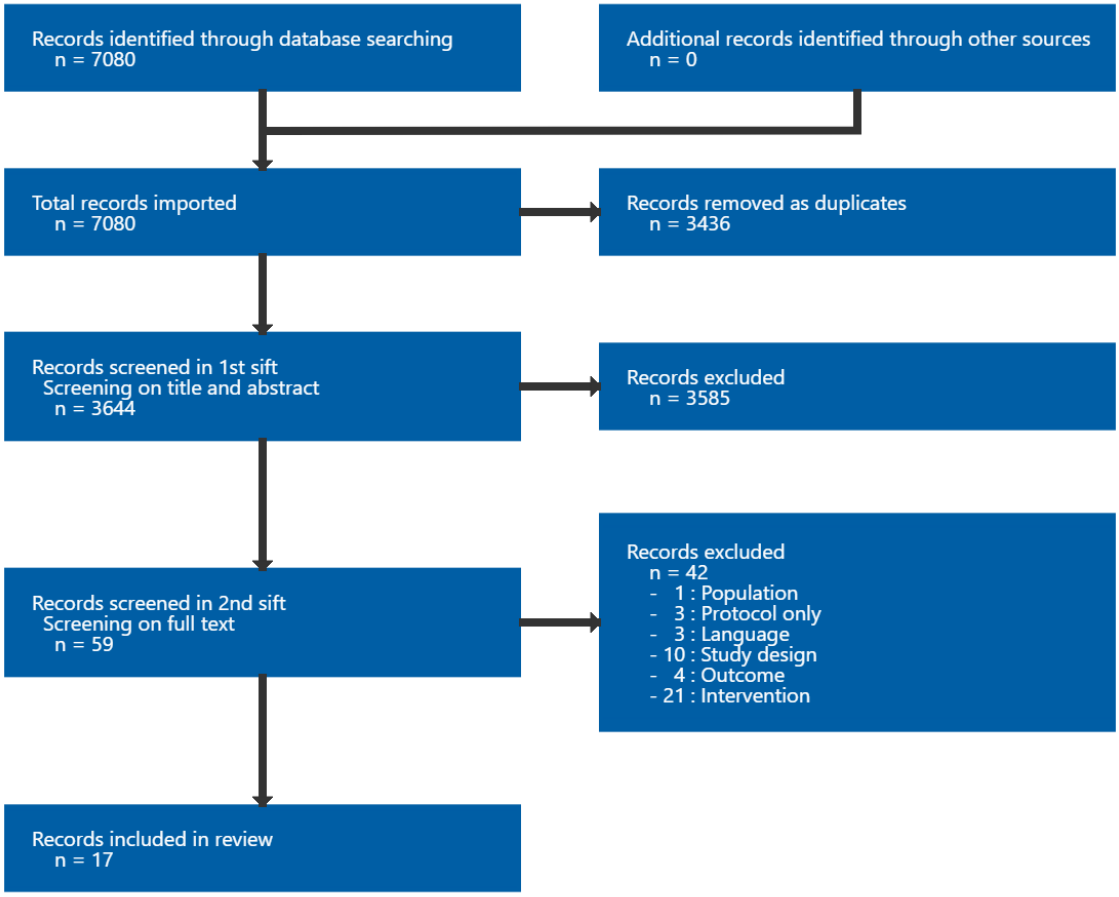
#	Searches	
1	MeSH DESCRIPTOR Climacteric	9
2	MeSH DESCRIPTOR Menopause	117
3	MeSH DESCRIPTOR Perimenopause	7
4	MeSH DESCRIPTOR postmenopause	209
5	(((menopau* or postmenopau* or perimenopau* or climacteri*)))	957
6	((("change of life" or "life change" or "life changes")))	38
7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6) IN NHSEED FROM 2012 TO 2022	33

3

Appendix C Effectiveness evidence study selection

Study selection for: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Table 5: Evidence tables

Abdelaziz, 2021

Bibliographic Reference Abdelaziz, Enas M; Elsharkawy, Nadia B; Mohamed, Sayeda M; Efficacy of Internet-based cognitive behavioral therapy on sleeping difficulties in menopausal women: A randomized controlled trial.; Perspectives in psychiatric care; 2021

Study details

Country where study was carried out	Saudi Arabia
Study dates	December 2020 to March 2021
Inclusion criteria	• menopausal women aged 50-60 years • the ability to read and write • experienced amenorrhea for at least 1 year (12 consecutive months without menstruation) • experienced poor sleep quality and insomnia in accordance with menopause • willing to provide written informed consent to participate in the study • a total score of >5 on the Pittsburgh Sleep Quality Index (PSQI), which indicates poor sleep, and a total score of >7 on the Insomnia Severity Index (ISI), which indicates insomnia • have a smartphone with Internet access • did not take sleeping medication
Exclusion criteria	• diagnosed as having sleep disturbances and had taken sleeping medications • serious or uncontrolled physical disorders • has insomnia disorder or other sleep disorders before menopause • receiving psychotropic medications or HRT • underwent hysterectomy • has cognitive impairments • had taken prescribed or nonprescribed clinical or herbal medications that influenced sleep

Patient characteristics	**Age, years - mean (SD):** All participants: 53.06 (4.28) Internet CBT: 53.90 (4.14) No treatment control: 52.23 (4.31) **Body mass index (BMI)** Not reported **Ethnicity** Not reported **Time since menopause, years - mean (SD):** Internet CBT: 4.60 (3.37) No treatment control: 4.30 (3.04) **Previous use of hormone replacement therapy (HRT)** Not reported **Duration of sleep difficulties - number (%)** **<6months** Internet CBT: 3 (7.5) No treatment control: 9 (22.5) **6 months to 1 year** Internet CBT: 28 (70.0) No treatment control: 16 (40.0) **1-2 years** Internet CBT: 5 (12.5) No treatment control: 9 (22.5) **>2 years** Internet CBT: 4 (10.0) No treatment control: 6 (15.0) **Perceived severity of hot flashes - number (%)** **Without symptoms** Internet CBT: 8 (20.0) No treatment control: 18 (45.0)

	Mild symptoms Internet CBT: 17 (42.5) No treatment control: 10 (25.0) **Moderate symptoms** Internet CBT: 10 (25.0) No treatment control: 12 (30.0) **Severe symptoms** Internet CBT: 5 (12.5) No treatment control: 0 (0.0) **Perceived severity of night sweating - number (%)** **Without symptoms** Internet CBT: 20 (50.0) No treatment control: 23 (57.5) **Mild symptoms** Internet CBT: 13 (32.5) No treatment control: 10 (25.0) **Moderate symptoms** Internet CBT: 7 (17.5) No treatment control: 6 (15.0) **Severe symptoms** Internet CBT: 0 (0.0) No treatment control: 1 (2.5)
Intervention(s)/control	**Internet CBT** • CBT intervention via six online modules (WhatsApp) • the program incorporated cognitive intervention (cognitive restructuring), psychoeducation (sleep environment improvement), and behavioural intervention (sleep hygiene education, stimulus control strategies, sleep restriction strategies, and relaxation training) • modules contained information on sleep and instructions for relaxation techniques, such as breathing exercises, progressive muscle relaxation (PMR), biofeedback, guided imagery, and meditation, to practice, and homework assignments • estimated time for module completion was one hour, and additional 20–30 min for homework assignments • each module contained a reflection of and feedback from the previous module, a PowerPoint presentation to schedule topics, researchers' instructions, homework assignments, and videos about the application of the

	recommended practical skills • weekly feedback via WhatsApp or email • a fixed time was allowed for discussion between researchers and participants via text messaging, phone calls, or email **No treatment (control group)** • limited interaction between researchers and participants • researchers answered the concerns and needs of the participants without intervention
Duration of follow-up	6 weeks
Sources of funding	Funded by the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia; grant number 1384754968
Sample size	N=98 randomised Internet CBT: n=49 randomised (n=40 analysed) No treatment control: n=49 randomised (n=40 analysed)

Outcomes

Study timepoints

- Baseline
- 6 weeks

Outcomes

Outcome	Internet CBT, Baseline, N = 40	Internet CBT, 6 weeks, N = 40	No treatment control, Baseline, N = 40	No treatment control, 6 weeks, N = 40
Sleep Quality (PSQI) Pittsburgh Sleep Quality Index; Global PSQI score with higher scores indicating poorer sleep quality Mean (SD)	10.5 (2.73)	6.9 (2.09)	9.63 (2.56)	9.53 (2.7)

Outcome	Internet CBT, Baseline, N = 40	Internet CBT, 6 weeks, N = 40	No treatment control, Baseline, N = 40	No treatment control, 6 weeks, N = 40
Discontinuation for any reason 6 weeks No of events	n = 0; % = 0	n = 9; % = 18.4	n = 0; % = 0	n = 9; % = 18.4

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information about concealment of the allocation sequence and any baseline differences observed between intervention groups appear to be compatible with chance)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Outcome data were not available for all, or nearly all, randomized participants and there is not evidence that the result was not biased by missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(It is likely that assessment of the outcome was influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one domain for this result)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Atema, 2019**

Bibliographic Reference Atema, Vera; van Leeuwen, Marieke; Kieffer, Jacobien M; Oldenburg, Hester S A; van Beurden, Marc; Gerritsma, Miranda A; Kuenen, Marianne A; Plaisier, Peter W; Lopes Cardozo, Alexander M F; van Riet, Yvonne E A; Heuff, Gijsbert; Rijna, Herman; van der Meij, Suzan; Noorda, Eva M; Timmers, Gert-Jan; Vrouenraets, Bart C; Bollen, Matthe; van der Veen, Henk; Bijker, Nina; Hunter, Myra S; Aaronson, Neil K; Efficacy of Internet-Based Cognitive Behavioral Therapy for Treatment-Induced Menopausal Symptoms in Breast Cancer Survivors: Results of a Randomized Controlled Trial.; Journal of clinical oncology : official journal of the American Society of Clinical Oncology; 2019; vol. 37 (no. 10); 809-822

3 **Study details**

Country where study was carried out	Netherlands
Study type	Randomised controlled trial (RCT)
Study dates	None specified
Inclusion criteria	• women with histologically confirmed BC • aged≥ 50 years of age at the time of diagnosis • had undergone chemotherapy and/or an oophorectomy (completed at a minimum of 4 months and a maximum of 5 years before study entry, with the exception of trastuzumab use) and/or endocrine treatment (including ongoing use) • disease free at the time of study entry • experienced treatment-induced problematic HF/ NS (as indicated by an average score of ≥ 2 on the problem rating subscale of the Hot Flush Rating Scale [HFRS]) for at least 2 months, with a minimum of 10 HF/NS in the past week.
Exclusion criteria	• women with a prior diagnosis of another type of cancer (except basal cell carcinoma) • serious overt cognitive or psychiatric comorbidity • did not speak Dutch • no Internet access • participating in concurrent studies/rehabilitation programs aimed at alleviating or coping with menopausal symptoms

Patient characteristics	**Internet-based cognitive behavioural therapy (iCBT)** **Age, years - mean (SD):** All participants: 47.4 (5.45) Guided iCBT: 47.5 (5.14) Self-managed iCBT: 47.7 (5.73) Waiting list control: 47.0 (5.50) **BMI, kg/m2 - mean (SD):** Guided iCBT: 26.41 (5.48) Self-managed iCBT: 26.22 (4.41) Waiting list control: 25.73 (4.16) **Ethnicity** Not reported **Time since diagnosis, years - mean (SD)** Guided iCBT: 3.2 (1.33) Self-managed iCBT: 3.0 (1.29) Waiting list control: 3.0 (1.33) **Time since diagnosis - Number (%)** **<1** Guided iCBT: 0 (0.0) Self-managed iCBT: 2 (2.4) Waiting list control: 1 (1.2) **1-2** Guided iCBT: 38 (44.7) Self-managed iCBT: 48 (56.5) Waiting list control: 43 (51.2) **3-5** Guided iCBT: 35 (41.2) Self-managed iCBT: 27 (31.8) Waiting list control: 30 (35.7) **>5** Guided iCBT: 12 (14.1) Self-managed iCBT: 8 (9.4)

	Waiting list control: 10 (11.9) **Previous use of hormone replacement therapy (HRT)** Not reported **Sleep difficulties** Not reported **Duration of HF/NS - Number (%)** **2-6 months** Guided iCBT: 4 (4.7) Self-managed iCBT: 4 (4.7) Waiting list control: 8 (9.5) **7-12 months** Guided iCBT: 15 (17.6) Self-managed iCBT: 15 (17.6) Waiting list control: 8 (9.5) **1-3 years** Guided iCBT: 46 (54.1) Self-managed iCBT: 45 (52.9) Waiting list control: 51 (60.7) **>3 years** Guided iCBT: 20 (23.5) Self-managed iCBT: 21 (24.7) Waiting list control: 17 (20.2)
Intervention(s)/control	**Guided Internet-based cognitive behavioural therapy (iCBT)** • 6 week internet CBT program focussed on HF/NS and included stress management and sleep problems topics • 6 modules which included self-reflection, psycho-education, assignments and a diary application to register HF/NS • information was provided through written texts and video clips presented by experts and BC survivors with similar menopausal symptoms. • Estimated time per module was 1 hour per week and an additional 30 minutes per day to carry out relaxation and homework assignments • weekly reminders • a telephone interview before the start of the program and weekly written feedback throughout provided by trained

	medical social workers and psychologists with access to the online entries of the women • additional contact could take place through a built-in e-mail application when required **Self-managed Internet-based cognitive behavioural therapy (iCBT)** • 6 week internet CBT program focussed on HF/NS and included stress management and sleep problems topics • six modules which included self-reflection, psycho-education, assignments and a diary application to register HF/NS • information was provided through written texts and video clips presented by experts and BC survivors with similar menopausal symptoms. • Estimated time per module was 1 hour per week and an additional 30 minutes per day to carry out relaxation and homework assignments • weekly reminders **Waiting list control (usual care)** • no specific programs or clinical pathways for dealing with menopausal symptoms • participants could complete the CBT program after the last follow-up assessment
Duration of follow-up	10 weeks and 24 weeks
Sources of funding	Supported by the Dutch Cancer Society (Grant No. NKI 2014-6788) and The Netherlands Cancer Institute
Sample size	N=254 randomised Guided iCBT: n=85 randomised (n=82 at 10 week follow-up; n=79 at 24 week follow-up) Self managed iCBT: n=85 randomised (n=80 at 10 week follow-up; n=77 at 24 week follow-up) Waiting list control: n=84 randomised (n=80 at 10 week follow-up; n=80 at 24 week follow-up) Analyses conducted as intention to treat

1 **Outcomes**

Outcome	Guided iCBT, Baseline, N = 85	Guided iCBT, 10 weeks, N = 85	Guided iCBT, 24 weeks, N = 85	Self-managed iCBT, Baseline, N = 85	Self-managed iCBT, 10 weeks, N = 85	Self-managed iCBT, 24 weeks, N = 85	Waiting list control, Baseline, N = 84	Waiting list control10 weeks, N = 84	Waiting list control, 24 weeks, N = 84
Perceived impact of HF/NS (HFRS problem rating) Hot flush rating scale (range 0-10 with higher scores indicating higher perceived impact of hot flushes/night sweats) Mean (SD)	4.98 (1.88)	3.27 (1.86)	3.34 (1.85)	4.89 (1.88)	3.33 (1.85)	3.41 (1.85)	4.7 (1.88)	4.18 (1.86)	3.96 (1.86)
Overall levels or menopausal symptoms (FACT-ES) Functional Assessment of Cancer Therapy-Endocrine Symptoms (range 0-72 with higher scores indicating fewer menopausal symptoms) Mean (SD)	50.23 (8.72)	53.88 (8.67)	53.02 (8.58)	51.22 (8.75)	53.81 (8.61)	54.61 (8.53)	50.01 (8.75)	50.82 (8.63)	50.4 (8.65)
Hot flush frequency (HFRS hot flush frequency) Hot flush rating scale (weekly frequency of hot flushes) Mean (SD)	55.22 (39.58)	39.44 (39.24)	40.35 (39.14)	48.79 (39.58)	38.76 (39.08)	34.03 (39.05)	48.5 (39.58)	46.1 (39.23)	52.54 (39.38)
Night sweats frequency (HFRS night sweats frequency) Hot flush rating scale (weekly frequency of night sweats)	18.29 (13.21)	10.34 (13.16)	11.46 (13.14)	18.17 (13.19)	14.28 (13.16)	12.07 (13.09)	18.75 (13.21)	19.25 (13.15)	17.56 (13.16)

Outcome	Guided iCBT, Baseline, N = 85	Guided iCBT, 10 weeks, N = 85	Guided iCBT, 24 weeks, N = 85	Self-managed iCBT, Baseline, N = 85	Self-managed iCBT, 10 weeks, N = 85	Self-managed iCBT, 24 weeks, N = 85	Waiting list control, Baseline, N = 84	Waiting list control10 weeks, N = 84	Waiting list control, 24 weeks, N = 84
Mean (SD)									
Sexual pleasure (SAQ pleasure) Sexual Activity Questionnaire (sexual pleasure subscale range 0-18 with higher scores indicating higher levels of sexual pleasure) Mean (SD)	7.03 (4.63)	7.61 (4.56)	7.58 (4.53)	6.07 (4.63)	6.46 (4.51)	7.14 (4.47)	7.32 (4.63)	7.44 (4.56)	6.95 (4.55)
Discomfort during sex (SAQ discomfort) Sexual Activity Questionnaire (sexual discomfort subscale range 0-6 with lower scores indicating lower levels of discomfort) Mean (SD)	2.34 (1.76)	2.19 (1.75)	2.05 (1.75)	2.17 (1.79)	1.9 (1.72)	1.83 (1.73)	2.11 (1.75)	2.19 (1.7)	2.23 (1.69)
Intercourse frequency (SAQ habit) Sexual Activity Questionnaire (sexual habit subscale range 0-3 with higher scores indicating more sexual activity) Mean (SD)	0.53 (0.71)	0.49 (0.71)	0.5 (0.71)	0.46 (0.71)	0.49 (0.71)	0.54 (0.71)	0.55 (0.71)	0.59 (0.71)	0.41 (0.71)
Anxiety (HADS) Hospital Anxiety and Depression Scale (anxiety subscale ranges 0-21 with higher	7.06 (4.01)	5.76 (3.95)	6.53 (3.92)	6.36 (4.01)	5.38 (3.91)	5.64 (3.88)	6.85 (4.01)	6.24 (3.95)	6.53 (3.94)

Outcome	Guided iCBT, Baseline, N = 85	Guided iCBT, 10 weeks, N = 85	Guided iCBT, 24 weeks, N = 85	Self-managed iCBT, Baseline, N = 85	Self-managed iCBT, 10 weeks, N = 85	Self-managed iCBT, 24 weeks, N = 85	Waiting list control, Baseline, N = 84	Waiting list control10 weeks, N = 84	Waiting list control, 24 weeks, N = 84
scores indicating more anxiety) Mean (SD)									
Physical functioning (SF-36 physical functioning) 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	77.94 (19.61)	79.42 (19.3)	79.49 (19.19)	80.94 (19.61)	81.08 (19.15)	81.91 (18.98)	78.27 (19.61)	77.58 (19.31)	77.64 (19.27)
Role limitations as a result of physical problems (SF-36 role physical) 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	60 (38.68)	69.41 (38.36)	61.97 (38.2)	65 (38.68)	68.91 (38.11)	66.68 (37.96)	61.61 (38.68)	69.57 (38.14)	65.7 (38.31)
Bodily pain (SF-36 bodily pain) 10 weeks; 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	65.12 (22.76)	65.92 (22.53)	66.86 (22.4)	66.51 (22.76)	68.72 (22.41)	68.73 (22.21)	67.56 (22.76)	66.72 (22.54)	67.07 (22.47)
General health perceptions (SF-36 general health)	62.75 (21.54)	63.76 (21.23)	62.79 (21.13)	61.77 (21.54)	62.19 (21.08)	62.94 (20.93)	64.4 (21.54)	63.63 (21.24)	62.01 (21.22)

Outcome	Guided iCBT, Baseline, N = 85	Guided iCBT, 10 weeks, N = 85	Guided iCBT, 24 weeks, N = 85	Self-managed iCBT, Baseline, N = 85	Self-managed iCBT, 10 weeks, N = 85	Self-managed iCBT, 24 weeks, N = 85	Waiting list control, Baseline, N = 84	Waiting list control10 weeks, N = 84	Waiting list control, 24 weeks, N = 84
36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)									
Vitality subscale of the SF-36 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	53.9 (18.16)	60.82 (17.94)	58.94 (17.82)	56.55 (18.16)	60.69 (17.83)	60.3 (17.66)	55.54 (18.16)	57.23 (17.94)	56.05 (17.89)
Social functioning SF-36 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	74.3 (21.75)	81.96 (21.52)	78.68 (21.4)	80.25 (20.59)	81.63 (20.36)	83.39 (20.16)	77.61 (20.51)	79.88 (20.35)	80.11 (20.27)
Role emotional SF-36 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher levels of functioning/well-being) Mean (SD)	75.29 (34.36)	79.36 (34.23)	75.38 (34.16)	77.26 (34.36)	80.49 (34.17)	78.74 (34.06)	77.78 (34.36)	82.55 (34.24)	75.46 (34.21)
Mental health SF-36 36-item Short Form Health Survey (range 0-100 with higher scores indicating higher	72.82 (16.46)	77.77 (16.26)	75.29 (16.16)	75.82 (16.46)	76.98 (16.16)	76.88 (16.02)	73.82 (16.46)	75.35 (16.26)	73.01 (16.23)

Outcome	Guided iCBT, Baseline, N = 85	Guided iCBT, 10 weeks, N = 85	Guided iCBT, 24 weeks, N = 85	Self-managed iCBT, Baseline, N = 85	Self-managed iCBT, 10 weeks, N = 85	Self-managed iCBT, 24 weeks, N = 85	Waiting list control, Baseline, N = 84	Waiting list control10 weeks, N = 84	Waiting list control, 24 weeks, N = 84
levels of functioning/well-being) Mean (SD)									
Sleep quality (GSQS) Groningen Sleep Quality Scale (range, 0-14 with higher scores indicating lower sleep quality) Mean (SD)	8.45 (3.86)	6.15 (3.82)	6.3 (3.8)	8.56 (3.85)	6.89 (3.79)	6.98 (3.75)	8.49 (3.86)	8.4 (3.82)	8.15 (3.81)
Discontinuation for any reason 10 weeks No of events		n = 3; % = 3.5			n = 5; % = 5.9			n = 4; % = 4.8	
24 weeks No of events		n = 6; % = 7			n = 8; % = 9.4			n = 4; % = 4.8	

1

2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information about concealment of the allocation sequence and any baseline differences observed between intervention groups appear to be compatible with chance)*
Domain 2a: Risk of bias due to deviations	Risk of bias for deviations from the	Low

Section	Question	Answer
from the intended interventions (effect of assignment to intervention)	intended interventions (effect of assignment to intervention)	
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Outcome data were not available for all, or nearly all, randomized participants and there is not evidence that the result was not biased by missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(It is likely that assessment of the outcome was influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one domain for this result)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Ayers, 2012**

Bibliographic Reference Ayers B; Smith M; Hellier J; Mann E; Hunter MS; Effectiveness of group and self-help cognitive behavior therapy in reducing problematic menopausal hot flushes and night sweats (MENOS 2): a randomized controlled trial.; Menopause (New York, N.Y.); 2012; vol. 19 (no. 7)

3 **Study details**

Country where study was carried out	United Kingdom, England
Study type	Randomised controlled trial (RCT)
Study dates	March 2009 to May 2010
Inclusion criteria	• English speaking

	• 18 years or older • having problematic HF/NS (hot flush/night sweats) score above 2 on the HFRS (hot flush rating scale) for at least a month • minimum weekly frequency of HF/NS of 10 • living within travelling distance of London • willing to maintain or report changes in menopausal treatment during the trial
Exclusion criteria	• non-English speaking • history of breast cancer • having medical or psychiatric conditions that would affect the ability to participate.
Patient characteristics	**Age, years - mean (SD):** All participants: 53.09 (5.4) Group CBT: 53.73 (5.9) Self-help CBT: 51.70 (4.4) No treatment control: 53.87 (5.7) **BMI (overweight/ obese) - number (%):** Group CBT: 19 (43%) Self-help CBT: 22 (49%) No treatment control: 23 (57%) **Ethnicity – number (%)** **White** Group CBT: 39 (82) Self-help CBT: 41 (87) No treatment control: 35 (78) **Asian** Group CBT: 2 (4) Self-help CBT: 1 (2) No treatment control: 1 (2) **Black** Group CBT: 5 (10) Self-help CBT: 4 (9) No treatment control: 6 (13)

	Other Group CBT: 2 (4) Self-help CBT: 1 (2) No treatment control: 3 (7) **Menopause status - Menopausal transition - number (%):** Group CBT: 17 (35%) Self-help CBT: 24 (51%) No treatment control: 15 (33%) **Menopause status - Postmenopausal:** Group CBT: 31 (65%) Self-help CBT: 23 (49%) No treatment control: 30 (67%) **Using HT - number (%):** Group CBT: 2 (4%) Self-help CBT: 1 (2%) No treatment control: 1 (2%) **Used HT in the past - number (%):** Group CBT: 15 (31%) Self-help CBT: 10 (21%) No treatment control: 14 (31%) **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**Group CBT** • 2 hour sessions, once a week for 4 weeks (8 hours in total). • Delivered by clinical psychologist. • Sessions focused on psychoeducation, stress management, paced breathing and CBT.

	• CBT of HF/NS based on a theoretical model of HF/NS. • Sessions audio recorded and 10% rated by a clinical psychologist for adherence to the manual. **Self-help CBT** • Self-help book completed during a 4-week period and two contacts with a clinical psychologist (one introductory session, and a telephone call 2 weeks into treatment. • Content of self-help CBT was identical to group CBT. • Participants received the CD for daily practice and homework. **No treatment (control group)** • Participants did not receive CBT treatment during the treatment phase. • Able to access their GP and other healthcare options. • Offered a form of CBT at the end of the study.
Duration of follow-up	6 and 26 weeks
Sources of funding	Not industry funded
Sample size	N=140 randomised Group CBT: n=48 randomised (n=46 analysed) Self-help CBT: n=47 randomised (n=40 analysed) No treatment control: n=45 randomised (n=43 analysed)

1 **Study arms**

2 **Group CBT (N = 48)**

3 **Self-help CBT (N = 47)**

4 **No treatment control (N = 45)**

5 **Outcomes**

Outcome	Group CBT, Baseline, N = 48	Group CBT, 6 weeks, N = 48	Group CBT, 26 weeks, N = 48	Self-help CBT, Baseline, N = 47	Self-help CBT, 6 weeks, N = 47	Self-help CBT, 26 weeks, N = 47	No treatment control, Baseline, N = 45	No treatment control, 6 weeks N = 45	No treatment control, 26 weeks, N = 45
SF-36 physical functioning Mean (SD)	83.19 (18.28)	81.43 (18.88)	86.92 (13.55)	87.23 (13.51)	90.47 (12.53)	86.5 (20.56)	74.67 (27.97)	80.38 (18.08)	73.59 (28.68)
SF-36 role-physical Mean (SD)	80.32 (36.09)	82.14 (32.33)	80.77 (34.63)	80.32 (29.46)	83.59 (28.12)	82.5 (32.92)	60.8 (42.55)	68.59 (37.04)	62.82 (45.11)
SF-36 bodily pain Mean (SD)	65.53 (23.39)	67.14 (20.52)	68.21 (19.04)	65.74 (22.82)	70.63 (20.94)	66.33 (23.27)	55.78 (22.41)	58.21 (26.44)	55.64 (24.37)
SF-36 general health Mean (SD)	68.83 (20.28)	69.76 (18.64)	72.95 (20.28)	68.09 (17.59)	74.84 (15.89)	73.17 (15.28)	69.09 (20.01)	67.95 (22.03)	68.59 (19.87)
SF-36 vitality	49.26 (21.72)	58.21 (22.95)	57.18 (24.78)	48.83 (17.76)	55 (19.92)	58 (19.01)	46.44 (20.02)	51.03 (21.74)	53.21 (19.31)

Outcome	Group CBT, Baseline, N = 48	Group CBT, 6 weeks, N = 48	Group CBT, 26 weeks, N = 48	Self-help CBT, Baseline, N = 47	Self-help CBT, 6 weeks, N = 47	Self-help CBT, 26 weeks, N = 47	No treatment control, Baseline, N = 45	No treatment control, 6 weeks N = 45	No treatment control, 26 weeks, N = 45
Mean (SD)									
SF-36 social functioning Mean (SD)	77.66 (25.17)	84.53 (20.81)	86.86 (22.39)	74.2 (23.37)	85.16 (20.93)	87.5 (19.14)	70.28 (28.49)	80.13 (24.12)	78.53 (28.53)
SF-36 role-emotional Mean (SD)	67.38 (39)	80.16 (31.29)	82.05 (34.92)	70.92 (36.53)	77.08 (34.33)	86.67 (28.5)	70.46 (41.43)	73.5 (38.37)	68.23 (42.84)
SF-36 Mental Health Mean (SD)	69.02 (19.64)	76.48 (14.39)	76.31 (19.88)	64.77 (15.37)	72.25 (12.61)	72.8 (14.8)	65.24 (21.57)	69.95 (19.68)	70.26 (16.64)
Hot flush frequency Mean (SD)	43.75 (34.31)	33.85 (36.39)	29.18 (47.3)	53.34 (50.21)	36.38 (30.21)	35 (37.21)	38.8 (43.41)	34.67 (41.23)	28.3 (33.22)
Night sweat frequency Mean (SD)	18.08 (12.29)	10 (9.62)	8.59 (11.83)	17.34 (12.16)	12.83 (11.85)	9.94 (8.78)	17.89 (13.04)	15 (12.85)	15.75 (18.92)
HF problem rating (1-10)	6 (2.15)	3.01 (2.11)	2.86 (2.11)	5.84 (1.93)	2.96 (1.76)	3.07 (1.93)	5.79 (2.76)	4.97 (2.44)	4.18 (2.45)

Outcome	Group CBT, Baseline, N = 48	Group CBT, 6 weeks, N = 48	Group CBT, 26 weeks, N = 48	Self-help CBT, Baseline, N = 47	Self-help CBT, 6 weeks, N = 47	Self-help CBT, 26 weeks, N = 47	No treatment control, Baseline, N = 45	No treatment control, 6 weeks N = 45	No treatment control, 26 weeks, N = 45
Mean (SD)									
WHQ sleep problems 6 weeks Mean (SD)	0.7 (0.3)	0.49 (0.36)	0.53 (0.32)	0.64 (0.31)	0.36 (0.3)	0.41 (0.31)	0.7 (0.31)	0.57 (0.35)	0.57 (0.36)
WHQ anxiety/fears Mean (SD)	0.46 (0.31)	0.23 (0.29)	0.26 (0.29)	0.43 (0.28)	0.29 (0.25)	0.26 (0.29)	0.43 (0.31)	0.36 (0.34)	0.33 (0.33)
WHQ depressed mood Mean (SD)	0.27 (0.22)	0.16 (0.2)	0.19 (0.2)	0.33 (0.23)	0.21 (0.19)	0.15 (0.18)	0.3 (0.28)	0.28 (0.24)	0.23 (0.2)
Discontinuation for any reason No of events	NA	n = 2; % = 4.2	n = 7; % = 14.6	NA	n = 7; % = 14.9	n = 8; % = 17	NA	n = 2; % = 4.4	n = 3; % = 6.7

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to	Risk of bias for deviations from the	Low

Section	Question	Answer
deviations from the intended interventions (effect of assignment to intervention)	intended interventions (effect of assignment to intervention)	
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Outcome data was available for 92% of randomized participants. There is no evidence that the result was not biased by missing outcome data and missingness in the outcome could depend on its true value, though this is not likely)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Cheng, 2020**

Bibliographic Reference Cheng, Philip; Kalmbach, David; Fellman-Couture, Cynthia; Arnedt, J Todd; Cuamatzi-Castelan, Andrea; Drake, Christopher L; Risk of excessive sleepiness in sleep restriction therapy and cognitive behavioral therapy for insomnia: a randomized controlled trial.; Journal of clinical sleep medicine: JCSM : official publication of the American Academy of Sleep Medicine; 2020; vol. 16 (no. 2); 193-198

3 **Study details**

Country where study was carried out	US
Study dates	None specified

Inclusion criteria	• postmenopausal women meeting Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for insomnia disorder • showed objective sleep disturbance via polysomnography at baseline as defined by wake after sleep onset ≥ 45 minutes.
Exclusion criteria	• prior or current Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition major depression per diagnostic interview • sleep-wake disorders other than insomnia (examined on polysomnography adaptation night and per patient report) • medications influencing sleep
Patient characteristics	**Age, years - mean (SD)** All participants (including those randomised to sleep restriction therapy): 56.44 (5.65) **Body mass index (BMI)** Not reported **Ethnicity (%)** Total sample: Non-Hispanic white: 52% Non-Hispanic Black: 39.3% **Age at menopause or last menstrual period** Not reported **Previous use of hormone replacement therapy (HRT)** Not reported **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**Insomnia CBT**

	• six face-to-face weekly sleep therapy sessions with a registered nurse specialized in behavioural sleep medicine • sessions covered behavioural (sleep restriction and stimulus control) and cognitive components (eg, cognitive restructuring), as well as relaxation strategies (eg, progressive muscle relaxation and autogenic training) and sleep hygiene education • sleep restriction and stimulus control were introduced during the first and second sessions and reviewed as necessary throughout the treatment **Sleep education (TAU)** • six weekly psychoeducation emails that also included sleep hygiene According to the study authors sleep hygiene was not considered the primary cause nor a sufficient therapeutic target in insomnia disorder and therefore served as an ideal minimal intervention control condition and real-world comparator.
Duration of follow-up	6 weeks
Sources of funding	None specified
Sample size	N=150 randomised Insomnia CBT: n=50 randomised Sleep education (TAU): n=50 randomised Note: N=6 participants at pre-treatment, and n=9 participants at post-treatment had technological errors or difficulties that precluded the valid and reliable scoring of the Multiple Sleep Latency Test. Subsequently this data was excluded from analyses. It was unclear as to which treatment group the excluded participants belonged.
Other information	Secondary analysis from Kalmbach 2019. The study was a three armed trial, but data was not extracted for the sleep restriction therapy group as the intervention was not relevant for this review.

Outcomes

Study timepoints

- Baseline
- 6 weeks

1 **Outcomes**

Outcome	Insomnia CBT, Baseline, N = 50	Insomnia CBT, 6 weeks, N = 50	Sleep education (TAU), Baseline, N = 50	Sleep education (TAU), 6 weeks, N = 50
Mean sleep onset latency (MSLT) Mean Sleep Latency Test; Range 0-20 with lower scores indicating more daytime sleepiness Mean (SD)	10.3 (6.2)	10.6 (5.4)	12.1 (5)	11.2 (5.4)

2

3 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information about the randomisation process nor concealment of the allocation sequence. Baseline differences observed between intervention groups appear to be compatible with chance)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(An appropriate analysis was not used to estimate the effect of assignment to intervention. Data was excluded from analyses, and the potential impact (on the estimated effect of intervention) of the failure to analyse participants in the group to which they were randomized was substantial)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(Outcome data were not available for nine participants where technological errors or difficulties precluded the valid and reliable scoring of the Multiple Sleep Latency Test. There is no evidence that the result was not biased by the missing outcome data. Missingness in the outcome could depend on its true value and it is likely that missingness in the outcome depended on its true value.)*

Section	Question	Answer
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(Due to technological errors or difficulties that precluded the valid and reliable scoring of the Multiple Sleep Latency Test, the measurement or ascertainment of the outcome could have differed between intervention groups)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There is no information on whether the result being assessed is likely to have been selected, on the basis of the results, from multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain and from multiple eligible analyses of the data)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in four domains)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Drake, 2019**

Bibliographic Reference Drake, Christopher L; Kalmbach, David A; Arnedt, J Todd; Cheng, Philip; Tonnu, Christine V; Cuamatzi-Castelan, Andrea; Fellman-Couture, Cynthia; Treating chronic insomnia in postmenopausal women: a randomized clinical trial comparing cognitive-behavioral therapy for insomnia, sleep restriction therapy, and sleep hygiene education.; Sleep; 2019; vol. 42 (no. 2)

3 **Study details**

Country where study was carried out	US
Study dates	None specified
Inclusion criteria	• postmenopausal women (12 consecutive months without menses) • reporting wake after sleep onset (WASO; wakefulness in the middle of the night after falling asleep) of an hour or more on ≥3 nights per week • meeting criteria for DSM-5 insomnia disorder that onset or was exacerbated during the perimenopausal or postmenopausal period per clinical interview with a registered nurse with specialty training in behavioural sleep medicine

	• endorse that current insomnia onset or worsened within ±6 months of menopause • objective sleep disturbance had to be evident per mean wake after sleep onset (WASO) of ≥45 min across two overnight polysomnography studies (adaptation night + baseline night, and neither night could have WASO of <30 min)
Exclusion criteria	• prior or current DSM-5 major depression per diagnostic interview • sleep–wake disorders other than insomnia [examined on PSG adaptation night (obstructive sleep apnoea defined as apnoea–hypopnea index of ≥15, periodic limb movements defined as arousal frequency of ≥15) and per patient report] • medications influencing sleep (prescription and non-prescription sleep aids, herbal supplements, and any antidepressants taken at night) Note: women receiving hormone therapy were permitted to participate
Patient characteristics	**Age, years - mean (SD):** All participants (including those randomised to sleep restriction therapy): 56.44 (5.64) Insomnia CBT: 55.32 (5.90) Sleep hygiene (TAU): 57.24 (5.55) **Body mass index (BMI)** Not reported **Ethnicity – number (%)** **White** Insomnia CBT: 24 (48) Sleep hygiene (TAU): 26 (52) **Black** Insomnia CBT: 22 (44) Sleep hygiene (TAU): 20 (40) **Hispanic or Latinx** Insomnia CBT: 0 (0) Sleep hygiene (TAU): 0 (0) **Multiracial** Insomnia CBT: 0 (0) Sleep hygiene (TAU): 0 (0) **Other**

	Insomnia CBT: 1 (2) Sleep hygiene (TAU): 1 (2) **Did not answer** Insomnia CBT: 3 (6) Sleep hygiene (TAU): 3 (6) **Years since last menstruation - mean (SD)** Insomnia CBT: 7.09 (6.65) Sleep hygiene (TAU): 7.33 (7.79) **Hormone replacement therapy - number (%)** Insomnia CBT: 0 (0.0) Sleep hygiene (TAU): 3 (6.0) Sleep restriction: 1 (2.0) **Wake after sleep onset – mean (SD)** Insomnia CBT: 49.07 (31.14) Sleep hygiene (TAU): 61.83 (39.5) **Vasomotor symptoms** Not reported
Intervention(s)/control	**Insomnia CBT** • 6 face-to-face weekly sleep therapy sessions with a registered nurse who specializes in behavioural sleep medicine • structured, multimodal treatment targeting sleep-disruptive behaviours and beliefs • sessions covered behavioural (sleep restriction and stimulus control) and cognitive (e.g. cognitive restructuring) components, relaxation strategies (e.g. progressive muscle relaxation and autogenic training) and sleep hygiene • fidelity monitoring **Sleep hygiene (TAU)** • 6 weekly emails on the basics of endogenous sleep regulation, the impact of sleep on health problems such as obesity, diabetes, and hypertension, the effects of stimulants and other sleep-disruptive substances, the

	relationship between sleep, diet, and exercise, and tips on creating a sleep-conducive bedroom environment According to the study authors sleep hygiene was not considered the primary cause nor a sufficient therapeutic target in insomnia disorder and therefore served as an ideal minimal intervention control condition and real-world comparator.
Duration of follow-up	6 weeks and 6 months
Sources of funding	Funded by the National Institute of Nursing Research (R01 NR013959, PI: Drake)
Sample size	N=154 randomised Insomnia CBT: n=52 randomised (n=50 analysed) Sleep hygiene (TAU): n=50 randomised (n=50 analysed)
Other information	Secondary analysis from Kalmbach 2019. The study was a three armed trial, but data was not extracted for the sleep restriction therapy group as the intervention was not relevant for this review

Study timepoints

- Baseline
- 6 weeks
- 6 months

Outcomes

Outcome	Insomnia CBT, Baseline, N = 50	Insomnia CBT, 6 weeks, N = 50	Insomnia CBT, 6 months, N = 41	Sleep hygiene (TAU), Baseline, N = 50	Sleep hygiene (TAU), 6 weeks, N = 50	Sleep hygiene (TAU), 6 months, N = 43
Insomnia Severity Index (ISI) 7-item self-reporting measure with higher scores indicating increasing insomnia severity Mean (SD)	14.94 (3.94)	7.24 (4.18)	6.95 (5.26)	15.36 (4.36)	14.24 (4.49)	13.44 (4.64)

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(it is unclear whether an appropriate analysis was used to estimate the effect of assignment to intervention, however the potential impact (on the estimated effect of intervention) of the failure to analyse participants in the group to which they were randomized was not substantial)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in one domain but is not at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

Duijts, 2012

Bibliographic Reference Duijts, Saskia F.A.; van Beurden, Marc; Oldenburg, Hester S.A.; Hunter, Myra S.; Kieffer, Jacobien M.; Stuiver, Martijn M.; Gerritsma, Miranda A.; Menke-Pluymers, Marian B.E.; Plaisier, Peter W.; Rijna, Herman; Lopes Cardozo, Alexander M.F.; Timmers, Gertjan; van der Meij, Suzan; van der Veen, Henk; Bijker, Nina; de Widt-Levert, Louise M.; Geenen, Maud M.; Heuff, Gijsbert; van Dulken, Eric J.; Boven, Epie; Aaronson, Neil K.; Efficacy of Cognitive Behavioral Therapy and Physical Exercise in Alleviating Treatment-Induced Menopausal Symptoms in Patients With Breast Cancer: Results of a Randomized, Controlled, Multicenter Trial; Journal of Clinical Oncology; 2012; vol. 30 (no. 33); 4124-4133

1 **Study details**

Country where study was carried out	The Netherlands
Study type	Randomised controlled trial (RCT)
Study dates	January 2008 to December 2009
Inclusion criteria	• Had primary breast cancer (stages T1-4, N0-1 and M0) • younger than 50 years • premenopausal at diagnosis • had received adjuvant chemotherapy, and/or hormonal therapy • disease free at study entry • reported at least a minimal level of menopausal symptoms • chemotherapy had to be completed at least 4 months before but no more than 5 years before study entry • hormonal therapy could still be ongoing. Patients received a letter about the study and were asked to complete a questionnaire about hot flashes, night sweats, and/or vaginal dryness. Eligibility depended on having had at least two of these symptoms “sometimes” or one of them “often” during the previous 2 weeks
Exclusion criteria	• Lack of basic proficiency in Dutch • serious cognitive of psychiatric problems • serious physical comorbidity • obesity (body mass index >35) • patients participating in concurrent studies targeted at menopausal symptoms or involving similar interventions.
Patient characteristics	**Age, years - mean (SD):** All participants (including those randomised to physical exercise and CBT/exercise groups: 48.2 (5.6) CBT: 48.2 (5.7) Control: 47.8 (6.0) **BMI, kg/m2 - mean (SD):** CBT: 26.1 (3.8) Control: 24.7 (4.4) **Ethnicity**

	Not reported **Age at menopause or last menstrual period** Not reported **Ongoing hormonal therapy - number, (%):** CBT: 80 (93%) Control: 81 (94.2%) **Time since completion of hormonal therapy- number, (%):** **<1 year** CBT: 6 (7%) Control: 3 (3.5%) **>1 year** CBT: 0 (0) Control: 2 (2.3%) **Sleep difficulties** Not reported **Hot flashes per day - mean (SD):** CBT: 5.2 (4.9) Control: 6.7 (7.1)
Intervention(s)/control	CBT: • 6 weekly group sessions of 90 minutes each • sessions included relaxation exercises • primary focus was hot flashes and night sweats • other focuses were symptoms such as vaginal dryness, problem areas such as body image and sexuality • booster session held 6 weeks after completion • sessions held by a clinical psychologist and 3 clinical social workers experienced in counselling women with breast cancer and specially trained in administering the CBT program.

	Control: • Control group were on a waiting list.
Duration of follow-up	12 weeks and 6 months
Sources of funding	Not reported
Sample size	The study was a four armed trial, but data was not extracted for the physical exercise group and CBT/exercise group as these interventions were not relevant for this review N=212 for the two included arms. CBT: n=109 randomised Control: n=103 randomised

1 **Outcomes**

Outcome	**CBT, 12 weeks, N = 109**	**CBT, 6 months, N = 109**	**Control, 12 weeks, N = 103**	**Control, 6 months, N = 103**
SF-36 physical functioning Mean (SD)	81.79 (16.6)	79.35 (18.76)	80.18 (17.08)	80.7 (18.79)
SF-36 bodily pain Mean (SD)	69.86 (23.38)	76.53 (23.71)	78.79 (23.78)	74.62 (23.68)
HF/NS problem rating Mean (SD)	3.03 (1.84)	2.83 (1.84)	3.72 (1.88)	3.31 (1.83)
Sexual activity questionnaire (SAQ)-	0.54 (0.79)	0.47 (0.69)	0.59 (0.79)	0.42 (0.69)

Outcome	CBT, 12 weeks, N = 109	CBT, 6 months, N = 109	Control, 12 weeks, N = 103	Control, 6 months, N = 103
Habit Mean (SD)				
Discontinuation for any reason 12 weeks No of events	n = 23; % = 21.1	n = 21; % = 19.3	n = 14; % = 13.6	n = 19; % = 18.4

1

2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Outcome data were not available for all, or nearly all, randomized participants (83% at T1 12-week follow-up), and there is no evidence that the result was not biased by missing outcome data. Missingness in the outcome could depend on its true value, however this is not likely. The percentage of available follow-up data did not differ significantly between groups.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(Questionnaires were self-reported and it is likely that assessment of the outcome was influenced by knowledge of the intervention received)*

Section	Question	Answer
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in one domain)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Fenlon, 2020**

Bibliographic Reference Fenlon D; Maishman T; Day L; Nuttall J; May C; Ellis M; Raftery J; Turner L; Fields J; Griffiths G; Hunter MS; Effectiveness of nurse-led group CBT for hot flushes and night sweats in women with breast cancer: Results of the MENOS4 randomised controlled trial.; Psycho-oncology; 2020; vol. 29 (no. 10)

3 **Study details**

Country where study was carried out	United Kingdom
Study type	Randomised controlled trial (RCT)
Study dates	February 2017 to January 2018
Inclusion criteria	• Women with primary breast cancer, or ductal carcinoma in situ. • Women who have completed all primary treatment. • Ages 16 or over. • Experiencing 7 or more hot flush and night sweats per week, with an overall rating of 4/10 on the Hot Flush Problem Rating Scale. • Ability to attend group sessions. • Signed informed consent.
Exclusion criteria	• Benign breast cancer. • Metastatic disease.

	• Current use of other mind-body therapies to help with hot flushes and night sweats, such as acupuncture, hypnosis and mindfulness.
Patient characteristics	**Age at baseline assessment, years - mean (SD)** CBT: 53.5 (9.78) Usual care: 55.2 (10.19) **BMI, kg/m2 - mean (SD)** CBT: 28.5 (4.61) Usual care: 28.1 (4.94) **Ethnicity white – number (%)** CBT: 58 (96.7) Usual care: 62 (95.4) **Time since last period - years, median (IQR)** CBT: 4.0 (1.0 to 8.0) Usual care: 4.0 (1.0 to 8.0) **Previous use of hormone replacement therapy (HRT)** Not reported **Sleep difficulties** Not reported **Baseline HFNS problem rating - mean (SD)** CBT: 6.9 (1.73) Usual care: 6.5 (2.13) **Baseline HFRDIS (hot flash related daily interference score - mean (SD)** CBT: 57.8 (21.20)

	Usual care: 51.8 (23.29) No baseline differences between groups
Intervention(s)/control	**Intervention - CBT:** • Women attend weekly group CBT sessions for 6 weeks (90 minute long session). • Sessions delivered by breast care nurse (BCN), who was trained by a clinical psychologist. • Sessions will follow a manual that includes: 1. psycho-education and the cognitive behavioural model 2. stress management 3. paced breathing 4. cognitive and behavioural strategies to improve wellbeing and for managing hot flushes; night sweats and sleep; and maintaining changes. **Control - usual care:** • Standard NHS care at the site. • This differed between site as there is no UK standard practice. • Generally, women given ad-hoc advice about hot flushes and night sweats. • For ethical reasons, participants were offered a version of self-help CBT after the final assessment at week 26.
Duration of follow-up	26 weeks
Sources of funding	Not industry funded
Sample size	N=130 randomised (127 analysed) CBT: 63 (61 analysed) Usual care: 67 (66 analysed) 3 participants withdrew
Other information	Hot Flushes and Night Sweats (HFNS) Problem Rating Scale:

	• measures the extent to which hot flushes and night sweats are problematic • 3 items are rated on a 10-point scale • higher scores indicate greater bother/impact • change of 2 points of the scale is considered clinically relevant. • The scale also assesses frequency, asking women to estimate how many HFNS they had in the past week. Pittsburgh Sleep Quality Index (PSQI) • Self-rated questionnaire, assesses sleep quality and disturbance • Validated for use in women with breast cancer. • The scores range from 0 to 21. A score >5 be considered as a significant sleep disturbance according to authors of the scale.

Outcomes

Study timepoints

- Baseline
- 9 weeks (midpoint)
- 26 weeks (endpoint)

Outcomes

Outcome	CBT, Baseline, N = 63	CBT, 9 weeks, N = 47	CBT, 26 weeks, N = 42	Usual care, Baseline, N = 67	Usual care, 9 weeks, N = 55	Usual care, 26 weeks, N = 57
Hot flash related daily interference scale (HFRDIS) 0 to 100, higher scores worse Mean (SD)	57.8 (21.2)	30.9 (22.79)	29.6 (25.23)	51.8 (23.29)	45.1 (24.9)	46.1 (24.83)
Total hot flush and night sweat	58 (35 to 84)	38.5 (16 to 73)	42 (17 to 63)	63 (28 to 91)	49 (22 to 80.5)	56 (28 to 77)

Outcome	CBT, Baseline, N = 63	CBT, 9 weeks, N = 47	CBT, 26 weeks, N = 42	Usual care, Baseline, N = 67	Usual care, 9 weeks, N = 55	Usual care, 26 weeks, N = 57
(HFNS) frequency Median (IQR)						
Hot flush and night sweats (HFNS) problem-rating score 1 to 10, higher score worse Mean (SD)	6.9 (1.73)	4.1 (2.01)	3.7 (2.16)	6.5 (2.13)	5.5 (2.61)	5.5 (2.45)
Sleep quality Pittsburgh Sleep Quality Index - 0 - 21, lower numbers are better Mean (SD)	2.9 (0.83)	NR (NR)	2.3 (0.78)	2.9 (0.74)	NR (NR)	2.9 (0.68)
Anxiety GAD-7 Median (IQR)	13 (10.5 to 16)	10 (7 to 14)	11 (7 to 14)	11 (8 to 15)	12 (9 to 15.1)	12 (9 to 17)

1

2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low

Section	Question	Answer
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(Outcomes are self-reported and it is likely that assessment of the outcome was influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in one domain)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Green, 2019**

Bibliographic Reference Green, Sheryl M; Donegan, Eleanor; Frey, Benicio N; Fedorkow, Donna M; Key, Brenda L; Streiner, David L; McCabe, Randi E; Cognitive behavior therapy for menopausal symptoms (CBT-Meno): a randomized controlled trial.; Menopause (New York, N.Y.); 2019; vol. 26 (no. 9); 972-980

3 **Study details**

Country where study was carried out	US
Study dates	September 2015 - April 2018
Inclusion criteria	• women aged 40 to 65 years of age • in the menopausal transition or postmenopausal as per the STRAW criteria or having surgically-induced menopause. • experiencing vasomotor symptoms that were frequent (≥4 hot flashes per day/night or 28 or more per week) • distressing (≥3 or more on the vasomotor subscale of the Greene Climacteric Scale) • interfering (≥30 or greater on the Hot Flash Related Daily Interference Scale [HFRDIS] • at least mild depressive symptoms (≥14 on the Beck Depression Inventory-II) • not taking HT or psychoactive medication, or, if taking these medications, the dose and type of medication was stable for ≥12 weeks before the baseline assessment

	• no changes in dose or type of HT and psychoactive medication throughout the 12-week CBT treatment or 12-week waitlist • not receiving concurrent psychological treatment • fluent in English As per the STRAW+10 guidelines: **menopause transition** was defined as either the early menopause transition [variability of 7 or more days in the menstrual cycle], late menopause transition [., no menstruation for at least 60 days and increased variability in menstrual cycle length], or the first part of early postmenopause [12 consecutive months without menstruation] **postmenopause** was defined as starting after 12 consecutive months without menstruation, continuing into the late postmenopause phase [graduate reduction in vasomotor symptoms, but often involving the onset or worsening of other symptoms, such as urogenital or sexual concerns.]
Exclusion criteria	• severe depression or active suicidal ideation • current psychosis or substance use disorder
Patient characteristics	**Age, years - mean (SD):** All participants: 53.08 (4.02) Menopause CBT: 53.27 (3.69) Waitlist control: 52.88 (4.39) **Body mass index (BMI)** Not reported **Ethnicity – number (%)** **African American** Menopause CBT: 0 (0) Waitlist control: 3 (8.8) **Asian/Pacific Islander** Menopause CBT: 2 (5.4) Waitlist control: 0 (0)

	White Menopause CBT: 34 (91.9) Waitlist control: 29 (85.3) **Other** Menopause CBT: 1 (2.7) Waitlist control: 1 (2.9) **Menopause staging - number (%)** **Perimenopausal** Menopause CBT: 13 (35.1) Waitlist control: 11 (32.4) **Postmenopausal** Menopause CBT: 18 (48.6) Waitlist control: 17 (50) **Medication use - number (%)** **Hormone therapy only** Menopause CBT: 1 (2.7) Waitlist control: 3 (8.8) **Hormone therapy + psychoactive medication** Menopause CBT: 3 (8.1) Waitlist control: 2 (5.9) **Sleep difficulties** Not reported **Diagnosed with current major depressive disorder/persistent depressive disorder - number (%)** **Yes** Menopause CBT: 26 (70.3) Waitlist control: 25 (73.5) **No**

	Menopause CBT: 11 (29.7) Waitlist control: 9 (26.5)
Intervention(s)/control	**Menopause CBT** • 12-weekly sessions of 2-hour sessions duration • a small-group format (up to eight participants per group; range 5-8) • weekly between-session exercises and participant progress was reviewed each week in group • treatment targeted to a range of menopausal symptoms (vasomotor and depressive symptoms, sleep difficulties, anxiety, and sexual concerns) **Waitlist Control** • did not receive Menopause CBT nor any other psychological intervention • offered Menopause CBT after the 12 week assessment Each treatment group was led by a PhD-level licensed clinical psychologist and graduate-level psychology trainee. A third staff member (a registered nurse or social worker not otherwise involved in the study) served as an observer, completing weekly checklists to monitor therapist adherence to the protocol. Supervision for assessments and therapy was provided weekly by a licensed clinical psychologist.
Duration of follow-up	12 weeks The intervention group were also followed up at 3 months post-treatment
Sources of funding	Funding for this study was obtained by Drs Green (PI), Frey, Fedorkow, and McCabe, from the Ontario Mental Health Foundation (Type A Grant)
Sample size	N=72 randomised Menopause CBT: n=37 randomised (n=28 completed, n=37 analysed) Waitlist control: n=35 randomised (n=21 completed, n=34 analysed) Note: n=23 completed 3-month follow up (menopause CBT only)
Other information	Modified intention to treat analyses; 1 participant from the waitlist control group was excluded from the analyses due to difficulties with comprehension when completing the study questionnaires

Study timepoints

- Baseline
- 12 weeks

Outcomes

Outcome	Menopause CBT, Baseline, N = 37	Menopause CBT, 12 weeks, N = 37	Waitlist control, Baseline, N = 35	Waitlist control, 12 weeks, N = 34
Vasomotor Severity (GCS-vm) Vasomotor subscale of the Greene Climacteric Scale; Range 0-6 with higher scores indicating more bothersome hot flashes/night sweats Mean (SD)	4.3 (1.41)	3.05 (1.78)	4.62 (1.37)	4.11 (1.53)
Anxiety (HAM-A) Hamilton Anxiety Scale; Range 0-56 with higher scores indicating higher levels of anxiety Mean (SD)	19.43 (7.23)	15.18 (7.78)	21.87 (7.03)	18.64 (7.16)
Sleep Quality (PSQI) Pittsburg Sleep Quality Inventory; Range 0-21 with higher scores indicating more sleep difficulties Mean (SD)	11.32 (3.27)	9.06 (3.85)	12.39 (5.52)	12.85 (5.61)
Sexual concerns, past month (FSFI) The Female Sexual Function Index; Range 0-95 with higher scores indicating more sexual function and satisfaction in the past month Mean (SD)	23.3 (10.01)	22.4 (10.87)	23.47 (9.55)	23.42 (10.16)
Sexual concerns current (GCS-sex) Greene Climacteric Scale; Range 0-4 with higher scores	2.14 (0.95)	1.57 (1.07)	1.91 (1.03)	1.82 (1.03)

Outcome	Menopause CBT, Baseline, N = 37	Menopause CBT, 12 weeks, N = 37	Waitlist control, Baseline, N = 35	Waitlist control, 12 weeks, N = 34
indicating more sexual concerns Mean (SD)				
Discontinuation for any reason 12 weeks No of events	n = 0; % = 0	n = 9; % = 24.3	n = 0; % = 0	n = 14; % = 40

1 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Low *(The study is judged to be at low risk of bias for all domains)*
Overall bias and Directness	Overall Directness	Directly applicable

2

3 **Green, 2020**

Bibliographic Reference	Green, S M; Donegan, E; McCabe, R E; Fedorkow, D M; Streiner, D L; Frey, B N; Objective and subjective vasomotor symptom outcomes in the CBT-Meno randomized controlled trial.; Climacteric: the journal of the International Menopause Society; 2020; vol. 23 (no. 5); 482-488

1 **Study details**

Country where study was carried out	US
Study dates	September 2015 and April 2018
Inclusion criteria	• women aged 40–65 years old • perimenopausal or postmenopausal as per the Stages of Reproductive Aging Workshop (STRAW) criteria or in surgically induced menopause • experiencing vasomotor symptoms that were frequent (≥4 hot flashes per day/night or 28 or more per week) • severe (≥3 or more on the vasomotor subscale of the Greene Climacteric Scale [GCS]), and interfering (≥30 or greater on the Hot Flash Related Daily Interference Scale [HFRDIS]) • having at least mild depressive symptoms (≥14 on the Beck Depression Inventory – II) • not taking hormone therapy or psychoactive medication, or, if taking these medications, the dose and type of medication were stable for ≥12 weeks prior to baseline • no changes in dose or type of medication throughout the study • no concurrent psychological treatment • fluent in English
Exclusion criteria	• severe depression or active suicidal ideation • current psychosis or substance use disorder
Patient characteristics	**Age, years - mean (SD):** All participants: 53.56 (4.14) Menopause CBT: 52.63 (4.04) Waitlist control: 54.59 (4.12) **Body mass index (BMI)** Not reported

Ethnicity – number (%)
African American
Menopause CBT: 0 (0)
Waitlist control: 2 (11.8)
Asian/Pacific Islander
Menopause CBT: 1 (5.3)
Waitlist control: 0 (0)
White
Menopause CBT: 18 (94.7)
Waitlist control: 15 (88.2)

Menopause staging - number (%)
Perimenopausal
Menopause CBT: 7 (36.8)
Waitlist control: 4 (23.5)
Postmenopausal
Menopause CBT: 12 (63.2)
Waitlist control: 13 (76.4)

Medication use (HT or anti-depressant/anti-anxiety medication) - number (%)
Menopause CBT: 10 (52.6)
Waitlist control: 7 (41.2)

Sleep difficulties
Not reported

Diagnosed with current major depressive disorder/persistent depressive disorder - number (%)
Menopause CBT: 13 (65.4)
Waitlist control: 12 (70.6)

Intervention(s)/control	**Menopause CBT** • 12-weekly sessions of 2-hour sessions duration • a small-group format (up to eight participants per group; range 5-8) • weekly between-session exercises and participant progress was reviewed each week in group • treatment targeted to a range of menopausal symptoms (vasomotor and depressive symptoms, sleep difficulties, anxiety, and sexual concerns) **Waitlist control** • did not receive Menopause CBT nor any other psychological intervention • offered Menopause CBT after the 12 week assessment Treatment groups were led by a PhD-level clinical psychologist and a graduate-level trainee
Duration of follow-up	12 weeks
Sources of funding	Funding was obtained by S. M. Green (PI), B. N. Frey, D. M. Fedorkow, and R. E. McCabe from the Ontario Mental Health Foundation (Type A Grant).
Sample size	N=72 randomised in the original study (Green 2019) N=36 (included in this secondary analyses) Menopause CBT: n=19 analysed Waitlist control: n=17 analysed
Other information	Secondary analyses of Green 2019 - includes two additional outcomes not previously reported; Vasomotor frequency and vasomotor bothersomeness

Study timepoints

- Baseline
- 12 weeks

1 **Outcomes**

Outcome	Menopause CBT, Baseline, N = 19	Menopause CBT, 12 weeks, N = 19	Waitlist control, Baseline, N = 17	Waitlist control, 12 weeks, N = 17
Vasomotor frequency Subjective frequency (biolog) Mean (SD)	12.71 (6.92)	9.31 (6.28)	13.72 (9.22)	11.09 (7.32)
Vasomotor bothersomeness In-the-moment bothersomeness (biolog); Range 0-10 with higher scores indicating greater severity or bother Mean (SD)	4.04 (1.81)	3.08 (1.78)	4.98 (1.76)	5.05 (1.73)

2

3 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Low *(The study is judged to be at low risk of bias for all domains)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Hardy, 2018**

Bibliographic Reference Hardy, Claire; Griffiths, Amanda; Norton, Sam; Hunter, Myra S; Self-help cognitive behavior therapy for working women with problematic hot flushes and night sweats (MENOS@Work): a multicenter randomized controlled trial.; Menopause (New York, N.Y.); 2018; vol. 25 (no. 5); 508-519

3 **Study details**

Country where study was carried out	United Kingdom (England)
Study dates	None specified
Inclusion criteria	• women employed within participating organisations • English speaking • aged 45-60 years • with problematic HFNS for at least 2 months (scoring above 2 on the Hot Flush Rating Scale, minimum frequency of 10 a week) • no current major physical or mental health problems
Exclusion criteria	None specified
Patient characteristics	**Age, years - mean (SD):** All participants: 54.09 (3.4) Self-help CBT: 54.04 (3.17) Waitlist control: 54.10 (3.53) **BMI – Mean (SD)** Self-help CBT: 25.66 (4.91) Waitlist control: 28.26 (4.12) **Ethnicity – Number (%)** **White British**

	Self-help CBT: 42 (70) Waitlist control: 45 (71.4) **Black British** Self-help CBT: 11 (18.3) Waitlist control: 14 (22.2) **Other** Self-help CBT: 7 (11.7) Waitlist control: 4 (6.4) **Menopausal status** **Menopause transition – Number (%)** Self-help CBT: 11 (20%) Waitlist control: 20 (35.7%) **Postmenopause – Number (%)** Self-help CBT: 44 (80%) Waitlist control: 36 (64.3%) **Last menstrual period, months – Mean (SD)** Self-help CBT: 48.29 (54.16) Waitlist control: 35.68 (51.69) **Previous use of HRT** Not reported **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**Self-help CBT**

	• adapted and shortened booklet from that used in the MENOS2 trial with additional sections covering work stress and how to discuss menopause at work • A5 sized, colour booklet with instructions and four chapters (with information, exercises and homework tasks) to be completed over four weeks • chapters covered psycho-education about menopause and HFNS, stress management, breathing/relaxation, and learning cognitive and behavioural strategies to help manage HFNS, stress and sleep, with individual goal setting and weekly homework • a relaxation and breathing exercise was also provided on a CD **Waitlist control** • access to their general practitioner and other health care options • participants were sent the SH-CBT booklet after the 20 week assessment
Duration of follow-up	6 weeks and 20 weeks
Sources of funding	Funded by Wellbeing of Women (RG1701)
Sample size	N=124 randomised Self-help CBT: n=60 randomised (n=46 analysed) [attrition 23.3%] Waitlist control: n=64 randomised (n=60 analysed) [attrition 6.2%] Note: Combined attrition 14.5%
Other information	Modified intention-to-treat analysis, with participants providing data on at least one post-randomisation assessment analysed in the group to which they were randomised

1 **Outcomes**

Outcome	Self-help CBT, Baseline, N = 46	Self-help CBT, 6 weeks, N = 46	Self-help CBT, 20 weeks, N = 46	Waitlist control,Baseline N = 60	Waitlist control, 6 weeks, N = 60	Waitlist control, 20 weeks, N = 60
HF/NS problem rating Hot flush rating scale (range 0-10 with higher scores indicating higher	6.25 (1.97)	4.38 (2.21)	4.36 (2.29)	6.8 (1.9)	6.16 (2.31)	5.8 (2.3)

Outcome	Self-help CBT, Baseline, N = 46	Self-help CBT, 6 weeks, N = 46	Self-help CBT, 20 weeks, N = 46	Waitlist control,Baseline N = 60	Waitlist control, 6 weeks, N = 60	Waitlist control, 20 weeks, N = 60
perceived impact of hot flushes/night sweats) Mean (SD)						
HF/NS frequency Hot Flush Rating Scale (number of hot flushes experienced in the previous week) Mean (SD)	53.13 (34.34)	40.59 (26.05)	34.28 (27.62)	54.28 (38.11)	54.02 (43)	46.03 (37.92)
Sleep Quality (PSQI) Pittsburg Sleep Quality Index (range 1-4 with higher scores indicating better sleep quality) Mean (SD)	1.82 (0.81)	1.3 (0.67)	1.4 (0.77)	1.85 (0.82)	1.69 (0.78)	1.66 (0.78)
WHQ anxiety/depression Revised Women's Health Questionnaire (23-items with higher scores indicating better perceptions of physical and emotional health) Mean (SD)	67.53 (22.12)	70.9 (22.3)	74.85 (23.97)	63.01 (19.97)	64.12 (22.31)	66.1 (21.42)
WHQ wellbeing Revised Women's Health Questionnaire (23 items with higher scores indicating better perceptions of physical and emotional health)	71.11 (15.65)	71.4 (19.72)	75.79 (16.44)	66.94 (19.47)	67.92 (19.58)	67.54 (17.3)

Outcome	Self-help CBT, Baseline, N = 46	Self-help CBT, 6 weeks, N = 46	Self-help CBT, 20 weeks, N = 46	Waitlist control,Baseline N = 60	Waitlist control, 6 weeks, N = 60	Waitlist control, 20 weeks, N = 60
Mean (SD)						
WHQ somatic symptoms Revised Women's Health Questionnaire (23-items with higher scores indicating better perceptions of physical and emotional health) Mean (SD)	50.37 (23.93)	53.48 (24.42)	58.41 (22.47)	47.67 (21.43)	49.22 (22.74)	49.94 (20.04)
WHQ memory and concentration Revised Women's Health Questionnaire (23-items with higher scores indicating better perceptions of physical and emotional health) Mean (SD)	50.37 (23.93)	48.47 (26.91)	51.33 (25.97)	47.67 (21.43)	42.41 (24.24)	44.25 (23.15)
Discontinuation for any reason 6 weeks No of events	NA	n = 16; % = 26.7	n = 3; % = 5	NA	n = 4; % = 6.7	n = 1; % = 1.6
20 weeks No of events						

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information about concealment of the allocation*

Section	Question	Answer
		sequence and any baseline differences observed between intervention groups appear to be compatible with chance)
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in at one domain, but not to be at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Hummel, 2017**

Bibliographic Reference Hummel, Susanna B; van Lankveld, Jacques J D M; Oldenburg, Hester S A; Hahn, Daniela E E; Kieffer, Jacobien M; Gerritsma, Miranda A; Kuenen, Marianne A; Bijker, Nina; Borgstein, Paul J; Heuff, Gijsbert; Lopes Cardozo, Alexander M F; Plaisier, Peter W; Rijna, Herman; van der Meij, Suzan; van Dulken, Eric J; Vrouenraets, Bart C; Broomans, Eva; Aaronson, Neil K; Efficacy of Internet-Based Cognitive Behavioral Therapy in Improving Sexual Functioning of Breast Cancer Survivors: Results of a Randomized Controlled Trial.; Journal of clinical oncology : official journal of the American Society of Clinical Oncology; 2017; vol. 35 (no. 12); 1328-1340

3 **Study details**

Country where study was carried out	Netherlands

Study dates	None specified
Inclusion criteria	• women with a history of breast cancer • aged 18 to 65 years • diagnosis of histologically confirmed breast cancer 6 months to 5 years before study entry • completion of breast cancer treatment (with the exception of maintenance endocrine therapy or immunotherapy) • disease free at time of study entry • sufficient command of the Dutch language • DSM IV–based diagnosis of a sexual dysfunction
Exclusion criteria	• no Internet access • serious psychiatric comorbidity (eg, depressive disorder, alcohol dependency) • treatment of another type of cancer (with the exception of cervix carcinoma in situ or basal cell carcinoma) • presence of severe relationship problems • concurrent therapy to alleviate problems with sexuality or intimacy • concurrent CBT for other psychological problems • participation in another trial investigating problems with sexuality or intimacy
Patient characteristics	**Age, years – mean (SD):** All participants: 51.1 (7.2) Internet CBT: 51.6 (7.7) Waitlist control: 50.5 (6.8) **Body mass index (BMI)** Not reported **Ethnicity** Not reported **Time since diagnosis, months - mean (SD)** Internet CBT: 38.1 (17.0) Waitlist control: 37.0 (15.6) **Time since diagnosis, years - number (%)**

	1 year Internet CBT: 4 (4.8) Waitlist control: 5 (4.5) **1-2 years** Internet CBT: 31 (36.9) Waitlist control: 33 (38.8) **3-5 years** Internet CBT: 49 (58.3) Waitlist control: 47 (55.3) **Menopause status - number (%)** **Pre** Internet CBT: 13 (15.5) Waitlist control: 13 (15.3) **Post** Internet CBT: 71 (84.5) Waitlist control: 72 (84.7) **Previous use of hormone replacement therapy** Not reported **Sleep difficulties** Not reported **Onset of sexual problems in relation to breast cancer treatment - number (%)** **Before** Internet CBT: 10 (11.9) Waitlist control: 11 (12.9) **During** Internet CBT: 57 (67.9) Waitlist control: 54 (63.5)

	After Internet CBT: 17 (20.2) Waitlist control: 20 (23.5)
Intervention(s)/control	**Internet CBT** • guided by a personal psychologist or sexologist • 20 weekly sessions that had to be completed within a maximum period of 24 weeks • tailored to the needs of the individual, including the choice of modules and homework exercises and the frequency of contact • modules included; put your problem into words, How is my relationship doing?, sex and my body, focus my attention, explore my body, Discovering my sexual arousal feelings (version for male partners), Discovering my sexual arousal feelings (female version), change my thoughts, my sexual preferences, and relapse prevention • sessions did not take place in real time, but rather consisted of an extensive reply (feedback, additional questions, and remarks) from the therapist in response to the completed homework assignments • contact between therapist and participant took place via e-mail • two evaluation interviews were scheduled by telephone, one halfway through and one at the end of therapy where the therapist reviewed with the client the extent to which goals had been achieved and set future goals (including maintenance of progress made after the end of therapy) **Waitlist control** • an information booklet was provided addressing sexuality issues after breast cancer treatment • a psychologist or sexologist telephoned the women at six weeks to discuss briefly any questions that had arisen after reading the booklet • participants were offered the possibility to complete the CBT program after completion of follow-up
Duration of follow-up	10 weeks (mid-treatment) and at end of treatment, maximum 24 weeks
Sources of funding	Supported by the Dutch Cancer Society (Grant No. NKI 2012-5388), the Pink Ribbon Foundation (Grant No. 2012.WO21.C138), and The Netherlands Cancer Institute
Sample size	N=169 randomised Internet CBT: n=84 randomised (n=75 analysed at midpoint; n=69 analysed at endpoint) Waitlist control: n=85 randomised (n=81 analysed at midpoint; n=82 analysed at endpoint)

Study timepoints

- Baseline
- 24 weeks

Outcomes

Outcome	Internet CBT, Baseline, N = 84	Internet CBT, 24 weeks, N = 69	Waitlist control, Baseline, N = 85	Waitlist control, 24 weeks, N = 82
Overall sexual functioning (FSFI) Female Sexual Function Index total; Range 2-36 with higher scores indicating better sexual functioning Mean (SD)	13.76 (6.92)	19.15 (9.53)	13.27 (7.75)	14.9 (8.61)
Sexual pleasure (SAQ) Sexual Activity Questionnaire pleasure; Range 0-18 with higher scores indicating higher levels of pleasure Mean (SD)	4.5 (3.06)	7.43 (4.35)	4.21 (2.86)	4.86 (3.52)
Discomfort during sex (SAQ) Sexual Activity Questionnaire discomfort; Range 0-6 with lower scores indicating lower levels of discomfort Mean (SD)	3.67 (1.86)	2.62 (1.57)	3.27 (2.05)	2.88 (1.91)
Intercourse frequency (SAQ) Sexual Activity Questionnaire habit; Range 0-3 with higher scores indicating more sexual activity than usual Mean (SD)	0.55 (0.99)	1.13 (1)	0.45 (0.77)	0.6 (0.81)
Menopausal symptoms (FACT-ES) Functional Assessment of Cancer Treatment - Endocrine Symptoms; Range 0-72 with higher scores indicating fewer menopausal symptoms	50.26 (8.46)	53.55 (9.05)	52.94 (8.2)	54.04 (7.61)

Outcome	Internet CBT, Baseline, N = 84	Internet CBT, 24 weeks, N = 69	Waitlist control, Baseline, N = 85	Waitlist control, 24 weeks, N = 82
Mean (SD)				
Anxiety (HADS) Hospital Anxiety and Depression Scale; Range 0-21 with higher scores indicating more psychological distress Mean (SD)	6.15 (3.41)	6.02 (3.46)	6.01 (4.31)	5.85 (3.91)
SF-36 physical functioning 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	79.4 (18.36)	79.64 (19.35)	82.1 (14.16)	82.87 (16.65)
SF-36 role limitations, physical 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	68.98 (35.48)	73.91 (37.48)	62.94 (40.75)	70.12 (40.72)
SF-36 bodily pain 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	71.31 (22.54)	72.3 (21.71)	71.78 (20.39)	72.18 (21.84)
SF-36 general health 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	65.24 (20.55)	63.01 (22.18)	67.52 (22.29)	65.96 (23.01)
SF-36 vitality 36-item Short Form Health Survey; Range 0-100 with higher	59.35 (16.09)	61.74 (20.97)	59.24 (19.22)	61.1 (19.95)

Outcome	Internet CBT, Baseline, N = 84	Internet CBT, 24 weeks, N = 69	Waitlist control, Baseline, N = 85	Waitlist control, 24 weeks, N = 82
scores indicating higher levels of functioning/well-being Mean (SD)				
SF-36 social functioning 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	79.61 (19.09)	79.71 (23.59)	81.18 (20.74)	80.79 (20.05)
SF36 role limitations (emotional) 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	86.35 (29.47)	81.16 (34.53)	75.69 (36.87)	77.64 (37.06)
SF-36 Mental Health 36-item Short Form Health Survey; Range 0-100 with higher scores indicating higher levels of functioning/well-being Mean (SD)	75.24 (14.49)	74.14 (16.72)	75.29 (16.92)	76.24 (16.47)
Discontinuation for any reason 24 weeks No of events	n = 0; % = 0	n = 15; % = 17.9	n = 0; % = 0	n = 3; % = 13.53

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2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(Outcome data was available for 89.3% of randomized participants and this differed significantly between groups. There is no evidence that the results were not biased by missing outcome data. Missingness in the outcome could depend on its true value and this is likely.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(It is likely that assessment of the outcome was influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one domain)*
Overall bias and Directness	Overall Directness	Directly applicable

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2 **Kalmbach, 2019**

Bibliographic Reference	Kalmbach, David A; Cheng, Philip; Arnedt, J Todd; Cuamatzi-Castelan, Andrea; Atkinson, Rachel L; Fellman-Couture, Cynthia; Roehrs, Timothy; Drake, Christopher L; Improving Daytime Functioning, Work Performance, and Quality of Life in Postmenopausal Women With Insomnia: Comparing Cognitive Behavioral Therapy for Insomnia, Sleep Restriction Therapy, and Sleep Hygiene Education.; Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine; 2019; vol. 15 (no. 7); 999-1010

3 **Study details**

Country where study was carried out	US

Study dates	None specified
Inclusion criteria	• postmenopausal women (12 consecutive months without menses) • reporting average wake after sleep onset (wakefulness in the middle of the night after falling asleep) of an hour or more on ≥ 3 nights per week • meeting criteria for chronic DSM-5 insomnia disorder that onset or worsened during the perimenopausal or postmenopausal period (as per clinical interview with a registered nurse with specialty training in behavioural sleep medicine) • objective sleep disturbance evident per mean wake after sleep onset of 45 minutes or more on two overnight polysomnography (PSG) studies (adaptation night + baseline night, neither of which could have wake after sleep onset < 30 minutes).
Exclusion criteria	• prior or current DSM-5 major depression as per diagnostic interview • sleep-wake disorders other than insomnia (examined on PSG adaptation night [obstructive sleep apnoea defined as apnoea-hypopnea index ≥ 15 events/h, periodic limb movements defined as arousal frequency ≥ 15] and per patient report) • medications influencing sleep (prescription and non-prescription sleep aids, herbal supplements, and any antidepressants taken at night) Note: women receiving hormone therapy were permitted to participate
Patient characteristics	**Age, years - mean (SD):** All participants (including those randomised to sleep restriction therapy): 56.44 (5.64) Insomnia CBT: 55.32 (5.90) Sleep hygiene therapy (TAU): 57.24 (5.55) **Body mass index (BMI)** Not reported **Ethnicity – number (%)** **White** Insomnia CBT: 24 (48) Sleep hygiene therapy (TAU): 26 (52) **Black**

	Insomnia CBT: 22 (44) Sleep hygiene therapy (TAU): 20 (40) **Hispanic or Latin** Insomnia CBT: 0 (0) Sleep hygiene therapy (TAU): 0 (0) **Multiracial** Insomnia CBT: 0 (0) Sleep hygiene therapy (TAU): 0 (0) **Other** Insomnia CBT: 1 (2) Sleep hygiene therapy (TAU): 1 (2) **Did not answer** Insomnia CBT: 3 (6) Sleep hygiene therapy (TAU): 3 (6) **Years since last menstruation - mean (SD):** Insomnia CBT: 7.09 (6.65) Sleep hygiene therapy (TAU): 7.33 (7.79) **Hormone replacement therapy - number (%)** Insomnia CBT: 0 (0.0) Sleep hygiene therapy (TAU): 3 (6.0) **Epworth Sleepiness Scale – mean (SD)** Insomnia CBT: 7.6 (3.35) Sleep hygiene therapy (TAU): 7.34 (3.21) **Hot flashes, daytime – mean (SD)** Insomnia CBT: 1.97 (1.42) Sleep hygiene therapy (TAU): 2.36 (1.80)

Intervention(s)/control	**Insomnia CBT** • 6 weekly face-to-face sleep therapy sessions with a registered nurse specialising in behavioural sleep medicine • targets sleep-disruptive behaviours and beliefs • sessions covered behavioural (sleep restriction and stimulus control) and cognitive (cognitive restructuring) components, relaxation strategies (progressive muscle relaxation and autogenic training) and sleep hygiene education • fidelity monitoring **Sleep hygiene therapy (TAU)** • 6 weekly emails including general, non-personalized information on: the basics of endogenous sleep regulation, the impact of sleep on health problems such as obesity, diabetes, and hypertension, the effects of stimulants and other sleep disruptive substances, the relationship between sleep, diet, and exercise; and tips on creating a sleep-conducive bedroom environment According to the study authors sleep hygiene was not considered the primary cause nor a sufficient therapeutic target in insomnia disorder and therefore served as an ideal minimal intervention control condition and real-world comparator.
Duration of follow-up	2 weeks and 6 months
Sources of funding	Funded by the National Institute of Nursing Research (R01 NR013959-05, PI: Drake).
Sample size	N=154 randomised Insomnia CBT: n=52 randomised (n=50 analysed); n=41 at 6-months follow-up Sleep hygiene (TAU): n=50 randomised (n=50 analysed); n=43 at 6-months follow-up Sleep restriction: n=52 randomised (n=50 analysed); n=42 at 6-months follow-up Note: Two participants in both the sleep restriction and insomnia CBT groups discontinued treatment for changes in medication or new onset comorbid sleep disorder, and subsequently were excluded from the analyses
Other information	The study was a three armed trial, but data was not extracted for the sleep restriction therapy group as the intervention was not relevant for this review

Study timepoints

- Baseline
- 6 weeks
- 6 months

Outcomes

Outcome	Insomnia CBT, Baseline, N = 52	Insomnia CBT, 6 weeks, N = 50	Insomnia CBT, 6 months, N = 41	Sleep hygiene, Baseline, N = 50	Sleep hygiene, 6 weeks, N = 50	Sleep hygiene, 6 months, N = 43
ESS daytime sleepiness Epworth Sleepiness Scale; Range 0-24 with higher scores indicating greater likelihood of falling asleep during the day Mean (SD)	7.6 (3.35)	6.64 (3.27)	6.7 (3.71)	7.34 (3.21)	7.72 (3.33)	7 (3.51)
SF-36 Energy 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)	52.5 (18.11)	61.9 (18.07)	67.79 (16.49)	52.7 (19.51)	52.1 (19.77)	54.55 (19.1)
SF-36 general health 36-item Medical Outcomes Study Short Form Health Survey,	73.2 (14.24)	73.7 (14.91)	73.37 (16.79)	72.7 (17.44)	75.4 (16.03)	73.07 (17.06)

Outcome	Insomnia CBT, Baseline, N = 52	Insomnia CBT, 6 weeks, N = 50	Insomnia CBT, 6 months, N = 41	Sleep hygiene, Baseline, N = 50	Sleep hygiene, 6 weeks, N = 50	Sleep hygiene, 6 months, N = 43
Range 0-100 with higher scores indicating better quality of life Mean (SD)						
SF-36 Physical Function 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)	89.8 (12.08)	91.1 (13.37)	92.21 (12.31)	84.4 (18.42)	85.7 (18.87)	83.98 (21.2)
SF-36 role limitations, physical 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)	74.5 (32.53)	79 (32.48)	89.53 (22.65)	64 (34.32)	67 (35.87)	73.86 (33.22)
SF-36 Emotional Wellbeing	76.96 (14.24)	81.36 (13.29)	81.67 (13.56)	75.2 (15.03)	76.8 (16.8)	73.18 (14.83)

Outcome	Insomnia CBT, Baseline, N = 52	Insomnia CBT, 6 weeks, N = 50	Insomnia CBT, 6 months, N = 41	Sleep hygiene, Baseline, N = 50	Sleep hygiene, 6 weeks, N = 50	Sleep hygiene, 6 months, N = 43
36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)						
SF36 role limitations (emotional) 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)	68.67 (38.34)	76 (35.66)	86.82 (30.98)	72.67 (36.07)	78.67 (32.13)	78.03 (32.9)
SF-36 social functioning 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life	82.75 (18.19)	85.5 (21.78)	89.53 (17.45)	79 (22.22)	85.25 (20.62)	84.09 (21.46)

Outcome	Insomnia CBT, Baseline, N = 52	Insomnia CBT, 6 weeks, N = 50	Insomnia CBT, 6 months, N = 41	Sleep hygiene, Baseline, N = 50	Sleep hygiene, 6 weeks, N = 50	Sleep hygiene, 6 months, N = 43
Mean (SD)						
SF-36 Pain 36-item Medical Outcomes Study Short Form Health Survey, Range 0-100 with higher scores indicating better quality of life Mean (SD)	77.3 (19.41)	77.05 (20.31)	78.37 (20.17)	73.55 (25.83)	69.7 (25.52)	68.35 (27.2)
Hot flashes, daytime Daily mean hot flashes Mean (SD)	1.97 (1.42)	1.8 (1.71)	1.63 (1.44)	2.36 (1.8)	2.21 (1.79)	1.67 (1.65)
Hot flashes, nighttime Daily mean hot flashes (assumed night sweat) Mean (SD)	1.72 (1.29)	1.4 (1.24)	1.33 (1.11)	1.69 (1.26)	1.48 (1.34)	1.31 (1.18)

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2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information about concealment of the allocation sequence and any baseline differences observed between intervention groups appear to be compatible with chance)*

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in one domain, but not to be at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

Keefer, 2005

Bibliographic Reference	Keefer, Laurie; Blanchard, Edward B; A behavioral group treatment program for menopausal hot flashes: results of a pilot study.; Applied psychophysiology and biofeedback; 2005; vol. 30 (no. 1); 21-30

Study details

Country where study was carried out	US
Study dates	None specified
Inclusion criteria	• women reporting any changes in their menstrual cycle length, flow or duration within the past 3–12 months • women who had not menstruated in the past 12 months but continued to experience daily vasomotor symptoms • women confirmed by their physician to meet the criteria outlined by the Stages of Reproductive Aging Workshop (STRAW, Soules, 2001) for the menopausal transition (Stages −1 to +1).

Exclusion criteria	• women who had never experienced menstrual cycle changes • women currently experiencing symptoms of a severe depression, psychosis or substance abuse disorder
Patient characteristics	**Age, mean (SD)** All participants: 51.0 (4.7) **Body mass index (BMI)** Not reported **Ethnicity** Not reported **Age at menopause or last menstrual period** Not reported **Previous use of hormone replacement therapy** n=19 menopausal and postmenopausal women who had never used hormone replacement therapy **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**Group CBT** • 8 weekly sessions of 90 minutes duration • 4-6 women per group • conducted by the principal investigator, a doctoral candidate in clinical psychology • participants monitored their vasomotor symptoms on the daily diaries, and kept track of their relaxation practices on standard forms • three active components to the group treatment:

	1. psychoeducation - shared discussion around symptoms and experiences of menopause, and the role that stress plays in perception of symptoms. 2. cognitive restructuring - restructuring negative beliefs about symptoms and menopause 3. paced respiration - inhalation for 3 seconds and exhalation for 7 seconds **Waitlist Control** • symptom monitoring only, women completed the post-wait list questionnaires and symptom diaries • participants started the treatment after 8 weeks
Duration of follow-up	8 weeks
Sources of funding	None specified
Sample size	N=19 randomised Group CBT: n=11 randomised and analysed Waitlist control: n=8 randomised and analysed

Study timepoints

- Baseline
- 8 weeks

Outcomes

Outcome	Group CBT, Baseline, N = 11	Group CBT, 8 weeks, N = 11	Waitlist control, Baseline, N = 8	Waitlist control, 8 weeks, N = 8
Total Vasomotor Frequency of vasomotor symptoms Mean (SD)	78.27 (44.73)	44.73 (62.43)	98.5 (64.98)	126.75 (121.85)
Distress Rating Range 0-10 with higher scores indicating	3.78 (2.22)	2.59 (2.71)	4.86 (1.48)	5.15 (1.6)

Outcome	Group CBT, Baseline, N = 11	Group CBT, 8 weeks, N = 11	Waitlist control, Baseline, N = 8	Waitlist control, 8 weeks, N = 8
increasing distress Mean (SD)				

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2 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(There is no information to answer any of the signalling questions)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and people delivering the interventions were aware of intervention groups during the trial and there is no information on whether there were deviations from the intended interventions. It is unclear whether an appropriate analysis was used to estimate the effect of assignment to interventions, and the potential impact (on the estimated effect of intervention) of the failure to analyse participants in the group to which they were randomized was substantial.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Some concerns *(The method of measuring the outcome was not inappropriate, and did not differ between intervention groups. The assessment of the outcome could have been influenced by knowledge of the intervention received, however this is unlikely)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There is no information on whether the result being assessed is likely to have been selected, on the basis of the results, from multiple eligible outcome measurements (e.g., scales, definitions, time points) within the outcome domain and from multiple eligible analyses of the data)*

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk in two domains)*
Overall bias and Directness	Overall Directness	Directly applicable

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2 **Mann, 2012**

Bibliographic Reference	Mann E; Smith MJ; Hellier J; Balabanovic JA; Hamed H; Grunfeld EA; Hunter MS; Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial.; The Lancet. Oncology; 2012; vol. 13 (no. 3)

3 **Study details**

Country where study was carried out	United Kingdom
Study type	Randomised controlled trial (RCT)
Study dates	March 2009 to August 2010
Inclusion criteria	• English speaking • women older than 18 • had at least 10 problematic HFNS (hot flush night sweats) per week - confirmed by a 2 week diary and a screening interview for a duration of 2 months or more • completed medical treatment for breast cancer (surgery, radiotherapy, chemotherapy) • no evidence of other cancers or metastases • women taking adjuvant endocrine treatment If women were taking treatments for HFNS consistently for 2 months or more, they were not excluded.
Exclusion criteria	• Those unable to attend sessions. • Those who were seeking treatment for mood disorders rather than for HFNS.
Patient characteristics	**Age at randomisation, years - mean (SD):**

	Intervention: 53.16 (8.10) Comparison: 54.05 (7.76) **Individuals younger than 50 years - number (%):** Intervention: 15 (32%) Comparison: 17 (35%) **BMI, kg/m2 - mean (SD):** Intervention: 27.13 (5.3) Comparison: 27.51 (6.9) **Ethnicity – number (%)** **White** Intervention: 42 (89) Comparison: 40 (82) **Black** Intervention: 4 (9) Comparison: 5 (10) **Other** Intervention: 1 (2) Comparison: 4 (8) **Pre-menopausal before diagnosis - number (%):** Intervention: 24 (51%) Comparison: 24 (49%) **Peri-menopausal before diagnosis - number (%):** Intervention: 9 (19%) Comparison: 8 (16%) **Post-menopausal before diagnosis - number (%):** Intervention: 12 (25%) Comparison: 16 (33%)

	Previous use of hormone replacement therapy (HRT) Not reported **Sleep difficulties** Not reported **Baseline HFNS problem-rating - mean (SD):** Intervention: 6.52 (2.43) Comparison: 6.12 (2.02)
Intervention(s)/control	**Intervention - group cognitive behavioural therapy (CBT):** • Psychoeducational, structured interactive with group discussions, handouts and weekly homework. • Paced breathing and relaxation were practiced at each session, with a take home CD. • Participants also received usual care. • 90 minute session per week for 6 weeks. • A clinical psychologist was trained to deliver the sessions with the help of an assistant. **Comparison - usual care:** • Women were followed up every 6 months by an oncologist or a clinical nurse specialist. • 77 (80%) had access to the cancer survivorship programme (those treated in hospitals in southeast London) - they were offered telephone support. • Women were sent an information leaflet and offered telephoned support every 2 weeks (maximum 10 calls). • Nurses gave information about HFNS, such as treatment options, symptom management and instructions for paced breathing and relaxation.
Duration of follow-up	9 and 26 weeks
Sources of funding	Not industry funded
Sample size	N=96 randomised Intervention: n=47 (43 analysed) Comparison: n=49 (45 analysed)

Study timepoints

- Baseline
- 9 weeks (midpoint)
- 26 weeks (endpoint)

Outcomes

Outcome	CBT, Baseline, N = 47	CBT, 9 weeks, N = 43	CBT, 26 weeks, N = 40	Usual care, Baseline, N = 49	Usual care, 9 weeks, N = 45	Usual care, 26 weeks, N = 40
SF-36 physical functioning Mean (SD)	66.17 (22.89)	75.38 (24.24)	74.13 (24.96)	74.89 (22.27)	79.23 (21.96)	73.88 (27.37)
SF-36 role-physical Mean (SD)	53.72 (43.29)	60 (40.35)	55.77 (43.1)	49.46 (40.31)	60.9 (39.65)	51.92 (44.2)
SF-36 bodily pain Mean (SD)	46.15 (22.73)	53.68 (23.98)	51 (22.5)	52.99 (21.64)	52.16 (22.57)	46.58 (22.18)
SF-36 general health Mean (SD)	48.1 (15.94)	51.84 (14.58)	50.34 (15.42)	49.32 (16.77)	47.68 (17.81)	44.98 (19.83)
SF-36 vitality Mean (SD)	35.33 (16.1)	39.63 (15.23)	40.31 (17.48)	38.13 (16.5)	38.89 (17.79)	38.96 (15.72)
SF-36 social functioning Mean (SD)	67.02 (31.43)	75.3 (25.39)	77.5 (27.18)	71.2 (28)	75.64 (25.96)	62.81 (29.48)
SF-36 role-emotional Mean (SD)	67.39 (42.45)	75.61 (38.02)	73.5 (37.6)	55.56 (42.64)	64.1 (40.02)	60.68 (42.49)

Outcome	CBT, Baseline, N = 47	CBT, 9 weeks, N = 43	CBT, 26 weeks, N = 40	Usual care, Baseline, N = 49	Usual care, 9 weeks, N = 45	Usual care, 26 weeks, N = 40
SF-36 Mental Health Mean (SD)	67.57 (17.89)	74.63 (14.22)	70.7 (19.24)	62.52 (17.37)	66.46 (14.2)	64.5 (16.06)
Hot flush frequency Mean (SD)	58.64 (32.16)	45.6 (38)	37.46 (41.41)	52.98 (37.93)	36.76 (29.18)	30.77 (25.4)
Night sweats frequency Mean (SD)	16.31 (14.84)	12.12 (9.93)	8.48 (9.13)	13.5 (10.13)	13.3 (8.69)	10.67 (9.97)
Hot flush and night sweats problem-rating scores Mean (SD)	6.52 (2.43)	3.53 (1.98)	3.13 (1.94)	6.12 (2.02)	4.95 (2.24)	4.6 (2.48)
WHQ sleep problems 0-1 lower scores better Mean (SD)	0.63 (0.3)	0.37 (0.31)	0.43 (0.37)	0.72 (0.29)	0.65 (0.32)	0.61 (0.34)
WHQ anxiety or fears 0 -1 lower scores better Mean (SD)	0.34 (0.25)	0.23 (0.27)	0.24 (0.31)	0.45 (0.3)	0.4 (0.33)	0.39 (0.31)
WHQ depressed mood 0 -1 lower scores better Mean (SD)	0.23 (0.26)	0.13 (0.16)	0.13 (0.19)	0.31 (0.27)	0.28 (0.24)	0.28 (0.26)

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1 **Critical appraisal**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Outcome data were available for 91.7% of randomized participants. There is no evidence that the result was not biased by missing outcome data. Missingness in the outcome could depend on its true value, however this is not likely.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in one domain, but not to be at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

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3 **McCurry, 2016**

Bibliographic Reference McCurry, Susan M; Guthrie, Katherine A; Morin, Charles M; Woods, Nancy F; Landis, Carol A; Ensrud, Kristine E; Larson, Joseph C; Joffe, Hadine; Cohen, Lee S; Hunt, Julie R; Newton, Katherine M; Otte, Julie L; Reed, Susan D; Sternfeld, Barbara; Tinker, Lesley F; LaCroix, Andrea Z; Telephone-Based Cognitive Behavioral Therapy for Insomnia in Perimenopausal and Postmenopausal Women With Vasomotor Symptoms: A MsFLASH Randomized Clinical Trial.; JAMA internal medicine; 2016; vol. 176 (no. 7); 913-20

1 **Study details**

Country where study was carried out	United States
Study type	Randomised controlled trial (RCT)
Study dates	September 2013 to August 2015
Inclusion criteria	• Aged 40 to 65 • Scoring 12 or higher on the Insomnia Severity Index (ISI) • Reporting 2 or more hot flashes daily • Perimenopausal or menopausal (menopausal defined as post-menopausal, no menstrual periods in the past 12 months, bilateral oophorectomy, or aged 55 or older with hysterectomy or endometrial ablation and perimenopausal defined as having had at least 1 lenses in the past 12 months or being younger than 55 years with a hysterectomy or endometrial ablation without bilateral oophorectomy)
Exclusion criteria	• Primary sleep disorder diagnosis • consumed more than 3 alcoholic drinks daily • had a current major illness interfering with sleep • had a job involving shift work (>3 times per week) • routinely used prescription sleeping medications (>3 times per week).
Patient characteristics	**Age, years - mean (SD):** All participants: 54.8 (4.2) CBT: 55 (3.5) MEC: 54.7 (4.7) **Body mass index (BMI)** Not reported **Ethnicity – number (%)** **White** CBT: 49 (92.5) MEC: 48 (90.6)

	African American CBT: 0 (0) MEC: 1 (1.9) **Other or unknown** CBT: 4 (7.5) MEC: 4 (7.5) **Menopausal status - number (%):** **Postmenopausal:** CBT: 34 (64.2) MEC: 34 (64.2) **Perimenopausal:** CBT: 16 (30.2) MEC: 15 (28.3) **Indeterminate:** CBT: 3 (5.7) MEC: 4 (7.5) **Previous use of hormone replacement therapy (HRT)** Not reported **Increase in sleep problems at menopause – number (%)** **Yes** CBT: 52 (98.1) MEC: 52 (98.1) **No** CBT: 1 (1.9) MEC: 0 (0) **Answer missing** CBT: 0 (0) MEC: 1 (1.9)

	Hot flashes per day – mean (SD) CBT: 7.1 (4.5) MEC: 7.8 (4.1)
Intervention(s)/control	**Intervention - CBT-Insomnia:** • Six 20 to 30 minutes telephone sessions over 8 weeks. • Participants were invited to have the first session in person but could be by telephone. • Treatment materials distributed at first sessions or mailed if it was a telephone session. • CBT-I components: education; sleep monitoring; sleep scheduling and goal setting behavioural homework and problem solving. • Sessions held by social worker and psychologist **Control - Menopause education control (MEC)** • Six 20 to 30 minutes telephone sessions over 8 weeks. • Participants were invited to have the first session in person but could be by telephone. • Treatment materials distributed at first sessions or mailed if it was a telephone session. • MEC components: education; sleep monitoring; support.
Duration of follow-up	Week 8 Week 24
Sources of funding	Not industry funded - funded by the National Institute on Aging, National Institutes of Health
Sample size	N=106 CBT-I: n=53 (51 analysed in primary analysis) MEC: n=53 (42 analysed in primary analysis)
Other information	Data reported as change from baseline score, mean and confidence intervals. Standard deviations calculated using confidence intervals

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Study timepoints

- Baseline
- 8 weeks (week 8 - baseline scores)
- 24 weeks (week 24 - baseline scores)

Outcomes

Outcome	CBT-I, Baseline, N = 53	CBT-I, 8 weeks, N = 47	CBT-I, 24 weeks, N = 44	MEC, Baseline, N = 53	MEC, 8 weeks, N = 41	MEC, 24 weeks, N = 37
Insomnia Severity Index (ISI) lower scores better Mean (SD)	15.6 (2.9)	-9.9 (4.26)	-10.7 (4.11)	16.8 (3.81)	-4.7 (4.44)	-6.7 (5.1)
Hot Flash Related Daily Interference Scale score Mean (95% CI)	NR (NR to NR)	-15.7 (-20.4 to -11)	-22.8 (-28.6 to -16.9)	NR (NR to NR)	-7.1 (-14.6 to 0.4)	-11.6 (-19.4 to -3.8)
Hot Flash Related Daily Interference Scale score Mean (SD)	NR (NR)	-15.7 (16)	-22.8 (19.24)	NR (NR)	-7.1 (23.8)	-11.6 (23.39)

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Allocation was random but no information on allocation concealment.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants were blinded to the intervention, and there were no deviations from intended intervention. Analysis was by intention to treat.)*

Section	Question	Answer
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Control arm had missing data but sensitivity analysis using a multiple imputation under assumptions that the missing data between intervention group would mirror missing data from control group.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Outcome assessors were blinded to the intervention.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Results and time points reported are as in the pre-specified protocol.)*
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in one domain but is not at high risk of bias for any domain)*
Overall bias and Directness	Overall Directness	Directly applicable

1

2 **Moradi Farsani, 2021**

Bibliographic Reference Moradi Farsani, Hadis; Afshari, Poorandokht; Sadeghniiat Haghighi, Khosro; Gholamzadeh Jefreh, Maryam; Abedi, Parvin; Haghighizadeh, Mohammad Hossein; The effect of group cognitive behavioural therapy for insomnia in postmenopausal women.; Journal of sleep research; 2021; vol. 30 (no. 5); e13345

3 **Study details**

Country where study was carried out	Iran
Study type	Randomised controlled trial (RCT)
Study dates	March 2018 - August 2018
Inclusion criteria	• menopausal women aged 45–60 years • women who were postmenopausal for 1–5 years (who were in the Stage +1a, +1b and +1c or early

	postmenopausal age according to the Stages of Reproductive Aging Workshop (STRAW) classification • meeting research diagnostic criteria for insomnia, with documented symptoms based on the Insomnia Severity Index (ISI; score ≥7) and Pittsburgh Sleep Quality Index (PSQI; score >5) • lack of severe anxiety and depression determined by the Beck Depression Inventory (BDI; scores >29) and Hamilton Anxiety Rating Scales (scores >30) The diagnostic criteria for insomnia disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) or the International Classification of Sleep Disorders (ICSD) were as follows: occurring ≥3 nights/week accompanied by daytime complaint or decreased functioning for ≥3 months. Also, lack of severe anxiety and depression was another inclusion criterion, which was determined based on the participants' answers to the Beck Depression Inventory (BDI; scores >29) and Hamilton Anxiety Rating Scales (scores >30), and women with severe anxiety and depression were not included in the study.
Exclusion criteria	• diagnosis or high clinical suspicion of a sleep disorder other than insomnia • psychiatric disorders (such as anxiety and severe depression, using over-the-counter sleeping pills) • uncontrolled medical disorder or pain syndrome that interfered with sleep, caused daytime sleepiness or was likely to be causally related to insomnia • current non-pharmacological insomnia treatment • previously failed trial of CBT-I • routine overnight shift work
Patient characteristics	**Age, years - mean (SD):** Insomnia CBT: 51.41 (3.00) Usual care: 52.35 (3.48) **BMI, kg/m2 - mean (SD):** Insomnia CBT: 29.00 (4.49) Usual care: 27.62 (4.86) **Ethnicity** Not reported

	Menopause age, years - mean (SD): Insomnia CBT: 48.32 (3.12) Usual care: 49.30 (2.75) **Previous use of hormone replacement therapy (HRT)** Not reported **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**Insomnia CBT** • Face to face, six weekly sessions of 60-minutes duration offered by an experienced therapist • CD on breathing and relaxation techniques for daily practice • sessions included general information about sleep and environmental factors that may affect sleep, stimulus control including instructions about factors that affect sleep and re-establishing a consistent sleep–wake schedule, sleep restriction for remaining in bed for a limited time to preserve actual sleep time and for creating mild sleep deprivation, which results in more efficient sleep, relaxation training to reduce somatic tension or intrusive thoughts interfering with sleep (this training was performed in the first 3 weeks), CBT to help change their incorrect beliefs and attitudes about sleep and insomnia (the participants received this training in the second 3 weeks) • conducted in groups of seven or eight participants • delivered by researcher trained in CBT - insomnia **Usual care control** • routine care including general information regarding sleep hygiene and controlling menopause complication • asked about their sleep, and if they had a problem with their sleep or if they were having hot flashes, then they would receive some herbal medicine to alleviate their hot flashes and some recommendations for sleep hygiene
Duration of follow-up	3 weeks, 6 weeks, and 10 weeks (4-weeks follow-up)

Sources of funding	Ahvaz Jundishapur University of Medical Sciences
Sample size	N=46 randomised Insomnia CBT: n=23 randomised (n=22 analysed) Usual care: n=23 randomised (n=23 analysed)

Study timepoints

- Baseline
- 3 weeks
- 6 weeks
- 10 weeks

Outcomes

Outcome	Insomnia CBT, Baseline, N = 22	Insomnia CBT, 3 weeks, N = 22	Insomnia CBT, 6 weeks, N = 22	Insomnia CBT, 10 week, N = 22	Usual care, Baseline, N = 23	Usual care, 3 weeks, N = 23	Usual care, 6 weeks, N = 23	Usual care, 10 weeks, N = 23
ISI score Insomnia Severity Index; Range 0-28 with higher scores indicating more severe insomnia Mean (SD)	17.95 (4.27)	13.04 (4.59)	7.23 (3.93)	7.5 (3.39)	18 (4.24)	18.13 (4.29)	18.91 (4.52)	17.83 (5.09)

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the	Risk of bias for deviations from the intended	Low

Section	Question	Answer
intended interventions (effect of assignment to intervention)	interventions (effect of assignment to intervention)	
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in one domain)*
Overall bias and Directness	Overall Directness	Directly applicable

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2 **Soori, 2019**

Bibliographic Reference Soori, M.; Kolivand, M.; Abolfathi Momtaz, Y.; Noori, P.; The effect of cognitive-behavioral group therapy on menopausal symptoms; Journal of Babol University of Medical Sciences; 2019; vol. 21 (no. 1); 215-222

3 **Study details**

Country where study was carried out	Iran
Study dates	2016
Inclusion criteria	• women with normal menopause and not due to medication or ovariectomy • aged 47 to 57 years • 1 – 4 years after the onset of menopause • no chronic or acute illness in the past 12 months so severe that the participant would be unable to attend sessions • not grieving the death of a loved one within the past three months • no specific stressors such as incurable disease of spouse or child • not using hormone therapy to reduce menopausal symptoms

	• fluent in Persian • no severe neurological illnesses or taking neurological drugs • no addiction • not using psychotropic drugs • no suicidal thoughts • no psychosis or suicide experience • not currently attending relaxation, yoga or similar classes • medical record in Hefdah-e-Shahrivar and Shahid Madani Health Centers in Tuyserkan in 2016
Exclusion criteria	• not attending two or more counselling sessions • use of hormone therapy during the study • the occurrence of an unanticipated stress in the course of counselling • dissatisfaction
Patient characteristics	**Age, years - mean (SD)** All participants: 53 (2.76) CBT Group: 53.15 (2.78) No treatment control: 52.84 (2.77) **BMI, kg/m2 - number (%)** **18.5-24.9** CBT Group: 9 (60%) No treatment control: 6 (40%) **25-29.9** CBT Group: 18 (45%) No treatment control: 22 (55%) **Above 30** CBT Group: 11 (52.4%) No treatment control: 10 (47.6%) **Ethnicity** Not reported

	Menopause duration, years - mean (SD) CBT Group: 2.83 (1.55) No treatment control: 2.37 (1.39) **Previous use of hormone replacement therapy** Not reported **Sleep difficulties** Not reported **Vasomotor symptoms** Not reported
Intervention(s)/control	**CBT group** • Groups of 10-12 people • 6 sessions of 30 minutes duration • CBT approach addressing menopausal symptoms and problems and helping to improve and treat them **No treatment (control group)** • one session of educational counselling after the assessments were done
Duration of follow-up	6 weeks
Sources of funding	None specified
Sample size	N=90 randomised CBT group: n=45 randomised (n=38 analysed) No treatment control: n=45 randomised (n=38 analysed)

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Study timepoints

- Baseline
- 6 weeks

Outcomes

Outcome	CBT group, Baseline, N = 45	CBT group, 6 weeks, N = 38	No treatment control, Baseline, N = 45	No treatment control, 6 weeks, N = 38
Anxiety Greene Climacteric Scale (21-items with higher values indicating more severity of symptoms) Mean (SD)	8.7 (3.9)	4.5 (2.6)	5.9 (3.6)	5.7 (3.3)
Vasomotor symptoms Greene Climacteric Scale (21-items with higher values indicating more severity of symptoms) Mean (SD)	3.02 (2.09)	1.4 (1.8)	3.65 (2.9)	3.8 (2.9)
Sexual dysfunction Greene Climacteric Scale (21-items with higher values indicating more severity of symptoms) Mean (SD)	1.7 (1.05)	0.71 (0.61)	1.6 (0.99)	1.6 (1.5)
Discontinuation for any reason No of events	n = 0; % = 0	n = 7; % = 15.5	n = 0; % = 0	n = 7; % = 15.5

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	High *(The allocation sequence was not adequately concealed)*

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(It appears as though an appropriate analysis was not used to estimate the effect of assignment to intervention and the potential impact (on the estimated effect of intervention) of the failure to analyse participants in the group to which they were randomized was substantial)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Some concerns *(The method of measuring the outcome was not inappropriate and did not differ between intervention group. The assessment of the outcome could have been influenced by knowledge of the intervention received, however this is unlikely.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one domain)*
Overall bias and Directness	Overall Directness	Directly applicable

BC: breast cancer; BCN: breast cancer nurse; BDI: Beck Depression Inventory; BMI: body mass index; CBT: cognitive behavioural therapy; DSM: Diagnostic and Statistical Manual; ESS: Epworth Sleepiness Scale; FSS: Fatigues Severity Scale; GAD-7: generalised anxiety disorder -7; GCS (vm): Greene Climacteric Scale (vasomotor subscale); GSQS: Groningen Sleep Quality Scale; HADS: Hospital Anxiety and Depression Scale; HAM-A: Hamilton Anxiety Scale – Anxiety; FACT-ES: Functional Assessment of Cancer Therapy-Endocrine Symptoms; FSDR-R: Female Sexual Distress Scale-Revised; FSFI: Female Sexual Function Index; HF/NS: hot flush/night sweat; HFRDIS: hot flash related daily interference score; HFRS: hot flush rating scale; ISI: Insomnia Severity Index; IQR: interquartile range; MEC: menopause education control; MSLT: Mean sleep onset latency; PSG: polysomnography; PSQI: Pittsburgh Sleep Quality Index; RCT: randomised controlled trial; SAQ: Sexual Activity Questionnaire; SD: standard deviation; SF: short form; SRT: sleep restriction therapy; STRAW: Stages of Reproductive Aging Workshop; TAU: treatment as usual; WASO: wake after sleep onset; WHQ: Women's Health Questionnaire

Appendix E Forest plots

Forest plots for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in Appendix F.

Comparison 1: Cognitive behavioural therapy versus treatment as usual

Figure 2: Vasomotor symptoms distress or bother (HFNS problem rating scale) at endpoint with stratification – Personal history of breast cancer/ Group CBT

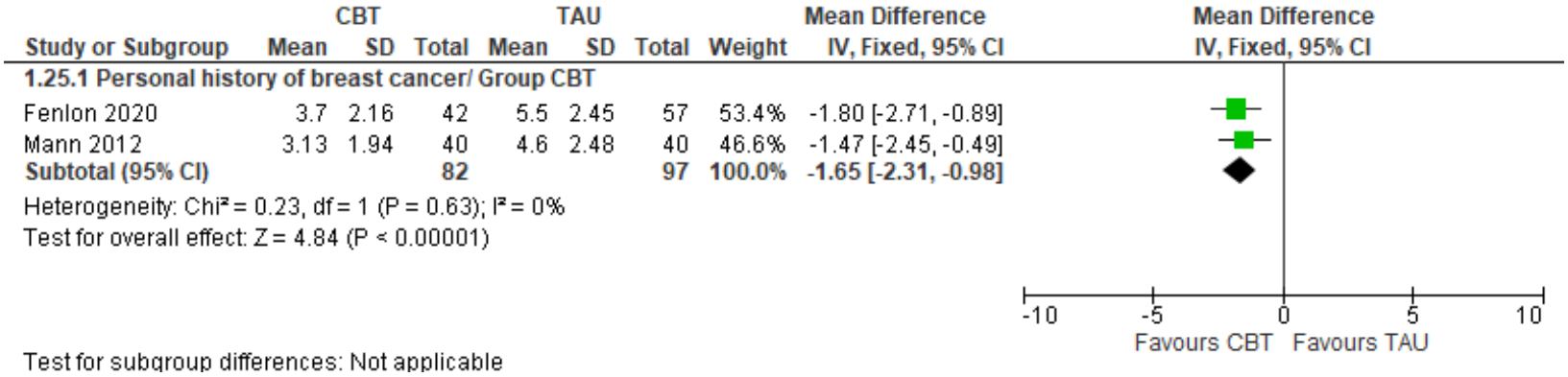


Figure 3: Difficulties with sleep (ISI) at endpoint with stratification – No personal history of breast cancer

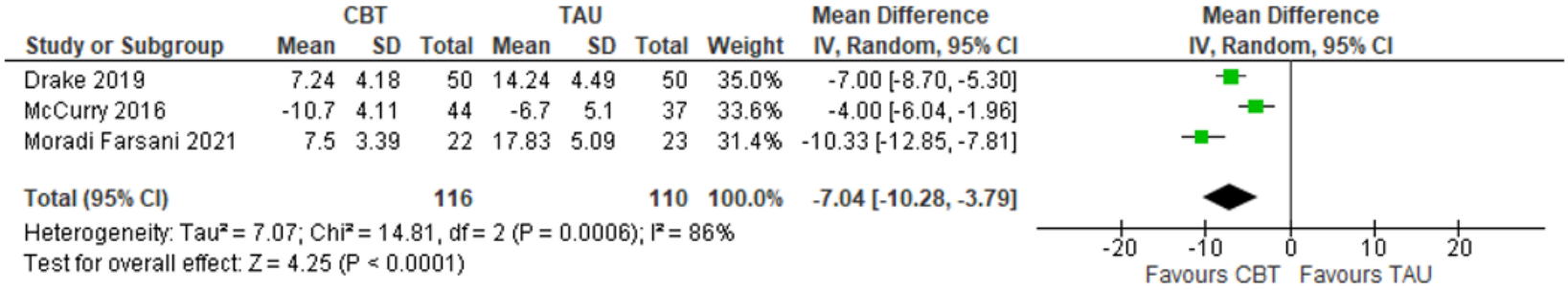


Figure 4: Difficulties with sleep (ISI) at endpoint with stratification – Individual CBT

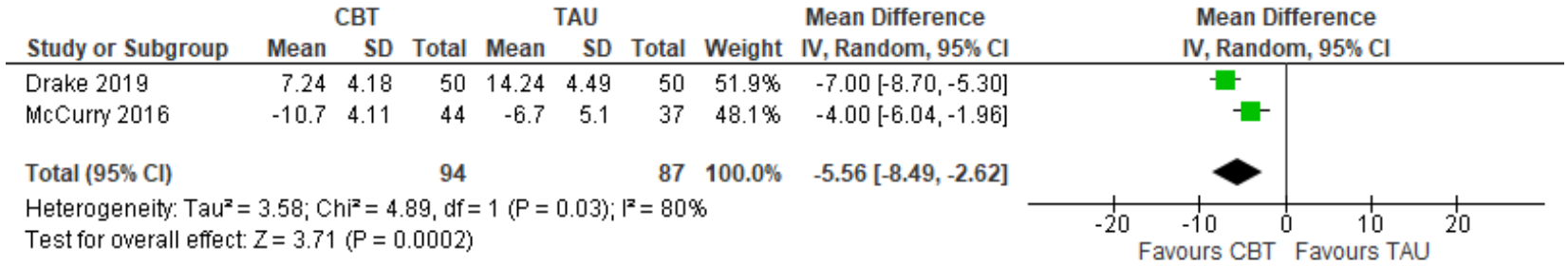
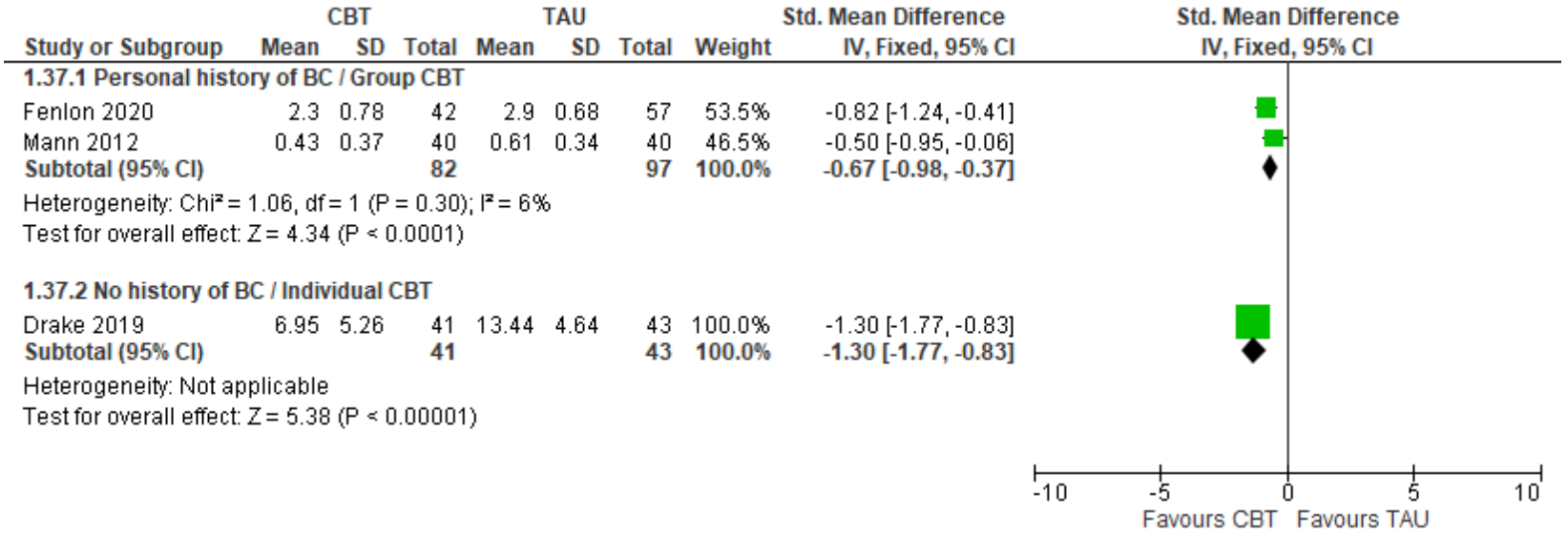


Figure 5: Difficulties with sleep (ISI, PSQI, WHQ) at follow up 6 months with stratification – Personal history of breast cancer/ Group CBT and no personal history of breast cancer/Individual CBT



Comparison 2: Cognitive Behavioural Therapy versus No treatment (critical outcomes)

Figure 6: Quality of life (SF-36 physical functioning) at endpoint with stratification – Personal history of breast cancer/ Duration ≥6 sessions

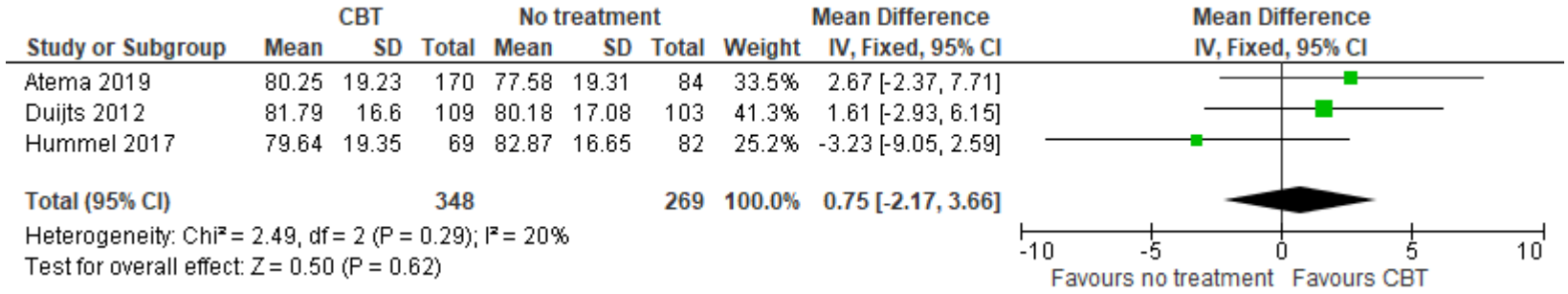


Figure 7: Quality of life (SF-36 physical functioning) at endpoint with stratification – Group CBT

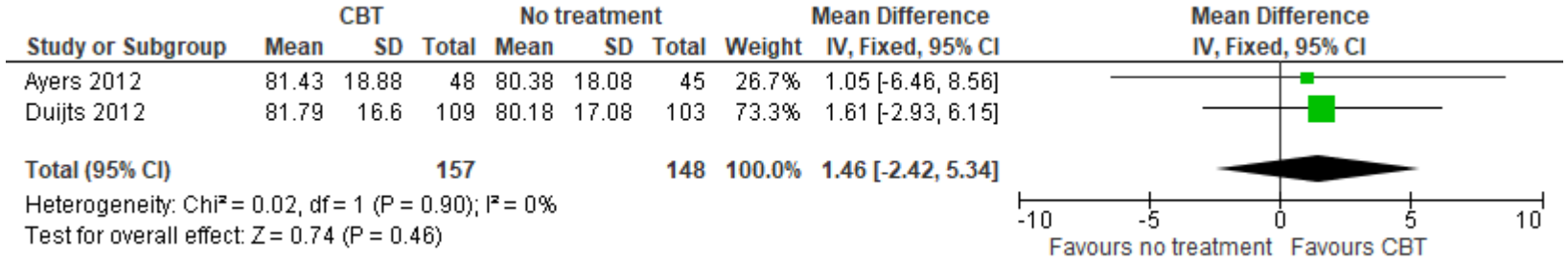


Figure 8: Quality of life (SF-36 physical functioning) at endpoint with stratification – Individual CBT

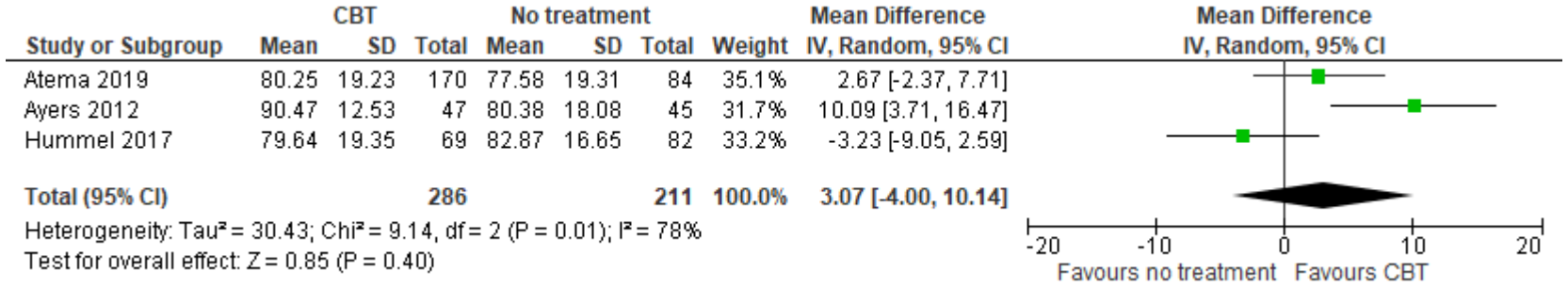


Figure 9: Quality of life (SF-36 physical functioning) at endpoint with stratification – Face to face CBT

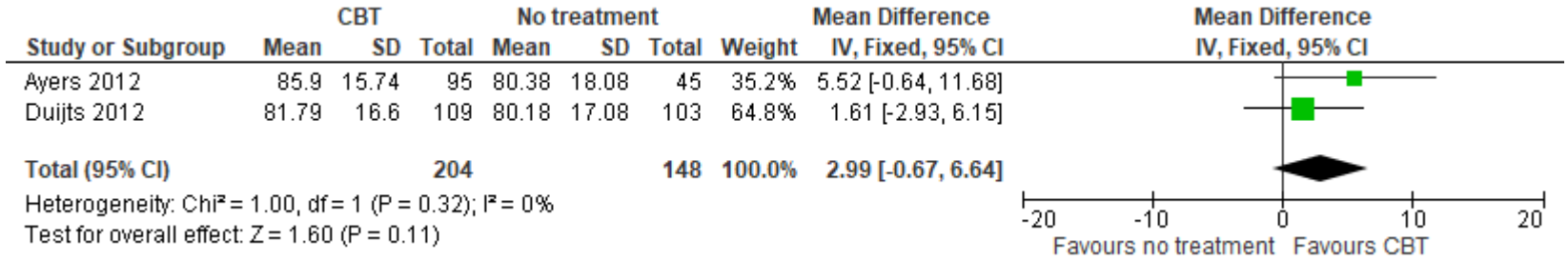


Figure 10: Quality of life (SF-36 physical functioning) at endpoint with stratification – Online CBT

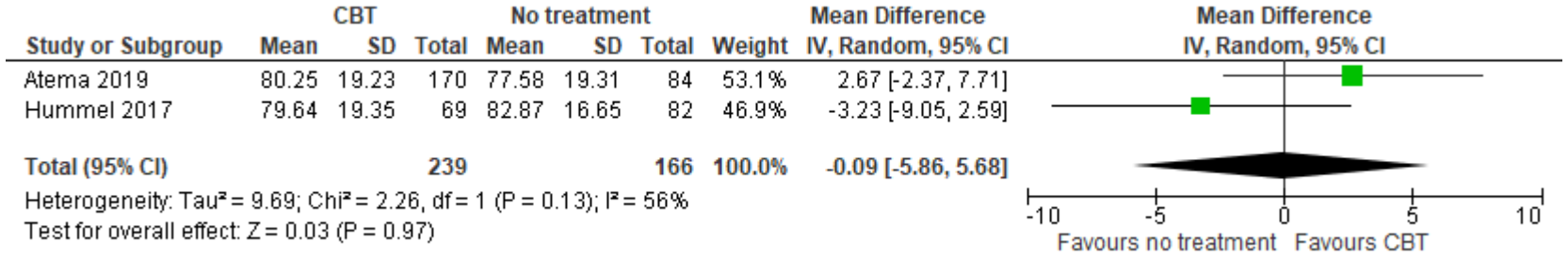


Figure 11: Quality of life (SF-36 physical functioning) at endpoint with stratification – Self-help CBT

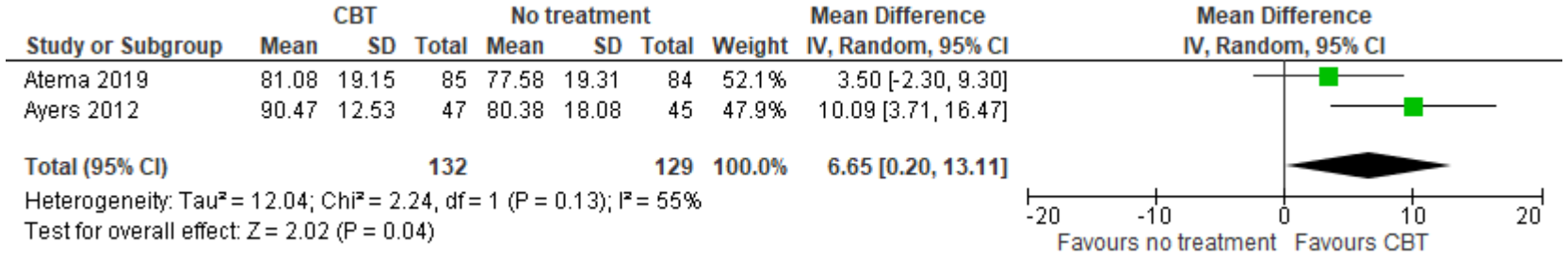


Figure 12: Quality of life (SF-36 physical functioning) at endpoint with stratification – Guided CBT

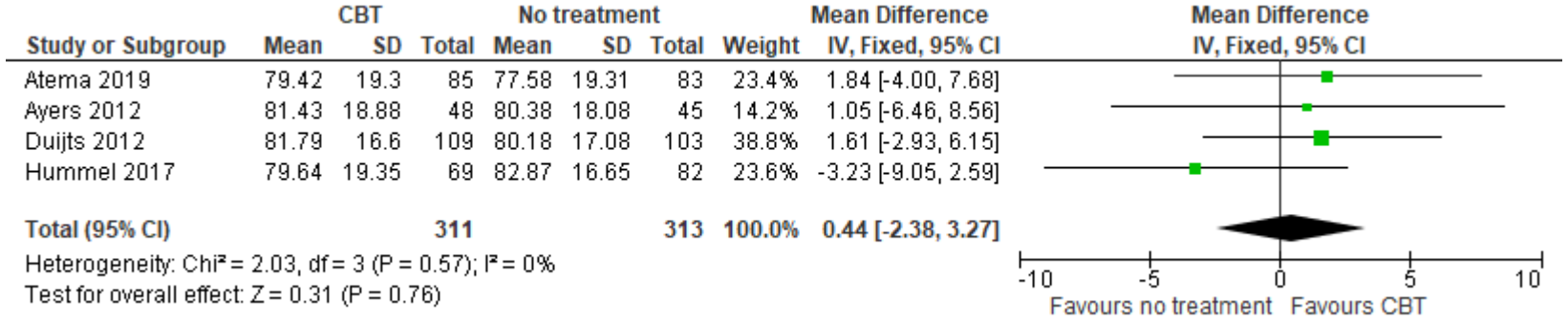


Figure 13: Quality of life (SF-36 physical functioning) at follow-up with stratification – Personal history of breast cancer/ Duration ≥6

sessions

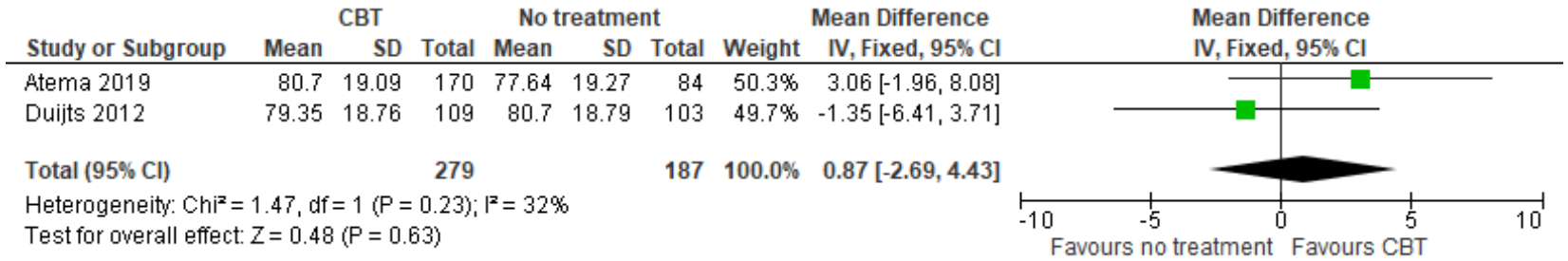


Figure 14: Quality of life (SF-36 physical functioning) at follow-up with stratification – Group CBT

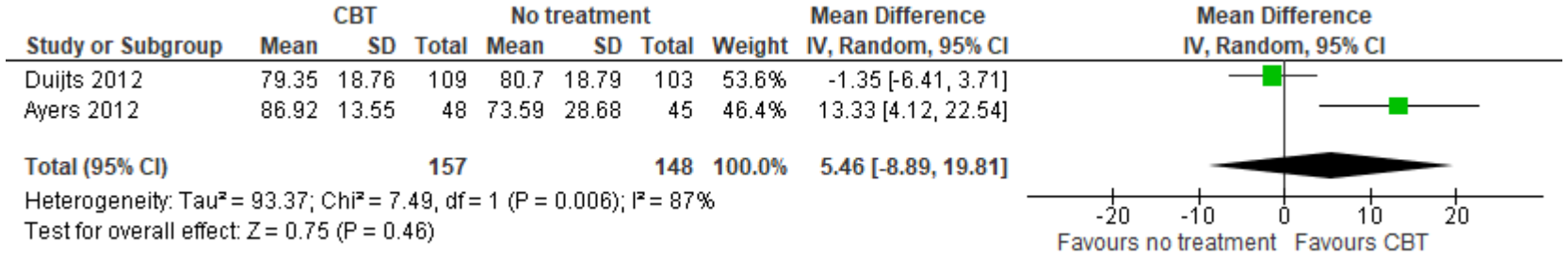


Figure 15: Quality of life (SF-36 physical functioning) at follow-up with stratification – Individual CBT

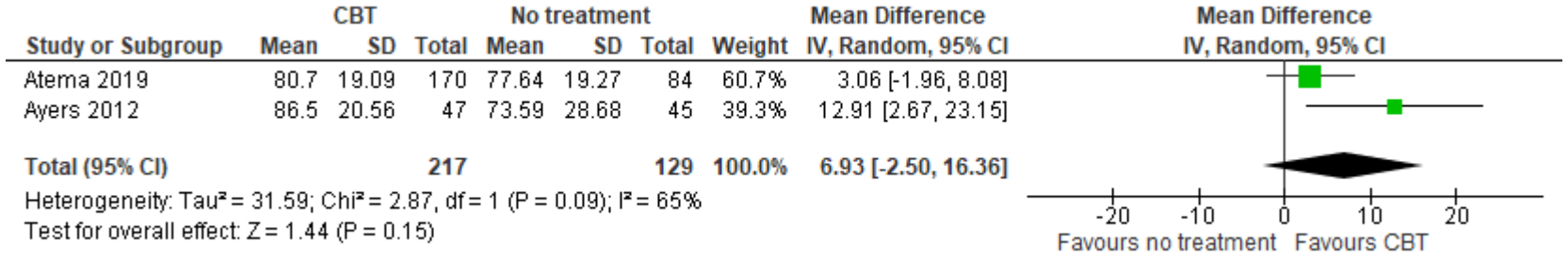


Figure 16: Quality of life (SF-36 physical functioning) at follow-up with stratification – Face to face CBT

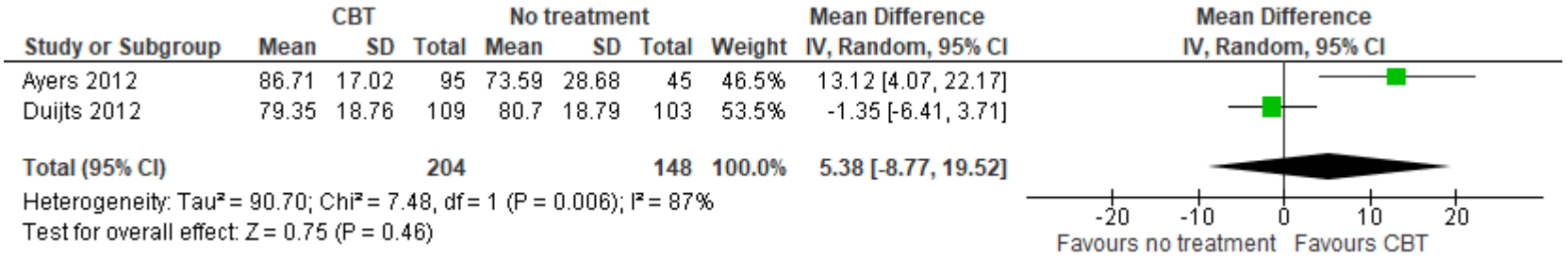


Figure 17: Quality of life (SF-36 physical functioning) at follow-up with stratification – Self-help CBT

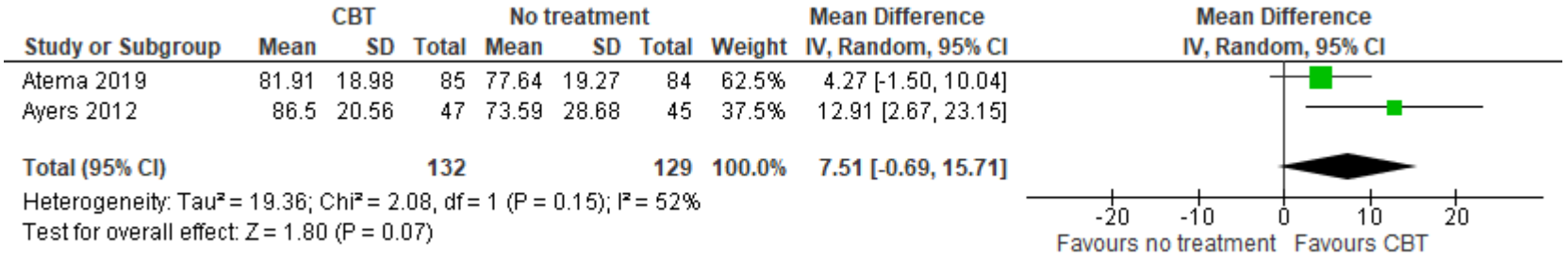


Figure 18: Quality of life (SF-36 physical functioning) at follow-up with stratification – Guided CBT

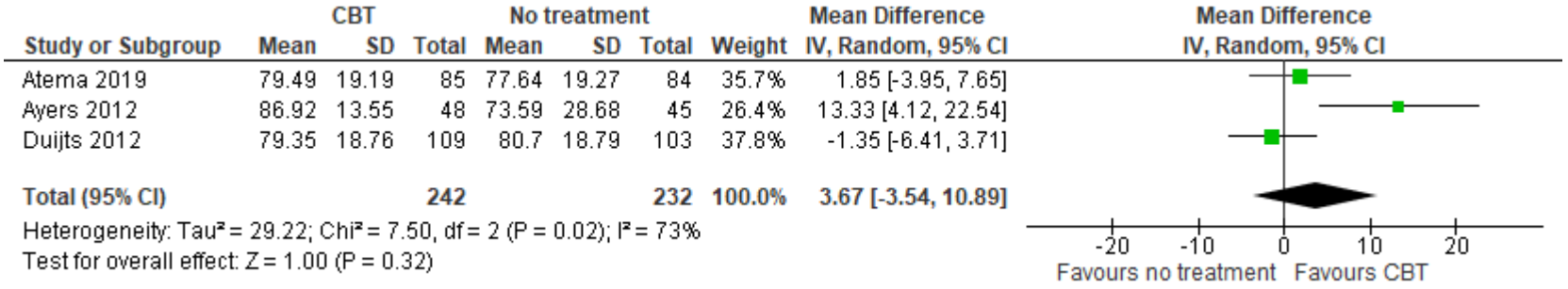


Figure 19: Quality of life (SF-36 social functioning) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions

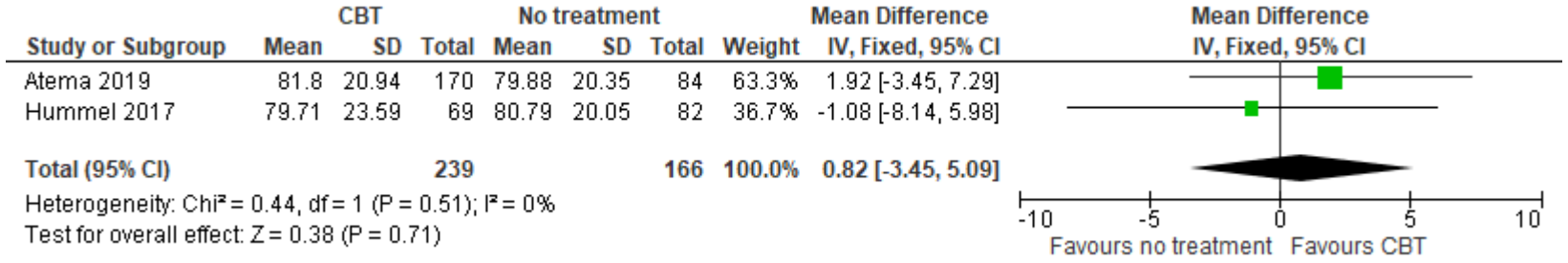


Figure 20: Quality of life (SF-36 social functioning) at endpoint with stratification – Individual CBT

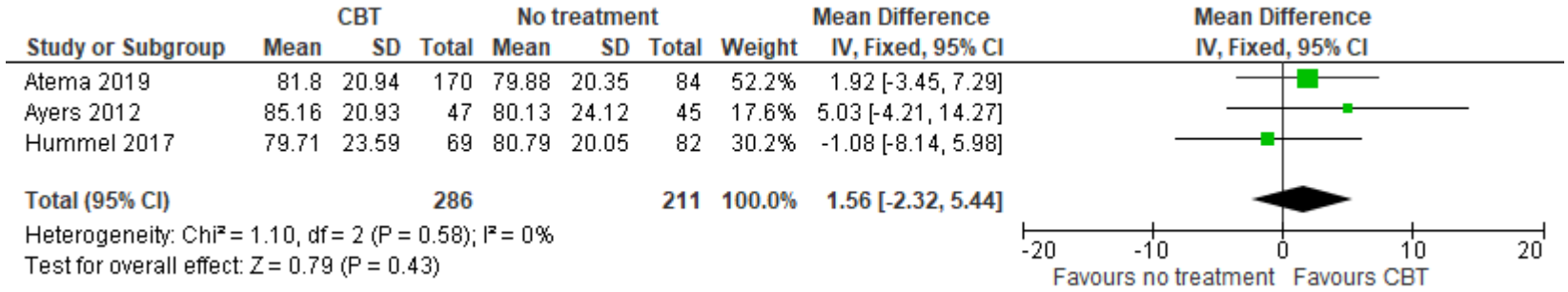


Figure 21: Quality of life (SF-36 social functioning) at endpoint with stratification – Online CBT

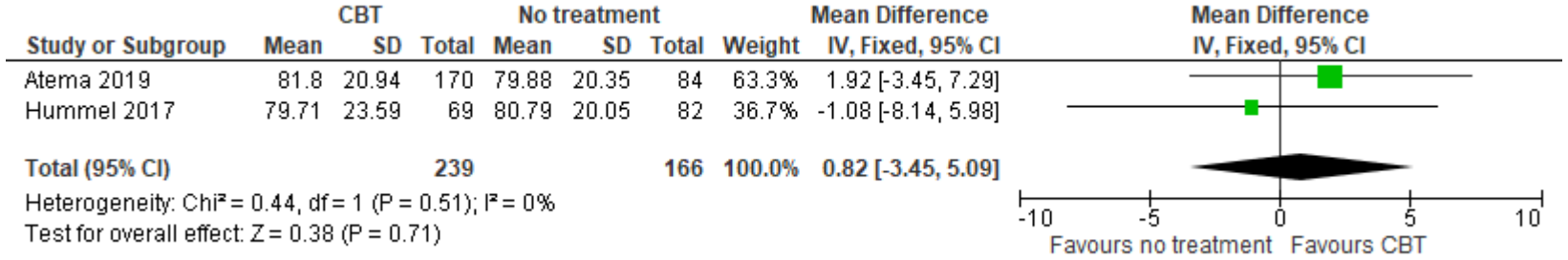


Figure 22: Quality of life (SF-36 social functioning) at endpoint with stratification – Self-help CBT

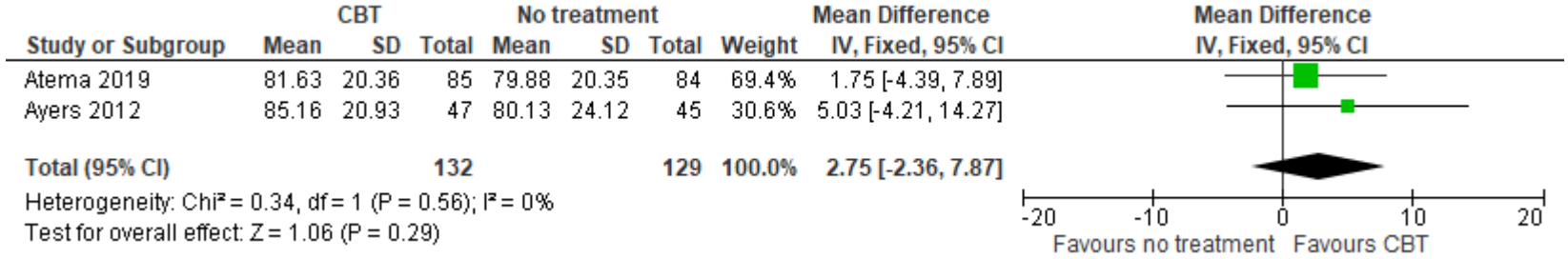


Figure 23: Quality of life (SF-36 social functioning) at endpoint with stratification – Guided CBT

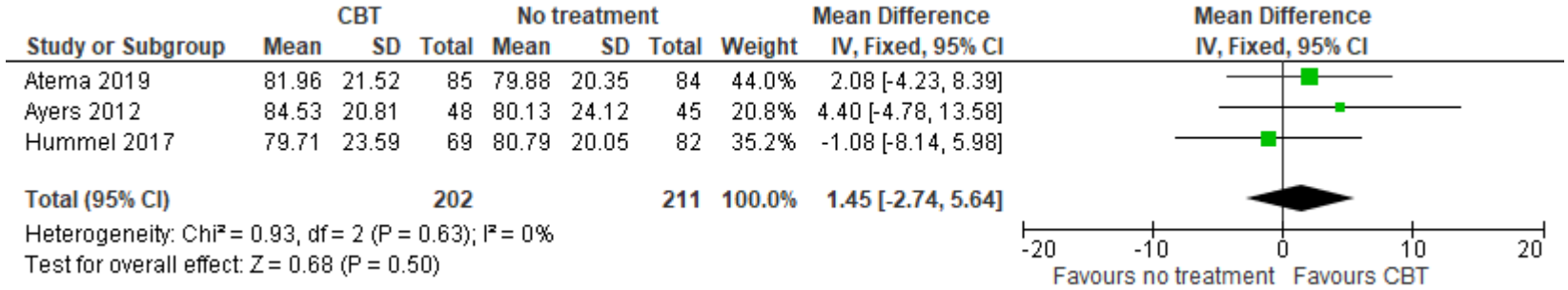


Figure 24: Quality of life (SF-36 social functioning) at follow-up with stratification – Individual CBT

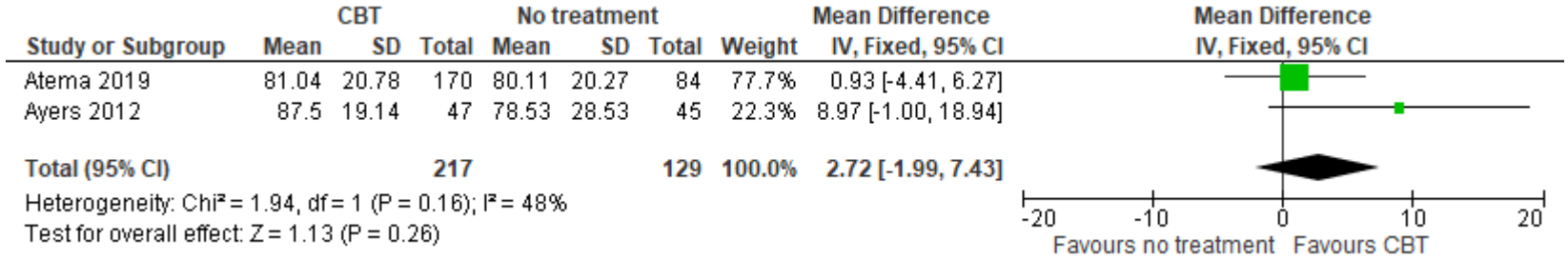


Figure 25: Quality of life (SF-36 social functioning) at follow-up with stratification – Self-help CBT

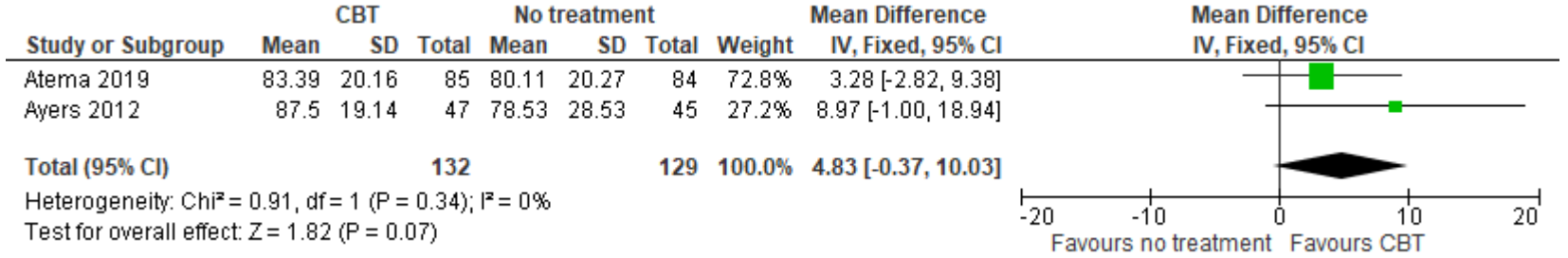


Figure 26: Quality of life (SF-36 social functioning) at follow-up with stratification – Guided CBT

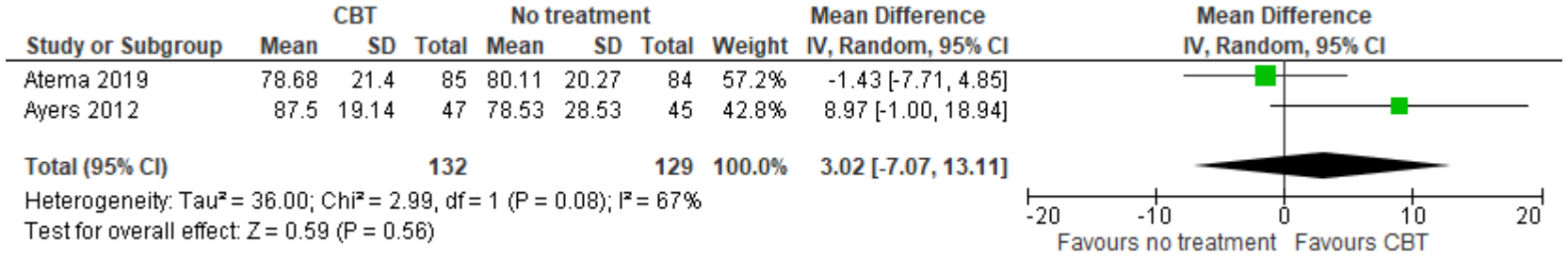


Figure 27: Quality of life (SF-36 physical role limitations) at endpoint with stratification – Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions

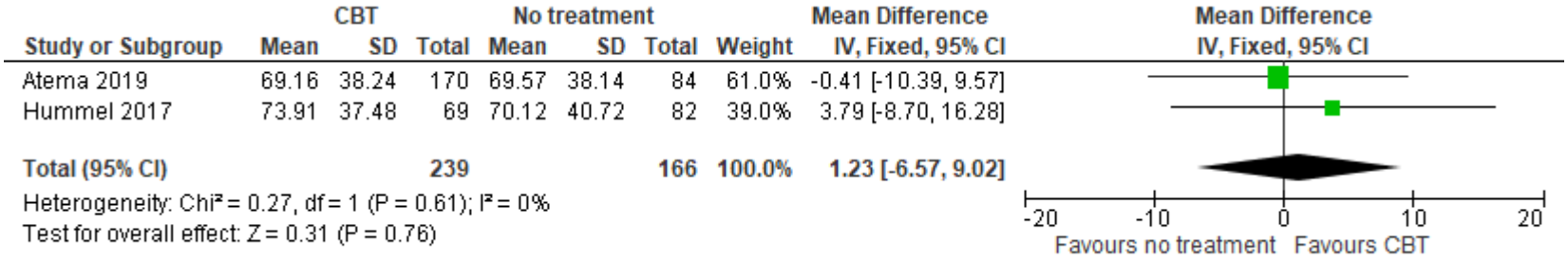


Figure 28: Quality of life (SF-36 physical role limitations) at endpoint with stratification – Individual CBT

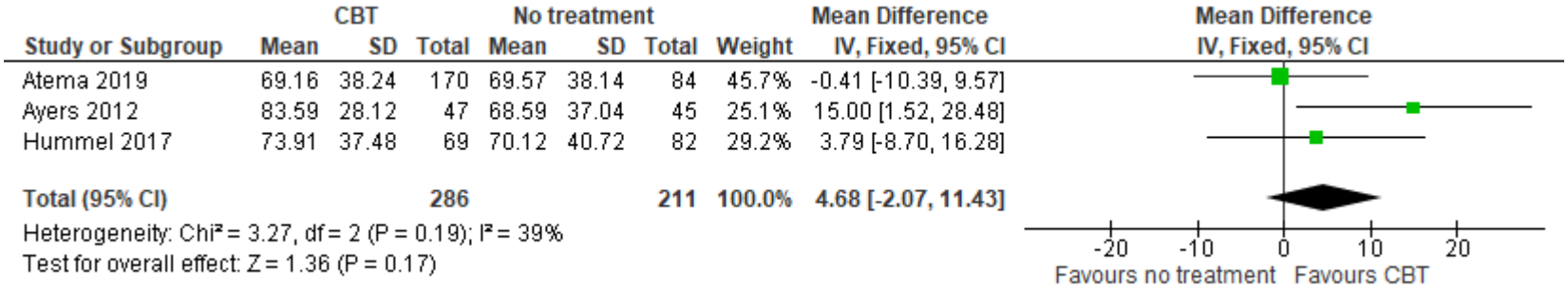


Figure 29: Quality of life (SF-36 physical role limitations) at endpoint with stratification – Self-help CBT

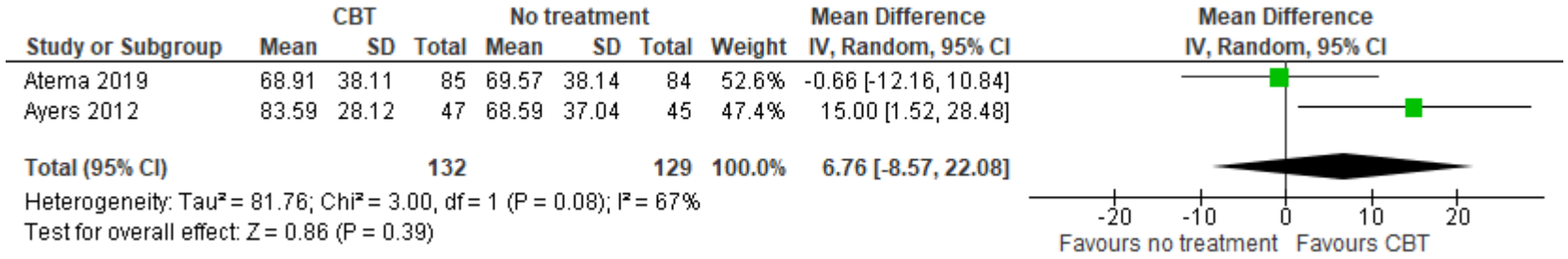


Figure 30: Quality of life (SF-36 physical role limitations) at endpoint with stratification – Guided CBT

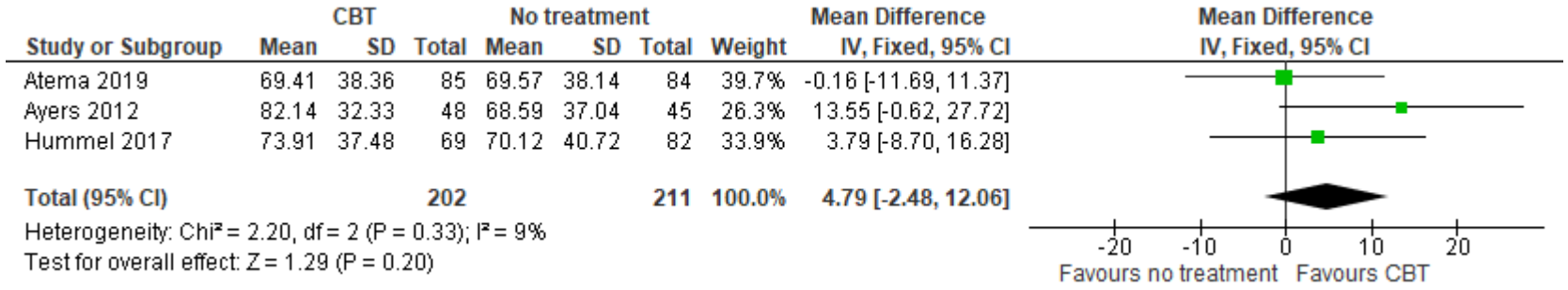


Figure 31: Quality of life (SF-36 physical role limitations) at follow-up with stratification – Individual CBT

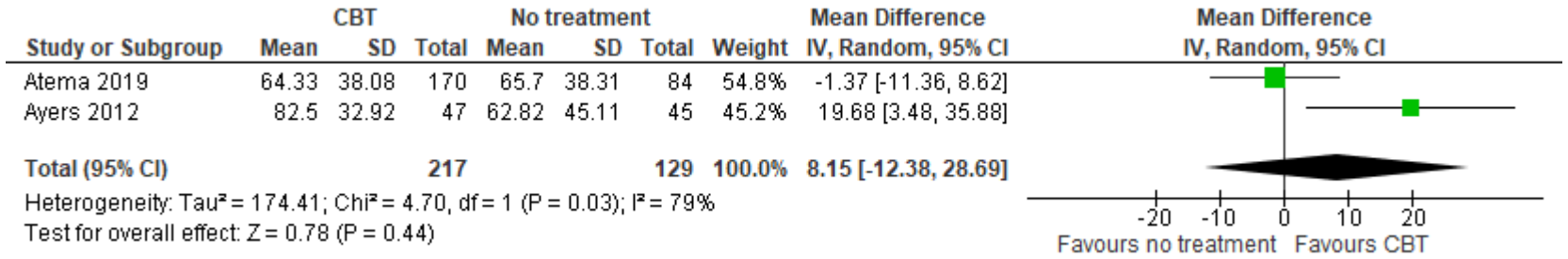


Figure 32: Quality of life (SF-36 physical role limitations) at follow-up with stratification – Self-help CBT

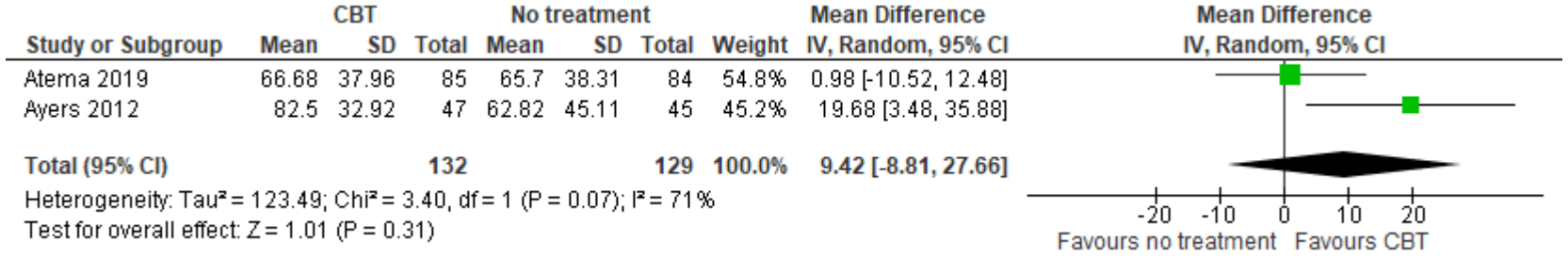


Figure 33: Quality of life (SF-36 physical role limitations) at follow-up with stratification – Guided CBT

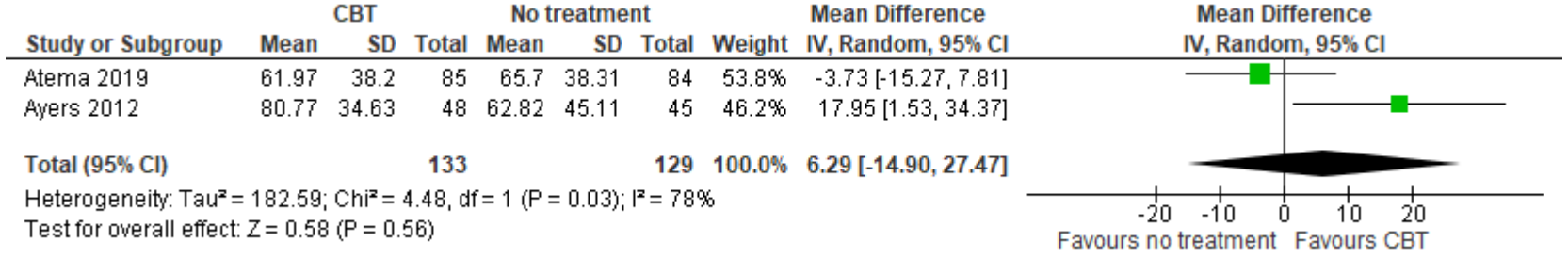


Figure 34: Quality of life (SF-36 emotional role limitations) at endpoint with stratification – Personal history of breast cancer/ Online

CBT/ Duration ≥6 sessions

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI
Atema 2019	79.93	34.2	170	82.55	34.24	84	62.0%	-2.62 [-11.57, 6.33]
Hummel 2017	81.16	34.53	69	77.64	37.06	82	38.0%	3.52 [-7.91, 14.95]
Total (95% CI)			**239**			**166**	**100.0%**	**-0.29 [-7.33, 6.76]**

Heterogeneity: Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.08 (P = 0.94)

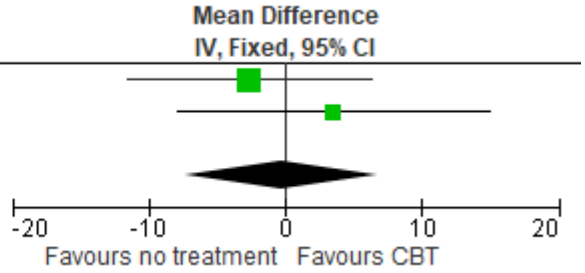


Figure 35: Quality of life (SF-36 emotional role limitations) at endpoint with stratification – Individual CBT

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI
Atema 2019	79.93	34.2	170	82.55	34.24	84	50.7%	-2.62 [-11.57, 6.33]
Ayers 2012	77.08	34.33	47	73.5	38.37	45	18.3%	3.58 [-11.32, 18.48]
Hummel 2017	81.16	34.53	69	77.64	37.06	82	31.0%	3.52 [-7.91, 14.95]
Total (95% CI)			**286**			**211**	**100.0%**	**0.42 [-5.95, 6.79]**

Heterogeneity: Chi² = 0.90, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.13 (P = 0.90)

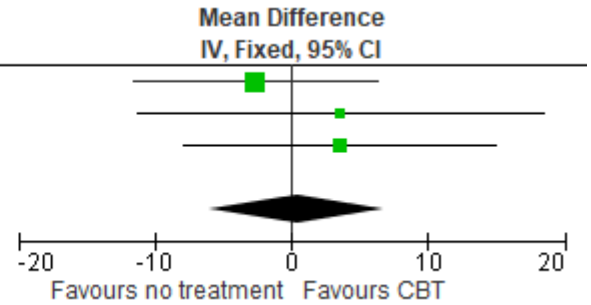


Figure 36: Quality of life (SF-36 emotional role limitations) at endpoint with stratification – Self-help CBT

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI
Atema 2019	80.49	34.17	85	82.55	34.24	84	67.6%	-2.06 [-12.37, 8.25]
Ayers 2012	77.08	34.33	47	73.5	38.37	45	32.4%	3.58 [-11.32, 18.48]
Total (95% CI)			**132**			**129**	**100.0%**	**-0.23 [-8.71, 8.25]**

Heterogeneity: Chi² = 0.37, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)

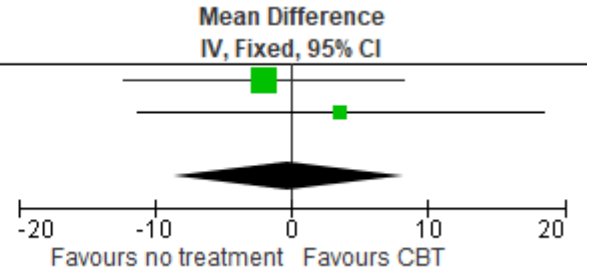


Figure 37: Quality of life (SF-36 emotional role limitations) at endpoint with stratification – Guided CBT

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI
Atema 2019	79.36	34.23	85	82.55	34.24	84	42.8%	-3.19 [-13.51, 7.13]
Ayers 2012	80.16	31.29	48	73.5	38.37	45	22.3%	6.66 [-7.62, 20.94]
Hummel 2017	81.16	34.53	69	77.64	37.06	82	34.9%	3.52 [-7.91, 14.95]
Total (95% CI)			**202**			**211**	**100.0%**	**1.35 [-5.40, 8.10]**

Heterogeneity: Chi² = 1.41, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.69)

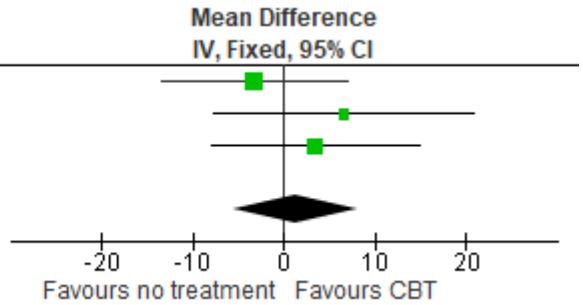


Figure 38: Quality of life (SF-36 emotional role limitations) at follow-up with stratification – Individual CBT

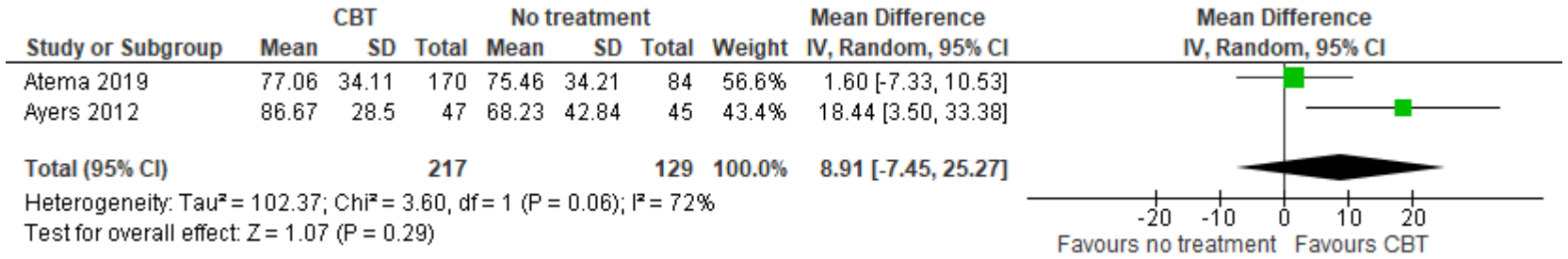


Figure 39: Quality of life (SF-36 emotional role limitations) at follow-up with stratification – Self-help CBT

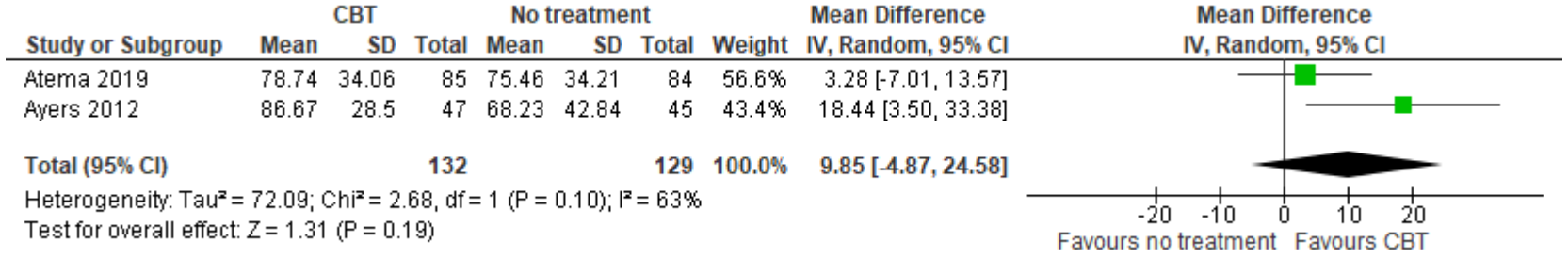


Figure 40: Quality of life (SF-36 emotional role limitations) at follow-up with stratification – Guided CBT

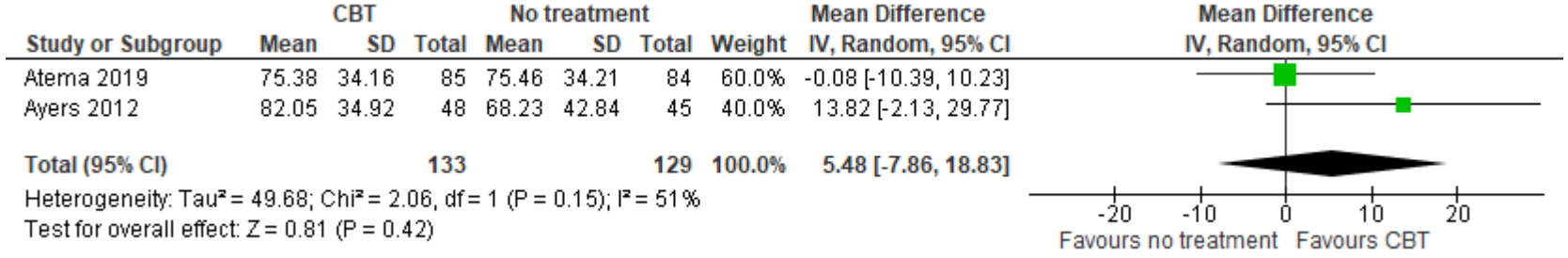


Figure 41: Quality of life (SF-36 bodily pain) at endpoint with stratification – Personal history of breast cancer/ Duration ≥6 sessions

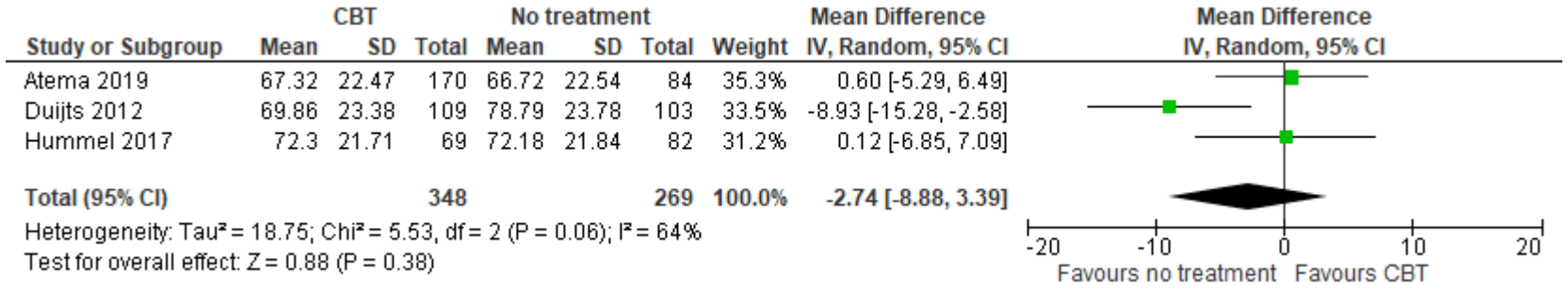


Figure 42: Quality of life (SF-36 bodily pain) at endpoint with stratification – Group CBT

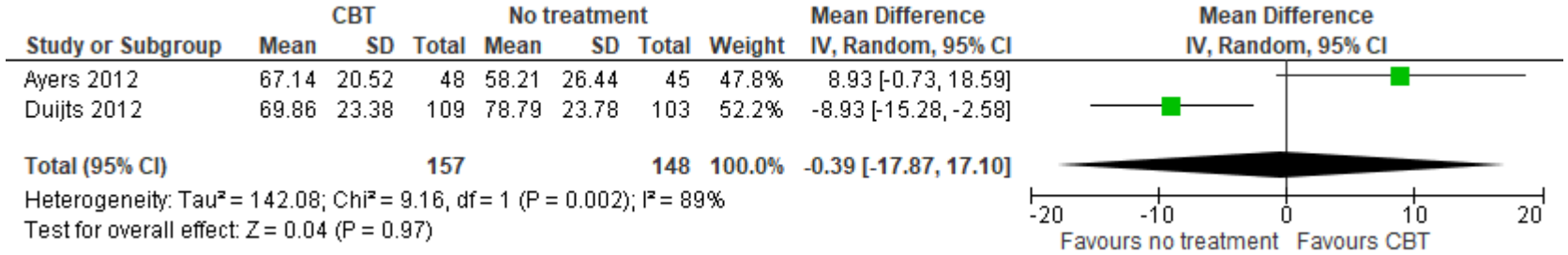


Figure 43: Quality of life (SF-36 bodily pain) at endpoint with stratification – Individual CBT

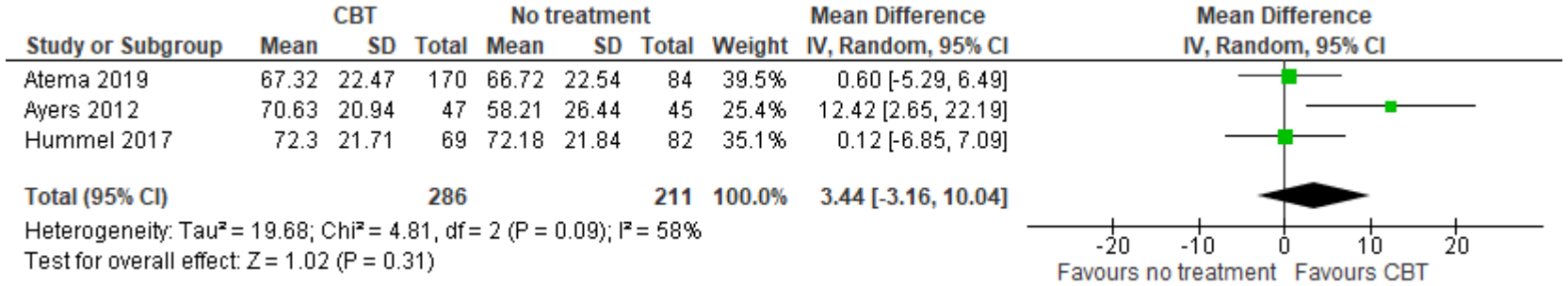


Figure 44: Quality of life (SF-36 bodily pain) at endpoint with stratification – Face to face CBT

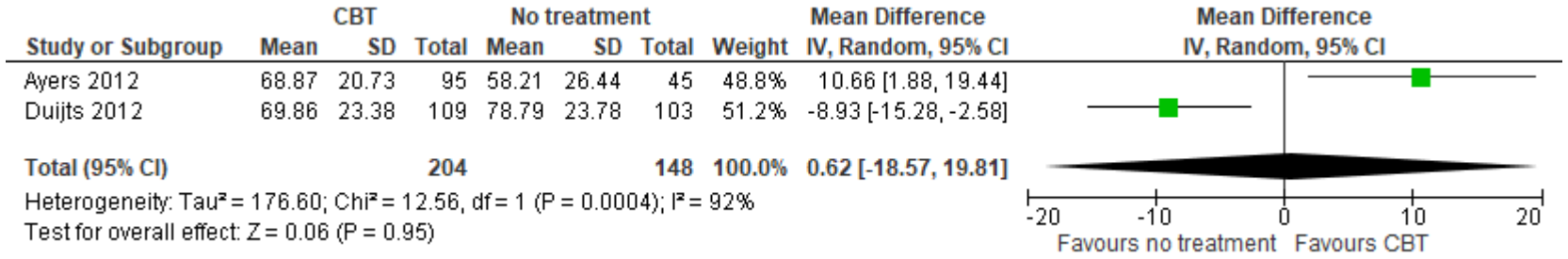


Figure 45: Quality of life (SF-36 bodily pain) at endpoint with stratification – Online CBT

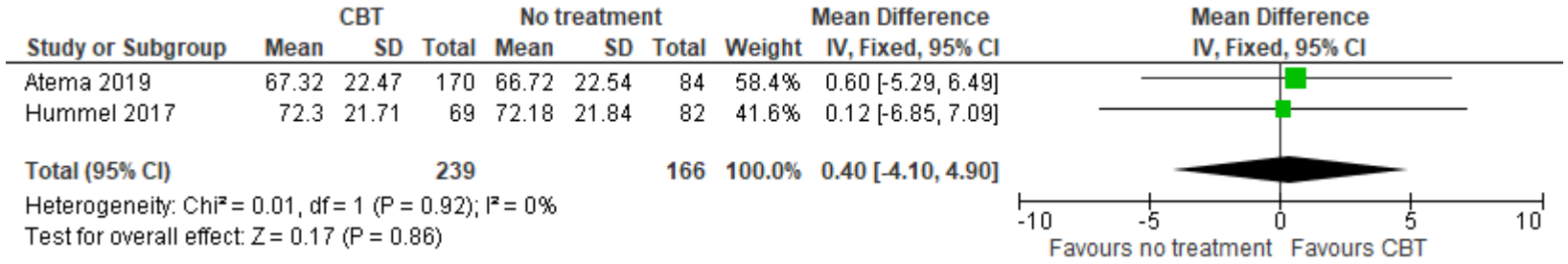


Figure 46: Quality of life (SF-36 bodily pain) at endpoint with stratification – Self-help CBT

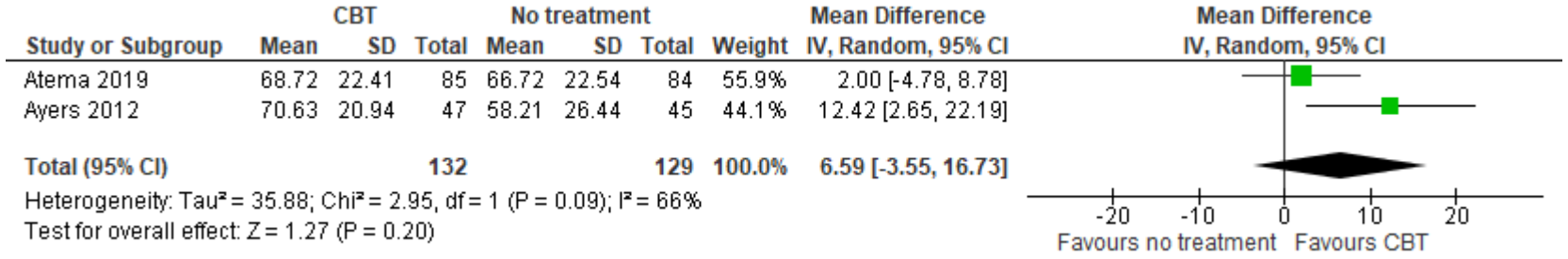


Figure 47: Quality of life (SF-36 bodily pain) at endpoint with stratification – Guided CBT

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Mean Difference IV, Random, 95% CI
Atema 2019	65.92	22.53	85	66.72	22.54	84	26.3%	-0.80 [-7.60, 6.00]
Ayers 2012	67.14	20.52	48	58.21	26.44	45	20.5%	8.93 [-0.73, 18.59]
Duijts 2012	69.86	23.38	109	78.79	23.78	103	27.2%	-8.93 [-15.28, -2.58]
Hummel 2017	72.3	21.71	69	72.18	21.84	82	25.9%	0.12 [-6.85, 7.09]
Total (95% CI)			**311**			**314**	**100.0%**	**-0.78 [-7.43, 5.88]**

Heterogeneity: Tau² = 31.82; Chi² = 9.95, df = 3 (P = 0.02); I² = 70%
Test for overall effect: Z = 0.23 (P = 0.82)

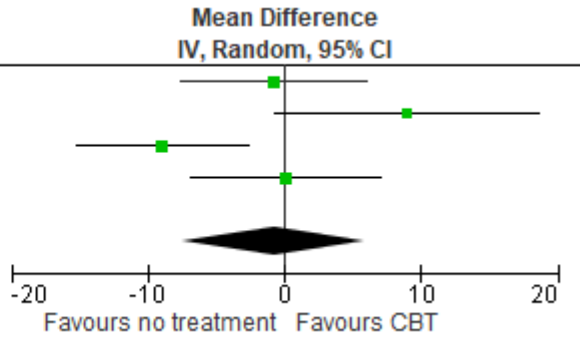


Figure 48: Quality of life (SF-36 bodily pain) at follow-up with stratification – Personal history of breast cancer/ Duration ≥6 sessions

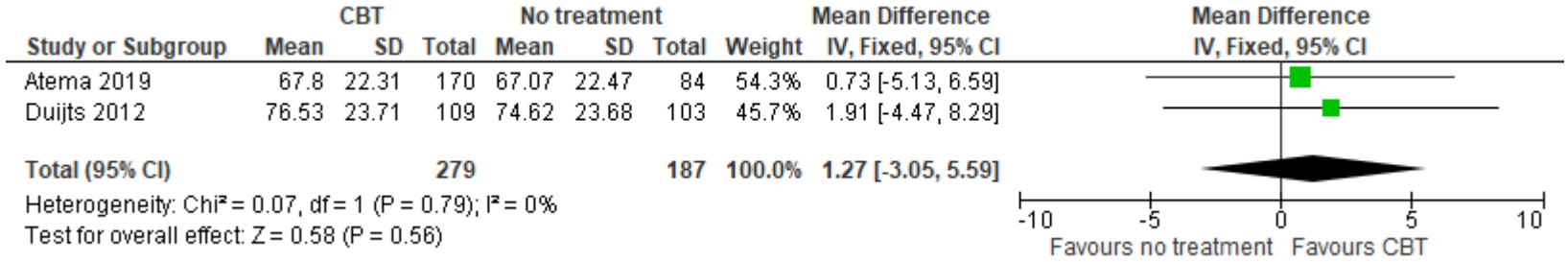


Figure 49: Quality of life (SF-36 bodily pain) at follow-up with stratification – Group CBT

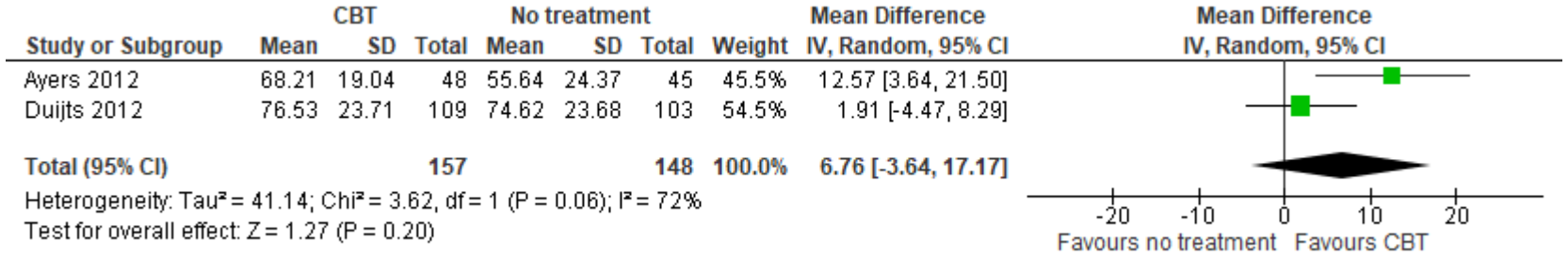


Figure 50: Quality of life (SF-36 bodily pain) at follow-up with stratification – Individual CBT

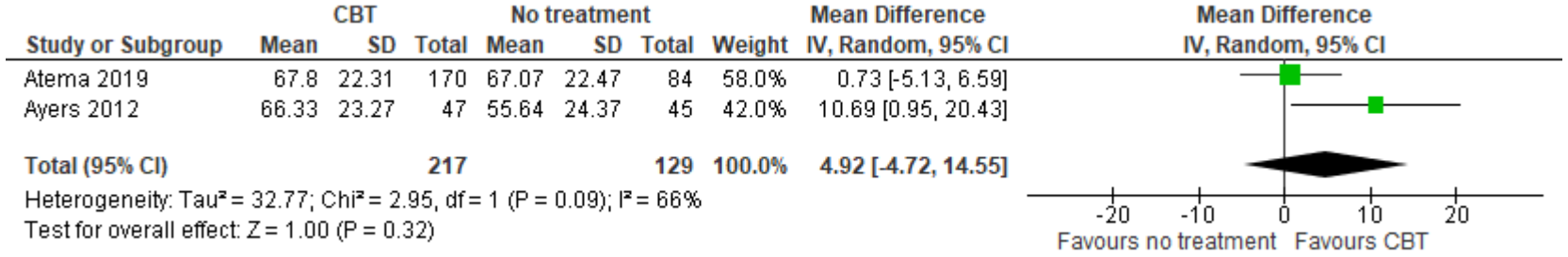


Figure 51: Quality of life (SF-36 bodily pain) at follow-up with stratification – Face to face CBT

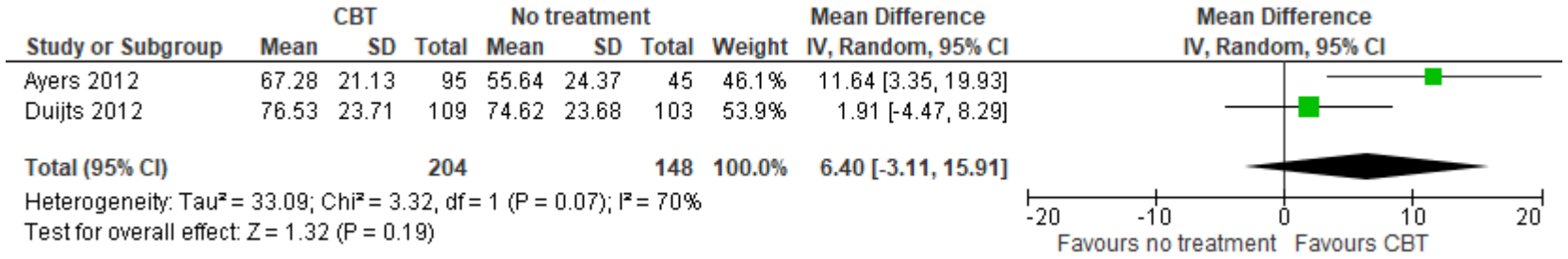


Figure 52: Quality of life (SF-36 bodily pain) at follow-up with stratification – Self-help CBT

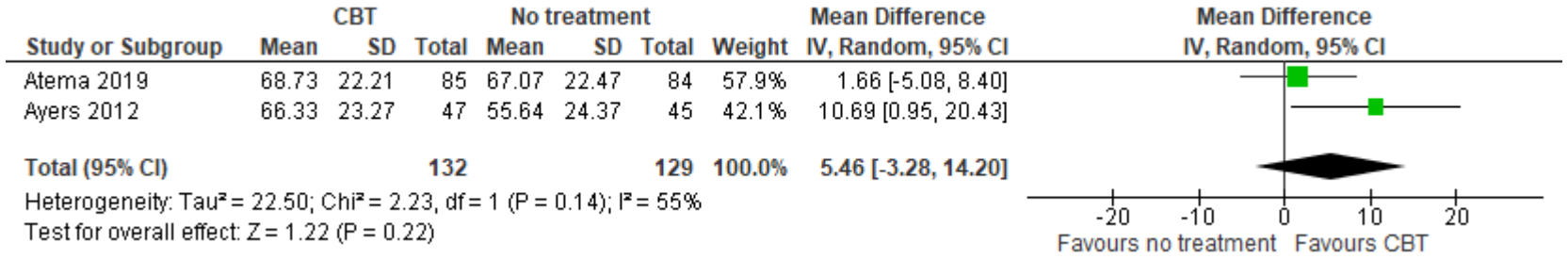


Figure 53: Quality of life (SF-36 bodily pain) at follow-up with stratification – Guided CBT

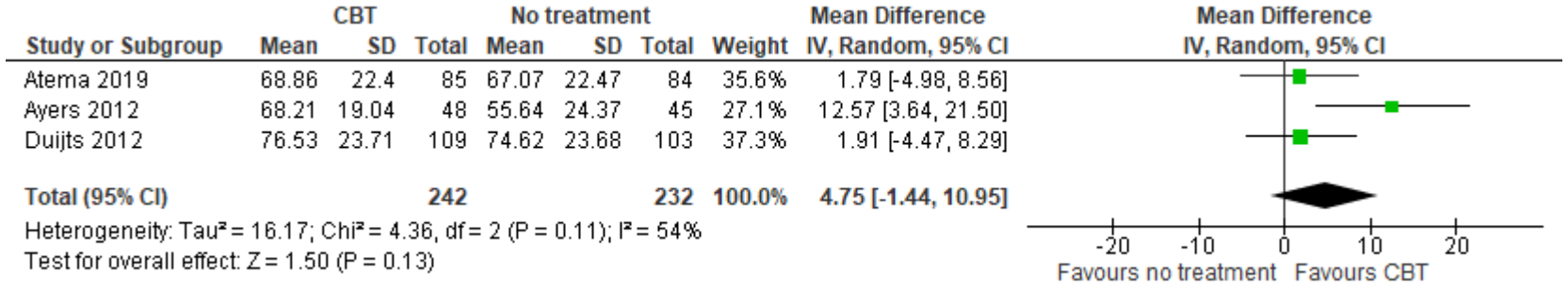


Figure 54: Quality of life (SF-36 general health) at endpoint with stratification – Personal history of breast cancer/ Online CBT/ Duration ≤6 sessions

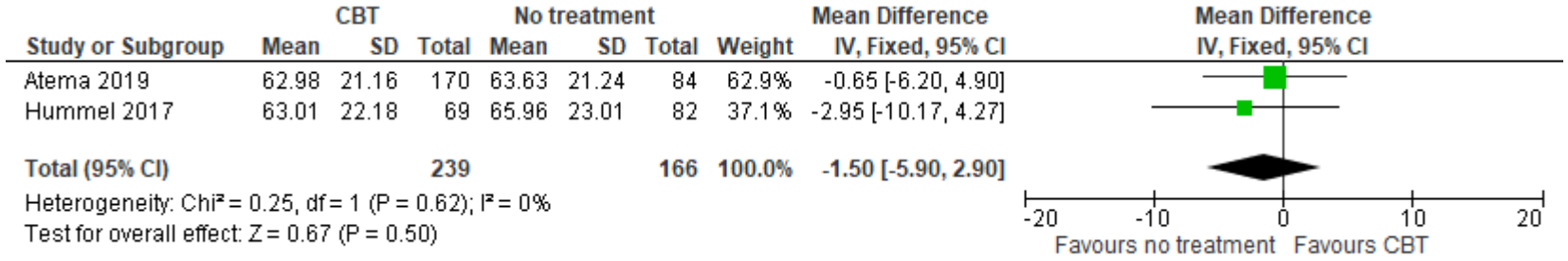


Figure 55: Quality of life (SF-36 general health) at endpoint with stratification - Individual CBT

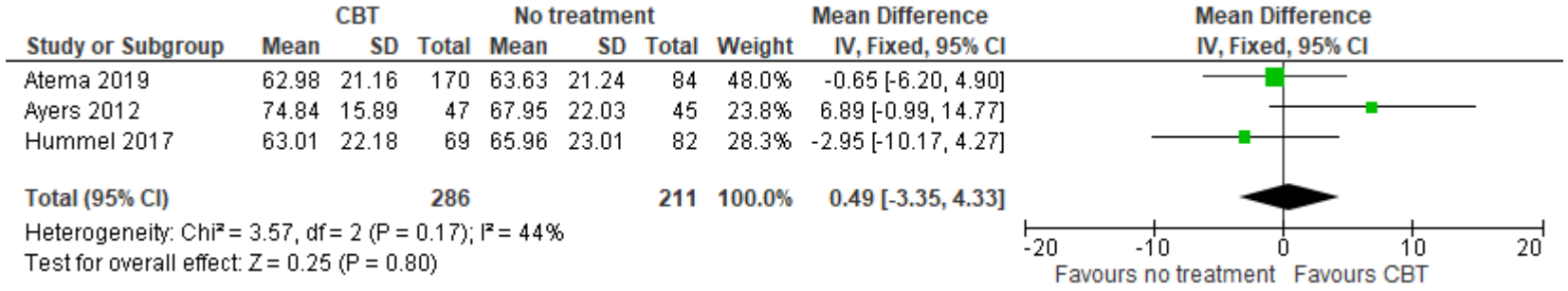


Figure 56: Quality of life (SF-36 general health) at endpoint with stratification – Self-help CBT

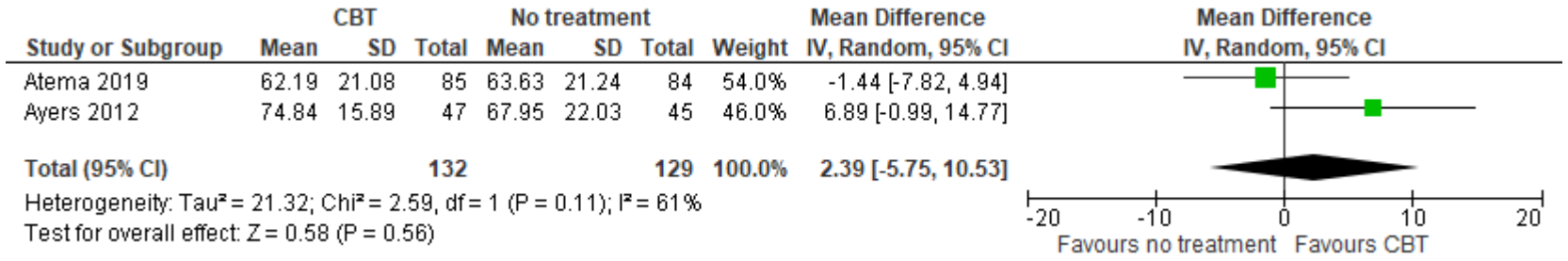


Figure 57: Quality of life (SF-36 general health) at endpoint with stratification – Guided CBT

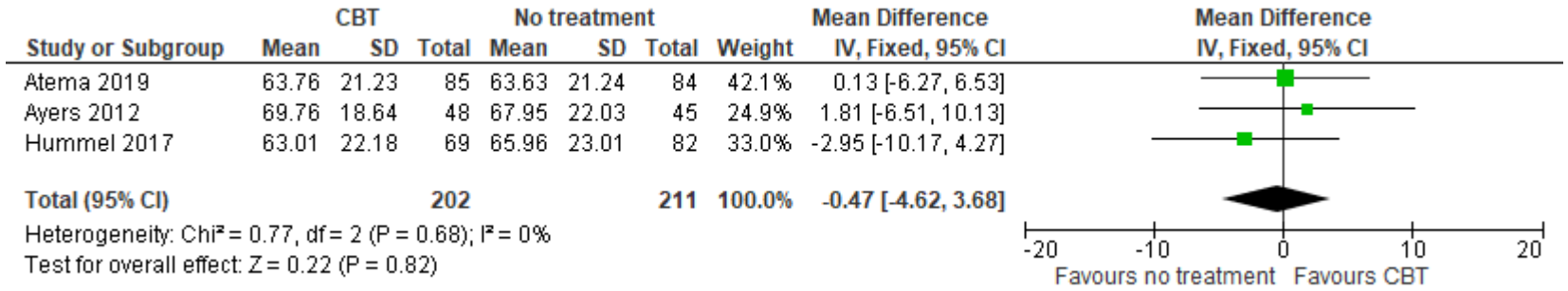


Figure 58: Quality of life (SF-36 general health) at follow-up with stratification – Individual CBT

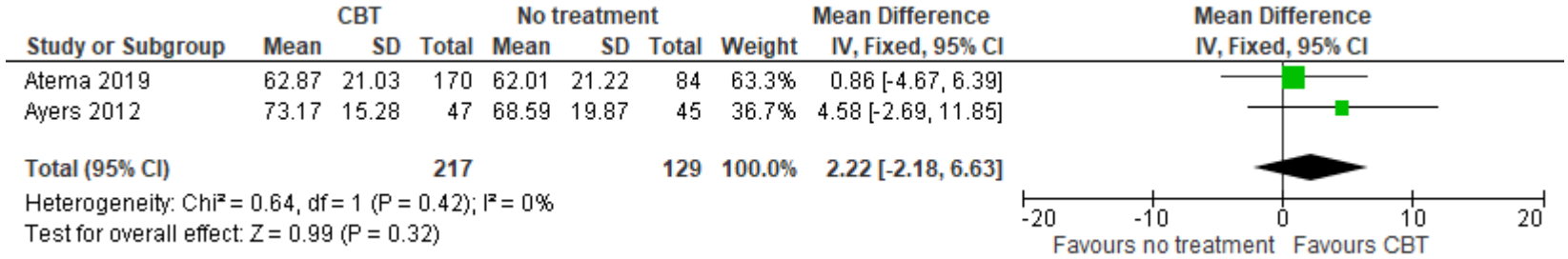


Figure 59: Quality of life (SF-36 general health) at follow-up with stratification – Self-help CBT

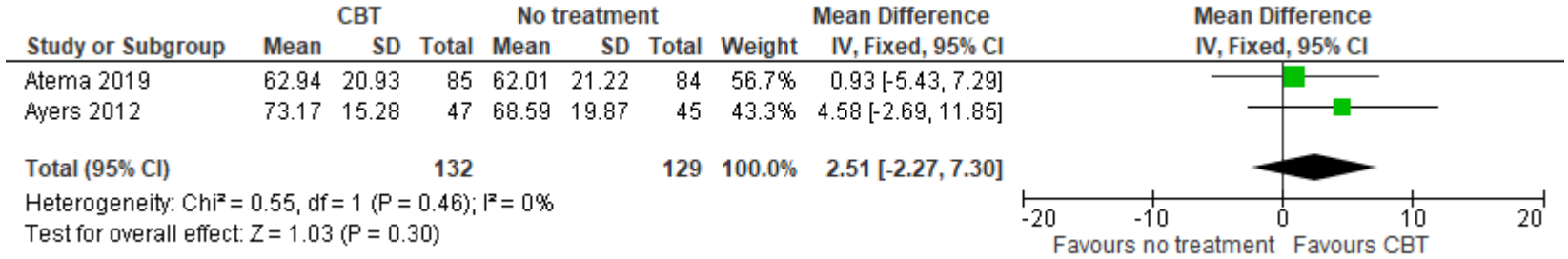


Figure 60: Quality of life (SF-36 general health) at follow-up with stratification – Guided CBT

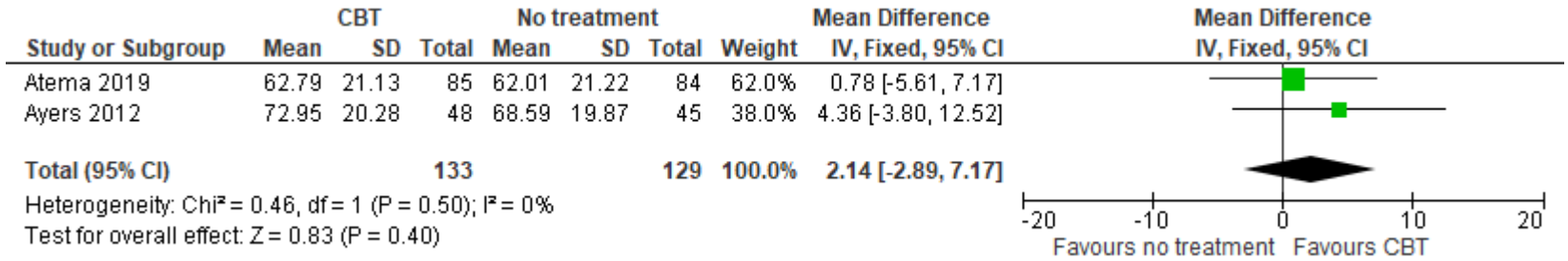


Figure 61: Quality of life (SF-36 vitality) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions

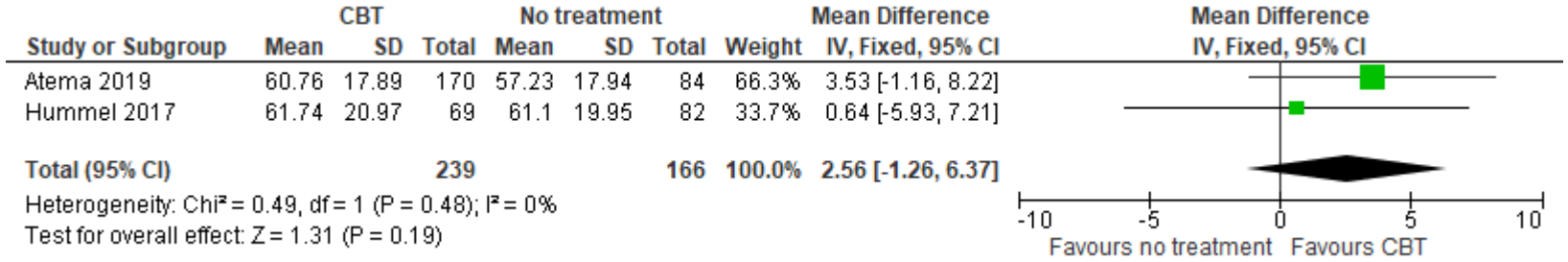


Figure 62: Quality of life (SF-36 vitality) at endpoint with stratification - Individual CBT

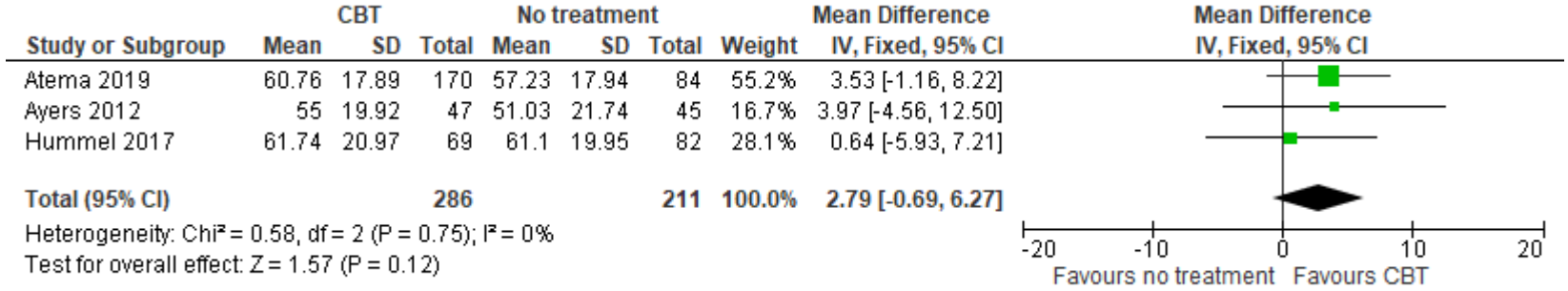


Figure 63: Quality of life (SF-36 vitality) at endpoint with stratification – Self-help CBT

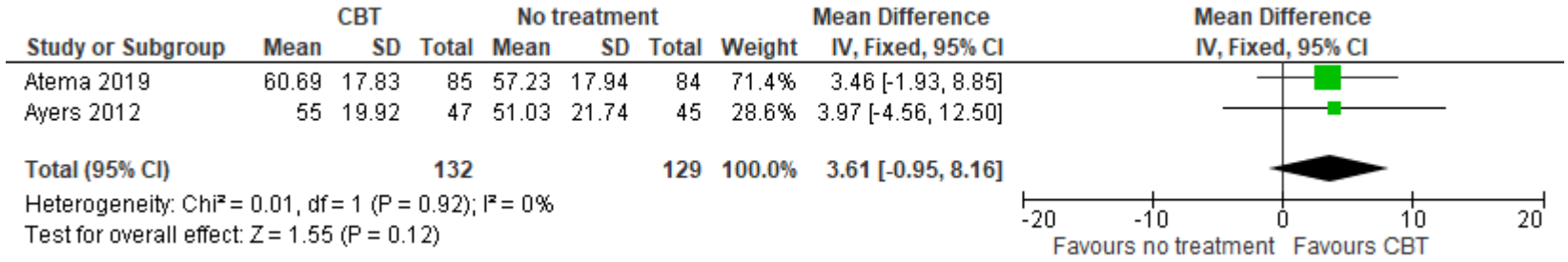


Figure 64: Quality of life (SF-36 vitality) at endpoint with stratification – Guided CBT

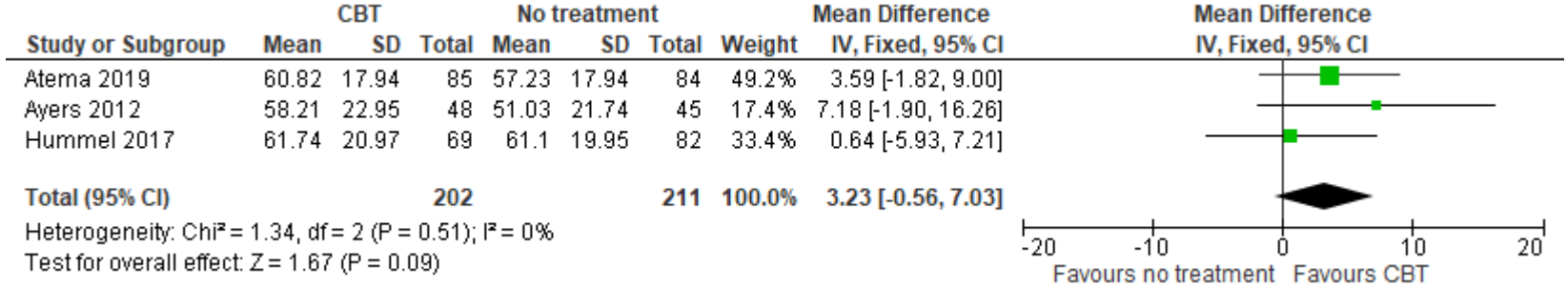


Figure 65: Quality of life (SF-36 vitality) at follow-up with stratification – Individual CBT

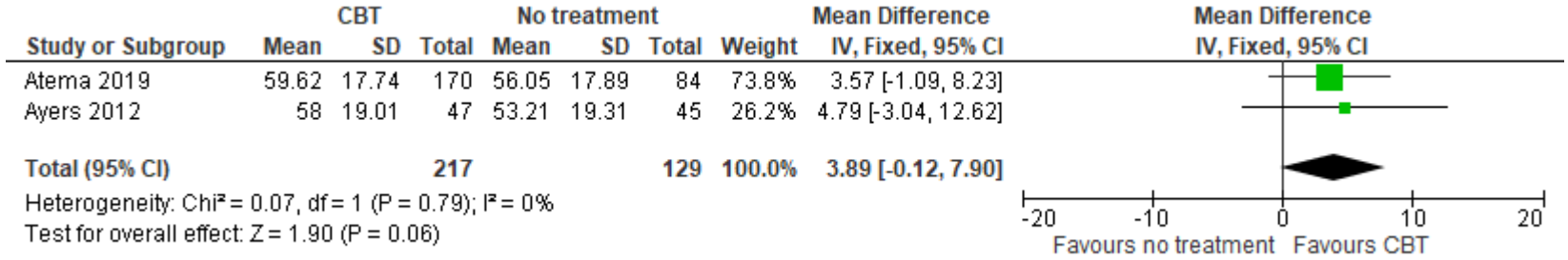


Figure 66: Quality of life (SF-36 vitality) at follow-up with stratification – Self-help CBT

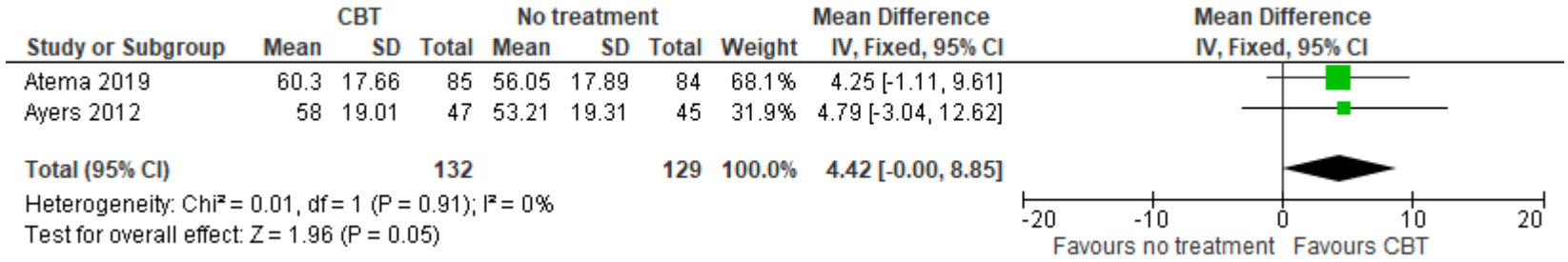


Figure 67: Quality of life (SF-36 vitality) at follow-up with stratification – Guided CBT

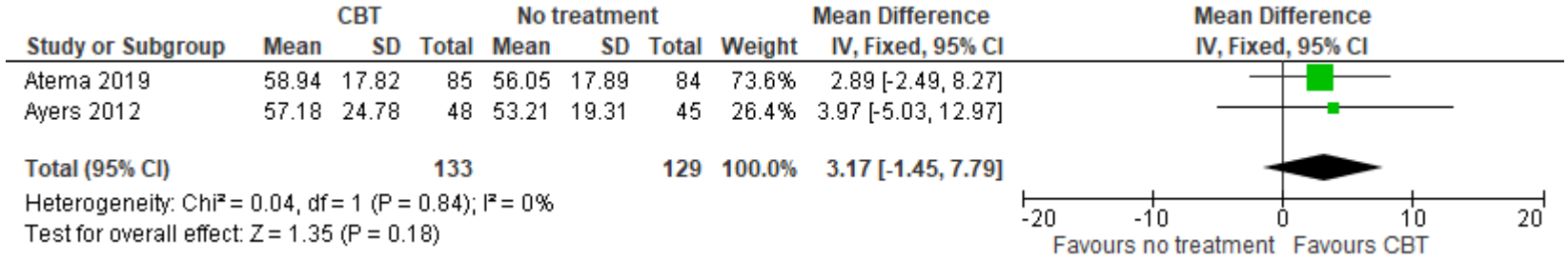


Figure 68: Quality of life (SF-36 mental health) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions

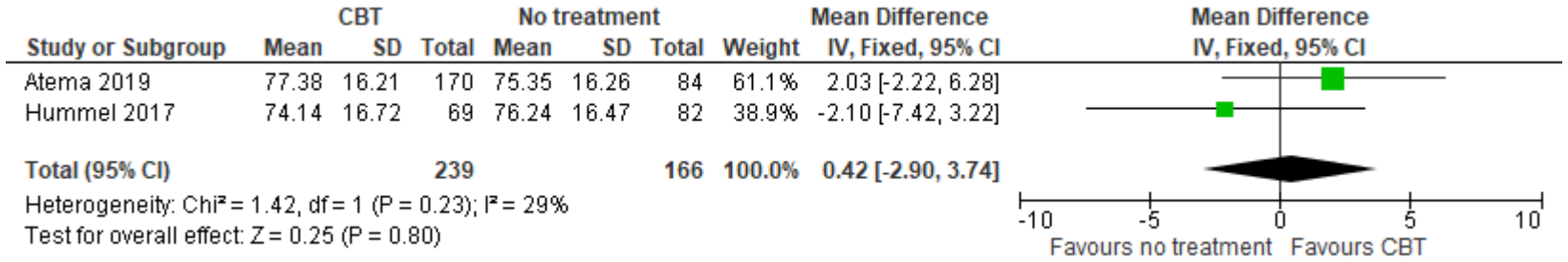


Figure 69: Quality of life (SF-36 mental health) at endpoint with stratification - Individual CBT

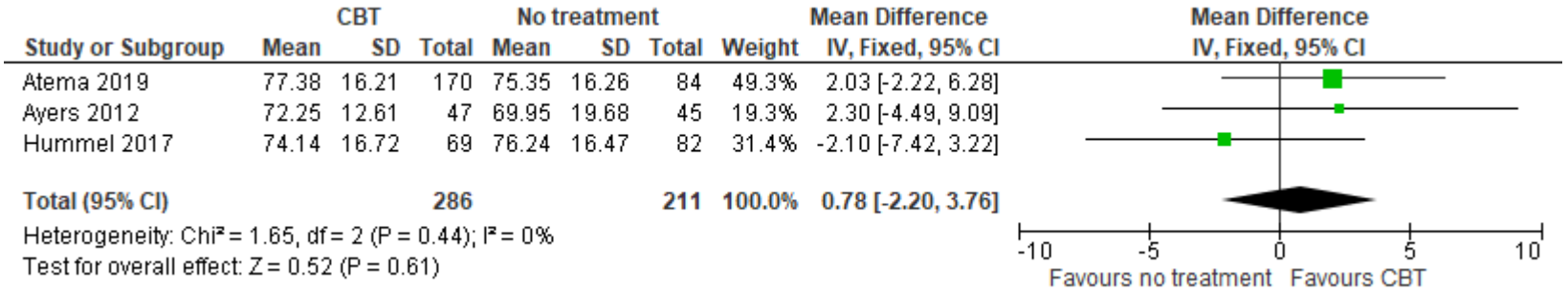


Figure 70: Quality of life (SF-36 mental health) at endpoint with stratification – Self-help CBT

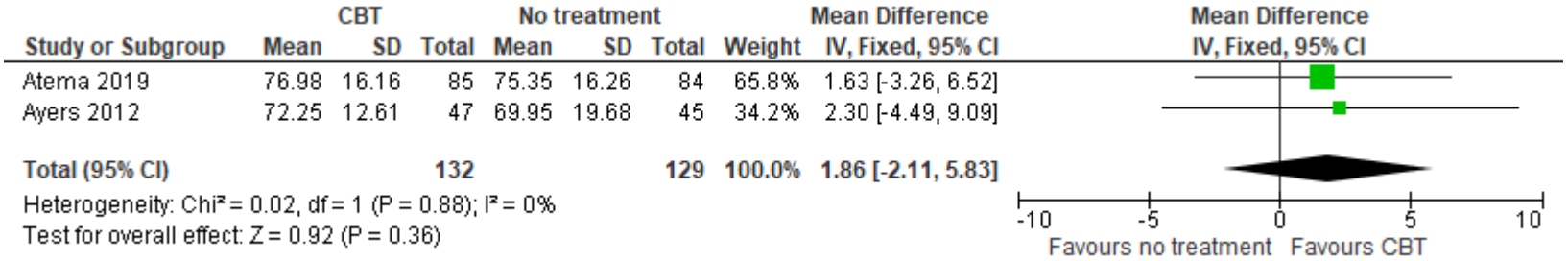


Figure 71: Quality of life (SF-36 mental health) at endpoint with stratification – Guided CBT

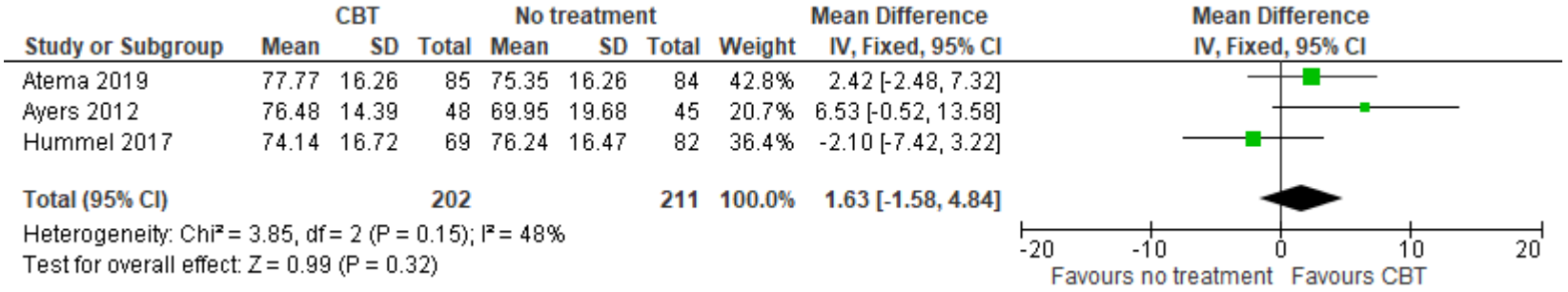


Figure 72: Quality of life (SF-36 mental health) at follow-up with stratification – Individual CBT

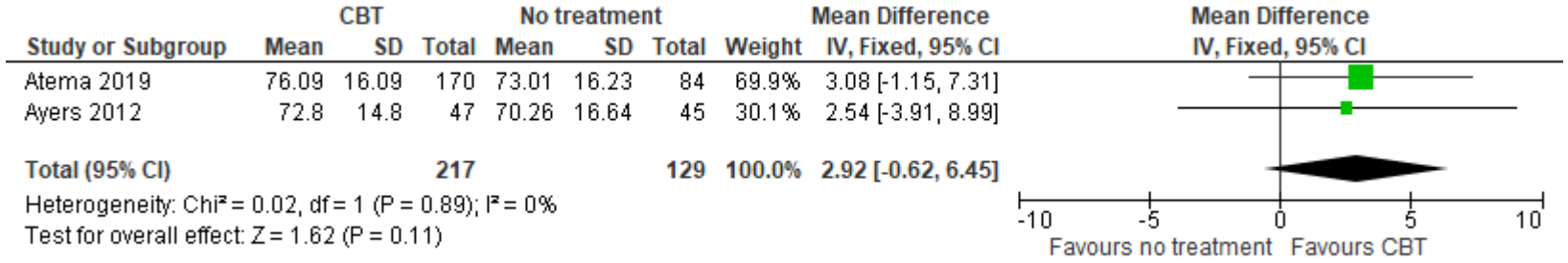


Figure 73: Quality of life (SF-36 mental health) at follow-up with stratification – Self-help CBT

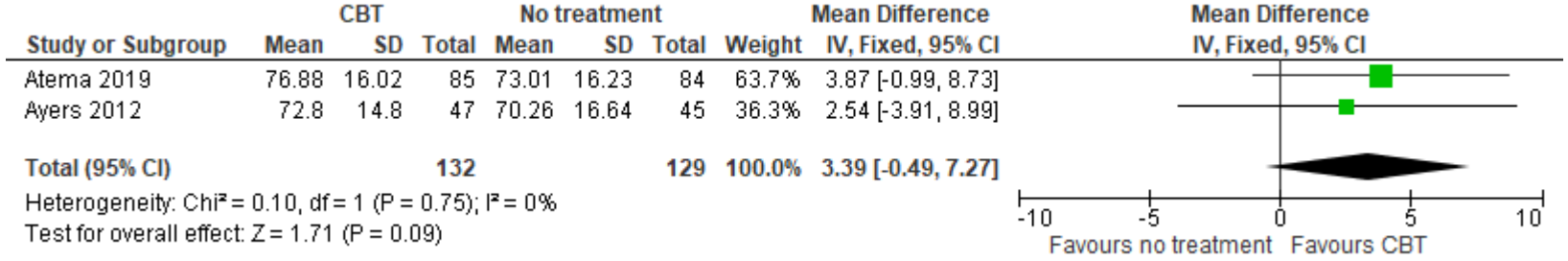


Figure 74: Quality of life (SF-36 mental health) at follow-up with stratification – Guided CBT

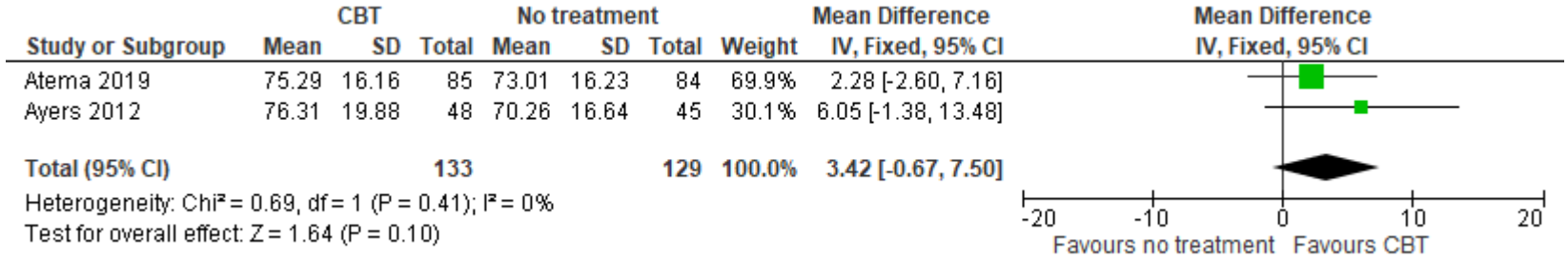


Figure 75: Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification – No personal history of breast cancer/ Duration <6 sessions

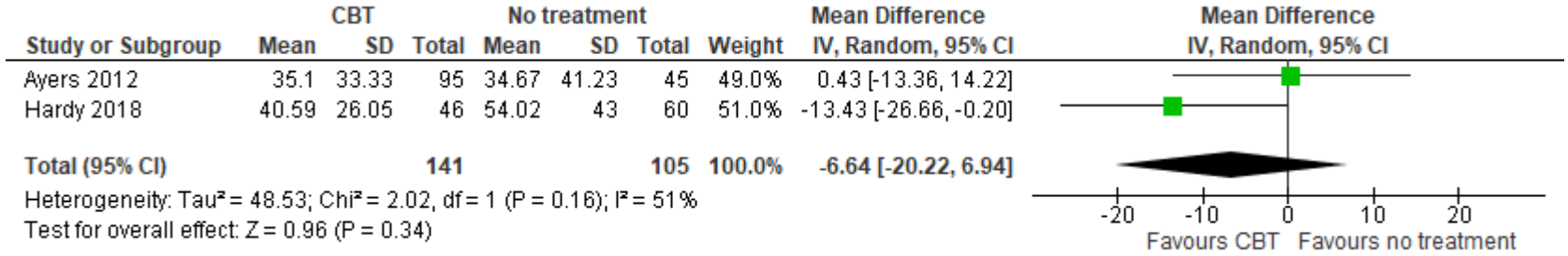


Figure 76: Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification – Individual CBT

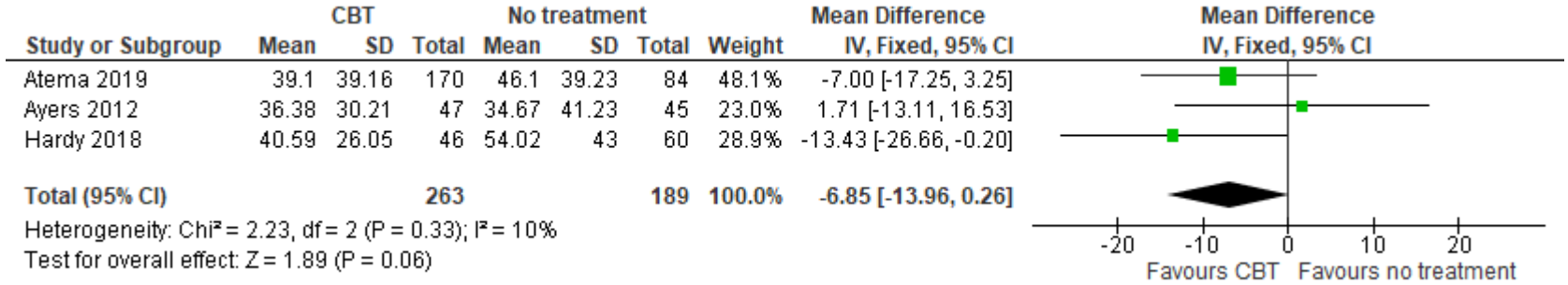


Figure 77: Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification – Online CBT

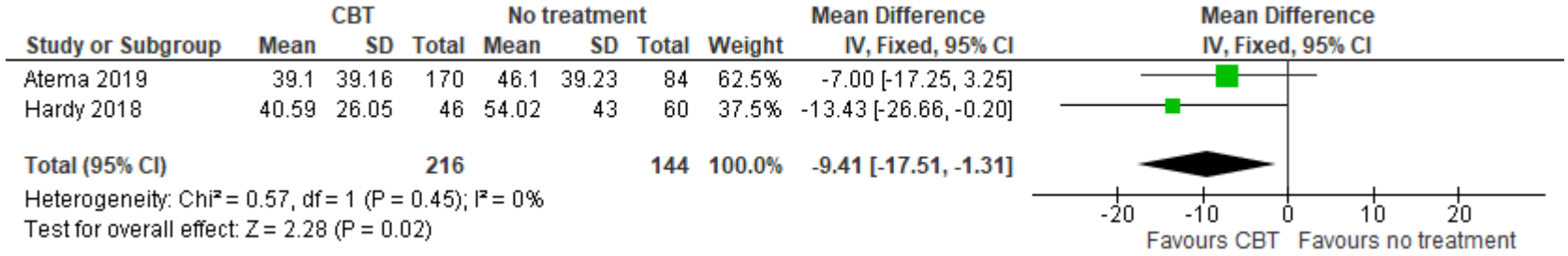


Figure 78: Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification – Self-help CBT

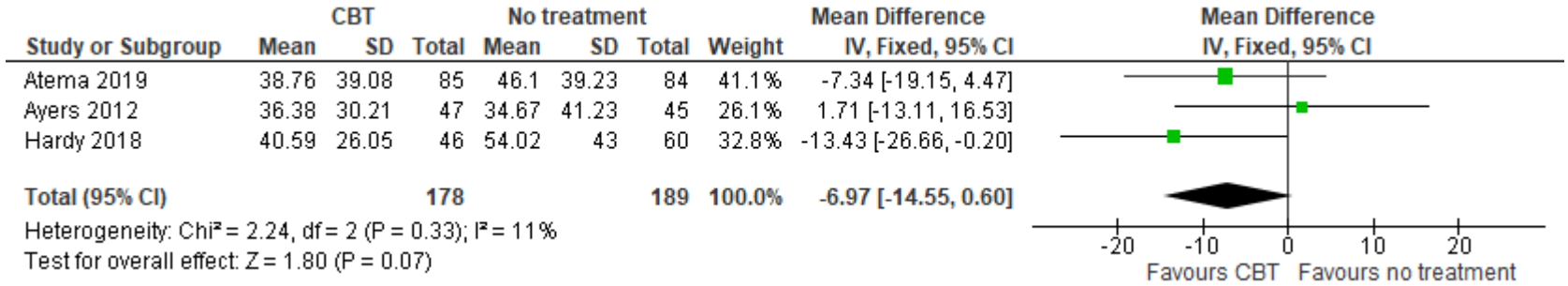


Figure 79: Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification – Guided CBT

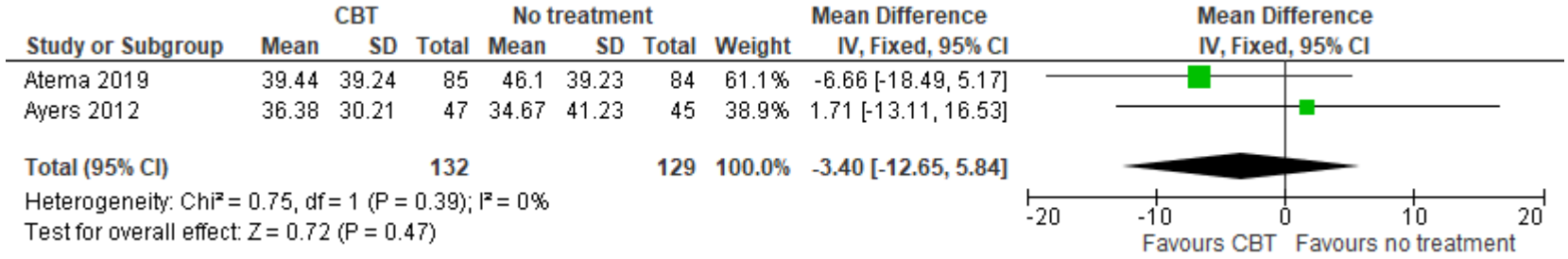


Figure 80: Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - No personal history of breast cancer/ Duration <6 sessions

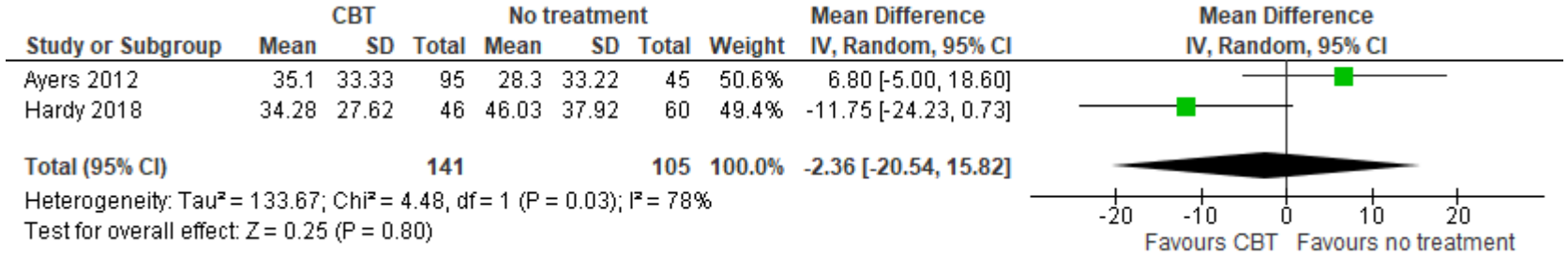


Figure 81: Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification – Individual CBT

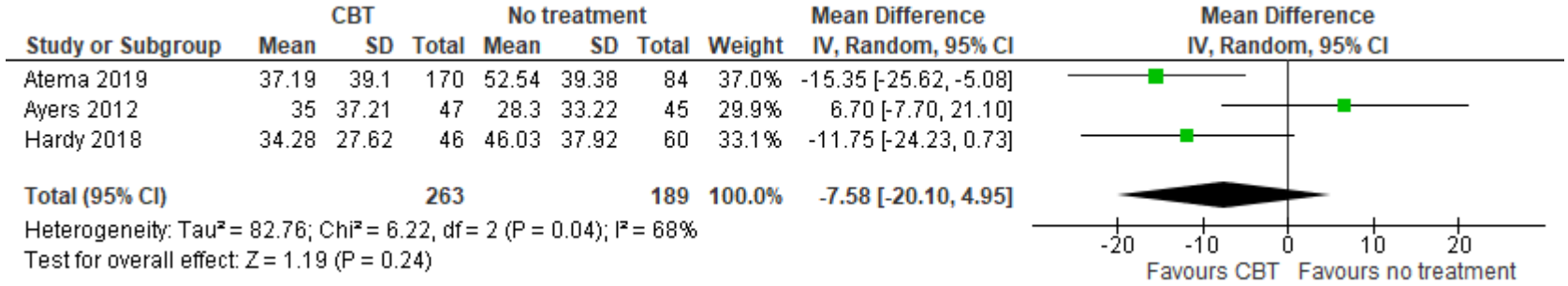


Figure 82: Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification – Online CBT

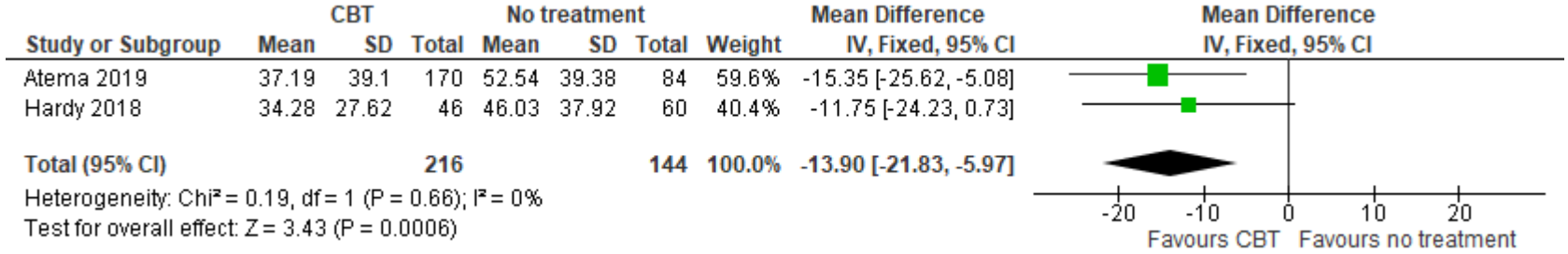


Figure 83: Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification – Self-help CBT

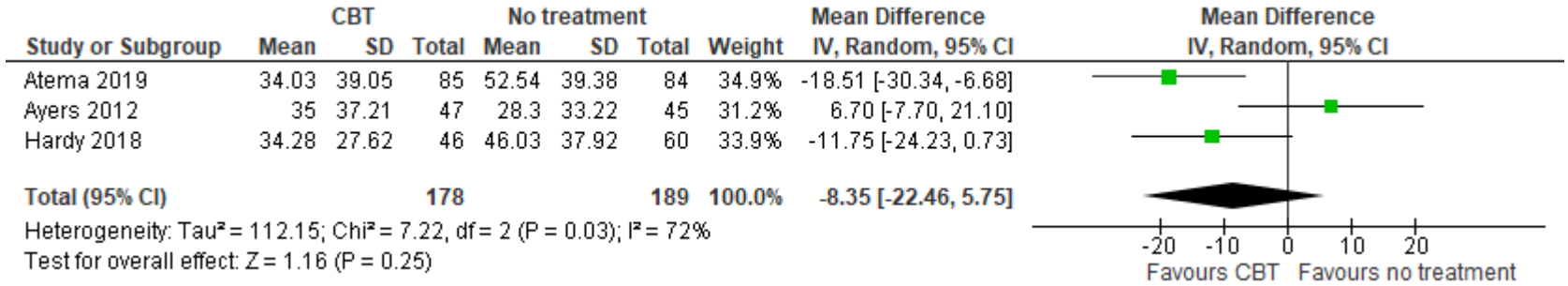


Figure 84: Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification – Guided CBT

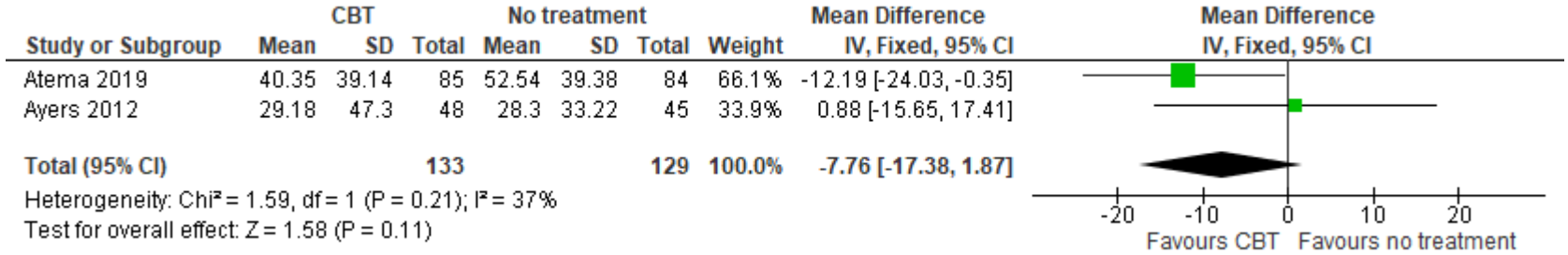


Figure 85: Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification – Individual CBT

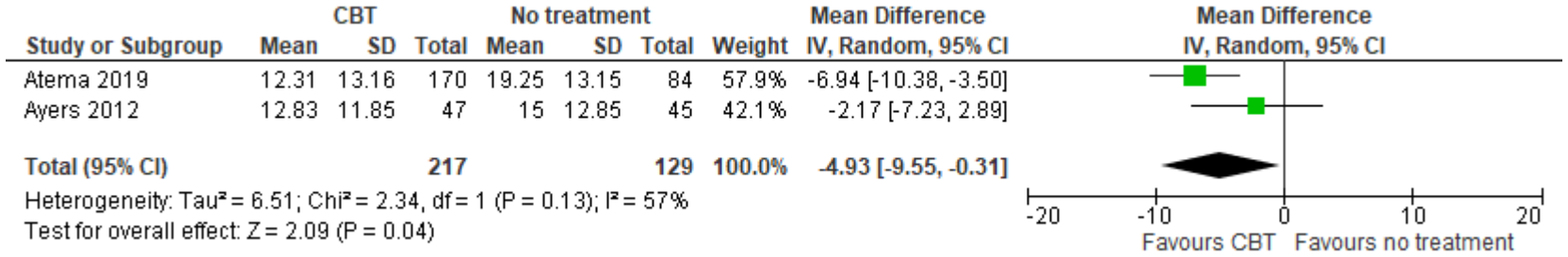


Figure 86: Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification – Self-help CBT

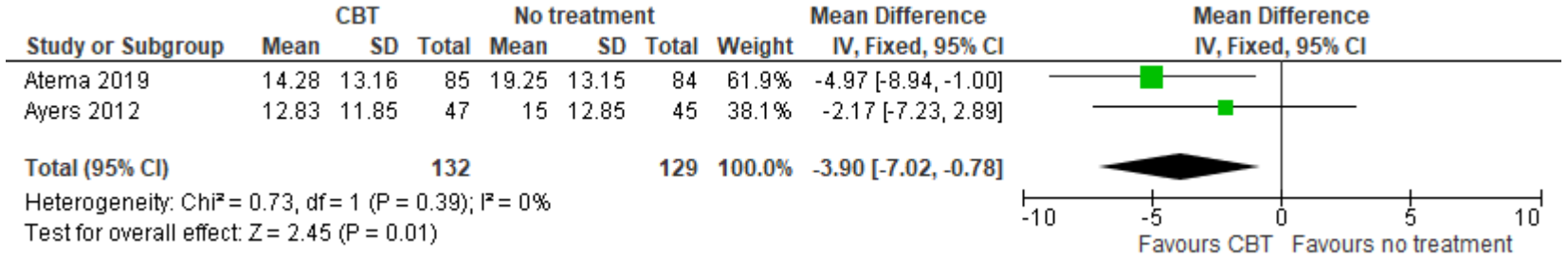


Figure 87: Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification – Guided CBT

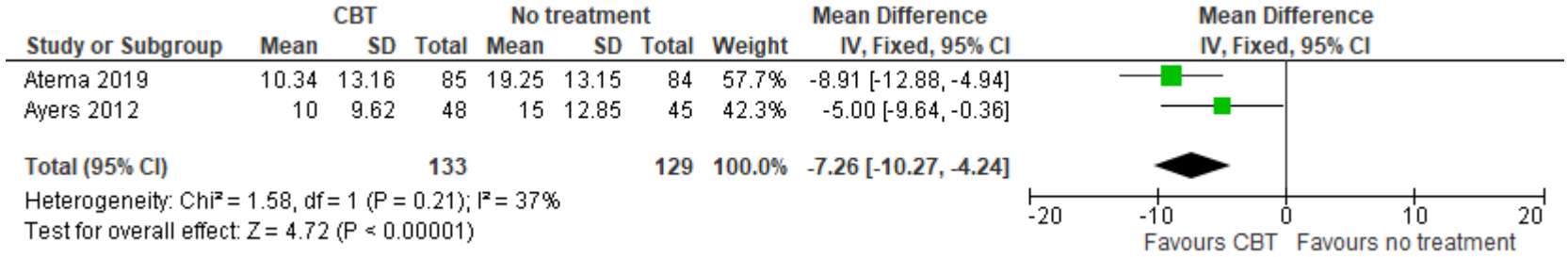


Figure 88: Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification – Self-help CBT

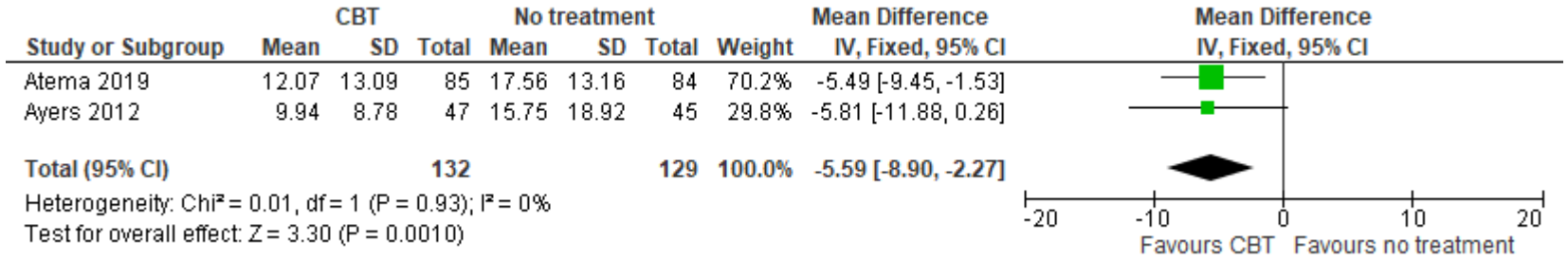


Figure 89: Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification – Guided CBT

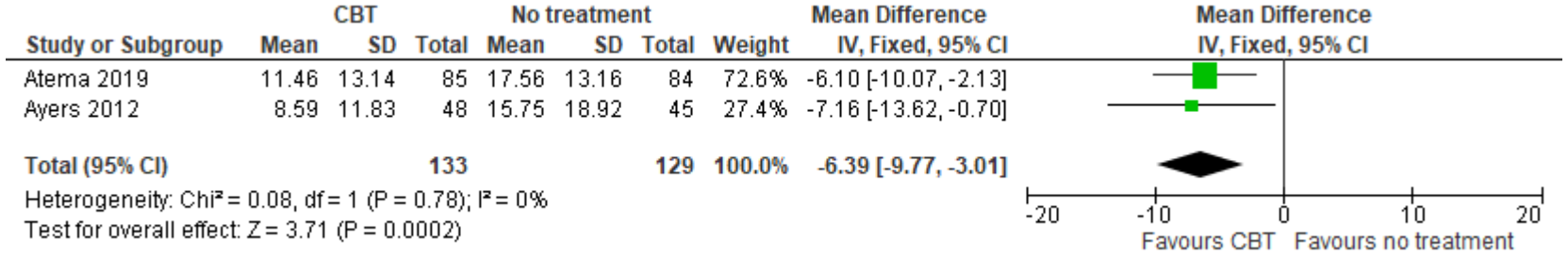


Figure 90: Vasomotor symptoms frequency (biolog, diary) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions

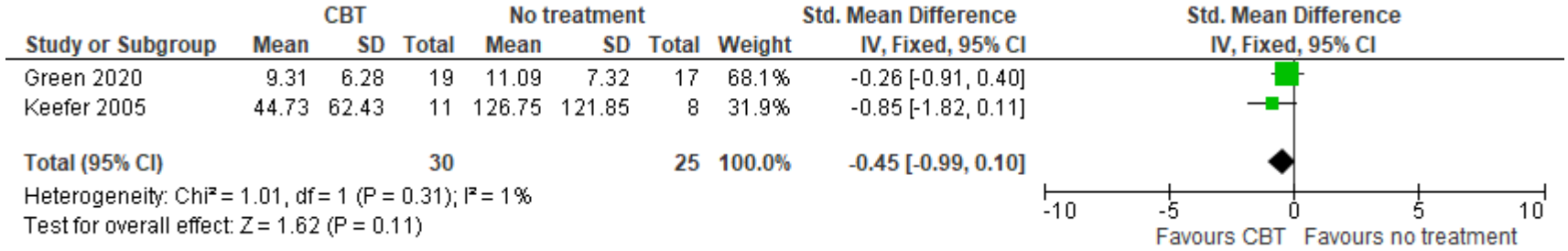


Figure 91: Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions

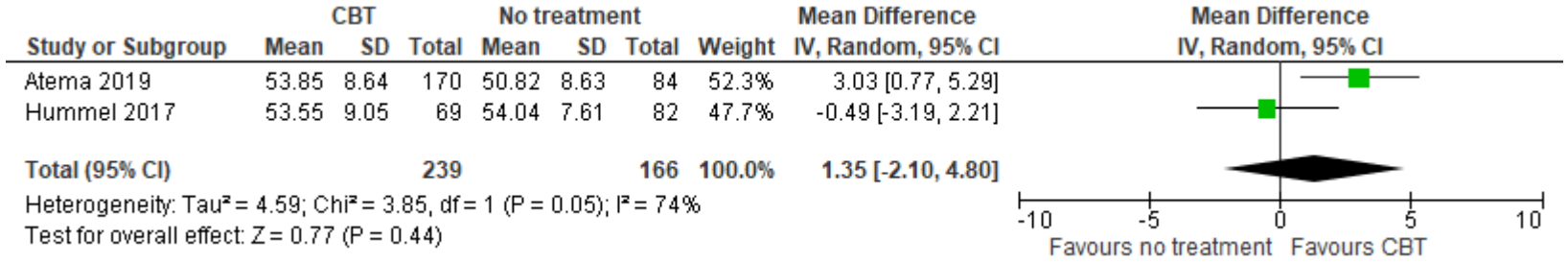


Figure 92: Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Guided CBT

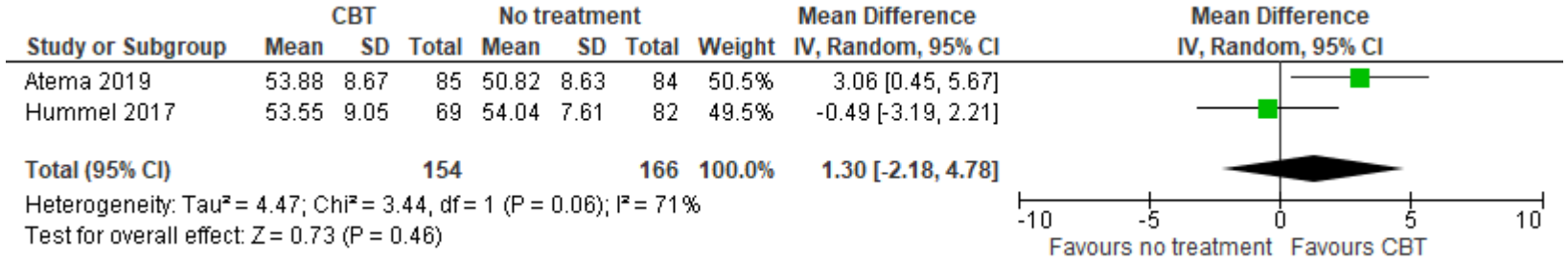


Figure 93: Vasomotor symptoms severity (GCS-vm) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions

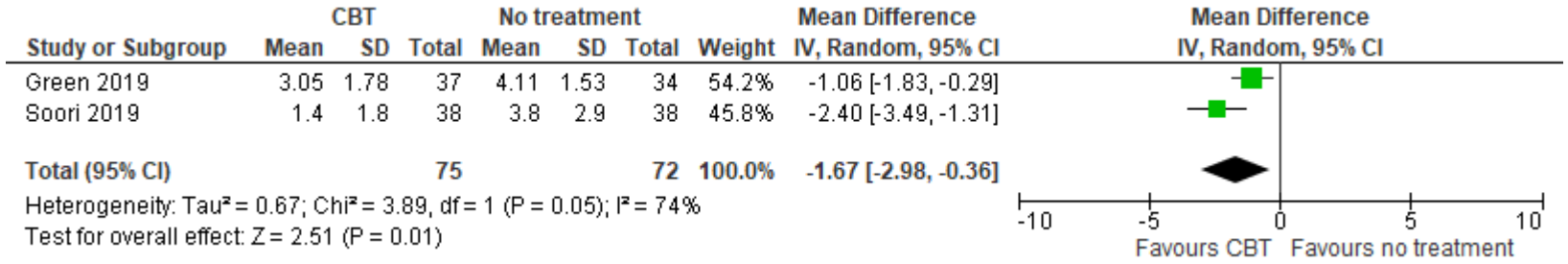


Figure 94: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions

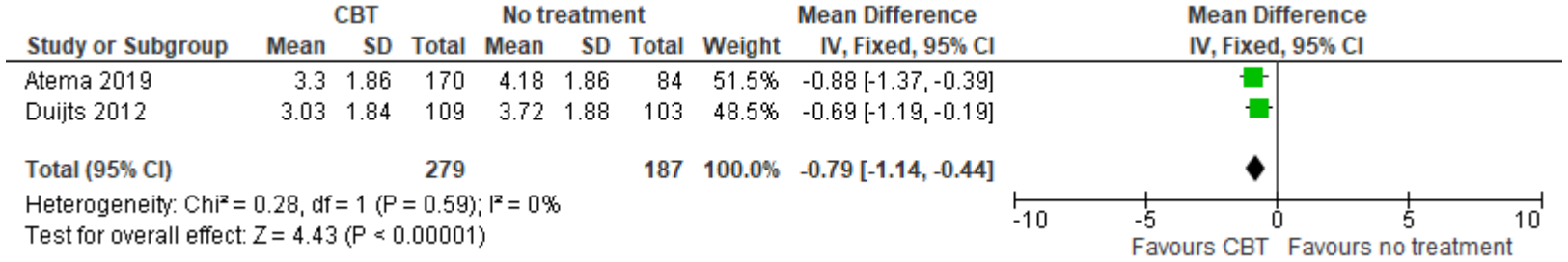


Figure 95: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – No personal history of breast cancer/ Duration <6 sessions

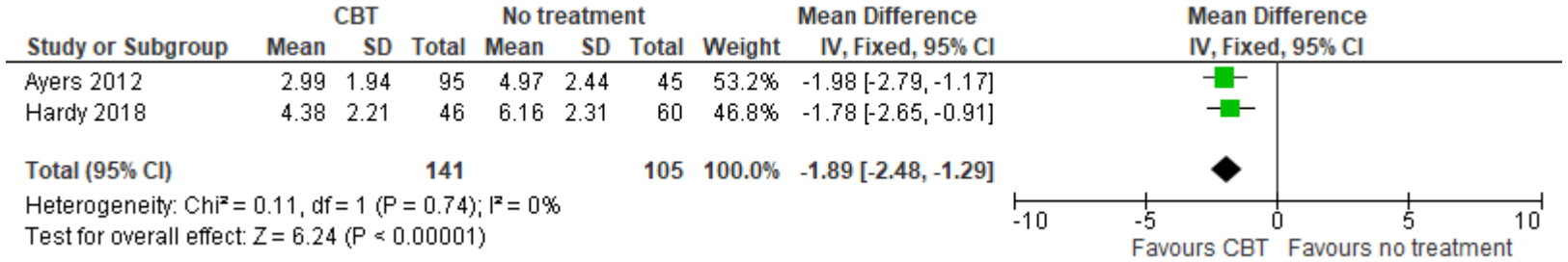


Figure 96: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Group CBT

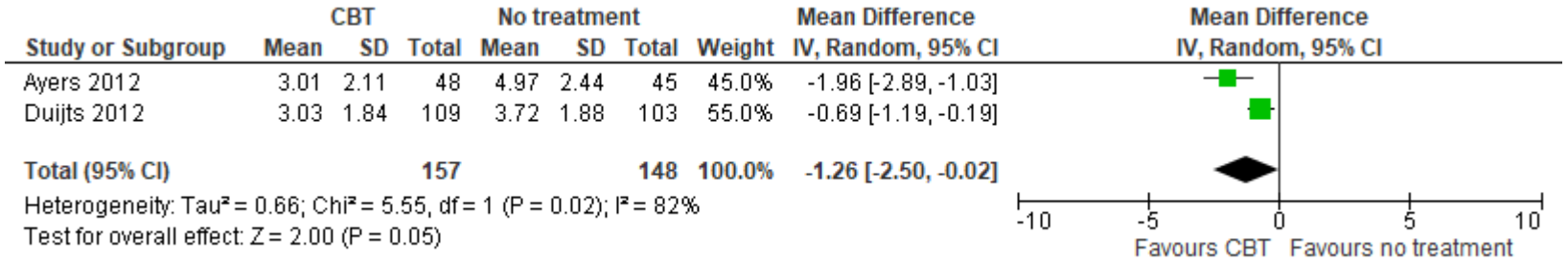


Figure 97: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Individual CBT

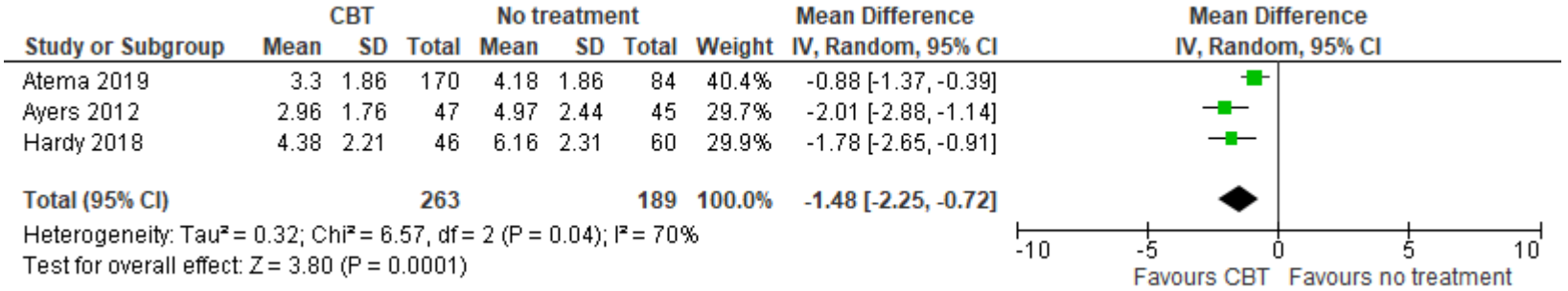


Figure 98: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Face to face CBT

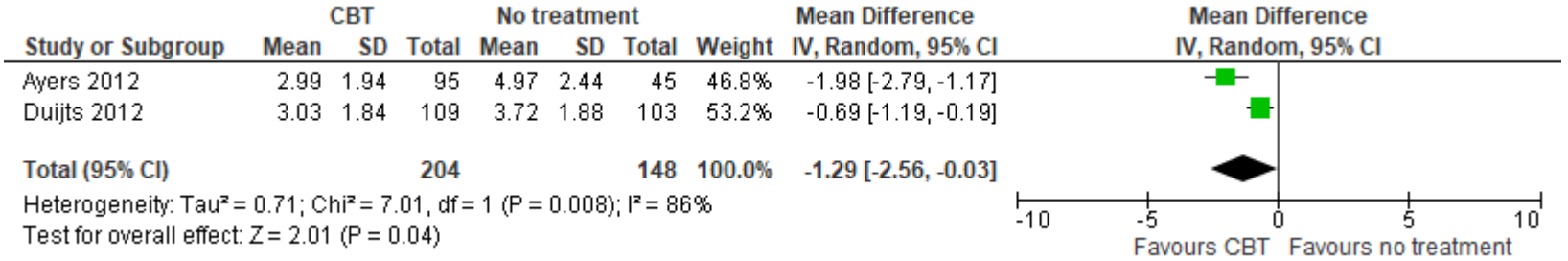


Figure 99: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Online CBT

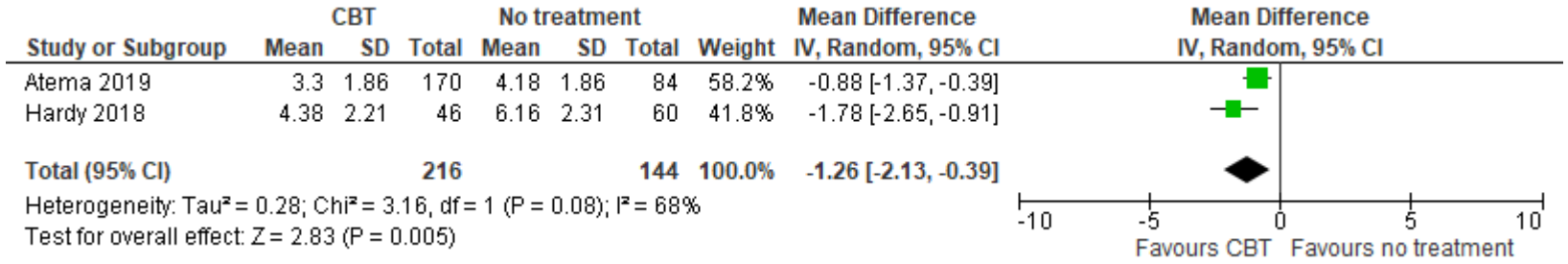


Figure 100: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Self-help CBT

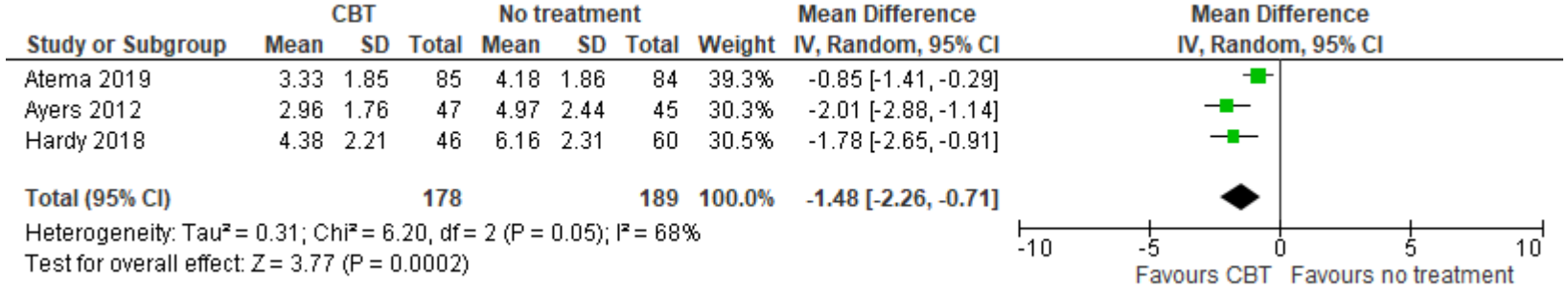


Figure 101: Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification – Guided CBT

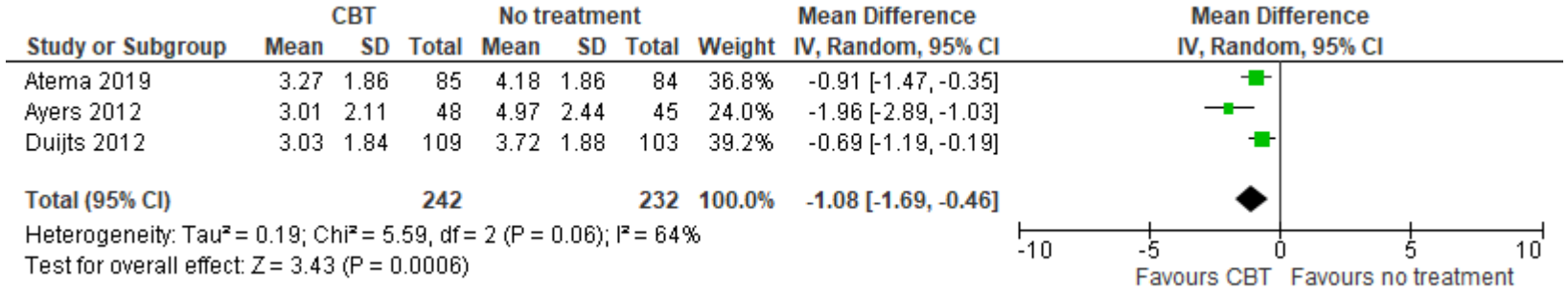


Figure 102: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Personal history of breast

cancer/ Duration ≥6 sessions

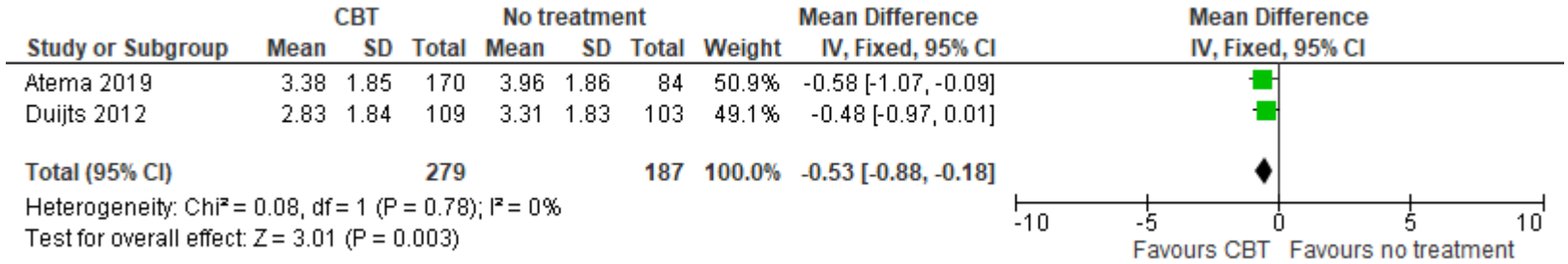


Figure 103: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – No personal history of breast cancer/ Duration <6 sessions

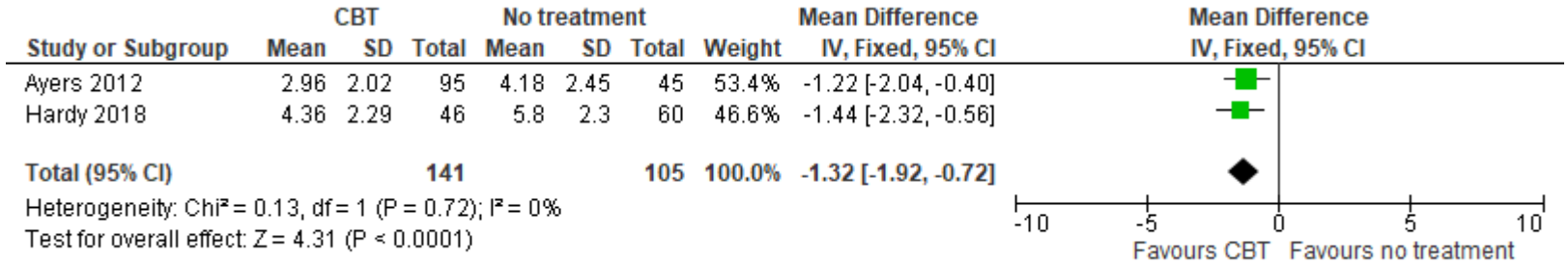


Figure 104: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Group CBT

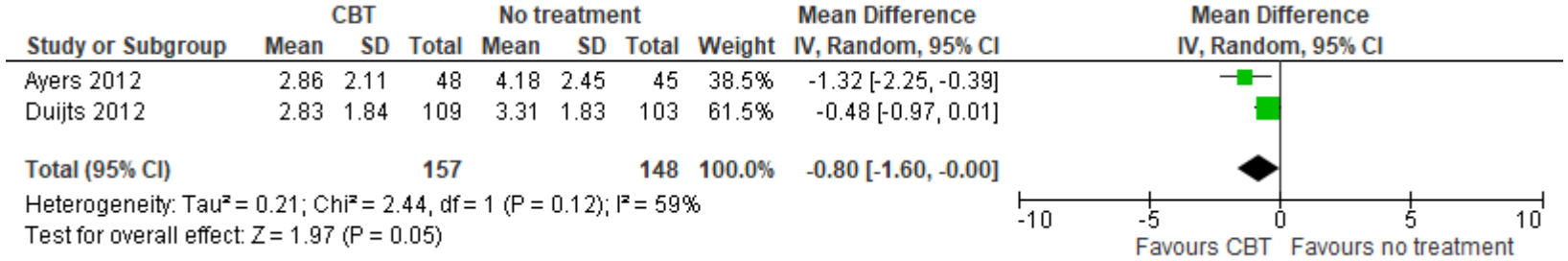


Figure 105: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Individual CBT

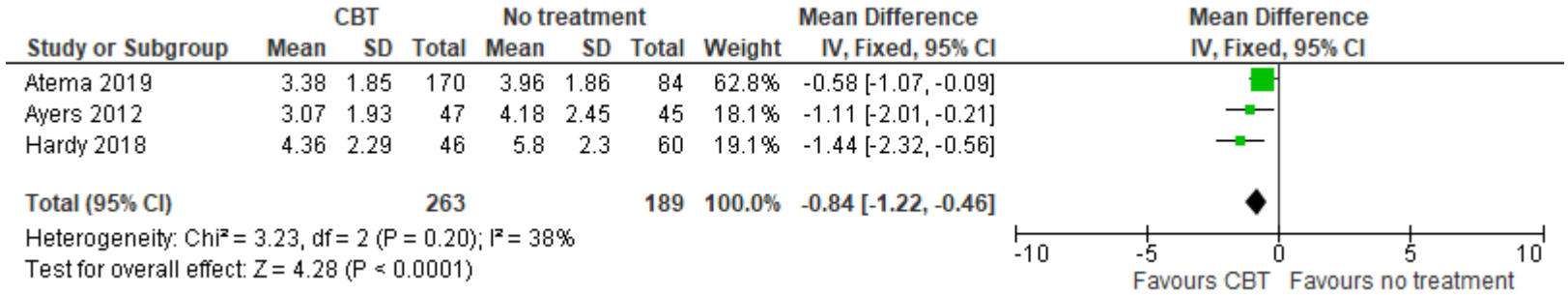


Figure 106: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Face to face CBT

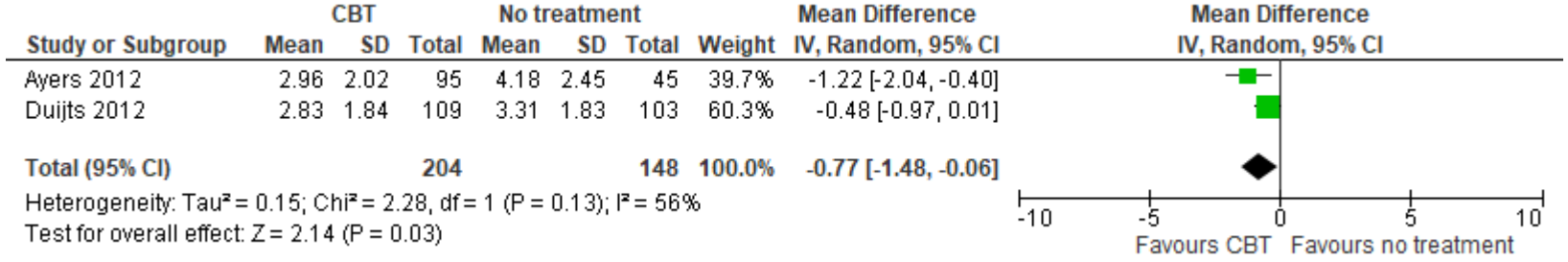


Figure 107: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Online CBT

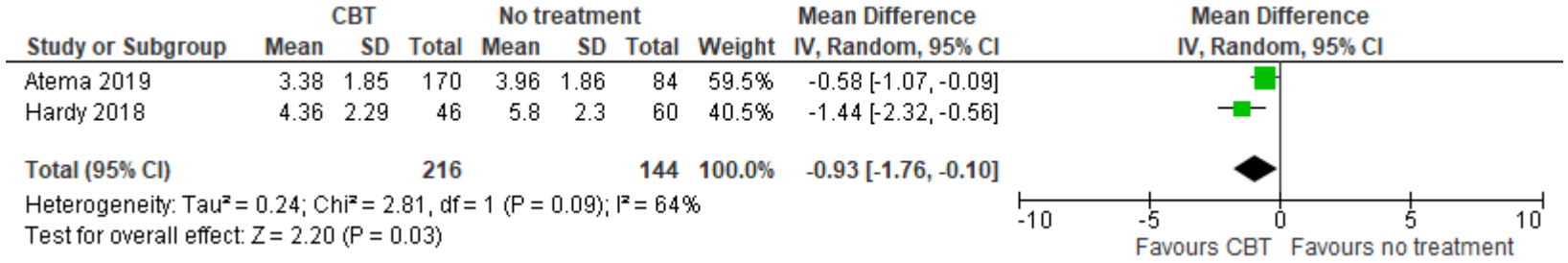


Figure 108: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Self-help CBT

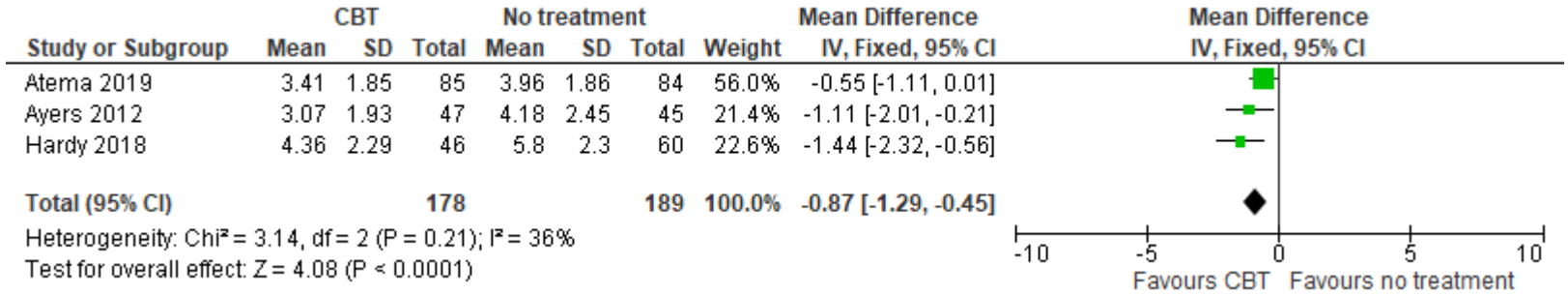


Figure 109: Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification – Guided CBT

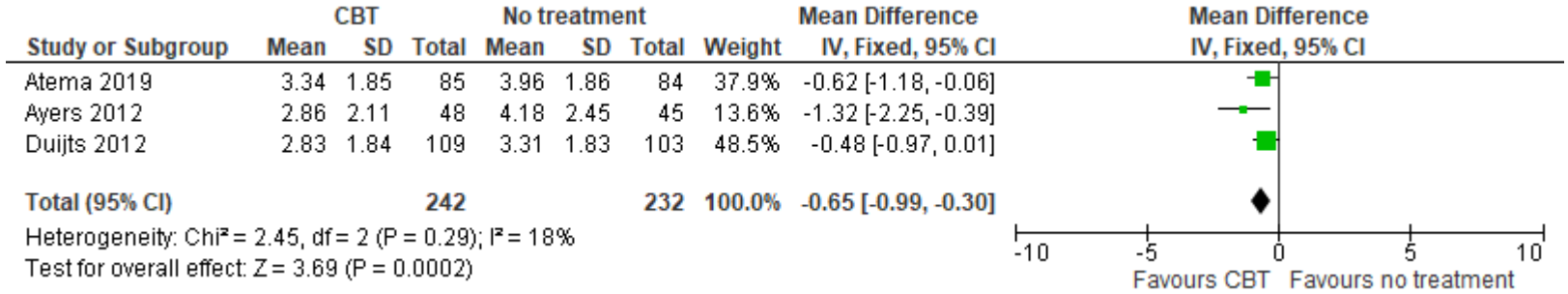


Figure 110: Vasomotor symptoms distress or bother (biolog, diary) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions

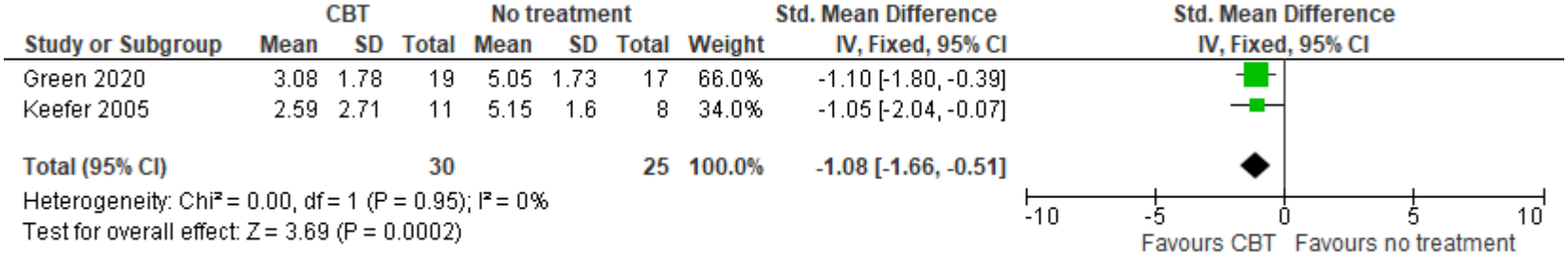


Figure 111: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – No personal history of breast cancer

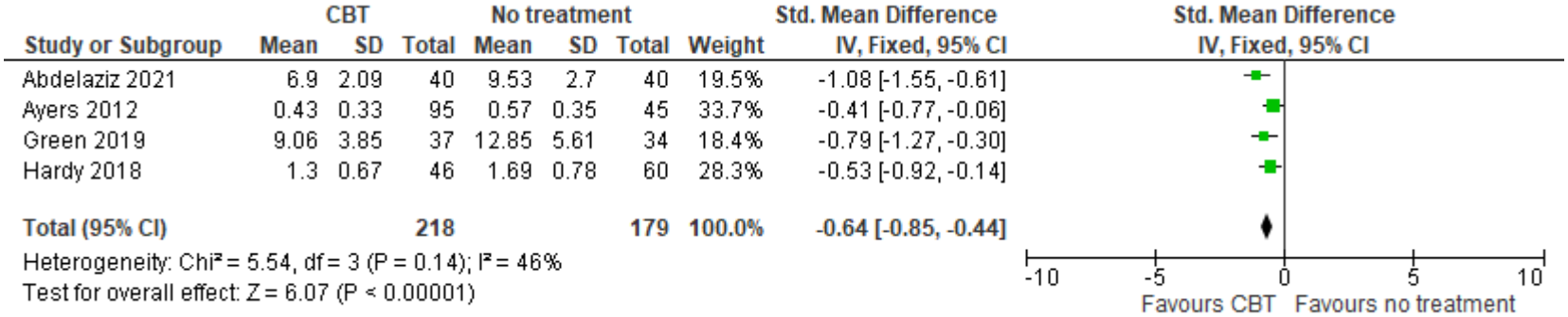


Figure 112: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Group CBT

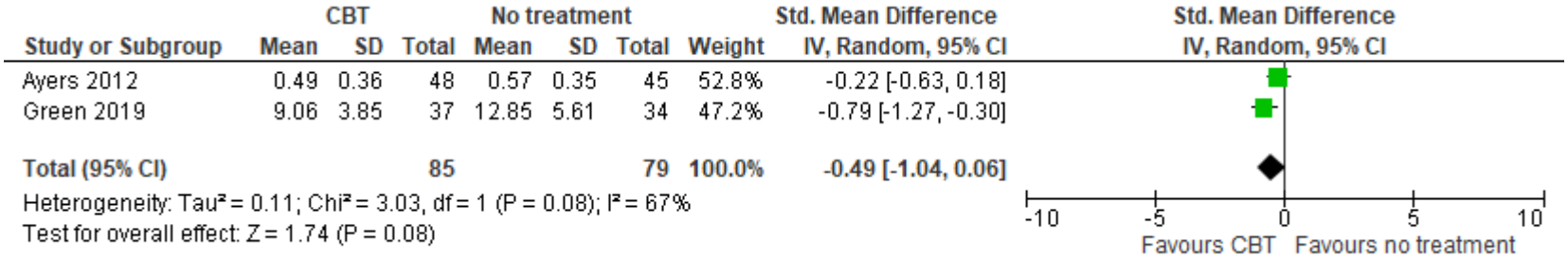


Figure 113: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Individual CBT

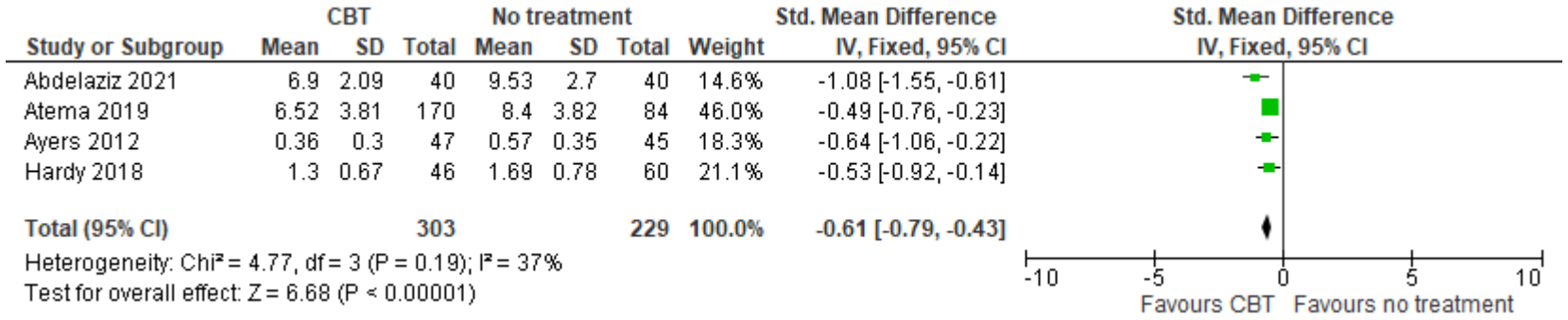


Figure 114: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Face to face CBT

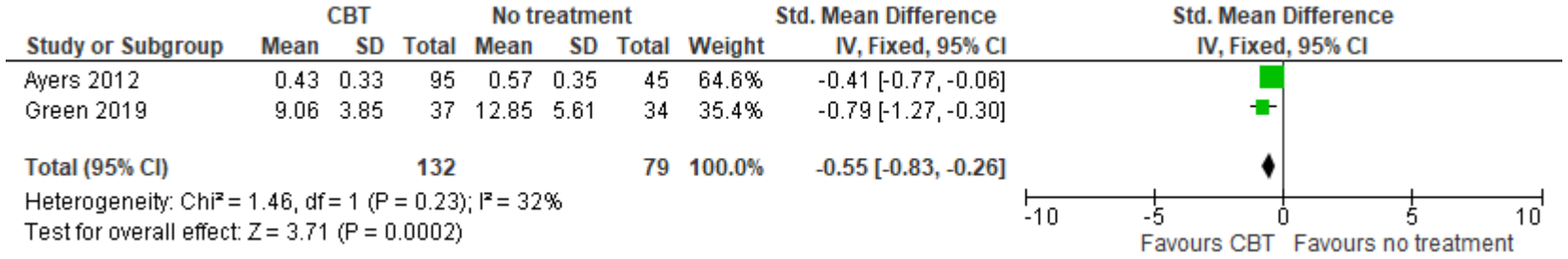


Figure 115: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Online CBT

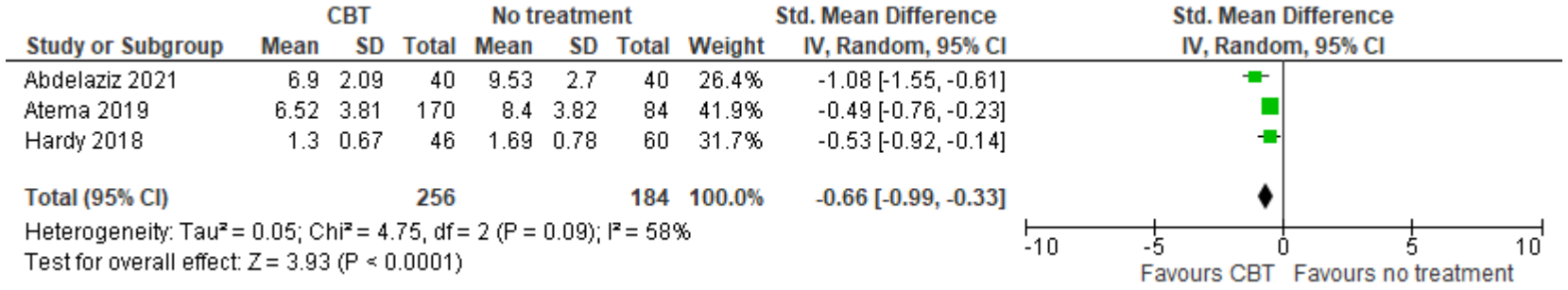


Figure 116: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Self-help CBT

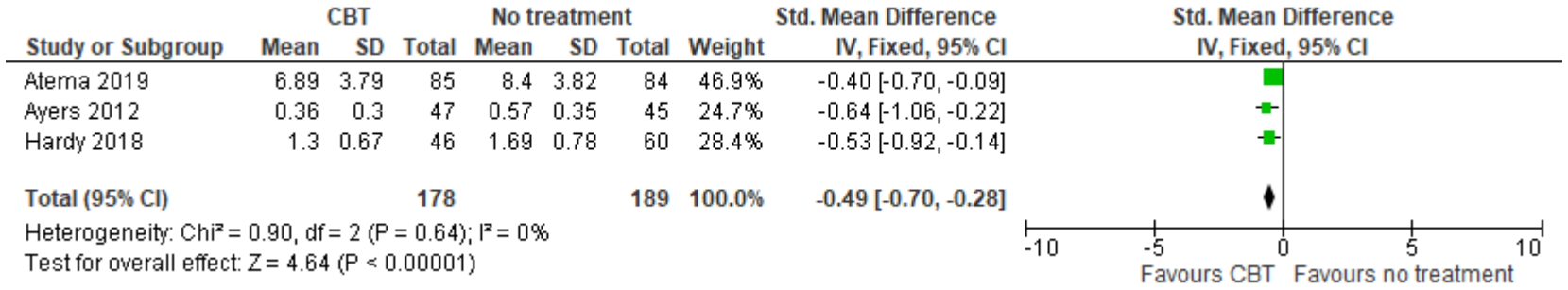


Figure 117: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Guided CBT

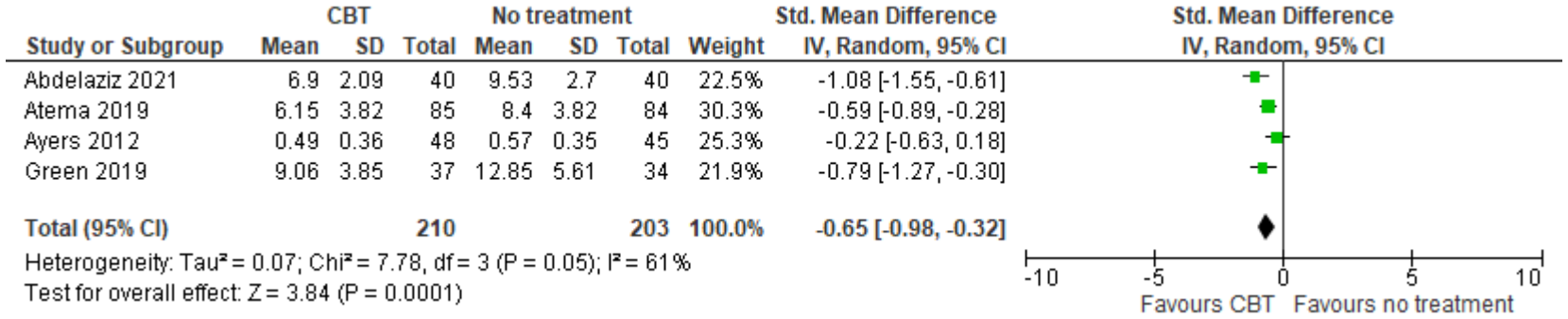


Figure 118: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Duration <6 sessions

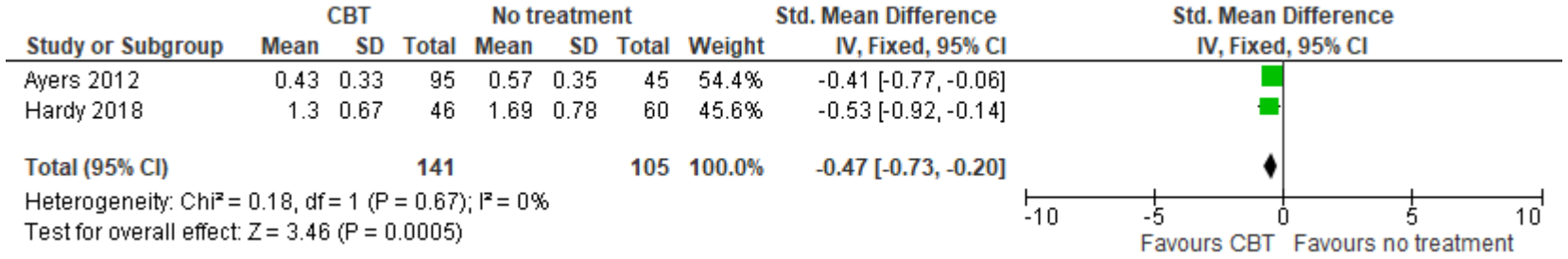


Figure 119: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification – Duration ≥6 sessions

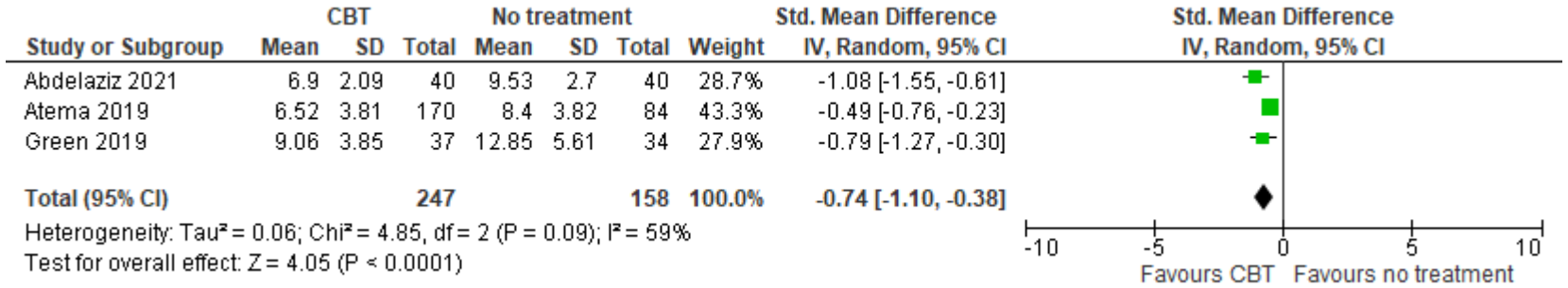


Figure 120: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – No personal history of breast cancer

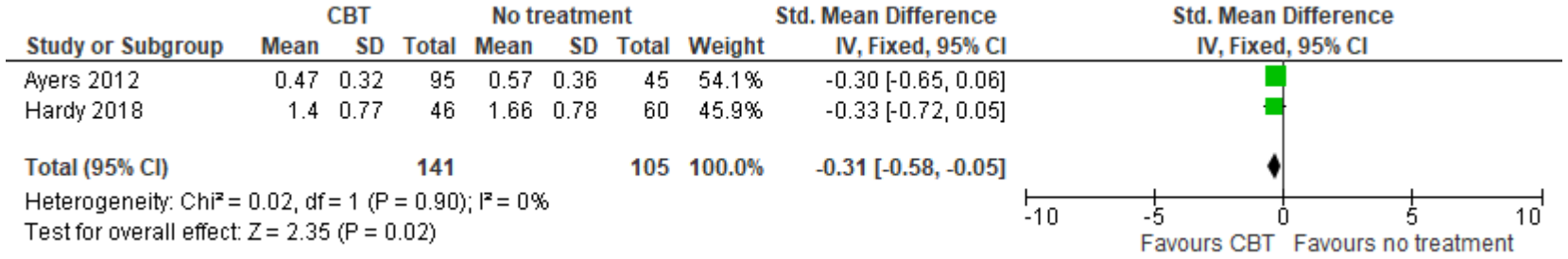


Figure 121: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – Individual CBT

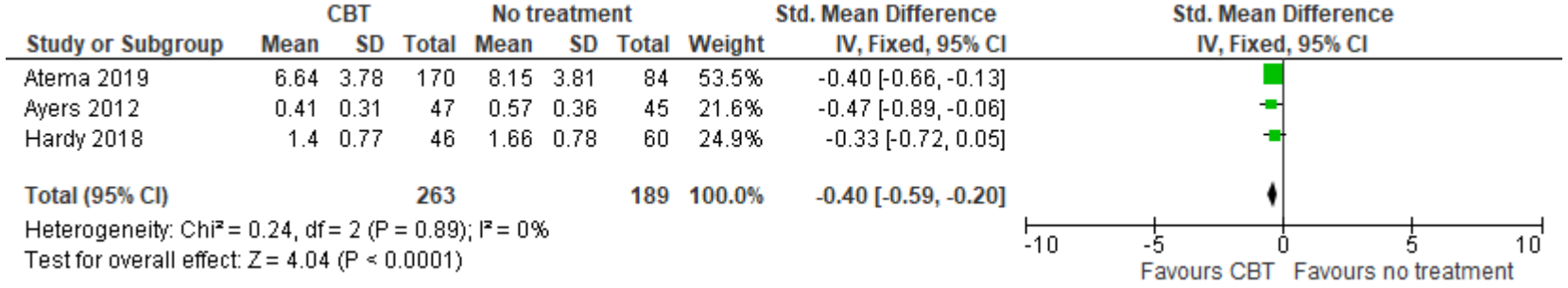


Figure 122: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – Online CBT

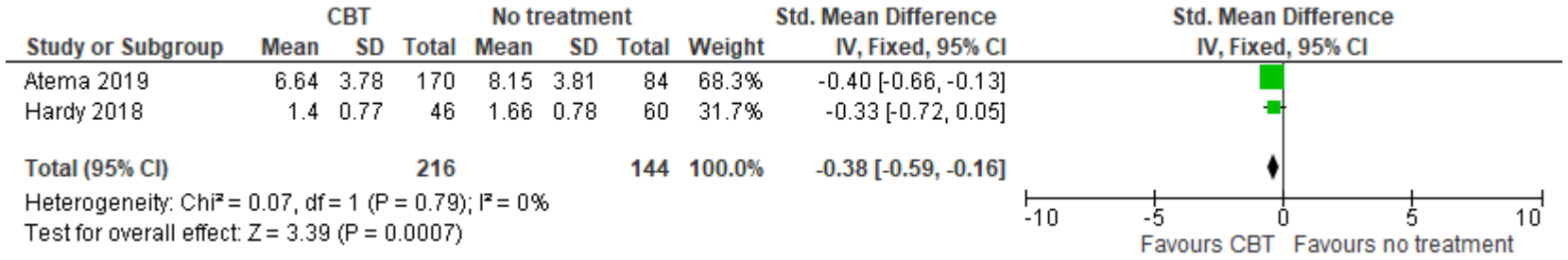


Figure 123: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – Self-help CBT

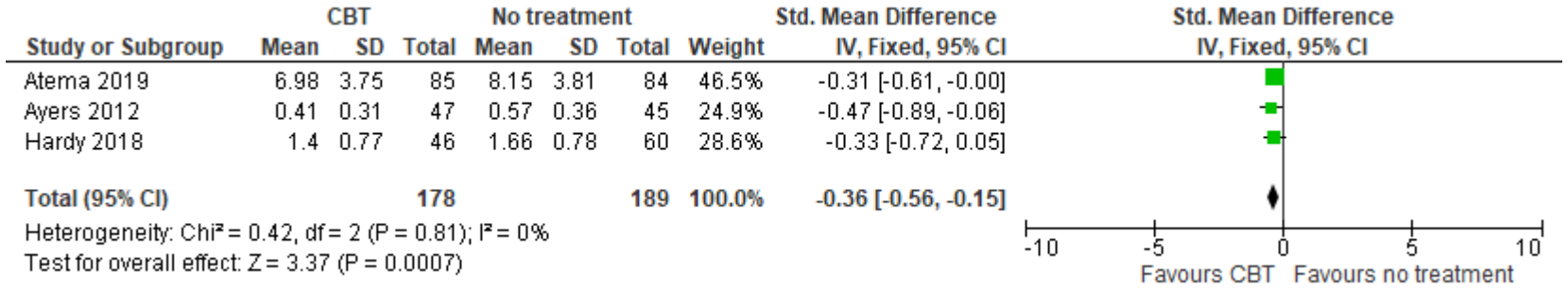


Figure 124: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – Guided CBT

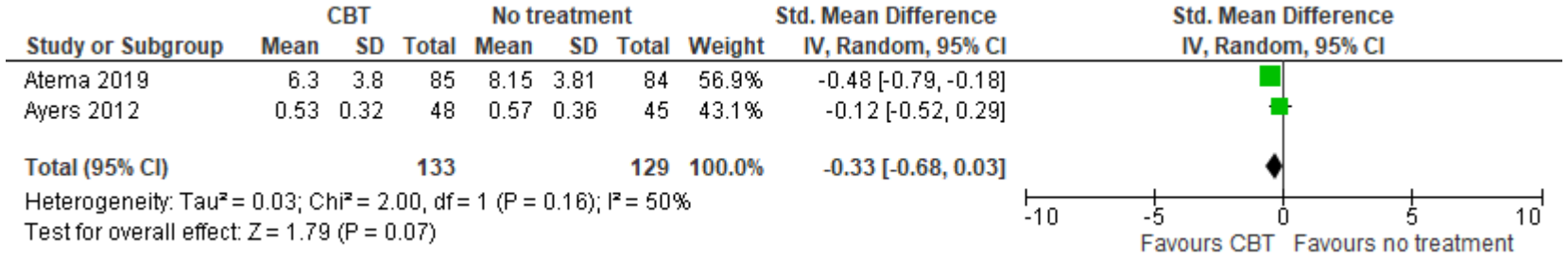
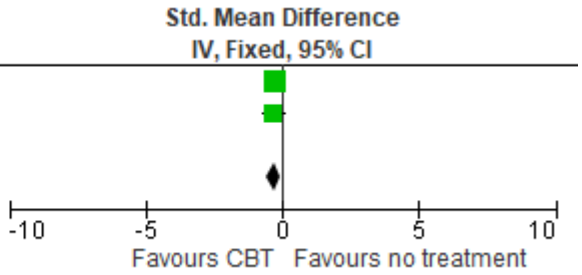


Figure 125: Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification – Duration <6 sessions

Study or Subgroup	CBT Mean	CBT SD	CBT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Ayers 2012	0.47	0.32	95	0.57	0.36	45	54.1%	-0.30 [-0.65, 0.06]
Hardy 2018	1.4	0.77	46	1.66	0.78	60	45.9%	-0.33 [-0.72, 0.05]
Total (95% CI)			**141**			**105**	**100.0%**	**-0.31 [-0.58, -0.05]**

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 2.35 (P = 0.02)



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Comparison 2: Cognitive Behavioural Therapy versus No treatment (important outcomes)

Figure 126: Discontinuation of treatment at endpoint with stratification - (no)/personal history of breast cancer

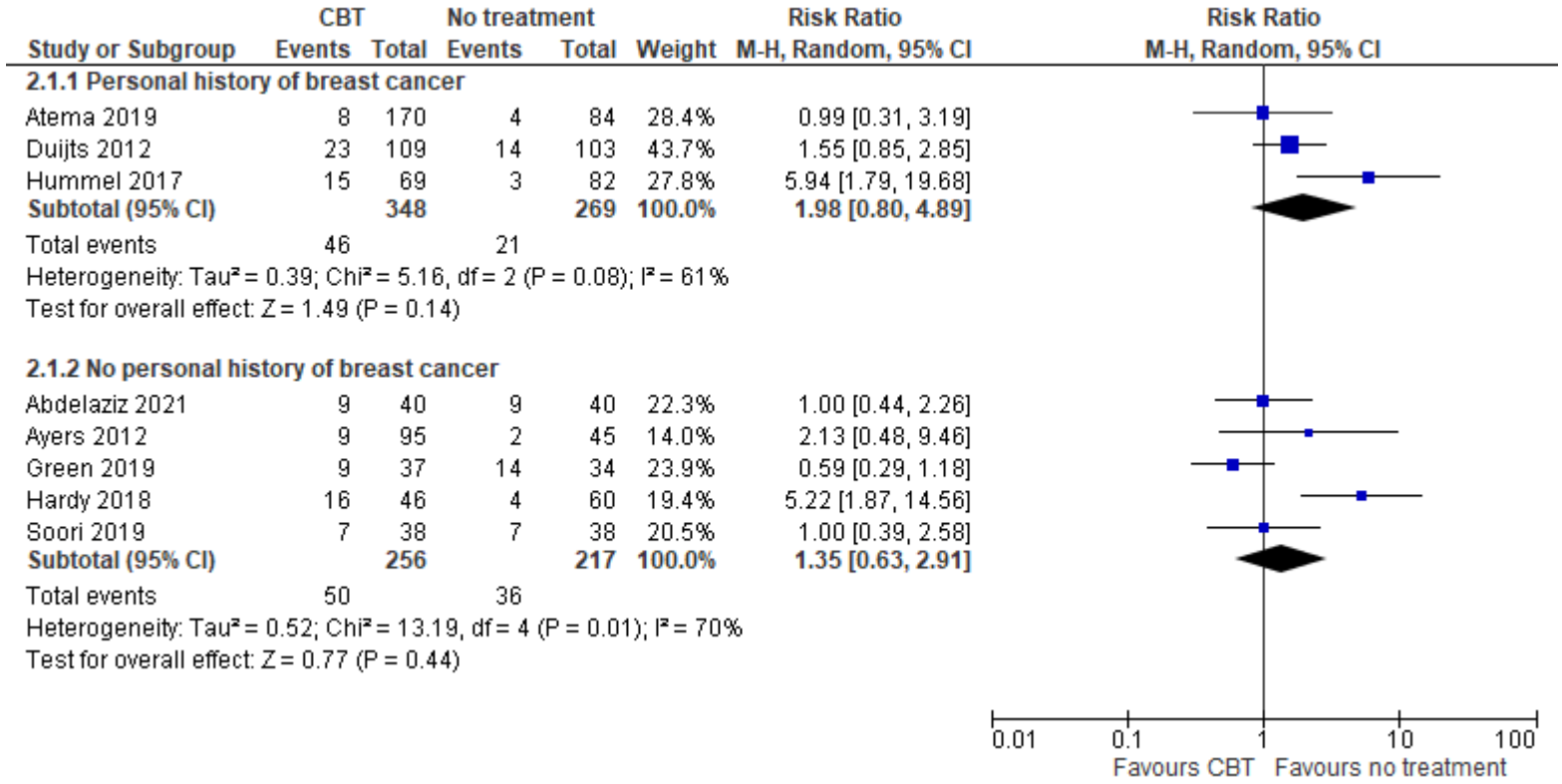


Figure 127: Discontinuation of treatment at follow-up with stratification - (no)/personal history of breast cancer

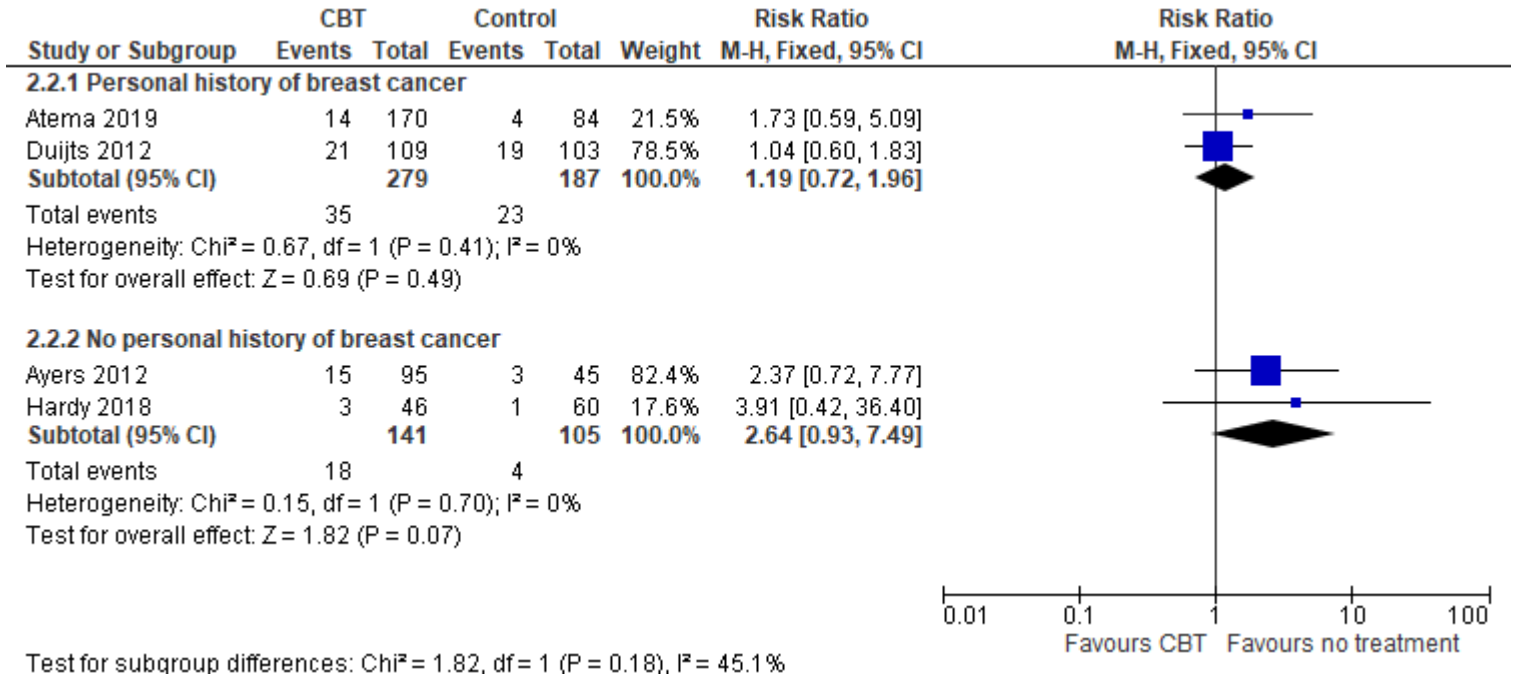


Figure 128: Altered sexual function (SAQ pleasure) at endpoint with stratification - Personal history of breast cancer

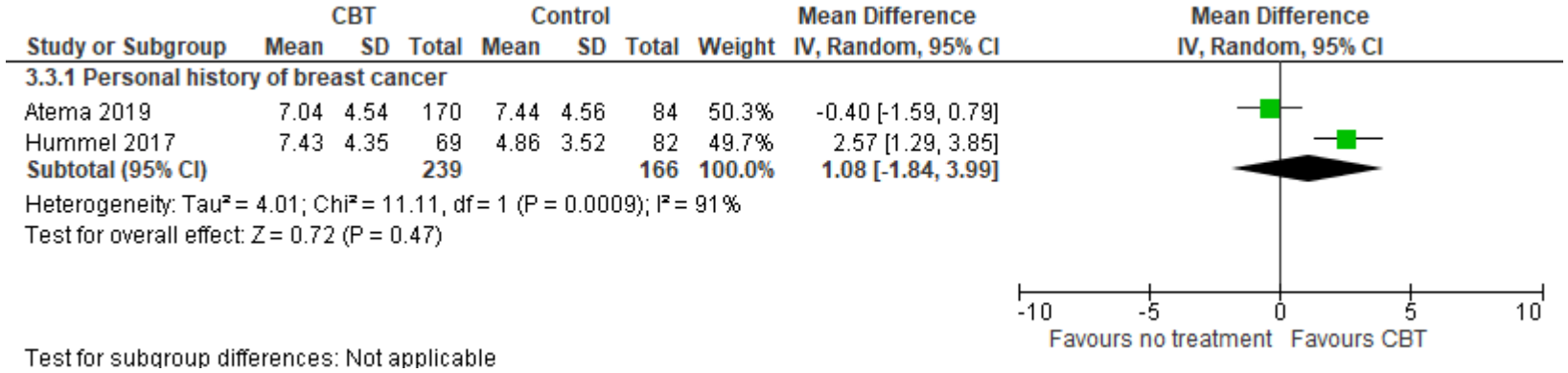


Figure 129: Altered sexual function (SAQ discomfort) at endpoint with stratification - Personal history of breast cancer

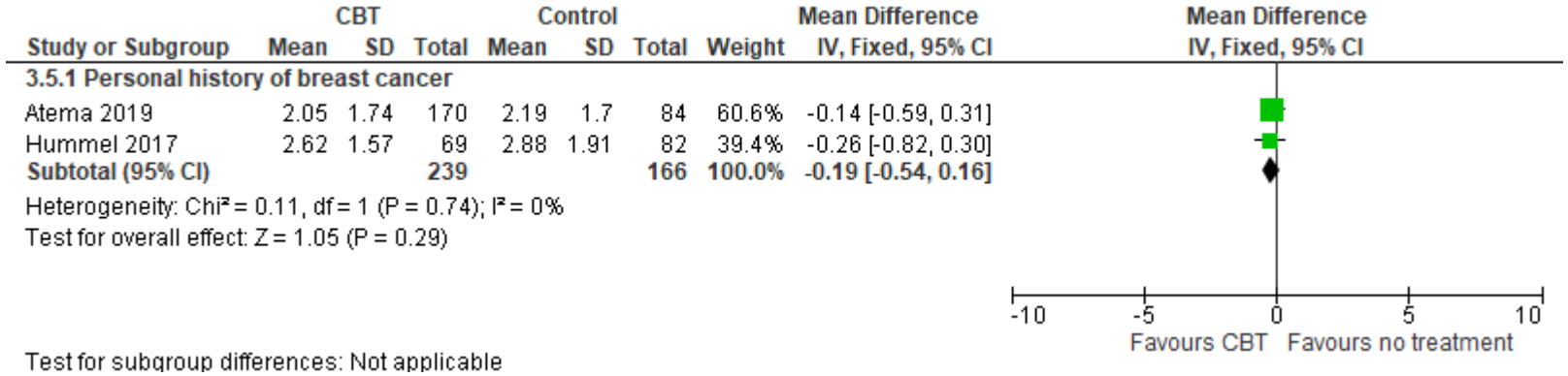


Figure 130: Altered sexual function (SAQ habit) at endpoint with stratification - personal history of breast cancer

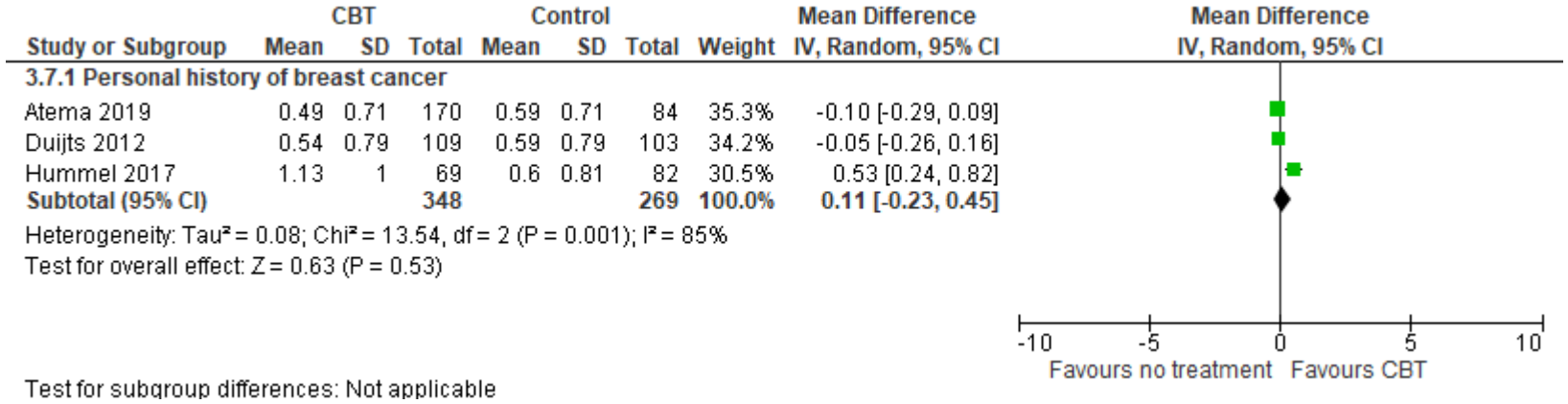


Figure 131: Altered sexual function (SAQ habit) at follow-up with stratification - personal history of breast cancer

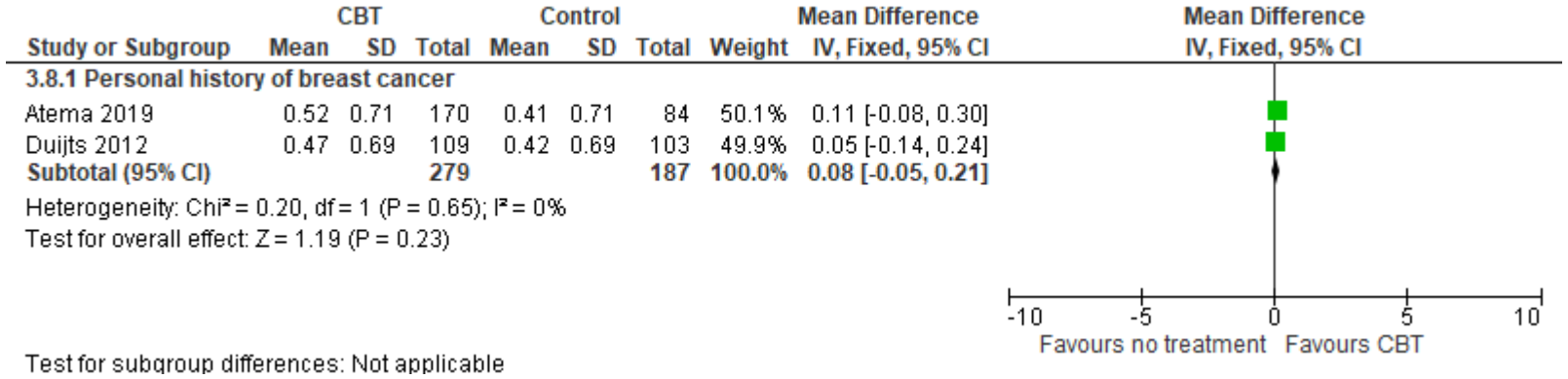


Figure 132: Altered sexual function (GCS-sex) at endpoint with stratification - no personal history of breast cancer

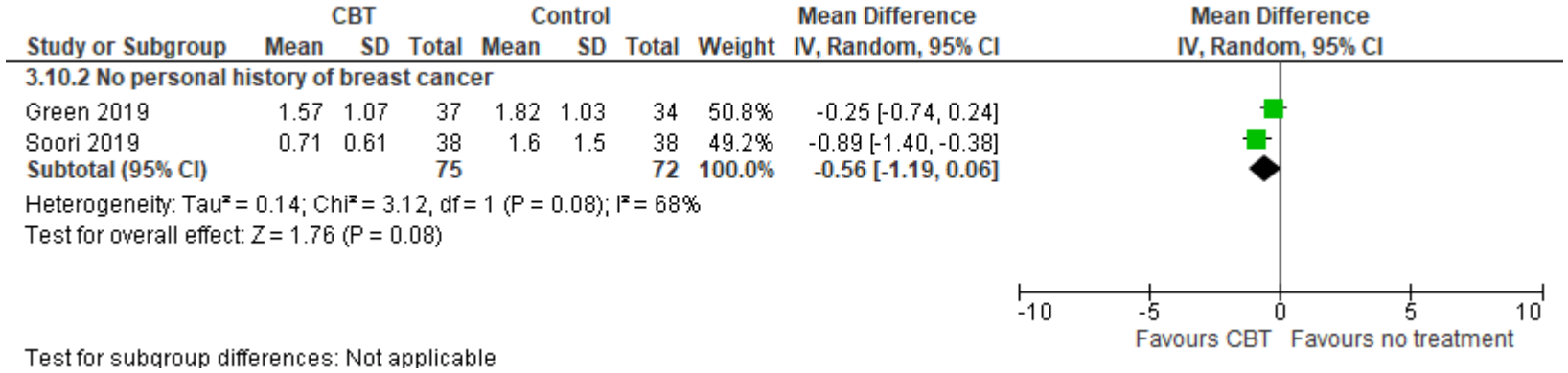


Figure 133: Psychological symptoms anxiety (HADS, WHQ, HAM-A, GCS) at endpoint with stratification - (no)/personal history of breast cancer

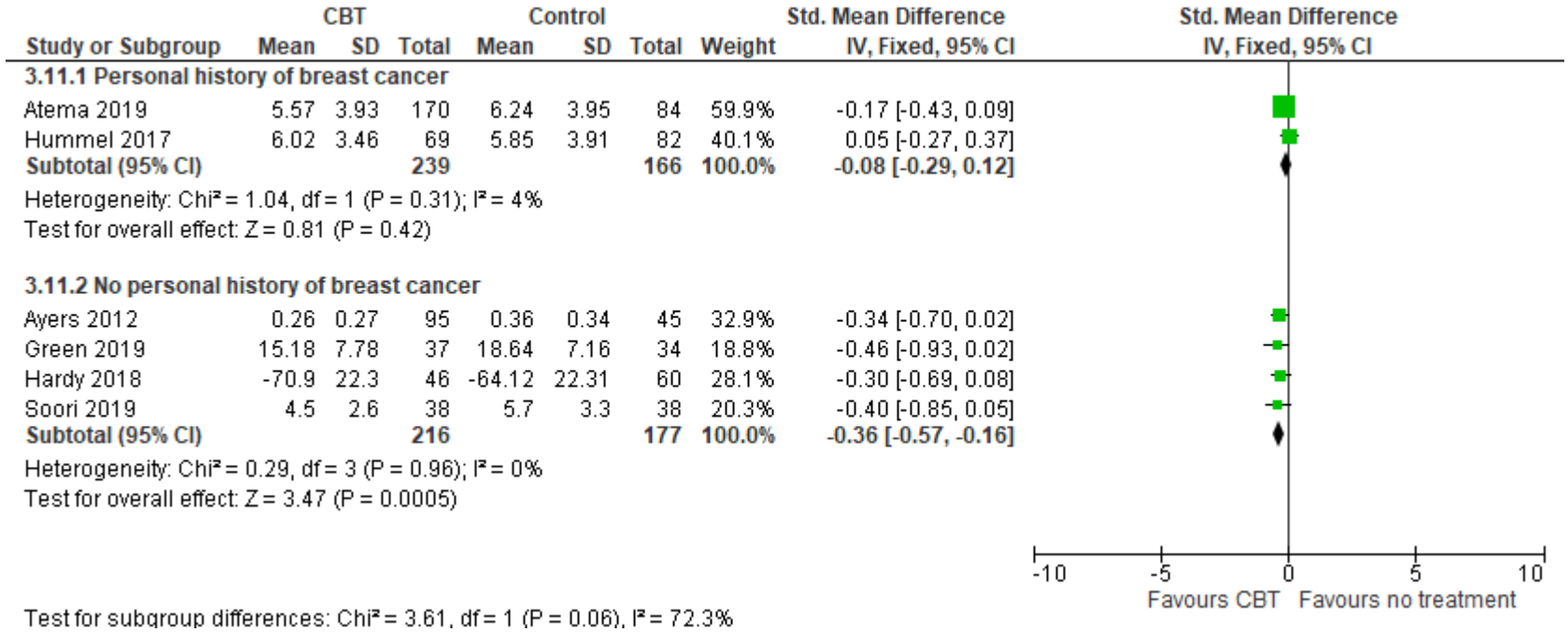
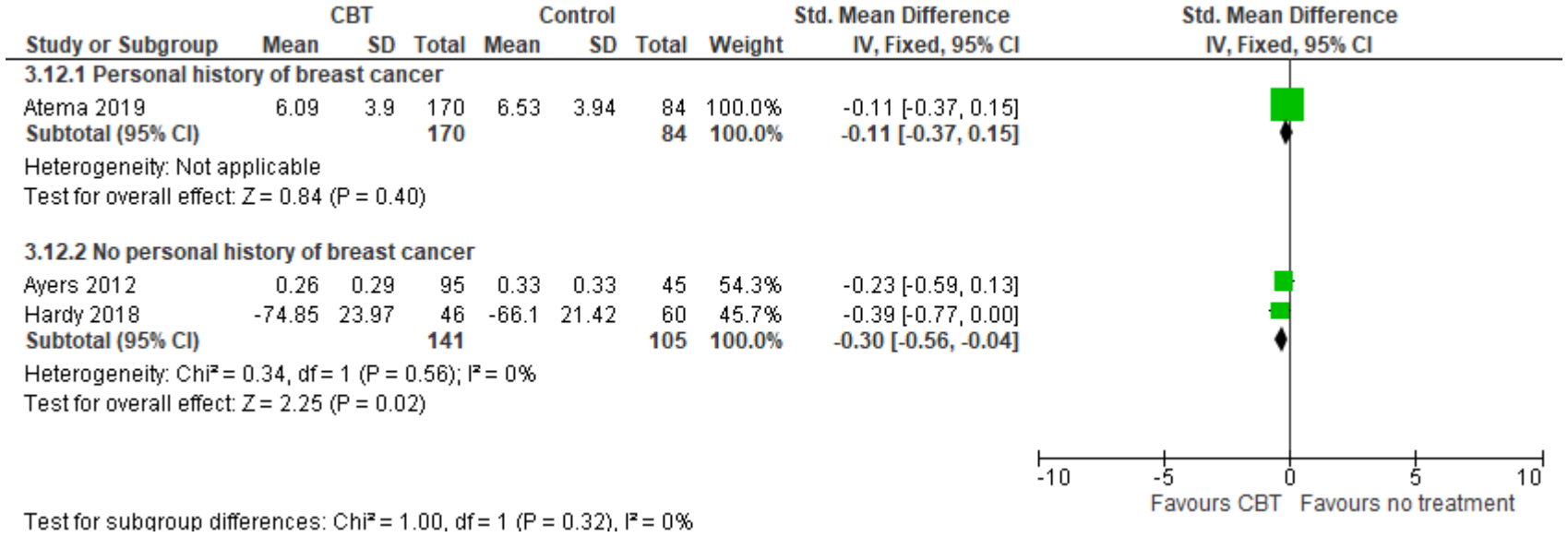


Figure 134: Psychological symptoms anxiety (HADS, WHQ) at follow-up with stratification - (no)/personal history of breast cancer



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Appendix F GRADE tables

GRADE tables for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Table 6: Comparison 1: Cognitive behavioural therapy versus treatment as usual

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	TAU (non-HRT)	Relative (95% CI)	Absolute		
Quality of life (SF-36 vitality) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 1.35 higher (5.94 lower to 8.64 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 9.8 higher (2.38 to 17.22 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 5.36 higher (2.42 lower to 13.14 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification – No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	50	-	MD 1.7 lower (7.77 lower to 4.37 higher)	MODERATE	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	40	40	-	MD 0.25 higher (11.23 lower to 11.73 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification – No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 5.4 higher (1.01 lower to 11.81 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Personal history of breast cancer/ Group CBT; range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 3.85 higher (15.28 lower to 22.98 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 12 higher (1.41 lower to 25.41 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	TAU (non-HRT)	Relative (95% CI)	Absolute		
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 6.2 higher (1.57 lower to 13.97 higher)	LOW	CRITICAL
Quality of life (SF-mental health) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 4.56 higher (1.38 lower to 10.5 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 12.82 higher (4.76 lower to 30.4 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification – No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	50	-	MD 2.67 lower (15.97 lower to 10.63 higher)	MODERATE	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 14.69 higher (2.26 to 27.12 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	50	-	MD 0.25 higher (8.06 lower to 8.56 higher)	MODERATE	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 4.42 higher (5.37 lower to 14.21 higher)	LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification – No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by higher values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 7.35 higher (1.69 lower to 16.39 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (Total HF/NS) at follow-up 26 weeks with stratification - Personal history of breast cancer / Group CBT (Better indicated by lower values)												
1 (Fenlon 2020)	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	42	57	-	median for CBT 42 (range 17 to 63), median for TAU 56 (range 28 to 77)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (hot flush) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Better indicated by lower values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 6.69 higher (8.36 lower to 21.74 higher)	LOW	CRITICAL
Vasomotor symptoms frequency – (hot flush) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Better indicated by lower values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	-	MD 0.41 lower (1.1 lower to 0.28 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (hot flush) at follow-up 6 months with stratification - No personal history of breast cancer/ Individual CBT (Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	TAU (non-HRT)	Relative (95% CI)	Absolute		
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	41	43	-	MD 0.04 lower (0.7 lower to 0.62 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency (night sweats) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Better indicated by lower values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 2.19 lower (6.38 lower to 2 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (night sweats) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Better indicated by lower values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	50	-	MD 0.08 lower (0.59 lower to 0.39 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency – (night sweats) at follow-up 6 months with stratification - No personal history of breast cancer/ Individual CBT (Better indicated by lower values)												
1 (Kalmbach 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	41	43	-	MD 0.02 higher (0.47 lower to 0.51 higher)	MODERATE	CRITICAL
Vasomotor symptoms distress or bother (HFRDIS) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-100; Better indicated by lower values)												
1 (McCurry 2016)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	44	37	-	MD 11.20 lower (20.64 to 1.76 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRDIS) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-100; Better indicated by lower values)												
1 (Fenlon 2020)	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	42	57	-	MD 16.50 lower (26.49 to 6.51 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFNS problem rating scale) at endpoint with stratification - Personal history of breast cancer/ Group CBT (Range of scores: 0-10; Better indicated by lower values)												
2[6]	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	82	97	-	MD 1.65 lower (2.31 to 0.98 lower)	VERY LOW	CRITICAL
Difficulties with sleep (ISI) at endpoint with stratification - No personal history of breast cancer (Range of scores: 0-28; Better indicated by lower values)												
3[7]	randomised trials	serious[1]	very serious[8]	no serious indirectness	no serious imprecision	none	116	110	-	MD 7.04 lower (10.28 to 3.79 lower) [MDs 4.00, 7.00 and 10.33 lower]	VERY LOW	CRITICAL
Difficulties with sleep (ISI) at endpoint with stratification - Group CBT (Range of scores 0-28; Better indicated by lower values)												
1 (Moradi Farsani 2021)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	22	23	-	MD 10.33 lower (12.85 to 7.81 lower)	MODERATE	CRITICAL
Difficulties with sleep (ISI) at endpoint with stratification - Individual CBT (Better indicated by lower values)												
2[9]	randomised trials	serious[1]	very serious[8]	no serious indirectness	no serious imprecision	none	94	87	-	MD 5.56 lower (8.49 to 2.62 lower)	VERY LOW	CRITICAL
Difficulties with sleep (ESS) at endpoint with stratification - No personal history of breast cancer/ Individual CBT (Range of scores: 0-24 Better indicated by lower values)												
1 (Kalmbach 2019)	randomised	serious[1]	no serious	serious[10]	serious[2]	none	50	50	-	MD 1.08 lower (2.37 lower to	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	TAU (non-HRT)	Relative (95% CI)	Absolute		
	trials		inconsistency							0.21 higher)		
Difficulties with sleep (MSLT) at endpoint with stratification – No personal history of breast cancer/ Individual CBT (Range of scores: 0-20; Better indicated by lower values)												
1 (Cheng 2020)	randomised trials	very serious[4]	no serious inconsistency	serious[10]	serious[2]	none	50	50	-	MD 0.6 higher (1.52 lower to 2.72 higher)	VERY LOW	CRITICAL
Difficulties with sleep (ISI, PSQI, WHQ) at follow-up 6 months with stratification - Personal history of breast cancer/ Group CBT (Better indicated by lower values)												
2[6]	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	82	97	-	SMD 0.67 lower (0.98 to 0.37 lower)	VERY LOW	CRITICAL
Difficulties with sleep (ISI, PSQI, WHQ) at follow-up 6 months with stratification - No personal history of breast cancer/ Individual CBT (Better indicated by lower values)												
1 (Drake 2019)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	41	43	-	SMD 1.3 lower (1.77 to 0.83 lower)	MODERATE	CRITICAL
Anxiety (WHQ) at endpoint with stratification - Personal history of breast cancer (Range of scores: 0-1; Better indicated by lower values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 0.15 lower (0.29 to 0.01 lower)	LOW	IMPORTANT
Anxiety (GAD -7) at follow-up 26 weeks with stratification - Personal history of breast cancer (Better indicated by lower values)												
1 (Fenlon 2020)	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	42	57	-	Median for CBT 11 (range 7 to 14), median for TAU 12 (range 9 to 17)	VERY LOW	IMPORTANT
Psychological symptoms low mood (WHQ) at endpoint with stratification - Personal history of breast cancer (Range of scores: 0-1; Better indicated by lower values)												
1 (Mann 2012)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 0.15 lower (0.25 to 0.05 lower)	LOW	IMPORTANT

BC: breast cancer; CBT: cognitive behavioural therapy; CI: confidence interval; ESS: Epsworth Sleepiness Scale; GAD-7: generalised anxiety disorder -7; HFNS: hot flush night sweats; HFRDIS: Hot flash related daily interference scale; HRT: hormone replacement therapy; ISI: insomnia severity index; MD: mean difference; MID: minimally important difference; MSLT: mean sleep latency test; PSQI: Pittsburgh Sleep Quality Index; SF-36: 36-item short form survey; SMD: standardised mean difference; TAU: treatment as usual; WHQ: women's health questionnaire; VMS: vasomotor symptoms

[1] Serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[2] 95% CI crosses 1 MID for continuous outcomes (for SF-36 vitality: combined = 9, BC history/group CBT = 8.25, no BC history/individual CBT = 9.76; for SF-36 general health : BC history/group CBT = 8.39; for SF-36 physical functioning: no BC history/individual CBT = 9.21; for SF-36 physical role limitations: combined=18.66, BC history/group CBT = 20.16, no BC history/individual = 17.16; for SF-36 mental health: combined = 8.10, BC history/group CBT = 8.69, no BC history/individual CBT = 7.52; for SF- emotional role limitations: BC history/group CBT = 21.23; for SF-36 social functioning: BC history/group CBT = 14; for SF-36 bodily pain, combined = 11.87, BC history/group CBT = 10.82, no BC history/individual CBT = 12.92; for VMS frequency HF BC/group = 18.97, no BC/individual =0.9; for VMS frequency NS BC/group = 5.07; for VMS HFNS problem rating = 1.04; for VMS HFRDIS = 11.67; for difficulties with sleep: ESS = 1.61, MSLT = 2.5 SMD = 0.5; for anxiety = 0.15; for depressed mood = 0.14)

[3] 95% CI crosses 2 MIDs for continuous outcomes (for SF-physical functioning: BC history/group CBT = 11.14)

[4] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[5] Sample size <200

[6] Fenlon 2020 and Mann 2012

[7] Drake 2019, McCurry 2016 and Moradi Farsani 2021

[8] Very serious heterogeneity unexplained by subgroup analysis

[9] *Drake 2019 and McCurry 2016*
[10] *Outcome indirect due to sleep scales used not specifically measuring difficulties with sleep but general daytime sleepiness*

Table 7: Comparison 2: Cognitive behavioural therapy versus no treatment (critical outcomes)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 physical functioning) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
3[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	348	269	-	MD 0.75 higher (2.17 lower to 3.66 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 5.52 higher (0.64 lower to 11.68 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	157	148	-	MD 1.46 higher (2.42 lower to 5.34 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	286	211	-	MD 3.07 higher (4.00 lower to 10.14 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Face to face CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	204	148	-	MD 2.99 higher (0.67 lower to 6.64 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Online CBT (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.09 lower (5.86 lower to 5.68 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 physical functioning) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 6.65 higher (0.20 to 13.11 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
4[10]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	311	313	-	MD 0.44 higher (2.38 lower to 3.27 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[11]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	187	-	MD 0.87 higher (2.69 lower to 4.43 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 13.12 higher (4.07 to 22.17 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
2[11]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	serious[4]	none	157	148	-	MD 5.46 higher (8.89 lower to 19.81 higher) [MD 1.35 lower, 13.33 higher]	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	217	129	-	MD 6.93 higher (2.50 lower to 16.36 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Face to face CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	serious[4]	none	204	148	-	MD 5.38 higher (8.77 lower to 19.52 higher) [MD 13.12 higher, 1.35 lower]	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 physical functioning) at follow-up with stratification - Online CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 3.06 higher (1.96 lower to 8.08 higher)	LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 7.51 higher (0.69 lower to 15.71 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical functioning) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[13]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	242	232	-	MD 3.67 higher (3.54 lower to 10.89 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.82 higher (3.45 lower to 5.09 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 4.71 higher (3.49 lower to 12.91 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 4.4 higher (4.78 lower to 13.58 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	286	211	-	MD 1.56 higher (2.32 lower to 5.44 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Online CBT (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.82 higher (3.45 lower to 5.09 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 2.75 higher (2.36 lower to 7.87 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 1.45 higher (2.74 lower to 5.64 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 0.93 higher (4.41 lower to 6.27 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 8.65 higher (0.67 lower to 17.97 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 8.33 higher (2.14 lower to 18.8 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	217	129	-	MD 2.72 higher (1.99 lower to 7.43 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 4.83 higher (0.37 lower to 10.03 higher)	LOW	CRITICAL
Quality of life (SF-36 social functioning) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 3.02 higher (7.07 lower to 13.11 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 1.23 higher (6.57 lower to 9.02 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 14.27 higher (1.86 to 26.68 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 13.55 higher (0.62 lower to 27.72 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	286	211	-	MD 4.68 higher (2.07 lower to 11.43 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[8]	no serious indirectness	serious[4]	none	132	129	-	MD 6.76 higher (8.57 lower to 22.08 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 4.79 higher (2.48 lower to 12.06 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 1.37 lower (11.36 lower to 8.62 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 18.81 higher (3.98 to 33.64 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 17.95 higher (1.53 to 34.37 higher)	LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	217	129	-	MD 8.15 higher (12.38 lower to 28.69 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 9.42 higher (8.81 lower to 27.66 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 physical role limitations) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	133	129	-	MD 6.29 higher (14.90 lower to 27.47 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.29 lower (7.33 lower to 6.76 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	95	45	-	MD 5.14 higher (7.87 lower to 18.15 higher)	MODERATE	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 6.66 higher (7.62 lower to 20.94 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	286	211	-	MD 0.42 higher (5.95 lower to 6.79 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 0.23 lower (8.71 lower to 8.25 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 1.35 higher (5.4 lower to 8.1 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1(Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 1.6 higher (7.33 lower to 10.53 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/ Duration < 6 sessions (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 16.11 higher (2.06 to 30.16 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 13.82 higher (2.13 lower to 29.77 higher)	LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	217	129	-	MD 8.91 higher (7.45 lower to 25.27 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 9.85 higher (4.87 lower to 24.58 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 emotional role limitations) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	133	129	-	MD 5.48 higher (7.86 lower to 18.83 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
3[1]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	348	269	-	MD 2.74 lower (8.88 lower to 3.39 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 10.66 higher (1.88 to 19.44 higher)	LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	very serious[13]	none	157	148	-	MD 0.39 lower (17.87 lower to 17.10 higher) [MD 8.93 higher, MD 8.39	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
										lower]		
Quality of life (SF-36 bodily pain) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	286	211	-	MD 3.44 higher (3.16 lower to 10.04 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Face to face CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	very serious[13]	none	204	148	-	MD 0.62 lower (18.57 lower to 19.81 higher) [MD 10.66 higher, MD 8.93 lower]	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Online CBT (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.4 higher (4.1 lower to 4.9 higher)	LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 6.59 higher (3.55 lower to 16.73 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
4[14]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	311	314	-	MD 0.78 lower (7.43 lower to 5.88 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[11]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	187	-	MD 1.27 higher (3.05 lower to 5.59 higher)	LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 11.64 higher (3.35 to 19.93 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 bodily pain) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	157	148	-	MD 6.76 higher (3.64 lower to 17.17 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	217	129	-	MD 4.92 higher (4.72 lower to 14.55 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Face to face CBT (Range of scores 0-100; Better indicated by higher values)												
2[5]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	204	148	-	MD 6.40 higher (3.11 lower to 15.91 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Online CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 0.73 higher (5.13 lower to 6.59 higher)	LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	132	129	-	MD 5.46 higher (3.28 lower to 14.20 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 bodily pain) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[15]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	242	232	-	MD 4.75 higher (1.44 lower to 10.95 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 1.5 lower (5.9 lower to 2.9 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 4.32 higher (2.99 lower to 11.63 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48	45	-	MD 1.81 higher (6.51 lower to 10.13 higher)	MODERATE	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	286	211	-	MD 0.49 higher (3.35 lower to 4.33 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	132	129	-	MD 2.39 higher (5.75 lower to 10.53 higher)	VERY LOW	CRITICAL
Quality of life (SF-36 general health) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 0.47 lower (4.62 lower to 3.68 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 0.86 higher (4.67 lower to 6.39 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 4.47 higher (2.35 lower to 11.29 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 4.36 higher (3.8 lower to 12.52 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	217	129	-	MD 2.22 higher (2.18 lower to 6.63 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 2.51 higher (2.27 lower to 7.3 higher)	LOW	CRITICAL
Quality of life (SF-36 general health) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	133	129	-	MD 2.14 higher (2.89 lower to 7.17 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 2.56 higher (1.26 lower to 6.37 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 5.59 higher (2.09 lower to 13.27 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 7.18 higher (1.9 lower to 16.26 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised	very	no serious	no serious	no serious	none	286	211	-	MD 2.79 higher (0.69 lower to 6.27	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
	trials	serious[2]	inconsistency	indirectness	imprecision					higher)		
Quality of life (SF-36 vitality) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 3.61 higher (0.95 lower to 8.16 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 3.23 higher (0.56 lower to 7.03 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 3.57 higher (1.09 lower to 8.23 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 4.38 higher (2.78 lower to 11.54 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 3.97 higher (5.03 lower to 12.97 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	217	129	-	MD 3.89 higher (0.12 lower to 7.9 higher)	LOW	CRITICAL
Quality of life (SF-36 vitality) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 4.42 higher (0 to 8.85 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 vitality) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	133	129	-	MD 3.17 higher (1.45 lower to 7.79 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.42 higher (2.9 lower to 3.74 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 13.44 higher (7.08 to 19.8 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 6.53 higher (0.52 lower to 13.58 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	286	211	-	MD 0.78 higher (2.2 lower to 3.76 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 1.86 higher (2.11 lower to 5.83 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at endpoint with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
3[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	202	211	-	MD 1.63 higher (1.58 lower to 4.84 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (SF-36 mental health) at follow-up with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 3.08 higher (1.15 lower to 7.31 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT/ Duration <6 sessions (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 4.31 higher (1.68 lower to 10.3 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at follow-up with stratification - Group CBT (Range of scores 0-100; Better indicated by higher values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 6.05 higher (1.38 lower to 13.48 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at follow-up with stratification - Individual CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	217	129	-	MD 2.92 higher (0.62 lower to 6.45 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at follow-up with stratification - Self-help CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 3.39 higher (0.49 lower to 7.27 higher)	LOW	CRITICAL
Quality of life (SF-36 mental health) at follow-up with stratification - Guided CBT (Range of scores 0-100; Better indicated by higher values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	133	129	-	MD 3.42 higher (0.67 lower to 7.5 higher)	LOW	CRITICAL
Quality of life (Revised WHQ wellbeing) at endpoint with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 3.48 higher (4.07 lower to 11.03 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Quality of life (Revised WHQ somatic symptoms) at endpoint with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 4.26 higher (4.85 lower to 13.37 higher)	LOW	CRITICAL
Quality of life (Revised WHQ memory and concentration) at endpoint with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 6.06 higher (3.84 lower to 15.96 higher)	LOW	CRITICAL
Quality of life (Revised WHQ wellbeing) at 6 months with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 8.25 higher (1.79 to 14.71 higher)	LOW	CRITICAL
Quality of life (Revised WHQ somatic symptoms) at 6 months with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 8.47 higher (0.23 to 16.71 higher)	LOW	CRITICAL
Quality of life (Revised WHQ memory and concentration) at 6 months with stratification - Self-help CBT (23-items; Better indicated by higher values)												
1 (Hardy 2018)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	46	60	-	MD 7.08 higher (2.44 lower to 16.6 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 7 lower (17.25 lower to 3.25 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - No personal history of breast cancer/ Duration <6 sessions (Weekly frequency of hot flushes; Better indicated by lower values)												
2[16]	randomised trials	serious[3]	serious[7]	no serious indirectness	serious[4]	none	141	105	-	MD 6.64 lower (20.22 lower to 6.94 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT**	**No treatment**	**Relative (95% CI)**	**Absolute**		
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Group CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48	45	-	MD 0.82 lower (16.67 lower to 15.03 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Individual CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	263	189	-	MD 6.85 lower (13.96 lower to 0.28 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Face to face CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	95	45	-	MD 0.43 higher (13.36 lower to 14.22 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Online CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
2[18]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	216	144	-	MD 9.41 lower (17.51 to 1.31 lower)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Self-help CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	178	189	-	MD 6.97 lower (14.55 lower to 0.60 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at endpoint with stratification - Guided CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132	129	-	MD 3.4 lower (12.65 lower to 5.84 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	170	84	-	MD 15.35 lower (25.62 to 5.08 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - No personal history of breast cancer/ Duration <6 sessions (Weekly frequency of hot flushes;												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Better indicated by lower values)												
2[16]	randomised trials	serious[3]	serious[7]	no serious indirectness	serious[4]	none	141	105	-	MD 2.36 lower (20.54 lower to 15.82 higher)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Group CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48	45	-	MD 0.88 higher (15.65 lower to 17.41 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Individual CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	263	189	-	MD 7.58 lower (20.10 to 4.95 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Face to face CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	95	45	-	MD 6.8 higher (5 lower to 18.6 higher)	MODERATE	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Online CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
2[18]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	216	144	-	MD 13.9 lower (21.83 to 5.97 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Self-help CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	178	189	-	MD 8.35 lower (22.46 lower to 5.75 higher)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS hot flush frequency) at follow-up with stratification - Guided CBT (Weekly frequency of hot flushes; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	133	129	-	MD 7.76 lower (17.38 lower to 1.87 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Weekly frequency of night sweats; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	170	84	-	MD 6.94 lower (10.38 to 3.5 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - No personal history of breast cancer/ Face to face CBT Duration <6 sessions (Weekly frequency of night sweats; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 3.6 lower (7.93 lower to 0.73 higher)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - Group CBT (Weekly frequency of night sweats; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 5 lower (9.64 to 0.36 lower)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - Individual CBT (Weekly frequency of night sweats; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	217	129	-	MD 4.93 lower (9.55 to 0.31 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - Self-help CBT (Weekly frequency of night sweats; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	132	129	-	MD 3.9 lower (7.02 to 0.78 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at endpoint with stratification - Guided CBT (Weekly frequency of night sweats; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	133	129	-	MD 7.26 lower (10.27 to 4.24 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - Personal history of breast cancer/ Individual CBT/ Duration ≥6 sessions (Weekly frequency of night sweats; Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	170	84	-	MD 5.79 lower (9.23 to 2.35 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - No personal history of breast cancer/ Face to face CBT /Duration <6 sessions (Weekly frequency of night sweats; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	95	45	-	MD 6.49 lower (12.39 to 0.59 lower)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - Group CBT (Weekly frequency of night sweats; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	48	45	-	MD 7.16 lower (13.62 to 0.7 lower)	LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - Online CBT (Weekly frequency of night sweats; Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	170	84	-	MD 5.79 lower (9.23 to 2.35 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - Self-help CBT (Weekly frequency of night sweats; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	132	129	-	MD 5.59 lower (8.90 lower to 2.27 higher)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (HFRS night sweats frequency) at follow-up with stratification - Guided CBT (Weekly frequency of night sweats; Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	133	129	-	MD 6.39 lower (9.77 to 3.01 lower)	VERY LOW	CRITICAL
Vasomotor symptoms frequency (biolog, diary) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions (Frequency of symptoms; Better indicated by lower values)												
2[19]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	30	25	-	SMD 0.45 lower (0.99 lower to 0.1 higher)	LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Personal history of breast cancer/ Online CBT/ Duration ≥6 sessions (Range of scores 0-72; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	239	166	-	MD 1.35 higher (2.10 lower to 4.80 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Individual CBT (Range of scores 0-72; Better indicated by higher values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
1 (Hummel 2017)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	69	82	-	MD 0.49 lower (3.19 lower to 2.21 higher)	LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Self-help CBT (Range of scores 0-72; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	85	84	-	MD 2.99 higher (0.39 to 5.59 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at endpoint with stratification - Guided CBT (Range of scores 0-72; Better indicated by higher values)												
2[8]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[4]	none	154	166	-	MD 1.30 higher (2.18 lower to 4.78 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at follow-up with stratification - Personal history of breast cancer/ Individual CBT/ Online CBT/ Duration ≥6 sessions (Range of scores 0-72; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	170	84	-	MD 3.42 higher (1.17 to 5.67 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at follow-up with stratification - Self-help CBT (Range of scores 0-72; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	85	84	-	MD 4.21 higher (1.62 to 6.8 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (FACT-ES) at follow-up with stratification - Guided CBT (Range of scores 0-72; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	85	84	-	MD 2.62 higher (0.02 to 5.22 higher)	VERY LOW	CRITICAL
Vasomotor symptoms severity (GCS-vm) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions (Range of scores 0-6; Better indicated by lower values)												
2[21]	randomised trials	serious[3]	serious[7]	no serious indirectness	serious[4]	none	75	72	-	MD 1.67 lower (2.98 to 0.36 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-10; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
2[11]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	187	-	MD 0.79 lower (1.14 to 0.44 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-10; Better indicated by lower values)												
2[5]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[22]	none	141	105	-	MD 1.89 lower (2.48 to 1.29 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Group CBT (Range of scores 0-10; Better indicated by lower values)												
2[5]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	serious[22]	none	157	148	-	MD 1.26 lower (2.50 to 0.02 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Individual CBT (Range of scores 0-10; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[22]	none	263	189	-	MD 1.48 lower (2.25 to 0.72 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Face to face CBT (Range of scores 0-10; Better indicated by lower values)												
2[5]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	serious[22]	none	204	148	-	MD 1.29 lower (2.56 to 0.03 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Online CBT (Range of scores 0-10; Better indicated by lower values)												
2[18]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[22]	none	216	144	-	MD 1.26 lower (2.13 to 0.39 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Self-help CBT (Range of scores 0-10; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[22]	none	178	189	-	MD 1.48 lower (2.26 to 0.71 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at endpoint with stratification - Guided CBT (Range of scores 0-10; Better indicated by lower values)												
3[15]	randomised	very	serious[7]	no serious	no serious	none	242	232	-	MD 1.08 lower (1.69 to 0.46 lower)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
	trials	serious[2]		indirectness	imprecision							
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Personal history of breast cancer/ Duration ≥6 sessions (Range of scores 0-10; Better indicated by lower values)												
2[11]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	187	-	MD 0.53 lower (0.88 to 0.18 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - No personal history of breast cancer/ Duration <6 sessions (Range of scores 0-10; Better indicated by lower values)												
2[16]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	141	105	-	MD 1.32 lower (1.92 to 0.72 lower)	MODERATE	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Group CBT (Range of scores 0-10; Better indicated by lower values)												
2[5]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	157	148	-	MD 0.80 lower (1.60 to 0.00 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Individual CBT (Range of scores 0-10; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	263	189	-	MD 0.84 lower (1.22 to 0.46 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Face to face CBT (Range of scores 0-10; Better indicated by lower values)												
2[5]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	204	148	-	MD 0.77 lower (1.48 to 0.06 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Online CBT (Range of scores 0-10; Better indicated by lower values)												
2[18]	randomised trials	very serious[2]	serious[7]	no serious indirectness	no serious imprecision	none	216	144	-	MD 0.93 lower (1.76 to 0.10 lower)	VERY LOW	CRITICAL
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Self-help CBT (Range of scores 0-10; Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	178	189	-	MD 0.87 lower (1.29 to 0.45 lower)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Vasomotor symptoms distress or bother (HFRS problem rating) at follow-up with stratification - Guided CBT (Range of scores 0-10; Better indicated by lower values)												
3[15]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	242	232	-	MD 0.65 lower (0.99 to 0.30 lower)	LOW	CRITICAL
Vasomotor symptoms distress or bother (biolog, diary) at endpoint with stratification - No personal history of breast cancer/ Group CBT/ Face to face CBT/ Guided CBT/ Duration ≥6 sessions (Range of scores 0-10; Better indicated by lower values)												
2[19]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	25	-	SMD 1.08 lower (1.66 to 0.51 lower)	MODERATE	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Personal history of breast cancer (Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	170	84	-	SMD 0.49 lower (0.76 to 0.23 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - No personal history of breast cancer (Better indicated by lower values)												
4[23]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	218	179	-	SMD 0.64 lower (0.85 to 0.44 lower)	LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Group CBT (Better indicated by lower values)												
2[24]	randomised trials	serious[3]	serious[7]	no serious indirectness	serious[20]	none	85	79	-	SMD 0.49 lower (1.04 to 0.06 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Individual CBT (Better indicated by lower values)												
4[25]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	303	229	-	SMD 0.61 lower (0.79 to 0.43 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Face to face CBT (Better indicated by lower values)												
2[24]	randomised trials	serious[3]	serious[7]	no serious indirectness	serious[20]	none	132	79	-	SMD 0.55 lower (0.83 to 0.26 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Online CBT (Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
3[26]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[20]	none	256	184	-	SMD 0.66 lower (0.99 to 0.33 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Self-help CBT (Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	178	189	-	SMD 0.49 lower (0.7 to 0.28 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Guided CBT (Better indicated by lower values)												
4[27]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[20]	none	210	203	-	SMD 0.65 lower (0.98 to 0.32 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Duration <6 sessions (Better indicated by lower values)												
2[16]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	141	105	-	SMD 0.47 lower (0.73 to 0.2 lower)	LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at endpoint with stratification - Duration ≥6 sessions (Better indicated by lower values)												
3[28]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[20]	none	247	158	-	SMD 0.74 lower (1.10 to 0.38 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Personal history of breast cancer (Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	170	84	-	SMD 0.4 lower (0.66 to 0.13 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - No personal history of breast cancer (Better indicated by lower values)												
2[16]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	141	105	-	SMD 0.31 lower (0.58 to 0.05 lower)	LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Group CBT (Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	48	45	-	SMD 0.12 lower (0.52 lower to 0.29 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	No treatment	Relative (95% CI)	Absolute		
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Individual CBT (Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	263	189	-	SMD 0.4 lower (0.59 to 0.2 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Face to face CBT (Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	95	45	-	SMD 0.3 lower (0.65 lower to 0.06 higher)	LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Online CBT (Better indicated by lower values)												
2[18]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	216	144	-	SMD 0.38 lower (0.59 to 0.16 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Self-help CBT (Better indicated by lower values)												
3[17]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[20]	none	178	189	-	SMD 0.36 lower (0.56 to 0.15 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Guided CBT (Better indicated by lower values)												
2[9]	randomised trials	very serious[2]	serious[7]	no serious indirectness	serious[20]	none	133	129	-	SMD 0.33 lower (0.68 to 0.03 lower)	VERY LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Duration <6 sessions (Better indicated by lower values)												
2[16]	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	141	105	-	SMD 0.31 lower (0.58 to 0.05 lower)	LOW	CRITICAL
Difficulties with sleep (PSQI, ISI, GSQS, WHQ) at follow-up with stratification - Duration ≥6 sessions (Better indicated by lower values)												
1 (Atema 2019)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[20]	none	170	84	-	SMD 0.4 lower (0.66 to 0.13 lower)	LOW	CRITICAL

1 *CBT: Cognitive behavioural therapy; CI: confidence interval; FACT-ES: Functional Assessment of Cancer Therapy-Endocrine Symptoms; GCS-vm: Greene Climacteric Scale-*
2 *vasomotor symptoms; GSQS: Groningen Sleep Quality Scale; HFRS: Hot flush rating scale; MD: mean difference; MID: minimal important difference; PQSI: Pittsburgh Sleep*

Quality Inventory; ROB 2: Cochrane risk of bias tool version 2; SF-36: 36-item Short Form Health Survey; SD: standard deviation; SMD: standardised mean difference; WHQ: Women's health questionnaire.

[1] Atema 2019, Duijts 2012 and Hummel 2017
[2] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
[3] Serious risk of bias in the evidence contributing to the outcomes as per RoB
[4] 95% CI crosses 1 MID (0.5x SD of the control group: for SF-36 physical functioning=9.3; SF-35 social functioning=10.4; SF-36 physical role limitations=20.4; SF-36 emotional role limitations=18.4; SF-36 bodily pain=11.3; SF-36 general health=10.7; SF-36 vitality=9.6; SF-36 mental health=8.5; Revised WHQ wellbeing=9.7; Revised WHQ somatic symptoms=10.7; Revised WHQ memory and concentration=10.7; HFRS hot flush frequency=19.8; HFRS night sweats frequency=6.5; FACT-ES=4.2; GCS-vm=1;)
[5] Ayers 2012 and Duijts 2012
[6] Atema 2019, Ayers 2012 and Hummel 2017
[7] Serious heterogeneity (I-squared inconsistency statistic of 50-80%)
[8] Atema 2019 and Hummel 2017
[9] Atema 2019 and Ayers 2012
[10] Atema 2019, Ayers 2012, Duijts 2012, and Hummel 2017
[11] Atema 2019 and Duijts 2012
[12] Very serious heterogeneity (I-squared inconsistency statistic of >80%)
[13] 95% CI crosses 2 MIDs (0.5x SD of the control group: for SF-36 bodily pain=11.3)
[14] Atema 2019, Ayers 2012, Duijts 2012 and Hummel 2017
[15] Atema 2019, Ayers 2012 and Duijts 2012
[16] Ayers 2012 and Hardy 2018
[17] Atema 2019, Ayers 2012 and Hardy 2018
[18] Atema 2019 and Hardy 2018
[19] Green 2020 and Keefer 2005
[20] 95% CI crosses 1 MID (+/-0.5 for SMD)
[21]Green 2019 and Soori 2019
[22] 95% CI crosses 1 MID (Published MID according to MENOS 2 study; HFRS problem rating=2)
[23] Abdelaziz 2021, Ayers 2012, Green 2019 and Hardy 2018
[24] Ayers 2012 and Green 2019
[25] Abdelaziz 2021, Atema 2019, Ayers 2012 and Hardy 2018
[26] Abdelaziz 2021, Atema 2019 and Hardy 2018
[27] Abdelaziz 2021, Atema 2019, Ayers 2012 and Green 2019
[28] Abdelaziz 2021, Atema 2019 and Green 2019

Table 8: Comparison 2: Cognitive behavioural therapy versus no treatment (important outcomes)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Control	Relative (95% CI)	Absolute		
Discontinuation of treatment at endpoint with stratification - Personal history of breast cancer (Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Control	Relative (95% CI)	Absolute		
3[1]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	none	46/348 (13.2%)	21/269 (7.8%)	RR 1.98 (0.80 to 4.89)	77 more per 1000 (from 16 fewer to 304 more)	VERY LOW	IMPORTANT
Discontinuation of treatment at endpoint with stratification - No personal history of breast cancer (Better indicated by lower values)												
5[5]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	none	50/256 (19.5%)	36/217 (16.6%)	RR 1.35 (0.63 to 2.91)	58 more per 1000 (from 61 fewer to 317 more)	VERY LOW	IMPORTANT
Discontinuation of treatment at follow-up with stratification - Personal history of breast cancer (Better indicated by lower values)												
2[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[7]	none	35/279 (12.5%)	23/187 (12.3%)	RR 1.19 (0.72 to 1.96)	23 more per 1000 (from 34 fewer to 118 more)	VERY LOW	IMPORTANT
Discontinuation of treatment at follow-up with stratification - No personal history of breast cancer (Better indicated by lower values)												
2[8]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[4]	none	18/141 (12.8%)	4/105 (3.8%)	RR 2.64 (0.93 to 7.49)	62 more per 1000 (from 3 fewer to 247 more)	LOW	CRITICAL
Altered sexual function (SAQ pleasure) at endpoint with stratification - Personal history of breast cancer (Range of scores 0-18; Better indicated by higher values)												
2[10]	randomised trials	very serious[2]	very serious[11]	no serious indirectness	serious[12]	none	239	166	-	MD 1.08 higher (1.84 lower to 3.99 higher) [MD 0.40 lower, MD 2.57 higher]	VERY LOW	IMPORTANT
Altered sexual function (SAQ pleasure) at follow-up with stratification - Personal history of breast cancer (Range of scores 0-18; Better indicated by higher values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 0.41 higher (0.78 lower to 1.6 higher)	LOW	CRITICAL
Altered sexual function (SAQ discomfort) at endpoint with stratification - Personal history of breast cancer (Range of scores 0-6; Better indicated by lower values)												
2[10]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	MD 0.19 lower (0.54 lower to 0.16 higher)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Control	Relative (95% CI)	Absolute		
Altered sexual function (SAQ discomfort) at follow-up with stratification - Personal history of breast cancer (Range of scores 0-6; Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	MD 0.29 lower (0.74 lower to 0.16 higher)	LOW	CRITICAL
Altered sexual function (SAQ habit) at endpoint with stratification - Personal history of breast cancer (Range of scores 0-3; Better indicated by higher values)												
3[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[12]	none	348	269	-	MD 0.11 higher (0.23 lower to 0.45 higher) [MD 0.10 lower, 0.05 lower, 0.53 higher]	LOW	CRITICAL
Altered sexual function (SAQ habit) at follow-up with stratification - Personal history of breast cancer (Range of scores 0-3; Better indicated by higher values)												
2[6]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	279	187	-	MD 0.08 higher (0.05 lower to 0.21 higher)	LOW	CRITICAL
Altered sexual function (FSFI) at endpoint with stratification - Personal history of breast cancer (Range of scores 0-95; Better indicated by higher values)												
1 (Hummel 2017)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[12]	none	69	82	-	MD 4.25 higher (1.33 to 7.17 higher)	VERY LOW	CRITICAL
Altered sexual function (FSFI) at endpoint with stratification - No personal history of breast cancer (Range of scores 0-95; Better indicated by higher values)												
1 (Green 2019)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[12]	none	37	34	-	MD 1.02 lower (5.91 lower to 3.87 higher)	MODERATE	CRITICAL
Altered sexual function (GCS-sex) at endpoint with stratification - No personal history of breast cancer (Range of scores 0-4; Better indicated by lower values)												
2[13]	randomised trials	serious[9]	serious[3]	no serious indirectness	serious[12]	none	75	72	-	MD 0.56 lower (1.19 to 0.06 lower)	VERY LOW	CRITICAL
Psychological symptoms anxiety (HADS, WHQ, HAM-A, GCS) at endpoint with stratification - Personal history of breast cancer (Better indicated by lower values)												
2[10]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	239	166	-	SMD 0.08 lower (0.29 lower to 0.12 higher)	LOW	CRITICAL
Psychological symptoms anxiety (HADS, WHQ, HAM-A, GCS) at endpoint with stratification - No personal history of breast cancer (Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Control	Relative (95% CI)	Absolute		
4[14]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[15]	none	216	177	-	SMD 0.36 lower (0.57 to 0.16 lower)	VERY LOW	IMPORTANT
Psychological symptoms anxiety (HADS, WHQ) at follow-up with stratification - Personal history of breast cancer (Better indicated by lower values)												
1 (Atema 2019)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	170	84	-	SMD 0.11 lower (0.37 lower to 0.15 higher)	LOW	CRITICAL
Psychological symptoms anxiety (HADS, WHQ) at follow-up with stratification - No personal history of breast cancer (Better indicated by lower values)												
2[8]	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[15]	none	141	105	-	SMD 0.3 lower (0.56 to 0.04 lower)	LOW	IMPORTANT
Psychological symptoms low mood (WHQ depressed mood) at endpoint with stratification - No personal history of breast cancer (Range of scores 0-1; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	serious[12]	none	95	45	-	MD 0.1 lower (0.18 to 0.02 lower)	LOW	IMPORTANT
Psychological symptoms low mood (WHQ depressed mood) at follow-up with stratification - No personal history of breast cancer (Range of scores 0-1; Better indicated by lower values)												
1 (Ayers 2012)	randomised trials	serious[9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	95	45	-	MD 0.06 lower (0.13 lower to 0.01 higher)	MODERATE	IMPORTANT

CBT: Cognitive behavioural therapy; CI: confidence interval; FSFI: Female Sexual Function Index; GCS: Greene Climacteric Scale; HADS: Hospital anxiety and depression scale; HAM-A: Hamilton Anxiety Rating Scale; MD: mean difference; MID: minimally important difference; OR: odds ratio; SAQ: Sexual activity questionnaire; RoB 2: Cochrane risk of bias tool version 2; SMD: standardised mean difference; WHQ: Women's health questionnaire.

[1] Atema 2019, Duijts 2012 and Hummel 2017

[2] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[3] Serious heterogeneity (I-squared inconsistency statistic of 50-80%)

[4] 95% CI crosses 1 MID for dichotomous variables (0.8 or 1.25)

[5] Abdelaziz 2021, Ayers 2012, Green 2019, Hardy 2018 and Soori 2019

[6] Atema 2019 and Duijts 2012

[7] 95% CI crosses 2 MIDs for dichotomous variables (0.80 and 1.25)

[8] Ayers 2012 and Hardy 2018

[9] Serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[10] Atema 2019, Hummel 2017

[11] Very serious heterogeneity (I-squared inconsistency statistic of >80%)

[12] 95% CI crosses 1 MID for continuous variables (0.5x SD of the control group: for SAQ pleasure=1.9; SAQ habit=0.4; FSFI=4.3; GCS-sex=0.5; WHQ depressed mood=0.14)

[13] *Green 2019 and Soori 2019*
[14] *Ayers 2012, Green 2019, Hardy 2018 and Soori 2019*
[15] *95% CI crosses 1 MID for continuous variables (+/-0.5 for SMD)*

Appendix G Economic evidence study selection

Study selection for: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

A single economic search was undertaken for all topics included in the scope of this guideline. See Supplement 2 for further information.

Appendix H Economic evidence tables

Economic evidence tables for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Table 9: Economic evidence tables for cognitive behavioural therapy versus waiting list control in people with a previous diagnosis of breast cancer

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Author and year: Verbeek 2019 **Country**: Netherlands **Type of economic analysis:** Cost utility **Source of funding:** Dutch Cancer Society and the Netherlands Cancer Institute	**Intervention:** 1) Guided internet based cognitive behavioural therapy (iCBT). Strong emphasis on hot flushes and night sweats but other symptoms addressed. Additional telephone intake and weekly online feedback. Total therapist time about 3 hours per person. 2)Self-managed iCBT. As for guided iCBT but without the telephone intake and weekly feedback. **Comparator:** Waiting list control. Usual care which did not involve any form of care aimed at coping with menopausal symptoms.	**Population:** 254 breast cancer survivors with treatment induced menopausal symptoms at 12 hospitals in the Netherlands between 2015 & 2017. Full discussion of population characteristics are discussed for Atema 2019 in the accompanying clinical evidence review. **Modelling approach**: Markov model **Source of baseline data:** Atema 2019 discussed in detail in the accompanying clinical evidence review **Source of effectiveness data:** Atema 2019 discussed	**Mean cost per participant:** Intervention: 1) €5315.55 2) €5118.22 Comparator: €4993.90 Difference (vs comparator): 1) €321.65 2) €124.32 **Mean outcome per participant (QALYs):** 1)4.119 2)4.117 Comparator: 3)4.106 Difference (vs comparator): 1)0.0138 2)0.0110	**ICER (per QALY gained):** 1) €23,330.50 2) €11,277.63 **Probability of being cost effective:** **€30k Threshold per QALY:** Self-managed iCBT (2) 68.9% probability of being the preferred option. **Sensitivity analysis:** Deterministic sensitivity analysis around all inputs into the model. Conclusions were sensitive to estimates around utility values, effectiveness of the	**Perspective:** Dutch health care payer **Currency**: Euro (€) **Cost year**: 2017 **Time horizon**: 5 years, sensitivity analysis varied from 3 to 7 years **Discounting**: 1.5% per annum for QALYs and 4.0% per annum for costs **Applicability**: Partially applicable **Limitations**: Minor limitations **Other comments**: Model largely based on results of Atema 2019 discussed in the accompanying clinical evidence review.

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
	Full description of interventions reported for Atema 2019 in the accompanying clinical evidence review.	in detail in the accompanying clinical evidence review **Source of utility data:** Health states for menopausal symptoms and reduction in menopausal symptoms, scored using the SF-36 and converted to EQ-5D-3L scores. These values were taken from Atema 2019 discussed in detail in the accompanying clinical evidence review. Recurrence of breast cancer utilities were taken from 1 EQ-5D-3L study of 361 consecutive breast cancer patients at I centre in Sweden. **Source of cost data:** Intervention costs were provided by 2 potential providers of the CBT programme. All healthcare utilisation costs were collected using the Dutch iMTA Medical Consumption Questionnaire during 1 RCT (Atema 2019)		intervention and cost reduction as a result of reducing menopausal symptoms.	
Author and year: Mewes 2015	**Intervention:** Cognitive behavioural therapy (CBT) – 6 weekly	**Population:** Hypothetical cohort of 48 year old women, premenopausal at time of	**Mean cost per participant:**	**ICER (per QALY gained):**	**Perspective:** Dutch health care payer

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Country: Netherlands **Type of economic analysis:** Cost utility **Source of funding:** Alpe d'HuZes, a foundation which is part of the Dutch Cancer Society	group sessions of 90 minutes each **Comparator:** Usual care/ waiting list control (WLC) Full description of interventions reported for Duijts 2012 in the accompanying clinical evidence review. Duijts 2012 considered physical exercise (PE) and CBT+PE. PE is outside the scope of this guideline and results from this intervention have not been reported in this evidence summary. CBT+PE was not considered by the economic model as it was considered more expensive and no more effective than CBT alone in Duijts 2012.	diagnosis, had undergone adjuvant chemotherapy and/or hormonal therapy, had experienced a treatment-induced menopause, and who reported at least a minimal level of menopausal symptoms. The cohort was matched to study characteristics from Duijt 2012 discussed in the accompanying clinical evidence report. premenopausal at time of diagnosis, had undergone adjuvant chemotherapy and/or hormonal therapy, had experienced a treatment-induced menopause, and who reported at least a minimal level of menopausal symptoms. **Modelling approach**: Markov model **Source of baseline data:**	Intervention: €2,983 Comparator: €2,798 Difference (vs comparator): €184 **Mean outcome per participant (QALYs):** 4.400 Comparator: 4.392 Difference (vs comparator): 0.0079	€22,502 **Probability of being cost effective:** **€30k Threshold per QALY:** CBT has a 49% probability of being cost effective compared to WLC and PE. Not reported excluding PE. **Sensitivity analysis:** Deterministic sensitivity analysis around all inputs into the model. Conclusions were sensitive to estimates around utility values and duration of effectiveness of the intervention.	**Currency**: Euro (€) **Cost year**: 2012 **Time horizon**: 5 years **Discounting**: 1.5% per annum for QALYs and 4.0% per annum for costs **Applicability**: Partially applicable **Limitations**: Minor limitations **Other comments**: Model largely based on results of Duijts 2019 discussed in the accompanying clinical evidence review.

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
		Duijt 2012 discussed in detail in the accompanying clinical evidence review. **Source of effectiveness data:** Duijt 2012 discussed in detail in the accompanying clinical evidence review. **Source of utility data:** SF-36 values were taken from individual patient data in Duijt 2012 discussed in detail in the accompanying clinical evidence review. Recurrence of breast cancer utilities were taken from from 1 EQ-5D-3L study of 361 consecutive breast cancer patients at I centre in Sweden. **Source of cost data:** Intervention and healthcare costs were collected during Duijt 2012 discussed in detail during the accompanying clinical evidence review. Recurrence costs taken from Retel 2010 an economic model of testing in early breast cancer.			

1 *CBT: Cognitive Behavioural Therapy; EQ-5D-3L: EuroQOL 5-Dimension three level; iCBT: Internet Based Cognitive Behavioural Therapy; ICER: Incremental Cost Effectiveness*
2 *Ratio; PE: Physical Exercises; QALY: Quality Adjusted Life Year; RCT: Randomised Controlled Trial; SF-36: 36 Item Short Form Survey; Vs: Versus; WLC: Waiting List Control*

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Appendix I Economic model

Economic model for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

Excluded effectiveness studies

Table 10: Excluded studies and reasons for their exclusion

Study	Reason for exclusion
Aaronson, N and Duijts, S (2008) Cognitive behavioral therapy (CBT) and physical exercise (PE) for climacteric symptoms in breast cancer patients experiencing treatment-induced menopause: a multicenter randomized trial (EVA project). Http://www.trialregister.nl/trialreg/admin/rctview.asp? TC=1165	- Protocol only Clinical trial entry only
Atema, V, van Leeuwen, M, Oldenburg, HSA et al. (2016) Design of a randomized controlled trial of Internet-based cognitive behavioral therapy for treatment-induced menopausal symptoms in breast cancer survivors. BMC cancer 16(1nopagination)	- Protocol only Published results assessed under Atema 2019
Atema, Vera, van Leeuwen, Marieke, Kieffer, Jacobien M et al. (2020) Internet-based cognitive behavioral therapy aimed at alleviating treatment-induced menopausal symptoms in breast cancer survivors: Moderators and mediators of treatment effects. Maturitas 131: 8-13	- Outcome Study does not report on the outcomes of the RCT in this report. RCT trial and results reported in Atema 2019
Atema, Vera, van Leeuwen, Marieke, Oldenburg, Hester S A et al. (2017) An Internet-based cognitive behavioral therapy for treatment-induced menopausal symptoms in breast cancer survivors: results of a pilot study. Menopause (New York, N.Y.) 24(7): 762-767	- Study design Not a randomised controlled trial
Ayen, I and Hautzinger, M (2004) Cognitive behavior therapy for depression in menopausal women. A controlled, randomized treatment study. Zeitschrift fur klinische Psychologie und Psychotherapie 33(4): 290-299	- Language Full text not in English (German)
Carmody, J.; Crawford, S.; Churchill, L. (2006) A pilot study of mindfulness-based stress reduction for hot flashes. Menopause 13(5): 760-769	- Study design Not a randomised controlled trial
Carmody, James Francis, Crawford, Sybil, Salmoirago-Blotcher, Elena et al. (2011) Mindfulness training for coping with hot flashes: results of a randomized trial. Menopause (New York, N.Y.) 18(6): 611-20	- Intervention Not cognitive behavioural therapy. Intervention is mindfulness only.
Chang, Yun-Chen; Hu, Wen-Yu; Chang, Yuh-Ming (2021) Cognitive-Behavioral Therapy to Alleviate Treatment-Induced Menopausal Symptoms in Women With Breast Cancer: A	- Study design Systematic review. Included studies checked and relevant RCTs have been identified by the

Study	Reason for exclusion
Systematic Review. Cancer nursing 44(5): 411-418	search and included. Majority of studies did not meet the study design criteria as they were not RCTs, therefore this systematic review was not included.
Conklin, Danette Y, Goto, Toyomi, Ganocy, Stephen et al. (2020) Manualized cognitive behavioral group therapy to treat vasomotor symptoms for women diagnosed with mood disorders. Journal of Psychosomatic Research 128	- Study design Not a randomised controlled trial
Darehzereshki, S; Dehghani, F; Enjezab, B (2022) Mindfulness-based stress reduction group training improves of sleep quality in postmenopausal women. BMC psychiatry 22(1)	- Intervention Not cognitive behavioural therapy. Intervention is mindfulness only.
Donohoe, Fionan, O'Meara, Yvonne, Roberts, Aidin et al. (2021) The menopause after cancer study (MACS) - A multimodal technology assisted intervention for the management of menopausal symptoms after cancer - Trial protocol of a phase II study. Contemporary clinical trials communications 24: 100865	- Protocol only Full results not yet published
Enjezab, B., Zarehosseinabadi, M., Farzinrad, B. et al. (2019) The effect of mindfulness-based cognitive therapy on quality of life in perimenopausal women. Iranian Journal of Psychiatry and Behavioral Sciences 13(1): e86525	- Intervention Not cognitive behavioural therapy. Mindfulness based cognitive intervention but not focused on cognitive behavioural therapy
Enjezab, B, Zarehosseinabadi, M, Farzinrad, B et al. (2019) Effect of mindfulness-based cognitive therapy on menopausal symptoms: a randomized clinical trial. Journal of mazandaran university of medical sciences 29(178): 85-97	- Language Full text not in English
Fujimoto, Kaoru (2017) Effectiveness of coaching for enhancing the health of menopausal Japanese women. Journal of women & aging 29(3): 216-229	- Intervention Not cognitive behavioural therapy, intervention is coaching
Ganz, P A, Greendale, G A, Petersen, L et al. (2000) Managing menopausal symptoms in breast cancer survivors: results of a randomized controlled trial. Journal of the National Cancer Institute 92(13): 1054-64	- Intervention Not cognitive behavioural therapy. Intervention is a comprehensive menopausal assessment which is followed by various treatments. Behavioural interventions are part of the intervention, but not specifically cognitive behavioural therapy, and less than 33% of participants received it.
Garcia, Marcelo C, Kozasa, Elisa H, Tufik, Sergio et al. (2018) The effects of mindfulness and relaxation training for insomnia (MRTI) on postmenopausal women: a pilot study. Menopause (New York, N.Y.) 25(9): 992-1003	- Intervention Not cognitive behavioural therapy. Intervention is mindfulness only.
Green, Sheryl M, Haber, Erika, McCabe, Randi E et al. (2013) Cognitive-behavioral group treatment for menopausal symptoms: A pilot study. Archives of Women's Mental Health 16(4): 325-332	- Study design Not a randomised controlled trial

Study	Reason for exclusion
Hashemian, Shervin-Sadat; Masom-Alipour, Soghra; Najimi, Arash (2020) Improving menopausal symptoms and reducing depression in postmenopausal women: Effectiveness of transferring experiences in group education. Journal of education and health promotion 9: 318	- Intervention Not cognitive behavioural therapy. Intervention is a group education on menopause
Hunter, Myra S, Coventry, Shirley, Hamed, Hisham et al. (2009) Evaluation of a group cognitive behavioural intervention for women suffering from menopausal symptoms following breast cancer treatment. Psycho-Oncology 18(5): 560-563	- Study design Not a randomised controlled trial
Hunter, Myra S and Liao, K. Lih-Mei (1996) Evaluation of a four-session cognitive-behavioural intervention for menopausal hot flushes. British Journal of Health Psychology 1(part2): 113-125	- Intervention Part patient-preference part randomised, however participants chose CBT and therefore there is a bias toward the intervention
Keefer, Laurie Anne (2003) The effect of a cognitive-behavioral group treatment on perimenopausal hot flashes and related symptoms. Dissertation Abstracts International: Section B: The Sciences and Engineering 64(6b): 2923	- Study design Dissertation
Khoshbooii, Robab, Hassan, Siti Aishah, Deylami, Neda et al. (2021) Effects of Group and Individual Culturally Adapted Cognitive Behavioral Therapy on Depression and Sexual Satisfaction among Perimenopausal Women. International journal of environmental research and public health 18(14)	- Outcome No outcomes matching the outcomes specified in the protocol
Larroy Garcia, Cristina and Gomez-Calcerrada, Sonia Gutierrez (2011) Cognitive-behavioral intervention among women with slight menopausal symptoms: a pilot study. The Spanish journal of psychology 14(1): 344-55	- Study design Not a randomised controlled trial
Lindh-Astrand, Lotta, Holm, Anna-Clara Spetz, Sydsjo, Gunilla et al. (2015) Internet-delivered applied relaxation for vasomotor symptoms in postmenopausal women: lessons from a failed trial. Maturitas 80(4): 432-4	- Study design Lessons learned from an RCT. RCT results published and assessed under Lindh-Astrand 2013
Lindh-Astrand, Lotta and Nedstrand, Elizabeth (2013) Effects of applied relaxation on vasomotor symptoms in postmenopausal women: a randomized controlled trial. Menopause (New York, N.Y.) 20(4): 401-8	- Intervention Not cognitive behavioural therapy. Intervention is an applied relaxation based on CBT, but not CBT
Moghadam, Fereshteh Salimi, Mahmoodi, Zohreh, Kabir, Kourosh et al. (2019) Effectiveness of a Multi-Dimensional Group Counseling Program Based on the GATHER Approach on the Quality of Life in Surgically Menopausal Women. Journal of menopausal medicine 25(3): 130-141	- Intervention Not cognitive behavioural therapy. Intervention is group counselling without a cognitive behavioural therapy component
Mollaahmadi, Leila, Keramat, Afsaneh, Changizi, Nasrin et al. (2019) Evaluation and	- Study design

Study	Reason for exclusion
comparison of the effects of various cognitive-behavioral therapy methods on climacteric symptoms: A systematic review study. Journal of the Turkish German Gynecological Association 20(3): 178-195	Systematic review. Included studies checked for relevance. Majority are not relevant due to not being randomised controlled trials, or not reporting outcomes that are relevant to this review. Other relevant studies have already been identified by the search and included.
Naeij, Ehtram, Khani, Soghra, Firouzi, Armin et al. (2019) The effect of a midwife-based counseling education program on sexual function in postmenopausal women: a randomized controlled clinical trial. Menopause (New York, N.Y.) 26(5): 520-530	- Intervention Not cognitive behavioural therapy. Intervention is a counselling education program
Reddy, Nethravathi Venkataswamy and Omkarappa, Dayananda Bittenahalli (2019) Cognitive-behavioral therapy for depression among menopausal woman: A randomized controlled trial. Journal of family medicine and primary care 8(3): 1002-1006	- Outcome No outcomes reported matching the outcomes in the protocol
Saensak, Suprawita, Vutyavanich, Teraporn, Somboonporn, Woraluk et al. (2014) Relaxation for perimenopausal and postmenopausal symptoms. The Cochrane database of systematic reviews: cd008582	- Intervention Included studies did not look at cognitive behavioural therapy. The interventions were around relaxation techniques.
Stefanopoulou, Evgenia and Grunfeld, Elizabeth Alice (2017) Mind-body interventions for vasomotor symptoms in healthy menopausal women and breast cancer survivors. A systematic review. Journal of psychosomatic obstetrics and gynaecology 38(3): 210-225	- Intervention Systematic review. Majority of the included studies are not CBT interventions. Included studies that are CBT based have already been identified by the search and assessed for relevance separately
Tran, Stephanie, Hickey, Martha, Saunders, Christobel et al. (2021) Nonpharmacological therapies for the management of menopausal vasomotor symptoms in breast cancer survivors. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 29(3): 1183-1193	- Intervention Only 3 of 12 included studies looking at CBT. They have already been identified by the search and included in the review.
Tunc Aksan, Aygul (2021) Effectiveness of cognitive behavioral therapies in women with breast cancer: A systematic review. Psikiyatride Guncel Yaklasimlar 13(1): 34-51	- Population Systematic review not focused on people with menopausal symptoms, therefore included studies not checked.
van Driel, C M, Stuursma, A, Schroevers, M J et al. (2019) Mindfulness, cognitive behavioural and behaviour-based therapy for natural and treatment-induced menopausal symptoms: a systematic review and meta-analysis. BJOG : an international journal of obstetrics and gynaecology 126(3): 330-339	- Intervention Systematic review. Majority of included studies are not CBT based. The studies that are CBT based have been identified by the search and assessed separately.
van Driel, Cmg, de Bock, G H, Schroevers, M J et al. (2019) Mindfulness-based stress reduction for menopausal symptoms after risk-reducing salpingo-oophorectomy (PURSUE study): a randomised controlled trial. BJOG : an international journal of obstetrics and	- Intervention Not cognitive behavioural therapy. Intervention is mindfulness based without a cognitive behaviour therapy component.

Study	Reason for exclusion
gynaecology 126(3): 402-411	
Velez Toral, Mercedes, Godoy-Izquierdo, Debora, Padial Garcia, Ana et al. (2014) Psychosocial interventions in perimenopausal and postmenopausal women: a systematic review of randomised and non-randomised trials and non-controlled studies. Maturitas 77(2): 93-110	- Intervention Systematic review focused on psychosocial interventions for self-caring and self-management of menopausal manifestations, and not looking at interventions for symptoms. Therefore included studies not checked.
Verbeek, Joost G E, Atema, Vera, Mewes, Janne C et al. (2019) Cost-utility, cost-effectiveness, and budget impact of Internet-based cognitive behavioral therapy for breast cancer survivors with treatment-induced menopausal symptoms. Breast cancer research and treatment 178(3): 573-585	- Outcome No clinical outcomes matching the protocol
Von Bultzingslowen, K; Pfeifer, M; Kroner-Herwig, B (2006) A cognitive-behavioral group intervention for menopausal women - Results of a randomized controlled study. Verhaltenstherapie 16(3): 184-192	- Language Full text not in English (German)
Wong, Carmen, Yip, Benjamin Hon-Kei, Gao, Ting et al. (2018) Mindfulness-Based Stress Reduction (MBSR) or Psychoeducation for the Reduction of Menopausal Symptoms: A Randomized, Controlled Clinical Trial. Scientific reports 8(1): 6609	- Intervention Not cognitive behavioural therapy. Intervention is a mindfulness-based stress reduction without a cognitive behavioural therapy component, and it is compared to an education programme.
Yazdani Aliabadi, Masoomeh, Javadnoori, Mojgan, Saki Malehi, Amal et al. (2021) A study of mindfulness-based stress-reduction training effects on menopause-specific quality of life in postmenopausal women: A randomized controlled trial. Complementary therapies in clinical practice 44: 101398	- Intervention Not cognitive behavioural therapy. Intervention is a mindfulness based intervention without a cognitive behavioural therapy component.
Yazdkhasti, M, Keshavarz, M, Khoei, Es Merghaati et al. (2012) The Effect of Support Group Method on Quality of Life in Post-menopausal Women. Iranian journal of public health 41(11): 78-84	- Intervention Not cognitive behavioural therapy. The intervention was a group session with various topics related to menopause discussed at each session, but without a cognitive behavioural therapy component.
Ye, Mengfei, Shou, Mengna, Zhang, Jian et al. (2022) Efficacy of cognitive therapy and behavior therapy for menopausal symptoms: a systematic review and meta-analysis. Psychological medicine 52(3): 433-445	- Intervention Systematic review. Many of the studies are not CBT based interventions. Studies with CBT based interventions have been checked and have already been identified by the search and have been assessed for inclusion separately

Excluded economic studies

No economic evidence was identified for this review. See Supplement 2 for further information.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the effectiveness of cognitive behavioural therapy for managing symptoms associated with the menopause?

No research recommendations were made for this review question.