

Review Article

Mindfulness as a tool for reducing stress in healthcare professionals: An umbrella review

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Abstract.

BACKGROUND: Health care providers (HCPs) and health care students experience a huge amount of stress due to high workloads and pressure to perform and are likely to develop anxiety, depression and burnout.

OBJECTIVE: The objective was to carry out an umbrella review of systematic and narrative reviews on the effectiveness of mindfulness-based interventions in reducing stress and improving well-being in HCPs and health care students.

METHODS: Systematic and narrative reviews that examined the impact of mindfulness-based interventions on HCPs and healthcare students' perceived stress were identified through a systematic search of three electronic databases: PubMed, Scopus and Web of Science.

RESULTS: Fifteen articles were included in the analysis: eleven systematic and four narrative reviews. Studies' quality varied from critically low to high. The different interventions showed positive results in reducing stress in both HCPs and students, with mindfulness-based stress reduction (MBSR) course having the major impact.

CONCLUSIONS: MBSR techniques and other mindfulness-based interventions resulted to be potentially effective in reducing stress. However, despite the vast amount of data collected by the studies and the promising results, several limitations affected the validity of the studies. Therefore, more research that considers the critical aspects of this field is required, in order to provide more reliable results.

Keywords: Mindfulness, stress reduction, healthcare professionals, umbrella review

1. Introduction

Health care providers (HCPs) are particularly exposed to various determinants of work-related stress [1, 2]. Usually, they face with organizational issues, diagnostic and therapeutic duties, as well as

have to face the suffering of people on a daily basis [3]. All these aspects are associated with the development of a progressive physical and psychological stressful status of HCPs, which consequently makes them more likely to develop anxiety, depression and burnout [4–6]. This can negatively have an impact on both patients and healthcare systems, by causing medical errors, longer patient hospital stay, and poorer patient care [7]. Attention has also been paid to healthcare students since they have to maintain

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clinical tasks and academic standards. These two stressors can affect their competency acquisition, and lead to depression and anxiety [8, 9]. In response to these concerns, several health and educational organizations started seeking possible solutions and strategies to reduce HCPs' and healthcare students' stress levels, as well as to improve well-being. One such strategy is mindfulness, through which HCPs and healthcare students learn to be purposefully alert and attentive to the present moment and to self-observe in an objective and detached manner. The first mindfulness intervention to be clinically evaluated was the mindfulness-based stress reduction (MBSR), a program that incorporates many types of meditation techniques and yoga postures [10, 11]. In recent years, other types of mindfulness-based interventions (MBIs) and meditation were evaluated. Results were promising, with most interventions showing a decrease in HCPs' anxiety, depression, stress, and burnout symptoms [12, 13]; some studies also analysed indirect elements, highlighting positive results for example on patients' satisfaction [13, 14]. There is evidence, based on systematic reviews already published, that MBSR and MBI interventions are useful tools able to reduce perceived stress symptoms, to improve mental health outcomes [9, 10, 15, 16] and positive results are reported on the prevention of burnout syndrome [17].

However, in many cases, several limitations do not allow studies providing statistically reliable results. Selection criteria, number of participants, duration of the intervention, lack of follow-up and other problems limit the robustness of evidences from these studies [4, 18, 19]. Moreover, the heterogeneity of the sample did not allow to objectively measure the outcomes. For these reasons, more research needs to be carried out, in order to better assess the methodology in this field. The present umbrella review aimed at:

- A) providing an overview of systematic and narrative reviews focusing on MBSR, MBIs interventions in HCPs and healthcare students;
- B) giving a summary and indicating implications for future research regarding mindfulness trainings and their impact on HCPs' health and wellness.

2. Materials and Methods

The umbrella review was performed during February 2020 following the Preferred Reporting Items for

Systematic Reviews and Meta-Analysis (PRISMA) Statement [20]. The study was based on a previously established protocol reviewed by a research team with expertise in knowledge synthesis and overview reviews. The study was not registered with PROSPERO or similar registers.

2.1. Identification of relevant studies

Systematic and narrative reviews that examined the impact of MBSR and other MBIs on HCPs and healthcare students' stress were identified through a systematic search of three electronic databases: PubMed, Scopus and Web of Science. All studies regardless time of publication were considered for inclusion. Moreover, we considered papers published in English, French and Italian. Eligible studies were selected by two researchers through a multi-step approach including title and abstract screening and full-text evaluation. The following search algorithm was used in both databases: "mindfulness AND (healthcare professionals OR nurse* OR doctor*) AND stress reduction AND review".

2.2. Study selection and eligibility criteria

The first selection was performed by filtering duplicated articles. Afterward, title and abstract screening was performed. Then full text assessment was performed. Systematic and narrative reviews were selected according to inclusion and exclusion criteria (Table 1) following the PICOS (Population, Intervention, Comparison, Outcomes and Study Design) search strategy tool.

2.3. Indicators of effectiveness

The effectiveness of the intervention was based on several outcome measures. The primary outcomes were the healthcare provider's and student's well-being and perceived stress, the secondary outcomes varied including mood, anxiety, burnout and performance.

2.4. Data extraction and quality assessment

Data were extracted and qualitatively assessed using the AMSTAR 1 tool for systematic reviews and the INSA tool for narrative reviews [21, 22]. AMSTAR consists of 11 items and has good face and content validity for measuring the methodological quality of systematic reviews. The INSA tool consists

Table 1
PICOS criteria for inclusion and exclusion of studies

	Include	Exclude
Population	HCPs, healthcare students	Patients, general population
Interventions	MBSR, MBIs	None
Comparators	Any	None
Outcomes	Well-being, perceived stress, anxiety, burnout, performance	None
Context/settings	Healthcare environment	Other environments
Timing	Pre-post intervention, before-after study	None
Study types and designs	Systematic reviews, narrative reviews	Other study designs

of 7 criteria and includes a point system according to which each valid answer corresponds to one point. A review awarded a total of 5 points will be considered good. The following study characteristics were extracted:

- author name;
- publication year;
- study design of included studies in the article;
- type of intervention;
- number of studies included in the review;
- primary and secondary outcome;
- participants;
- follow-up (where applicable);
- results.

2.5. Data synthesis

In order to organize the amount of data, results have been grouped on the basis of the type of intervention. Three main subcategories were finally identified: MBSR, MBIs, other techniques.

3. Results

The search strategy initially resulted in a total of 54 references, of which 31 remained after deduplication. Another 10 articles were excluded after title and abstract screening. 21 full-text articles were then selected and read. Six papers were removed from the final review, since they were not reviews. Finally, 15 studies were included in the umbrella review, of which eleven were systematic reviews and four were narrative reviews (Fig. 1). Most reviews were conducted in the USA, Canada and Australia. One review was conducted in Ireland, and another in Lebanon. The characteristics of reviews are shown in Table 2.

3.1. Quality of included reviews

Findings of the quality assessment are presented in Tables 3 and 4. None of the systematic reviews reached the maximum of the AMSTAR score. Moreover, all studies failed to satisfy AMSTAR items 4, 5, 11. In particular, the authors did not state whether they searched for reports regardless of their publication type (e.g., grey literature) (AMSTAR item 4), did not provide a list of included and excluded studies (AMSTAR item 5) and did not acknowledge any potential sources of support or cp (AMSTAR item 11).

The final assessment of the systematic reviews varied from critically low to moderate. Among narrative reviews, the study carried out by Irving and colleagues reached all seven items of the INSA score, the study conducted by West five, the remaining two reached very low scores, hence being judged as very low-quality studies.

3.2. Mindfulness-based stress reduction

Most of the reviews examined studies that evaluated the effect of MBSR techniques on HCPs and healthcare students. The MBSR program developed by Kabat-Zinn was mainly conducted, consisting in 8 weekly 2.5-h sessions and one full-day silent retreat between the 6th and 7th class [11]. There was a general agreement regarding the results, since they found out that MBSR has an effective role in reducing stress in a targeted sample. However, the overall high heterogeneity of the participants, between and within the reviews, represents a first obstacle to properly evaluate the results. Perceived stress and burnout were the most frequently evaluated outcomes, and their assessment was performed by using the Perceived Stress Scale (PSS) [23] and the Maslach Burnout Inventory (MBI) [24]. Lamothe et al. primarily evaluated perceived stress, finding that MBSR is able to decrease it, and similarly, positive findings regarding burnout, anxiety and mental well-being resulted from

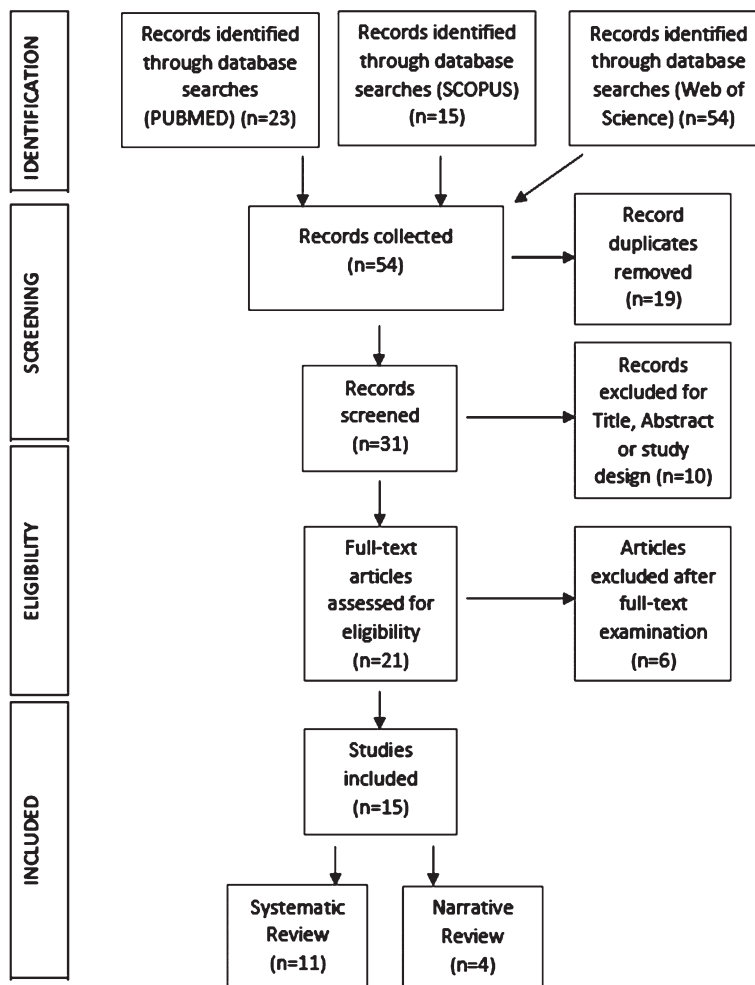


Fig. 1. The PRISMA flowchart and the study selection process.

the analysis of the studies. Mindfulness outcomes were also evaluated through different questionnaires, showing similar results. Some variants of MBSR were also developed, since a need for adaptation was required in many cases, with shorter and more intensive MBSR courses [19]. Spinelli et al. used the Hedge's to quantify the effect of various MBSR techniques on the measured outcomes, finding a significant moderate association for several parameters: anxiety, depression, psychological distress and perceived stress. They also analysed some studies that considered a follow-up ranged from 4 to 80 weeks after the intervention, finding small to moderate effect on stress [4]. Smith et al. evaluated different types of MBSR courses mainly for healthcare students and nurses, and measured different outcomes, again reporting positive effects on them [12]. Stillwell et al. focused on pre-post studies, specifically investi-

gating the immediate effect of MBSR techniques and other stress management courses, and demonstrating a reduction in perceived stress after the intervention in all the analysed studies [25].

Burton et al. [26] performed a meta-analysis on 7 out of 9 papers included in their systematic review and found that MBSR, MBSR-M and MBIs are interventions that have a significant impact on decreasing stress levels for HCPs. The results of the meta-analysis shows a medium effect ($r=0.342$; $CI=0.202-0.468$).

Gilmartin et al. [16] performed a systematic review using the results of 14 papers, of which 50% were RCTs. 83% of the studies reported statistically significant improvements in stress score levels after completion of the intervention. Moreover, two thirds of the studies reveal positive changes in levels of anxiety, resiliency, and burnout symptoms.

Table 2
Characteristics of the reviews included in the umbrella review

First Author, Year	Review type	Study design of included studies in the Review	Type of intervention	Studies included in the Review	Primary outcome	Secondary outcome	Participants	Follow-up	Effectiveness	AMSTAR/ INSA score
Lamothe, 2015 [16]	Systematic review	RCT, quasi-experimental, pre-post (no control)	Not specified	39	Mental health, physical health and physical well-being, Mindfulness	Sense of coherence	Healthcare students, HCPs	Not specified	MBSR is associated with favorable effects on HCPs' mental health and levels of mindfulness. Nonetheless, no clear conclusion can be drawn, due to the lackness of an item-level analysis and the weight of specific items on scores and subscores.	8
Gilmartin, 2017 [24]	Systematic review	Any study design	MBSR, other MBIs Brief MBIs	14	Perceived stress, anxiety, depression	Burnout, resiliency	In hospital employed physicians, nurses, nursing students, medical trainees	Not specified	MBIs are mainly associated with improvement of stress and anxiety. Notably, interventions which were adapted to increase accessibility by providers, showed positive results in self-management of reactions to stressful work environments. However not all interventions improved study outcomes.	7
Everson, 2018 [25]	Systematic review	Not specified	Empathy and communication skills training, patient experience focused programs, film based training and mindfulness training	15	Empathic concern	None	Healthcare students, HCPs	Not specified	Some evidence for the effectiveness of MBSR, programs that incorporate the film Wit, and provision of empathy content over the full course of a healthcare degree has been seen. However, a clear impact on EC could not be identified.	6
Stillwell, 2017 [22]	Systematic review	Quasi-experimental, RCTs, quantitative studies	Stress management course, MBSR techniques	8	Perceived stress	None	Healthcare graduate students within USA	Not specified	In all studies, self-care interventions reduced perceived stress in graduate health science students. All studies had small sizes and were conducted in single-cite university settings, having the potential of bias.	3
Burton, 2017 [26]	Systematic review	RCTs	MBSR-M, other MBIs	9	Perceived stress	None	HCPs	Not specified	MBIs are able to significantly decrease stress levels for HCPs. The results of the meta-analysis revealed a significant value of $r = 0.342$ (CI = 0.202–0.468), showing a medium effect	7

(Continued)

Table 2
(Continued)

First Author, Year	Review type	Study design of included studies in the Review	Type of intervention	Studies included in the Review	Primary outcome	Secondary outcome	Participants	Follow-up	Effectiveness	AMSTAR/ INSA score
Ghawadra, 2019 [27]	Systematic review	RCTs, Quasi-experimental	MBSR	9	Perceived stress, anxiety, depression	Burnout, life satisfaction	Nurses	Six weeks – four months	MBSR has a positive impact on the psychological well-being of nurses. The mindfulness interventions had effects on improvements of the primary outcomes, such as stress level, reduced in six studies, and anxiety and depression levels, reduced in three studies	6
Lomas, 2018 [28]	Systematic review	RCTs	MBIs	81	Burnout, distress, anxiety, depression, and stress.	None	HCPs	Not specified	Mindfulness based interventions are associated with positive outcomes in relation to the chosen measures, and especially for burnout	7
O'Driscoll, 2017 [9]	Systematic review	Randomized and non-randomized controlled trial	MBSR techniques	11	Stress, mood	Mindfulness levels	Health or social care undergraduate students	6 months	Benefits have been reported in participants' stress, mood and mindfulness levels, as well as anxiety, well-being, self-compassion and coping abilities. No significant relationship between the number of class hours and effect on psychological distress was reported. Follow-up made in two studies showed no sustained effect. Gender and personality have emerged as factors which potentially affect the results achieved through MBIs.	4
van der Riet, 2018 [26]	Systematic review	Quantitative, qualitative and mixed	Mindfulness meditation	16	Stress reduction, depression, anxiety and burnout	Well-being and empathy	Nursing students, nurses		Engagement in MM programs, especially when accompanied by regular practice, has a significant impact on stress, depression, anxiety, burnout, and well-being. MM has proven to be a protective strategy that builds emotional regulation.	5
Smith, 2014 [12]	Systematic review	Randomized and non-randomized control trials, pre-post test, phenomenology and descriptive	MBSR courses	13	Stress	Burnout, anxiety, focus, self-improvement, empathy	Students, nurses	Not specified	MBSR has been found to decrease nurses' stress and increase nurses' ability to focus, increase attention, and decrease distractive, ruminative thoughts and behaviors.	2

Spinelli, 2019 [4]	Systematic review	RCT, quasi-experimental, pre-post (no control)	MBSR, MBSR-M, other MBIs	38	Anxiety, burnout, depression, psychological distress, stress	Well-being, psychical health, performance, cognitive, clinical, mindfulness	HCPs, HCPs-IT	Not specified	Larger intervention effects were found with HCPs, MBSR intervention, and inactive controls. MBSR had the largest effect on stress, MBIs-O on burnout and MBSR-M on anxiety, depression, and psychological distress. Well-being outcomes were most effected by meditation.	8
Romani, 2014 [5]	Narrative review	Not specified	Stress management courses, Balint sessions, stretching exercise	15	Burnout, stress	Performance, well-being, others	Medical students, physicians	Not specified	Multidisciplinary actions such as changes in the work environmental factors and stress management programs that help people to cope better with stressful events, showed promising solutions to manage burnout. Yet, no rigorous studies could prove this.	2
Raab, 2014 [3]	Narrative review	Not specified	Mindfulness, MBSR	Not specified	Not specified	Not specified	HCPs	Not specified	Mindfulness interventions have potential to reduce stress and burnout and increase empathy and self-compassion, as well as clinical care outcomes, although more research in this field is required.	1
Irving, 2009 [23]	Narrative review	RCT, NRCT, pre-post, qualitative	MBSR, mindfulness meditation	10	Psychological symptoms, empathy, burnout, relaxation	Not specified	Nursing and medical students, HCPs	Not specified	Despite the promising findings for both clinical and non-clinical populations, research on mindfulness has been limited by several issues. Research initiatives with a combined focus upon process and outcome variables and diversified research methods are recommended.	7
West, 2018 [6]	Narrative review	Not specified	Not specified	Not specified	Burnout, stress	Not specified	Physicians	Not specified	Many gaps regarding burnout knowledge remain. Effective remedies should be taken from all stakeholders in healthcare delivery.	5

Table 3
Quality assessment of included systematic reviews according to AMSTAR

Author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Final rating
Lamothe, 2015	1	1	1	0	0	1	1	1	1	1	0	8
Gilmartin, 2017	0	1	1	0	0	1	1	1	1	1	0	7
Everson, 2018	1	0	1	0	0	1	1	1	0	1	0	6
Stillwell, 2017	0	1	1	0	0	0	1	0	0	0	0	3
O'Driscoll, 2017	0	0	1	0	0	1	0	0	1	1	0	4
van der Riet, 2018	1	1	1	0	0	1	1	0	0	0	0	5
Smith, 2014	0	0	1	0	0	1	0	0	0	0	0	2
Spinelli, 2019	1	1	1	0	0	1	1	1	1	1	0	8
Burton, 2017	1	1	1	0	0	1	0	1	1	1	0	7
Ghawadra, 2019	0	1	1	0	0	1	1	1	0	1	0	6
Lomas, 2018	1	0	1	0	0	1	1	1	1	1	0	7

Table 4
Quality assessment of included narrative reviews according to INSA

Author, year	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Final rating
Romani, 2014	0	0	0	0	1	0	1	2
Raab, 2014	1	0	0	0	0	0	0	1
Irving, 2009	1	1	1	1	1	1	1	7
West, 2018	1	0	0	1	1	1	1	5

A systematic review, performed by Ghawadra et al. [27] on papers on the effect of MBSR intervention on nurses, found the MBSR has a positive impact on the psychological well-being of these HCPs. These interventions are able to improve the primary outcomes, such as stress level, reduced in 66% of studies, and anxiety and depression levels, reduced in 33% of the studies.

O'Driscoll et al., in their review, accounted studies performing follow-up monitoring, but interestingly a lack of sustained effect was reported, suggesting that a continuous MBSR course should be followed to maintain the positive effects on stress reduction [9]. The two narrative reviews that analysed this type of intervention, published by Raab and Irving et al., also agreed that MBSR could represent a promising tool for HCPs and healthcare students to manage stress, burnout, and other mental and physical affections [3, 25]. In particular, Raab focused on the concept of self-compassion as an attitude enhanced by MBSR training, which eventually leads to a reduction in maladaptive cognitive coping tendencies and a better management of stress. Nonetheless, all these studies underlined difficulties in properly interpreting data. Apart from the consistent heterogeneity reported in many studies, a limited number of participants and contrasting results made it difficult to perform a sensitive analysis. Moreover, most reviews reported a high-risk bias in the primary studies.

3.3. Mindfulness-based interventions

Apart from the main MBSR intervention other mindfulness-based interventions were evaluated to analyze the effect on stress in the targeted population. Van der Riet et al. mainly focused on nurses and nursing students and considered various mindfulness meditation (MM) techniques to reduce stress. The results of this review identified that MM can have positive impact on stress, anxiety, depression and burnout among nurses and nursing students [17]. However, the authors also put forward that the majority of papers included in the review described small scale localized studies which limit the generalizability of the results [17]. Spinelli et al. considered some other MBIs among the studies. It was reported that while MBSR intervention had the largest effect on stress, other MBIs were more effective on burnout [4, 28]. Gilmartin et al. included studies that incorporated different MBIs, some focusing only on mindfulness, others including mindfulness within multifaceted resiliency programs to reduce medication errors, others used a combination of lecture, discussion, and group or independent practice sessions. The dose, duration, and settings of the different interventions also varied. Outcomes regarding the providers' mental and physical health were measured through different scores, and most of the studies reported statistically significant improvements; no

significant improvement on medical errors reduction was reported [16]. Moreover, Raab et al. also considered other MBIs along with MBSR courses as instruments for HCPs to face stress, burnout, depression. They also underlined the importance of empathy and compassion as fundamental characteristics for working with the suffering of people and argued that both MBSR and other MBIs also contribute to balance these aspects [3].

3.4. Other techniques

Different approaches to reduce stress, burnout, and generally to improve HCPs and students' mental and physical health, as well as to enhance their attitude and competence to work or study, were examined by some other studies. Apart from MBSR and MBIs, other types of courses were evaluated to verify the efficacy that they may have had. In particular, Romani et al. considered studies that analyzed various stress management courses:

- sociopsychological training;
- sessions of open discussions and problem solving within a flexible, group-determined set of agenda items;
- single, all-day stress management workshop;
- meditation and breathing exercises [5].

Some of them resulted in positive effects, others, such as the second, demonstrated no improvement in the measured outcomes. Other included studies by Romani et al. analysed Balint sessions, showing an important improvement in patient-centred care and self-esteem among general practitioners. Similar results were obtained for studies that evaluated some exercises, especially stretching exercises in the workplace. Finally, some occupational interventions were considered to verify the improvement of the practitioner's well-being, in particular giving priority to physicians' well-being as much as the quality of care, or identifying factors that produce stress, and trying to reduce them. Everson et al. focused mainly on programs that promote health professional students' empathic concern [29]. The interventions were divided into four categories: empathy and communication skills training, patient experience focused programs, film-based training and mindfulness training. Again, contrasting results did not allow the studies to provide a statistically significant conclusion.

4. Discussion

This umbrella review examined eleven systematic and four narrative reviews focusing on MBSR and MBI techniques to reduce stress among HCPs and healthcare students. Hilton et al. [30] already created an evidence map summarizing the impact of mindfulness interventions, also for HCPs. However, they did not perform a systematic review.

4.1. Stress

The results suggest that the techniques evaluated can be effective in helping this target population to cope with stress. Due to high demand and workplace stress, HCPs and healthcare students may experience high levels of stress, and mindfulness-based interventions were generally found to reduce symptoms and to improve mental health outcomes [14, 25–27]. Other MBIs and stress management interventions also led to a better mental health state in participants [15, 16]. The most overall evaluated outcome was perceived stress, that was most often measured using the PSS. In most studies perceived stress decreased after the intervention. Comparison among interventions showed different outcomes, with MBSR having the largest effect on stress reduction.

4.2. Burnout

Burnout was also frequently measured, mainly using Maslach Burnout Inventory, which reported positive results. Van der Riet et al demonstrated that mindfulness meditation has proven to be a protective strategy that builds emotional regulation, and this can have a preventive impact on burnout development [17].

4.3. Anxiety, depression and well-being

Beyond these two major aspects (stress and burnout), various measurements of well-being, physical health, performance, empathy, or even patients' satisfaction were performed, showing less positive results.

As far as concerns anxiety and depression, O'Driscoll et al. [9] and Raab et al. [3] underline the potential benefit of MBSR through the mediation of compassion and self-compassion. These effects are of particular interest for the HCPs, for improving work relationships (i.e., job satisfaction) and increasing perceived comfort with patients.

van der Riet et al. [17] and Spinelli [3] demonstrated that engagement in Mindfulness Meditation programs, especially when accompanied by regular practice, appeared to be most effective in increasing well-being.

4.4. Limitations

Several limitations must be acknowledged in this review. First of all, most studies included in the single reviews had small sample sizes, and a grade of heterogeneity varying from moderate to high for different outcomes, having the potential for bias [15, 25]. In many studies there a control group was lacking, making it difficult to provide evident outcomes. Furthermore, the intervention settings often varied within the studies, mainly due to the difficulty for participants to attend the courses at the same time of the day due to different work-shifts. Consequently, it was difficult to recommend a standardized MBSR or MBIs approach to better evaluate the outcome [4]. Besides, almost all studies did not include follow-up observations, making it difficult to establish the long-term effect of the interventions [14]. Furthermore, the studies that used a follow-up, showed no sustained effects, suggesting that MBSR courses should be continually implemented in order to maintain the benefits over time [9].

Another limitation was the choice of some studies to include together different types of HCPs and students, not considering the difference that can be present among them, especially for students, which were certainly exposed to different factors compared to HCPs. For all these reasons, the quality of the studies was generally affected, and this review could not fully clarify the effectiveness of the analyzed methods in reducing stress in HCPs and healthcare students.

5. Conclusions

Stress has been identified as a risk factor for health among both HCPs and healthcare students. The high prevalence of workplace stress as well as the complex and demanding nature of healthcare underline the need for implementing strategies to increase resilience. The present review summarized studies that focused on the efficacy and effectiveness of MBSR and MBI techniques to reduce stress.

However, we need to recognize that while both MBSR and other MBIs techniques can be effective in reducing stress, the review also identified limita-

tions and consequently roadways for further research. There is sufficient evidence to use these techniques in longitudinal education training of both HCPs and healthcare students.

From the methodological point of view, future research should focus on the standardization of the intervention, sufficient sample sizes to empower hypothesis testing, a separate analysis of HCPs and students, conduction of follow-up investigations to assess the continuation of the intervention efficacy and application of better instruments of analysis, such as developing more focused questionnaires for HCPs.

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Conflict of interest

The authors declare no conflict of interest.

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