The impact of greenspace or nature-based interventions on cardiovascular health or cancer-related outcomes: A systematic review of experimental studies

Jean C. Bikomeye¹, Joanna S. Balza¹, Jamila L. Kwarteng²,³, Andreas M. Beyer³,⁴, Kirsten M. M. Beyer¹,³*,

¹ Division of Epidemiology & Social Sciences, PhD Program in Public and Community Health, Institute for Health & Equity, Medical College of Wisconsin, Milwaukee, WI, United States of America, ² Division of Community Health, Institute for Health & Equity, Medical College of Wisconsin, Milwaukee, WI, United States of America, ³ MCW Cancer Center, Medical College of Wisconsin, Milwaukee, WI, United States of America, ⁴ Division of Cardiology, Department of Medicine, Cardiovascular Center, Medical College of Wisconsin, Milwaukee, WI, United States of America

* kbeyer@mcw.edu

Abstract

Significance
Globally, cardiovascular disease (CVD) and cancer are leading causes of morbidity and mortality. While having different etiologies, CVD and cancer are linked by multiple shared risk factors, the presence of which exacerbate adverse outcomes for individuals with either disease. For both pathologies, factors such as poverty, lack of physical activity (PA), poor dietary intake, and climate change increase risk of adverse outcomes. Prior research has shown that greenspaces and other nature-based interventions (NBIs) contribute to improved health outcomes and climate change resilience.

Objective
To summarize evidence on the impact of greenspaces or NBIs on cardiovascular health and/or cancer-related outcomes and identify knowledge gaps to inform future research.

Methods
Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 and Peer Review of Electronic Search Strategies (PRESS) guidelines, we searched five databases: Web of Science, Scopus, Medline, PsycINFO and GreenFile. Two blinded reviewers used Rayyan AI and a predefined criteria for article inclusion and exclusion. The risk of bias was assessed using a modified version of the Newcastle–Ottawa Scale (NOS). This review is registered with PROSPERO, ID # CRD42021231619.
Results & discussion

Of 2565 articles retrieved, 31 articles met the inclusion criteria, and overall had a low risk of bias. 26 articles studied cardiovascular related outcomes and 5 studied cancer-related outcomes. Interventions were coded into 4 categories: forest bathing, green exercise, gardening, and nature viewing. Outcomes included blood pressure (BP), cancer-related quality of life (QoL) and (more infrequently) biomarkers of CVD risk. Descriptions of findings are presented as well as visual presentations of trends across the findings using RAW graphs. Overall studies included have a low risk of bias; and alluvial chart trends indicated that NBIs may have beneficial effects on CVD and cancer-related outcomes.

Conclusions & implications

(1) Clinical implication: Healthcare providers should consider the promotion of nature-based programs to improve health outcomes.

(2) Policy implication: There is a need for investment in equitable greenspaces to improve health outcomes and build climate resilient neighborhoods.

(3) Research or academic implication: Research partnerships with community-based organizations for a comprehensive study of benefits associated with NBIs should be encouraged to reduce health disparities and ensure intergenerational health equity. There is a need for investigation of the mechanisms by which NBIs impact CVD and exploration of the role of CVD biological markers of inflammation among cancer survivors.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of global morbidity and mortality [1,2]. In 2019, CVD accounted for approximately 18.6 million deaths globally [3]. In the 2020 Lancet global burden of disease (GBD) report, ischemic heart disease (IHD) and stroke, both CVD, were the top-ranked causes of disability adjusted life years (DALYs) in both 50–74 years and 75 years and older age groups [4]; and respectively responsible for 16% and 11% of the total global deaths, in 2019 [2]. In the US, 126.9 million adults had some form of CVD from 2015 and 2018 [3]. Costs associated with CVD from 2016 to 2017 totaled $363.4 billion ($216.0 billion in direct costs and $147.4 billion in lost productivity due to morbidity or mortality) [3]. In addition to the CVD burden, cancer was the sixth leading cause of global mortality in 2019, and a significant contributor to global morbidity [2]. Further, in 2020 alone, 19.3 million new cancer cases were diagnosed; and this number is expected to become 28.4 million cases in 2040, a 47% rise from 2020 [5]. There were almost 10.0 million cancer deaths in 2020 [5]. In 2017, the financial burden of cancer in the US was approximately 1.8% of gross domestic product or nearly $350 billion [6]. The cancer-related healthcare cost was $161.2 billion while the cost associated with premature mortality was $150.7 billion; and the cost of productivity loss from morbidity was $30.3 billion [6].

CVD and cancer have close co-morbid linkages due to multiple shared risk factors [7], which put cancer survivors at a disproportionate risk for CVD [1,8]. CVD and cancer are closely linked in a bidirectional causal relationship whereby having one of the diseases puts the patient at an increased risk of having the other [8,9]. With multiple common risk factors such as obesity, smoking, and inadequate or low physical activity (PA), co-occurrence of both diseases is a major clinical problem [8]. Each disease affects the treatment of the other, and therefore, has a detrimental impact on individual’s quality of life (QoL) and survival [8]. For
instance, cancer survivors have increased CVD risk due to cardiotoxic effects of some cancer treatment therapies such as anthracyclines [10,11] and increased risk for CVD mortality [12,13]. Vice versa, there is an increased risk for cancer incidence post CVD diagnosis [14].

Another commonality between CVD and Cancer is how both pathologies are impacted by the environment. In the 2019 GDB risk factor hierarchy, level 1 risk factors include behavioral, environmental or occupational, and metabolic factors [4]. Neighborhood social and built environments, including nature and greenspaces are key determinants of health and important factors in predicting health outcomes [15], including for CVD [16,17] and cancer [18]. Recent estimates suggest that 70% to 80% of CVD burden might be attributable to non-genetic environmental factors, such as lifestyle choices, socioeconomic status (SES), air pollution, lack of neighborhood greenness [19,20] and poorer residential neighborhood characteristics [21]

Neighborhood environmental factors play a key role in influencing obesogenic behaviors [22] such as “food deserts” where grocery stores and food choices are limited [23], and “food swamps” with high concentration of fast-food restaurants selling calorie-dense and nutrient deficient “junk food” with limited healthier food options [24]. Other environmental factors such as limited or poor-quality greenspaces [22,25] and safety concerns [26,27] may reduce use of greenspaces [28,29] and lead to inadequate PA [30]. The double burden of food deserti-

fication and food swamps, along with the abovementioned neighborhood-level social risk factors intersect in predisposing individuals to obesity [31]. Inadequate PA and obesity are the two main drivers of high levels of CVD [32,33] and cancer [34] in the US. Additionally, neigh-
borhood disadvantage exposes residents to chronic stress [35] which increases their risk to CVD [36,37] through different biological and pathological processes such as increased levels of cumulative burden of chronic stress and life events, known as allostatic load [38], higher levels of systemic inflammation and differential DNA methylation [39]. On the other hand, neigh-
borhood or community advantage, including increased access to greenspace has been associ-

ated with stress reduction [40] as well as weight loss and reduced obesity [41].

Neighborhood material deprivation or neighborhood disadvantage, including reduced neighborhood greenspace quality and quantity, and poor neighborhood social environments have been linked to an increased risk of CVD and cancer [42,43]. For example, in a study with a sample of 25–64-olds in Sweden, among whom 60% had lived at their current addresses for more than five years, neighborhood deprivation, measured by the Care Needs Index [44], was a predictor of CVD risk factors (i.e.: smoking, low PA, and obesity), except for hypertension (HTN) and diabetes that became non-significant in adjusted models [45]. After adjusting for individual level factors (i.e. age, gender, marital status, immigration status, urbanization, and SES), individuals living in highly deprived neighborhoods were significantly more likely to smoke, be physically inactive, and obese, compared to those living in moderately deprived neighborhoods [45]. Similarly, in another sample of Swedish adults aged 25–74 years (n = 73 159), followed from January 1st, 1990, to December 31st, 2008, age-standardized prostate cancer mortality rate was 1.5 times higher in men living in high-deprived neighborhoods than in those living in affluent neighborhoods [46]. Greenspace has been implicated in reducing socio-economic inequities that contribute to neighborhood deprivations [47]. It is important to note that Sweden is more or less of an egalitarian country, which might indicate that these relationships might have higher gradient in countries with high rates of socio-economic inequalities, such as the US [48].

In the US, neighborhood deprivation has been associated with adverse CVD and cancer outcomes [49,50]. In a study with a sample of 25–64 year-olds (1988–1994, n = 9,961), residing in a deprived neighborhood increased residents’ probability of having an adverse CVD risk profile, independent of individual’s SES [49]. Similar findings were observed in both the Jackson Heart Study [43] and the Dallas Heart Study [51]. In the Jackson Heart Study,
neighborhood disadvantages increased CVD risk in a socioeconomically diverse sample of African Americans [43]. For each standard deviation increase in neighborhood disadvantage, CVD risk increased by 25% (hazard ratio = 1.25; 95% confidence interval (CI) = 1.05, 1.49) [43]. In the Dallas heart study, a multilevel regression analysis with a sample of 1174 (18–65 year-olds); found that residing in more deprived neighborhoods was significantly associated with increased BP and incidence of HTN over time during a 9-year period [51]. Individuals living in more deprived neighborhoods had 1.69 times greater odds of developing HTN (OR = 1.69, 95% CI 1.02, 2.02) [51]. Further, in another study, authors used census tract data to investigate the relationship between a 10-year change (1990 to 2000) in neighborhood SES and mortality among 288,555 participating individuals, aged 51–70 years, who enrolled in the National Institutes of Health-AARP Diet and Health Study in 1995–1996 (baseline) and did not move during the study [50]. Mortality data were assessed by linking census tract data to the Social Security Administration Death Master File between 2000 and 2011. Improvement in neighborhood SES was associated with a lower mortality rate, while SES deterioration was associated with a higher mortality rate for both cancer and CVD [50].

Neighborhood built or social environments have been linked with cancer outcomes [18] through multiple studies. In their "Multi-level Biological and Social Integrative Construct (MBASIC)" framework, Lynch and Rebbeck integrated macro-environment (i.e.: health care policy, neighborhood, or family structure), individual factors (i.e.: behaviors, carcinogenic exposures, socioeconomic factors, and psychological responses) and biological factors (i.e.: cellular biomarkers and inherited susceptibility variants) to represent the multifactorial and complex nature of cancer etiology [52]. This model has been deemed essential in cancer etiology research [18]. Subsequent research has linked poor neighborhood built and social environments to adverse health outcomes across the entire cancer control continuum including cancer risk [53,54], cancer incidence [55,56], cancer diagnosis [57], cancer treatment [58], cancer survivorship [59], cancer survival [57,60], and cancer mortality [18,61].

In addition to poorly built or social neighborhood environments, global climate change is also adversely impacting health, including poorer CVD and cancer outcomes [62,63]. Extensive literature reviews suggest that increased temperature is associated with higher extreme weather events-related morbidity and mortality, particularly cardiovascular (CV) and respiratory events [64,65]. The higher burden of warmer temperatures on CV health includes increased risk of myocardial infarction (MI) [66] and mortality for IHD in North America [67]. A 2008 study found that for every increase of 4.7˚C in mean daily temperature, there was a 2.6% increase in CV mortality in California (95% confidence interval (CI): 1.3, 3.9) [67].

Greenspace is a major component of the built neighborhood environment and has been linked with increased neighborhood property values [68–70]. Additionally, greenspace has been linked with many positive health outcomes [71], including lower odds of being overweight or obese, a major risk factor for both CVD and cancer [41]. Some of empirically investigated benefits of greenspace on CV health include increased angiogenic capacity [72], reduced CVD risk [17,73], decreased CVD morbidity [74], and decreased CVD mortality [19,75,76]. Similarly, some of the benefits of greenspace on cancer outcomes include enhanced cancer prevention initiatives [77,78], reduced cancer incidence [78,79], improved cancer survivorship [78,80], and reduced prostate cancer mortality [81]. Additionally, greenspace helps in sequestering carbon and contributing to greenhouse gases reduction, therefore is a viable intervention for the adverse impacts of climate change on both environmental and human health [82].

There is growing literature evidence on the impact of greenspace on improving clinical outcomes in CVD and cancer patients through different interventions such as “park prescription” programs and other nature-based interventions (NBI) [83–86]. Some of this evidence was found through experimental studies, suggesting possible causal relationships, and
opportunities for specific interventions to improve CVD and cancer-related health outcomes. However these experimental studies have not yet been systematically reviewed to bring all existing evidence together [1]. In this review, we sought to systematically summarize findings from experimental studies with greenspace interventions and identify potential literature gaps for future research. We use an expanded definition of greenspace exposure that include forest bathing, nature viewing, nature visit, parks visits, gardening, etc. We conducted a systematic review of studies that have investigated the impact of greenspace or NBI on two main health outcomes: CVD and cancer. CVD outcomes include morbidity and mortality across different CVD conditions. Cancer-related outcomes include different measures across the cancer control continuum including cancer risk, prevention, detection, diagnosis, treatment, survivorship, end of life or mortality, as well as cancer-related QoL.

2. Methods

This review followed a pre-defined protocol that was developed following the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) statement and checklist [87,88]; and was pre-registered with PROSPERO, ID # CRD42021231619. This review then followed the PRISMA 2020 reporting guidelines [89]. The PRISMA chart is illustrated in Fig 1; and the PRISMA 2020 27-items checklist is annexed in Appendix A.

2.1. Literature search

A comprehensive literature search was developed in collaboration with a medical librarian and peer reviewed using the Peer Review of Electronic Search Strategies (PRESS) guideline [105]. The following citation databases were searched on March 10th, 2021: Web of Science, Scopus, Medline, APA PsycINFO, and GreenFile. Searches were limited to articles written in English. Databases were chosen because we sought to include all citation databases of peer-reviewed literature with comprehensive citation data for many different academic disciplines (Web of Science), source neutral literature curated by independent subject matter experts (Scopus), medical sciences from the National Library of Medicine’s bibliographic database (Medline), literature in the field of psychology (PsycINFO) and literature focused on nature or greenspace.
Search strategies were created using medical subject headings (MeSH) and keywords combined with database-specific advanced search techniques. MeSH terms and keywords were identified to represent greenspace interventions, CVD, and cancer. Keywords related to greenspace or NBI (i.e.: park prescription, wilderness therapy, forest bathing, forest therapy, green exercise, etc.), CVD outcomes (i.e.: heart failure (HF), stroke, coronary artery disease (CAD), MI, cardiac arrest, major adverse CV event (MACE), etc.) and cancer-related outcomes (i.e.: cancer prognosis, cancer incidence, cancer mortality, etc.). A full search strategy is annexed in Appendix B.

A total of 2565 results from literature searches (Medline: 348, PsycINFO: 68, Scopus: 1161, Web of Science: 972 and Greenfile: 16) were downloaded into EndNote where duplicate articles ($n = 1126$) were removed. 1439 unique publications were uploaded into Rayyan AI, an online tool for systematic review [90,91] available at https://www.rayyan.ai/. The web app facilitated article screening and eased collaboration between two independent reviewers.

### 2.2. Article selection process

The following PICO framework [92] of inclusion and exclusion criteria was followed:

- **P (Population):** No restriction. All ages, genders, races/ethnicities, healthy or diseased individuals are included.

- **I (Interventions):** Exposure to greenspace or NBIs such as forest bathing, greening exercise, nature viewing, or gardening.

- **C (Comparison):** All types of controls, or simple pre-post experiments without formal controls.

- **O (Outcomes):** CVD or cancer-related outcomes

1. CVD related outcomes include BP and MACE, as defined in previous studies [93–95] including: occurrence of fatal and nonfatal MI, HF, cerebrovascular disease or CV accident or stroke (fatal and nonfatal), and coronary artery bypass grafting (CABG) and cardiac arrest. Both preventive measures (indicators of good CV health among healthy individuals) and restorative measures (indicators of improved CV health among individuals with CVD) are all considered.

2. Cancer-related outcomes include lifestyle changes (i.e., gardening continuation after intervention) and QoL during cancer survivorship, and cancer outcomes (i.e.: cancer prognosis, cancer incidence, cancer mortality, etc.). We used the National Cancer Institute definition of cancer survivorship in defining the cancer survivor’s population which proposes that survivorship starts the first time the patient was told by a healthcare provider that they have cancer until the end of life [96].

Since the overall goal of the review is to look at the impact of interventions on outcomes, Using Rayyan, search results were systematically screened by two reviewers (J.C.B and J.S.B) to determine eligibility. Reviewers first screened articles’ titles against eligibility criteria, excluding any article that did not clearly meet the PICO criteria by reading articles’ titles. Conflicts were resolved and the process was repeated, screening full abstracts, and then article’s methods section. If a conflict could not be resolved between the two reviewers, a third mediator (KMMB) was consulted. Finally, the reference lists of all included articles were screened to identify relevant publications not retrieved by electronic database searches.

### 2.3. Eligibility criteria

Inclusion and exclusion criteria are summarized in Table 1.
2.4. Data extraction and reporting

Extracted data are summarized in Tables 3 and 4 and include: (1) Studies’ geographical information (City, state, country); (2) Studies’ urbanicity setting (rural, semi-urban, or urban) where applicable; (3) type of greenspace or nature-based interventions + controls description where applicable, (4) assumptions made or hypotheses; (5) Measures of any CVD related outcome (incidence, morbidity, or CVD related mortality); (6) Measures of any cancer-related outcome (anything from the cancer control continuum, cancer-related quality of life (QOL), or cancer-related mortality; (7) cancer type under investigation (specific or any type); (8) Covariates adjusted for including (a) individuals level variables such as demographic information (when available); socioeconomic information (when available); comorbidity information (when available); and (b) neighborhood factors (when available) such as social environment factors, and other neighborhood-built environment characteristics; (9) Statistical analyses conducted; (10) Studies strengths and weaknesses. We used the following information to create alluvial charts as a visual representation of trends across studies by outcomes of interest, a method that was previously used in previous systematic reviews [97]:

1. Article reference
2. Study country
3. Intervention type
4. CVD outcomes or cancer-related outcomes
5. Conclusion (weather a statistical test found the intervention to be significantly beneficial: Beneficial effect, or no statistically significant difference between control and experimental groups: Not significant; or whether beneficial changes were observed in the control group instead of in the interventional or experimental group: Significant in controls.

Two excel datasets used to create alluvial charts for (1) CVD, and (2) cancer-related outcomes are respectively annexed in Appendices C1 and C2.

3. Results

3.1. PRISMA 2020 chart illustrating our articles screening process

From 2,565 articles initially retrieved from database searches, 31 articles meeting our pre-defined criteria remained after screening, as illustrated in Fig 1. At the abstract screening stage, 45 articles were excluded because they did not meet at least one of our pre-defined
Table 2. Risk of bias assessment of included studies using a Modified version of the Newcastle–Ottawa Scale.

| Study: Author (year) | Final score | Representativeness of exposed group Non-exposed group | Ascertainment of exposure | Baseline difference | Groups compatibility | Outcome assessment | Exposure duration | Groups follow up |
|----------------------|-------------|-------------------------------------------------------|---------------------------|---------------------|---------------------|--------------------|-------------------|-----------------|
| 1 Mao et al., 2012 [100] | 9           | 1 1 1 1 1 2 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 2 Navalta et al., 2019 [101] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                              |                           |                     |                     |                    |                   |                 |
| 3 Engell et al., 2020 [102] | 5           | 0 1/2 1/2 1/2 0 1 1 1 1                              |                           |                     |                     |                    |                   |                 |
| 4 Duncan et al., 2014 [103] | 6.5         | 1 1/2 1/2 1/2 1/2 1 1 1 1                            |                           |                     |                     |                    |                   |                 |
| 5 Furuyashiki et al., 2019 [104] | 4           | 1 0 0 0 0 0 1 1 1                                   |                           |                     |                     |                    |                   |                 |
| 6 Grazuleviciene et al., 2016 [105] | 9           | 1 1 1 1 1 2 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 7 Lee et al., 2011 [106] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                              |                           |                     |                     |                    |                   |                 |
| 8 Li et al., 2016 [107] | 5           | 0 1/2 1/2 1/2 0 1 1 1 1                              |                           |                     |                     |                    |                   |                 |
| 9 Mao et al., 2017 [108] | 9           | 1 1 1 1 1 2 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 10 Mao et al., 2012 [109] | 9           | 1 1 1 1 1 2 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 11 Niedermeier et al., 2017 [110] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                            |                           |                     |                     |                    |                   |                 |
| 12 Chen et al., 2018 [111] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 13 Ochiai et al., 2015 [112] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 14 Peterfalvi et al., 2021 [113] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 15 Pretty et al., 2005 [114] | 8           | 1 1 1 1 1 1 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 16 Song et al., 2018 [115] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                            |                           |                     |                     |                    |                   |                 |
| 17 Tsutsumi et al., 2017 [116] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 18 White et al., 2015 [117] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                            |                           |                     |                     |                    |                   |                 |
| 19 Bielnis et al., 2019 [118] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 20 Yu et al., 2017 [119] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 21 Koura et al., 2016 [120] | 4           | 1 0 0 0 0 0 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 22 McEwan et al., 2021 [121] | 6           | 1 ½ 1/2 1/2 0 1 1 1 1                             |                           |                     |                     |                    |                   |                 |
| 23 Park et al., 2017 [122] | 7.5         | 1 1 1 1 1 1 1 1 1                                  |                           |                     |                     |                    |                   |                 |
| 24 Song et al., 2013 [123] | 6           | 1 1/2 1/2 1/2 0 1 1 1 1                            |                           |                     |                     |                    |                   |                 |
| 25 Wu et al., 2020 [124] | 9           | 1 1 1 1 1 2 1 1 1                                  |                           |                     |                     |                    |                   |                 |
inclusion criteria. Each one of the excluded studies was either not experimental, or not looking at one of the outcomes of interest.

### 3.2. Risk of bias assessment

The risk of bias for 31 included studies was assessed using a modified version of Newcastle–Ottawa Scale (NOS). Two reviewers (J.C.B. and J.S.B.) independently assessed articles on eight pre-defined items including representativeness of exposed cohort, similarity of cohorts’ origins, similarity of exposed vs non-exposed cohorts (compatibility), ascertainment of exposure, baseline differences, outcome assessment, exposure duration (enough to observe outcome), and cohorts follow up.

#### Table 2. (Continued)

| Study: Author (year) | Final score | Representativeness of exposed group | Non-exposed group | Ascertainment of exposure | Baseline difference | Groups compatibility | Outcome assessment | Exposure duration | Groups follow up |
|----------------------|-------------|------------------------------------|-------------------|--------------------------|---------------------|---------------------|-------------------|------------------|-----------------|
| 26 Lanki et al., 2017 [125] | 6 | 1 | 1/2 | 1/2 | 0 | 1 | 1 | 1 | 1 |
| 27 Bail et al., 2018 [126] | 7 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 |
| 28 Blair et al., 2013 [127] | 4 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| 29 Demark-Wahnefried et al., 2018 [128] | 8 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 30 Li et al., 2008 [129] | 6 | 1 | ½ | ½ | 0 | 1 | 1 | 1 | 1 |
| 31 Li et al., 2007 [130] | 4 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| Average (±SD) Score | 6.0 (±1.8) | | | | | | | | |

**Item assessment description:**

Representativeness of exposed group: One star was given if the study population reflected the title or abstract of the article (i.e., the group is representative (or somewhat representative of the community average). For example, a study that only used male subjects, but the title/abstract did not specify that the ‘community’ was males (leaving room for confusion), did not receive a star. However, a study that said in the title they were assessing results in a “population of healthy young males” and then used healthy young males, did receive a star.

Non-exposed group: One star was given if two groups (exposed or not exposed) were drawn from the same population. Half of a star was given if the same group served as the control group (on a different day or time in which they were not exposed to the intervention). No star was given if it was a simple pre-exposure and post-exposure measurement with no control group OR if the two groups (exposed or not exposed) were not drawn from the same population.

Ascertainment of exposure: One star was given for studies where participants were randomly assigned to be in control or exposure group. Half of a star was assigned if the same sample was the control one day then the experiment another day or time, or if the two groups were similar but not random. No star if there was no control group.

Baseline difference: One star was given if there was a control group, and there was no baseline difference. Half a star was given if the same group served as their own controls, by repeating the experiment twice, once with exposure and once without (as a control) and there was no difference at baseline. No star given if there was no control group, there were differences between the group at baseline, or if this was not reported.

Compatibility and controlling factors between groups: If the study design controlled for two or more factors in both groups that may have impacted the outcome (i.e., diet, caffeine, sleep) they were given 2 stars. If they had two compatible groups but controlled for only one or no factors, they were given one star. No star was given for simple preexposure/postexposure tests with no control group.

Outcome assessment: One star was given if the study clearly defines outcomes and how they were assessed.

Exposure duration: One star was given if raters perceive that exposure duration was long enough to observe differences in outcomes.

Cohorts follow up: One star was given if all subjects were followed up until completion or if there if raters perceive the number of subjects lost to follow as small enough to not introduce any bias.
Table 3. Characteristics for 26 studies with Cardiovascular outcome.

| Author and year | Country, City, State/Urbanicity setting | Sample Size | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention Green space description | Exposure description | Hypothesis/Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses
|-----------------|----------------------------------------|-------------|------------|--------------------|------------------------|--------------------------------------|---------------------|----------------------|-------------|---------------------|----------------------|----------|-------------------|
| Mao et al., 2012 | Hangzhou city, Zhejiang Province, China Urban | n (± 24: 12 for both the control and the experimental groups) | Experimental study | 7 days duration from 23 to 30 July 2011 | Age 60 to 75 years | Forest bathing Two daily pre-determined unsurpassed pace walks for 1.5h with 20 minutes rest during the walk, one in the morning and another one in the afternoon. Participants had a pre-determined daily schedule for the 7 days | A broad-leafed evergreen forest experience whereby predominant species are Ormosia hosiei, Cinnamomum camphora, Magnolia officinalis, subsp., bobea, and Nyssa sinensis. The control group was sent to an urban area | There is a therapeutic effect of forest bathing on hypertension in elderly subjects. | Demographic factors: Age, body mass index, Socioeconomic: N/A | HTN BP indicators, CV disease-related pathological factors including endothelin-1, homocysteine, angiotensinogen, angiotensin II, angiotensin II type 1 receptor, angiotensin II type 2 receptor as well as inflammatory cytokines interleukin-6 and tumor necrosis factor alpha (TNF-α) | Kolmogorov-Smirnov test and Levene’s test were respectively used for normality and homogeneity of variances test for comparison between two groups Mann-Whitney U test or Wilcoxon Signed Ranks test for two independent or related samples | No baseline difference in all biomarkers investigated. Participants who experienced a 7-day forest bathing trip showed a significant decrease in systolic BP (SBP) and diastolic BP (DBP) compared with that of the city group. Pulse pressure decreased No change in heart rate (HR) | Limitation of participants site and age range. Forest bathing has therapeutic effects on HTN reduces BP and prevents CV disorders. |
| Navalla et al., 2019 | USA State and city not specified Urban | n (7 males and 3 females) | Experimental study | 30 mins | Age 29.2 (± 7.3) | Walk in green and brown environments for 30 mins self-paced walking (WALK) in indoor, outdoor urban, green, and two brown environments. No control group (use of repeated measures in different environments) | Exercise in a natural setting would provide similar beneficial psychophysiological and perceptual effects. | Demographic factors: Age, Height, and mass Socioeconomic: N/A | Comorbidity: N/A | Environmental factors: N/A | HR, BP, and measures of stress, comfort, and calm | Analysis was done with a 3 (Time: Pre-ST, Post-ST, Post-Walk) X 5 (Environment: Indoor, urban, green, brown, brown below sea level) ANOVA with repeated measures on both factors. HR was elevated in urban vs. green (p = 0.05) SBP was lower after ST compared to PRE and WALK (p = 0.05) | No limitation lies on the study population and small number of population, budget limitations. The study was supplemented in a natural setting which includes ambient noise, the presence of non-study personnel, past memories of visits to the particular setting, physical discomfort, and odors. Exercise in a desert environment is as beneficial as exercise in a green environment. |
| Engell et al., 2020 | Norway Urbanicity not specified Urban | 9 male students | Experimental study | 7-days | Age: mean (SD) = 23.35 (± 2.34) | View of a modest natural environment while sitting after physical exertion | A window view with a forest dominated while sitting after physical exertion. The field land and forest were fully or partially covered in snow in all seasons. No control group (All participants were engaged in the same activity) | Three hypotheses 1) Resting with a window view of a natural environment improves cognitive function 2) Taking a break in front of a window, viewing a natural environment after minor physical activity produces more efficient heart rate responses. 3) Taking a break in front of a window, viewing a natural environment after minor physical activity causes reduced heart rate responses. | Demographics and potential confounders (amount of sleep, mood state, current health, exercise history current week, consumption of potentially confounding substances) Socioeconomic factors: N/A Comorbidity: N/A | Measures of choice reaction time (CRT) and HR variability (HRV): intervals between successive heartbeats | Within-subjects repeated measures and HR Wilcoxon signed-ranks test with rank-frerated correlation Improvements in CRTs and HR after resting with a window view and compared to resting without a view Suggests greater effect of cognitive enhancement and physiological restoration in resting after exercise with view to natural environment. | No limitation of participants site and age range. Limitation: Most sample size Cognitive enhancement and physiological restoration after exercise in resting with a window view of a natural environment compared to resting without its view. |

(Continued)
| Author and year | Country, City, State, Urbanicity setting | Sample Size | Study type | Follow-up duration | Age (Mean ± SD, years) | Intervention | Greenspace description + Greenspace type and Control group | Exposure | Hypothesis/ Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses | Conclusions |
|----------------|------------------------------------------|-------------|------------|-------------------|------------------------|-------------|-------------------------------------------------------------|----------|------------------------|------------|----------------------|---------------------|----------|----------------------|-------------|
| Dong et al., 2014 [103] | Coventry, UK Urban | 14 children (7 boys, 7 girls) | Experimental study | 15 min | 10 (± 1) | Exercise in green environment | Control condition: viewing a blank screen. Experimental condition: watching a film of cycling in a forest environment (Through the Forest World of Nature). Participants in control scenario wore virtual reality glasses to maintain moderate intensity of 15 min. | Changes in POMS items: Pressure, Restlessness, Vigor, Fatigue, and Depression. | N/A | Socioeconomic factors: Gender, Education, Occupation, Income, and Marital Status. | Environmental factors: N/A | Randomized controlled trial | No difference in POMS items between experimental and control groups. | Limitations: Study was conducted in a controlled environment, which may not reflect real-world conditions. |
| Burry et al., 2019 [104] | Hiroshima City, Japan Urban | 61 | Experimental study | 16 – one-day long sessions for 3 years (2012 – 2014) | Age range: 19–39 Mean: 44.0 ± 9.6 | Forest bathing | Within a national park, Vegetation: natural forests with a temperate climate. No control group. Authors collected measurements of outcomes before and after a forest bathing intervention. | There are physiological and psychological effects of forest bathing on people of working age with and without depression tendencies. | N/A | Demographic factors: Age, Gender, and SES. | Environmental factors: N/A | Cluster-randomized trial | Reduction in depression scores after forest bathing. | The limitations of this study include the potential for selection bias, as only people who choose to participate in forest bathing may differ from those who do not. |
| Guarino et al., 2016 [105] | Kaunas City, Lithuania Urban | 20 male and female half in experimental and half in control groups | Experimental study | 7 days | 45–75 years Mean: 62.3 (± 12.6 years) | Green exercise: City Park or urban street environment | Green space exposure: urban park environment (green park terrain). Control group was exposed to an urban street environment. | Changes in HR and BP were measured before and after walking in a city. | N/A | Demographic factors: Age, Gender, and SES. | Environmental factors: N/A | Randomized controlled trial | Reduction in HR and BP after forest bathing. | Limitations of this study include the small sample size and the potential for selection bias, as only people who choose to participate in forest bathing may differ from those who do not. |
| Ito et al. 2011 [106] | Hokiolo, Japan Urban | 12 males half in experimental and half in control groups | Experimental study | 15 min exposure to forest or urban environmental stimuli (observation period) 3 day – 2 night field experiment | 21.2 (± 9.9) years | Forest bathing and urban control: 15 minutes of viewing an urban or forest stimuli (12 – 14th September 2006). | Changes in HR and BP were measured before and after walking in a city. | N/A | Demographic information: Age, Gender, and SES. | Environmental factors: N/A | Randomized controlled trial | Reduction in HR and BP after forest bathing. | Limitations of this study include the small sample size, which may lead to weak statistical power, the potential for selection bias, as only people who choose to participate in forest bathing may differ from those who do not. |

*Note: Table continues on the next page.*
| Author and year | Country, City, State | Sample Size | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention | Exposum description, Green space type and Control group | Exposure duration | Hypothesis/ Assumption | Covariates | Statistical Analyses | Findings | Strengths & Weaknesses | Conclusions |
|----------------|----------------------|-------------|------------|-------------------|------------------------|-------------|------------------------------------------------------|------------------|-------------------------|------------|------------------------|----------|-----------------------|-------------|
| Li et al., 2016 [107] | Agematso, Nagano Prefecture, Japan Urban | 19 males | Experimental study | 4 weeks | 51.2 (± 8.8) | Forest bathing | Walking for 2.6 km for 80 min each in both morning and afternoon on Saturdays | Forest Environment: forest park. The control group was sent to the urban region with no trees | Walking in a forest environment would improve cardiovascular function. | Demographic factors: Age, Height (cm), Body weight (kg) BMI Socioeconomic factors: Smoking status Comorbidity: N/A Environmental factors: N/A | CV parameters BP and PR Mood state (POMS) Metabolic parameters: Urinary adrenaline; Urinary dopamine; Serum adiponectin | Paired t-test | Forest bathing reduces PR, increases vigor, and decreases depression, fatigue, anxiety, and confusion. After forest bathing, there is decrease of Urinary adrenaline and Urinary dopamine compared to urban walking. The increase in Serum adiponectin. | The limitation is that the order of exposure was not controlled or counterbalanced. Sample size is not large enough. Forest bathing has a positive effect on health and psychological and physiological situation. |
| Mao et al., 2017 [108] | Hangzhou City, China Urban | 33 | Experimental study | 4 days: From 20 to 24 August 2015 | Forest bathing | Forest bathing is thought to be beneficial to CAD patients, such as those with chronic heart failure, and may even provide therapeutic advantages. | Demographic factors: Age, Gender, Height, Weight, BMI Socioeconomic factors: New York Heart Association Class Comorbidity: N/A Environmental factors: N/A | Chronic HF Biomarkers for BP BNP and NT-Pi BNP, CV disease-related factors Oxidative indicators Profile of Mood States Air quality | Kolmogrov-Smirnov test and Levene's test were respectively used for normality and homogeneity of variance. t-test for comparison between two groups Mann-Whitney U test or Wilcoxon Signed Ranks test for two independent or related samples Chi-squared test for count data Kruskal-Wallis test for multi-group comparisons with p < 0.05 Bonferroni adjustment | Forest bathing decreases brain norepinephrine (NE), and components of the renin-angiotensin system (RAS) including renin, angiotensin I, angiotensin II and AngII receptor type 1 or 2 (AT1 or AT2), inflammatory cytokines including interleukin-6 (IL-6) and TNF-α, and other markers of oxidative stress. | Forest bathing reduces brain norepinephrine (NE), and components of the renin-angiotensin system (RAS) including renin, angiotensin I, angiotensin II and AngII receptor type 1 or 2 (AT1 or AT2), inflammatory cytokines including interleukin-6 (IL-6) and TNF-α, and other markers of oxidative stress. Limitations are small sample size, indicators were measured in a specific time, climatic factors were not controlled. Forest bathing has a therapeutic role for CV disorders. |
| Mao et al., 2017 [109] | Zhejiang, China Urban | 20 male university students | Experimental study | 2 days | 20.79 (± 1.54 years) | Forest bathing | Broad-leaved evergreen forest with urban area controls. The control group was sent in urban city. | There are yet to be any direct demonstration of whether forest bathing has any other health benefits | Demographic factors: Age, weight, BMI Socioeconomic factors: N/A Comorbidity: N/A Environmental factors: N/A | Serum total SOD Lipid peroxidation (malondialdehyde) Serum and plasma Serum cortisol and testosterone Lymphocyte assay The profile of mood states (POMS) | Kolmogrov-Smirnov test and Levene's test were respectively used for normality and homogeneity of variance. t-test for comparison between two groups Mann-Whitney U test for non-normally distributed data | There were no differences in baseline values for all biomarkers between the two groups. There's reduction of oxidative stress and pro-inflammatory level compared to those exposed in forest Serum cortisol levels were lower for the forest group than those of urban area. Concentration of plasma endothelin-1 (ET-1) was lower than those in forest group. Increased vigor after exposure to forest and POMS lower after the forest exposure. | There were no differences in baseline values for all biomarkers between the two groups. There's reduction of oxidative stress and pro-inflammatory level compared to those exposed in forest Serum cortisol levels were lower for the forest group than those of urban area. Concentration of plasma endothelin-1 (ET-1) was lower than those in forest group. Increased vigor after exposure to forest and POMS lower after the forest exposure. Limitations: small sample sizes, results don't reflect in old or rural people, climatic data such as air pollution, air quality not considered. Forest bathing has benefits to human health. |
| Author and year | Study Type | Sample Size | Country | Site | Setting | Age (Mean ± SD, years) | Sex | Follow up duration | Intervention Greenspace type | Age | Hypothesis/Assumption | Findings | Strengths & Weaknesses |
|----------------|------------|-------------|--------|-----|--------|------------------------|-----|-------------------|----------------------------|-----|----------------------|----------|----------------------|
| Ochiai et al., 2017 | Randomized controlled trial study | 42 | Innsbruck, Austria | Mountain hiking | 56 (± 13.0) | Forest bathing | Natural forest | Pre-treatment | 3 hours | Mountain hiking | Decrease in HRV and BP, no significant differences in salivary cortisol levels between groups. The control group showed an increase in cortisol. | Limitations: small sample size, lack of control group, insufficient duration of intervention. |
| Peterfalvi et al., 2021 | Cross-over design | 12 | Nagano Prefecture, Japan | Mountain hiking | 48.61 (± 10) | Forest bathing | Natural forest | Pre-treatment | 2-day | Forest bathing therapy program | Decrease of SBP and HRV, increase of Vigor and Mood | Limitations: small sample size, lack of control group, insufficient duration of intervention. |
| Ochiai et al., 2015 | Pre-test post-test design | 16 female | Nantou, Taiwan | Forest bathing | 38.5 | Forest bathing | Natural forest | Pre-treatment | 2-day | Forest bathing therapy program | Decrease of HRV and BP, increase of Vigor and Mood | Limitations: small sample size, lack of control group, insufficient duration of intervention. |
| Ochiai et al., 2018 | Pre-test post-test design | 7.83 (± 1.53) | Nantou, Taiwan | Forest bathing | 40.61 (± 10) | Forest bathing | Natural forest | Pre-treatment | 1 day | Forest bathing therapy program | Decrease of HRV and BP, increase of Vigor and Mood | Limitations: small sample size, lack of control group, insufficient duration of intervention. |

(Continued)
### Table 3. (Continued)

| Author and year | Country, City, Setting | Sample Size | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention | Exposure description | Hypothesis/Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses |
|-----------------|------------------------|-------------|------------|--------------------|-----------------------|--------------|---------------------|----------------------|------------|--------------------|----------------------|----------|------------------------|
| Pretty et al., 2005 [14] | Colchester, UK Urbanicity not specified | 100 (55 female, 45 males) | Experimental study | 24.6 (± 9.9) | Green exercise: With controls running without exposure to scenery images | Randomized exposure to a sequence of 30 scenes projected on a wall whilst exercising. The scenes were categorized as rural, pleasant, rural unpleasant, urban pleasant, urban unpleasant. The control group was set to run without being exposed to any visual. | There may be a synergistic benefit to engaging in physical activities while being directly exposed to nature. | Demographic factors, Age, Socioeconomic factors, N/A Comorbidity, N/A Environmental factors, N/A | BP and two psychological measures (self-esteem and mood) | One-way ANOVA test | No significant differences in any of the measures between the groups before the intervention. Reduced BP, increased self-esteem. Rural and urban pleasant scenes of exercise than exercise-only control. Green exercise has benefits of exercise. Limitation: no exposure to real scenes of environment, while considering types of duration, intensity of physical activity. Greens exercise has important health benefits. |
| Song et al., 2018 [15] | Japan [Noda Hospital], Urbanicity not specified | 14 patients (Males, 4 females, 10) | Experimental study | 78.6 (± 9.6) | Nature viewing: Bonsai was used as visual stimuli | Bonsai has characteristic of mimicking natural landscapes and has been used in daily life in Japan since a long time ago. Japanese cypress bonsai trees. The control group had no experimental stimulus. | Viewing bonsai induces relaxation | Demographic factors, Age, gender, Socioeconomic factors, N/A Comorbidity, N/A Environmental factors, N/A | Autonomic nervous activity, HR, PR, Prefrontal cortex activity | Paired t-tests were used to compare physiological responses between before and after viewing bonsai (pre- vs post-measurement) and between the two stimuli (bonsai vs. control) while Wilcoxon signed-rank test was used to compare psychological responses. | Increased parasympathetic nervous activity. Decreased sympathetic nervous activity. Increased perceptions of feeling “comfortable” and “relaxed.” | Limitation: studying psychological responses while viewing bonsai in healthy young people, small sample size. Viewing bonsai induces physiological and psychological relaxation. |
| Tsutsumi et al., 2017 [16] | Japan, Urbanicity not specified | 12 healthy men | Experimental study | 22.2 (± 1.7) | Nature viewing: Divided into two groups of 6 each and exposed to either rural or forest scenery using the Visual Analogue Scale based on individual preference | Stimulation by viewing an individual’s preferred video or forest scenery. Watch 90 min DVDs of sea with natural sounds and forest with natural sounds. No control groups. Two groups of six based on their preference for rural or forest scenery and each indicator was compared between them by using a pre post study design. | Viewing an individual’s chosen film of the sea or forest has an influence on relaxation. | Demographic factors, Male gender, Socioeconomic factors, N/A Comorbidity, N/A Environmental factors, N/A | HRV Biotracer Index System, Description statistics, Wilcoxon Signed-Rank test for the R-Pain, POMS and the Multi-trait-Method U-test for the HK, HJ, and RS were used | Differences in a decrease in HR, increase in high frequency, and sustained arousal level | Limitations: Healthy men in 30s, age range limited, no use of videos of personal preference. Viewing an individual’s preferred video of each forest had a relaxation effect. Video relaxation therapy should be considered. |

(Continued)
| Author and year | Country, City, Study type | Sample Size | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention | Green space exposure | Exposure description & green space type and control group | Hypothesis / Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses | Conclusions |
|-----------------|---------------------------|-------------|------------|--------------------|------------------------|-------------|---------------------|---------------------------------------------------------|------------------------|-------------|---------------------|------------------------|----------|---------------------|-------------|
| White et al., 2015 | Southwestern England, UK | 37 postmenopausal women | Experimental study | 1 week | 50.11 (±3.09) | Green exercise | Cycling on a stationary exercise bike for 15 min while facing either a blank wall (Control) or while watching one of three videos: Urban (Grey), Countryside (Green), Coast (Blue). | Hypothesis: participants’ physiological and psychological relaxation can be influenced by a short-term forest leisure program. There is a utility of a forest near Obetyn on the Red-breasted nature reserve for forest leisure. | Demographic factors: Age, BMI, Socioeconomic factors: N/A. Comorbidity: N/A. Environmental factors: N/A. | | | | Repetitive measures of variance (ANOVA’s) to examine the effect of Time of measurement and environment type for each variable. | Outcomes were more positive in a simulated green and blue environment. Blue environment led to shorter exercise duration and increased participants’ willingness to repeat it again in blue setting. | | |
| Bielinis et al., 2019 | Poland, Urban | 21 | Experiment | 2-day | 23.86 ± 2.67 | Forest recreation – forest bathing | Forested area of the nature reserve | Two hypotheses: Participants’ physiological and psychological relaxation can be influenced by a short-term forest leisure program. There is a utility of a forest near Obetyn on the Red-breasted nature reserve for forest leisure. | Demographic factors: Age, Gender, weight, height, BMI. Socioeconomic factors: N/A. Comorbidity: N/A. Environmental factors: N/A. | Psychological measures: PR, BP. | Paired sample t-test was applied to compare pre-test and post-test measurements and Cohen’s d was used to estimate the effect size. | Negative mood markers were reduced after forest recreation; restoration and vitality was increased PR, SBP and mean arterial pressures reduced after the program. | Limitations: design was applied to one group, no control group, no socio-economic factors, and stress hormone levels were not assessed. | Forest recreation lowers stress. |
| Yu et al., 2017 | Taiwan, central Taiwan | 128 | Experimental study | 2-hours | 60.8 (±7.44 years) | Forest bathing | Planted forest containing Populus simoncina and Phyllostachis pubescens. No control group. The study used a one group post–post field experimental design | There are physiological and psychological effects of a short–forest bathing program on middle-aged and older people. | Demographic factors: Gender. Socioeconomic factors: N/A. Comorbidity: Diabetes, hypertension, heart disease. Other diseases: Environmental factors: N/A. | Physiological responses, PR, SRP, DBP, HRV, and psychological indices. | Paired sample t-test was applied to compare pre-test and post-test measurements and Cohen’s d was used to estimate the effect size. | Significant reduction in PR, SBP and DBP after the program. No significant changes in HRV Forest bathing reduced mood states but vigorous activity increased. Lowered anxiety level. | Limitations: Failure to collect information of confounding variables such as socio-economic status. Environmental factors, habits (e.g., smoking, exercise, etc.) and personality (e.g., nature lover). Environmental factors such as forest aesthetics, types and levels of pollutions and environmental conditions were not considered as covariates. Short forest bathing program has health benefits, therapeutic properties, and leads to relaxation. |
| Kwon et al., 2016 | Japan, not specified | 7 (5 females and 2 males) | Experimental design | 5–7 minutes | 76.2 (±6.7) | Horticultural therapeutic gardens | Walking in a horticultural therapeutic garden. No control group. The study used a pre–post study design | There are benefits of horticultural therapy for all people’s well-being that are reachable. | Demographic factors: Gender, age. Socioeconomic factors: N/A. Comorbidity: Dementia. Environmental factors: N/A. | | | | The therapeutic horticulture system (SHS) was enhanced post intervention. | Limitations not specified. Stress reduction effect of walking may last after the walk even among participants with moderate to severe dementia. | |
| Author and Year | Country, City, Urbanicity setting | Sample Size | Study type | Follow-up duration | Age (Mean ± SD, years) | Intervention | Exposure description | Green-space type and Control group | Hypothesis/Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses

**McBride et al., 2021 [21]**

- United Kingdom
- City not specified
- Urbanicity not specified
- 41 (50 females, 11 males)
- Experimental design
- 3 months
- 18 years and older
- Forest bathing
- Three groups were used in 3X3 experimental design: Forest bathing, Compassionate Mind Training, Forest Bathing + Greenspace. The control combined with Compassionate Mind Training.
- Compassionate Mind Training (CMT) control condition would similarly to Forest Bathing.
- Demographic factors: age, gender, height, weight, BMI, smoking status, habitual alcohol consumption, weight, Compassion, NT/AN A
- Environmental factors: N/A
- Multiple Analysis of Variance (MANOVA) and Cohen’s d was used to estimate the effect size. Independent t-tests were used to assess any differences in HRV scores between conditions at baseline.
- Wellbeing and HRV
- Positive emotions, mood disturbance, rumination, nature connection and compassion improved HRV increased.
- Limitations: Parametric assumptions were limited by forest bathing session, women were only attracted to sessions, the hypothesis was not considered socioeconomically deprived individuals with need have no access to high-quality greenspace, non-comparable HRV data from previous studies considered, effects of pandemic, forest bathing has positive health effects and improves wellbeing.

**Park et al., 2017 [22]**

- Seoul, South Korea
- Urban
- 21 women
- Gardening study/Pilot study
- 7.5 weeks
- Gardening intervention as a low to moderate PA intervention (green exercise) 15-session of gardening program (twice a week, average 90 minutes per session) from Sept to Nov 2015.
- Planning a garden, making a garden plot, planting, sowing, mulching, fertilizing, watering, weeding, harvesting, garden maintenance, and cleaning the garden plot: Exercise intensity of gardening intervention. The control group matched on gardening intervention was composed by the participants from the senior community centers.
- Gardening intervention has impacts on blood vasculature, and immunity in women over 70 years old.
- Demographic factors: Age (year); Height (cm); Body composition; Resting HR (beats/min); Education; Elementary school graduate or less; Marital states; Socioeconomic Income; Compassion; Anxious; Blood pressure; Cholesterol; Asthma; Thyroid; Heart disease; Blood circulation; Hip pain; Osteoporosis; Backache; Environmental factors: N/A
- Lipid profiles, BP, Pro-inflammatory proteins (TNF-α and Monocyte chemoattractant protein-1 (MCP-1) in peripheral blood mononuclear cells (PBMC), and Inflammatory markers: Inducible nitric oxide synthase (iNOS), Receptor for advanced glycation end products (RAGE), and the NADPH oxidase p47.
- Chi-square tests were used to compare different variables. Wilcoxon signed-rank test was used to compare before and after measurements.
- Gardening intervention as PA improves high density lipoprotein (HDL) profile, SBP and DBP and reduces oxidative stress. Improved immunity in the intervention group. Reduced of TNF-α and RAGE.
- No significant change for MCP-1, INOD, and NADPH oxidase p47.
- Limitations: small duration and small sample size.
- Gardening intervention has positive effects on lipid profiles, BP and therefore reduce the risk for CVD. Gardening intervention has positive effects on some inflammatory markers (TNF-α) and oxidative stress (RAGE) of women aged over 70 years.

**Song et al., 2018 [23]**

- Chiba, Japan
- Urban
- 13 males
- Experimental study
- 15 minutes
- 22.5 ± 3.1 years old
- Urban parks (test) City area (control)
- Urban green park: Prescribed 15-minute walk sessions in an urban park (test) and in the city area (control). The control was the city areas around the urban park (city area).
- Urban parks have similar health benefits to natural environments.
- Demographic factors: Male gender, age; Socioeconomic factors: N/A; Environmental factors: N/A
- HR and HRV psychological responses.
- Paired t-test Wilcoxon signed-rank test.
- HR lower when walking in urban park than city.
- Walking in the urban park enhanced the mood and decreased negative feelings and anxiety.
- Limitations: Female population not considered, age groups not considered, other ethnicities not considered, small sample size.
- Walking in urban parks has health benefits and relaxing effects in winter.

**Wu et al., 2020 [24]**

- Hangzhou city, Zhejiang province, China
- Urban
- 31 (control group (n=11), Forest group (n=20)
- Experimental study/shoot study
- 3 days
- Forest bathing with Ginkgo biloba camphora (C. camphora)
- Demographic factors: gender; age; body mass index (BMI); Socioeconomic factors: N/A; Environmental factors: N/A
- Hypertension, Hyperlipidemia, cardiac function class
- Environmental factors: N/A
- BP, pulse oxygen saturation. HR, HRV.
- Levels of plasma beta-CRP Profile of mood status (POMS)
- Categorical variables were compared by Chi-square analysis. Independent sampled t-test or paired samples t-test was used to compare continuous outcomes.
- No significant differences at baseline across all variables. D RP reduced in forest group. Pulse oxygen saturation levels higher than control group.
- Negative POMS was lower after forest bathing and there was a higher positive score.
- Limitations: Sample size was small, elderly population, short intervention. C. Camphora environment has good analgesic effects on patients with HFN.

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(Continued)
| Author and year | Country, City, State | Sample Size | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention & Greenspace exposure | Hypothesis/ Assumption | Covariates | CV related outcome | Statistical Analyses | Findings | Strengths & Weaknesses Conclusions |
|----------------|----------------------|-------------|------------|-------------------|-----------------------|-------------------------------------|------------------------|------------|-------------------|----------------------|----------|-------------------------------|
| Lanki et al., 2017 [125] | Helsinki, Finland Urban | 36 (female) | Experimental study | 15-min period of sitting and viewing the environment, and a 30-min period of unhurried walking | 30–60 years | Green Exercise Visit three different type of environments, namely urban forest, urban park, and (built-up) city center. No control group: Before and after viewing measures were taken, when visiting environment types. Participants were considered as their own controls | Psychophysiological responses to visits to green area are dependent on the quality of the area. | Demographic factors: age, female gender | SBP, DBP, HR and HRV were measured before and after the forest experience | Descriptive statistics Regression models | Visits to the green environments were associated with lower HR and higher HRV than visits to city center. No difference in BP was observed between the green environments and city center | Limitations: No inclusion of both sexes. Even short visits to green areas may lead to beneficial changes in CV risk factors |

https://doi.org/10.1371/journal.pone.0276517.t003
| Author and year | Country City State | Sample Size | Study type | Follow-up duration | Age (Mean ± SD, years) | Intervention Group | Greenspace type | Control group | Hypothesis/Assumption | Contraindations | Statistical analyses | Cancer-related outcome | Findings | Strengths & Weaknesses/Conclusion |
|----------------|---------------------|-------------|------------|-------------------|------------------------|-------------------|----------------|---------------|----------------------|----------------|-------------------|-------------------|---------|----------------------|
| Bell et al., 2018 | Birmingham, Alabama, USA | Total: 82 | Intervention Group: 46 | Total: 82 | 2 years | Greenspace type: | Neighborhood | Community | There is a feasibility of a supervised vegetable gardening intervention and health-related outcomes among breast cancer survivors (BSC) | Demographic factors: Age, Maternal status, Body weight status. Socioeconomic factors: Current smoker, Race, Education; Rural area of residence; At risk of weight gain. Control group: BSC allocated to either 1 year vegetable gardening intervention or a wait control group | Within-group comparisons of baseline to post intervention change scores, between groups were compared using the paired t-test and the chi-square test | Health-related outcomes among breast cancer survivors (BSC); Vegetable consumption; PA; Health-related QoL; Physical performance; Anthropometrics and Biomarkers. | Compared with the control group, those in the intervention indicated the enhancement in PA. The study reported the accrued benefits in self-esteem, satisfaction, and satisfaction Improved vegetable consumption, Continued gardening posttwo years | Limitations: modest sample size, no attention control group, low location area Feasibility of municipal, home-based vegetable gardening intervention Improvement in health behavior and outcomes among cancer survivors (BSC). |
| Rait et al., 2013 | aluminum, USA | 12 cancer survivors (eight adults, four children) | Feasibility study/ pilot study | 1 year | Adult survivors: 56.3 ± 4.4; Child survivors: 9.8 (1.0) | Vegetable gardening | Greenspace type: | Community | Gardening increases fruit and vegetable intake, physical activity, quality of life, and physical functioning in cancer survivors, both children and adults | Descriptive statistics due to lack of power | Adult and child cancer survivors | Intervention well accepted and feasible among older adults | Limitations: Small sample size, lack of attention control group, use of self-report Feasibility of providing intervention Improved fruit and vegetable consumption PA; and physical function in cancer survivors |
| Demark-Wahnefried et al., 2018 | aluminum, USA | 46 | Feasibility study/ Pilot Randomized Controlled Trial | 1 year | Age 60+ | Seasonal vegetable gardening at nutritious homes | Greenspace type: | Community | Vegetable gardening can be feasible among older cancer survivors and is related to other health-related outcomes | Discriptive statistics due to lack of power | Adult and child cancer survivors | Assess the effects on fruit and vegetable intake, physical activity, quality-of-life, and physical function | Intervention well accepted and feasible among older adults and children | Limitations: lack of statistical power, modest sample size, relying on self-reported data, the increased child/old type 1 error associated with multiple comparisons. Feasibility of the study: Improved fruit and vegetable consumption, reassessment of worth and quality of life. Improve health, health behaviors and wellbeing of older cancer survivors |
| Li et al., 2018 | Tokyo, Japan | 12miles | Experimental study | 3 days | 45.1 (4.7) | Forest bathing | Greenspace type: | Community | There is an effect of forest bathing in glioma NK activity | Descriptive factors: Age, male gender. Socioeconomic factors: Education, Lifetime habits of cigarette smoking, alcohol consumption, eating breakfast, sleeping hours, working hours, physical exercise, mental balance, and mental stress. Anxiety, Type of cancer (Breast, prostate, colorectal), Cancer treatment, No. of comorbidities | Two-way ANOVA with repeated measures One-way ANOVA with repeated measures Paired t-test Unpaired t-test | Natural killer cells (NK) activity, number of NK and T-cells, and granulocytes, perforin, and granzymes A/B expressing lymphocytes. Adrenocortical hormone | Limitations not specified Forest bathing trip has effects on health and the effects last for 7 days. Phytochemicals reduce stress and contribute partially to NK cell activity. | (Continued)
Table 4. (Continued)

| Author and year | Country | City | State | Sample Size  | Study type | Follow up duration | Age (Mean ± SD, years) | Intervention Exposure type + Hypothesis | Exposure description + Greenspace type and Control group | Hypothesis/ Assumption | Covariates | Statistical analyses | Cancer-related outcome | Findings | Strengths & Weaknesses | Conclusions |
|-----------------|---------|------|-------|--------------|------------|--------------------|------------------------|------------------------------------------|--------------------------------------------------------|------------------------|------------|----------------------|------------------------|----------|---------------------|------------|
| Li et al., 2007 [130] | Tokyo, Japan | Urban |       | 12 males     | Experimental study | 3 days          | 43.1 (±1.1)          | Forest bathing                  | Three day/two-night trip to three different forest fields. Blood prior to the trip was sampled as a control. | There are effects of forest bathing on human NK activity. | Demographic factors: Age, male gender; Socioeconomic factors: lifestyle habits of cigarette smoking, alcohol consumption, eating habits, sleeping hours, physical exercise, nutritional balance, and mental stress. Comorbidity: N/A Environmental factors: N/A | Paired t-test | Natural killer (NK), NK cells, perforin, granzymes and granulysin expression in peripheral blood lymphocytes (PBL). Proportions of NK, T cells, perforin, and granzymes ALB-expressing cells in PBL | NK activity increased. Increased NK, perforin, granulysin, and granzymes ALB-expressing cells | Limitations not specified. Forest bathing trip increase NK activity due to increasing the number of NK cells and induction of intracellular anti-cancer proteins |

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and follow up after greenspace intervention. Two assessors discussed discrepancies between scores until a consensus was reached through a joint re-evaluation of the article, a method that has been used in previous studies [98]. This graphical representation shows an overall trend in findings across all studies included. Acronyms: SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BNP: Brain natriuretic peptide; HRV: Heart rate variability; RAS: Renin-angiotensin system components; PNSA: Parasympathetic Nervous System Activity; SNSA: Sympathetic Nervous System Activity; hsCRP: High sensitivity C-reactive protein; TNF-α: Tumor necrosis factor alpha; HR: Heart rate; MDA: Malondialdehyde; RAGE: Receptor for advanced glycation end products; iNOS: Inducible nitric oxide synthase; MCP-1: Monocyte chemoattractant protein-1; ET-1: Endothelin-1; PP: Pulse pressure; AdipoQ: Adiponectin; Hcy: Homocysteine; NADPH oxidase p47: HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

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3.3. Summary characteristics of 31 articles included in the review

Data from included studies is summarized in two tables (3 and 4). Table 3 summarizes 26 studies with CV outcomes, and Table 4 summarizes 5 studies with cancer-related outcomes. Reported items include citation, study location, urbanicity setting, sample size, study type, follow up/duration, covariates, age, interventions, greenspace exposure type, CV health or cancer-related outcomes, statistical analyses conducted, main findings, study strengths and weaknesses, and conclusions.
3.4. Study design and demographics

All included studies used some kind of experimental designs. Thirteen (13) studies used simple pre-post study designs, some studies used the same group as the control and experimental group (on a different day/time) and measured statistical differences with paired sample t-tests [103,106,107,111,112,115,118,119,123,126,128–130], and eight (8) studies used randomized control and experimental groups and measured statistical differences with independent sample t-tests [100,104,105,108,109,113,124,129]. Sample sizes ranged from 7 [120] to 155 [104] with an average sample size of 33.5. Study participants’ mean age ranged from 10 years [103] to 80.3 years [122]. Twenty (20) studies included both male and female participants, 7 included males only [106,107,112,116,123,129,130], and 4 included females only [111,117,122,125]. No study specified nonbinary gender conforming or transgender identity.

3.5. Statistical analyses

Various statistical approaches were used in describing data and testing effects of NBI on outcome measures of CV health and cancer-related QoL. Descriptive statistics reported means and standard deviations as well as frequency distributions [105,111,116,125,127]. In addition to descriptive statistics, inferential statistics were used to determine statistical differences observed pre and post intervention. Some studies used specific tests for normality and homogeneity of variances such as Kolmogorov-Smirnov and Levene’s tests [100,108,109] or Shapiro-Wilk test [104,105]. Studies with normally distributed data used parametric tests such as t-tests, chi square, spearman correlation or regression [104]. Studies with categorical outcome variables used Chi squared test for statistical independence or association between samples [104,108,122,124,126,128]; and some studies with dichotomous outcome variables incorporated McNemar’s test [126,128] to determine if there are differences between two related groups. Other studies used regression models to test predictions of interventions effects on dependent continuous outcomes variables [104,125]; and studies with more than two groups to compare during interventions used ANOVA to test for statistical differences between groups’ means [101,103,110,114,117,121,129]. Other studies used post adjustment tests such as Bonferroni post-hoc pairwise comparisons or partial eta squared (η²) test [103] or Cohen’s d test [118,119] for effect size estimation. In addition to parametric tests, studies with non-normally distributed outcome variables used nonparametric tests such as Mann Whitney U test for between subjects’ comparisons or Wilcoxon Signed Rank tests for within subjects’ comparisons to compare statistical differences between samples [100,102,116,122,123,104–106,108,109,112,113,115] or Kruskal-Wallis test for multi-group comparisons with post hoc Bonferroni adjustment [108]. One study used schematic views in representing their findings and did not specify the statistical test used [120].

3.6. Geographic distribution and urbanicity setting

Sixteen (16) studies were carried out in Asia, mostly in Japan and China, 12 in Europe, and 3 in North America. No study from other parts of the world (Africa, South America, and Australia) was identified. 22 studies were conducted in urban areas while 9 studies did not specify their urbanicity setting; and no study reported a rural setting for the experiment.

3.7. Summary of findings

Of 31 studies included in this review, 26 examined CV health related outcomes (Table 3) while 5 examined cancer-related outcomes (Table 4). Results of these studies are described separately for CV and cancer outcomes.
3.7.1. Greenspace or NBIs on cardiovascular health. Twenty-six (26) out of 31 studies included in the review looked at measures of CV health. Out of those 26 studies, 8 studies were conducted in Japan [104,106,107,112,115,116,120,123], 4 in China [100,108,109,124], 4 in the UK [103,114,117,121], and 2 in Taiwan [111,119]. One study was conducted in each of the following countries: Korea [122], Austria [110], Hungary [113], Poland [118], Lithuania [105], Finland [125], US [101] and Norway [102] (Fig 2). The most widely used intervention was forest bathing, quite common in Japan and China, followed by green exercise, nature viewing and gardening (Fig 2). The most reported outcomes were DBP, SBP, and HR, measured in 18 out of 26 studies. HRV was next and was measured in 5 out of those 26 studies, followed by measures of both the parasympathetic and sympathetic nervous systems, measured in 4 out of 26 studies. Few outcomes looked at stress measures of the cardiac myocyte such as the brain natriuretic peptide (BNP), Endothelin-1 (ET-1) and some components of the Renin-angiotensin system (RAS). Other outcomes investigated are measures of cholesterol such as high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Most statistical tests conducted across all studies found that greenspace or NBI led to beneficial CV health outcomes (Beneficial effect), and some found no statistically significant difference (Not significant) (Fig 2).

3.7.2. Greenspace or nature-based interventions on cancer-related outcomes. Five (5) out of 31 studies looked at cancer-related outcomes. Of those 5 studies, 3 were conducted in the US [126–128] while 2 were conducted in Japan [129,130]. Three US studies focused on vegetable gardening interventions while two Japanese studies focused on forest bathing interventions. Japanese studies looked at number of natural killer (NK) cells and their activity while US studies examined more diverse outcomes. Four of the outcome measures were related to positive health behaviors such as improved vegetable consumption habits [126–128], improved fruit consumption habits [127,128], increased PA [126,127] and gardening continuation [126]. Other outcomes were related to measures of physical fitness including strength [127], endurance [127], agility [127], and the two-minute-step test [126]. Three outcome measures were focused on overall health including weight loss [127], overall QoL [127,128], and reassurance of worth [128]. Three outcome measures were related biological markers including cortisol, a measure of stress [128], telomerase activity, a measure of aging [126,128], and interleukin-6 (IL-6), a pro-inflammatory biomarker and measure of systemic inflammation [128] (Fig 3). Observed trend suggests NBI’s health protective effects on cancer outcomes (Beneficial effect) with few exceptional outcomes that were not statistically significant (Not significant) or significant only in control groups whereby control groups had better outcomes than the experimental groups (Significant in controls) (Fig 3). The ‘significance in control groups’ does not, in any way, suggest negative effect of the intervention. It is also not same as “not significant”.

4. Discussion

4.1. Greenspace interventions and outcomes
This review focused on NBIs or greenspace interventions. Diverse types of experimental exposure to greenspace were identified, including forest bathing, green exercise, vegetable gardening, and nature viewing (Figs 2 and 3). Outcomes investigated were related to CV health or cancer. Study locations were distributed across three continents including Asia, Europe, and North America. As hypothesized, observed trends suggest overall beneficial effects of greenspace interventions on both CV health and cancer-related outcomes, with some exceptions on few outcome measures.

4.1.1. Forest bathing. Forest bathing “Shinrin-yoku” is a conscious and contemplative practice of being immersed in the sights, sounds, touches, tastes and smells of the forest [131]. This practice was developed in Japan in the 1980s as a physiological and psychological exercise
and part of the national health program [132,133]. Its purpose was in twofold: (1) reduce burnout from the stressful work environment; and (2) inspire residents to reconnect with and protect the country’s forests [133]. Scientists have then investigated its benefits on physical, mental, emotional, and social health outcomes [134]. Forest bathing is known to boost immunity [113,130,135], a plausible central pathway between nature exposure and human health benefits [136].

In this review, forest bathing was the most common intervention (15 out of 31 studies). Forest bathing was deployed in different forms including short forest recreation programs [113,118], forest therapy programs [111,112], longer slow walks in forests [100,104,107–109,124,129,130], forest viewing vs urban viewing [106], and full forest immersion experience, comprised of sessions of slowly moving in silence through woodland, stopping to observe using all of senses (sight, smell, touch, hearing, and taste) and engaging in slow and relaxing breathing to ensure discovery and mindful appreciation of the woodland [119,121]. In 15 studies with forest bathing intervention, 6 were conducted in Japan [104,106,107,112,129,130], 4 in China [100,108,109,124], 2 in Taiwan [111,119], and one in Hungary [113], Poland [118], and UK, respectively [121].

Most statistical tests conducted found beneficial effects of forest bathing on outcome measures for CV health with few exceptions that did not find statistically significant associations. Few non-significant associations included some outcome measures including diastolic blood pressure (DBP) [107,111,113,118], systolic blood pressure (SBP) [107,124], HR [104,109,111,113,124], pulse pressure [109], and HRV [119]. One study found no statistical significance in both PSNA and SNSA [119]. Other remaining statistical tests conducted across various studies found significant beneficial effects. The first beneficial outcome observed is in
measures of heart function such as reduced DBP [100,104,112,119,124], reduced SBP [100,104,111,112,118,119], lower HR [106,107,109,112,118,119], and increased HRV [121,124]. Another measured outcome that can impact CV health was stress. Stress reduction is salutogenic and was empirically observed with a decrease in stress hormones levels including urinary dopamine [107], adrenaline [112], and serum cortisol [109,112] after the intervention. Stress reduction was also observed with indicators of autonomic nervous system, such as enhanced parasympathetic nervous system activity (PNSA) [106] and suppressed sympathetic nervous system activity (SNSA) [106].

Improved systemic inflammatory profile is another beneficial outcome that was observed through reduction in both pro-inflammatory biomarkers and increase in anti-inflammatory biomarkers after forest bathing interventions. Reduced pro-inflammatory biomarkers include endothelin (ET-1) [100,108,109], IL-6 [100,108,109], tumor necrosis factor alpha (TNF-α) [109], homocysteine (Hcy) [100], and high sensitivity C-reactive protein (hsCRP) [124]. Increased anti-inflammatory biomarkers include serum adiponectin [107]. There were numerical differences between pre and post measures for two measured biomarkers of inflammation within the intervention groups, but no statistically significant differences were observed. Those non-statistically significant tests were for TNF-α [100,108] and hsCRP [108], and were reported in the alluvial chart as “Not significant”.

Measures of oxidative stress were also improved after forest bathing interventions, as observed through lower levels of malondialdehyde (MDA) in experimental group post-intervention [108,109]. Last but not least, measured CVD pathological factors biomarkers were improved after forest bathing interventions as observed though serum reduction of constituents of the renin angiotensin system (RAS) (renin [108], angiotensin II (Ang II) [108], angiotensinogen (AGT) [100,108], angiotensin II type 1 receptor (AT1) [100,108], and angiotensin II type 2 receptor (AT2) [100,108]) and the brain natriuretic peptide (BNP), a biomarker of HF [108]. One study found mild reduction in renin and angiotensin II (Ang II) in the experimental group, although changes were not statistically significant [100]; and this was reported as “Not significant” in alluvial charts.

Most statistical tests conducted found beneficial effects of forest bathing on cancer-related measured outcomes including enhanced immune functioning observed through increase in number of NK cells [129,130] and their activity [129,130]. The forest bathing ‘outcome-conclusion’ chart is illustrated in Fig 4.

Forest bathing is a promising intervention to improve CV health and QoL, particularly during cancer survivorship. Clinical practitioners, particularly those working in cardio-oncology specialties should examine more closely these non-invasive interventions and incorporate them in the standard of care to optimize CV health outcomes for cancer survivors through increased use of nature prescription programs, in addition to the clinical standards of care.

4.1.2. Green exercise. Another commonly used intervention was green exercise (8 out of 31 studies). Green exercise has been defined as any PA occurring in a natural environment [114]. In this study, exercising with a view of nature through a window, on pictures, or on televisions was also considered “green exercise”. Diverse green exercise interventions were used in studies included in this review, but most of them used nature visual stimuli. Duncan et al., 2014 had participants in the intervention arm of their study cycle for 15 min whilst watching a film of cycling in a forest environment [103]. Like Duncan et al., 2014, Pretty et al., 2005, had participants watch different scenes of videos projected on a wall whilst exercising on a treadmill [114] while Song et al., 2018’s participants viewed Bonsai, small plants in container with restriction to roots or food storage capability [137]. The Bonsai used as a visual stimulus had characteristic mimicking natural landscapes that has been historically used in daily life in Japan [115]. White et al., 2015 also had their participants in the intervention arm cycle on a
stationary exercise bike for 15 min while watching one of three videos: Urban (Grey), Countryside (Green), or Coast (Blue) [117]. Grazuleviciene et al., 2016 had the participants in intervention arm of their experiment walk in a pine forest park [105]. Lanki et al., 2017’s intervention consisted of a visit to an urban greenspace (forest or park) [125] with 15 min visit of sedentary viewing greenspace and 30 min of walking in greenspace [125]. Navalta et al., 2021 used exercise in a desert environment (brown environment) as a nature-based intervention to test if there are similar benefits to those anticipated in green environments [101]. Niedermeier et. al., 2017 used mountain hiking as green exercise [110].

Green exercise has been shown to improve both physical and mental health [114,138] and higher enjoyment of exercise [139]. Some of the positive health outcomes previously associated with green exercise include greater feelings of revitalization and positive engagement [140], and improvement in measures of mood and self-esteem [141] such as depression, tension, and anger [142,143]. Green exercise has been suggested by previous scholars as a potential workplace intervention to reduce job stress and promote restoration [144]. Chronic stress has been linked to increased CVD risk [145–147], including a 40–50% increase in the occurrence of coronary heart disease in prospective observational studies [145,148].

In our review, interventions with green exercise were conducted in different countries, including the UK [103,114,117], Lithuania [105], Finland [125], Austria [110], Japan [123] and the US [101]. Green exercise was found to be positively associated with many outcome measures related to CV health with few statistical tests that found no significant associations or no
numerical difference at all. Green exercise’s beneficial CV health outcomes include observed reduction in SBP [103,114,117], DBP [105,114,117], HR [117,123,125], and increase in HRV [123,125]. Another significant change observed was a reduction in cortisol, a measure of stress [105]. Some studies did not find a significant difference on measures of SBP [101,105,110,125], DBP [101,103,110,125], and HR [101,110,114], including one study that found no association between green exercise and one measure of CV health, HR [103]. For studies that looked at cancer-related outcomes, none used a green exercise intervention. The green exercise ‘outcomes-conclusions’ chart is illustrated in Fig 5.

No study in this review investigated the impact of “green exercise” on cardiotoxicity among cancer survivors. This literature gap suggests the need for empirical investigation on the role of greenspaces in reducing risks for cardiotoxicity in this highly vulnerable population and testing the use of such interventions in Cardio-oncology clinics to optimize CV health and improve cancer survivorship care. Additionally, only one statistical test investigated the impact of green exercise on CV biological markers by looking at cortisol. Future studies should investigate more biomarkers, including additional stress biomarkers and CVD pathological factors such as the components of the renin angiotensin system and inflammatory biomarkers such as IL-6, hsCRP, TNF-α etc..

4.1.3. Vegetable gardening. Gardening interventions provide individuals with hands-on experience planting, growing, and harvesting fruits and vegetables, which may promote consumption of fruits and vegetables [149,150]. Individual benefits of gardening activities include increased PA, access to fresh air, landscape beautification and enjoyment [151]. Gardening interventions have been linked to many health benefits [152] including improved physical
health [153,154] and mental health [155–157]. Gardening has been proposed as a strategy for health promotion in aging women [158] and its prescription, along with other conservation activities are recommended to improve health and wellbeing in aging population [159]. In the cancer care continuum, gardening interventions have been linked to positive health outcomes and improved survival [160,161]. Some specific benefits of gardening during cancer survivorship include improved dietary habits, improved PA, and improved QoL [162].

In this review, vegetable gardening interventions were conducted in Japan [120], South Korea [122] and the US [126–128]. Two studies looked at CV health related outcomes [120,122] while three studies looked at cancer-related outcomes [126–128]. Most studies found beneficial effects of gardening interventions on outcome measures related to CV health and cancer-related QoL, with some exceptions that found no statistically significant changes (not significant), or significant only among controls. Those ‘not significant’ exceptions include some statistical tests on outcome measures of weight loss and overall QoL in one feasibility study in cancer survivors [127], some biomarkers including the monocyte chemoattractant protein-1 (MCP-1), NADPH oxidase p47, and the inducible nitric oxide synthase protein (iNOS) [122], stress hormone cortisol and IL-6 [128], and low-density lipoprotein (LDL) [122]. Two tests found significance among controls, one on overall QoL [128] and another one on telomerase activity [126], an enzyme responsible for maintenance of telomeres length by addition of guanine-rich repetitive sequences in both gametes and stem and tumor cells [163].

Included studies in this review showed beneficial effects of gardening interventions on stress [120], total cholesterol and HDL [122], BP [122], dietary habits [126–128], positive self-care behaviors [126,127], physical performance [127], increased reassurance of worth [128] and improved aging process [128]. Stress reduction benefits were observed through proxy measures with enhanced parasympathetic nervous system activity (PNSA) [120] and suppression of sympathetic nervous system activity (SNSA) [120]. Benefits on blood cholesterol level were measured through improved high-density lipoprotein (HDL), or good cholesterol profile [122]. Beneficial outcomes in BP were measured with both decreased SBP [122] and decreased DBP [122]. Improvement in dietary habits was observed through improved vegetable and fruit consumption [126–128]. Positive self-care behaviors were observed through improved PA [126,127] and gardening continuation [126]. Physical performance improvement was observed through improvement in the 2-minute-step test [126] and other measures including improved strength [127], improved endurance [127] and improved agility [127]. Increased reassurance of worth was measured with self-reported assessments of psychosocial measures [128]. Improvement in aging process was observed through a decrease in telomerase activity [128]. The gardening interventions impact on both CV health and cancer-related outcomes, along with the overall conclusion are graphically illustrated in Fig 6.

Observed trends (Fig 6) suggest that gardening is a promising intervention to improve outcomes related to CV health and QoL during cancer survivorship. Cardio-oncologists should keep close collaborations with primary care providers in optimizing the cancer survivorship care by including these innovative interventions to improve CV health and survivorship experience. Community leaders, including local government and other community-based organizations should work together to ensure presence, accessibility, and use of community gardens. In addition to supporting positive healthy gardening behaviors, those gardens also have potential to increase access to healthier foods options for residents in “food deserts” and “food swamps” neighborhoods [164–166]. Such gardens could also enhance biodiversity, local ecosystem, water management and contribute to local climate change resilience strategies [167]. Additionally, continuous targeted messaging campaigns should be in place to remind those at increased risk of the benefits associated with gardening. Academic partners should come in to continuously evaluate impact and suggest best practices to ensure maximum benefits from all
the resources set aside for such a community wide intervention to support intergenerational equity. Future studies should incorporate more biological measures including pathological factors for CVD such as biomarkers of oxidative stress and more inflammatory biomarkers in addition to IL-6, the only pro-inflammatory biomarker that was investigated in vegetable gardening interventions studies included.

4.1.4. Nature Viewing. Exposure to natural environments including viewing them has been linked with improved restoration and cognitive capacity [102] and autonomic function recovery after acute mental stress [168]. In this review, we found studies that tested nature viewing effects on measures of CV health including HR, SBP, DBP, PSNA and SNSA. Those studies were carried out in two countries, Japan [115,116] and Norway [102]. Statistical tests found beneficial effects of nature viewing on CV health including reduction in HR [102,116], enhanced PSNA [115,116] and suppressed SNSA [115]. Tests on measures of SBP and DBP were not statistically significant [116]. The nature viewing interventions on both CV health outcomes, along with the overall conclusion are graphically illustrated in Fig 7.

Contrary to other NBI in this review (forest bathing, green exercise, and vegetable gardening), nature viewing intervention did not measure a single biological marker of inflammation.

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Future studies should investigate nature viewing’s impact on biomarkers including CVD pathological factors such as the components of the renin angiotensin system and pro-inflammatory biomarkers such as IL-6, hsCRP, and TNF-α. Such knowledge would complement current behavioral self-care plans particularly for cancer survivors in reducing risk for cardiotoxicity; and nature viewing is a relatively harmless intervention, amenable to change and relatively easier to implement.

Presented all together, this review suggests that forest bathing and gardening interventions have the most beneficial outcomes (Figs 4 and 6) compared to other interventions (nature viewing or green exercising) which are also beneficial, but to a less extent (Figs 5 and 7). Intervention specific alluvial charts suggest more thickness for “beneficial effect” for forest bathing and gardening compared to nature viewing or green exercise. These findings have implications for increasing use of forest bathing and/or gardening interventions to improve CVD and/or cancer outcomes. Nature viewing and green exercise interventions remain also very important in improving outcomes. The clinical use of these interventions would be best assessed with patient preference and what interventions they are most likely to adhere to.

4.2. Limitations

While this review is methodologically rigorous, it has some limitations. First, in the risk of bias assessment, we used a modified version of the Newcastle Ottawa Scale because there was no validated tool that accurately assessed all types of studies included in our review. While the official NOS has been validated for case-control and cohort studies, the scoring guide created...
for this study by modifying the scale to capture factors related to experimental or pre-post studies has not been validated, and it’s scoring can be subjective. This subjectivity was attenuated by ensuring that two reviewers (J.C.B. and J.S.B.) independently assess all studies. Secondly, we reported trends across all relevant statistical tests conducted in all included studies with alluvial charts to visualize our results summary, but no meta-analysis was done to suggest any statistical inference for all the articles if taken altogether. Therefore, our trend across all studies should be seen as a descriptive summary of findings; and any inference made should consider all studies collectively. Thirdly, not all included studies measured, adjusted for, or reported the same variables. This is why we used alluvial chart to summarize similar trends instead of conducting a meta-analysis to deduct any statistical inference for all studies combined. Last, this review is not immune to other limitations discussed by the authors of the included studies, which may include small sample size, lab errors, potential misclassification, or other measurement errors. Regardless of the limitations, this review is an outstanding summary of impact of greenspace or nature based interventions on both CV health and cancer-related outcomes and highlight benefits with direct implication for clinical and public health practice.

5. Conclusion

This review sought to assess the impact of greenspace or NBI on: (1) CV health, and (2) cancer-related outcomes.

Interventions used included a Japanese tradition of forest bathing or “shinrin-yoku,” green exercise, gardening, and nature viewing. CV health related outcomes include measures of BP, HR, HRV, autonomic nervous system activity, stress biomarkers including cortisol, oxidative stress measures such as iNOS, RAGE, and NADPH oxidase p47, CVD pathological factors including lipid profile, components of the renin angiotensin system, pro-inflammatory biomarkers including IL-6, hsCRP, TNF-α, ET-1, Hcy, MDA, and MCP-1 and anti-inflammatory biomarkers including adiponectin. Cancer-related outcome measures include measures of physical performance such as physical strength, endurance, and agility; personal behaviors such as vegetable and fruits consumption, PA, and weight loss; biological markers including stress markers (cortisol), inflammatory markers (IL-6), some components of the renin angiotensin system (RAS), and some immune function markers including both the count of natural killer cells as well as their activity.

An overall trend across studies suggests beneficial effects of greening and NBI on both CV health and cancer-related outcomes, although not all studies found a significant benefit. Cardio-oncologists, along with primary care providers should incorporate these innovative interventions in the standard of care to optimize both CV and cancer-related health outcomes. Future studies should combine multiple measures of CVD pathological factors including components of the renin angiotensin system (renin, Ang II, AGT, AT1 and AT2), multiple markers of oxidative stress, multiple measures of both pro and anti-inflammatory biomarkers, and multiple biomarkers of stress. Other direct and relatively easier measures such as BP, HR, pulse pressure and HRV would be important to add to this line of investigation. Additionally, future studies should pay more attention to some populations with higher CVD risk such as cancer survivors to order to investigate the premise of such innovative population-based approaches in reducing cardiotoxicity from cancer treatment therapies and optimize the survivorship experience.

Existing conceptual models such as the “Greenspace and Health Equity model” [169] or the “Greenspace in Cardio-Oncology model” [1] can be very useful in future research on greenspace and CardioOncology disparities. There is a need for increased research funding from relevant
organizations such as the American Heart Association, the American Cancer Society, and National Health Institutes including the National Cancer Institute. This knowledge will promote a more robust understanding of the role of greenspace and NBI on CV and/or cancer-related outcomes as well as their critical contribution to climate resilient neighborhoods. The focus on biomarkers is particularly relevant for clinical practice as more biomarkers can clinically be measured and greenspace interventions impact on CV health can be continuously assessed during all stages of the cancer care continuum. Such practice can help reduce risks for MACE, reduce mortality, and improve cancer survivorship quality and survival.

**Supporting information**

S1 Checklist. The PRISMA 2020 checklist: Appendix A.

(SDOCX)

S1 File. The full databases search strategy and alluvial charts data files: Appendices B and C.

(SDOCX)

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**Author Contributions**

Conceptualization: Jean C. Bikomeye, Kirsten M. M. Beyer.

Data curation: Jean C. Bikomeye, Joanna S. Balza, Kirsten M. M. Beyer.

Formal analysis: Jean C. Bikomeye.

Funding acquisition: Kirsten M. M. Beyer.

Investigation: Jean C. Bikomeye, Kirsten M. M. Beyer.

Methodology: Jean C. Bikomeye, Joanna S. Balza, Jamila L. Kwarteng, Andreas M. Beyer, Kirsten M. M. Beyer.

Project administration: Jean C. Bikomeye, Joanna S. Balza, Kirsten M. M. Beyer.

Resources: Jean C. Bikomeye, Jamila L. Kwarteng, Andreas M. Beyer, Kirsten M. M. Beyer.

Software: Jean C. Bikomeye, Joanna S. Balza.

Supervision: Kirsten M. M. Beyer.

Validation: Jean C. Bikomeye, Jamila L. Kwarteng, Andreas M. Beyer, Kirsten M. M. Beyer.

Visualization: Jean C. Bikomeye.

Writing – original draft: Jean C. Bikomeye, Kirsten M. M. Beyer.

Writing – review & editing: Jean C. Bikomeye, Joanna S. Balza, Jamila L. Kwarteng, Andreas M. Beyer, Kirsten M. M. Beyer.

**References**

1. Bikomeye J.C.; Beyer A.M.; Kwarteng J.L.; Beyer K.M.M. Greenspace, Inflammation, Cardiovascular Health, and Cancer: A Review and Conceptual Framework for Greenspace in Cardio-Oncology
Greenspace interventions on CVD and cancer related outcomes

1. World Health Organization. The top 10 causes of death Available online: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed on Jan 21, 2021).

2. Vos T.; Lim S.S.; Abbafati C.; Abbas K.M.; Abbasi M.; Abbasi-Santouri M.; Abubakar H.; Abd-Allah F.; Abdala H.; et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020, 396, 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9 PMID: 33069326

3. Sung H.; Ferlay J.; Siegel R.L.; Laversanne M.; Soerjomataram I.; Jemal A.; Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2021, 71, 209–249. https://doi.org/10.3322/caac.21660 PMID: 33538338

4. The Cancer Atlas. The Economic Burden of Cancer Available online: https://canceratlas.cancer.org/ taking-action/economic-burden/ (accessed on Apr 27, 2021).

5. The World Health Organization. The top 10 causes of death Availab le online: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed on Jan 21, 2021).

6. Rohrmann S.; Witassek F.; Erne P.; Rickli H.; Radovanovic D. Treatment of patients with myocardial infarction depends on history of cancer. Eur. Heart. J. Acute Cardiovasc. Care 2018, 7, 639–645, https://doi.org/10.1177/2048872617729636 PMID: 28927294

7. Braveman P.; Grusky D.M.; Devree E.; Jha P.; Krieger N.; et al. Myocardial infarction: The rising burden of cardiovascular disease in the United States. Circ. Res. 2020, 126, 152–168. https://doi.org/10.1161/CIRCRESAHA.119.324711 PMID: 31953060

8. Bertero E.; Ameri P.; Maack C. Bidirectional Relationship Between Cancer and Heart Failure: Old and New Issues in Cardio-oncology. Card. Fail. Rev. 2019, 5, 106–111, https://doi.org/10.15420/cfr.2019.1.2 PMID: 31179021

9. Bikomeye J.C.; Terwoord J.M.; Santos J.H.; Beyer A.M. Emerging mitochondrial signaling mechanisms in cardio-oncology: beyond oxidative stress. Am. J. Physiol. Heart Circ. Physiol. 2022, https://doi.org/10.1152/ajpheart.00231.2022 PMID: 35930448

10. Barac A.; Murtagh G.; Carver J.R.; Chen M.H.; Freeman A.M.; Herrmann J.; Iliescu C.; Ky B.; Mayer E.L.; Okwuosa T.M.; et al. Cardiovascular health of patients with cancer and cancer survivors: A roadmap to the next level. J. Am. Coll. Cardiol. 2015, 65, 2739–2746, https://doi.org/10.1016/j.jacc.2015.04.059 PMID: 26112199

11. Ameri P.; Canepa M.; Anker M.S.; Belenkov Y.; Bergler-Klein J.; Cohen-Solal A.; Farmakis D.; López-Fernández T.; Lainscak M.; Pudil R. Cancer diagnosis in patients with heart failure: epidemiology, clinical implications and gaps in knowledge. Eur. J. Heart Fail. 2018, 20, 879–887. https://doi.org/10.1002/ejhf.1165 PMID: 29464808

12. Jackson R.J. The impact of the built environment on health: an emerging field. Am. J. Public Health 2003, 93, 1382. https://doi.org/10.2105/ajph.93.9.1382 PMID: 12948946

13. Chow C.K.; Lock K.; Teo K.; Subramanian S. V.; McKee M.; Yusuf S. Environmental and societal influences acting on cardiovascular risk factors and disease at a population level: a review. Int. J. Epidemiol. 2009, 38, 1580–1594, https://doi.org/10.1093/ije/dyn258 PMID: 19261658

14. Bhatnagar A. Environmental Determinants of Cardiovascular Disease. Circ. Res. 2017, 121, 162–180. https://doi.org/10.1161/CIRCRESAHA.117.306458 PMID: 28684622

15. Gomez S.L.; Shariff-Marco S.; Derouen M.; Keegan T.H.M.; Yen I.H.; Mujahid M.; Satariano W.A.; Glaser S.L. The impact of neighborhood social and built environment factors across the cancer continuum: Current research, methodological considerations, and future directions. Cancer, 2015, https://doi.org/10.1002/cncr.29345 PMID: 25847484

16. Yeager R.A.; Smith T.R.; Bhatnagar A. Green environments and cardiovascular health. Trends Cardiovasc. Med. 2020, 30, 241–246. https://doi.org/10.1016/j.tcm.2019.06.005 PMID: 31248691

17. Riggs D.W.; Yeager R.; Conklin D.J.; DeJarnett N.; Keith R.J.; DeFilippis A.P.; Rai S.N.; Bhatnagar A. Residential proximity to greenness mitigates the hemodynamic effects of ambient air pollution. Am. J. Physiol. Circ. Physiol. 2021, 320, H1102–H1111, https://doi.org/10.1152/ajpheart.00689.2020 PMID: 33416460
21. Riggs D.W.; Yeager R.A.; Bhatnagar A. Defining the Human Envirome: An Omics Approach for Assessing the Environmental Risk of Cardiovascular Disease. *Circ. Res.* 2018, 122, 1259–1275, https://doi.org/10.1161/CIRCRESAHA.117.311230 PMID: 29700071

22. Casagrande S.S.; Whitt-Glover M.C.; Lancaster K.J.; Odums-Young A.M.; Gary T.L. Built Environment and Health Behaviors Among African Americans: A Systematic Review. *Am. J. Prev. Med.* 2009, 36, 174–181, https://doi.org/10.1016/j.amepre.2008.09.037 PMID: 19135908

23. Blanchard T.C.; Matthews T.L. *Retail concentration, food deserts, and food-disadvantaged communities in rural America.* University of Nebraska Press Lincoln; Lincoln, 2007;

24. Cooksey-Stowers K.; Schwartz M.B.; Brownell K.D. Food Swamps Predict Obesity Rates Better Than Food Deserts in the United States. *Int. J. Environ. Res. Public Health* 2017, 14, 1366, https://doi.org/10.3390/ijerph14111366 PMID: 29135909

25. Sallis J.F.; Floyd M.F.; Rodríguez D.A.; Saelens B.E. Role of built environments in physical activity, obesity, and cardiovascular disease. *Circulation* 2012, 125, 729–737. https://doi.org/10.1161/CIRCULATIONAHA.110.969022 PMID: 22311885

26. Weimann H.; Rylander L.; van den Bosch M.A.; Albin M.; Ska˚rbäck E.; Grahn P.; Björk J. Perception of safety is a prerequisite for the association between neighborhood green qualities and physical activity: Results from a cross-sectional study in Sweden. *Health Place* 2017, 45, 124–130, https://doi.org/10.1016/j.healthplace.2017.03.011 PMID: 28359908

27. Janssen I. Crime and perceptions of safety in the home neighborhood are independently associated with physical activity among 11–15 year olds. *Prev. Med. (Baltim)*. 2014, 66, 113–117. https://doi.org/10.1016/j.ypmed.2014.06.016 PMID: 24963893

28. de la Barrera F.; Reyes-Paècke S.; Harris J.; Bascuñán D.; Farías J.M. People’s perception influences on the use of green spaces in socio-economically differentiated neighborhoods. *Urban For. Urban Green.* 2016, 20, 254–264.

29. Gozalo G.R.; Morillas J.M.B.; González D.M. Perceptions and use of urban green spaces on the basis of size. *Urban For. Urban Green.* 2019, 46, 126470.

30. Cohen D.A.; Han B.; Derose K.P.; Williamson S.; Marsh T.; Rudick J.; McKenzie T.L. Neighborhood poverty, park use, and park-based physical activity in a Southern California city. *Soc. Sci. Med.* 2012, 75, 2317–2325, https://doi.org/10.1016/j.socscimed.2012.08.036 PMID: 23010338

31. Malambo P.; Kengne A.P.; De Villiers A.; Lambert E.V; Puoane T. Built environment, selected risk factors and major cardiovascular disease outcomes: a systematic review. *PLoS One* 2016, 11, e0166846. https://doi.org/10.1371/journal.pone.0166846 PMID: 27808835

32. Belin L.; Huang R.-C. Childhood obesity, Hypertension, the metabolic syndrome and adult cardiovascular disease. *Clin. Exp. Pharmacol. Physiol.* 2008, 35, 409–411, https://doi.org/10.1111/j.1440-1618.2008.04887.x PMID: 18307730

33. van Emmerik N.M.A.; Renders C.M.; van der Veer M.; van Buuren S.; van der Baan-Slootweg O.H.; Kist-van Holthe J.E.; HiraSing R.A. High cardiovascular risk in severely obese young children and adolescents. *Arch. Dis. Child.* 2012, 97, 818 LP–821, https://doi.org/10.1136/archdischild-2012-301877 PMID: 22826539

34. Bianchini F.; Kaaks R.; Vainio H. Overweight, obesity, and cancer risk. *Lancet Oncol.* 2002, 3, 565–574, https://doi.org/10.1016/s1470-2045(02)00849-6 PMID: 12177794

35. Elliott M. The stress process in neighborhood context. *Health Place* 2000, 6, 287–299. https://doi.org/10.1016/s1353-8292(00)00010-1 PMID: 11027954

36. Augustin T.; Glass T.A.; James B.D.; Schwartz B.S. Neighborhood Psychosocial Hazards and Cardiovascular Disease: The Baltimore Memory Study. *Am. J. Public Health* 2008, 98, 1664–1670, https://doi.org/10.2105/AJPH.2007.125138 PMID: 18630886

37. Albert M.A.; Durazo E.M.; Slopen N.; Zaslavsky A.M.; Buring J.E.; Silva T.; Chasman D.; Williams D. R. Cumulative psychological stress and cardiovascular disease risk in middle aged and older women: Rationale, design, and baseline characteristics. *Am. Heart J.* 2017, 192, 1–12, https://doi.org/10.1016/j.ahj.2017.06.012 PMID: 28938955

38. Guidi J.; Lucente M.; Sonino N.; Fava G.A. Allostatic Load and Its Impact on Health: A Systematic Review. *Psychother. Psychosom.* 2021, 90, 11–27, https://doi.org/10.1159/000510696 PMID: 32799204

39. Giurgescu C.; Nowak A.L.; Gillespie S.; Nolan T.S.; Anderson C.M.; Ford J.L.; Hood D.B.; Williams K. P. Neighborhood environment and DNA methylation: implications for cardiovascular disease risk. *J. Urban Heal.* 2019, 96, 23–34, https://doi.org/10.1007/s11524-018-0341-1 PMID: 30635842

40. Jones R.; Tarter R.; Ross A.M. Greenspace Interventions, Stress and Cortisol: A Scoping Review. *Int. J. Environ. Res. Public Health* 2021, 18, 2802.
41. Luo Y.-N.; Huang W.-Z.; Liu X.-X.; Markevych I.; Bloom M.S.; Zhao T.; Heinrich J.; Yang B.-Y.; Dong G.-H. Greenspace with overweight and obesity: A systematic review and meta-analysis of epidemiological studies up to 2020. *Obes. Rev.* 2020, 21, e13078, [https://doi.org/10.1111/obr.13078](https://doi.org/10.1111/obr.13078) PMID: 32677149

42. Tamura K.; Langerman S.D.; Ceasar J.N.; Andrews M.R.; Agrawal M.; Powell-Wiley T.M. Neighborhood social environment and cardiovascular disease risk. *Curr. Cardiovasc. Risk Rep.* 2019, 13, 1–13. [https://doi.org/10.1007/s12170-019-0601-5](https://doi.org/10.1007/s12170-019-0601-5) PMID: 31482004

43. Barber S.; Hickson D.A.; Wang X.; Sims M.; Nelson C.; Diez-Roux A. V Neighborhood disadvantage, poor social conditions, and cardiovascular disease incidence among African American adults in the Jackson Heart Study. *Am. J. Public Health* 2016, 106, 2219–2226.

44. Malmström M. *Care Need Index, Social Deprivation and Health*. Epidemiological Studies in Swedish Health Care; Lund University, 2000; ISBN 9162838644.

45. Cubbin C.; Sundquist K.; Ahlen H.; Johansson S.-E.; Winkleby M.A.; Sundquist J. Neighborhood deprivation and cardiovascular disease risk factors: protective and harmful effects. *Scand. J. Public Health* 2006, 228–237. [https://doi.org/10.1080/14034940500327935](https://doi.org/10.1080/14034940500327935) PMID: 16754580

46. Li X.; Sundquist K.; Sundquist J. Neighborhood deprivation and prostate cancer mortality: a multilevel analysis from Sweden. *Prostate Cancer Prostatic Dis.* 2012, 15, 128–134. [https://doi.org/10.1038/pcan.2011.46](https://doi.org/10.1038/pcan.2011.46) PMID: 21986984

47. Sugiyama T.; Villanueva K.; Kuiman M.; Francis J.; Foster S.; Wood L.; Giles-Corti B. Can neighborhood green space mitigate health inequalities? A study of socio-economic status and mental health. *Health Place* 2016, 38, 16–21. [https://doi.org/10.1016/j.healthplace.2016.01.002](https://doi.org/10.1016/j.healthplace.2016.01.002) PMID: 26796324

48. Bor J.; Cohen G.H.; Galea S. Population health in an era of rising income inequality: USA, 1980–2015. *Lancet* 2017, 389, 1475–1490, [https://doi.org/10.1016/S0140-6736(17)30571-8](https://doi.org/10.1016/S0140-6736(17)30571-8) PMID: 28402829

49. Cubbin C.; Hadden W.C.; Winkleby M.A. Neighborhood context and cardiovascular disease risk factors: the contribution of material deprivation. *Etnh. Dis.* 2001, 11, 687–700. PMID: 11763293

50. Xiao Q.; Berrigan D.; Powell-Wiley T.M.; Matthews C.E. Ten-year change in neighborhood socioeconomic deprivation and rates of Total, cardiovascular disease, and Cancer mortality in older US adults. *Am. J. Epidemiol.* 2018, 187, 2642–2650. [https://doi.org/10.1093/aje/kwy181](https://doi.org/10.1093/aje/kwy181) PMID: 30137194

51. Claudel S.E.; Adu-Brimpong J.; Banks A.; Ayers C.; Albert M.A.; Das S.R.; de Lemos J.A.; Leonard T.; Polek C.; Hardie T.; Deatrick J.A. Breast cancer survivorship experiences of urban Hispanic women. *Cancer Causes Control* 2019, 30, 631–647. [https://doi.org/10.1007/s10552-011-9736-5](https://doi.org/10.1007/s10552-011-9736-5) PMID: 21318584

52. Hossain F.; Danos D.; Prakash O.; Gilliland N.; Simonson N.; Leonardi C.; Yu Q.; Wu X.-C.; Miele L. Neighborhood social determinants of triple negative breast cancer. *Front. public Heal.* 2019, 7, 18. [https://doi.org/10.3389/fpubh.2019.00018](https://doi.org/10.3389/fpubh.2019.00018) PMID: 30834239

53. Gomez S.L.; Glaser S.L.; McClure L.A.; Shema S.J.; Keegan T.H.M.; Satariano W.A. The California Neighborhoods Data System: a new resource for examining the impact of neighborhood social and built environment on breast cancer risk: the neighborhoods and breast cancer study 2017.

54. Krieger N.; Quesenberry C.J.; Peng T.; Horn-Ross P.; Stewart S.; Brown S.; Swallen K.; Guillermo T.; Suh D.; Alvarez-Martinez L.; et al. Social class, race/ethnicity, and incidence of breast, cervix, colon, lung, and prostate cancer among Asian, Black, Hispanic, and White residents of the San Francisco Bay Area, 1988–92 (United States). *Cancer Causes Control* 1999, 10, 525–537, [https://doi.org/10.1023/a:1008950210967](https://doi.org/10.1023/a:1008950210967) PMID: 10616822

55. Hiatt R.A.; Breen N. The social determinants of cancer: a challenge for transdisciplinary science. *Am. J. Prev. Med.* 2008, 35, S141–50, [https://doi.org/10.1016/j.amepre.2008.05.006](https://doi.org/10.1016/j.amepre.2008.05.006) PMID: 18619394

56. Conroy S.M.; Shariff-Marco S.; Koo J.; Yang J.; Keegan T.H.M.; Sangaramoorthy M.; Hertz A.; Nelson D.O.; Cockburn M.; Satariano W.A. Racial/ethnic differences in the impact of neighborhood social and built environment on breast cancer risk: the neighborhoods and breast cancer study 2017.

57. Gomez S.L.; Press D.J.; Lichtensztajn D.; Keegan T.H.M.; Shema S.J.; Le G.M.; Kurian A.W. Patient, hospital, and neighborhood factors associated with treatment of early-stage breast cancer among Asian American women in California. *Cancer Epidemiol. Biomarkers Prev.* 2012, 21, 821–834, [https://doi.org/10.1158/1055-9965.EPI-12-0475](https://doi.org/10.1158/1055-9965.EPI-12-0475) PMID: 22402290

58. Polec C.; Hardie T.; Deatrick J.A. Breast cancer survivorship experiences of urban Hispanic women. *J. Cancer Educ.* 2020, 35, 923–929, [https://doi.org/10.1007/s13187-019-01543-0](https://doi.org/10.1007/s13187-019-01543-0) PMID: 31098836
60. Cheng I.; Shariff-Marco S.; Koo J.; Monroe K.R.; Yang J.; John E.M.; Kurian A.W.; Kwan M.L.; Henderson B.E.; Bernstein L.; et al. Contribution of the neighborhood environment and obesity to breast cancer survival: the California Breast Cancer Survivorship Consortium. *Cancer Epidemiol. Biomarkers Prev.* 2015, 24, 1282–1290, https://doi.org/10.1158/1055-9966.EPI-15-0055 PMID: 26063477

61. Fleisch Marcus A.; Illescas A.H.; Hohl B.C.; Llanos A.A.M. Relationships between social isolation, neighborhood poverty, and cancer mortality in a population-based study of US adults. *PLoS One* 2017, 12, e0173370. https://doi.org/10.1371/journal.pone.0173370 PMID: 28273125

62. Baaghideh M.; Mayvaneh F. Climate change and simulation of cardiovascular disease mortality: A case study of Mashhad, Iran. *Iran. J. Public Health* 2017, 46, 396. PMID: 28435826

63. Cheng X.; Su H. Effects of climatic temperature stress on cardiovascular diseases. *Eur. J. Intern. Med.* 2010, 21, 164–167. https://doi.org/10.1016/j.ejim.2010.03.001 PMID: 20493415

64. Kovats R.S.; Campbell-Lendrum D.; Matthies F. Climate change and human health: Estimating avoidable deaths and disease. *Risk Anal.* 2005, 25, 1409–1418, https://doi.org/10.1111/j.1539-6924.2005.00688.x PMID: 16506971

65. Patz J.A.; Campbell-Lendrum D.; Holloway T.; Foley J.A. Impact of regional climate change on human health. *Nature* 2005, 438, 310–317. https://doi.org/10.1038/nature04188 PMID: 16292302

66. Bhaskaran K.; Hajat S.; Haines A.; Herrett E.; Wilkinson P.; Smeeth L. Effects of ambient temperature on the incidence of myocardial infarction. *Heart* 2009, 95, 1760–1769. https://doi.org/10.1136/hrt.2009.175000 PMID: 19635724

67. Basu R.; Ostro B.D. A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. *Am. J. Epidemiol.* 2008, 168, 632–637. https://doi.org/10.1093/aje/kwn170 PMID: 18663214

68. Martin C.W.; Maggio R.C.; Appel D.N. The contributory value of trees to residential property in the Austin, Texas metropolitan area. *J. Arboric.* 1989, 15, 72–75.

69. Morales D.J. The contribution of trees to residential property value. *J. Arboric.* 1980, 6, 305–308.

70. Anderson L.M.; Cordell H.K. Influence of trees on residential property values in Athens, Georgia (USA): A survey based on actual sales prices. *Landsc. Urban Plan.* 1988, 15, 153–164.

71. Twogih-Bennett C.; Jones A. The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes. *Environ. Res.* 2018, 166, 628–837, https://doi.org/10.1016/j.envres.2018.06.030 PMID: 29982151

72. Yeager R.; Riggs D.W.; DeJarnett N.; Tollerson D.J.; Wilson J.; Conklin D.J.; O’Toole T.E.; McCracken J.; Lorkiewicz P.; Xie Z.; et al. Association between residential greenness and cardiovascular disease risk. *J. Am. Heart Assoc.* 2018, 7, https://doi.org/10.1161/JAHA.118.009117 PMID: 30561265

73. Dalton A.M.; Jones A.P. Residential neighbourhood greenspace is associated with reduced risk of cardiovascular disease: A prospective cohort study. *PLoS One* 2020, 15, 1–16, https://doi.org/10.1371/journal.pone.0226524 PMID: 31899764

74. Komar P.; Bauwelinc M.; Zijlema W.; Bartoll X.; Cirach M.; Vandenheede H.; Nieuwenhuijzen M.; Borrell C.; Dadvand P. Greenspace and cardiovascular morbidity: a comparative study in two European cities. *Environ. Epidemiol.* 2019, 3, 25.

75. Gascon M.; Triguero-Mas M.; Martinez D.; Dadvand P.; Rojas-Rueda D.; Plasencia A.; Nieuwenhuijzen M.J.; Martinez D.; Dadvand P.; Rojas-Rueda D.; et al. Residential green spaces and mortality: A systematic review. *Environ. Int.* 2016, 86, 60–67, https://doi.org/10.1016/j.envint.2015.10.013 PMID: 26540085

76. Liu X.X.; Ma X.L.; Huang W.Z.; Luo Y.N.; He C.J.; Zhong X.M.; Dadvand P.; Browning M.H.E.M.; Li L.; Zou X.G.; et al. Green space and cardiovascular disease: A systematic review with meta-analysis. *Environ. Pollut.* 2022, 301, 118990, https://doi.org/10.1016/j.envpol.2022.118990 PMID: 35181451

77. Wray A.; Olstad D.L.; Minaker L.M. Smart prevention: a new approach to primary and secondary cancer prevention in smart and connected communities. *Cities* 2018, 79, 53–69.

78. Porcherie M.; Linn N.; Le Gall A.R.; Thomas M.-F.; Faure E.; Rican S.; Simos J.; Cantoreggi N.; Vailant Z.; Cambron L. Relationship between Urban Green Spaces and Cancer: A Scoping Review. *Int. J. Environ. Res. Public Health* 2021, 18, 1751.

79. Datzmann T.; Markevych I.; Trautmann F.; Heinrich J.; Schmitt J.; Tesch F. Outdoor air pollution, green space, and cancer incidence in Saxony: a semi-individual cohort study. *BMJ Public Health* 2018, 18, 1–10.

80. Nakau M.; Imanishi J.; Imanishi J.; Watanabe S.; Imanishi A.; Baba T.; Hirai K.; Ito T.; Chiba W.; Morimoto Y. Spiritual care of cancer patients by integrated medicine in urban green space: a pilot study. *Explores* 2013, 9, 87–90, https://doi.org/10.1016/j.explore.2012.12.002 PMID: 23452710

81. Iyer H.S.; James P.; Valeri L.; Hart J.E.; Pernar C.H.; Mucci L.A.; Holmes M.D.; Laden F.; Rebbeck T.R. The association between neighborhood greenness and incidence of lethal prostate cancer: A
prospective cohort study. *Environ. Epidemiol.* (Philadelphia, Pa.) 2020, 4. https://doi.org/10.1097/ EE9.0000000000000091 PMID: 32656487

82. Bikomeye J.C.; Rublee C.S.; Beyer K.M.M. Positive Externalities of Climate Change Mitigation and Adaptation for Human Health: A Review and Conceptual Framework for Public Health Research. *Int. J. Environ. Res. Public Health* 2021, 18, 2481, https://doi.org/10.3390/ijerph18052481 PMID: 33802347

83. Razani N.; Kohn M.A.; Wells N.M.; Thompson D.; Flores H.H.; Rutherford G.W. Design and evaluation of a park prescription program for stress reduction and health promotion in low-income families: The Stay Healthy in Nature Everyday (SHINE) study protocol. Contemp. Clin. Trials 2016, 51, 8–14. https://doi.org/10.1016/j.cct.2016.09.007 PMID: 27693759

84. Messiah S.E.; Jiang S.; Kardys J.; Hansen E.; Nardi M.; Forster L. Reducing childhood obesity through coordinated care: Development of a park prescription program. *World J. Clin. Pediatr.* 2016, 5, 234. https://doi.org/10.5409/wjcp.v5.i3.234 PMID: 27610338

85. Müller-Riemenschneider F.; Petrunoff N.; Sia A.; Ramiah A.; Ng A.; Han J.; Wong M.; Choo T.B.; Uijtdewilligen L. Prescribing physical activity in parks to improve health and wellbeing: protocol of the park prescription randomized controlled trial. *Int. J. Environ. Res. Public Health* 2018, 15, 1154. https://doi.org/10.3390/ijerph15061154 PMID: 30720784

86. Müller-Riemenschneider F.; Petrunoff N.; Yao J.; Ng A.; Sia A.; Ramiah A.; Wong M.; Han J.; Tai B.C.; Uijtdewilligen L. Effectiveness of prescribing physical activity in parks to improve health and wellbeing: the park prescription randomized controlled trial. *Int. J. Behav. Nutr. Phys. Act.* 2020, 17, 1–14.

87. Moher D.; Libarati A.; Tetzlaff J.; Altman D.G. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 2009, 6, e1000097, https://doi.org/10.1371/journal.pmed.1000097 PMID: 19621072

88. Moher D.; Shamseer L.; Clarke M.; Gherisi D.; Liberati A.; Petticrew M.; Sheller K.; Stewart L.A. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst. Rev.* 2015, 4, 1. https://doi.org/10.1186/s40647-014-0009-4 PMID: 25954246

89. Page M.J.; McKenzie J.E.; Bossuyt P.M.; Boutron I.; Hoffmann T.C.; Mulrow C.D.; Shamseer L.; Tetzlaff J.M.; Akl E.A.; Brennan S.E.; et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMA* 2021, 372, n71, https://doi.org/10.1136/bmj.n71 PMID: 3782057

90. Ouzzani M.; Hammady H.; Fedorowicz Z.; Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst. Rev.* 2016, 5, 210, https://doi.org/10.1186/s13643-016-0384-4 PMID: 27919275

91. Khabsa M.; Elmagarmid A.; Ilyas I.; Hammad H.; Ouzzani M. Learning to identify relevant studies for systematic reviews using random forest and external information. *Mach. Learn.* 2015, 1–18, https://doi.org/10.1007/s10994-015-5535-7

92. Nang C.; Piano B.; Lewis A.; Lycett K.; Woodhouse M. Using the PICOS model to design and conduct a systematic search: a speech pathology case study. Edith Cowan University, Joondalup, Australia, 2015.

93. Kokkinos P.F.; Faselis C.; Myers J.; Narayan P.; Sui X.; Zhang J.; Lave C.J.; Moore H.; Karasik P.; Fletcher R. Cardiorespiratory Fitness and Incidence of Major Adverse Cardiovascular Events in US Veterans: A Cohort Study. *Mayo Clin. Proc.* 2017, 92, 39–48, https://doi.org/10.1016/j.mayocp.2016.09.013 PMID: 2876315

94. Trialists’ Collaboration B.P.L.T. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. *BMJ* 2008, 336, 1121–1123, https://doi.org/10.1136/bmj.39548.738368.BE PMID: 18480116

95. Wang T.J.; Gona P.; Larson M.G.; Tofler G.H.; Levy D.; Newton-Cheh C.; Jacques P.F.; Rifai N.; Selhub J.; Robins S.J.; et al. Multiple Biomarkers for the Prediction of First Major Cardiovascular Events and Death. *N. Engl. J. Med.* 2006, 355, 2631–2639. https://doi.org/10.1056/NEJMoa055373 PMID: 17182988

96. National Cancer Institute Definition of survivorship—NCI Dictionary of Cancer Terms Available online: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/survivorship (accessed on Jan 14, 2021).

97. Bikomeye J.; Balza J.; Beyer K. The Impact of Schoolyard Greening on Children’s Physical Activity and Socioemotional Health: A Systematic Review of Experimental Studies. *Int. J. Environ. Res. Public Health* 2021, 18, 535, https://doi.org/10.3390/ijerph18020535 PMID: 33561082

98. Veronese N.; Cereda E.; Solmi M.; Fowler S.A.; Manzato E.; Maggi S.; Manu P.; Abe E.; Hayashi K.; Allard J.P.; et al. Inverse relationship between body mass index and mortality in older nursing home residents: a meta-analysis of 19,538 elderly subjects. *Obes. Res. an Off. J. Int. Assoc. Study Obes.* 2015, 16, 1001–1015, https://doi.org/10.1111/obr.12309 PMID: 26252230
99. Luchini C.; Stubbs B.; Solmi M.; Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. *World J Meta-Anal*, 2017, 5, 80–84. https://doi.org/10.13105/wjma.v5.i4.80

100. Mao G.-X.; Cao Y.-B.; Lan X.-G.; He Z.-H.; Chen Z.-M.; Wang Y.-Z.; Hu X.-L.; Lv Y.-D.; Wang G.-F.; Yan J. Therapeutic effect of forest bathing on human hypertension in the elderly. *J. Cardiol.*, 2012, 60, 495–502. https://doi.org/10.1016/j.jcc.2012.08.003 PMID: 22948092

101. Navalta J.W.; Bodell N.G.; Tanner E.A.; Aguilar C.D.; Radzak K.N. Effect of exercise in a desert environment on physiological and subjective measures. *Int. J. Environ. Health Res.*, 2021, 31, 121–131. https://doi.org/10.1080/09603123.2019.1631961 PMID: 31240953

102. Duncan M.J.; Clarke N.D.; Birch S.L.; Tallis J.; Hankey J.; Bryant E.; Eyre E.L. The effect of green exercise on blood pressure, heart rate and mood state in primary school children. *Int. J. Environ. Res. Public Health*. 2014, 11, 3678–3688.

103. Furuhashi A.; Tabuchi K.; Norikoshi K.; Kobayashi T.; Oriyama S. A comparative study of the physiological and psychological effects of forest bathing (Shinrin-yoku) on working age people with and without depressive tendencies. *Environ. Heal. Prev. Med.* Med. 2019, 24, 46. https://doi.org/10.1186/s12990-019-0800-1 PMID: 31228960

104. Grazuleviciene R.; Venclovienė J.; Kubilius R.; Grizas V.; Danileviciute A.; Dedele A.; Andrusaityte S.; Vakarelikas K.; Kveiatė R. Psychological and physical effects of forest therapy on middle-aged males with high-normal blood pressure. *Int. J. Environ. Res. Public Health*. 2017, 14, 11. https://doi.org/10.3390/ijerph14080905 PMID: 28800067

105. Mao G.; Cao Y.; Wang B.; Wang S.; Chen Z.; Wang J.; Xing W.; Ren X.; Lv X.; Dong J.; et al. The Salutary Influence of Forest Bathing on Elderly Patients with Chronic Heart Failure. *Int. J. Environ. Res. Public Health*. 2017, 14, 31. https://doi.org/10.3390/ijerph14030368 PMID: 28362327

106. Mao G.; Lan X.; Cao Y.; Chen Z.; He Z.; Lv Y.; Wang Y.; Hu X.; Wang G.; Yan J. Effects of Short-Term Forest Bathing on Human Health in a Broad-Leaved Evergreen Forest in Zhejiang Province, China. *Biomed. Environ. Sci.* 2012, 25, 317–324, https://doi.org/10.3967/0895-3988.2012.03.010 PMID: 22840583

107. Li Q.; Kobayashi M.; Kumeda S.; Ochiai T.; Miura T.; Kagawa T.; Imai M.; Wang Z.; Otsuka T.; Kawada T. Effects of Forest Bathing on Cardiovascular and Metabolic Parameters in Middle-Aged Males. *Evidence-Based Complement. Altern. Med. eCAM*. 2016, 2016, 2587381. https://doi.org/10.1155/2016/2587381 PMID: 27493670

108. Chen H.T.; Yu C.P.; Lee H.Y. The effects of forest bathing on stress recovery: Evidence from middle-aged females of Taiwan. *Forests*. 2018, 8.

109. Ochiai H.; Ikei H.; Song C.; Kobayashi M.; Takamatsu A.; Miura T.; Kagawa T.; Li Q.; Kumeda S.; Imai M.; et al. Physiological and psychological effects of forest therapy on middle-aged males with high-normal blood pressure. *Int. J. Environ. Res. Public Health*. 2015, 12, 2532–2542.

110. Peterfalvi A.; Meggyes M.; Makszin L.; Farkas N.; Miko E.; Miseta A.; Szereday L. Forest Bathing Always Makes Sense: Blood Pressure-Lowering and Immune System-Balancing Effects in Late Spring and Winter in Central Europe. *Int. J. Environ. Res. Public Health*. 2021, 18, 20. https://doi.org/10.3390/ijerph18042067 PMID: 33672536

111. Pretty J.; Peacock J.; Sellens M.; Griffin M. The mental and physical health outcomes of green exercise. *Int. J. Environ. Health Res.* 2005, 15, 319–337. https://doi.org/10.1080/09603120500155963 PMID: 16416750

112. Song C.; Ikei H.; Nara M.; Takayama D.; Miyazaki Y. Physiological Effects of Viewing Bonsai in Elderly Patients Undergoing Rehabilitation. *Int. J. Environ. Res. Public Health*. 2018, 15, 25. https://doi.org/10.3390/ijerph15122635 PMID: 30477254

113. Tsuchumi N.; Nogaki H.; Shimizu Y.; Stone T.E.; Kobayashi T. Individual reactions to viewing preferred video representations of the natural environment: A comparison of mental and physical reactions. *Japan J. Nurs. Sci. JJNS*. 2017, 14, 3–12. https://doi.org/10.1111/jjns.12131 PMID: 27160351

114. White M.P.; Pahl S.; Ashbulyk K.J.; Burton F.; Depledge M.H. The effects of exercising in different natural environments on psycho-physiological outcomes in post-menopausal women: A simulation.
118. Bielinis E.; Bielinis L.; Krupińska-Szeluga S.; Lukowski A.; Takayama N. The effects of a short forest recreation program on physiological and psychological relaxation in young Polish adults. *Forests* 2019, 10.

119. Yu C.P.; Lin C.M.; Tsai M.J.; Tsai Y.C.; Chen C.Y. Effects of Short Forest Bathing Program on Autonomic Nervous System Activity and Mood States in Middle-Aged and Elderly Individuals. *Int. J. Environ. Res. Public Health.* [Electronic Resour. 2017, 14, 9. https://doi.org/10.3390/ijerph14080897 PMID: 28792445]

120. Koura S.; Ikeda A.; Rappe E.; Park S.A. Effects of horticultural therapeutic garden on autonomic nervous system among elderly people with dementia and the value of people-plants relationships. *Acta Hort.* 2016, 1121, 27–32.

121. McEwan K.; Giles D.; Clarke F.J.; Kotera Y.; Evans G.; Terebenina O.; Minou L.; Teeling C.; Basran J.; Wood W.; et al. A pragmatic controlled trial of forest bathing compared with compassionate mind training in the UK: Impacts on self-reported wellbeing and heart rate variability. *Sustain.* 2021, 13, 1–20.

122. Park S.A.; Lee A.Y.; Park H.G.; Son K.C.; Kim D.S.; Lee W.L. Gardening intervention as a low- to moderate-intensity physical activity for improving blood lipid profiles, blood pressure, inflammation, and oxidative stress in women over the age of 70: A pilot study. *HortScience* 2017, 52, 200–205.

123. Song C.; Joung D.; Ikeda H.; Igarashi M.; Aga M.; Park B.J.; Miwa M.; Takagaki M.; Miyazaki Y. Physiological and psychological effects of walking on young males in urban parks in winter. *J. Physiol. Anthropol.* 2013, 32.

124. Wu Q.; Ye B.; Lv X.; Mao G.; Wang S.; Chen Z.; Wang G. Adjunctive therapeutic effects of cinnamonum camphora forest environment on elderly patients with hypertension. *Int. J. Gerontol.* 2020, 14, 327–331.

125. Lanki T.; Siiponen T.; Ojala A.; Korpela K.; Pennanen A.; Tiittanen P.; Tsunetsugu Y.; Kagawa T.; Tyrnänen L. Acute effects of visits to urban green environments on cardiovascular physiology in women: A field experiment. *Environ. Res.* 2017, 159, 176–185. https://doi.org/10.1016/j.envres.2017.07.039 PMID: 28602208

126. Bail J.R.; Fruge A.D.; Cases M.G.; De Los Santos J.F.; Locher J.L.; Smith K.P.; Cantor A.B.; Cohen H.J.; Demark-Wahnefried W. A home-based mentored vegetable gardening intervention demonstrates feasibility and improvements in physical activity and performance among breast cancer survivors. *Cancer* 2018, 124, 3427–3435. https://doi.org/10.1002/cncr.31559 PMID: 29832460

127. Blair C.K.; Madan-Swain A.; Locher J.L.; Desmond P.A.; de Los Santos J.; Affuso O.; Glover T.; Smith K.; Carley J.; Lipsitz M.; et al. Harvest for health gardening intervention feasibility study in cancer survivors. *Acta Oncol.* (Madr) 2013, 52, 1110–1118. https://doi.org/10.3109/0284186X.2013.770165 PMID: 23438359

128. Demark-Wahnefried W.; Cases M.G.; Cantor A.B.; Fruge A.D.; Smith K.P.; Locher J.; Cohen H.J.; Tsuruta Y.; Daniel M.; Kaia R.; et al. Pilot Randomized Controlled Trial of a Home Vegetable Gardening Intervention among Older Cancer Survivors Shows Feasibility, Satisfaction, and Promise in Improving Vegetable and Fruit Consumption, Reassurance of Worth, and the Trajectory of Central Adipos. *J. Acad. Nutr. Diet.* 2018, 118, 689–704.

129. Li Q.; Morimoto K.; Kobayashi M.; Inagaki H.; Katsumata M.; Hirata Y.; Hirata K.; Suzuki H.; Li Y.J.; Wakayama Y. Visiting a forest, but not a city, increases human natural killer activity and expression of anti-cancer proteins. *Int. J. Immunopathol. Pharmacol.* 2008, 21, 117–127. https://doi.org/10.1177/039463200802100113 PMID: 18336737

130. Li Q.; Morimoto K.; Nakada A.; Inagaki H.; Katsumata M.; Shimizu T.; Hirata Y.; Hirata K.; Suzuki H.; Miyazaki Y.; et al. Forest Bathing Enhances Human Natural Killer Activity and Expression of Anti-Cancer Proteins. *Int. J. Immunopathol. Pharmacol.* 2007, 20, 3–8, https://doi.org/10.1177/03946320070200202 PMID: 17903349

131. Miyazaki Y. *Shinrin Yoku: The Japanese art of forest bathing.* Timber Press, 2018; ISBN 1604698799.

132. Global Wellness Institute Definition of Forest Bathing Available online: https://globalwellnessinstitute.org/wellnessevidence/forest-bathing/ (accessed on Apr 10, 2021).

133. FITZGERALD, S. The secret to mindful travel? A walk in the woods Available online: https://www.nationalgeographic.com/travel/article/forest-bathing-nature-walk-health (accessed on Apr 10, 2021).

134. Li Q. Introduction of Forest Medicine-Effects of Forest Bathing/Shinrin-Yoku on Human Health. *For. Public Heal.* 2020, 2.

135. Li Q. Effect of forest bathing trips on human immune function. *Environ. Health Prev. Med.* 2010, 15, 9–17. https://doi.org/10.1007/s12199-008-0068-3 PMID: 19568839

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136. Kuo M. How might contact with nature promote human health? Promising mechanisms and a possible central pathway. Front. Psychol. 2015, 6. https://doi.org/10.3389/fpsyg.2015.01093 PMID: 26379564

137. Bonsai Empire Definition and meaning of Bonsai Available online: https://www.bonsaiempire.com/origin/what-is-bonsai (accessed on Apr 22, 2021).

138. Gladwell V.F.; Brown D.K.; Wood C.; Sandercoc G.R.; Barton J.L. The great outdoors: how a green exercise environment can benefit all. Extrem. Physiol. Med. 2013, 2, 3. https://doi.org/10.1186/2046-7648-2-3 PMID: 23849478

139. Lahart I.; Darcy P.; Gidlow C.; Calogiuri G. The effects of green exercise on physical and mental well-being: A systematic review. Int. J. Environ. Res. Public Health 2019, 16, 1352. https://doi.org/10.3390/ijerph16081352 PMID: 30991724

140. Thompson Coon J.; Boddy K.; Stein K.; Whear R.; Barton J.; Depledge M.H. Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental well-being than physical activity indoors? A systematic review. Environ. Sci. Technol. 2011, 45, 1761–1772. https://doi.org/10.1021/es102947t PMID: 21291246

141. Barton J.; Pretty J. What is the best dose of nature and green exercise for improving mental health? A multi-study analysis. Environ. Sci. Technol. 2010, 44, 3947–3955. https://doi.org/10.1021/es903183r PMID: 20337470

142. Barton J.; Hine R.; Pretty J. The health benefits of walking in greenspaces of high natural and heritage value. J. Integr. Environ. Sci. 2009, 6, 261–278.

143. Pretty J.; Peacock J.; Hine R.; Sellens M.; South N.; Griffin M. Green exercise in the UK countryside: Effects on health and psychological well-being, and implications for policy and planning. J. Environ. Plan. Manag. 2007, 50, 211–231.

144. Calogiuri G.; Evensen K.; Weydahl A.; Andersson K.; Patil G.; Ihlebæk C.; Raanaas R.K. Green exercise as a workplace intervention to reduce job stress. Results from a pilot study. Work 2016, 53, 99–111.

145. Steptoe A.; Kiivimäki M. Stress and cardiovascular disease. Nat. Rev. Cardiol. 2012, 9, 360–370. https://doi.org/10.1038/nrcardio.2012.45 PMID: 22473079

146. Steptoe A.; Kiivimäki M. Stress and cardiovascular disease: an update on current knowledge. Annu. Rev. Public Health 2013, 34, 337–354. https://doi.org/10.1146/annurev-publichealth-031912-114452 PMID: 23297662

147. Esch T.; Stefano G.B.; Fricchione G.L.; Benson H. Stress in cardiovascular diseases. J. Psychosom. Res. 2002, 52, 1–23. https://doi.org/10.1016/s0022-3999(01)00302-6 PMID: 11801260

148. Black P.H.; Garbutt L.D. Stress, inflammation and cardiovascular disease. J. Psychosom. Res. 2009, 6, 261–278. https://doi.org/10.1016/j.jpsychores.2008.07.016 PMID: 19051686

149. Community Preventive Services Task Force, T. Community Preventive Services Task Force Finding and Rationale Statement—Nutrition: Gardening Interventions to Increase Fruit and Vegetable Consumption Among Children. 2017.

150. Kim S.-O.; Park S.-A. Garden-Based Integrated Intervention for Improving Children’s Eating Behavior for Vegetables. Int. J. Environ. Res. Public Health 2020, 17, 1257, https://doi.org/10.3390/ijerph17041257 PMID: 32075303

151. Quinn J.; Trinklein D. Vegetable Gardening: Missouri Master Gardener Core Manual Available online: https://extension.missouri.edu/publications/mg5 (accessed on Apr 11, 2021).

152. Soga M.; Gaston K.J.; Yamura Y. Gardening is beneficial for health: A meta-analysis. Prev. Med. reports 2017, 5, 92–99. https://doi.org/10.1016/j.pmedr.2016.11.007 PMID: 27981022

153. Nicklett E.J.; Anderson L.A.; Yen I.H. Gardening is beneficial for health: A meta-analysis. J. Appl. Gerontol. 2016, 35, 678–690. https://doi.org/10.1177/0733464814536308 PMID: 25515757

154. Park S.-A.; Lee A.-Y.; Son K.-C.; Lee W.-L.; Kim D.-S. Gardening intervention for physical and psychological health benefits in elderly women at community centers. Horttechnology 2016, 26, 474–483.

155. Ohly H.; Gentry S.; Wigglesworth R.; Bethel A.; Lovell R.; Garside R. A systematic review of the health and well-being impacts of school gardening: synthesis of quantitative and qualitative evidence. BMC Public Health 2016, 16, 1–36.

156. Clatworthy J.; Hinds J.; Camic P.M. Gardening as a mental health intervention: a review. Ment. Heal. Rev. J. 2013.

157. Page M. Gardening as a therapeutic intervention in mental health. Nurs. Times 2008, 104, 28–30. PMID: 19051686

158. Infatino M. Gardening: a strategy for health promotion in older women. J. N. Y. State Nurses. Assoc. 2004, 35, 10–17. PMID: 15884480
159. Husk K.; Lovell R.; Garside R. Prescribing gardening and conservation activities for health and well-being in older people. *Maturitas* 2018, 110, A1–A2. [https://doi.org/10.1016/j.maturitas.2017.12.013](https://doi.org/10.1016/j.maturitas.2017.12.013) PMID: 29279141

160. Cutillo A.; Rathore N.; Reynolds N.; Hilliard L.; Haines H.; Whelan K.; Madan-Swain A. A literature review of nature-based therapy and its application in cancer care. *J. Ther. Hortic.* 2015, 25, 3–15.

161. Fillon M. Home gardening: an effective cancer therapy. *JNCI J. Natl. Cancer Inst.* 2014, 106.

162. Cases M.G.; Frugé A.D.; Jennifer F.; Locher J.L.; Cantor A.B.; Smith K.P.; Glover T.A.; Cohen H.J.; Daniel M.; Morrow C.D. Detailed methods of two home-based vegetable gardening intervention trials to improve diet, physical activity, and quality of life in two different populations of cancer survivors. *Contemp. Clin. Trials* 2016, 50, 201–212. [https://doi.org/10.1016/j.cct.2016.08.014](https://doi.org/10.1016/j.cct.2016.08.014) PMID: 27565830

163. Zvereva M.I.; Shcherbakova D.M.; Dontsova O.A. Telomerase: structure, functions, and activity regulation. *Biochemistry. (Mosc.)* 2010, 75, 1563–1583, [https://doi.org/10.1134/s0006297910130055](https://doi.org/10.1134/s0006297910130055) PMID: 21417995

164. Garcia M.T.; Ribeiro S.M.; Germani A.C.C.G.; Bógus C.M. The impact of urban gardens on adequate and healthy food: a systematic review. *Public Health Nutr.* 2018, 21, 416–425. [https://doi.org/10.1017/S1368980017002944](https://doi.org/10.1017/S1368980017002944) PMID: 29160186

165. Diekmann L.O.; Gray L.C.; Baker G.A. Growing ‘good food’: Urban gardens, culturally acceptable produce and food security. *Renew. Agric. Food Syst.* 2020, 35, 169–181.

166. Barthel S.; Isendahl C. Urban gardens, agriculture, and water management: Sources of resilience for long-term food security in cities. *Ecol. Econ.* 2013, 86, 224–234.

167. Cabral I.; Costa S.; Weiland U.; Bonn A. Urban gardens as multifunctional nature-based solutions for societal goals in a changing climate. In *Nature-Based Solutions to Climate Change Adaptation in Urban Areas*; Springer, Cham, 2017; pp. 237–253.

168. Brown D.K.; Barton J.L.; Gladwell V.F. Viewing nature scenes positively affects recovery of autonomic function following acute-mental stress. *Environ. Sci. Technol.* 2013, 47, 5562–5569. [https://doi.org/10.1021/es305019p](https://doi.org/10.1021/es305019p) PMID: 23590163

169. Bikomeye J.C.; Namin S.; Anyanwu C.; Rublee C.S.; Fersching J.; Leinbach K.; Lindquist P.; Hoppe A.; Hoffman L.; Hegarty J.; et al. Resilience and Equity in a Time of Crises: Investing in Public Urban Greenspace Is Now More Essential Than Ever in the US and Beyond. *Int. J. Environ. Res. Public Heal.* 2021, *Vol. 18, Page 84202021, 18, 8420, [https://doi.org/10.3390/ijerph18168420](https://doi.org/10.3390/ijerph18168420) PMID: 34444169