



AKADÉMIAI KIADÓ

# The potential of psilocybin use to enhance well-being in healthy individuals – A scoping review

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## REVIEW ARTICLE



### ABSTRACT

*Background and aims:* This scoping review employed a multifaceted conceptualization of well-being to examine how psilocybin use affects well-being and related sub-concepts in healthy individuals. It investigated which factors influence the relationship between psilocybin use and well-being, what research protocols have been employed, and what underlying mechanisms have been proposed in existing studies. *Methods:* A comprehensive literature search in line with the PRISMA guidelines was conducted. Scopus, PubMed, PsycINFO, Web of Science, and Google Scholar were searched for peer-reviewed articles about psilocybin and well-being in healthy populations. *Results:* Studies were heterogeneous in regard to study objectives, study design, study procedure, sample size and psilocybin dosage. In all studies, psilocybin use led to positive well-being-related outcomes for the majority of participants. Facets of well-being positively affected by psilocybin use in this review were self-acceptance, positive relationships, and meaning/purpose in life. *Conclusions:* This scoping review provided preliminary evidence for the beneficial effects of psilocybin on well-being and related sub-concepts such as self-acceptance, positive relationships, and meaning/purpose in life in healthy individuals. Ego-dissolution, unity, connectedness, and mystical-type experiences are interrelated concepts that seem to be crucial for explaining such positive well-being-related effects of psilocybin. Under conducive conditions, the use of psilocybin may contribute to healthy functioning, through broad and sustained improvements in a variety of well-being concepts. Due to the heterogeneous nature of the studies, more definite conclusions require further research with a rigorous and homogeneous design.

### KEYWORDS

psilocybin, well-being, scoping review

## INTRODUCTION

### What is psilocybin?

Psilocybin is a psychoactive compound that can induce psychedelic effects (Griffiths, Richards, McCann, & Jesse, 2006). It is a tryptamine alkaloid that naturally occurs in a variety of Psilocybe mushroom species, also known as *magic mushrooms*. Along with lysergic acid diethylamide (LSD), mescaline and N, N-dimethyltryptamine (DMT), psilocybin is a classic psychedelic, which is defined as “a drug which, without causing physical addiction, craving, major physiological disturbances, delirium, disorientation, or amnesia, more or less reliably produces thought, mood, and perceptual changes otherwise rarely experienced except in dreams, contemplative and religious exaltation, flashes of vivid involuntary memory, and acute psychosis” (Grinspoon & Bakalar, 1979, p. 9). Such profound changes in various perceptual modalities, mood, and cognition are also referred to as an altered state of consciousness (Studerus, Kometer, Hasler, & Vollenweider, 2011).

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## A brief history and current application of psilocybin

Psilocybin was brought into Western countries by the American banker and amateur mycologist R. Gordon Wasson, who travelled to Mexico in order to document the traditional indigenous use of psilocybin mushrooms in 1955 (Johnson, Hendricks, Barrett, & Griffiths, 2019). By the end of the 1960s, a large number of studies had explored the therapeutic potential of psilocybin and other classical psychedelic drugs such as LSD, DMT and mescaline (Grinspoon & Bakalar, 1981). Soon after, however, classical psychedelic drugs began to be taken recreationally in uncontrolled settings. They became heavily associated with the countercultural movement of the 1960s, and were depicted as dangerous drugs of abuse (Rucker, Iliff, & Nutt, 2018; Studerus et al., 2011). Consequently, psychedelics were placed in Schedule 1 of the United Nations (UN) Convention on Drugs in 1967, legally defining them as having no accepted medical use and the maximum potential for harm and dependence. Following their prohibition in most countries of the world, clinical research into the medical use of these substances soon ceased (Rucker et al., 2018).

Nowadays, psychedelic research is surging, with a renewed interest into clinical applications of these substances. Psilocybin has been successfully utilized in numerous randomized controlled trials for treating a variety of psychiatric disorders, including depression and anxiety associated with advanced cancer (Ross et al., 2016), obsessive-compulsive disorder (Moreno, Wiegand, Taitano, & Delgado, 2006), tobacco use disorder (Garcia-Romeu, Griffiths, & Johnson, 2014), alcohol use disorder (Bogenschutz et al., 2015), and major depressive disorder (Carhart-Harris et al., 2021; Davis et al., 2021). As a consequence of promising results, the United States Food and Drug Administration (FDA) granted “breakthrough therapy” status to the use of psilocybin for treatment-resistant depression (Reiff et al., 2020). However, the revival of interest in psychedelics has not been limited to its application for the treatment of psychiatric disorders. Modern-era studies have also explored the potential application of psilocybin in healthy individuals (e.g., Griffiths et al., 2006; Kometer et al., 2012; Kraehenmann et al., 2015; Rucker et al., 2022; Wittmann et al., 2007). Such research has been conducted with the aim to study neuropharmacological mechanisms of psilocybin related to time perception, emotional processing, or cognitive functioning and to examine its acute and long-lasting psychological effects.

## Neurobiological mechanisms of psilocybin

For a better understanding of the psychological effects of psilocybin, it is useful to consider the underlying neurobiological mechanisms of psychedelic states. Psilocybin and other classical psychedelic drugs mainly exert their effects on the serotonin 5-HT<sub>2A</sub> receptor, where they act as agonists and thus stimulate the receptor (Nutt, 2019). A functional magnetic resonance imaging (fMRI) study investigating the neural correlates of the psychedelic state showed that the

main effect of psilocybin is to decrease brain blood flow and blood oxygen level-dependent (BOLD) activity predominantly in the default mode network (DMN; Carhart-Harris et al., 2012). The DMN is a network of brain regions associated with metacognitive thinking, reflecting on the past and future, and with mind wandering (Carhart-Harris et al., 2014). Specific, internalized mental states are a key shared feature of a range of conditions that have been treated with psilocybin such as affective disorders or substance use disorders (Nutt, Erritzoe, & Carhart-Harris, 2020). During a psychedelic experience, an entropic brain state is induced, the integrity of communication between brain regions of the DMN seems to be decreased and brain networks that usually function more independently are increasingly connected (Carhart-Harris et al., 2017; Tagliazucchi et al., 2016). This leads to a compromised modular but enhanced global brain connectivity, which is argued to allow individuals to think in new ways (Carhart-Harris et al., 2014).

## A multidimensional conceptualization of well-being

In order to examine how psilocybin can affect well-being, a clear conceptualization is first needed, since a variety of approaches to defining well-being exist in the literature (Dodge, Daly, Huyton, & Sanders, 2012).

In general, two opposing philosophical traditions rooted in ancient Greek philosophy are relevant to today’s conceptualizations of well-being: hedonism and eudaimonism (Ryan & Deci, 2001). In the hedonistic view, well-being is equated with pleasure, comfort, and enjoyment. In the eudaimonistic view, it is equated with pursuing meaningful goals and the common good by means of exercising one’s personal virtues and potentials (Delle Fave, Massimini, & Bassi, 2011). Most contemporary psychological models posit that well-being is constituted of both hedonic and eudaimonic components (Wagner, Gander, Proyer, & Ruch, 2019).

Two prominent and widely applied theories of well-being are the PERMA model by Martin Seligman, and the Six-Factor Model of Psychological Well-being (Ryff, 1989; Seligman, 2011; see Fig. 1).

The name of the PERMA model stems from the five elements that well-being consists of according to Seligman (2011), namely *positive emotion*, *engagement*, *positive relationships*, *meaning*, and *accomplishment*. *Positive emotion* is directly linked to related concepts such as happiness and life satisfaction. It is seen as the hedonistic component of well-being (the “pleasant life”). It encompasses positive emotions such as pleasure, rapture, ecstasy, comfort, and warmth that are commonly referred to as subjective well-being. *Engagement* reflects “being in flow” and the loss of self-consciousness during an absorbing activity (the “engaged life”). It means living in the present moment and focusing entirely on the here-and-now. *Relationships* encompass feeling supported, loved, valued and having positive interactions with significant others. *Meaning* refers to the feeling of belonging to and serving something greater than oneself (the “meaningful life”). It may be pursued in various ways, for example through a profession, religion,



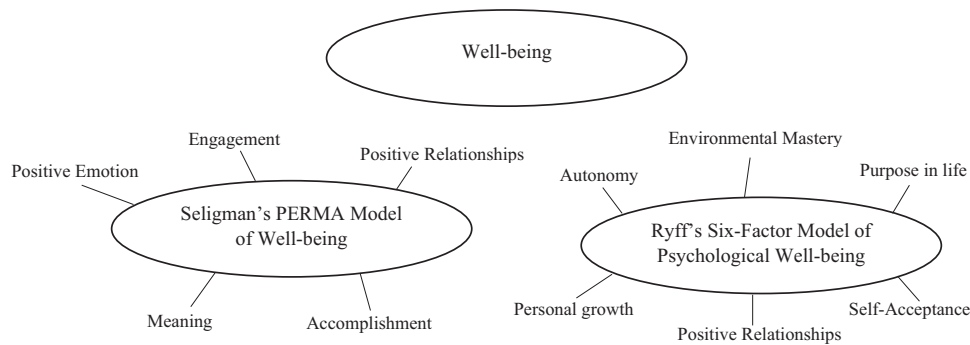


Fig. 1. A conceptualization of well-being informed by Seligman's PERMA model of well-being and Ryff's six-factor model of psychological well-being

creative endeavors, or political commitment. *Accomplishment* (or achievement) is referred to as a sense of mastery and competence (the “achieving life”). It involves the concepts of perseverance and attaining goals.

According to the Six-Factor Model of Psychological Well-being, the six factors contributing to a person's psychological well-being are *self-acceptance*, *positive relationships with others*, *autonomy*, *environmental mastery*, *purpose in life*, and *personal growth*. *Self-acceptance* involves holding positive attitudes towards oneself. The concept of *positive relationships*, similar to Seligman's conceptualization, emphasizes the importance of warm and trusting relationships. *Autonomy* refers to qualities of independence, self-determination, and regulating behavior independent of social pressure. *Environmental mastery* involves being able to manage one's environmental factors and activities such as everyday affairs, to create situations that benefit personal needs, and to make effective use of opportunities. *Purpose in life*, similarly to Seligman's concept of meaning, encompasses a sense of directedness and a conviction that life holds meaning. Lastly, *personal growth* can be described as continually developing one's potential and welcoming new experiences. These two models serve as a useful basis for a multidimensional conceptualization of well-being which can be employed to investigate in what way well-being is affected by the use of psilocybin.

### Psilocybin – action mechanisms and positive effects on well-being

Despite the fact that several recent studies point towards a positive effect of psilocybin on well-being and its related sub-concepts (Carbonaro et al., 2016; Griffiths et al., 2006, 2011, 2018; Griffiths, Richards, Johnson, McCann, & Jesse, 2008; Haijen et al., 2018; Mans et al., 2021; Mason, Mischler, Uthaug, & Kuypers, 2019; Nicholas et al., 2018; Smigielski et al., 2019), the underlying action mechanisms are not fully understood (Andersen, Carhart-Harris, Nutt, & Erritzoe, 2021). In the early literature, it has been proposed that its positive effects are strongly tied to the ability of the substance to yield mystical-type experiences and profound existential insights (Pahnke, 1969). The concept of a mystical experience is composed of (1) feeling a sense of

internal unity, the feeling of becoming one with all existing objects and individuals, (2) a sense of sacredness, (3) a noetic quality, meaning that the experience is perceived as an encounter with ultimate reality, (4) a positive mood (feelings of awe, joy, and ecstasy), (5) transcendence of time and space, and (6) ineffability meaning that the experience cannot be easily put into words (Stace, 1960). Pahnke's (1969) proposition seems to be supported by more recent studies as well, indicating that psilocybin use can lead to profound personal insights, which have the potential to provoke sustained positive changes in personality, attitudes, and values, and can lead to increased self-compassion, purpose in life, connectedness with oneself, others, and the world (e.g. Smigielski et al., 2019; Studerus et al., 2011; Watts, Day, Krzanowski, Nutt, & Carhart-Harris, 2017).

In one of the most prominent clinical trials investigating the effect of psilocybin in healthy individuals, Griffiths et al. (2006) found that 67% of the participants rated their psychedelic experience to be among the most meaningful and spiritually significant events of their lives. Even after 14 months, about two-thirds of the participants still rated the experience as the most meaningful one of their lives and felt a persisting increased sense of well-being and life satisfaction (Griffiths et al., 2008). Another study that examined retrospective survey data from individuals who had used psilocybin in the past year found that having a mystical experience was linked to high scores in positive changes such as increased gratitude and empathy (Russ, Carhart-Harris, Maruyama, & Elliott, 2019).

Furthermore, Studerus et al. (2011) pooled data from eight different trials involving psilocybin administration in healthy individuals and reported that 90% rated it as an enriching experience, and nearly 40% of the participants reported long-lasting positive change regarding their connection with nature and the environment.

Roseman, Nutt, and Carhart-Harris (2018) conducted a clinical trial on the efficacy of psilocybin for treatment-resistant depression and found that Oceanic Boundlessness (OBN)—a state conceptually closely linked to the mystical-type experience, characterized by feelings of blissfulness, insightfulness, disembodiment, and experience of unity—was the main predictive factor for long-term positive therapeutic outcomes.



On a related note, Smigielski et al. (2019) administered psilocybin in a mindfulness group retreat and showed that the extent of ego dissolution, characterized by increased union with one's surroundings, dissolved ego boundaries, and a loss of the self (Nour, Evans, Nutt, & Carhart-Harris, 2016), predicted positive changes in psycho-social functioning of participants four months later. These results have been interpreted as support for the notion that the temporary loss of the ego and self-boundaries induced by psilocybin diminishes self-referential and egocentric processing and in turn fosters an altered perspective towards oneself, others, and the environment (Smigielski et al., 2019). In a review about the effect of psychedelics on human functioning, Jungaberle et al. (2018) concluded that the current body of literature provides preliminary evidence for the beneficial effects of psychedelics in terms of well-being in both clinical and healthy populations.

## Objectives

These findings indicate that psilocybin may have the potential to enhance the well-being of healthy individuals by bringing meaning, connectedness, and novel perspectives into people's lives. Therefore, the objective of this scoping review is to provide an overview of contemporary research on psilocybin use and its effect on well-being with a unique focus on healthy individuals, employing a rigorous well-being conceptualization. Moreover, we aim to examine which factors influence this relationship. The following research questions result from the previously formulated objectives:

1. How does psilocybin affect well-being in healthy individuals?
2. Which factors influence the relation between psilocybin use and well-being in healthy individuals?

Additionally, we explored which research protocols have been employed in studies on psilocybin use and well-being in healthy individuals, what underlying mechanisms of improved well-being have been proposed in the literature, and which facets of well-being were influenced by psilocybin use.

## METHODS

### Overview

A scoping review was conducted to map out existing evidence, identify gaps in the research field, and provide implications for further research. Scoping reviews differ from systematic reviews in a number of ways. First, scoping reviews provide a broader overview of a specific topic, since research is usually included irrespective of study quality and study design (Arksey & O'Malley, 2005). This is useful if the evidence on a topic is scarce (Tokgöz, Hrynyschyn, Hafner, Schönfeld, & Dockweiler, 2021) as is the case for research on psilocybin and the effect on well-being in healthy individuals. Existing studies employ different study designs

with highly heterogeneous quality of evidence, and many lack standardized measures and rigorous models of well-being. Therefore, generalized claims about the effectiveness of psilocybin use, as one would expect in a systematic review, cannot be made. Hence, conducting a scoping review is appropriate, since its aim is to provide an overview of the currently available evidence, which can point towards the need to employ more in-depth conceptualizations, and identify general knowledge gaps in a specific line of research (Tricco et al., 2016).

### Literature search

A comprehensive literature search in line with the PRISMA guidelines (Page et al., 2021) was conducted. Scopus, PubMed, PsycINFO, Web of Science, and Google Scholar were searched for peer-reviewed articles including experimental and non-experimental studies about psilocybin and well-being. To identify fitting studies, the search terms psilocybin and well-being (including its related sub-concepts described in Fig. 1) were employed. The following search string was used in Scopus, PubMed, PsycINFO, and Web of Science: psilocybin AND wellbeing (OR "well-being" OR "well being" OR "autonomy" OR "environmental mastery" OR "personal development" OR "personal change" OR "personal growth" OR "purpose in life" OR "life change" OR "meaning" OR "self-acceptance" OR "positive emotions" OR "positive relations" OR "accomplishment" OR "engagement"). A search of Google Scholar with the terms psilocybin and well-being was finally used to identify missing articles.

### Inclusion and exclusion criteria

Inclusion criteria were studies with data about psilocybin and well-being or its sub-concepts (as shown in Fig. 1) in *healthy functioning participants*. Exclusion criteria were studies that were not published in English, *micro-dosing* studies (the practice of consuming very low, sub-hallucinogenic doses), studies focusing on individuals with a clinically diagnosed condition/illness (e.g., depression, eating disorders, substance use disorders, neurodegenerative disorders), studies about other psychedelic substances (e.g. LSD), studies solely examining positive outcomes not included in the conceptualization of well-being employed in this paper (e.g., empathy or mindfulness), and studies published prior to 1990, as many studies of this "first wave" of psychedelic research were criticized for containing methodological flaws (Wheeler & Dyer, 2020). First, duplicates were removed and the title and abstracts of search results were screened. Articles that did not match the inclusion and exclusion criteria were removed. The identified full-text articles were then further screened and assessed for eligibility.

## RESULTS

In total, 13 studies met the inclusion criteria and were included in this review (see Fig. 2). All studies entailed data





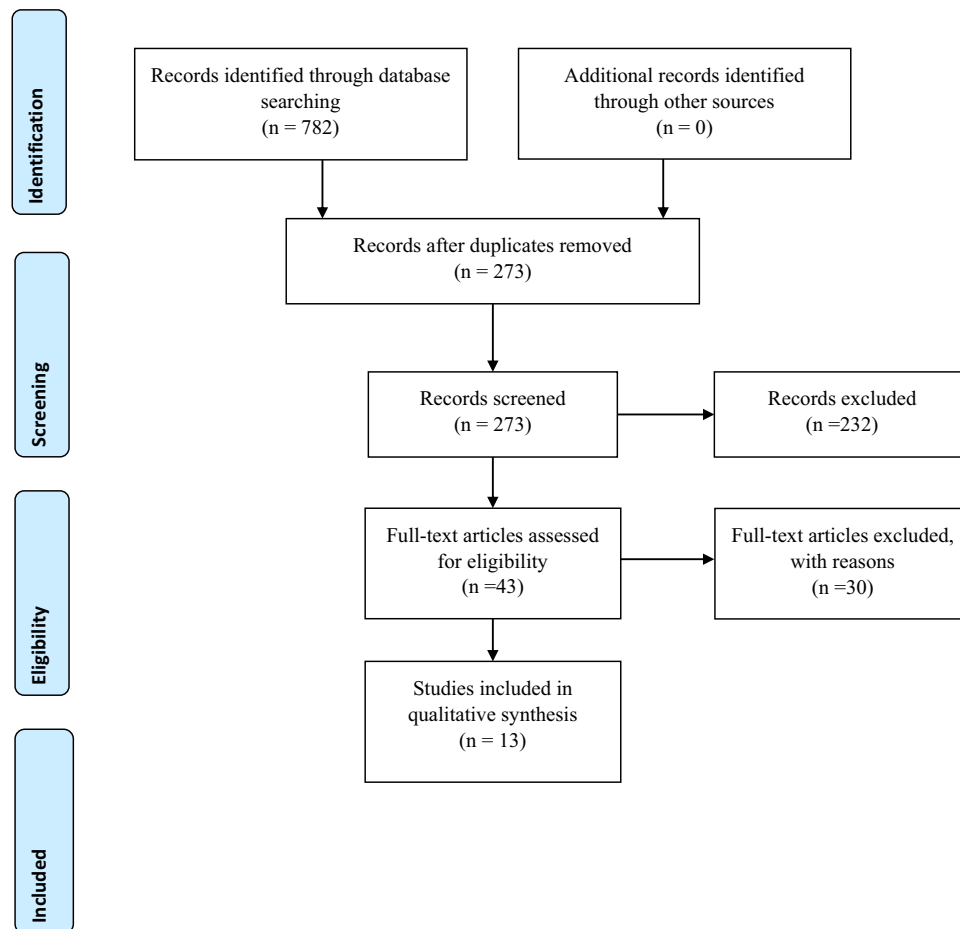


Fig. 2. Prisma flow chart

about healthy individuals who have used psilocybin in the past and outcome measures related to well-being (e.g., subjective well-being, life satisfaction, positive mood). The initial search yielded 782 results. Duplicates were removed, and 273 results remained. After scanning titles and abstracts, 232 articles were excluded because they did not match the inclusion and exclusion criteria. Hence, 43 full-text articles were further screened and assessed for eligibility. Thirty articles were excluded for multiple reasons: First, in some studies, well-being or related constructs were measured but scores were not provided. Moreover, studies that solely reported positive outcomes unrelated to the conceptualization of well-being in this study were excluded. This was the case for studies focusing on concepts such as mindfulness, empathy, or nature connectedness. Lastly, some studies only focused on neurobiological measures and were therefore removed. The selected studies are presented in Table 1 and are further described below.

### Objectives of the studies, conceptualization, and measurement of well-being

All of the studies contained data about the well-being-related effects of psilocybin use in healthy individuals. Two studies were conducted with the primary aim of examining the

effect of psilocybin on well-being specifically (Mans et al., 2021; Mason et al., 2019). In some studies, the primary objective was to investigate constructs such as mindfulness, creativity, or empathy, but well-being measures were nevertheless included as a secondary outcome measure. In most of the studies, well-being was not explicitly conceptualized but a variety of measurement instruments were employed that can be related to the well-being conceptualization of this paper. One study explicitly provided a well-being conceptualization (Mans et al., 2021). The authors treated well-being as an umbrella construct and used a variety of well-being measures that were clustered into different aspects of well-being.

Six of the studies employed the Persistent Effects Questionnaire (PEQ) as the main outcome measure related to well-being (Griffiths et al., 2006, 2008, 2011, 2018; Madsen et al., 2020; Nicholas et al., 2018). This instrument contains subscales about positive changes in mood, social effects, and attitudes about life and oneself. From these subscales of the questionnaire, inferences to the well-being conceptualization of this paper can be made since they are closely linked conceptually. The subscale *positive attitude about life* from the PEQ includes items related to the concept of meaning/purpose in life (e.g., “your life has more meaning”), *positive attitude about self* includes questions related to

Table 1. Summary of studies that investigate the effect of psilocybin in healthy individuals and entail well-being outcome measures

Reference	Study Design	Study Objectives and Sample Size ( <i>N</i> )	WB Concepts	Procedure, WB-related outcome measures, measurement timing	Dosage	Outcomes
Barrett et al. (2020)	Open-label, within-subjects, longitudinal pilot study	Long-term enduring impact of psilocybin on affect and associated brain function ( <i>N</i> = 12)	Positive emotions (joy, contentment, pride, amusement)	One individual session DPES One day before, one week after, and one month later	25 mg of psilocybin per 70 kg of bodyweight	One month post-psilocybin, positive emotions remained elevated
Carbonaro et al. (2016)	Cross-sectional survey study	An online survey about individuals' single most psychologically difficult or challenging experience after consuming psilocybin mushrooms ( <i>N</i> = 1993)	WB and life satisfaction	Questionnaire with one item retrieved from the PEQ, asking if psilocybin use affected participants' current sense of WB or life satisfaction, in regards to their single most difficult psilocybin experience, answered on a 7-point Likert scale	Median reported weight of dried psilocybin mushrooms = 4 g ( <i>N</i> = 1,203), median weight of fresh mushrooms = 21–30 g ( <i>N</i> = 148)	76% of the participants reported an increase and 8% reported a decrease in WB due to their most psychologically difficult or challenging psilocybin experience
Carhart-Harris and Nutt (2010)	Cross-sectional survey study	User perceptions of the benefits and harms of hallucinogenic drug use ( <i>N</i> = 503)	WB, self-acceptance	Questionnaire with open-ended questions about perceived health benefits and risks of psilocybin use  One item asking whether lifetime psilocybin use has had a long-term effect on participants' WB, answered on a 5-point Likert scale	Not specified	In the open-ended answers, 35% of psilocybin users commented on perceived benefits (e.g. improved self acceptance) and 12% commented on perceived risks of psilocybin use (e.g. increased anxiety)  2.4% of psilocybin users attributed a negative effect to the use of psilocybin on WB, and 0.2% a very negative effect  87% of psilocybin users attributed a positive or very positive effect to the use of psilocybin on WB
Griffiths et al. (2018)	Double-blind, randomized, active placebo, planned comparison between and within group	Changes in psychological functioning resulting from psilocybin use in combination with meditation and other spiritual practices ( <i>N</i> = 75)	Positive emotions (joy, contentment, pride, amusement), WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects, meaning/purpose in life	Two groups with two individual sessions of high-dose psilocybin, whereas one group received high support for spiritual practices One group with two individual low-dose psilocybin session (active placebo) PEQ, DPES, PIL Baseline and 6 months later	Low-dose group (active placebo): 1mg/70 kg psilocybin High-dose groups: 20mg/70 kg on session one and 30mg/70 kg on session two	Positive significant changes on all well-being-related measures in both high-dose groups compared to the low-dose group except for positive emotions as measured with the DPES  72% of the high-dose standard support and 92% of the high-dose high support group attributed a moderate to very high increase in WB or life satisfaction to the use of psilocybin  No decrease of WB or life satisfaction Positive outcomes were predicted by the intensity of psilocybin-occasioned mystical experience and rates of engagement with meditation and other spiritual practices

(continued)





Table 1. Continued

Reference	Study Design	Study Objectives and Sample Size (N)	WB Concepts	Procedure, WB-related outcome measures, measurement timing	Dosage	Outcomes
Griffiths et al. (2011)	Double-blind, quasi-random, placebo-controlled	Evaluation of the psychological effects of different psilocybin doses (N = 18)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Five individual sessions, with four active doses in either ascending or descending order PEQ, written comments One month after each session, 14 months later	0, 5, 10, 20, 30 mg/70 kg	94% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin Positive significant changes on all well-being-related measures, which were sustained at the 14-month follow-up 89% rated moderate or higher changes in positive behavior at the 14-month follow-up, such as better social relationships, increased physical and psychological self-care and increased spiritual practice No decrease of WB or life satisfaction Persisting positive effects increased with increasing dose
Griffiths et al. (2008)	Follow-up	Persistence of positive changes in psychological functioning following psilocybin administration (N = 36)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Psilocybin administered on one of two or three individual sessions PEQ, 14–16 months later	30 mg/70 kg	Positive changes on all well-being-related measures were sustained 64% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin No decrease of WB or life satisfaction
Griffiths et al. (2006)	Double-blind, counterbalanced comparison	Acute and long-term psychological effects of a high dose of psilocybin (N = 36)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Psilocybin on one of two or three individual sessions, placebo during the other sessions PEQ, PANAS-X, two months later	30 mg/70 kg Placebo: methylphenidate hydrochloride (40 mg/70 kg)	Participants rated their psilocybin experiences as having substantial personal meaning Positive significant changes on all PEQ well-being-related measures (WB or life satisfaction, positive mood, attitude about life, attitude about self, positive social effects) 79% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin No difference in positive affect as measured with the PANAS-X between the two conditions

(continued)

Table 1. Continued

Reference	Study Design	Study Objectives and Sample Size ( <i>N</i> )	WB Concepts	Procedure, WB-related outcome measures, measurement timing	Dosage	Outcomes
Lutkajtis (2021)	Qualitative phenomenological approach	Four individuals' experiences during and following a psilocybin truffle retreat in the Netherlands ( <i>N</i> = 4)	WB, positive emotion, self-acceptance, positive relationships, personal growth, environmental mastery	One session in a group retreat setting Semi-structured interview questions, asking participants to describe their journey since the retreat, including any significant after-effects and changes Eight to twelve months later	30–40 g of psilocybin truffles	Personally significant changes to health and well-being due to behavioural lifestyle changes, an increased sense of self-love, self-acceptance, self-confidence, positive emotions, an increased interest in spirituality and improved interpersonal connection
Madsen et al. (2020)	Open label, within-subject study	Long-term changes in mindfulness, neocortical 5-HT <sub>2A</sub> receptor binding and psychological functioning ( <i>N</i> = 10)	Positive mood, attitude about life, attitude about self, positive social effects	One individual session PEQ Three months later	14 mg/70 kg ( <i>N</i> = 4) and 21 mg/70 kg ( <i>N</i> = 6)	Positive changes on all well-being-related measures
Mans et al. (2021)	Longitudinal survey study	Sustained, multifaceted improvements in mental well-being following psychedelic experiences <sup>a</sup> (baseline: <i>N</i> = 654, final follow up: <i>N</i> = 64)	Mental well-being (positive affect, satisfying interpersonal relationships and positive functioning), meaning in life, social connectedness Life satisfaction	Repeated survey entailing 14 measures related to WB <sup>b</sup> WEMWBS MLQ SCS Seven days before, one day before, one day later, 14 days later, 28 days later, two years later	Not specified	Positive changes in two out of three clusters of WB outcomes that remained statistically significant up to 2 years post-experience
Mason et al., 2019 <sup>a</sup>	Open label, within subject study	Assessment of the sub-acute effects of psilocybin on creative thinking, empathy, and well-being in a psilocybin retreat ( <i>N</i> = 22)		One guided session in a group retreat setting SWLS Baseline, one day later, seven days later	An average (SD) of 34.2 g (8.9) of psilocybin truffles Final (average) psilocin consumption of 27.1 mg	Persistent significant increase in life satisfaction after one week
Nicholas et al. (2018)	Open-label within-subject study	Positive subjective effects of high dose psilocybin in healthy volunteers ( <i>N</i> = 12)	WB/life satisfaction, positive mood, attitude about life, attitude about self positive social effects	Three individual sessions with escalating doses PEQ One month later	21mg/70 kg; 31.5mg/70 kg; 42mg/70 kg)	Positive changes on all well-being-related measures 83.3% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin Moderate decrease of WB or life satisfaction for one participant

(continued)





Table 1. Continued

Reference	Study Design	Study Objectives and Sample Size (N)	WB Concepts	Procedure, WB-related outcome measures, measurement timing	Dosage	Outcomes
Smigielski et al. (2019)	Double-blind randomized, placebo controlled	Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat (N = 39)	Self-acceptance, meaning/purpose in life	One guided session in a group retreat setting LCI-R Four months later	22.05mg/70 kg Placebo: lactose	Increased appreciation for life, self-acceptance and quest for meaning/sense of purpose significantly different from the placebo group The extent of self-dissolution contributed to the global change in attitude and behaviour, the experience of unity predicted self-acceptance, and sacredness and ineffability contributed to the change in appreciation of life

Note. DPES = Dispositional Positive Emotion Scale. LCI-R = Life Changes Inventory, Revised. PANAS-X = Positive and Negative Affect Scale - X. PEQ = Persisting Effects Questionnaire. PIL = Purpose in Life Test. MLQ = Meaning in Life Questionnaire. RCT = Randomised Controlled Trial. SCS = Social Connectedness Scale. SWLS = Satisfaction with Life Scale. WB = well-being. WEMWBS = Warwick-Edinburgh Mental Well-being Scale.

<sup>a</sup> The authors included other classic psychedelic compounds besides psilocybin (i.e. LSD, ayahuasca, DMT/5-MeO-DMT and mescaline), and did not distinguish between the effects of these substances.

<sup>b</sup> Only measures relevant to the well-being conceptualization of this paper were included.

self-acceptance (e.g., “your self-confidence/self-assurance has increased”), and *positive social effects* include questions related to positive relationships (e.g., “you have a more positive relationship with others”). The PEQ also contains a final item that asks participants on a 7-point Likert scale whether they believe that the experience of using psilocybin and the contemplation about the experience led to changes in their current sense of personal well-being or life satisfaction. In one study using the PEQ, this item was not reported (Madsen et al., 2020).

Three other studies also examined life satisfaction. One of them used the final item of the PEQ, asking about changes in well-being/life satisfaction (Carbonaro et al., 2016). Carhart-Harris and Nutt (2010) used a similar ad-hoc item, asking whether lifetime psilocybin use has had a long-term effect on participants’ well-being, and answered on a 5-point Likert scale. The last study used the Satisfaction with Life Scale (Mason et al., 2019).

Besides the PEQ, the Positive and Negative Affect Scale - X (PANAS-X) and the Dispositional Positive Emotion Scale (DPES) were used as additional questionnaires that also examined positive emotions (Barrett, Doss, Sepeda, Pekar, & Griffiths, 2020; Griffiths et al., 2006, 2018).

Furthermore, in one study, the Purpose in Life test (PIL) was employed, which is related to the well-being sub-concepts of meaning/purpose in life (Griffiths et al., 2018). The conceptually closely related Meaning in Life Questionnaire (MLQ) was used by Mans et al. (2021). Moreover, the authors employed another 13 well-being measures, of which two further measures are relevant to the well-being conceptualization of this paper. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS) was used as the primary outcome measure and includes the concepts of positive affect, interpersonal relationships, and positive functioning. The Social Connectedness Scale (SCS) can be related to the concept of positive relationships as well. In another study, the Life Changes Inventory (LCI) was used, which entails a subscale related to self-acceptance and a subscale related to meaning/purpose in life (Smigielski et al., 2019). In the study by Lutkajtis (2021), descriptions of semi-structured interviews and related key themes were provided, which entailed information related to improvements in well-being and several sub-concepts.

## Study design and sample size

Regarding the study design, the thirteen studies were rather heterogeneous. There were eight experimental studies, of which four were open-label and double-blind studies, respectively, one study with follow-up data, two cross-sectional survey studies, one longitudinal survey study, and one qualitative interview study. All studies in which psilocybin was administered in a controlled setting included a sample size in the double-digit range, with a total of 228 participants. Three survey studies assessed experiences with psilocybin in a non-experimental, uncontrolled setting, and entailed a total of 3,150 participants (Carbonaro et al., 2016; Carhart-Harris & Nutt, 2010; Mans et al., 2021).

## Study procedure and dosage

Studies varied in setting, amount of dosing sessions, form of psilocybin administration, and the actual dosage. In most of the studies, psilocybin was administered in individual sessions. Three studies were conducted in a group retreat setting (Lutkajtis, 2021; Mason et al., 2019; Smigielski et al., 2019). The three survey studies asked about psilocybin use in an uncontrolled setting (Carbonaro et al., 2016; Carhart-Harris & Nutt, 2010; Mans et al., 2021).

In most studies, the researchers administered synthetic psilocybin in the form of a capsule. Dosage ranged from a low dose of 5 mg of psilocybin per 70 kg of body weight (Griffiths et al., 2011) to 42 mg/70 kg (Nicholas et al., 2018). Most studies involved dosing sessions that can be considered a high dose of psilocybin ( $\geq 25$  mg psilocybin; Johnson, Richards, & Griffiths, 2008). Five studies did not use synthetic psilocybin. They varied in dose and form of administration.

Most studies involved screening procedures to assess the eligibility of participants (Griffiths et al., 2006, 2008, 2011, 2018; Lutkajtis, 2021; Madsen et al., 2020; Mason et al., 2019; Nicholas et al., 2018; Smigielski et al., 2019). They were required to be medically and psychiatrically healthy and without personal or family histories of psychotic disorders or bipolar I or II disorder. The seven experimental studies that involved individual dosing sessions followed research protocols similar to each other (Barrett et al., 2020; Griffiths et al., 2006, 2008, 2011, 2018; Madsen et al., 2020; Nicholas et al., 2018), in line with safety guidelines for human hallucinogen research (Johnson et al., 2008). Before the dosing sessions, multiple preparatory meetings with the monitoring staff were conducted, with the purpose of building rapport and trust, explaining safety precautions, and reviewing life history and current life circumstances of participants. In all studies, music was played during the session and two monitors of the research staff were present to offer support and reassurance in case of anxiety. Except for Madsen et al. (2020), it was furthermore described that sessions took place in an aesthetic living-room-like environment, whereby participants were instructed to sit on a couch, using an eye mask to block external visual distractions. After the psilocybin session, participants were offered further meetings to discuss and reflect upon their experiences. The three experimental studies that were conducted in group retreat settings, followed different schedules and procedures regarding the duration of stay, and activities before and after the sessions, but they all shared common features as well. In all studies, preparatory activities such as meditation exercises and meetings with facilitators and other participants took place, psilocybin was consumed under supervision in a comfortable surrounding accompanied by music, and after the experience, participants had the opportunity to discuss their experience with the facilitators and other participants.

## Well-being-related outcomes

In all studies, the majority of participants reported that psilocybin use had positive psychological implications.

In more than half of the studies, the percentage of participants who felt a sense of increased well-being or life satisfaction following the use of psilocybin was reported. Most participants indicated a moderate to very high increase in their sense of well-being, ranging from 64% (Griffiths et al., 2008) to 94% (Griffiths et al., 2011).

In the experimental studies, the most commonly identified well-being outcomes were related to the PEQ: an increased sense of well-being or life satisfaction, heightened mood, more positive attitudes about life (related to meaning/purpose in life), positive attitudes about oneself (related to self-acceptance) and positive social effects (related to positive relationships). In all studies that employed the PEQ, these concepts were elevated after the use of psilocybin, up to 14 months after the ingestion (Griffiths et al., 2008, 2011). Those studies employing a control condition found these effects to be significantly higher than for the control group (Griffiths et al., 2006, 2008, 2011, 2018).

Other questionnaires also revealed that psilocybin use led to an increase in a variety of well-being (sub-)concepts. Smigielski et al. (2019) reported significant improvements for all well-being-related concepts that were assessed with the Life Changes Inventory, Revised (LCI-R), namely appreciation of life, self-acceptance, and quest for meaning/purpose in life. Similarly, meaning/purpose in life was significantly increased in two further studies, as measured with the PIL (Griffiths et al., 2018) and the MLQ (Mans et al., 2021). Mans et al. (2021) also found a significant increase in mental well-being as measured with the WEMWBS, which entails the concepts of positive affect, satisfying interpersonal relationships and positive functioning. Furthermore, the authors found lasting improvements in social connectedness, reflected by significantly increased SCS scores.

Three studies provided qualitative data that also indicate improvements in a number of well-being-related outcomes such as positive relationships, self-acceptance, optimism, and positive lifestyle changes (Carhart-Harris & Nutt, 2010; Griffiths et al., 2011; Lutkajtis, 2021).

Regarding positive mood, improvements were detected in most studies (Barrett et al., 2020; Griffiths et al., 2006, 2008, 2011, 2018; Madsen et al., 2020; Nicholas et al., 2018).

## Action mechanisms

Underlying mechanisms that constitute the positive effects of psilocybin on well-being were only scarcely investigated. In multiple studies, however, positive outcomes were linked to the substance's ability to evoke mystical-type experiences. In Griffiths et al. (2008), correlation analyses between measures of mystical experience and ratings of personal meaning and spiritual significance were performed with subsequent regression analysis, controlling for the intensity of drug effects. Scores for mystical experience were significantly related to high ratings of personal meaning and spiritual significance at follow-up. From these results, the authors inferred that having a mystical experience can be considered an underlying action mechanism for positive



outcomes of psilocybin use. In another study, hierarchical regression analysis revealed that the intensity of the psilocybin-occasioned mystical experience was predictive of various long-term positive outcomes (Griffiths et al., 2018). Finally, in the study by Smigielski et al. (2019), regression analysis revealed that various concepts related to mystical-type experiences were predictive of long-term positive outcomes. The extent of self-dissolution contributed to the global change in attitude and behaviour, the experience of unity predicted self-acceptance and sacredness, whereas ineffability contributed to the change in appreciation of life.

### Adverse effects

In general, serious adverse events (e.g., physical discomfort, disorientation, severe anxiety, panic, or psychotic-like reactions) did not occur in the experimental studies. Only one participant attributed a moderate decrease in well-being to the use of psilocybin (Nicholas et al., 2018). In multiple studies, minor adverse effects such as acute distress, anxiety, and dysphoria were reported, but these effects were of short duration, well managed by the study staff, or were described as cathartic (Griffiths et al., 2006, 2011, 2018; Lutkajtis, 2021). In most studies taking place in a controlled environment, no adverse effects were reported (Barrett et al., 2020; Griffiths, 2008; Madsen et al., 2020; Mason et al., 2019; Smigielski et al., 2019). In contrast to that, adverse effects were reported in the two cross-sectional survey studies. In Carhart-Harris and Nutt (2010), 2.6% of psilocybin users attributed a negative effect on well-being to the use of the substance and 13% of psilocybin users reported that the use was associated with physical or mental health problems (e.g., persistent psychotic symptoms, depressive symptoms). In the survey study on participants' worst "bad trip" by Carbonaro et al. (2016), 11% percent of participants put themselves or others at risk of physical harm after using psilocybin, with 2.6% exhibiting physically aggressive or violent behaviour towards themselves or others, and 2.7% requiring medical help at a hospital or emergency department. Three individuals reported experiencing psychotic-like symptoms and three individuals reported a subsequent suicide attempt.

### Limitations

A limitation that applies to most studies and might restrict the generalizability of data results lies in the sample homogeneity regarding socioeconomic status and ethnicity. In most studies, a large majority of participants were predominantly white, well-educated individuals. Additionally, samples of experimental studies might be unrepresentative due to the exclusion of participants who are subject to risk factors such as history of drug abuse or psychiatric illness. Moreover, in the three survey studies, convenience samples were employed, which may have facilitated a selection bias, as participants were mainly recruited on websites with a relatively favorable view of psychedelic drug use. Similarly, individuals with positive attitudes towards psychedelic drugs might have been more inclined to take part in the

experimental studies. Furthermore, limitations that apply to web-based questionnaires more generally were high rates of non-completion, difficulty in assessing the truthfulness of respondents, the subjective nature of data, and the lack of a control group. Additionally, one of the survey studies included other classical psychedelics besides psilocybin (Mans et al., 2021). Several experimental studies also lacked control groups or had difficulties to maintain the blinding procedures due to the perceptible effects of psilocybin (Smigielski et al., 2019), which also could have led to expectancy effects. Lastly, small sample sizes of experimental studies potentially limited statistical power.

## DISCUSSION

In this scoping review, the current literature about the use of psilocybin and its effect on well-being in healthy individuals was investigated, employing a rigorous, multifaceted conceptualization of well-being. The aim was to examine well-being-related outcomes of psilocybin use and identify factors that contribute to such outcomes. Additionally, this review explored what research protocols have therefore been employed, what underlying action mechanisms have been proposed in the literature, and which facets of well-being are influenced by psilocybin use in healthy individuals.

The data revealed subsequent improvements in a wide range of well-being (sub-) concepts after the use of psilocybin in all studies included in this review. These findings lend support to the view that a low number of high-dose psilocybin administration sessions can have broad and sustained positive implications for well-being of healthy individuals.

Following the conceptualization of well-being in this review, *self-acceptance*, *positive relationships*, and *meaning/purpose in life* were facets of well-being that stood out to consistently show significant improvements in multiple studies. These results are consistent with data obtained in a qualitative study of patients with treatment-resistant depression who underwent psilocybin-assisted therapy (Watts et al., 2017). Patients in the study reported an improved connection to the self and a boosted sense of self-worth and self-compassion. They reported strengthened bonds with loved ones, and an improved sense of meaning, purpose, and hope. Furthermore, in another qualitative study on participants' experiences in psilocybin-assisted psychotherapy, all participants described significant insights or positive changes concerning close personal relationships (Belser et al., 2017). They also reported "new feelings of empowerment and personal agency to live meaningful lives, and a sense of belonging within their communities and the larger universe" (Belser et al., 2017, p. 369).

The well-being facets of autonomy, accomplishment, engagement, and personal growth were only implicitly mentioned or not reported at all as well-being-related outcomes of psilocybin use. Hereby, it is important to consider that none of these concepts were explicitly assessed by the well-being-related measurement instruments employed in





the reviewed studies. Thus, it remains unclear whether these well-being facets do not occur due to the lack of adequate measurement instruments or because they are not as relevant for positive well-being-related outcomes of psilocybin use.

### Action mechanisms

Most studies did not elaborate on underlying action mechanisms explaining positive outcomes of psilocybin use. However, as described in the Results section, a central role was attributed to the occurrence of mystical-type experiences in multiple articles. This finding is frequently reported in the scientific literature on psilocybin (e.g., [Doblin, 1991](#); [Haijen et al., 2018](#); [Kangaslampi, Hausen, & Rauteenmaa, 2020](#); [Ross et al., 2016](#); [Russ et al., 2019](#)). Other concepts that have been linked to the mystical-type experiences and to positive outcomes of psilocybin use are *feelings of unity*, *connectedness*, and *ego dissolution*. According to [Stace \(1960\)](#), a central part that lies at the core of the mystical-type experience is a feeling of unity, which involves an experience of the complete dissolution of the self, a loss of the sense of personal identity. Therefore mystical-type experiences have been conceptually closely tied to the concept of ego dissolution which is supported by literature that finds a unitive experience to correlate highly with scores of ego dissolution ([Nour et al., 2016](#)). It has been put forward that through this blurring of lines between self and others, and an inclusion of others in the construct of the self, an increased sense of connectedness with external objects or entities is achieved ([Forstmann, Yudkin, Prosser, Megan Heller, & Crockett, 2020](#)). In line with this, the concept of “connectedness” has been commonly theorized to be a central mechanism leading to positive outcomes of psilocybin use ([Aday, Mitzkovitz, Bloesch, Davoli, & Davis, 2020](#); [Carhart-Harris, Erritzoe, Haijen, Kaelen, & Watts, 2018](#); [Watts et al., 2017](#)). [Watts et al. \(2017\)](#), for example, found that an increased connection towards oneself, others, and the world was a central theme in patient reports of psilocybin experiences. Similarly, in the study by [Smigielski et al. \(2019\)](#), regression analyses showed that feelings of unity are linked to increased self-acceptance and that ego-dissolution generally predicted positive outcomes. The authors argued that self-referential and egocentric processing is diminished as a result of psilocybin use, which can reshape one’s perspective towards oneself, others, and the environment.

These proposed mechanisms may bring forward possible explanations for why self-acceptance, positive relationships, and meaning/purpose in life seem to be well-being facets affected by psilocybin use. Feelings of unity, ego dissolution, and a sense of connectedness as part of the mystical experience might facilitate a sense of belonging and an altered perspective towards oneself, others, and the world that is more benevolent and accepting.

### Adverse effects

Concerning studies conducted in a controlled setting, either a few minor adverse effects such as acute distress and anxiety

or no adverse effects at all were evident. [Carbonaro et al. \(2016\)](#) concluded that risks of dangerous behavior or prolonged psychological problems are extremely low in laboratory studies of psilocybin with carefully screened, well-prepared, and supported participants. This underpins the relative safety of administering psilocybin under conducive conditions and is consistent with previous research. In a pooled analysis of 110 healthy psilocybin research participants, for example, the authors found low rates of sustained negative psychological symptoms, and no subsequent drug abuse, persisting perception disorders, prolonged psychosis-like symptoms, or other long-term impairment of functioning ([Studerus et al., 2011](#)). Psilocybin has low physiological toxicity, is not associated with compulsive drug craving or withdrawal symptoms, and is considered to be non-addictive ([Johnson et al., 2008](#); [Teixeira et al., 2021](#)). Moreover, two independent studies in the United States found no evidence of a link between psychedelic use and mental health concerns or suicidality ([Johansen & Krebs, 2015](#); [Krebs & Johansen, 2013](#)). In fact, an additional study found that lifetime use of psilocybin is associated with a decreased likelihood of psychological distress and suicidality ([Hendricks, Johnson, & Griffiths, 2015](#)).

Rates and severity of both acute and enduring adverse effects were comparatively higher in the cross-sectional survey studies in comparison to studies conducted in controlled laboratory settings. Such differences are argued to arise due to factors such as lack of psychological screening and preparation, absence of physical comfort and social support during the session, and inappropriate dosage ([Carbonaro et al., 2016](#)). It has been acknowledged that unsupervised use of psilocybin can be potentially harmful. The most likely risk is overwhelming distress or anxiety, which can escalate to dangerous behaviors such as self-harm or violence ([Johnson et al., 2008](#)).

### Promoting positive results – the importance of set and setting

Such potential adverse effects highlight the importance of non-pharmacological factors for shaping the outcome of psychedelic experiences. Adequate *set* and *setting* are crucial determinants for positive outcomes of a psychedelic experience ([Elsey, 2017](#); [Haijen et al., 2018](#); [Pahnke, 1969](#)). *Set* refers to the characteristics of the person taking the drug and *setting* refers to the characteristics of the environment. To account for this, modern-day clinical trials adhere to safety guidelines for human hallucinogen research ([Johnson et al., 2008](#)).

This way, a proper *set* of participants in research is ensured by employing a screening process that excludes individuals with cardiovascular conditions and with a history of psychotic disorders ([Aday et al., 2020](#)). Additionally, preparation sessions are recommended to take place, with the aim of building rapport, fostering the ability to be emotionally open to the psychedelic experience, and enhancing psychological flexibility ([Johnson et al., 2008](#)). In order to provide a pleasant *setting*, psilocybin studies usually



take place in a comfortable environment with psychological support available (Andersen et al., 2021; Roseman et al., 2018). In conclusion, adequate screening and preparation procedures, a supportive setting, appropriate dosage, psychological support, and proper integration of the experience promote positive outcomes and minimize adverse effects.

### Limitations

This review should be viewed in light of its limitations. The primary aim of this scoping review was to provide an initial and broad overview of the available evidence in the field, irrespective of study quality. Therefore, studies were included independently of methodological rigor or quality, which is considered a common limitation of the scoping review methodology (Arksey & O'Malley, 2005). As described in the Results section, several studies featured small and homogenous samples, were potentially subject to self-selection or expectancy biases, and lacked adequate control conditions.

Moreover, only a small number of studies were included in this review. Although there is a recent renewed interest in psychedelic research (Chi & Gold, 2020), current drug laws restrict the use of psilocybin for research in healthy individuals. Permission to investigate psychedelic drugs is granted to a very limited number of research labs only and is associated with high administrative and financial burdens (Nutt, King, & Nichols, 2013).

Furthermore, this scoping review focused on outcomes related to a predefined conceptualization of well-being. Several factors external to Ryff's and Seligman's well-being models such as *mindfulness* (Madsen et al., 2020; Smigielski et al., 2019), *empathy* (Mans et al., 2021), *optimism* (Mans et al., 2021), and *resilience* (Lutkajtis, 2021; Mans et al., 2021) have also been related to the positive effect of psilocybin on well-being.

### Future research

Future research should focus on increasing the representativeness and generalizability of results, to assess whether psilocybin use can effectively and safely improve well-being of healthy individuals. Larger, more diverse samples with varying socioeconomic status, ethnicities, and attitudes towards psychedelic drugs are therefore needed. Additionally, more comprehensive well-being measures should be used in future studies. Such data would allow to make more meaningful claims about the efficacy of psilocybin to improve well-being particularly in healthy individuals. Moreover, rigorous double-blind, placebo-controlled, crossover experimental designs with standardized dosages should be employed, to minimize blinding and expectancy effects, and increase the reliability of results.

### CONCLUSION

This scoping review provided preliminary evidence regarding the effect of psilocybin use on well-being. Moving

beyond the focus on clinical populations and clinical outcomes, this research focused on healthy individuals.

To the authors' knowledge, this study was the first to employ a rigorous well-being conceptualization in the context of psilocybin use, which revealed more precisely how and which well-being (sub-) concepts are affected by psilocybin. Following Ryff's and Seligman's conceptualization, *self-acceptance*, *positive relationships*, and *meaning/purpose in life* were well-being sub-concepts consistently reported to be improved by psilocybin use. *Ego-dissolution*, *unity*, *connectedness*, and *mystical-type experiences* are interrelated concepts that seem to be crucial for explaining such positive well-being-related effects of psilocybin. Under conducive conditions, the use of psilocybin can contribute to enhanced functioning in healthy individuals, including broad and sustained improvements in a variety of well-being concepts.

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