Nature-based treatment for chronic pain

A literature review of the physiological and psychological parameters connected with chronic pain and influenced by contact with nature

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Final Version: 18 November 2020

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1. Introduction

Chronic pain is a condition that affects an undefined but large proportion of the UK population (estimated at 25-50% of adults) and is an area of research where there is a body of academic work. The impact of contact with nature on both mental and physical health has been explored, with some suggestion of causal links, but the clinical evidence of impact remains limited. Given the nature and extent of chronic pain, there is potential to seek clinical evidence of the impact of nature-based interventions on the lived experience of the condition. If proven, this would be work of clinical significance.

In order to define a research project, it is necessary to conduct a literature review which brings together existing evidence on the intersection of nature and health, the impact of context and patient attitude on chronic pain, and the efficacy of existing interventions in the management of chronic pain. This project brings together two departments at UWE Bristol and Dorothy House, a hospice supporting patients experiencing chronic pain, and will conduct that literature review.

The outputs from the review will offer scope for future research, in order to establish 'Nature-based treatments for chronic pain' as a research and practice field.

The review is structured as follows. The main narrative literature review is contained in Section 2. Section 4 contains some recommendations for possible follow-on activities for Dorothy House to consider. Section 5 adopts a more didactic structure, offering a Q&A around nature contact for chronic pain management which may be useful for clients or other audiences/stakeholders. Section 6 contains a more detailed examination of the methodologies deployed by many of the scientific papers reviewed. The key intention here is to allow Dorothy House to readily determine which papers used more objective versus subjective approaches to exploring the linkages between chronic pain and nature contact. In the final section, we note a number of researchers around the world who may be key to further exploring this fascinating if complex area of research and clinical practice.

2. Literature review

Chronic pain is usually identified as a pain lasting more than three months (Stanhope, Breed and Weinstein, 2020; Turk, Wilson and Cahana, 2011), separating it from acute pain, a temporary condition lasting less than three months. It is estimated that around 1.9 billion people, 25% of the world's population, suffer from chronic pain (Mills, Nicolson and Smith, 2019), including 43.5% of the people of Great Britain (Stanhope, Breed and Weinstein, 2020). Chronic pain is influenced by an array of internal and external factors, including psychological, immunological, economic, environmental and social factors (Stanhope, Breed and Weinstein, 2020; Evans et al., 2008), making it hard to find the best therapy to prevent and treat it. The main treatments to date have been pain relievers (including opioids), together with antidepressants and anti-inflammatory drugs (Danilov et al., 2020; DeBar et al., 2018; Turk, Wilson and Cahana, 2011). These incur health and social costs - including treatment and medication costs, loss of working days, and loss of wellbeing - of around

$139.3 billion a year in Australia (Pezzullo, 2019), and between $560-$635 billion a year in US (Gaskin and Richard, 2012). In the UK, back pain alone costs around £11.6 billion a year (Versus Arthritis, 2019).

Complementary and Alternative Medicine (CAM) approaches have evolved to try to cure chronic pain with, for example, massage, acupuncture, spinal manipulation (Tick et al., 2018; Johnson and Cosgrove, 2015), medication therapy, psychotherapy, behavioural therapy, and coping-pain skills (DeBar et al., 2018; Tick et al., 2018; Kurklinsky et al., 2016). However, none of these multidisciplinary and interdisciplinary treatments contain nature-contact solutions, an area of growing interest in recent years because of the wide range of benefits nature can provide to human health (Frumkin et al., 2017; Capaldi et al., 2015; Bowler et al., 2010). Contact with nature, conceptualised as visiting a greenspace and experiencing its sounds and views, has been shown to reduce stress, depression, anxiety, fatigue and sadness, and improve positive feelings, such as vitality and energy, mood, self-esteem, and health-related quality of life (Capaldi et al., 2015; Verra et al., 2012; Bowler et al., 2010). Moreover, it has been proved that natural stimuli can help promote mental focus and the restoration of direct attention, necessary for cognitive tasks and activated when thinking about pain, while also stimulating the parasympathetic nervous system, seat of indirect attention, which is activated when feeling relaxed (Wells et al., 2019; Capaldi et al., 2015; Bowler et al., 2010). A range of physiological factors also seem to be affected by natural settings, including an improved immune system, a decrease in blood pressure and mortality (Stanhope, Breed and Weinstein, 2020), and a decrease in the cortisol level, pulse rate, and blood flow to the prefrontal cortex, which is associated with mental illnesses (Song et al., 2015). Heart rate and heart rate variability (HRV), salivary cortisol, and the Natural Killer (NK) number are the biophysical parameters most used to predict nature's outcomes on human health (Han et al., 2016; Song et al., 2015; Li, 2010; Li et al., 2008; Evans et al., 2008). Part of the immune system, Natural Killer (NK) cells are lymphocytes responsible of the removal of infected or damaged cells, and they fight against tumour cells (Eissmann, 2020). To be able to detect and destroy infected cells they need to release proteins, proteases (granzymes) and proteins (perforin and granulysin) (Lieberman, 2015).

Where then is the research underpinning the use of nature contact as a treatment for chronic pain? Despite a wide range of studies in this field, the majority represent small sample case studies which are not easily generalizable (Song et al., 2015; Li, 2010; Li et al., 2008), or theoretical research (Stanhope, Breed and Weinstein, 2020; Frumkin et al., 2017; Capaldi et al., 2015; Bowler et al., 2010). Most rehearse the possible benefits of nature exposure, with little consideration of influencing or confounding variables, such as accessibility to greenspace, the socioeconomic status of the person visiting the greenspace, previous experiences with nature, and the long-term effects of nature on human health. Almost all of the literature cited (peer-reviewed and grey literature) included urban parks, forests, grasslands, and waterways in the definition of greenspace or natural environment, without considering more remote or exotic environments such as tropical forests, mountains or deserts, which might be the only available nature settings for certain populations around the world.

Chronic pain is significantly associated with depression, stress, anxiety, sleep problems, difficulties in approaching everyday activities (Han et al., 2016; Evans et al., 2008), immune system functionality (Li, 2010, Li et al., 2008), and attention fatigue (Wells et al., 2019). However, only a limited amount of research has been undertaken on the specific question of nature-based treatment for chronic pain (Stanhope, Breed and Weinstein, 2020; Wells et al., 2019; Han et al., 2016; Kang et al., 2015; Verra et al., 2012). Analysing the effect of nature-based therapies on these psychological and physiological parameters might help us understand its indirect effect on chronic pain.

All five studies evaluating the benefits of nature-based treatments on chronic pain are composed of a small group of participants, mainly white, over 40 (Wells et al., 2019; Han et al., 2016; Kang et al., 2015; Verra et al., 2012), female (Wells et al., 2019; Kang et al., 2015), with no mental health issues and part of the middle class economically. Verra et al. (2012) focussed on horticultural therapy, which was added to a multidisciplinary program entailing psychotherapy, physical exercise, and drug therapy. Wells et al. (2019) studied the psychological responses of nearby nature on people affected by pain-catastrophising pain. Two studies investigated the effects of forest therapy: Han et al. (2016) analysed people with chronic widespread pain, while Kang et al. (2015) focussed on chronic neck pain. Stanhope, Breed and Weinstein (2020) proposed a theoretical study of all of the benefits given by different natural elements to people with a chronic condition of pain. Except for the Wells et al. (2019) study, both physiological and psychological effects were measured, giving an objective and a subjective view of the effects of the nature therapy.

The research by Han et al. (2016) involved spending two days and one night in a forest while experts provided relaxation, refreshment, and attention restoration therapies and psychoeducational treatment for coping with pain and stress. Meditation was promoted and music played during the evening. Measurements were taken at the beginning of the first day and at the end of the therapy. HRV, NK cells, pain, depression and health-related quality of life were measured. HRV is an index of the relaxation status of a person. When the heart rate decreases, and the HRV increases, the sympathetic nervous system is resting, while the parasympathetic system is activated. The latter is activated when people are asleep or relaxed, aiding recovery from attention fatigue and focusing only on the indirect attention. Sympathetic system activity is also a symptom of anxiety and stress (Wells et al., 2019). Attention, sleep and stress are related to chronic pain, and these measurements provide a physiological, objective view of the changes of these emotions. NK cells are cells of the immune system, similar to cytotoxic t-lymphocytes, which kill damaged, infected or tumour cells. They regulate the immune system, reducing inflammatory diseases, which seem to be connected with cardiovascular issues, stress and depression (Rook, 2013), with the latter two often found in patients experiencing chronic pain.

In the other forest therapy research, Kang et al. (2015), unlike Han et al. (2016), used trigger points in the posterior neck region (TRPs) and the cervical range of motion (C-ROM) to assess directly the impact that a forest bath has on pain reduction, together with psychological measurements of pain, neck pain, and lifestyle. Two groups were formed for this study, one doing just forest therapy for five days, with two hours of walking every morning and free time afterwards, and the other one adding stretching exercises aimed at the neck and shoulders, for two hours every afternoon. Both

studies revealed a decrease in the sensation of pain and an improvement in the related quality of life. For the first group, depression also improved, and the NK and HRV increased, showing relaxation and immunoregulation. Forest bathing alone and with exercise showed, surprisingly, similar positive results, except for the TRPs measure, which had more beneficial effects when stretching and exercising. C-ROM, a measure of the movement that your neck can achieve, was not improved in the same way with the participants doing added exercise. Why one of the two objective measurements improved more with exercise and the other did not is unclear. However, from the analysis of these two studies, nature-based treatment seemed to improve pain, depression and the immune system. A study assessing the effect of forest bathing without any psychological therapy should be undertaken to better understand the potential of nature for treating chronic pain.

When a horticultural therapy, composed of seven one-hour sessions of gardening, stress and tension reduction therapy, botany, physical activity, and a break time to reflect on coping skills, was added to a multidisciplinary program provided by a Swiss pain centre (Verra et al., 2012), all the psychological parameters, namely depression, anxiety, pain, quality of life, and vitality, were enhanced in a positive way. Anxiety had just a minor change for people experiencing the multidisciplinary treatment, but improved for people undertaking the horticultural therapy. However, when evaluating the six-minute walk test (6mWT), a physiological test used for people suffering from fibromyalgia, and the Back Performance Scale (BPS), a test used for people with chronic back pain, no differences were encountered for the study groups. This study shows that nature, and activities in a natural space, have a more beneficial effect on the psychological side of human health. In fact, an interdisciplinary treatment for chronic pain, comprising of physical activity, occupational therapy (to increase independence and participation in life activities), and cognitive behaviour therapy, with specialists dealing with stress, anxiety and behaviour change, also used the 6mWT to measure improvements in movement disability related to pain intensity. The results showed a significant improvement in the patients' movement (Kurklinsky et al., 2016). This may confirm that nature acts partially in the physiological parameters connected to pain. However, interdisciplinary treatments are also efficient in managing chronic pain.

The Wells et al. study (2019) did not undertake any special treatment but analysed to what degree residents of a suburb of New York City used nearby nature, and how it affected their mental health. The study focussed on people suffering pain-catastrophising pain, a condition in which pain is felt to overwhelm the person. Pain-catastrophising is divided into three subgroups: rumination, helplessness and magnification. In this condition, all the attention is concentrated on the sensation of pain and, therefore, a distraction therapy might be the best solution to reduce not the actual pain, but the intensity of it. Rumination is the best predictor of pain intensity, and it is defined as the constant thought about, and preoccupation with, something. As specified before, direct attention, which requires neurological effort and is needed to focus on important skills, is connected with the sympathetic neural system, while the indirect, or involuntary attention, is the one activated when interesting stimuli from the outside are perceived. It does not require any mental effort and, at the same time, direct attention restores. Nature is full of stimuli for the brain, engaging the indirect attention, and thus diverting thoughts away from pain. In the study, pain intensity, pain catastrophising, psychological resilience, and the nearby nature were evaluated. Nearby nature did

not influence directly pain intensity, but did influence the association between pain intensity and pain catastrophising, and rumination and pain intensity. The results were not affected by age, gender or income, nor by the time spent in nature. This means that the pain intensity is indirectly reduced by nature by moderating rumination and pain catastrophising. In this small case study, nature seems to have a non-direct effect on pain. It needs to be mentioned, nonetheless, that while greenness percentage and plant biodiversity were determined during the study, how biodiversity and the amount of green in the neighbourhood affected the human health was not specified in the results. An evaluation of these two variables may have provided a better understanding of the effect of nature on people's health.

From this short review of the few articles available regarding the relationship between nature-based treatment and chronic pain management, nature seems to help reduce both pain sensation and all the negative psychological and functional effects that come with it. Racial and ethnic differences, as well as previous experiences with nature and pro-environmental behaviour, are rarely mentioned as covariates in these studies. These parameters may be able to alter the effects of nature on chronic pain (Frumkin et al., 2017). A recent study, however, showed that white, black, and other ethnic minorities feel the same about nature: they do not have feelings of fear about it, and they feel more restored and at peace when experiencing it (Taylor, 2018). Regarding previous experiences in nature or people's preferences, two studies investigating the psychological outcomes achieved when people were using greenspaces involved participants who had already chosen voluntarily the specific environment. Therefore, the positive outcomes may be exaggerated by the self-selection of the environment (Carrus et al., 2015; Fuller et al., 2007).

Further research is needed to validate this theory, and to thoroughly understand more precisely which components of nature influence mental and physical health. The next section will examine the effects of nature on the physiological and psychological parameters of human health.

The psychological parameters involved in chronic pain are:

- Depression
- Stress
- Anxiety
- Attention fatigue
- Other parameters, such as connectedness to nature, quality of life, self-esteem, meaningful life, and pain-catastrophising

The physiological parameters influencing and influenced by chronic pain are:

- Natural Killer (NK) cells, together with perforin, granulysin and granzymes
- Cortisol
- Adrenaline
- Heart Rate Variability (HRV)
- Blood pressure and pulse rate
- Prefrontal cortex activity
- Circadian rhythm

As previously mentioned, chronic pain is significantly associated with depression (Stanhope, Breed and Weinstein, 2020; Han et al., 2016; Cino, 2014; Verra et al., 2012; Evans et al., 2008). Numerous studies have demonstrated that contact with nature can help with depression (Stanhope, Breed and Weinstein, 2020; Chun, Chang and Lee, 2017; Soga, Gaston and Yamaura, 2017; Han et al., 2016; Bratman et al., 2015; Taylor et al., 2015; Marselle, Irvine and Warber, 2014; Rook, 2013; Verra et al., 2012; Park et al., 2010). Nature works in different ways on depression. Contact with nature decreases negative feelings, such as depression, perhaps because of the Biophilia theory, which explains that humankind has evolved for most of its life in natural environments, and only in recent years have humans developed and inhabited urban cities. As a consequence, humans are still deeply connected with nature, which makes their mental health improve every time they are exposed to nature, either visually or through direct contact (Wyles et al., 2019; Seymour, 206; Capaldi et al., 2015; Carrus et al., 2015). Moreover, some studies have evaluated positive outcomes for people walking or exercising in nature. Physical activity is known to reduce cardiovascular diseases, obesity and may decrease the likelihood of cancer, while improving social connection and mobility (Kaczynski and Henderson, 2007), enhancing mental health, positive feelings, and cognitive behaviour (Marselle, Irvine and Warber, 2014). Physical activity, therefore, influences the health of a person, and reduces the potential for musculoskeletal pain, which may become a long-lasting disability. Walking in a natural environment enhances these benefits and also improves mental wellbeing. Short-term, light exercise is preferred to long, intense sessions (Marselle, Irvine and Warber, 2014; Barton and Pretty, 2010). Finally, natural environments contain a range of different plants, animals, and microorganisms (known as microbiome when describing a whole group of microorganisms present in a certain environment) (Stanhope, Breed and Weinstein, 2020). Environmental microbiome positively affects the human microbiome, especially in the gut through probiotics, for example. It also influences the brain and neurotransmitters, indirectly affecting mediators of chronic pain (Stanhope, Breed and Weinstein, 2020). Influencing the human microbiome will, therefore, likely reduce pain. Natural microbiome and phytoncides (organic volatile compounds secreted by trees) increase the production of Natural Killer cells and the activity of the immune system (Stanhope, Breed and Weinstein, 2020; Frumkin et al., 2017). A strong immune system reduces stress, depression, cardiovascular diseases, and the development of inflammation, which is connected with chronic pain development. The positive influence of various microorganisms on the human microbiome can be explained with the Old Friend Mechanism: our body was used to being connected with a diversity of microorganisms, which made our immune system capable of recognising which microbes were harmless and which could be defined as pathogens. In our newly-developed cities, we lost contact with many of those microbes, and our body lost the power to recognise harmful and harmless microorganisms and began to weaken. Previously we would have been able to fight *Salmonella spp*. without serious issue, but nowadays it is considered a very dangerous disease. Being in a natural environment, with all its elements, animals, plants and microorganisms, allows the human immune system to connect with these 'Old Friends' and enhance its functioning (Rook, 2013).

Stress is another negative feeling that normally comes with chronic pain (Stanhope, Breed and Weinstein, 2020; Kurklinsky et al., 2016; Hannibal and Bishop, 2014; Evans et al., 2008). As with

depression, exercising in nature brings about a reduction in negative feelings such as stress. Moreover, just being in a natural environment reduces stress (Wyles et al., 2019; Frumkin et al., 2017; Capaldi et al., 2015; Taylor et al., 2015; Park et al., 2010), with Gascon et al. (2017) concluding blue spaces lower stress and other negative emotions even more. The sights and sounds of nature also decrease stress (Stanhope, Breed and Weinstein, 2020; Bratman et al., 2015), even when seen through virtual reality (White et al., 2018). Lastly, activities involving engaging with nature, such as gardening and horticultural therapy, seem to improve the mental and physical benefits that nature and exercise may have on human health (Soga, Gaston and Yamaura, 2017; Verra et al., 2012).

Anxiety is another of the main psychological factors connected with chronic pain (Stanhope, Breed and Weinstein, 2020; Han et al., 2016; Kurklinsky et al., 2016; Cino, 2014; Evans et al., 2008), and many studies suggest nature improves anxiety as it does with stress and depression (Chun, Chang and Lee, 2017; Frumkin et al., 2017; Soga, Gaston and Yamaura, 2017; Song et al., 2015).

Another important parameter to consider is attention. The attention that focuses on cognitive tasks and life's goals, but also on pain and negative feelings, is called direct attention. When attention is extremely focussed on one particular emotion, normally a negative feeling, a person is experiencing a maladaptive behaviour, called rumination (Wells et al., 2019; Bratman et al., 2015). The part of the brain designated for these activities is called the prefrontal cortex (Park et al., 2010). Nature has the ability to involve the indirect attention and decrease direct attention fatigue (Wells et al., 2019; Wyles et al., 2019; Frumkin et al., 2017; Soga, Gaston and Yamaura, 2017; Bratman et al., 2015; Capaldi et al., 2015; Bowler et al., 2010), and to decrease the blood flow to the prefrontal cortex (Bratman et al., 2015; Song et al., 2015; Park et al., 2010). One study measured the activity of the prefrontal cortex with neuroimaging, which can measure long-lasting rumination activities. Outcomes proved that rumination and prefrontal cortex activity can be effectively reduced with exposure to nature (Bratman et al., 2015). This explains the connection between attention, rumination and pain, previously discussed in this paper (Wells et al., 2019). Virtual reality may also offer an escape from this maladaptive behaviour and reduce acute pain and pain sensation (White et al., 2018).

Finally, studies revealed that blue spaces, especially coastal areas, promote happiness, life satisfaction and relaxation (Wyles et al., 2019; Gascon et al., 2015), as do rural and Protected and Designated Areas (PDAs) (Wyles et al., 2019). Natural environments also enhance positive effects, such as vigour (Soga, Gaston and Yamaura, 2017; Song et al., 2015; Park et al., 2010), mood (Capaldi et al., 2015; Song et al., 2015; with physical activity, see Barton and Pretty, 2010), and self-esteem (with a short-term exposure to the natural environments or a whole day in it, see Barton and Pretty, 2010). Quality of life can also be enhanced either by nature on its own (Han et al., 2016), or through exercising in nature (Kaczynski and Henderson, 2007), gardening activities (Soga, Gaston and Yamaura, 2017), and when visiting nature frequently (White et al., 2017).

In general, contact with nature does not seem to have any negative effects in this context. However, it is worth remembering that even if positive outcomes are the most common, some researchers have found no impact, for example, between biodiversity and psychological wellbeing

(Carrus et al., 2015), or between physical activity and the presence of urban greenspaces (Kaczynski and Henderson, 2007) and blue spaces (Gascon et al., 2017). In these studies, health parameters were the same before and after a nature visit. Additionally, benefits may change with the seasons. A study which analysed the physiological and psychological benefits of a walk in a park during different seasons showed that during winter time, the activity of the sympathetic system did not decrease as it did during spring and autumn (Song et al., 2015).

The number and activity of NK cells are enhanced by phytoncides for their antimicrobial properties. Some examples of phytoncides are limonene and alpha-pinene. They are normally not found in a city or urban area, but in the presence of plants (Stanhope, Breed and Weinstein, 2020; Li et al., 2008). As they are part of the immune system, when the number and activity of NK cells increase, there is an improvement in the immunoregulation. NK cells and their related proteins and proteases seem to increase every time when in the presence of a natural environment (Stanhope, Breed and Weinstein, 2020; Frumkin et al., 2017; Han et al., 2016; Li, 2010; Li et al., 2008). NK activity is also enhanced by the natural microbiome (Frumkin et al., 2017; Rook, 2013) and by negative air ions (Stanhope, Breed and Weinstein, 2020), electrically charged atoms or molecules emitted by plants, water or found in rays of sunlight (Jiang, Ma and Ramachandran, 2018), all elements of the natural environments. Immunoregulation decreases inflammatory diseases, connected with stress, depression and cardiovascular diseases (CVD) (Rook, 2013). Moreover, NK cell activity is inhibited by stress, raised adrenaline (Li, 2010) and raised cortisol (Park et al., 2010). A continuous release of cortisol, due to chronic stress, may cause immune system dysfunction, muscular-skeletal damage and cardiovascular issues (Evans et al., 2008), all associated with pain. Indeed, NK cells have been used as a therapy to manage pain (Stanhope, Breed and Weinstein, 2020; Li et al., 2008).

Cortisol mobilises glucose, which gives the body enough energy to fight an inflammation and escape from danger. Cortisol is released when feeling stressed. Short-term stress responses to pain are adaptive. However, long-term and repeated stress may cause maladaptive responses that cause a cortisol dysfunction, which can generate widespread nerve and tissue damage, fibromyalgia and chronic pain. Maladaptive behaviours, such as catastrophising behaviour, may cause an exaggeration of the fear and thought of pain, increasing stress levels and, therefore, cortisol levels (Hannibal and Bishop, 2014; Evans et al., 2008). Cortisol is, hence, directly related to stress, but it is also associated with depression and pain in a positive correlation (Evans et al., 2008), and high levels of cortisol can reduce the activity of the NK cells (Park et al., 2010). Studies show nature exposure can decrease the level of cortisol, measured through salivary tampons (Song et al., 2015; Park et al., 2010), which is a measure of relaxation. Exposure to nature is, furthermore, likely to reduce pain outcomes through lowering the cortisol level.

Adrenaline is related to the stress hormones, hence a reduction in adrenaline, lowers stress (Li, 2010; Li et al., 2008) and, as explained previously, NK cells decrease with an increase of adrenaline and stress. Forest therapy reduced the level of urine adrenaline (Li, 2010; Li et al., 2008).

Heart rate variability, pulse rate, blood pressure can also be affected by contact with nature. A study investigating the effect of a 15 minute-walk alone in an urban park showed a decrease in

HRV, and an increase in the High Frequency (HF), which is a measure of the parasympathetic nervous system activity and thus describes relaxation. This was seen in spring and autumn, but not in winter, where HRV enhanced but not the HF (Song et al., 2015). A forest bathing experiment also demonstrated a decrease in HRV, together with blood pressure and pulse rate, which helps with relaxation and stress. HF and LF (Low Frequency) are both components of the HRV. The HF/LF measure is an index of the sympathetic nervous system and, as such, it describes stress. HF enhanced during the forest bathing, while HF/LF decreased (Park et al., 2010). A more recent forest therapy experiment also revealed an improvement in HRV when in a forest (Han et al., 2016).

Circadian rhythm, a process that regulates sleep, is also influenced by natural environments, most precisely through the natural microbiome, the enhancement of vitamin D, natural sounds, phytoncides (Stanhope, Breed and Weinstein, 2020), sunlight exposure, and physical activity (Stanhope, Breed and Weinstein, 2020; Seymour, 2016). A regular circadian rhythm promotes physical and mental health.

In summary, these are the main chronic pain influencers:

- Depression is connected with stress, rumination, cortisol, inflammation, and the immune system
- Stress is connected with depression, cortisol, rumination, inflammation, the immune system, NK cells, and adrenaline
- NK cells are connected with adrenaline, stress, and cortisol
- Cortisol is connected with stress, depression, NK cells
- Adrenaline is connected with stress and NK cells

All of the above are directly or indirectly connected with chronic pain and are affected by the natural environment.

In conclusion, nature can provide a wide range of benefits for human health, and also on the psychological and physiological parameters connected with chronic pain and pain outcomes. For pain-related physical disabilities, such as neck movement impairment and walking disabilities, the effect of nature seems to be varied. One study showed, through the 6mWT, that horticultural therapy did not improve the movement disability of the patients involved in the treatment (Verra et al., 2012). However, another interdisciplinary treatment did show an improvement to movement (Kurklinsky et al., 2016), and Kang et al. (2015) showed an enhancement in neck movement when bathing in a forest. More studies are needed to understand the real, direct effects that nature has on chronic pain. Despite the limited evidence that connects nature with chronic pain management, what emerges from this literature review is that being in a natural environment provides for a range of benefits and it seems not to have any negative aspects. Qing Li, author of *Forest Bathing: How Trees Can Help You Find Health and Happiness*, explains that the key to attaining the most benefits from nature is to use all five senses, hear the sound of birds and insects, smell the scent of flowers, see the landscape, taste fruits, and touch the natural elements. This can be done through a forest therapist or without, but the important thing is to choose a place that we like: a forest or a park or

anywhere there are trees. We can also choose the activity we would like to perform in it. The most essential element is just to find a place and an activity that most relaxes us, and with the help of the environment and its phytoncides, the effects will be more powerful.

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4. Recommendations for future activities for Dorothy House

The following are suggestions for possible activities that may be appropriate for Dorothy House clients, based on the review undertaken:

- Bring nature into the hospice through gardening or through 'contact with pets' schemes.
- Bring nature into the hospice through guided walks by guides with body cameras, possibly even live so that hospice clients can direct the guides to look at specific things.
- Developing small areas of nature adjacent to or within hospice facilities and giving clients a chance to physically touch and experience them.
- Creating soundscapes within the hospice or parts of the hospice – e.g. birdsong – at certain times.
- Cleaning-up activities in natural sites.
- Bring nature into the hospice with wallpapers of natural pictures.
- Create walking paths made of different natural elements (sand, water, grass, leaves) to engage the tact sense.
- Pick seasonal fruits and herbs, possibly with an expert, and make a barbecue/dinner with them.
- Forest-therapy experience.
- Aloe massage.
- Promote therapy sessions outside (weather permitting).

In the course of the research we became aware of the work of Steve England, who may be a useful future consultee:

> Steve England is a naturalist and conservationist living in Bristol. He conducts guided tours and volunteering activities in nature, in which he explains all the natural elements encountered. See: http://steveengland.co.uk/

5. Questions regarding nature contact and chronic pain

1. Is there evidence to suggest varying impacts of contact with nature amongst patients with more or less extreme chronic pain?

One of the few studies (Stanhope, Breed and Weinstein, 2020) reporting the relationship between chronic pain and nature-based treatment is a literature review of research analysing the various aspects of nature, namely, microbiome, sunlight exposure, phytoncides, natural sights and sounds, negative air ions, and the presence of nature around a residential area. Only one of the papers they evaluated reported a specification of the pain of the people involved in the study, which was a severe musculoskeletal condition. In this case, living close to a greenspace reduced the severe pain complaints, however, differentiation between severity and intensity of the pain was not assessed. Research by Han et al. (2016) did not specify the intensity of the chronic pain of the people recruited for the study, nor did it explore the effect of forest therapy on people with different pain severity. Kang et al. (2015) involved people with pain over 4 on the Visual Analog Scale (VAS). Similarly, another paper included only people with a pain level of more than 5 on a scale between 0 and 10 (Wells et al., 2019), and the Interdisciplinary Program in Zurzach did not accommodate people with psychiatric and severe somatic disorders (Verra et al., 2012). Differences in pain were never explored in these studies, therefore differences in the impact of nature-based treatment on people's pain level is difficult to evaluate.

2. How long do positive impacts on pain last after contact with nature? Does evidence suggest other variables (type of contact, starting pain score, previous experience of nature) impact on the durability of positive impacts?

All the papers analysing the relationship between chronic pain and nature-based treatment measured the physiological and/or psychological indices before and after the treatments proposed for the research: forest therapy (Han et al., 2016), forest therapy compared with forest therapy with stretching exercises (Kang et al., 2015), and horticultural therapy (Verra et al., 2012). However, an article regarding the effect of forest therapy on the human immune system, assessed through the measurements of the number and activity of Natural Killer (NK) cells and related components (perforin, granulysin and granzymes) (Li, 2010), provided measurements before a forest therapy experiment, immediately after, and after 7 and 30 days. Results showed an increase of these parameters up to 30 days after the therapy, even though the figures decreased over time. An increase in immune system activity corresponds to a sense of relaxation, reduction in tumour development and its related pain (Li, 2010), and a reduction of inflammation, which is seen to be associated with stress and depression (Rook, 2013), both of which are normally present in people with chronic pain (Stanhope, Breed and Weinstein, 2020; Han et al., 2016; Verra et al., 2012). This indirectly demonstrates that forest therapy can have long lasting positive effects on human health. However, during the Li (2010) study, participants were fully immersed in nature and walked for two or four hours per day. Positive prolonged benefits may, therefore, have been caused by the undertaking of physical activity. However, to have prolonged physical and mental benefits through

physical activity, it would be necessary to have repeated workouts, and it would be useful to know if the participants had undertaken any other physical activity between the end of the experiment and the last measurement, 30 days later. Evidence suggests that activities in nature, such as exercise in greenspaces and gardening, provide a major beneficial effect on pain (Stanhope, Breed and Weinstein, 2020). This may be caused by physical activity and social interaction, although an Italian study (Carrus et al., 2015) demonstrated that people felt more restored when contemplating nature, rather than reading or talking. Similarly, an English national survey demonstrated that walking is the activity that makes people more connected to nature (Wyles et al., 2019). This may be caused by the promotion of physical activity and the more immersion in the soft and engaging stimuli that nature has to offer, and that fosters relaxation and stress reduction, compared to activities such as reading, talking or working out.

The studies evaluating chronic pain and nature-based treatment did not provide information about previous nature experiences of the participants and did not verify beneficial or negative effects of contact with nature on people with a different starting pain score.

Long-term exposure seems to ameliorate the lifestyle of a person, reducing mental distress (Capaldi et al., 2015), and improving wellbeing (Carrus et al., 2015). One study assessed the positive benefits of a natural environment on the human immune system and it revealed that, to be effective, contact with nature needs to be an enduring experience (Rook, 2013).

3. Does the impact vary between habitats? Is there a correlation between biodiversity recorded in the area of contact and the scale of the impact on pain?

Wells et al. (2019) assessed the amount and type of nature, meant as the quality of the area and biodiversity level, close to a residential area. However, when drawing conclusions from the results, no specification of the greenspace typology was included, and therefore it is not clear if the effects caused by nearby nature on people's health may have varied across different types of greenspace. Carrus et al. (2015) assessed people's preferences regarding the location and biodiversity of a greenspace, and their choice was for a more diverse habitat in a peri-urban space, giving the subjects a strong sense of wellbeing and restorativeness. In one study, people felt that their life was better when living in a neighbourhood with a large amount of nature (evaluative wellbeing) (White et al., 2017). In an English national survey called MENE, people replied to questions regarding the natural environments and their emotional outcomes when seeing or visiting them. Results demonstrated that people prefer rural, coastal area, and PDAs sites (Protected and Designated Areas), which are known to have a high ecological quality (no litter, degradation) and contain more biodiversity. These sites made people feel more connected to nature and relaxed. Connectedness is correlated with life satisfaction, positive feelings, and more pro-environmental behaviour (Wyles et al., 2019).

People also seem to prefer to do their physical activity in natural environments. Physical activity reduces musculoskeletal disorders, obesity, and cardiovascular diseases, and a natural habitat may indirectly improve the physical health of a person, reducing pain from obesity and musculoskeletal

conditions (Kaczynski and Henderson, 2007). As phytoncides, volatile organic anti-microbial compounds secreted by trees, enhance the activity and number of Natural Killer (NK) cells, a more diverse natural habitat, specifically with a wide range of different tree species, should further improve the functionality of the immune system of people in those habitats (Li et al., 2008). Plant biodiversity also improves wellbeing, and increases a sense of reflection and being unique (Fuller et al., 2007). If biodiversity is defined as a range of different animals, plants and microorganisms, a more diverse natural habitat should ameliorate human health, and indirectly, pain outcome, as it has a range of microbes which, in the past, were connected with our gut flora but which we lack in modern urban societies. These microorganisms were keeping the human immune system active and efficient. By eliminating this innate connection, the immune system stops recognising harmful pathogens and become more susceptible to microorganisms, such as Salmonella species, which were previously tolerated by the human body. This creates chronic inflammation and cardiovascular diseases (Rook, 2013).

4. Does the relationship between the length of contact with nature and the average reduction in pain score show a normal distribution and if so, what is the optimum length of contact (i.e., the shortest time with the greatest reduction in pain score)?

In general, repeated, short-term exposure to greenspace is preferred to a long-term exposure. Specifically, self-esteem and mood increase during short exposure to greenspace. A whole day spent in greenspace also benefits self-esteem and mood, but this may be due to taking part in activities such as social interaction, picnicking and camping, which increase relaxation and social cohesion (Barton and Pretty, 2010). Greenspace exposure, in this case, follows a U-shape distribution, opposite to a Gaussian, normal distribution, although this is a correlation between nature contact and general health parameters, and does not specifically include pain outcomes. Conversely, increased wellbeing and restorativeness was felt by people visiting urban or peri-urban greenspaces for a longer period of time (Carrus et al., 2015). Similarly, a greater sense of connection to nature, associated with life satisfaction, wellbeing, positive effects, and mental restoration was felt when people were visiting coastal environments, rural areas and areas with high ecological quality and biodiversity for longer period of time (in this case, more than 30 minutes) (Wyles et al., 2019). In a paper by Wells et al. (2019), the length of exposure did not influence the pain intensity and the pain-catastrophising relationship. A systematic review of the effects of contact with nature on human health (Frumkin et al., 2017) reported that short-term exposure to phytoncides is likely to improve NK cell activity. However, as mentioned by Rook (2015), repeated contact over time, rather than long-term exposure, is associated with an improvement in the lifestyle of a person and in the reduction of mental distress (Capaldi et al., 2015).

5. Is there evidence that positive impacts of contact with nature are stronger or weaker amongst those who report a previous interest in wildlife or the environment?

The people involved in the research of Carrus et al. (2015) completed a questionnaire regarding the subjective psychological and physiological outcomes felt after an experience in a greenspace.

However, participants had already chosen to visit that specific site, hence, the positive results achieved may be influenced by this. No specification of previous interest in nature was examined. Similarly, Fuller et al. (2007) examined the psychological parameters of the users of 15 different greenspaces. People were, therefore, not asked to visit a natural environment but it was already in their intention to do so. Frumkin et al. (2017) asserts that many papers fail to appraise if participants have had previous experiences with nature.

6. Methodology and measurements of the physiological and psychological factors

Authors and affiliations	Article title	Methodology/Study characteristics	Measurements
Q. Li [1], K. Morimoto [2], M. Kobayashi [1], H. Inagaki [1], M. Katsumata [1], Y. Hirata [1], K. Hirata [1], H. Suzuki [1], Y.L. Li [1], Y. Wakayama [1], T. Kawada [1], B.J. Park [3], T. Ohira [3], N. Matsui [3], T. Kagawa [3], Y. Miyazaki [3], A.M. Krensky [4] *1 Department of Hygiene and Public Health, Nippon Medical School, Tokyo* *2 Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine, Osaka* *3 Forestry and Forest Products Research Institute, Tsukuba, Japan* *4 Department of Pediatrics, Stanford University School of Medicine, Stanford, CA, USA*	Visiting a forest, but not a city, increases human natural killer activity and expression of anti-cancer proteins	Forest bathing. Day 1: 2h walk in a forest and sleep in a nearby hotel. Day 2: 2h walk in the morning and 2h walk in the afternoon. Day 3: return to Tokyo after completing a questionnaire and drawing blood. City tour. Day 1: 2h walk in the city. Day 2: 2h walk in the morning and 2h in the afternoon. Day 3: return to Tokyo after completing a questionnaire and drawing blood. 2.5km for each course, resembling normal daily physical activity.	Physiological analysis. • White blood cell (WBC) counts • NK activity, proportions of NK and T cells, and granulysin, perforin, and granzymes A/B were measured • Adrenaline concentration in urine was also determined. Phytoncides were measured.
Richard A. Fuller [1], Katherine N. Irvine [2], Patrick Devine-Wright [2], Philip H. Warren [1], Kevin J. Gaston [1] *1 Department of Animal and Plant Sciences, University of Sheffield, Sheffield, UK* *2 Institute of Energy and Sustainable Development, De Montfort University, Leicester, UK*	Psychological benefits of greenspace increase with biodiversity	Greenspace biodiversity identification. Interviews with 312 users of the greenspaces.	Ecological survey in each 10x10m quadrant of 15 greenspaces. Butterflies and birds survey. Psychological analysis: 5-point Likert scale about: recovery from mental fatigue and the opportunity for reflection, derived from attention restoration theory, attachment to, and personal identity gained from, the greenspace, reflection, distinct identity, continuity with past, and attachment.

Kayleigh J. Wyles [1,2], Mathew P. White [3], Caroline Hattam [2], Sabine Pahl [4], Haney King [5], Melanie Austen [2] *1 University of Surrey, Guildford, UK* *2 Plymouth Marine Laboratory, Plymouth, UK* *3 European Centre for Environment & Human Health, University of Exeter Medical School, UK* *4 Plymouth University, Plymouth, UK* *5 Natural England, Worcester, UK*	Are Some Natural Environments More Psychologically Beneficial Than Others? The Importance of Type and Quality on Connectedness to Nature and Psychological Restoration	English MENE (Monitor of Engagement with the Natural Environment) survey. Survey between 2009 and 2014. 4,515 participants.	Recalled connectedness to nature (RCN). Recalled restoration (RR). Environment type: (urban green, rural green, and coastal) Environment quality: [PDA (Protected or Designated Areas) or Non-PDA]. Socioeconomic and demographic data. Activity undertaken and companion Length of the visit.
Mathew P. White [1], Sabine Pahl [1,2], Benedict W. Wheeler [1], Michael H. Depledge [1], Lora E. Fleming [1] *1 European Centre for Environment and Human Health, University of Exeter Medical School, UK* *2 Department of Psychology, Plymouth University, UK*	Natural environments and subjective wellbeing: Different types of exposure are associated with different aspects of wellbeing	English MENE (Monitor of Engagement With the Natural Environment) survey. 7,272 participants. Urban/Peri-Urban population.	SWB (Subjective Well-Being), divided in: evaluative wellbeing, eudaimonic wellbeing, positive and negative experiential wellbeing. Exposure was operationalised in terms of: neighbourhood nature (% local area categorised as green/blue space), visit frequency (frequency of recreational visits over the previous 12 months), and specific visits (whether individuals visited nature 'yesterday'). Socioeconomic and demographic data.
Mark S. Taylor [1], Benedict W. Wheeler [1,2,3], Mathew P. White [2], Theodoros Economou [1,2,3], Nicholas J. Osborne [2] *1 Department of Public Health, Fakulta Zdravotnictva a Socialnej Prace, University of Trnava, Trnava, Slovakia* *2 European Centre for Environment & Human Health, University of Exeter Medical School, University of Exeter, Truro Campus, Knowledge Spa, Royal Cornwall Hospital, Truro, UK* *3 Exeter Climate Systems, University of Exeter, Exeter, UK*	Research note: Urban street tree density and antidepressant prescription rates—A cross-sectional study in London, UK	Data collection during 2009/2010 obtained from: data.london.gov.uk Ordnance Survey and ArcGIS.	Antidepressant prescriptions in London. Street trees in London. Socioeconomic data, age and prevalence of smoking people.

Qing Li *Department of Hygiene and Public Health, Nippon Medical School, Sendagi, Bunkyo-ku, Tokyo, Japan*	Effect of forest bathing trips on human immune function	12 healthy males selected, age between 37-55. Forest bathing trip. Day 1: 2h walk. Day 2: 2h walk in the morning and 2h walk in the afternoon. Blood and urine sample collection. Day 3: return to Tokyo. Completion of a questionnaire and collection of blood and urine sample. Day 7: collection of blood and urine sample. Day 30: collection of blood and urine sample. 2.5km for each course, resembling normal daily physical activity. 12 healthy males selected, age range: 35-56. City tour. Same as above. 13 healthy women selected, age range: 25-43. Forest bathing trip. Same as above.	Physiological analysis. • NK activity, NK number, and granulysin, perforin, and granzymes A/B were measured • Adrenaline concentration in urine was also determined. Phytoncides were measured.
Jin-Woo Han [1], Han Choi [1], Yo-Han Jeon [1], Chong-Hyeon Yoon [2], Jong-Min Woo [1,3], Won Kim [1,3] *1 Stress Research Institute, Inje University, Seoul, Korea* *2 Department of Rheumatology, Uijeongbu St. Mary's Hospital, Catholic University, Uijeongbu, Korea* *3 Department of Psychiatry, Seoul Paik Hospital, Inje University School of Medicine, Korea*	The Effects of Forest Therapy on Coping with Chronic Widespread Pain: Physiological and Psychological Differences between Participants in a Forest Therapy Program and a Control Group	Full-time employees between 25-49. 3 forest bathing trips+ 3 control groups. Day 1 of forest trip: pre-test measurements in the hospital, reach the site and, then, indoor and outdoor activities aimed at providing relaxation, refreshment, and attention restoration, plus music therapy and a psychoeducation on coping with pain and stress. Day 2: exercises and mindfulness-based meditation in the forest. The program ended with post-test measurements. Control group: pre- and post-measurements, but no psychological	Physiological measures. • Heart rate variation (HRV) measure through. electrocardiography electrode to measure HRV. • NK cells determined using the NK Vue-Kit. Psychological measures: • Pain through VAS Pain. • Depression through Beck Depression Inventory. • Health related quality of life through EQ-VAS.

		or therapeutic treatments and no visit to natural sites.	
Giuseppe Carrus [1], Massimiliano Scopelliti [2], Raffaele Lafortezza [3], Giuseppe Colangelo [3], Francesco Ferrini [4], Fabio Salbitano [5], Mariagrazia Agrimi [6], Luigi Portoghesi [6], Paolo Semenzato [7], Giovanni Sanesi [3] *1 Department of Education, Experimental Psychology Laboratory, Roma Tre University, Italy 2 Department of Human Studies, Libera Università Maria Ss. Assunta (LUMSA), Italy* *3 Department of Agricultural and Environmental Science, University of Bari, Italy* *4 Department of Agrifood Production and Environmental Sciences, University of Florence, Italy* *5 Department of Agriculture, Food and Forest Systems Management, University of Florence, Italy* *6 Department for Innovation in Biological, Agro-food and Forest systems, Tuscia University, Italy* *7 Department of Land, Environment, Agriculture and Forestry, University of Padua, Italy*	Go greener, feel better? The positive effects of biodiversity on the well-being of individuals visiting urban and peri-urban green areas	Selection of 4 green urban areas: 1= urban location, low biodiversity, 2= urban location, high biodiversity, 3= peri-urban location, low biodiversity, 4= peri-urban location, high biodiversity. Questionnaire for 569 visitors of the four parks.	Species richness, tree canopy, beauty, artificiality vs natural quality. Likert-type scale for: length and frequency of visits, crowding, main activity performed, perceived restorativeness, psychological and physical benefits experienced in the environment.
Martin L. Verra [1], Felix Angst [2], Trudi Beck [3], Susanne Lehm nn [4], Roberto Brioschi [5], Renata Schneiter [6], André Aeschlimann [7] *1 Director at the Physiotherapy Institute, Inselspital, Bern University Hospital, Switzerland, and research assistant at the rehabilitation clinic (RehaClinic), Bad Zurzach, Switzerland* *2 Head of research at RehaClinic, Bad Zurzach* *3 Lecturer in the Department of Social Sciences, Zurich University of Applied Sciences, Duebendorf, Switzerland* *4 Research nurse* *5 Clinical psychologist at RehaClinic, Bad Zurzach* *6 Professor in the School of Life Sciences and Facility Management, Zurich University of Applied Sciences, Wädenswil, Switzerland* *7 Medical director at RehaClinic, Bad Zurzach*	Horticultural Therapy for Patients With Chronic Musculoskeletal Pain: Results of a Pilot Study	79 patients of an interdisciplinary 4-week pain program in Zurich selected. 37 for a pain program with horticultural activities, and 42 as a control group (no horticultural therapy). The program has three main components: drug therapy, exercise therapy, and psychotherapy.	Tests used for pain and related disabilities: • The West Haven-Yale Multidimensional Pain Inventory (MPI) assessed the pain and its consequences in terms of symptoms, disability, activity, behaviour, mood, and social relationships. • The Medical Outcome Study Short Form-36 (SF-36) assessed the health-related quality of life (QOL).

			• The Hospital Anxiety and Depression Scale (HADS) assessed anxiety and depression. • The Coping Strategies Questionnaire (CSQ) assessed active and passive coping strategies. • Back Performance Scale (BPS) for participants with chronic back pain and the 6-minute Walk Test (6-MWT) for participants with fibromyalgia.
Jo Barton [1], Jules Pretty [1] *1 Interdisciplinary Centre for Environment and Society, Department of Biological Sciences, University of Essex, Colchester, UK*	What is the Best Dose of Nature and Green Exercise for Improving Mental Health? A Multi-Study Analysis	Literature review of 10 studies of the University of Essex. 1252 participants in total.	Psychological measurements. • Self-esteem with The Rosenberg Self-Esteem Scale (RSE). • Changes in mood with the Profile of Mood States (POMS). Duration of green exercise was measured and divided in subgroups. Age was a covariance.
Boram Kang [1], Taikon Kim [1], Mi Jung Kim [1], Kyu Hoon Lee [1], Seungyoung Choi [1], Dong Hun Lee [1], Hyo Ryoung Kim [2], Byol Jun [2], Seen Young Park [2], Sung Jae Lee [2], Si-Bog Park [1] *1 Department of Rehabilitation Medicine, Hanyang University College of Medicine, Seoul, Korea* *2 Department of Integrative Medicine, Korea University College of Medicine, Seoul, Korea*	Relief of Chronic Posterior Neck Pain Depending on the Type of Forest Therapy: Comparison of the Therapeutic Effect of Forest Bathing Alone Versus Forest Bathing With Exercise	64 subjects selected. 32 for Forest-bathing alone. 32 for Forest-bathing with exercise. Both groups walked 2h in the morning for 5 days. Forest-bathing with exercise group, for 2h each afternoon, did additional stretching and strengthening exercises targeting muscles in the cervical and shoulder regions. Measurements on the first and last day of therapy.	• Evaluation of pain level with VAS. • Neck pain affection to everyday activities with Neck Disability Index (NDI). • Assessment of individual's health status with EQ VAS/EQ index. • Self-reported measurements of pain with McGill Pain Questionnaire (MPQ). • The number of trigger points in the posterior neck region (TRPs). • Cervical range of motion C-ROM.
Chorong Song [1], Harumi Ikei [1,2], Miho Igarashi [1] Michiko Takagaki [1], Yoshifumi Miyazaki [1]	Physiological and Psychological Effects of	Each of the 23 males selected for the study walked in an urban park for 15	Physiological measurements.

1 Center for Environment, Health and Field Sciences, Chiba University, Kashiwa, Chiba, Japan *2 Forestry and Forest Products Research Institute, Matsunosato, Tsukuba, Ibaraki, Japan*	a Walk in Urban Parks in Fall	minutes and in a city area for 15 minutes. Questionnaires were completed before and after each walk. HRV was measured during the walk.	• Heart rate variability (HRV) measured with a portable electrocardiograph, together with High Frequency (HF) and Low Frequency (LF). Psychological measurements. • Profile of Mood State (POMS). • State-Trait Anxiety Inventory (STAI). • The semantic differential (SD) method to assess artificiality, relaxation and comfort.
Kimberly David Evans 1, Bill Douglas 2, Neville Bruce 3, Peter D. Drummond 1 *1 School of Psychology, Murdoch University* *2 Pain Clinic, Fremantle Hospital* *3 School of Anatomy and Human Biology, University of Western Australia, Perth, Western Australia*	An Exploratory Study of Changes in Salivary Cortisol, Depression, and Pain Intensity After Treatment for Chronic Pain	18 participants for a 4-week pain management program. Participants attended a 2-hour physiotherapy class each day, psychoeducational seminars, and relaxation training sessions. Saliva samples were taken on the 3 days before and on the 3 days after the program. Subjective responses were taken before and after the program.	• Pain perception assessed with Numerical Graphic Rating Scale (NGRS). • Depression assessed with Zung Self-Rating Depression Scale (ZSDS). • Health-related quality of life assessed with The Medical Outcome Study Short Form-36 (SF-36). • Total medication usage assessed with Medication Quantification Scale (MQS). • Salivary cortisol measurement.
Melissa R. Marselle 1,2, Katherine N. Irvine 2,3, Sara L. Warber 4 *1 Department of Psychology, Edge Hill University, Ormskirk, UK.* *2 Institute of Energy and Sustainable Development, De Montfort University, Leicester, UK.* *3 Social, Economic and Geographical Sciences Research Group, The James Hutton Institute, Aberdeen, UK.*	Examining Group Walks in Nature and Multiple Aspects of Well-Being: A Large-Scale Study	Walking for Health program in England. 1516 participants in total for a group walk (people who attended at least one group walk in a 13-week period of time) and a non-group walk (people not participating in a group walk for 6 months prior to the experiment and during it).	• Stressful life events assessed with The List of Threatening Experiences. • Frequency and duration of other nature walks assessed with a questionnaire. • Physical activity assessed with a questionnaire.

4 Department of Family Medicine, University of Michigan, Ann Arbor, Michecigan, USA		Measurements collated at the beginning of the study and 13 weeks later (end of the study).	• Depression assessed with Major Depressive Inventory (MDI). • Perceived stress assessed with the Perceived Stress Scale (PSS). • Negative and positive affect assessed with The Positive and Negative Affect Schedule. • Mental well-being assessed with Warwick Edinburgh Mental Well-being Scale. • Social well-being assessed with the Appraisal subscale of the Interpersonal Support Evaluation List (ISEL).
Nancy M. Wells [1], Kimberly A. Rollings [2], Anthony D. Ong [3], M. Carrington Reid [4] *1 Department of Design and Environmental Analysis, College of Human Ecology, Cornell University, Ithaca, NY, United States,* *2 School of Architecture, Department of Psychology, University of Notre Dame, Notre Dame, IN, United States* *3 Department of Human Development, College of Human Ecology, Cornell University, Ithaca, NY, United States* *4 Division of Geriatric and Palliative Medicine, Joan and Sanford I. Weill Department of Medicine, Weill Cornell Medical College, New York, NY, United States*	Nearby Nature Buffers the Pain Catastrophizing–Pain Intensity Relation Among Urban Residents With Chronic Pain	81 community-dwelling adults with chronic pain were enrolled. Chronic pain was most commonly due to lower back pain and osteoarthritis of the hip and/or knee. Participants completed a 14-day diary and questionnaires containing pain measures.	• Daily pain intensity assessed with a questionnaire. • Pain catastrophising assessed with a questionnaire that considered rumination, helplessness, and magnification. • Psychological resilience assessed with the Ego-Resiliency Scale. • Neuroticism assessed with the International Personality Item Pool (IPIP). • Nearby nature assessed with Google Maps. Time in nature, age and gender were considered.
Eric I. Rosenberg [1], Inginia Genao [2], Ian Chen [3], Alex J. Mechaber [4], Jo Ann Wood [5], Charles J. Faselis [6], James Kurz [7], Madhu Menon [8], Jane O'Rorke [9], Mukta Panda [10], Mark Pasanen [11],	Complementary and Alternative Medicine Use by Primary Care Patients with Chronic Pain	Self-reported current CAM (Complementary and Alternative Medicine) usage by 463 patients with chronic pain disorders. Cognitively impaired people excluded.	SF-36 Health Survey. Pain Self-Efficacy Questionnaire (PSEQ).

Lisa Staton [10], Diane Calleson [7], Sam Cykert [7] *1 University of Florida, Gainesville, Florida* *2 Yale University, New Haven, Connecticut* *3 Eastern Virginia Medical School, Norfolk, Virginia* *4 University of Miami, Miami, Florida* *5 University of Minnesota, Minnesota* *6 George Washington University, Washington, DC; 7 University of North Carolina at Chapel Hill, Chapel Hill, North Carolina* *8 University of Pittsburgh Medical Center, McKeesport, Pennsylvania* *9 University of Texas, San Antonio, Texas* *10 University of Tennessee College of Medicine-Chattanooga Unit, Chattanooga, Tennessee* *11 University of Vermont, Burlington, USA*			
Bum Jin Park [1], Yuko Tsunetsugu [2], Tamami Kasetani [3], Takahide Kagawa [2], Yoshifumi Miyazaki [1] *1 Center for Environment, Health and Field Sciences, Chiba University, Kashiwa, Japan* *2 Forestry and Forest Products Research Institute, Ibaraki, Japan* *3 Chiba Prefectural Agriculture and Forestry Research Center Forestry Research Institute, Haniya, Japan*	The physiological effects of Shinrin-yoku (taking in the forest atmosphere or forest bathing): evidence from field experiments in 24 forests across Japan	Experiments in 24 forests in Japan. In each experiment 6 people walked in a forest, 6 in a city. 280 young males in total. Day 1. About 15 minutes walking in the selected area. About 15 minutes viewing the landscape. Measurements before and after the walk, and before and after the view. Day 2. Cross-check study. Each subject did the same things in the other setting. Measurements before and after the walk, and before and after the view.	Psychological measurement. • Profile of Mood States (POMS), measuring: anxiety, depression, anger, fatigue and vigour. Physiological measurements. • Pulse rate, blood pressure, measured by a digital blood pressure monitor. • Heart rate variability (HRV), measured by a portable electrocardiograph. • High Frequency (HF), component of the parasympathetic nervous activity, and Low Frequency (LF)/HF, component of the sympathetic nervous activity. • Salivary cortisol concentration.
Min Ho Chun [1], Min Cheol Chang [1], Sung-Jae Lee [2]	The effects of forest therapy on depression and anxiety in	59 patients, manly male, average age of 60 years, recruited from a stroke welfare centre.	Psychological measures. • The Beck Depression Inventory (BDI) and The Hamilton

1 Department of Physical Medicine and Rehabilitation, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea *2 Department of Integrative Medicine, College of Medicine, Korea University, Seoul, Republic of Korea*	patients with chronic stroke	30 participants of a forest group, 29 for an urban group. 4 days, 3 nights. Forest therapy program consisted of: meditation, experiencing the forest through all five senses, and walking in the forest. The urban group: meditation and walking activities.	Depression Rating Scale (HAM-D17), both for depression. • Spielberger State-Trait Anxiety Inventory (STAI), for anxiety. Physiological measurements. • Reactive oxygen metabolites (d-ROMs) and biological antioxidant potentials (BAPs), associated with psychological stress.
Gregory N. Bratman 1, J. Paul Hamilton 2, Kevin S. Hahn 3, Gretchen C. Daily 4,5, James J. Gross 3 *1 Emmett Interdisciplinary Program in Environment and Resources, Stanford University, Stanford* *2 Laureate Institute for Brain Research, School of Community Medicine, Tulsa* *3 Department of Psychology, Stanford University, Stanford* *4 Center for Conservation Biology, Department of Biology, and Woods Institute, Stanford University, Stanford* *5 Global Economic Dynamics and the Biosphere, Royal Swedish Academy of Sciences, and Stockholm Resilience Centre, Stockholm, Sweden*	Nature experience reduces rumination and subgenual prefrontal cortex activation	38 participants (males and females, mean age = 26 years old) with no diagnosis of neurologic or psychiatric disorder invited to the experiment. 19 people for a 90-minute nature walk, 19 for a 90-minute urban walk. The urban walk took place in a busy thoroughfare, while the natural setting comprised grassland with scattered oak trees and shrubs. 10 photographs taken to evaluate the surrounding environment. Tests before and after walk.	Psychological measures. • Self-reported measure of rumination through the Reflection Rumination Questionnaire (RRQ). Physiological measurements. • Activity in the subgenual prefrontal cortex (sgPFC) by using a neuroimaging method called arterial spin labelling (ASL), able to detect effects associated with longer-lasting psychological phenomena such as rumination.

7. List of associations and researchers contacted by email

National Association of Drug Diversion Investigators (NADDI)	"NADDI does not conduct research or collect statistical data, thus could not be of any assistance to your project. The National Institutes of Health (NIH) and the Center for Disease Control and Prevention (CDC) may be the best resource for your project."
The National Institute of Environmental Health Sciences (NIEHS)	Follow-up email sent. No answer
Chronic Pain Association of Canada	"Our organization does not conduct studies. We provide education and advocacy for chronic pain patients. I'm sorry we cannot be of more help. If you complete your study and wish us to promote it via social media, please let us know and it can be passed through the proper channels."
American Academy of Pain Medicine (AAPM)	"Thank you for contacting the American Academy of Pain Medicine (AAPM). In response to your inquiry, any research that the Academy would have on this topic can be found in the *Pain Medicine* Journal. Please visit this link to browse through the journal: https://academic.oup.com/painmedicine/search-results?page=1&q=nature%20based%20treatment%20for%20chronic%20pain&fl_SiteID=5414&SearchSourceType=1&allJournals=1. Additionally, you might want to reach out to the following organizations. These organization are dedicated to patients with pain, and might have more research!" • Agency for Healthcare Research and Quality (AHRQ) • American Chronic Pain Association (ACPA) • Chronic Pain Research Alliance • National Association of Drug Diversion Investigators (NADDI) • Patient Mind Inc. • U.S. Pain Foundation
Pain Association Scotland	Follow-up email sent. No answer
World Institute of Pain	Follow-up email sent. No answer
American Society of Regional Anesthesia and Pain Medicine	"I have consulted with some of my colleagues and we do not have any resources on this subject. It is certainly an interesting topic to study. I also would be happy to connect you to people who might be able to help you share your findings."
Advancing Expert Care (Hospice and Palliative Nurses Association)	Follow-up email sent. No answer
American Society for Pain	Follow-up email sent. No answer

Management Nursing (ASPMN)	
Bateman Horne Center	Follow-up email sent. Reply: “At this time we do not have any studies like that. I’m sorry we can’t help”.
The British Pain Society	Follow-up email sent. No answer
The Australian Pain Society	“Unfortunately, the APS doesn’t have any research in this area and we wish you well on your literature review.”
Australian Pain Management Association	“Thanks for your email, but unfortunately we don't have anything that would be of use to you for your research. Wishing you the best in your studies.”
U.S. Pain Foundation	Follow-up email sent. Reply: “Unfortunately, we do not have any research regarding nature-based therapies.”
Chronic Pain Research Alliance	Follow-up email sent. No answer
Gyanunlimited: a Hub of Alternative Medicine and Holistic Health	Follow-up email sent. No answer
International Association for the Study of Pain (IASP)	“I’ve attached the resources page of our website. Here I hope you’ll to be able to find a source for more information on what you’re looking for. https://www.iasp-pain.org/Resources?navItemNumber=650”
American Chronic Pain Association	Follow-up email sent. No answer
Consiglio Nazionale delle Ricerche	“There is not much done on the beneficial effects of nature on patients with chronic pain, if not a very recent study by Johns Hopkins and published in the Journal of Alternative and Complementary Medicine, which says that sounds from nature can help this category of patients to live with the disease. In general, the beneficial effects of nature intended as environmental enrichment are well documented in the general population and during aging, increasing hippocampal neurogenesis, frontal cortex activity and promoting the quality of life and perceived well-being. A new line of research has recently opened from Japan, not tested on patients yet, but on healthy subjects which says that prolonged exposure to natural environments such as forests, for this goes by the denomination of Forest-Therapy, induce well-being inasmuch as nature releases substances that act on immune system by strengthening it. This is exactly what I am collaborating on with the University of Florence for a project that should start as soon as conditions allow. Last year I participated in a study that evaluated the effects of mindfulness intended as environmental enrichment in aged workers of various Tuscan municipalities to understand how the different rural and urban environments and could amplify the neurobiological effects of mindfulness and we found that those who live in rural contexts already had a greater predisposition to physical and mental awareness and a greater capacity for relaxation. These were healthy subjects, but surely if we could hypothesize an implication on patients suffering from chronic pain, also in that case nature, through sensory stimulation, could increase the benefits. There are many works on **mindfulness** and **fibromyalgia** for example. It is no coincidence that one of the protocols used, the **Snoezelen Method**, developed in Northern Europe for the management of

	neurodegenerative diseases and then applied to other pathologies, is based precisely on sensory stimulation coming from nature, a sort of virtual reality."
UNIVPM- Ufficio Ricerca (Research Office)	Follow-up email sent. Reply: "I have sent an email to the doctor Pamela Barbadoro. She turned the message to Anesthesiology even though her group may have data from the multipurpose on the spread of the use of herbal medicine / homeo / manual treatments in the general population with chronic pain and the associated variables". No reply from Barbadoro.
Cure-naturali (Natural treatments)	Follow-up email sent. Reply: "With regard to specific professionals who treat chronic pain with therapies and/or natural remedies, I have no contacts to report. However, I know a doctor who, here in Italy, has been dealing with this problem for years, is Dr. Enzo Primerano, here a reference: http://www.dolorecronico.org/. I would contact him for any further contacts and references or, even, have an answer to your questions."
Istituto di Medicina Naturale (Institute of Natural Medicine)	Follow-up email sent. No answer
Il Portale del Dolore Cronico (Chronic Pain Portal) by Enzo Primerano	Follow-up email sent. No answer
Vivere Senza Dolore (Live Without Pain)	Follow-up email sent. No answer
Lovell Rebecca, leader of the Defra Research Fellowship, studying human health and natural Environments	"We run a blog that has all our research https://beyondgreenspace.net/published-papers/, reports https://beyondgreenspace.net/reports-summaries/ etc on nature-health links. Two other good papers: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0203000 and https://www.sciencedirect.com/science/article/pii/S0013935118303323"
European Centre for Environment and Human Health, University of Exeter Medical School Knowledge	"Your email made its way to me. This sounds like an interesting piece of work. The best thing I would suggest is for you to have a look at our blog site: https://beyondgreenspace.net/ We write about our research there, and you can find links to lots of our published papers: https://beyondgreenspace.net/published-papers/ You also have expertise locally, for example Helen Hoyle who works in this area - https://people.uwe.ac.uk/Person/HelenHoyle "
Helen Hoyle	Follow-up email sent. No answer
Jessica Stanhope Author: *Exposure to greenspaces could reduce the high global burden of pain* Jessica.stanhope@adelaide.edu.au	"Thank you for your email, and apologies for my late reply. You are right there isn't a lot of evidence yet, but I may have some ideas to help you move forward. Are you available for a Zoom meeting on Thursday or Friday (Australian Central Time)? I think that's probably going to be easier than email or phone?" Very productive 1-hour interview conducted with Dr Stanhope, 11 September 2020.

Qing Li Author: *Effect of forest bathing trips on human immune function* qing-li@nms.ac.jp	"Please read my following books to get some information. Shinrin-Yoku in the UK by Penguin Random House https://www.penguin.co.uk/books/308285/shinrin-yoku Forest Bathing in the USA by Viking Books https://www.penguinrandomhouse.com/books/579709/forest-bathing-by-dr-qing-li/9780525559856/"
Nancy M. Wells Author: *Nearby Nature Buffers the Pain Catastrophizing–Pain Intensity Relation Among Urban Residents with Chronic Pain* nmw2@cornell.edu	Follow-up email sent. No answer
Kyu Hoon Lee Author: *Relief of Chronic Posterior Neck Pain Depending on the Type of Forest Therapy: Comparison of the Therapeutic Effect of Forest Bathing Alone Versus Forest Bathing With Exercise* dumitru1@hanyang.ac.kr	Follow-up email sent. No answer
Jin-Woo Han Author: *The Effects of Forest Therapy on Coping with Chronic Widespread Pain: Physiological and Psychological Differences between Participants in a Forest Therapy Program and a Control Group* moc.liamg@sserts.wjnah	Follow-up email sent. No answer