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Nature-based rehabilitation for patients with longstanding stress-related disorders – an updated report

Ahlborg Jr G, Bergenheim A, Eriksson M, Jivegård L, Sundell G, Svanberg T, Svensson M, Bernhardsson S.

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Nature-based rehabilitation for patients with longstanding stress-related disorders – an updated report
[Grön rehabilitering för patienter med långvarig stressrelaterad ohälsa – uppdaterad rapport]

Ahlborg G[1*], Bergenheim A[2], Eriksson M[3], Jivegård L[4], Sundell G[5], Svanberg T[3], Svensson M[4], Bernhardsson S[4]

[1]Institute of Stress Medicine, Region Västra Götaland, Gothenburg, Sweden
[2]Närhälsan Rehabilitation Uddevalla, Region Västra Götaland, Gothenburg, Sweden
[3]Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
[4]HTA-centrum of Region Västra Götaland, Gothenburg, Sweden.
[5]Psykiatrimottagning utmattningssyndrom, Gothenburg, Sweden

[*]Corresponding author

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1. Abstract

Background: In December 2018 mental illness diagnoses comprised 53% and 40% of all cases of sick leave among women and men respectively, and stress-related diagnoses accounted for approximately 20% of all cases in Sweden. The diagnosis "*Exhaustion disorder*" (ED) is used in Sweden to define patients with exhaustion as a consequence of identifiable stressor(s) present for at least six months. Diagnostic criteria include: exhaustion, cognitive dysfunction, sleep disturbance, reduced tolerance to further stress, and somatic symptoms. Patients with stress-related disorders usually receive psychological support, physical activity, guidance and medication as needed for symptoms of depression and anxiety. Nature-based rehabilitation (NBR) is not standardised but is always led by a multi-disciplinary rehabilitation team, usually including a physiotherapist, an occupational therapist, a psychotherapist/psychologist and personnel with competences related to garden/gardening and nature. In 2016, a Health Technology Assessment (HTA) report on NBR for patients with longstanding stress-related disorders was published (Bernhardsson et al., 2016), indicating uncertainty of effect of NBR compared with other rehabilitation programmes, but perceived positive effects reported in qualitative studies. The present HTA report is an update of the 2016 report and includes both the previous studies and those identified in a new systematic search.

Questions at issue: 1) Is multidisciplinary, group-based, NBR more effective than either multidisciplinary, group-based, rehabilitation that is not nature-based, or any other rehabilitation that is not nature-based, for patients with longstanding (>6 months) stress-related disorders, in terms of health-related quality of life (HRQoL), sick leave, work ability, healthcare consumption, perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain or insomnia/sleep disturbances? 2) What are the experiences and perceived effects of participating in NBR in patients with longstanding stress-related disorders?

Methods: During July 2019, systematic literature searches were conducted in PubMed, Embase, the Cochrane Library, Cinahl, Amed, PsycInfo and a number of HTA databases. At least two authors independently screened titles, abstracts, full-text articles for inclusion and thereafter appraised study quality and extracted data. The certainty of evidence from the quantitative studies was appraised according to GRADE. The qualitative studies were synthesised and the certainty of evidence was appraised according to CERQual.

Results: Four RCTs, two controlled cohort studies and four qualitative studies were included in the report. Most quantitative studies had major study limitations. Regarding outcomes critical for decision-making, there may be little or no difference in sick-leave, healthcare consumption (frequency of general practitioner (GP) contacts), or HRQoL after NBR compared with non-NBR or other rehabilitation for patients with longstanding stress-related disorders (GRADE ⊕⊕OO). For all other outcomes in the quantitative studies, the certainty of evidence was very low (GRADE ⊕OOO). No studies reported cognitive disability and pain. The qualitative studies were considered relevant regarding context, population and intervention, and quality was generally assessed as high. The synthesis resulted in 16 descriptive themes organised under four broad, analytical, themes: state of mind, experiences of garden and nature, insights, and changes. The experiences and perceived effects of participating in NBR and spending time in a nature environment were described as positive for recovery. Eleven of the descriptive themes were based on explicit results from at least three of the four studies. Confidence in the evidence of the qualitative findings ranged from moderate to low, primarily due to the low number of studies.

Concluding remarks: The effectiveness of NBR compared with other forms of rehabilitation in patients with longstanding stress-related disorders remains poorly studied. Regarding critical outcomes, there may be little or no difference in sick-leave, healthcare consumption, or HRQoL after NBR compared with non-NBR or other rehabilitation for patients with longstanding stress-related disorders (GRADE ⊕⊕OO). Effects on all other studied outcomes are uncertain. Qualitative studies suggest patients experience positive health effects from being in natural environments and working in a garden. There is thus qualitative evidence of a perceived positive effect of NBR on long-standing stress related disorders, but no quantitative evidence that NBR is more effective than other forms of rehabilitation for longstanding stress-related disorders.

2. Svensk sammanfattning – Swedish summary

Bakgrund: I december 2018 utgjorde i Sverige psykiatriska diagnoser 53% respektive 40% av all sjukskrivning bland kvinnor respektive män och stress-relaterade diagnoser stod för ca 20% av alla sjukskrivningar. Diagnosen Utmattningssyndrom (eng *Exhaustion disorder, ED*) används i Sverige vid utmattning som konsekvens av identifierbara stressorer som funnits i minst sex månader. Diagnoskriterier är: utmattning, kognitiva besvär, sömnsvårigheter, nedsatt stresstålighet och fysiska symtom. Vanliga åtgärder vid stress-relaterad ohälsa är psykologiskt stöd, fysisk aktivitet, rådgivning och vid behov läkemedelsbehandling för symtom på depression och ångest. Den svenskutvecklade rehabiliteringsformen "Grön Rehab" (eng *Nature-based rehabilitation, NBR*) är inte standardiserad men leds alltid av ett multidisciplinärt rehabiliteringsteam som i regel består av fysioterapeut, arbetsterapeut, psykolog och personal med trädgårdskompetens. 2016 publicerade HTA-centrum en HTA-rapport angående NBR för patienter med långvarig stress-relaterad ohälsa (Bernhardsson et al., 2016). Föreliggande HTA-rapport är en uppdatering av rapporten från 2016 och är baserad på de studier som då ingick samt nytillkomna studier.

Frågeställningar: 1) Är multidisciplinär, gruppbaserad, NBR mer effektiv än antingen multidisciplinär, gruppbaserad rehabilitation som inte är naturbaserad eller annan rehabilitering som inte är naturbaserad, för patienter med långvarig (>6 månader) stressrelaterad ohälsa, vad gäller hälsorelaterad livskvalitet, sjukskrivning, arbetsförmåga, sjukvårdskonsumtion, upplevd stress, depression, ångest, trötthet/utmattning, kognitiva besvär, smärta eller insomni/sömnsvårigheter? 2) Vilka är erfarenheterna och upplevda effekter av att genomgå NBR hos patienter med långvarig stressrelaterad ohälsa?

Metod: Systematiska litteratursökningar gjordes i juli 2019 i PubMed, Embase, Cochrane Library, Cinahl, Amed, PsycInfo och ett antal HTA-databaser. Minst två författare läste och selekterade artiklar samt utvärderade studiekvalitet och extraherade data. Tilltron till de kvantitativa studiernas resultat värderades enligt GRADE och tilltron till de kvalitativa studiernas resultat enligt CERQual.

Resultat: Fyra RCT:er, två kontrollerade kohortstudier och fyra kvalitativa studier inkluderades i rapporten. De flesta av de kvantitativa studierna hade betydande metodologiska brister. Vad gäller utfall som är kritiska för beslutsfattande visade studierna liten eller ingen skillnad i sjukskrivning, vårdkonsumtion (antal läkarkontakter) eller hälsorelaterad livskvalitet mellan NBR och annan, icke-naturbaserad, rehabilitering för patienter med långvarig stressrelaterad ohälsa (GRADE ⊕⊕○○). För övriga utfall i de kvantitativa studierna var det vetenskapliga underlaget otillräckligt (GRADE ⊕○○○). Ingen av studierna rapporterade kognitiva besvär eller smärta. De kvalitativa studierna bedömdes som relevanta avseende kontext, population och intervention och metodologisk kvalitet var överlag god. Den kvalitativa syntesen resulterade i 16 deskriptiva teman som organiserades under fyra analytiska teman: *sinnesstämning, erfarenheter av trädgård och natur, insikter* och *förändringar*. Patienternas erfarenheter och upplevda effekter av rehabilitering i trädgård/natur var att detta var positivt för tillfrisknande. Elva av de deskriptiva temana baserades på explicita resultat från minst tre av de fyra studierna. Tillförlitligheten till de kvalitativa studiernas resultat varierade från måttlig till låg, främst pga det låga antalet studier.

Sammanfattande slutsatser: Effektiviteten av NBR jämfört med andra rehabiliteringsformer för patienter med långvarig stressrelaterad ohälsa är fortfarande otillräckligt studerad. Naturbaserad rehabilitering skulle kunna resultera i liten eller ingen skillnad i de kritiska utfallen sjukskriving, vårdkonsumtion (antal läkarkontakter) och hälsorelaterad livskvalitet jämfört med icke-naturbaserad rehabilitering för patienter med långvarig stressrelaterad ohälsa För övriga utfall är det vetenskapliga underlaget otillräckligt. De kvalitativa studierna visar att patienterna har positiva upplevelser av NBR, men de kvantitativa studierna visade inget stöd för ett mer positivt resultat i effektivitet jämfört med andra former av rehabilitation för långvarig stressrelaterad ohälsa.

The above summaries were written by representatives from the HTA-centrum. The HTA report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers, and is ended with a concluding summary.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 29 January 2020

Regional board for quality assurance of activity-based HTA	
Bergenheim, Anna	PT, PhD
Bergh, Christina	MD, Professor
Bernhardsson, Susanne	PT, Associate professor
Hakeberg, Magnus	OD, Professor
Jivegård, Lennart	MD, Senior university lecturer
Larsson, Anders	MD, PhD
Nelzén, Olle	MD, Associate professor
Petzold, Max	Statistician, professor
Rylander, Christian	MD, Associate professor
Sjögren, Petteri	DDS, PhD
Sjövall, Henrik	MD, Professor
Skogby, Maria	RN, PhD
Strandell, Annika	MD, Associate professor
Svanberg, Therese	HTA librarian
Svensson, Mikael	Health economist, Professor
Wallerstedt, Susanna	MD, Professor
Wartenberg, Constanze	Psychologist, PhD

DDS Doctor of dental surgery
MD Medical doctor
PhD Doctor of Philosophy
OD Odontology doctor
PT Physiotherapist
RN Registered Nurse

3. Summary of quantitative findings

Outcome	Study design Number of studies	Absolute effect	Certainty of evidence GRADE[1]
Sick leave	2 RCTs, 1 cohort study	Days/month with sick leave compensation: 9 vs 7 days; Δ 2 days (95% CI -2 to 5); ns Proportion on sick-leave 12 month after intervention: 21% vs 33%; Δ 12%; ns Proportion with sickness benefits or compensation 20 months after intervention: 75% vs 60%; Δ 15%; ns	⊕⊕○○[2] ⊕○○○[3]
Self-assessed work ability	1 cohort study	Work ability index[3] (0–10) Intergroup difference in change 0–3 months: Δ 0.70 (95% CI -0.43 to 1.84); ns 3–6 months: Δ 0.46 (CI -0.86 to 1.78); ns	⊕○○○[4]
Healthcare consumption	1 RCT, 1 cohort study	Median no. of GP contacts during 12 months after intervention: 13 (range 0-67) vs 14 (range 5-35) Intragroup difference 12 months after vs 12 months before intervention: p<0.01 vs p<0.05 Intergroup difference after intervention (effect size): r=-0.396 vs r=-0.249; statistical significance NR No. of outpatient visits one year after/one year before intervention: SMR 0.84 (95% CI 0.81-0.87) vs 0.92 (95% CI 0.90-0.93); Intergroup difference p< 0.05 No. of hospital days one year after/one year before intervention: SMR 0.47 (95% CI 0.43-0.52) vs 0.94 (95% CI 0.87-1.0) Intergroup difference p< 0.05	⊕⊕○○[5] ⊕○○○[6]
Health-related quality of life	1 RCT	Psychological General Well-Being Index: Post-treatment 61.44 (SD 15.51) vs 59.62 (SD 18.87); ns 3 months 63.31 (SD 18.58) vs 63.38 (SD 21.51); ns 6 months 63.28 (SD 14.47) vs 65.92 (SD 19.91); ns 12 months 63.51 (SD 16.81) vs 64.86 (SD 21.87); ns	⊕⊕○○[7]
Perceived stress	1 RCT, 1 cohort study	DASS21 subscale stress difference pre and post intervention Intergroup diff.: $F_{1.28}$ = 5.442; p=0.027; eta squared = 0.163 PSS-10, change from baseline to 3 months: -4.61 (95% CI -6.52 to -2.71) vs -4.16 (95% CI -6.59 to -1.73) Intergroup difference Δ 0.45 (-3.54 to 2.63); ns PSS-10, change from baseline to 6 months: -1.15 (95% CI -3.53 to 1.23) vs -1.82 (95% CI -4.69 to -1.06) Intergroup difference Δ 0.67 (-3.07 to 4.40); ns	⊕○○○[8]
Depression	1 RCT	DASS21 subscale depression score difference pre and post intervention: ns between groups	⊕○○○[8]
Anxiety	1 RCT	DASS21 subscale anxiety score difference pre and post intervention: ns between groups	⊕○○○[8]
Exhaustion/ burnout	2 RCTs, 1 cohort study	Mean total SMBQ score post-intervention and at 3, 6, and 12 months: ns between groups at any time point (scores not presented)	⊕⊕○○[9]

NR=Not reported; GP=General practitioner; SMR=Standard morbidity ratio; ns=non-significant; DASS21=Depression anxiety stress scale, 21 items; PSS-10=Perceived stress scale, 10 items; SMBQ=Shirom-Melamed burnout questionnaire

[1]**Certainty of evidence**

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[2]Downgraded two steps for serious study limitations (e.g. unclear randomisation procedure, lack of blinding, unclear reasons for dropout) and serious imprecision (few "events", confidence interval does not exclude negative effect)
[3]Downgraded three steps for study design and very serious study limitations (baseline differences, poorly reported confounders, compliance, numbers and reasons for dropout)
[4]Downgraded three steps for study design and very serious study limitations (risk of selection bias and high dropout rate)
[5]Downgraded two steps for serious study limitations (e.g. lack of intergroup analysis) and serious inconsistency (only one small RCT, unclear reproducibility).
[6]Downgraded three steps for study design and very serious study limitations (baseline differences, poorly reported confounders, compliance, size and reasons for dropout)
[7]Downgraded two steps for serious study limitations (lack of blinding, self-reported outcome measures, unbalanced and high frequencies of missing data) and serious inconsistency (only one small RCT, unclear reproducibility).
[8]Downgraded three steps for very serious study limitations (unclear randomisation, no blinding, unclear baseline differences, lack of follow-up, unclear drop-out rate, unclear results presentations) and problems with precision and consistency (only one small RCT, few "events", unclear reproducibility).
[9]Downgraded two steps for very serious study limitations (unclear randomisation, lack of blinding, unclear baseline differences, lack of follow-up, unclear drop-out rate)

4. Summary of qualitative findings

Summary of review finding	Studies contri-buting to the review finding	CERQual assessment of confi-dence in the evidence	Explanation of CERQual assessment
State of mind during NBR			
Patients described how nature's peace and quiet had a calming impact on their state of mind.	1,2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen across all four included studies.
Patients expressed that NBR made them feel joy in daily tasks.	1,2,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies of which two provided sufficiently rich data.
Patients experienced that NBR created a sense of belonging to a greater whole and helped patients to find meaning and values.	2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies.
Patients described themselves as becoming one with nature during NBR, enabling them to get closer to their feelings.	2,3	Low confidence	Moderate concerns about adequacy as the data come from a very small number of studies and the finding was seen in two of the four studies. The studies were of moderate to high quality.
Patients described how sensory experiences in the garden helped them to be in the present.	2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies.
Experiences of garden and nature			
Patients experienced that the garden gave a sense of safety and security.	2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies.
Patients experienced that the therapeutic garden met their needs.	2,4	Low confidence	Moderate concerns about adequacy as the data come from a very small number of studies and the finding was seen in two of the four studies of which only one provided sufficiently rich data. The studies were of high quality.
The garden was perceived as an undemanding, tolerant and permissive setting.	2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies.
Patients described that NBR helped them slow down and adjust to nature's slower pace.	1,2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen across all four included studies.
Nature was experienced as a restorative environment that facilitated recovery.	1,2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen across all four included studies.
Insights gained by NBR			
Patients described gaining self-acceptance through kinship with nature, which helped them come to terms with being ill.	3,4	Low confidence	Moderate concerns about adequacy as the data come from a very small number of studies and the finding was seen in two of the four studies. The studies were of moderate to high quality.
Patients experienced that NBR increased their awareness of own needs and destructive patterns in daily life.	1,4	Low confidence	Moderate concerns about adequacy as the data come from a very small number of studies and the finding was seen in two of the four studies. The studies were of high quality.
Nature was perceived as a source of creativity and energy, making room for new ideas and affecting inner strength.	1,2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen across all four included studies.
Changes as a consequence of NBR			
Patients' experiences in nature and the garden helped them see things differently and develop new perspectives.	3,4	Low confidence	Moderate concerns about adequacy as the data come from a very small number of studies and the finding was seen in two of the four studies. The studies were of moderate to high quality.
The patients developed new approaches to tasks in their daily life.	1,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen in three of the four studies.
NBR was perceived as increasing empowerment, which enabled the patients to move forward.	1,2,3,4	Moderate confidence	Minor concerns about adequacy as the data come from a small number of studies. The studies were of moderate to high quality. The finding was seen across all four included studies.

NBR=Nature-based rehabilitation. 1=Pålsdottir 2014a, 2=Pålsdottir 2014b, 3=Sahlin 2012, 4=Sidenius 2017

5. Abbreviations/Acronyms

CBT = Cognitive behaviour therapy
DASS21 = Depression anxiety stress scale, 21 items
GP = General practitioner
ED = Exhaustion disorder
HRQoL = Health-related quality of life
NBR = Nature-based rehabilitation
OHS = Occupational healthcare service
PGWB = Psychological general well-being
PMU = Psykiatrimottagning Utmattningssyndrom (Psychiatric clinic for Exhaustion disorder)
PTSD = Posttraumatic stress disorder
RCT = Randomised controlled trial
SMBQ = Shirom-Melamed burnout questionnaire
SMR = Standard morbidity ratio
VGPV= Region Västra Götaland Primary Care
VGR = Region Västra Götaland

6. Background

Stress-related disorders
Mental health problems are estimated to be one of the major contributors to work disabilities globally (Salomon *et al,* 2012; Vos *et al,* 2012). In Sweden, the prevalence of sick leave caused by mental health problems increased around the turn of the millennium (Henderson *et al,* 2005; Stefansson *et al,* 2006) and stress-related illness is the most common cause of sick leave from work (Försäkringskassan, 2017). After having risen dramatically between 1997 and 2003, the trend was reversed and sick leave due to mental illness was reduced (Åsberg *et al,* 2010). A general increase in sick leave has been observed again in Sweden since 2010, and mental illness comprises a substantial part. The proportion of mental illness diagnoses of all started cases of sick leave has increased from 17% in 2006 to 27% in 2016 (Försäkringskassan, 2017). In December 2018 mental illness diagnoses comprised 53% of all ongoing cases of sick leave among women and 40% among men (Försäkringskassan, 2019a). Stress-related diagnoses (F43) accounted for 24% among women and 12% among men (Försäkringskassan, 2019b).

According to WHO's International Classification of Diseases, ICD-10 (ICD-10-SE 2016), stress-related illness is classified into the following diagnoses:
• Acute stress reaction (F43.0)
• Posttraumatic stress disorder (PTSD) (F43.1)
• Adjustment disorder (F43.2)
• Other reactions to severe stress (F43.8)
• Exhaustion disorder (Utmattningssyndrom) (F43.8A)

In this cluster the clinical diagnosis "*Exhaustion disorder*" (ED) was proposed by the National Board of Health and Welfare in Sweden for use in clinical practice to define patients with exhaustion that has developed as a consequence of identifiable stressor(s) that have been present for at least six months. Per this definition, ED is a longstanding stress-related disorder. Exhaustion disorder was accepted as a separate diagnosis (F43.8A), in Sweden in 2005. The term is not commonly used in other countries (Socialstyrelsen, 2003), where the diagnoses adjustment disorder, other reactions to severe stress, depression, and anxiety are more commonly used for such conditions. The diagnoses *Acute stress reaction* and *Post-traumatic stress disorder* (*PTSD)* are used when a person has been exposed to a specific traumatic event that includes death/death threat or serious violence, or being a witness to such a situation.

Examples of symptoms are flash-backs and avoidance of what is related to the trauma. The difference between these two diagnoses is the duration of symptoms; *Acute stress reaction* refers to an immediate reaction after exposure whereas *PTSD* has a longer duration of symptoms (more than one month). *Adjustment disorder* is used as a diagnosis when emotional and behavioural changes are seen as a consequence of identifiable stressors, but at a maximum of six months after the stressor/s occurred (whereas ED has the criteria at least six months of duration). *Other reactions to severe stress* is used as a diagnosis when the criteria are not met for any of the other stress-related diagnoses, but the symptoms still cause significant suffering and loss of functions (American Psychiatric Association, DSM-5, 2013).

The diagnostic criteria for ED include the following main symptoms: exhaustion, cognitive dysfunction, sleep disturbance, reduced tolerance to further stress, and somatic symptoms (Swedish National Board of Health and Welfare, 2003). The complete diagnostic criteria are presented in Appendix 6. Lack of energy and cognitive problems often become long-lasting (Jonsdottir *et al,* 2013). The severity of ED symptoms ranges from mild to severe reduction in functioning, which may entail a risk of reduced quality of life and disability, as well as reduced work ability and activities in daily living for several months or even years (Pålsdottir *et al,* 2014A).

In 2016, a Health Technology Assessment (HTA) report on Nature-based rehabilitation (NBR) for patients with longstanding stress-related disorders was published (Bernhardsson *et al,* 2016). It was based on one randomised controlled trial (RCT), two controlled cohort studies, and three qualitative studies, all published before 2015. The conclusions drawn were that NBR was poorly studied, that it was uncertain whether there are any differences between the results of NBR and those of other rehabilitation programmes, that qualitative studies suggested perceived positive health effects from NBR, and that more studies were needed. The present HTA report is an update of the 2016 report and includes both the previous studies and those identified in a new systematic search in August 2019.

Prevalence and incidence

Estimates of prevalence of ED in Swedish working populations range between five percent and 22% (Norlund *et al,* 2010; Hallsten *et al,* 2002; Lindblom *et al,* 2006). No Swedish prevalence studies of other stress-related disorders have been found. In a registry-based national study in Denmark, incident cases of adjustment disorders and reactions to severe stress were calculated for the period 1995-2011 (Gradus *et al,* 2014). Incidence rates were 97 and 29 per 100,000 person years, respectively, among adults. A large increase was observed from 2007 and onwards.

In the regional patient registry VEGA for treatment within VGR primary care (VGPV), 31,980 and 41,752 patients aged 18 to 70 years received a stress-related diagnosis (F43,0-F43,9) in 2014 and 2018, respectively. These numbers correspond to 2.9% and 3.7%, respectively, of all listed patients of these ages in VGPV. Between 2014 and 2018, all diagnoses within this category increased in number, except Other reaction to stress (F43,9P). For Other reaction to severe stress (F43,8), the numbers were 10,141 (0.9%) in 2014 and 16,306 (1,5%) in 2018, and for ED separately the numbers were 7,285 (0.7%) and 11,768 (1.0%), respectively.

Present treatment

After assessment and diagnosis, most patients with stress-related disorders receive individualised treatment in primary care or occupational healthcare service (OHS). The provided care varies depending on local resources but may include a combination of psychological support, physical activity, behavioural therapy, or group-based patient education (e.g. sleep and stress), if needed in combination with medication for symptoms of depression and anxiety. According to current regional medical guidelines in Region Västra Götaland (VGR), patients with mild ED should be managed within primary care and occupational health care (Region Västra Götaland, 2019). Stakeholders such as the Social Insurance Agency, employers and the OHS are often involved in the process of return-to-work activities. Patients with severe ED often receive specialised psychological treatments, occupational therapy, physiotherapy and psycho-education.

This type of treatment and rehabilitation is typically provided by multidisciplinary teams within the approach of so-called multimodal rehabilitation. Thus ”usual care” for these patients shows large variation.

Some patients with severe ED and comorbidity with anxiety and depression are offered contact with specialist psychiatry when treatment of comorbidity is needed. In VGR patients with severe ED and chronic psychiatric comorbidity can receive multimodal rehabilitation, involving several interventions provided by different professions, at the subspecialised clinic Psykiatrimottagning utmattningssyndrom (PMU) (Psychiatric clinic Exhaustion disorder).

The normal pathway through the healthcare system and current wait time for medical assessment/treatment

Patients who perceive symptoms related to stress normally seek care at primary health care or OHS centres. Some primary care centres have a triage system to direct patients to physiotherapy, occupational therapy or psychological treatment directly, depending on their symptoms. Availability of multidisciplinary teams in primary care and occupational health care within VGR varies. Some units offer stress management courses that typically run over a period of 8-10 weeks. A specific form of stress management within the multidisciplinary approach is Nature-based rehabilitation (NBR).

According to VGR quality criteria/requirements (Krav- och Kvalitetsboken), average waiting time for a first assessment by a general practitioner should be maximum seven days. Actual waiting times for this condition have not been possible to assess. Average waiting time for a first assessment by physiotherapist or occupational therapist in Närhälsan (VGR primary care) is usually less than seven days, often as little as one day due to the current “drop in” systems in place at many rehabilitation units. Waiting times to psychologist/psychotherapist are often longer and can vary from two weeks to six months.

Number of patients per year who undergo nature-based rehabilitation

The vast majority of patients with stress-related disorders are treated in primary care. In 2018, NBR was provided to approximately 350 patients with longstanding stress-related disorders, at nine units in VGR. This number corresponds to 0.8% of the total number of patients with a stress-related diagnosis. The number of patients treated with NBR is somewhat uncertain because the number treated in some units in VGR was not possible to verify. Furthermore, the proportion of all patients with stress-related symptoms and ED, respectively, who are offered NBR, is unknown. A few other units in VGR also provide NBR, but because their activities are work-oriented and typically not provided by healthcare staff, these units are not considered in this report.

Present recommendations from medical societies or health authorities

No present national or international recommendations from medical societies or health authorities have been identified regarding the use of NBR or nature-assisted therapy for individuals with stress-related mental illness. No records were found in a web-based search performed at the relevant international authorities (NICE, UK; APA, USA; WHO Guidelines).

A 2014 brief report from SBU on ”green rehabilitation for stress-related ill health” and its effect on return to work did not identify any relevant studies but reported that the authors of the two included systematic reviews concluded that ”green rehabilitation may have positive effect, but more studies are required” (SBU, 2014).

Current regional medical guidelines from VGR for the management of ED highlight the importance of identifying the most important stressors for the patient, regardless of the severity of the disease, and recommend that treatment is individualised according to the patient’s needs. Treatment includes lifestyle advice about regular life needs and activities including sleep, meals and individual or group-based physical activity, and workplace measures (Region Västra Götaland, 2019). Everyday physical activity, as well as education in stress management and relaxation skills, is particularly recommended. The guidelines also recommend multidisciplinary interventions, including physiotherapy, occupational therapy, and psychological treatment such as cognitive behavioural therapy and/or psychodynamic group therapy.

Furthermore, the guidelines emphasise that the timing of interventions and a holistic perspective are important, and that the primary goal of interventions should be to support the patient in returning to work (Region Västra Götaland, 2019).

7. Nature-based rehabilitation

Because of increasing numbers of employees on long-term sick leave due to stress-related disorders, an NBR programme was initiated and directed to the employees of VGR. Conventional rehabilitation of employees in VGR is provided by the organisation's own occupational health service, where a team-based rehabilitation model has been developed for this patient group (Sahlin 2014, Doctoral thesis). Region Västra Götaland started a similar but nature-based rehabilitation for this patient group called "Grön rehabilitering" ("Green rehabilitation") in 2006. Patients indicate benefits from this treatment and clinical experience suggests that this type of rehabilitation has a favourable outcome. A positive effect of nature on stress recovery has been suggested (Ulrich et al, 1991, Berto *et al,* 2014).

The number of NBR programmes in Sweden for patients with stress-related mental disorders increased quickly during the first decade of the 21st century. A lack of recommended rehabilitation programmes for this patient group has opened up for the establishment of NBR as an intervention for longstanding stress-related disorders. The intervention was originally developed at the Swedish University of Agricultural Sciences at Alnarp. There is no commonly accepted standardisation of NBR but it is always led by a multi-disciplinary rehabilitation team, usually including a physiotherapist, an occupational therapist, a psychotherapist/psychologist and personnel with competences related to the garden and nature. Each profession contributes to the content of the programmes on an inter-disciplinary basis. The duration of an NBR programme can range from eight to 28 weeks depending on the mission. The participants often come in groups of eight individuals. The intensity of NBR usually ranges between two and four hours per day, two to four days per week. The NBR activities include mild and limited sensory stimulation and therapeutic activities, in a specially designed garden or selected nature environment.

As NBR is neither internationally nor nationally standardised nor has a clear-cut definition, it is difficult to compare it with multi-disciplinary team rehabilitation in general. One difference is that the ordinary multi-disciplinary team lacks the "green" professions (e.g. gardener, biologist or other profession with competencies related to nature/garden). Other important differences are the presumed stress reducing effects inherent with nature and garden environments, and the use of symbolic activities/opportunities in nature. On the other hand, the programs can be similar in content regarding components such as psycho-educative talks about how to prevent stress, bodily exercises, mindfulness, and creative workshops.

Internal evaluations, published as well as unpublished, from NBR programmes have suggested promising results for individuals with long term sick leave due to stress-related mental disorders in their return-to-work rehabilitation (Sahlin & Ahlborg, 2010). Gröna Rehab Botaniska has a stated aim that the participants during the later part of the programme should phase in work or studies and phase out the programme. All participants at Gröna Rehab Botaniska are employed in VGR and on average they have been on sick leave for 26 months (range from three months to 12 years).

In view of the increasing prevalence of stress-related mental disorders and the accompanying burden for the individual as well as for the society, it is important to find effective methods for rehabilitation and to further develop methods that seem to be promising as well as to do further research comparing NBR with other methods.

8. Focused questions

1. Is multidisciplinary, group-based, nature-based rehabilitation (NBR) more effective than either multidisciplinary, group-based, rehabilitation that is not nature-based, or any other rehabilitation that is not nature-based, for patients with longstanding (>6 months) stress-related disorders, in terms of health-related quality of life (HRQoL), sick leave, work ability, healthcare consumption, perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain or insomnia/sleep disturbances (the latter added in this up-dated report)?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

PICO 1

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
C: Rehabilitation that is multidisciplinary, group-based but not nature-based
O: Outcomes

- Critical for decision making: HRQoL, sick leave, work ability, healthcare consumption
- Important for decision making: perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain, insomnia/sleep disturbances
- Not important for decision making: none

PICO 2

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
C: Any other rehabilitation that is not nature-based
O: Outcomes

- Critical for decision making: HRQoL, sick leave, work ability, healthcare consumption
- Important for decision making: perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain, insomnia/sleep disturbances
- Not important for decision making: none

2. What are the patients' experiences of participating in NBR?

PIO: P= Patients, I= Intervention, O=Outcome

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
O: Outcomes

- Patients' experiences

9. Methods

Systematic literature search (Appendix 1)

During July 2019 two authors (TS, ME) performed systematic searches in PubMed, Embase, the Cochrane Library, AMED, CINAHL and PsycInfo to update the original HTA report from 2016, Nature-based rehabilitation for patients with longstanding stress-related disorders. Reference lists of relevant articles were scrutinised for additional references. Search strategies, eligibility criteria and a flowchart of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all authors. All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

The included studies were critically appraised using checklists from the SBU for assessment of randomised controlled trials, cohort studies, and qualitative studies, respectively. The main findings of each article were extracted and tabulated by one author and verified by another, and summarised per outcome in Appendices 4.1-4.8. A summary result per outcome and the associated certainty of evidence are presented in a Summary-of-findings table (page 8). The certainty of evidence was defined according to the GRADE system (Atkins *et al,* 2004; GRADE Work group). The main findings of the qualitative studies and the performed synthesis thereof have been summarised in Appendix 5. Certainty of evidence in the qualitative findings was assessed using GRADE-CERQual (Lewin *et al,* 2015), and the results are presented in a Summary-of-qualitative-findings table (page 9). The CERQual system was developed by a GRADE working group and offers a similar, systematic and transparent way of grading certainty of evidence in the findings from qualitative studies, as the GRADE system does for quantitative studies. Certainty of evidence is assessed in four domains (coherence, relevance, adequacy of data, and methodological limitations of the included studies) and is graded as high, moderate, low or very low (Lewin *et al,* 2015).

Synthesis of qualitative studies

A qualitative synthesis of the results from the four qualitative studies was performed by three of the authors, experienced in qualitative methodology. The aim was to describe experiences and perceived effects from participating in NBR, with special focus on the nature and garden components, in patients with stress-related disorders. Data were extracted on characteristics of the four studies and all relevant text presenting results, after which a thematic analysis was conducted using qualitative synthesis methodology (Thomas and Harden, 2008). The extracted data were inductively coded by one author and verified by another. Two authors then independently sorted the codes into preliminary descriptive themes. Disagreements were resolved in consensus among three authors, who discussed and revised the descriptive themes and identified the review findings.

Ongoing research

A search in Clinicaltrials.gov (2019-10-15) using the search terms ((Stress OR exhaustion OR Stress-related OR stress-induced OR adjustment disorder* OR adaptation syndrome OR burnout OR burn-out OR pain OR anxiety OR depression OR fatigue OR insomnia OR sleep disturbance*) AND (nature-based OR nature-supported OR nature-assisted OR Gardening OR garden OR horticult*)) OR ((nature-based OR nature-supported OR nature-assisted) AND (treatment OR rehabilitation OR therap*)) identified 156 studies.

10. Results

Search results and study selection (Appendix 1)

The updated literature search identified 539 records after removal of duplicates. After reading the abstracts, 523 articles were excluded. Another ten articles were excluded by two authors in consensus after reading the articles in full text. The remaining six articles were sent to all authors, and four studies were finally included. Together with the six articles from the original HTA report, a total of ten articles were included in the synthesis. A flowchart of the search results is presented in Appendix 1.

Included studies

A total of ten articles (six from the previous report and four added in this updated report) were included: four articles reporting results from three RCTs, two non-randomised controlled studies and four qualitative studies. Three recent RCT articles were identified (Corazon *et al,* 2019 and Stigsdotter *et al,* 2018; Vujcic *et al,* 2017), of which the first two stemmed from one RCT comparing an NBR intervention with control treatment but reporting different outcomes. One RCT (Försäkringskassan, 2013) and two controlled cohort studies (Währborg *et al,* 2014; Willert *et al,* 2014) from the previous report were also included. All quantitative studies had serious study limitations, several had unclear precision, and there were major problems with directness in one RCT (Försäkringskassan, 2013) and some problems in one cohort study (Willert *et al,* 2014).

One recent qualitative study (Sidenius *et al,* 2017) was identified in addition to the three earlier ones (Pålsdottir *et al,* 2014A and B; Sahlin *et al,* 2012), presenting participants' experiences of NBR. The quality of all four qualitative studies was considered generally good, even though some limitations were identified.

Included studies, their design, and patient characteristics are presented in Appendix 2. Excluded studies and the reasons for exclusion are presented in Appendix 3.

Main findings from quantitative studies

<u>Outcomes, critical for decision-making</u>

Sick leave (Appendix 4:1)

Sick leave was reported in two RCTs and one cohort study, all PICO 2. One of the RCTs, conducted in VGR, compared NBR with a control group receiving usual care in patients with mainly ED. The other RCT, a non-inferiority study conducted in Denmark, compared NBR with cognitive behavioural therapy (CBT) in patients with adjustment disorder and/or reaction to severe stress. The cohort study compared NBR with controls, matched for main condition, age and sex and recruited from the Skåne Health Care register, receiving usual care. The primary outcome was any kind of sickness benefit or compensation, thus including sick leave. All studies used registry data for the outcome. The Swedish RCT and the cohort study had major methodological limitations. The Danish RCT had some limitations and problems with precision in intergroup analysis (performed by the present authors) due to small numbers. The RCTs showed significantly fewer patients on sick leave in both groups but no significant intergroup difference in sick leave after 20 or 12 months, respectively. Also the cohort study reported no significant intergroup difference in sick leave for NBR compared with the control group.

<u>Conclusion:</u> NBR may result in little or no difference in sick-leave compared with non-nature-based rehabilitation (usual care/CBT) for patients with longstanding stress-related disorders.
Low certainty of evidence (GRADE ⊕⊕○○).

Self-assessed work ability (Appendix 4:2)
Self-assessed work ability was reported in a Danish cohort study comparing NBR (an all-outdoors vocational rehabilitation programme) with a stress and job management intervention comprising primarily indoor activities (PICO 1), for individuals on long-term sick leave due to sustained stress-related symptoms. The study reported improved self-assessed work ability in both groups three months after the intervention, but no significant intergroup difference. There were no statistically significant intra- or intergroup changes in self-assessed work ability between three and six months.

Conclusion: It is uncertain whether NBR results in any difference in self-assessed work ability compared with non-nature-based, multidisciplinary, group-based rehabilitation for patients with longstanding stress-related disorders.
Very low certainty of evidence (GRADE ⊕OOO).

Healthcare consumption (Appendix 4:3)
Healthcare consumption was reported in an RCT with a non-inferiority design conducted in Denmark, comparing NBR with CBT in patients with adjustment disorder and/or reaction to severe stress, and in a Swedish cohort study comparing patients in an NBR programme with controls receiving usual care recruited from a healthcare register in Region Skåne (both PICO 2). In the RCT, the number of GP contacts during the 12 months before intervention was compared to those 12 months after the intervention, based on registry data. The number of GP contacts decreased significantly in both groups, but intergroup difference was not reported. In the cohort study, referrals were made due to long-term sick leave for patients diagnosed with depressive disorders and/or reactions to severe stress. The number of healthcare visits was significantly reduced for the cases one year after compared with one year before the intervention (a relative reduction of 16% for the NBR versus 8% for the controls, intergroup difference $p<0.05$). The decrease was significantly greater in NBR participants compared with controls concerning primary healthcare and inpatient days in psychiatric health care.

Conclusion: NBR may result in little or no difference in the frequency of GP contacts compared with CBT treatment for patients with longstanding stress-related disorders. Low certainty of evidence (GRADE ⊕⊕OO). It is uncertain whether NBR results in fewer healthcare visits than usual care for patients with longstanding stress-related disorders.
Very low certainty of evidence (GRADE ⊕OOO).

Health-related quality of life (Appendix 4:4)
Health-related quality of life measured as psychological general well-being was studied in a Danish RCT comparing NBR with CBT (PICO 2) in patients with adjustment disorder and/or reaction to severe stress. A self-report questionnaire (PGWBI) was used before and after the intervention, and 3, 6, and 12 months thereafter. The study had serious limitations. Besides relying on self-reports and not being blinded, there were more missing data in the control group and imputation was applied. There was no significant intergroup difference in well-being score, although intragroup difference was significant in both groups.

Conclusion: NBR compared with cognitive behaviour therapy may result in little or no difference in health-related quality of life, measured as psychological general well-being, for patients with longstanding stress-related disorders.
Low certainty of evidence (GRADE ⊕⊕OO).

Outcomes important for decision-making

Perceived stress (Appendix 4:5)
Perceived stress was studied in a Serbian RCT comparing NBR with non-NBR for patients with adjustment disorder or reaction to severe stress, anxiety or depression disorders, and in a Danish cohort study comparing NBR with a stress and job management programme, for individuals on long-term sick leave due to sustained stress-related symptoms (both PICO 1). The RCT was small (n=16+14) and perceived stress was measured by a subscale of the Depression Anxiety Stress Scale at the start and end of the intervention. The difference in change in stress score was significant (intergroup difference p=0.027). The study had major limitations.

The control programme in the cohort study comprised similar activities but was performed indoors. The study had major limitations. There were no significant intergroup differences, although both study groups reported a significant decrease in perceived stress after three months of rehabilitation.

Conclusion: It is uncertain whether NBR results in any difference in perceived stress compared with non-nature-based multidisciplinary rehabilitation for patients with longstanding stress-related disorders. Very low certainty of evidence (GRADE ⊕○○○).

Depression (Appendix 4:6)
Depression was studied in a Serbian RCT comparing NBR with non-NBR (PICO 1) for patients with adjustment disorder or reaction to severe stress, anxiety or depression disorders. The RCT was small (n=16+14) and self-reported depression was measured by a subscale of the Depression Anxiety Stress Scale at the start and end of the intervention. The study had major limitations. The intergroup difference in depression score was not significant.

Conclusion: It is uncertain whether NBR results in any difference in depression compared with non-nature-based multidisciplinary rehabilitation for patients with longstanding stress-related disorders. Very low certainty of evidence (GRADE ⊕○○○).

Anxiety (Appendix 4:7)
Anxiety was studied in a Serbian RCT comparing NBR with non-NBR (PICO 1) for patients with adjustment disorder or reaction to severe stress, anxiety or depression disorders. The RCT was small (n=16+14) and self-reported anxiety was measured by a subscale of the Depression Anxiety Stress Scale at the start and end of the intervention. The study had major limitations. The intergroup difference in anxiety score was non-significant.

Conclusion: It is uncertain whether NBR results in any difference in anxiety compared with non-nature-based multidisciplinary rehabilitation for patients with longstanding stress-related disorders. Very low certainty of evidence (GRADE ⊕○○○).

Exhaustion/burnout (Appendix 4:8)
Burnout was studied in a Danish RCT comparing NBR with CBT (PICO 2) in patients with adjustment disorder and/or reaction to severe stress. A self-report questionnaire (SMBQ) was used before and after intervention, and 3, 6, and 12 months thereafter. The study had serious limitations. There was no significant intergroup difference in burnout score (not presented), although it decreased significantly after the intervention in both groups, and remained so at all follow-ups.

Conclusion: NBR may result in little or no difference in exhaustion/burnout compared with cognitive behaviour therapy for patients with longstanding stress-related disorders (GRADE ⊕⊕○○).

Cognitive disability, pain or **insomnia/sleep disturbances** were not reported in any of the included studies.

Main findings from qualitative studies

Patient experiences
Experiences of participating in NBR among patients with longstanding stress-related disorders were studied in four qualitative studies (n=89). These studies reported that participants in NBR experienced positive health effects from rehabilitation in natural environments and working in a garden. The most recent study stemmed from the same NBR project in the Nacadia Therapy Garden in Copenhagen as the two RCTs described on p. 17 (Sidenius *et al, 2017*). Two of the other qualitative studies concerned the NBR programme in the health garden at the Swedish University of Agricultural Sciences in Alnarp, Sweden (Pálsdóttir *et al,* 2014A and B). The fourth reported experiences by participants in an NBR programme at the Botanical Garden in Gothenburg (Gröna Rehab), Sweden (Sahlin *et al,* 2012). All used semi-structured interviews for data collection from 11 to a maximum of 43 patients. The studies were considered relevant regarding context, population and intervention, and quality for the four qualitative studies was assessed as moderate to high. There were some limitations, however, mainly regarding description of participants and researcher preunderstanding.

Sixteen descriptive themes emerged in the qualitative analysis on which the review findings were based (Appendix 5). These were organised in the present report under four broad, analytical themes (or domains) relating to the type of experiences and perceived effects of the nature and garden components of NBR: 1) State of mind; 2) Experiences of garden and nature; 3) Insights gained; 4) Changes (of perspectives, approaches and capabilities). The experiences and perceived effects of participating in NBR and spending time in a nature environment were described as positive for recovery. Nature and garden helped the patients slow down, feel calm, safe, and part of a whole. The environment met their needs and increased their self-awareness and self-acceptance and was considered a source of energy and creativity. It promoted the development of new perspectives and approaches in daily life, which made them feel empowered to go forward.

<u>Conclusion:</u> Participating in NBR is experienced as giving positive health effects by patients with longstanding stress-related disorders (GRADE-CERQual moderate to low confidence in the evidence).

11. Ethical aspects

Using a technology for which there are no clear patient benefits compared with other interventions, and where the costs are higher, may constitute an ethical dilemma due to possible displacement effects. On the other hand, there may also be ethical consequences of discontinuing a treatment option that is perceived as beneficial both by patients (as reported in the qualitative studies) and healthcare providers.

Another ethical issue is how patients are selected and offered NBR. The existing capacity is clearly very limited in relation to the large population with stress-related disorders, and only a fraction of patients can be offered the intervention. A narrow selection may have ethical implications in terms of equal treatment and justice. Should NBR be introduced at other units than where it is currently offered, there is a risk for a displacement effect on both the studied population and other patient groups. Compared with other treatment programs for patients with ED, proven benefits may be small or non-existent, but so is the risk; no adverse effects were reported in any of the studies. The quality of the evidence is low, meaning that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

12. Organisational aspects

Time frame for the putative introduction of NBR
Since 13 years, NBR is offered as an option for rehabilitation of patients with long-standing stress-related disorders within VGR. One unit, Gröna Rehab, offers this intervention to patients employed by VGR, the other providers accept patients from the general public.

Present use of NBR in other regions in Sweden
NBR is used in other areas in Sweden, notably at the Swedish University of Agricultural Sciences in Alnarp, where the concept was conceived in 2002. Today Alnarp is used for patients with PTSD and distress from migration experiences. At present about 25 units in Sweden use the concept in some form.

Consequences of NBR for personnel
The consequences of introducing NBR are mostly on an educational level, as physiotherapists, occupational therapists and psychotherapists/psychologists need to be trained in the specific theories and methods used in NBR. This training is on the other hand not voluminous, as the professionals mostly work according to their original professional training.

Consequences for other clinics or supporting functions in the Region Västra Götaland
Many patients, physicians and other healthcare professionals are requesting NBR as a treatment option. Many primary healthcare centres are presently not able to accommodate this patient group adequately according to experiences from on-going research projects conducted by the Institute of Stress Medicine. A lack of resources and suitable gardens within primary care settings makes it difficult to implement NBR on a larger scale in VGR as a treatment option for patients with stress-related illness.

13. Economic aspects

Estimated costs of currently used technologies

The average cost per patient, including staff costs, for usual care in outpatient settings, in the category that includes stress-related illnesses (F43.0, F43.1, F43.2, F43.8, F3.8A), is estimated at 25,700 SEK per year (Sveriges Kommuner och Regioner, 2019).

Expected costs of NBR

Since specific implementation (treatment length, staff intensity, etc.) differs among the units that treat patients with NBR, the expected costs will vary from unit to unit. The expected costs are based on estimates from units with slightly more detailed utilisation data (Nestegården NBR and Grevegården NBR). Nestegården treated in the year 2019 32 patients with a total NBR utilisation/visits of 578 (managed by 1 full-time position) and Grevegården treated 28 patients with a total NBR utilisation/visits of 710. The cost per patient, including staff costs, in this set-up is in the range of 29,000 to 34,000 SEK.

Total change in costs

The total change in cost per patient is expected to be in the interval of 29,000-34,000 SEK if NBR is offered in addition to usual care, or in the interval 3,300-8,300 SEK if it completely replaces usual care. The degree to which NBR can replace usual care is uncertain. It can be assumed that NBR would replace other forms of team rehabilitation, but not other components of usual care, e.g. GP visits, medication.

There is currently uncertainty in the total number of patients offered NBR, and as such, there is also uncertainty regarding the total cost consequences of NBR. With an approximate number of 350 patients annually, the total cost for NBR would be in the range of 10-12 million SEK per year if it is offered in addition to usual care or in the range of 1-3 million SEK if it would completely replace usual care.

Possibility to adopt and use NBR within the present budget

The total added costs of offering NBR depends on to what degree it can replace any existing treatments for this patient group (e.g. CBT, pharmaceutical treatment, etc.). Under the basic assumption that NBR will be offered as an additional treatment option for the most severely ill patients, NBR is a cost-increasing treatment and will displace other healthcare services within the present budget. If NBR completely replaces usual care, it will require some (but relatively minor) additional resources.

If external funding is retrieved (e.g. from Försäkringskassan, as for "Gröna vägen" in Borås), it is possible to offer NBR without displacing other healthcare services in the primary care sector.

Available economic evaluations or cost advantages/disadvantages

No published health-economic analyses of NBR were identified in the literature search.

14. Discussion

Summary of main results

The main finding in this systematic review is that there is no evidence that NBR is more effective than other forms of rehabilitation in patients with longstanding stress-related disorders. The systematic searches carried out in the present updated HTA report identified four new articles. Three more RCTs and one qualitative study were added to the one RCT, two controlled cohort studies, and three qualitative studies included in the previous HTA report. Two of the new publications stemmed from the same Danish RCT but reported different outcomes.

The findings in the present analysis regarding outcomes critical for decision-making show that there may be little or no difference in sick-leave, frequency of GP contacts, or health-related quality of life after NBR compared with non-NBR or other rehabilitation for patients with longstanding stress-related disorders. It is uncertain whether any differences exist regarding self-assessed work-ability or frequency of healthcare visits in general. Regarding outcomes important for decision making, there may be little or no difference in exhaustion/burnout, and uncertainty concerning perceived stress, depression and anxiety, after NBR compared with non-NBR or other rehabilitation for this patient group. All RCTs showed significant positive intragroup effects of NBR on the outcome in focus, but no significant intergroup differences when compared with control treatment. The certainty of evidence for all outcomes in the two studies comparing NBR with rehabilitation that is multidisciplinary, group-based but not nature-based was very low. For the outcomes in the four studies that compared NBR with other rehabilitation that is not nature-based, certainty of evidence was low (although for number of general healthcare visits, certainty of evidence was very low).

The qualitative synthesis, aiming to describe experiences and perceived effects of the nature and garden components of NBR of the participants in the four qualitative studies, resulted in 16 descriptive themes organised under the four broad themes *State of mind*, *Experiences of garden and nature*, *Insights*, and *Changes*. The experiences and effects of nature and garden were reported as positive for recovery by promoting e.g. calmness, a sense of safety, self-awareness, new perspectives and empowerment, according to the interviewed patients. Eleven of the descriptive themes were based on explicit results from at least three of the four studies, strengthening our confidence that the findings are a reasonable representation of the phenomenon of interest. Even though the evidence base for the experienced benefits is small, the qualitative data were relevant, adequate and highly consistent, supporting that the conclusions made are appropriate. For most findings, we had no or very minor concerns regarding methodological limitations, relevance, coherence, and adequacy of the data.

Overall completeness and applicability of evidence

The recent Danish RCT, which reported four outcomes in two publications, had a better design and less serious limitations than the other quantitative studies, which contributed to the upgraded certainty of evidence to GRADE ⊕⊕○○ for sick-leave, compared with the previous HTA report. In this study, NBR was compared with a control intervention that was not group-based, and multidisciplinary only in the sense that the patients received usual care by healthcare professionals, supplemented by individual CBT (recommended treatment by the health authorities). The Serbian RCT had serious limitations and altogether there is a lack of good quality studies comparing the effects of NBR with non-NBR or treatment as usual. One problem is that blinding of patients and/or care providers is not possible in this type of interventions. However, blinding of the researchers performing the data analyses and evaluation /interpretation of the results could be aimed for.

The cost analysis revealed that with an approximate number of 350 annual NBR patients, the expected additional cost associated with NBR is in the range of 10 to 12 million Swedish kronor per year in VGR.

The environmental contexts and study groups participating in NBR were reasonably similar and relevant, but the control conditions varied among the quantitative studies. The experiences and perceived effects expressed by the patients in the qualitative studies suggest a positive effect by NBR in patients with long-standing stress-related disorders. There is no contradiction between the patients' positive experiences of NBR in the qualitative studies and the lack of difference between NBR and comparators in the quantitative studies since the quantitative studies suggest positive intragroup changes in both NBR and control groups.

Agreements and disagreements with other studies and reviews

Although few studies have been published on NBR for patients with stress-related disorders, there is a wealth of scientific literature addressing different aspects of the relations between nature and health. A systematic review of quantitative (of which 6 RCTs) and qualitative studies by Annerstedt & Währborg (2011) showed that nature-assisted therapy, including e.g. horticultural therapy, improved various outcomes in 30 of 35 included studies, for adult and paediatric patients with various mental and physical disorders. A recent systematic review of controlled studies showed that nature-based activities, including walking and seated relaxation in natural environments, gave better effects compared with control interventions, on mental health outcomes such as psychological wellbeing, psychosocial function, psychophysiological stress response, and cognitive performance (Mygind *et al,* 2019). A systematic review and meta-analysis of controlled and uncontrolled studies on gardening and horticultural therapy in various populations, showed positive effects on e.g. depression, anxiety and quality of life (Soga *et al,* 2016). However, of the included 21 studies only six referred to patients with psychiatric disorders of some relevance for the present HTA report, four of which were from the same research group, context and design, and without control group. Hence, there is some, but inconsistent, support for nature and garden as positive environments for various health conditions. The systematic reviews referred above suffer from great heterogeneity in terms of populations, interventions and outcomes.

Implications for research

There is a need for large, properly designed randomised controlled trials including blinded observers for important outcomes. There is also a need for improved routines within VGR so that costs can be correctly attributed for the interventions used and economic effectiveness of NBR can be investigated. A separate rehabilitation registry with detailed codes for, e.g., diagnosis, rehabilitation unit, type and length of intervention/treatments, health professionals involved, would be helpful for adequate follow-up.

15. Future perspectives

Scientific knowledge gaps

In spite of some more RCTs evaluating NBR in this, compared with the previous, HTA report, there is still a clear knowledge gap concerning effects of participation in an NBR programme. The findings of this report highlight a need for further research in the area, with special emphasis on methodological rigour.

Ongoing research

Of 156 identified ongoing studies in clinicaltrials.gov, only one was relevant for this HTA report. An ongoing controlled cohort study in Denmark (Id NCT04073524) aims to assess the effects of an NBR programme (The Wild Man Programme) on quality of health (primary outcome) and perceived stress (secondary outcome) in male participants. The intervention group is compared with a matched group receiving treatment as usual. The study also aims to examine which natural environments best work as supportive environments in the rehabilitation.

16. Participants in the project

The question was nominated by

Ulf Svensson, MD, medical advisor, Regional knowledge centre for mental health (Koncernkontoret/Kunskapsstöd för psykisk hälsa), Region Västra Götaland, Gothenburg, Sweden

Participating healthcare professionals

Gro Sundell, RN, Manager of specialist Burnout unit (Psykiatri affektiva Psykiatrimottagning utmattningssyndrom), Region Västra Götaland; master's degree in geriatric nursing and specialist in psychiatric nursing, Gothenburg, Sweden
Gunnar Ahlborg jr, MD, PhD, Senior physician and Associate professor, Institute of Stress Medicine, Region Västra Götaland, Gothenburg, Sweden

Participants from the HTA-centrum

Anna Bergenheim, PT, PhD, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Susanne Bernhardsson, PT, Associate professor, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Lennart Jivegård, MD, Senior university lecturer, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Maud Eriksson, medical librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
Therese Svanberg, medical librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
Mikael Svensson, professor, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden

Administrative support

Pernilla Rönnholm, project coordinator, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden

External reviewers

Robert Eggertsen, MD, professor, Mölnlycke Healthcare Centre, Mölnlycke, Sweden
Ulla Karilampi, psychologist, PhD, Sahlgrenska University Hospital, Gothenburg, Sweden

Declaration of interests

None of the participants have any conflicts of interest to declare. Gunnar Ahlborg Jr was co-author of one of the included publications and did not assess the methodological quality of this study.

Project time

The HTA was accomplished during the period 13/06/2019 to 29/01/2020.
Literature searches were made on 25 July 2019.

Appendix 1
PICO, study selection, search strategies, and references

Focused questions:

1. Is multidisciplinary, group-based, nature-based rehabilitation (NBR) more effective than either multidisciplinary, group-based, rehabilitation that is not nature-based, or any other rehabilitation that is not nature-based, for patients with longstanding (>6 months) stress-related disorders, in terms of health-related quality of life (HRQoL), sick leave, work ability, healthcare consumption, perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain or insomnia/sleep disturbances (the latter added in this up-dated report)?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

PICO 1

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
C: Rehabilitation that is multidisciplinary, group-based but not nature-based
O: Outcomes
- Critical for decision making: HRQoL, sick leave, work ability, healthcare consumption
- Important for decision making: perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain, insomnia/sleep disturbances
- Not important for decision making: none

PICO 2

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
C: Any other rehabilitation that is not nature-based
O: Outcomes
- Critical for decision making: HRQoL, sick leave, work ability, healthcare consumption
- Important for decision making: perceived stress, depression, anxiety, fatigue/exhaustion, cognitive disability, pain, insomnia/sleep disturbances
- Not important for decision making: none

2. What are the patients' experiences of participating in NBR?

PIO: P= Patients, I= Intervention, O=Outcome

P: Patients with longstanding (>6 months) stress-related disorders without ongoing drug abuse
I: Multidisciplinary, group-based, nature-based rehabilitation
O: Outcomes
- Patients' experiences

Eligibility criteria

Study design:
Randomised controlled trials
Non-randomised controlled studies
Qualitative studies

Language:
English, Swedish, Norwegian, Danish

Publication date:
2015-

Selection process – flow diagram

Identification

Studies included in previous version of review (n=6)

Records identified through database searching (n =774)

Additional records identified through other sources (n =3)

Screening

Records after duplicates removed (n =539)

Records screened by HTA librarians (n =539)

Records excluded by HTA librarians. Did not fulfil PICO or other eligibility criteria (n =523)

Eligibility

Full-text articles assessed for eligibility by HTA librarians (n =16)

Full-text articles excluded by HTA librarians, with reasons (n =10)
8 = wrong patient/population
1 = wrong intervention
1= wrong comparison

Full-text articles assessed for eligibility by project group (n =6)

Full-text articles excluded by project group, with reasons (n =2)
See Appendix 3

Included

New studies included (n =4)
See Appendix 2

Total no. of studies included in synthesis (n=10)
See Appendix 2

Search strategies

Database: PubMed
Date: 25 July 2019
No. of results: 276

Search	Query	Items found
#26	**Search #18 AND #19 Filters: Swedish; Norwegian; English; Danish**	**276**
#20	Search #18 AND #19	289
#19	Search "2015/12/01"[crdt] : "2019/07/25"[crdt]	4454415
#18	Search #16 NOT #17	620
#17	Search (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])	1745458
#16	Search #14 NOT #15	622
#15	Search ((eukaryota[mh]) NOT (eukaryota[mh] AND humans[mh]))	5244639
#14	Search #10 OR #13	933
#13	Search #11 AND #12	110
#12	Search treatment OR rehabilitation OR therapy OR therapies	10753444
#11	Search nature-based[tiab] OR nature-supported[tiab] OR nature-assisted[tiab]	367
#10	Search #6 AND #9	861
#9	Search #7 OR #8	11091
#8	Search nature-based[tiab] OR nature-supported[tiab] OR nature-assisted[tiab] OR gardening[tiab] OR garden[tiab] OR horticultural[tiab] OR horticulture[tiab]	11089
#7	Search "Horticultural Therapy"[Mesh]	53
#6	Search #1 OR #2 OR #4 OR #5	1732245
#5	Search pain[tiab] OR anxiety[tiab] OR depression[tiab] OR fatigue[tiab] OR insomnia[tiab] OR sleep disturbance*[tiab]	1050860
#4	Search stress[tiab] OR exhaustion[tiab] OR stress-related[tiab] OR stress-induced[tiab] OR adjustment disorder*[tiab] OR adaptation syndrome[tiab] OR burnout[tiab] OR burn-out[tiab]	717832
#2	Search "Adjustment Disorders"[Mesh]	4159
#1	Search "Stress, Psychological"[Mesh]	123743

Database: Embase 1974 to 2019 July 24 (OvidSP)
Date: 25 July 2019
No. of results: 207

#	Searches	Results
1	exp job stress/	8513
2	exp mental stress/	77242
3	exp burnout/	15765
4	exp adjustment disorder/	3532
5	(stress or exhaustion or stress-related or stress-induced or adjustment disorder$ or adaptation syndrome or burnout or burn-out or pain or anxiety or depression or fatigue or insomnia or sleep disturbance$).ab,kw,ti.	2325788
6	1 or 2 or 3 or 4 or 5	2359573
7	exp horticultural therapy/	90
8	(nature-based or nature-supported or nature-assisted or gardening or garden or horticultural or horticulture).ab,kw,ti.	12374

9	7 or 8	12383
10	6 and 9	1073
11	(nature-based or nature-supported or nature-assisted).ab,kw,ti.	557
12	(treatment or rehabilitation or therapy or therapies).af.	10778860
13	11 and 12	164
14	10 or 13	1183
15	(exp eukaryote/ not (exp eukaryote/ and human)).sh.	5458469
16	14 not 15	786
17	limit 16 to dc=20151201-20190725	329
18	**limit 17 to ((embase or medline) and (danish or english or norwegian or swedish) and (article or article in press or conference paper or note or "review"))**	**207**

Database: AMED, CINAHL, PsycInfo (EBSCOhost Research Databases)
Date: 25 July 2019
No. of results: 198

#	Undran	Resultat
S8	**S4 NOT S5** Avgränsare - Publikationsdatum: 20150101-20191231 Utökning - Sök med relaterade ord Begränsa genom att Language: - english Sökinställningar - Hitta alla mina söktermer Databas - AMED - The Allied and Complementary Medicine Database;CINAHL;PsycINFO	**198**
S7	S4 NOT S5	238
S6	S4 NOT S5	615
S5	((MH "Plants+") NOT (MH "Plants+" AND MH "Human"))	68,846
S4	S1 OR S2 OR S3	640
S3	TI ((stress OR exhaustion OR stress-related OR stress-induced OR adjustment disorder* OR adaptation syndrome OR burnout OR burn-out OR pain OR anxiety OR depression OR fatigue OR insomnia OR sleep disturbance*) AND (nature-based OR nature-supported OR nature-assisted OR Gardening OR garden OR horticultural OR horticulture)) OR ((nature-based OR nature-supported OR nature-assisted) AND (treatment OR rehabilitation OR therapy OR therapies))	96
S2	AB ((stress OR exhaustion OR stress-related OR stress-induced OR adjustment disorder* OR adaptation syndrome OR burnout OR burn-out OR pain OR anxiety OR depression OR fatigue OR insomnia OR sleep disturbance*) AND (nature-based OR nature-supported OR nature-assisted OR Gardening OR garden OR horticultural OR horticulture)) OR ((nature-based OR nature-supported OR nature-assisted) AND (treatment OR rehabilitation OR therapy OR therapies))	533
S1	((MW Stress OR MW exhaustion OR MW Stress-related OR MW stress-induced OR MW adjustment disorder* OR MW adaptation syndrome OR MW burnout OR MW burn-out OR MW pain OR MW anxiety OR MW depression OR MW fatigue OR MW insomnia OR MW sleep disturbance*) AND (MW nature-based OR MW nature-supported OR MW nature-assisted OR MW Gardening OR MW garden OR MW horticultural OR MW horticulture)) OR ((MW nature-based OR MW nature-supported OR MW nature-assisted) AND (MW treatment OR MW rehabilitation OR MW therapy OR MW therapies))	113

Database: The Cochrane Library
Date: 25 July 2019
No. of results: 93
Cochrane reviews 1
Trials 92

ID	Search	Hits
#1	stress or exhaustion or stress-related or stress-induced or adjustment disorder* or adaptation syndrome or burnout or burn-out or pain or anxiety or depression or fatigue or insomnia or sleep disturbance*:ti,ab,kw	292704
#2	nature-based or nature-supported or nature-assisted or gardening or garden or horticultural or horticulture:ti,ab,kw	369
#3	#1 and #2	111
#4	nature-based or nature-supported or nature-assisted:ti,ab,kw	41
#5	treatment or rehabilitation or therapy or therapies:ti,ab,kw	905708
#6	#4 and #5	26
#7	**#3 or #6** **with Cochrane Library publication date from Dec 2015 to Jul 2019**	**93**

The web-sites of **SBU** and **Folkehelseinstituttet** were visited 25 Jul 2019.
Nothing relevant to the question at issue was found.

Reference lists
A comprehensive review of reference lists brought 3 new records.

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Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 2 – Characteristics of included studies

Author, Year, Country	Study design	Study follow up (months)	Study groups; Intervention vs control	Patients (n) I + C	Mean age (years)	Men (%)	Study population	Outcome variables
Försäkringskassan, 2013, Sweden	RCT	30	NBR vs usual care	141 + 98	42	0	Women with reduced work ability due to mental illness, primarily ED	Sick leave
Vujcic, 2017, Serbia	RCT	0?	NBR vs non-NBR	16+14	45	30	Patients with adjustment disorder or reaction to severe stress, anxiety or depression disorders	Perceived stress, anxiety, depression
Corazon, 2018, Denmark	RCT (non-inferiority study)	12	NBR vs CBT	43+41	47.9+44.9	18	Patients incapacitated from work for at least 3 months with adjustment disorder and/or reaction to severe stress	Sick leave, health care consumption
Stigsdotter, 2018, Denmark	RCT (non-inferiority study)	12	NBR vs CBT	43+41	47.9+44.9	18	Patients incapacitated from work for at least 3 months with adjustment disorder and/or reaction to severe stress	Health-related quality of life (general well-being), exhaustion (burnout)
Willert, 2014, Denmark	Controlled cohort	7	NBR vs non-nature-based rehabilitation	48 + 45	45	17	Patients on long-term sick leave due to sustained stress-related symptoms	Self-assessed workability, perceived stress
Währborg, 2014, Sweden	Controlled cohort	24	NBR vs usual care	103 + 678	46	11	Patients on sick leave for at least 3 months due to a diagnosis of reactions to severe stress and/or depression	Sick leave, healthcare consumption
Sahlin, 2012, Sweden	Qualitative	N/A	NBR	11	43	27	Patients with ED and/or depression and anxiety	-
Palsdottir, 2014A, Sweden	Qualitative and quantitative[1]	N/A	NBR	21	47	10	Patients with adjustment disorder, reaction to severe stress, or depression	-
Palsdottir, 2014B, Sweden	Qualitative	N/A	NBR	43	46	19	Patients on long-term sick leave for adjustment disorder, reaction to severe stress, or depression	-
Sidenius, 2017, Denmark	Qualitative	N/A	NBR	14	N/R	N/R	Patients with inability to work for at least 3 months with adjustment disorder and/or reaction to severe stress	-

NBR=Nature-based rehabilitation; ED=Exhaustion disorder; N/A=Not applicable; PGWBI=Psychological General Well-Being Index; SMBQ= Shirom-Melamed Burnout Questionnaire; DASS21=Depression Anxiety Stress Scale 21 items; N/R=Not reported. [1]Quantitative part = case series and therefore excluded

Report: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 3 - Excluded studies

Author, year	Reason for exclusion
Grahn, 2017	Case series
Sidenius, 2017	Wrong study aim, case series

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:1
Outcome variable: Sick leave

* + No or minor problems
? Some problems
\- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results: Intervention NBR	Results: Control Non nature-based interventions	Comments	Directness*	Study limitations*	Precision*
Försäkringskassan, 2013, Sweden	RCT	n=239 I=141 C=98	I=41 C=21	Days/month with sick leave compensation At baseline: 14 At 20 months: 9* Intergroup difference at 20 months: Δ 2* (95% CI -2 to 5*) n.s.	 At baseline: 12.5 At 20 months: 7*	A major part of the participants received social insurance benefits. A decrease in sick leave was observed in both groups. 20 months was chosen since it was the mean follow-up time	-	-	?
Corazon, 2018, Denmark	RCT	n=84 I=43 C=41	I=9 C=11	Total number of months on sick leave during 12 months before vs 12 months after the intervention n.s. Proportion of subjects on sick-leave At baseline one month before intervention: 88% At 12 months after intervention: 21% Intragroup difference: p<0.001 Intergroup difference: 12% n.s.	 At baseline one month before intervention: 80% At 12 months after intervention: 33% Intragroup difference: p<0.01	Non-inferiority-study Total number of months on sick leave not given. No statistical analysis of the difference between the groups.	+	?	?/-
Währborg, 2014, Sweden	Cohort study	n=781 I=103 C=678		Proportion of subjects with any kind of sickness benefits or compensation At baseline: 90% At 20 months: 75%* Intergroup difference at 20 months: Δ 15%* n.s.	 At baseline: 95% At 20 months: 60%*	No significant differences between intervention and control regarding any kind of sickness benefits before or after rehabilitation programme	+	-	?

NBR=Nature-based rehabilitation
*) estimated from figures in the report/article

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:2
Outcome variable: Self-assessed work ability

* + No or minor problems
? Some problems
\- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results: Intervention NBR	Results: Control Non nature-based, multidisciplinary, group-based rehabilitation	Comments	Directness*	Study limitations*	Precision*
Willert, 2014, Denmark	Cohort	n=93 I=48 C=45		Baseline		Control intervention was a stress & job management program, similar in scope but with all activities performed indoors.	?	-	?
				WAI score 2.24; SD 2.31	WAI score 2.41; SD 2.40 n.s.				
				Change 0-3 month					
				1.81; 95% CI 1.09 to 2.52 intragroup difference (*p*<0.01) SMD=0.80; 95% CI 0.48 to 1.12	1.10; 95% CI 0.22 to1.98 intragroup difference (*p*=0.01) SMD=0.49; 95% CI 0.10 to 0.88				
				Intergroup difference: Δ 0.70; 95% CI -0.43 to 1.84 (n.s.); SMD=0.31; 95% CI 0.19 to 0.82					
				Change 3-6 months					
				0.64; 95% CI -0.20 to 1.49 n.s.	0.18; 95% CI -0.82 to 1.20 n.s.				
				Intergroup difference: Δ 0.46; 95% CI -0.86 to 1.78 n.s.					

NBR=Nature-based rehabilitation; WAI=work ability index. Range 0–10; 0 indicates having no ability to work and 10 indicates the lifetime best work ability of the individual; SD=standard deviation; CI=confidence interval; SMD=standardized mean difference

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:3
Outcome variable: Healthcare consumption

* + No or minor problems
? Some problems
\- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results: Intervention NBR	Results: Control Non nature-based rehabilitation	Comments	Directness*	Study limitations*	Precision*
Corazon, 2018, Denmark	RCT	n=84 I=43 C=41	I=6 C=6	Total number of contacts with a GP during 12 months before vs 12 months after intervention During the 12 months before intervention Md=18 (Min 1; Max 42) During the 12 months after intervention Md=13 (Min 0; Max 67) Intragroup difference: $p<0.01$ Effect size: r = -0.396	 Md=21 (Min 6; Max 103) Md=14 (Min 5; Max 35) $p<0.05$ r = -0.249	Non-inferiority study. No statistical analysis of difference between the groups.	+	?	?/-
Währborg, 2014, Sweden.	Cohort study	n = 781 I = 103 C= 678		Any kind of outpatient health care visit Mean number of outpatient visits per patient: One year before intervention 28.7 One year after intervention 24.1 One year after/one year before (SMR/rate) 0.84 (95% CI 0.81–0.87) Intergroup difference: $p < 0.05$ Outpatient primary health care visit One year after/one year before (SMR/rate) 0.72 (95% CI 0.68–0.77)	 18.3 16.8 0.92 (95% CI 0.90–0.93) 0.92 (95% CI 0.90–0.95)	NBR program was 12 weeks. Controls were retrieved from the Skåne Health Care Register and were matched for main condition, age and sex. Controls received usual care (not specified). 65% in the NBR group and 70% in the control group had exhaustion syndrome. 27% in the NBR group and 29% in the control group had depression.	+	-	?

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:3
Outcome variable: Healthcare consumption

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients n=	With drawals - dropouts	Results: Intervention NBR	Results: Control Non nature-based rehabilitation	Comments	Directness*	Study limitations*	Precision*
				Intergroup difference: $p < 0.05$					
				Bed days in hospital One year after/one year before (SMR/rate)					
				0.47 (95% CI 0.43–0.52)	0.94 (95% CI 0.87–1.0)				
				Intergroup difference: $p < 0.05$					
				Bed days in hospital for psychiatric health care: One year after/one year before (SMR/rate)					
				0.35 (95% CI 0.31–0.39)	0.76 (95% CI 0.69–0.82)				
				Intergroup difference: $p < 0.05$					

NBR=Nature-based rehabilitation; SMR=standard morbidity ratio; HCC=healthcare contacts; HD=hospital days

Project: Nature-based rehabilitation for patients with long-standing stress-related disorder
Appendix 4:4
Outcome variable: Health related quality of life/general well-being

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness*	Study limitations*	Precision*
				Intervention NBR	Control Non nature-based rehabilitation				
Stigsdotter, 2018, Denmark	RCT	n=84 I= 43 C=41	I=4 C=4	PGWBI total score: Baseline 46.59 (sd 15.38) End NBR 61.44 (sd 15.51) 3 months 63.31 (sd 18.58) 6 months 63.28 (sd 14.47) 12 months 63.51 (sd 16.81) Intragroup Effect size partial η^2 = 0.044; partial ω^2=0.l25	PGWBI total score: Baseline 49.24 (sd 16.64) End CBT 59.62 (sd 18.87) 3 months 63.38 (sd 21.51) 6 months 65.92 (sd 19.91) 12 months 64.86 (sd 21.87) Intragroup Effect size partial η^2 = 0.088; partial ω^2=0.067 Overall effect of any treatment $F(4.144)=5.23$, $p<0.01$; partial η^2 =0.13 ns. between groups	Non-inferiority studie. Intention-to-treat analysis with LOCF imputation. More participants with incomplete data in the control group.	+	?/-	+

PGWBI=Psychological General Well-Being Index; LOCF=Last observation carried forward.

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:5
Outcome variable: Perceived stress

* + No or minor problems
? Some problems
\- Major problems

Author, year, country	Study design	Number of patients n=	With-drawals - dropouts	Results: Intervention NBR	Results: Control Non nature-based, Multidisiplinary, group-based rehabilitation	Comments	Directness*	Study limitations*	Precision *
Willert, 2014, Denmark	Cohort study	n=93 I=48 C=45	I=6 C=21	Change in PSS-10 from baseline to 3 months		Control intervention was a stress & job management program, similar in scope but with all activities performed indoors.	?	-	?
				-4.61 (95% CI -6.52 to -2.71)	-4.16 (95% CI -6.59 to -1.73)				
				Intergroup difference: Δ 0.45 (95%CI -3.54 to 2.63), n.s.					
				Change in PSS-10 from baseline to 6 months					
				-1.15 (95% CI -3.53 to 1.23)	-1.82 (95% CI -4.69 to 1.06)				
				Intergroup difference: Δ 0.67 (95% CI -3.07 to 4.40); n.s.					
Vujcic, 2017, Serbia	RCT	n=30 I=16 C=14	0	DASS21 subscale stress difference pre and post intervention Intergroup difference: $F_{1.28} = 5.442$; p=0.027; eta squared=0.163		Small sample with no follow-up period after the end of treatment. Randomisation procedure not described and DASS subscale average group scores only given in graphic form.	?	-	?/-

PSS-10 = Perceived Stress Scale, 10-item version. Total score range 0-40; higher score indicates more frequent symptoms; CI = confidence interval; DASS21 = Depression Anxiety Stress Scale 21 items.

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:6
Outcome variable: Depression

* +	No or minor problems
?	Some problems
-	Major problems

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness*	Study limitations*	Precision*
				Intervention NBR	Control Non nature-based, multidisciplinary, group-based rehabilitation				
Vujcic, 2017, Serbia	RCT	n=30 I=16 C=14	0	DASS21 subscale depression score difference pre and post intervention ns. between groups		Small sample with no follow-up period after the end of treatment. Randomization procedure not described and DASS subscale average group scores not presented.	?	-	?/-

DASS21 = Depression Anxiety Stress Scale 21 items.

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders
Appendix 4:7
Outcome variable: Anxiety

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness*	Study limitations*	Precision*
				Intervention NBR	Control Non nature-based, multidisciplinary, group-based rehabilitation				
Vujcic, 2017, Serbia	RCT	n=30 I=16 C=14	0	DASS21 subscale anxiety score difference pre and post intervention n.s. between groups		Small sample with no follow-up period after the end of treatment. Randomization procedure not described and DASS subscale average group scores not presented.	?	-	?/-

DASS21 = Depression Anxiety Stress Scale 21 items

Project: Nature-based rehabilitation for patients with long-standing stress-related disorders
Appendix 4:8
Outcome variable: Exhaustion/burnout

* + No or minor problems
? Some problems
\- Major problems

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness*	Study limitations*	Precision*
				Intervention NBR	Control Non nature-based rehabilitation				
Stigsdotter, 2018, Denmark	RCT	n=84 I= 43 C=41	I=4 C=4	Mean total SMBQ score at baseline, end NBR, 3, 6, and 12 months χ^2 (4) = 45.35, p<0.001	Mean total SMBQ score at Baseline, end NBR, 3, 6, and 12 months χ^2 (4) = 33.15, p<0.001 n.s. between groups at all time points	Non-inferiority study. Secondary outcome. Intention-to-treat analysis with LOCF imputation. SMBQ scores not presented. More participants in the control group with incomplete data.	+	?/-	+

SMBQ = Shirom-Melamed Burnout Questionnaire; LOCF = Last observation carried forward

Project: Nature-based rehabilitation for patients with longstanding stress-related disorders

Appendix 5. Analytical and descriptive themes from the qualitative synthesis

Analytical themes	**Descriptive themes**
State of mind during NBR	Calming impact of nature
	Joy in daily tasks
	Finding meaning and sense of belonging
	Being one with nature
	Being in the present
Experiences of garden and nature	Garden giving a sense of safety and security
	Garden meeting needs
	Garden as an undemanding and permissive setting
	Adjusting to nature's slower pace
	Nature as a restorative environment
Insights gained by NBR	Gaining self-acceptance
	Increased self-awareness
	Insights of nature as source of creativity and energy
Changes as a consequence of NBR	Developing new perspectives
	Developing new approaches
	Moving forward through empowerment

Appendix 6
Diagnostic criteria Exhaustion disorder

Table 1. Diagnostic criteria for stress-related exhaustion disorder as proposed by the Swedish National Board of Health and Welfare

A. Physical and mental symptoms of exhaustion of at least two weeks' duration. The symptoms have developed in response to one or more identifiable stressors, which have been present for at least six months.

B. Markedly reduced mental energy, which is manifested by reduced initiative, lack of endurance, or increase in time needed for recovery after mental effort.

C. At least four of the following symptoms have been present most of the day, nearly every day, during the same 2-week period:

1) Persistent complaints of impaired memory
2) Markedly reduced capacity to tolerate demands or to work under time pressure
3) Emotional instability or irritability
4) Insomnia or hypersomnia
5) Persistent complaints of physical weakness or fatigue
6) Physical symptoms such as muscular pain, chest pain, palpitations, gastrointestinal problems,vertigo or increased sensitivity to sounds

D. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
E. The symptoms are not due to the direct physiological effects of a substance (such as drug abuse or medication) or a general medical condition (such as hypothyroidism, diabetes and infectious disease).
F. If criteria for major depressive disorder, dysthymic disorder or generalized anxiety disorder are met, exhaustion disorder is considered a co-morbid condition.

Sources:

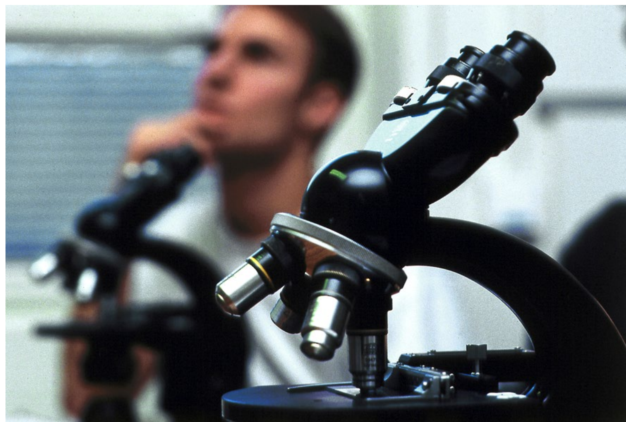
1. Swedish National Board of Health and Welfare. Utmattningssyndrom. Stressrelaterad psykisk ohälsa. (Exhaustion Syndrome. Stress related mental poor health) (in Swedish) Stockholm; 2003. Bjurner & Bruno AB:2003. ISBN 91-7201-786-4.
2. Ändringar i och tillägg till klassifikation av sjukdomar och hälsoproblem 1997 (KSH97) alfabetisk förteckning. (Changes in and supplement to classifications of diseases and health problems 1997- an alphabetic list.) 2005 (in Swedish).

Components of this Health Technology Assessment

- ☑ Description of methods
- ☑ PICO
- ☑ Full literature search
- ☑ Flowchart
- ☑ Selection based on relevance
- ☑ Quality assessment
- ☑ Data tabulation
- ☑ Evidence synthesis
- ☐ Meta-analysis
- ☑ Certainty of evidence by GRADE
- ☑ Summary
- ☑ Economical aspects
- ☑ Organisational aspects
- ☑ Ethical aspects
- ☑ Ongoing studies
- ☑ Excluded articles
- ☑ Participation of experts
- ☑ External review
- ☑ Knowledge gaps identified
- ☑ Conflict of interest reported

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

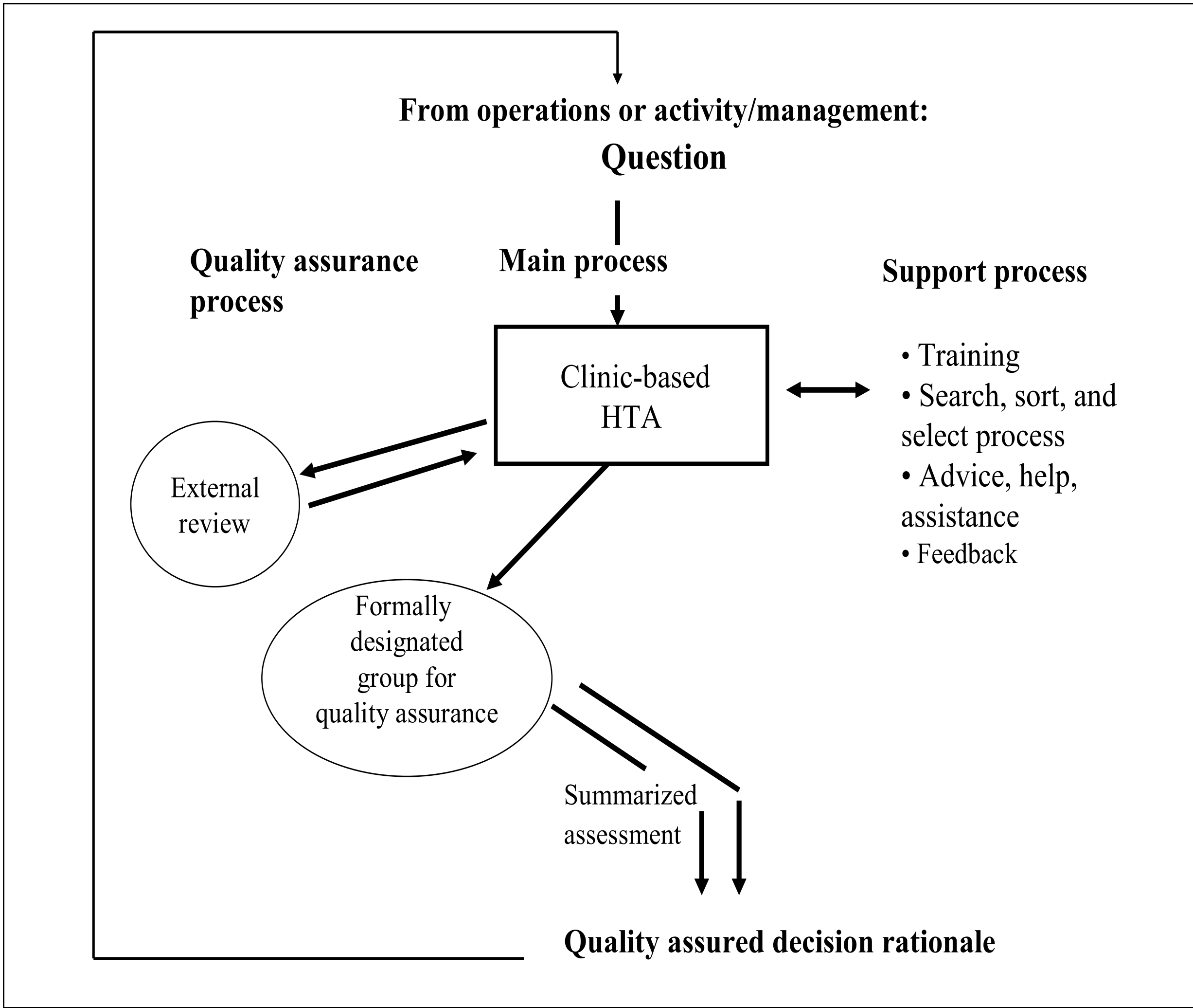
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the certainty of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High certainty of evidence	= (GRADE⊕⊕⊕⊕)
Moderate certainty of evidence	= (GRADE ⊕⊕⊕O)
Low certainty of evidence	= (GRADE ⊕⊕OO)
Very low certainty of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh
Professor, MD
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/htacentrum