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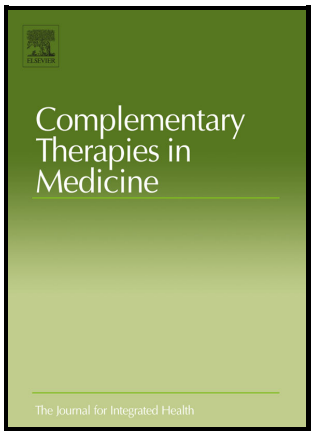

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A systematic review and meta-analysis of the effect of whole body cryotherapy on mental health problems

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon request.

Abstract

Objective: To give an overview of the nature and methodological quality of studies on whole body cryotherapy (WBC) as add-on intervention for mental health problems.

Methods: A meta-analysis according to PRISMA guidelines was conducted (Prospero registration: CRD42020167443). Databases MEDLINE, PsycINFO and the Cochrane Library were searched. Risk of bias was scored according to the Cochrane ROBINS-I-tool to which an extra bias-dimension of allegiance bias was added. Within and between Hedges' *g* pooled effect sizes were calculated for the main aspect of mental health measured. Treatment efficacy was examined using a random effects model. Heterogeneity was examined through identification of visual outliers and by I^2 statistics.

Results: Out of 196 articles coming up from the search, ten studies met all inclusion criteria, six of which were (randomized) controlled trials. Together these studies report on a total of 294 participants receiving WBC. The within-group pooled effect size for mental health problems is large (Hedges' g = 1.63, CI: 1.05-2.21), with high heterogeneity (I^2 = 93%). Subgroup analyses on depressive symptoms and quality of life (QOL) showed a diminution of heterogeneity to moderate. Effect sizes for depressive symptoms are very large (Hedges' g = 2.95, CI: 2.44-3.45) and for QOL medium (Hedges' g = 0.70, CI: 0.15-1.24). The between-group pooled effect size is medium (Hedges' g = 0.76, CI: 0.17-1.36).

Conclusions: Results indicate preliminary evidence for WBC as efficacious add-on intervention for mental health problems, especially depressive symptoms. Further research in the form of RCTs with larger numbers of participants is needed.

Keywords

cryotherapy, cold therapy, psychiatric somatic therapies, mental disorders, mental health

HIGHLIGHTS

• Whole body cryotherapy (WBC) is a procedure in which participants enter a cryo-cabin (enclosed space) with an air temperature of -110 degrees Celsius for approximately three minutes.

• In the professional world of sports WBC has been used for some decades. Research shows that WBC leads to better exercise capacity, more regular circadian rhythm, improved quality of sleep and less tiredness in athletes. These effects are also desired aims of treatment in people with certain psychiatric disorders.

• Recently studies appeared which measured the effect of WBC on mental health. So far, no meta-analysis was conducted on this subject.

• Currently there is a lack of low-cost, easily accessible treatment possibilities for most psychiatric disorders.

• This meta-analysis demonstrates that there is preliminary evidence for efficacy of WBC as an add-on intervention for mental health problems, especially where depressive symptoms are concerned.

1 | INTRODUCTION

From time immemorial it has been known that cooling down of the body can have a beneficial effect on body and mind. It was a known practice during Antiquity, mentioned a.o. by Hippocrates (460 BC) in his writings[1] and it lasted during the Middle Ages.[2] In our present time, the effects of swimming in cold water or taking cold showers or baths (4-10 degrees Celsius) are still being researched, especially in Northern countries.[3–5] The presupposition of the various interventions is that cooling down of the body leads to a physiological reaction which reinforces the immune system and induces physical activity.[4,6]

Until the 80s of the last century, psychiatric patients in the United States were wrapped in cold, wet sheets.[7] Purpose of this was to calm down patients with heightened agitation and to activate patients who had too little initiative (apathy).[8] Recently the use of cold therapy has re-entered psychiatry in several forms. The two most known are bathing in cold water or entering cooled air chambers. With cooling by water, temperatures vary between 0-15 degrees Celsius, or - when the water is salted - even lower. Research in this field is done by both scientists[4,5,9], but also by large groups of followers in less academic settings.[10] With the second method, cooling is effectuated by means of cold air in temperature-controlled chambers or cabins. In these devices the cryogenic temperatures measure between -60 to even -200 degrees Celsius.[11,12] This method is mostly referred to as whole body cryotherapy (WBC)[12], since it's the only method in which the whole body

including the head is cooled. Recently, a third method has been developed in which water-perfused suits are worn.[13] All of these methods vary greatly in their procedure. Consequently, there is a large variety in results of drop in skin temperature. This is due to difference in heat transmission coefficients in different environments (water, air, etc.) and due to the fact there are no uniform standardized protocols.

During cold therapy and in particular WBC, strong variations in skin temperature induced by exposure to extreme cold, lead to the stimulation of cutaneous thermoreceptors and therefore to the stimulation of the thermoregulation centre in the hypothalamus.[12] During exposure to cold, the thermoregulatory system attempts to maintain a constant core temperature (around 37 degrees Celsius) by means of skin vasoconstriction and by increasing the metabolic rate through shivering. Lower skin temperature through WBC leads to a decrease in heart rate and an increase of blood pressure (both diastolic and systolic).[14,15] During a severe cold exposure, such as WBC, skin temperature decreases rapidly due to the mentioned vasoconstriction and direct skin cooling, most profoundly in the extremities.[16,17] Skin temperature can drop 10 degrees Celsius there, especially in calves and forearms.[18] The range of change depends on both BMI[14,18] and gender.[19–21] Core and muscle temperatures hardly drop during WBC.[16,18] As we will demonstrate below, WBC has been applied within various fields that mainly focus on the somatic benefits of the procedure. Some of the findings obtained within these fields suggest that WBC also holds promise as a procedure to advance mental health.

Since the 70s, several forms of WBC have been applied in people suffering from autoimmune diseases such as multiple sclerosis[22,23], ankylosing spondylitis[5,7,24] and rheumatoid arthritis.[25] Autoimmune diseases are diseases in which the immune system is overactive and causes increased inflammatory reactions, which in their turn cause tissue damage.[6] Research shows that WBC applied to patients with autoimmune diseases leads to a reduction of their somatic complaints and pain. Researchers argue that this effect is achieved because WBC has a suppressing effect on the immune system.[11,23] The above research also shows a decrease of cellular micro inflammation in the form of lower levels of pro-inflammatory cytokines* and oxidative stress† after treatment with WBC.

Apart from its application in autoimmune diseases, WBC or cooling down via other means as mentioned above is used increasingly in the professional world of sports due to its supposed effects on physical recovery after sports activities.[26,27] There are several studies on the effects of WBC on exercise induced muscle damage (EIMD) e.g. recovery from EIMD.[27,28] A Cochrane review also concludes that cold therapy (in the form of cold water) has a positive effect on the recovery of muscles after exercise.[29] In addition to this, the possible recovery-inducing effects of WBC were studied in specific sports, a.o. athletics[11,26,30,31],

* Pro-inflammatory cytokines are proteins that are produced within cells as their over-reaction against a presumed enemy. They are a product of the immune system. Sometimes it is supposed there is a link between the derailing of the immune system and an increased oxidative stress, but that has not been conclusively established (Fonda et al., 2014). However it is clear though that reversely, pro-inflammatory cytokines increase oxidative stress markers.

† Oxidative stress is a condition of the metabolism in which more than a normal physiological amount of reactive oxygen compound is formed within the cell. These reactive oxygen compounds can damage the DNA.

kayaking[32], volleyball[33], basketball[34] and swimming.[35] All of these studies show improvement of performance through WBC or cooling down by cold water. Compared to control groups, the groups which were treated with cold therapy showed better exercise capacity, more regular circadian rhythm, improved quality of sleep, less tiredness, lower levels of pro inflammatory cytokines* and decrease of oxidative stress† on the cellular level. These results agree with recent findings from research into cold therapy in healthy participants outside the professional world of sports.[36,37]

Certain effects of cold therapy found in the studies discussed above, such as behavioural activation, increased exercise capacity and improvement of quality of sleep and sleep efficiency[26,28] are also the desired aims of treatment in people with psychiatric disorders. For example, it has been duly known that improvement of the circadian rhythm mediates mood enhancement.[38] Originally, it was assumed that remission in symptom levels of mood disorders automatically leads to an improvement in quality of sleep. However, the opposite appears to be the case.[39] The same holds true for an increased exercise capacity and behavioural activation: there is now proof that these factors favourably influence mood enhancement and reduce levels of anxiety.[40–43] In addition, the key target of treatment in many psychiatric disorders according to guidelines consists of improvement of exercise capacity and behavioural activation.[44]

Since the beginning of the 21st century, several studies have been published on the effect of cold therapy on mental health. For the sake of uniformity and comparability of studies we decided to concentrate on the method applied by cold-air chambers (WBC) only. Apart from these methodological arguments, there is also a very practical aspect for this. Only one study on the use of cold therapy in another form (cold showers) in patients with mental health problems (that meets all other criteria about quality and number of participants, see part two Material and Method) is currently available.[4]

Although there are studies that show positive results of WBC, their number is limited, and only small samples were used. So far no systematic review or meta-analysis of WBC in mental illnesses has been executed.

Currently there is a lack of affordable, easy accessible treatment possibilities for most psychiatric disorders.[45,46] Most evidence-based treatment is expensive and labour intensive for both professionals and patients.[44,45] In most countries there are waiting lists for mental health centres.[47] It is expected that the number of people suffering from psychiatric disorders will increase in both the Western and Non-Western countries.[48,49] We are therefore looking for new effective alternatives for current treatments or effective add-on treatments that preferably have the potential to target multiple symptom clusters: so-called transdiagnostic interventions. Since the launch of the network theory[50,51] and the insight that many psychiatric diagnoses are a combination of a limited amount of symptoms, the search for (add-on) interventions aimed at these common symptoms (i.e. transdiagnostic domains) seems worthwhile.[52–54]

If WBC would be effective as an add-on intervention for people suffering from mental illnesses, this could contribute to solve the above-mentioned problem. The application of WBC for mental health problems fits in with the transdiagnostic approach since it targets common symptoms in psychiatric disorders like sleeping problems and inactivity. Moreover, WBC is relatively inexpensive, quick and easily accessible. Especially if compared to traditional healthcare with it's highly trained professionals (high financial costs) and long waiting lists (high burden of disease-costs). Furthermore WBC can be initiated by the patient itself, as long as he or she is screened by a medical doctor. All these aspects taken together

can stimulate the empowerment of patients. The use of WBC appears to be safe in view of studies done so far with participants using WBC and studies focusing on the technical and safety aspect of the procedure.[55] It's very important, as said, that patients are seen beforehand by a medical doctor who checks upon possible physical or mental contra indications for WBC. A list of exclusion criteria can be found in Appendix 2. Furthermore it's important that the technical installations meet international safety requirements such as set by the European Union for example, and that a notified body approved the marking of installations.

For these reasons the present study aims at giving a meta-analytical review of the effect of WBC on psychopathology. More specifically, the aim of the study is five-fold:

Aims of the study

(1) To investigate the current body of knowledge concerning the influence of Whole Body Cryotherapy (WBC) on mental health.
(2) To assess the psychological effect of WBC on people with different conditions.
(3) To define the methodology and quality of the existing studies.
(4) To formulate an indication whether WBC can be an effective additional treatment for patients with mental health problems.
(5) To suggest further steps in research on the use of WBC in order to improve mental health.

2 | MATERIAL AND METHOD

2.1 Guidelines and registration

The systematic review and meta-analysis followed the guidelines as provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[56] The research protocol was registered in advance at the Prospero database of the University of York[57] under number: CRD42020167443 (registration completed 24th of April 2020).

2.2 Identification of studies

See figure 1 Flowchart. In PICO terms the research question is: **Could WBC be effective as additional treatment for patients with mental health problems?** On basis of this question, four categories of search terms were formulated: *'Patients suffering from mental illnesses'* (Patient), '*Cryotherapy'* (Intervention), *'Treatment as usual',* (Comparison), and *'Outcome'* (Outcome). For each of the PICO-elements all possible meSH terms, thesaurus terms, key words and synonyms were mapped. Three databases were selected in which possibly relevant articles could be found: MEDLINE (the following variants were used: MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations), PsycINFO, and the Cochrane Library (of which was used: the EBM Reviews - Cochrane Database of Systematic Reviews). The search was done by means of the search system Ovid. See Appendix A for a survey of the search grid.

Combining the three databases (excluding an overlap of 6 articles) resulted in 188 publications. Next, the contents of the overlapping articles were studied. All these turned out to originate from one research group of the Medical Faculty of the University of Wroclaw (Poland). Between 2003 and 2020 this Faculty published several articles on the effect of cryotherapy on patients with mental disorders. We therefore contacted this Faculty, which yielded two more articles. By studying references we discovered two more titles. An auto-

alert search order was installed to keep us informed of the most recent publications. This was last checked on July 1st, 2020. This led to a total of 196 articles of which the abstracts were checked.

2.3 Inclusion and Exclusion criteria

Two consecutive selection phases were established. Considering the fact that cryotherapy is a relatively new field of study with a wide range of applications and methods, we wanted to start with fairly broad inclusion criteria in order to get a thorough knowledge of the whole field of study. The inclusion criteria for the first phase were: use of a so-called cryo-chamber or other method to cool the whole body and the fact that the tests were done on human adults. All types of studies were included, and no language restrictions were applied.

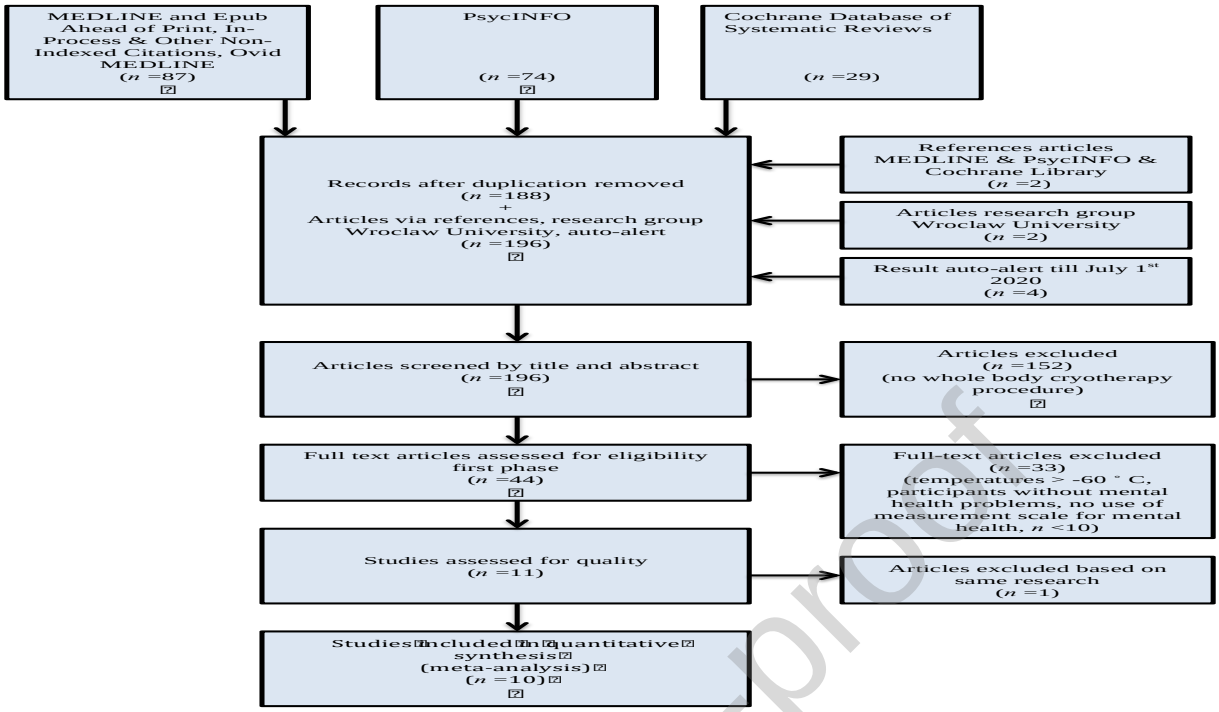
Two independent reviewers JD and MT, each blinded to the findings of the other reviewer, independently screened titles and abstracts of all studies that met the first set of inclusion criteria. Papers that potentially met the pre-defined inclusion criteria were included for full-text analyses. Both at the initial screening and the full text analysis any disagreements were resolved by discussion or - if discrepancies or uncertainty persisted - through consulting another independent reviewer, AN. Thus 152 articles were excluded.

Then the inclusion criteria were further narrowed. From literature research it appeared that the application of WBC is very variable as regards temperature and duration of the intervention.[12] In this meta-analysis we decided to investigate only the application of WBC where there is at least a cooling to -60 degree Celsius or rather even lower down to -110 in a cryo-cabin. As a matter of fact from literature it appears that this effectuates the intended cardiovascular and thermal physiological response, while this does not necessarily happen in higher temperatures or a non-complete cooling down as e.g. in water.[11,14] Other added inclusion criteria were: the presence of mental health problems in participants and the use of a measurement scale that assesses mental health issues. Also, we selected only studies in which the amount of participants was at least $n = 10$. In this way a selection of eleven articles was left. On second reading two of these articles were found to be based on the same research. The whole search strategy can be provided by the authors on request.

2.4 Data extraction

From the included full-text articles the same reviewers extracted the relevant characteristics and data concerning the mental health of participants. Corresponding (and in case of inconsistencies primary) authors of the articles were contacted to clarify any omitted data or study characteristics. Where possible, intention-to-treat data were used. Characteristics that were defined beforehand were: authors, year of publication, type of intervention, number of sessions, dose, mental health aspect, primary outcome measure, *n*, percentage attrition, female/male ratio and age. For the determination of which outcomes to use and which primary measurement instrument was selected, a protocol was written that is available on request by the authors. In advance - as registered in PROSPERO - subgroup analyses were planned according to: type of health issue measured, different research groups and different study designs.

FIGURE 1 Flowchart of the study inclusion/exclusion process



2.5 Risk of bias

After a literature research on the keywords and meHS terms *risk of bias* in PsychINFO and PubMed, there appears to exist no golden standard tool to define risk of bias in the assessment of heterogeneous research designs. The tools found in the literature research were evaluated on their utility according to their content and by studying other meta-analyses in which they were used. This was effectuated for the following risk of bias tools: ROBINS-I, COSMIN, ACROBAT-NRSI, Newcastle-Ottawa Scale (NOS), Scottish International Guideline network Tool (SIGN), CONSORT- checklist and the AHRQ system to rate the strength of scientific evidence. We decided to apply the Cochrane risk of bias tool (ROBINS-I), as this has the highest standard of scientific foundation and linked up best with the majority of the studies that was assessed here.[58]

Besides the various risks of bias that are part of the Cochrane tool, the risk of 'researcher allegiance', described by Cuijpers (2006) was additionally assessed. We decided to include this type of bias as WBC is a relatively new intervention and articles were published by a restricted number of research groups. Risk domains of researcher allegiance were identified as: utterances of authors on the superiority of the method in the article or elsewhere via other channels, vested interests in WBC-enterprises, concentration on the specific research field of WBC regarding publications and non-objective utterances on WBC in either the article or in the correspondence contact between authors of the included articles and the authors of the meta-analysis.

Regarding the scoring scales, the Cochrane rating was adopted (low, moderate, serious, critical, unclear). In the visual display we preferred to render the rating on a visual analogue scale in relation to the scores instead of reducing them to three levels (low, some concerns, high), as in the Robvis-tool (which is usually used in combination with ROBINS-I). In this way, the reader can envisage which risks of bias have been established and which weight they carry.

2.6 Statistical analyses

A power calculation was performed taking into account the ten selected articles to estimate whether enough studies with sufficient sample size were included in the meta-analysis to reach relevant conclusions.[59] This resulted in a power of > 0.80, which is sufficient.

All calculations were made with a software program especially designed for conducting meta-analyses called 'Comprehensive Meta-Analysis' (CMA).[60]

Hedges' *g* ($[mean_1\text{-}mean_2]/[SD_1^2 + SD_2^2])/2$) was chosen as effect size estimate because of its superiority in accuracy when pooling studies with relatively small sample sizes since it corrects for bias in small samples.[61] Values can technically range from minus to plus infinity, where commonly observed values of 0.8, 0.5 and 0.2 refer to effect sizes of respectively large, medium and small magnitude.[62]

Within-group effect sizes were computed based on the mean pre- and post-treatment scores of the primary outcome, their *SD*s, as well as the correlation between pre- and post-treatment scores. Between-group effect sizes were calculated comparing intervention groups with their control groups for pre- to post-treatment changes. Not all articles provided means and *SD*s. In case of missing data, all corresponding authors were contacted to provide these data. For the calculation of within-group Hedges' *g* effect sizes, the pre- to post Spearman correlation is needed. In case authors were unable to provide the correlation, a conservative estimate of $r = 0.70$ was made. [63,64]

The results of the included studies were pooled using a random-effects model under the assumption that 1) the true effect sizes estimated by individual studies were drawn from a distribution of true effects rather than a single value, and 2) an expectation of substantial heterogeneity across studies given the differences in included interventions. Ninety-five per cent confidence intervals were used throughout. Results were published in the form of a forest plot. Assessment of heterogeneity between studies was evaluated visually and with I^2-statistic. Regarding visual inspection of heterogeneity, effect size data of a given study was identified as an outlier if either the upper or lower limit of the 95% CI fell outside the range of the pooled 95% CI.[64,65] I^2 ranges from 0% (no heterogeneity) to 100% (the differences between the effect size can completely be explained by chance alone) and it is assumed that a percentage of 25% indicates low heterogeneity, 50% moderate and 75% high heterogeneity.[66]

Subgroup analyses were succeedingly performed and stratified by type of mental health problem, study design and origin by research group - as put down in the Prospero registration preceding the analysis. Subgroup analyses were conducted according to the mixed effects model[67], in which studies within subgroups are pooled with the random effect model, while tests for differences between subgroups are conducted with the fixed effects model. A funnel plot to analyse publication bias could not be made, as this type of analysis requires a minimum of 30 studies.[64]

3 | RESULTS

3.1 Study characteristics and data

Table 1 shows all included studies and their main characteristics. In total ten studies met the inclusion criteria.[68–77] Not all articles provided means, *SD*s and correlations in their tables.

Within eight months time we managed to obtain all the necessary means and *SD*s that were missing from the corresponding or primary authors.

There was one article[75] from which it was possible to retract the Spearman correlation directly. The rest of the articles didn't provide this information. We tried to retrieve these data in hindsight. In three cases authors were unable to provide them.[69,75,78] All collected data can be obtained from authors upon request.

3.2 Risk of bias

Table 2 provides an overview of the potential risk of bias of the included studies per article according to the Cochrane ROBINS-I tool. Table 3 shows the application of the Cochrane Robvis-tool that creates an overview of each bias when pooled.

Looking at the total of included studies, risk of bias arriving from the randomization or selection process was low to moderate (50% 'low risk' and 50% 'some concerns'). Risk of bias due to deviations from intended interventions was low for all studies (100% 'low risk'). Bias due to missing outcome data was low in seven studies, moderate in one study and serious in two studies (70% 'low risk', 10% 'some concerns', 20% 'high risk'). The two studies with high risk in bias of missing outcome data had relatively high attrition percentages not compensating these dropout numbers in their final conclusions (using completer instead of intent-to-treat data). Bias in measurement of the outcome was moderate in nine studies and low in one study (10% 'low risk', 90% 'some concerns'). Bias in selection of the reported results and bias due to researchers allegiance were low for all studies (100% 'low risk'). Overall 80% of the studies showed 'some concerns' and 20% a 'high risk of bias'.

3.3 Meta-analytic outcomes

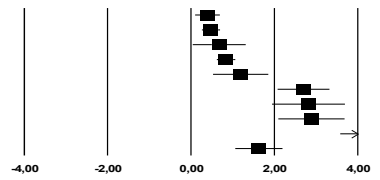
3.3.1 Within-group analyses

One study was excluded from further analysis at this stage, as we encountered a serious outlier[69] that appeared to be unrealistic, Hedges' g = 49.0, and would have strongly impacted the pooled effect size. An additional argument to delete this study was that *SD*s of 0 were reported simultaneously with a range in score, which is impossible (as 0 implies no variation and therefore no range in scores). The authors were contacted again but could not provide additional data to enlighten this concern.

Figure 2 displays the forest plot of the pooled effect sizes. The remaining nine studies show a pooled Hedges' g = 1.63 (95% CI: 1.05-2.21). Considerable heterogeneity among studies was found. Three outliers could be identified from the forest plot and I^2 was 93%, which is high.

FIGURE 2 Within-group pre- to post effect sizes and forest plot for all WBC studies [59,60,62–66]

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Happe et al. (2016)	0,396	0,159	0,025	0,085	0,707	2,498	0,013
Pawlk et al. (2019)	0,478	0,118	0,014	0,246	0,710	4,042	0,000
Rymaszewska et al. (2018)	0,676	0,330	0,109	0,029	1,323	2,047	0,041
Szczepanska-Gieracha et al. (2014)	0,839	0,120	0,014	0,604	1,075	6,982	0,000
Vitenet et al. (2018)	1,189	0,345	0,119	0,513	1,865	3,446	0,001
Rymaszewska & Ramsey (2008)	2,700	0,325	0,106	2,062	3,338	8,300	0,000
Rymaszewska et al. (2019)	2,815	0,453	0,205	1,927	3,703	6,213	0,000
Rymaszewska et al. (2020)	2,887	0,411	0,169	2,081	3,693	7,019	0,000
Rymaszewska et al. (2003)	5,708	1,095	1,198	3,563	7,853	5,215	0,000
	1,625	0,296	0,087	1,046	2,205	5,495	0,000

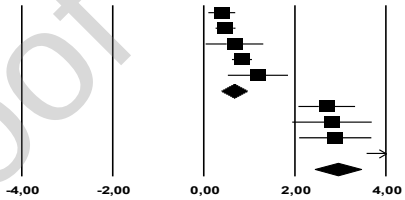


3.3.2 Subgroup analyses

Figures 3 and 4 show the results of a series of subgroup analyses we conducted as reported beforehand in PROSPERO. Studies with symptom levels of depression as a primary outcome showed significantly larger effect sizes (Hedges' g = 2.95, CI: 2.44-3.45), than studies focusing on other mental health outcomes (Hedges' g = 0.67, CI: 0.38-0.94), $p < .001$. Heterogeneity in both subgroups dropped. Looking at the forest plot there were no outliers in the depression group, and one outlier in the other mental health aspects group. I^2 dropped to 57.1% (moderate) and 57.9% (moderate), respectively.

FIGURE 3 Within-group pre- to post effect sizes and forest plot for depression studies (coded 1) versus other aspects of mental health (coded 0)

Group by depression	Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
0,00	Happe et al. (2016)	0,396	0,159	0,025	0,085	0,707	2,498	0,013
0,00	Pawlk et al. (2019)	0,478	0,118	0,014	0,246	0,710	4,042	0,000
0,00	Rymaszewska et al. (2018)	0,676	0,330	0,109	0,029	1,323	2,047	0,041
0,00	Szczepanska-Gieracha et al. (2014)	0,839	0,120	0,014	0,604	1,075	6,982	0,000
0,00	Vitenet et al. (2018)	1,189	0,345	0,119	0,513	1,865	3,446	0,001
0,00		0,659	0,143	0,020	0,379	0,938	4,617	0,000
1,00	Rymaszewska & Ramsey (2008)	2,700	0,325	0,106	2,062	3,338	8,300	0,000
1,00	Rymaszewska et al. (2019)	2,815	0,453	0,205	1,927	3,703	6,213	0,000
1,00	Rymaszewska et al. (2020)	2,887	0,411	0,169	2,081	3,693	7,019	0,000
1,00	Rymaszewska et al. (2003)	5,708	1,095	1,198	3,563	7,853	5,215	0,000
1,00		2,945	0,260	0,067	2,436	3,454	11,338	0,000

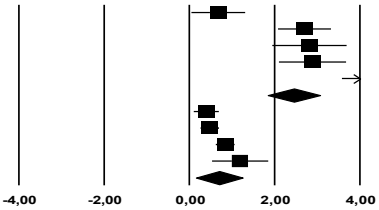


Studies with quality of life (QOL) as a primary outcome showed significantly smaller effect sizes (Hedges' g = 0.70, CI: 0.15-1.24), than studies focusing on other mental health outcomes (Hedges' g = 2.45, CI: 1.84-3.06), $p < .001$. A reduction of heterogeneity was found; visual inspection of the forest plots showed no outliers in the studies focusing on QOL, whereas two outliers were observed in the studies focusing on non-QOL outcomes. I^2 dropped to 68.3% (QOL) and 89.6% (non-QOL), indicating moderate and large heterogeneity, respectively.

A third subgroup analysis investigating differential effects in RCTs versus uncontrolled trials showed no significant differences in effect size, nor a reduction in heterogeneity.

FIGURE 4 Within-group pre- to post effect sizes and forest plot for QOL-studies (coded 1) versus other aspects of mental health (coded 0)

Group by quality of life	Study name	Hedges' g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
0,00	Rymaszewska et al. (2018)	0,676	0,330	0,109	0,029	1,323	2,047	0,041
0,00	Rymaszewska & Ramsey (2008)	2,700	0,325	0,106	2,062	3,338	8,300	0,000
0,00	Rymaszewska et al. (2019)	2,815	0,453	0,205	1,927	3,703	6,213	0,000
0,00	Rymaszewska et al. (2020)	2,887	0,411	0,169	2,081	3,693	7,019	0,000
0,00	Rymaszewska et al. (2003)	5,708	1,095	1,198	3,563	7,853	5,215	0,000
0,00		2,448	0,312	0,097	1,837	3,060	7,852	0,000
1,00	Happe et al. (2016)	0,396	0,159	0,025	0,085	0,707	2,498	0,013
1,00	Pawlk et al. (2019)	0,478	0,118	0,014	0,246	0,710	4,042	0,000
1,00	Szczepanska-Gieracha et al. (2014)	0,839	0,120	0,014	0,604	1,075	6,982	0,000
1,00	Vitenet et al. (2018)	1,189	0,345	0,119	0,513	1,865	3,446	0,001
1,00		0,695	0,279	0,078	0,149	1,242	2,494	0,013

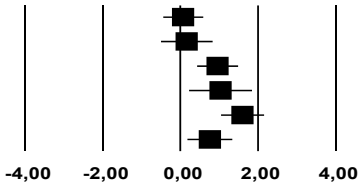


3.3.3 Between-group analysis

Figure 5 shows the results of the between-group analysis. Hedges' g = 0.76 (CI: 0.17-1.36). No visual outliers can be detected in the forest plot. I^2 statistics showed moderate heterogeneity (73,44%). Subgroup analyses were not performed, as the number of included studies was too small.[64]

FIGURE 5 Between-group effect sizes and forest plot of RCT-studies

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Pawik et al. (2019)	0,075	0,270	0,073	-0,455	0,605	0,276	0,782
Happe et al. (2016)	0,164	0,349	0,121	-0,519	0,847	0,472	0,637
Rymaszewska et al. (2020)	0,958	0,279	0,078	0,411	1,506	3,431	0,001
Vitenet et al. (2018)	1,038	0,423	0,179	0,209	1,867	2,453	0,014
Rymaszewska & Ramsey (2008)	1,600	0,292	0,085	1,028	2,172	5,481	0,000
	0,763	0,304	0,092	0,168	1,359	2,513	0,012



4. DISCUSSION

4.1 Summary of evidence

To our knowledge this is the first meta-analysis evaluating the study quality and effect of cryotherapy for mental health problems. Nine studies were found on the subject, which met all inclusion criteria and of which all data could be retraced.

WBC showed a large effect from pre-treatment to post-treatment for all mental health problems it is applied to (Hedges' g = 1.63, CI: 1.05-2.21). When narrowed down to specific aspects of mental health heterogeneity was reduced for two subgroups. For depressive symptoms, WBC resulted in a very large effect (Hedges' g = 2.45, CI: 2.44-3.45). The effect of WBC was medium for studies focusing on quality of life (Hedges' g = 0.70, CI: 0.15-1.24).

The between-group effect sizes that could be calculated for RCTs, demonstrated that WBC was more effective than a waiting list condition, physical exercise, sham WBC (of -10˚ Celsius) or local cryotherapy. The between group effect sizes also demonstrate WBC to be an effective add-on treatment to pharmacotherapy and cognitive behavioural therapy (the treatment as usual condition) for patients with depression and fibromyalgia. The overall between-group effect size is medium (Hedges' g = 0.76).

Overall, this meta-analysis demonstrates preliminary evidence for efficacy of WBC as an add-on intervention for mental health problems, especially where it concerns depressive symptoms.

4.2 Strengths and Limitations

The current study has a number of strengths and limitations. We will discuss both simultaneously while pointing out several aspects of the study below.

First, all studies into the effect of WBC on mental health problems produced so far, have relatively small numbers of participants (n = 55 being the maximum). By pooling effect sizes, power was augmented resulting in more valuable conclusions on the efficacy of WBC for mental health patients. Still, the total number of participants is small (n = 294). Moreover, the small number of included studies did not enable us to create a funnel plot, such that publication bias could not be evaluated.

Second, most studies show concerns when it comes to overall risk of bias. This is mainly due to methodological shortcomings in the randomization process, with half of the studies being uncontrolled trials. Another shortcoming in quality is that a number of studies have based their analyses on completer data instead of intent to treat (ITT) data. This can hamper generalization of use in daily clinical practice since analysis without ITT data are considered less valid.[79]

On the other hand, bias due to deviations from intended interventions, bias in selection of the reported results and bias due to researchers allegiance were overall low. This can be explained by the fact that the inclusion criteria were strict and that the WBC procedure in itself is straightforward. Still there are some, albeit small differences in the various WBC procedures that were followed (dose, frequency). A frequency of ten daily sessions in a row (or with a two day break) seems optimal. During such a period of treatment, temperature should be -60˚C for 30 seconds followed by 150 seconds of exposure to at least the same temperature but preferably lower (for example -100˚C to -120˚C).[14]

Third, by getting into contact with corresponding authors we retraced almost all relevant data. However, we had to estimate three correlations. We took a conservative guess in order not to overrate effect sizes. It would add to the value of results if we could have obtained all missing data.

Fourth, between-study heterogeneity was considerable in this meta-analysis. Although, the application of WBC within the field of mental health is expanding, it is still in its infancy as is also reflected in the number of studies that could be included. For this meta-analysis, we primarily focussed on the *intervention type*, that is application of WBC within the general mental health field. This focus resulted in heterogeneity of treated diagnoses and outcome measures. With respect to heterogeneity in outcome measures, all of the included outcome measures have in common that they assess mental health aspects. Also note that a large number of studies have demonstrated a moderate to strong relation (i.e. inverse correlation) between quality of life and symptom levels of psychiatric disorders, also in patients with somatic complaints.[80–84]

To further deal with between-study heterogeneity, we performed two subgroup analyses. This way, we narrowed down our focus to assess potential variation in effects. Focussing on the studies that used quality of life as the primary outcome measure, the specific outcomes to assess quality of life varied across studies. This gives a less robust result compared to an analysis of results based on the same instrument, as was possible for the depression subgroup analysis. The same kind of limitation holds true for the variety in control conditions in the between group analysis. This complicates a general conclusion on the efficacy of WBC. Assuming the application of WBC will continue to increase, future meta-analyses should focus on the application of WBC within homogeneous subgroups such as mental health diagnoses.

Finally we want to remark some limitations due to the inability to differentiate between participants within studies. For example none of the included studies differentiated in its results according to participant's gender, while the literature shows that female bodies are cooling down in a different and quicker way than male bodies do.[19–21] The same goes for differences of BMI among participants, or whether participants were moving or not inside the cold-chamber. Both factors are known to influence the degree of cooling down the skin and thereby potentially influence effects of WBC.[12,14–16,18,85]

For WBC-studies on depression specifically, inclusion criteria were broad (presence of a depressive episode) and results did not assess potential effects of initial symptoms levels of depression, or discriminate between patients with or without medication (except for one).[77]It's not clear whether WBC could be a useful add-on to pharmacotherapy or that the effect is different when applied to patients not using any anti-depressant medication. It is worthwhile to differentiate between effect sizes based on various combinations of WBC, pharmacotherapy and psychotherapy. WBC might be used as a substitute for pharmacotherapy for certain patients. This would mean a significant reduction of side effects since no side effects are reported with WBC.

All of the limitations discussed above pertain to methodological shortcomings and issues regarding the generalizability of findings. Resolving these issues may provide further knowledge regarding a) the full potential of WBC for mental health problems, and b) which individuals will profit most under which circumstances (personalized medicine). Yet, another issue regarding WBC that is currently unclear, and will additionally aid in achieving these goals, is knowledge on the working mechanisms that are responsible for the effects of WBC on mental health. As reviewed in the introduction, WBC leads to healthier sleeping patterns, augments quality of sleep, stimulates activation, creates a better physical condition in patients with psychological problems and reduces fatigue. It is obvious that these results will have impact on mental health and alleviate depressive symptoms. Yet, what causes these improvements is still unclear.

According to some researchers, the results of lower levels of pro-inflammatory cytokines and decrease of oxidative stress on cellular level as found in patients with auto-immune diseases, sportspeople and healthy participants[26,30–37], are responsible for these effects. Since 2017, studies have shown up suggesting that inflammatory processes are associated with the onset of depressive and anxiety disorders and possibly other mental illnesses.[86–90] Until now only two of the studies included in this meta-analysis did measure levels of biomarkers: oxidative stress (measured: TAS‡) and cytokines (measured: hs-CRP§, IL-6¶, IL-10). Neither of them found significant differences in these levels before and after WBC.[76,77], and none of these studies assessed the mediational effect of inflammatory processes on symptom reduction or quality of life. Future studies should assess mediators of WBC on both the biological, as well as the behavioral (sleep, activation) level whereby a sound methodological design facilitating causal inference (e.g. RCTs) should be applied.

Although underlying mechanisms are still not well understood, results of the current meta-analyses suggest that WBC is a useful add-on intervention in the treatment of mental illnesses - depressive symptoms in particular. WBC appears to target multiple symptom clusters, which is in line with a transdiagnostic approach. The idea of this approach is to identify the crucial 'hub' of symptoms for a particular patient, e.g. which symptom forms the most central part in a person's network of symptoms maintaining the disorder.[91] Treating this central hub might discontinue the maintenance of the related processes. In this way the hysteresis (the fact that the system remains out of balance although the initial trigger cause of the disorder has

‡ Total antioxidant status

§ High sensitivity C-reactive protein

¶ Interleukin

disappeared) is ended, thereby paving the way to recovery. In case of the cluster 'depression', central processes or 'hubs' in the network are often sleeping problems and anhedonia.[50] WBC might function as an intervention that disconnects part of these hubs, thereby calming down the whole system and reducing the overall burden of disease.

The reason WBC seems to be effective in other mental health problems as well, might be explained because - according to the network theory - sleep problems are on the top list as main hub for many individuals with mental health problems.[51]

If future research would provide further evidence for the effectiveness of WBC for certain mental health problems and further insight into its mechanisms would be gained, WBC could function as a new intervention. If we know how and for whom it works, there might be advantages of the treatment. WBC is a simple, quick and relatively low-cost procedure that can be applied outside medical settings. Patients themselves can initiate it as long as a MD screens them for contraindications. This low-threshold aspect could potentially contribute to empowerment of patients and help with destigmatization. WBC could not only be applied as an add-on to regular treatment, but may also function as part of a relapse plan or as an early intervention in case of recurrent symptoms.

5. Conclusion

WBC seems a potential promising add-on intervention for people suffering from mental health problems. Further research with better methodological quality is necessary, preferably in the form of randomized controlled trials using a uniform procedure. In future studies it is recommended that both biomarkers and behavioural processes that may mediate results are included to gain more insight on the working mechanisms of WBC.

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APPENDIX 1. Search grid

TABEL 1

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily – 1946 to July 1st, 2020

OR\AND	**P**atient/**P**opulations/**P**roblem	**I**ntervention	**C**omparison	**O**utcome
PICO filled-in	Patients suffering from mental illnesses	Cyrotherapy	Treatment as usual	Complaint reduction
Synonyms	1.	2.	3.	4.

	Ambulant Anxiety Disorders BDI-II Bipolar Disorder Depression Depression symptoms DSM 5 Disorders Hamilton Anxiety Scale Hamilton Depression Scale Hamilton Scale IDS Inpatients Major Depression Mental Disorders Mental Illness Mood Disorder Mood Disturbances Outpatient Oxidative Stress Panic Attacks PHQ-9 Psychiatric Patients Psychiatric Hospital	Cold Effects Cold Therapy Cryotherapy Low Temperature Thermoregulation Whole body WBCT Whole Body Cryo Therapy	Anti-depressants Behavioural therapy CBT Cognitive Behavioural Therapy Cognitive Therapy Pharmacotherapy Interpersonal Therapy Psychodynamic Therapy Treatment Outcomes	Activation Adjuvant Treatment Auxiliary Treatment Complaint Reductions Decrease of Symptoms Energy Health Improvement Immune System Life Satisfaction Mental Health Mood Enhancement Mood Improvement Quality of Life
Thesaurus/ MeSH terms	5. Antidepressive Agents Anxiety Disorders Bipolar Disorder Burnout, professional Depression Depressive Disorder, Major Mental Disorders Oxidative Stress	6. Cryotherapy	7. Cognitive Behavioural Therapy Psychoanalytic Therapy Psychotherapy Therapeutics	8. Affect Exercise Motivation Treatment Outcome Quality of Life

	Psychiatric Status Rating Scales Psychiatry Stress Disorders Stress, Psychological			
Keywords/ Title words/ Abstract words	9. Depression.mp Depression.tw Mood Disorders.tw Mood Disorders.mp Mental Ilness.tw Mental Ilness.mp Mood Disturbances.tw Mood Disturbances.mp DSM 5 Diagnosis.mp DSM 5 Diagnosis.tw DSM 5.mp DSM 5.tw Oxidative Stress.mp Oxidative Stress.tw Psychiatric Patients.mp Psychiatric Patients.tw Psychopathology.mp Psychopathology.tw	10. Cold Effects.mp Cold Effects.tw Cold therapy.mp Cold Therapy.tw Cryo Chamber.mp Cryo Chamber.tw Cryotherapy.mp Cryotherapy.tw Low Temperature.mp Low Termperature.tw Thermoregulation.mp Thermoregulation.tw Whole Body.mp Whole Body.tw WBCT.mp WBCT.tw Whole Body Cryo Therapy.mp Whole Body Cryo Therapy.tw	11.	12.
Limits	13. Human, Adults			

TABEL 2

PsycINFO 1806 to July 1st 2020

Thesaurus/ MeSH Terms	14. Affective Disorders Antidepressant Drugs Anxiety disorders Bipolar Disorder Comorbidity Diagnostic and Statistical Manual Depression Emotional States Major Depression Mental Disorders Mental Health Services Oxidative Stress Panic Attack Panic Disorders Personality Disorders Psychiatric Hospitalization Psychiatric Hospitals Psychiatric Patients Psychiatric Units Psychodiagnosis Psychological Stress Psychometrics Psychopathology	15. Cryotherapy Cold Effects	16. Cognitive Behaviour Therapy Cognitive Therapy Interpersonal Psychotherapy Psychoanalysis Psychodynamics Psychotherapy Treatment	17. Adjunctive Treatment Behavioural Activation System Exercise Health Promotion Life Satisfaction Mental Health Motivation Quality of Life
Keywords/ Title words/ Abstract words	18. Depression.mp Depression.tw Mood Disorders.tw Mood Disorders.mp Mental Ilness.tw Mental Ilness.mp	19. Cold Effects.mp Cold Effects.tw Cold therapy.mp Cold Therapy.tw Cryotherapy.mp Cryotherapy.tw	20.	21.

	Mood Disturbances.tw Mood dDsturbances.mp DSM 5 Diagnosis.mp DSM 5 Diagnosis.tw DSM 5.mp DSM 5.tw Oxidative Stress.mp Oxidative Stress.tw Psychiatric Patients.mp Psychiatric Patients.tw Psychopathology.mp Psychopathology.tw	Low Temperature.mp Low Termperature.tw WBCT.mp WBCT.tw Whole Body Cryo Therapy.mp Whole Body Cryo Therapy.tw		
Limits	22. Humans and Adults			

TABEL 3

EBM Reviews – Cochrane Database of Systematic Reviews 2005 to July 1st, 2020

Keywords	23. Affective Disorders Antidepressive Agents Antidepressant Drugs Anxiety Disorders Bipolar Disorder Burnout, professional Comorbidity Depression Depressive Disorder, Major Diagnostic and statistical manual Emotional States	24. Cryotherapy	25.	26.

	Major Depression Mental Disorders Mental Health Services Oxidative Stress Panic Attack Panic Disorders Personality Disorders Psychiatric Hospitalization Psychiatric Hospitals Psychiatric Patients Psychiatric Status Rating Scales Psychiatric Units Psychiatry Psychodiagnosis Psychological Stress Psychometrics Psychopathology Stress Disorders Stress, Psychological			
Keywords with extensions	27. Depression.mp Depression.tw Mood Disorders.tw Mood Disorders.mp Mental Ilness.tw Mental Ilness.mp Mood Disturbances.tw Mood Disturbances.mp DSM?5 Diagnosis.mp DSM?5 Diagnosis.tw DSM?5.mp DSM?5.tw	28. Cold Effects.mp Cold Effects.tw Cold therapy.mp Cold Therapy.tw Cryo Chamber.mp Cryo Chamber.tw Cryotherapy.mp Cryotherapy.tw Low Temperature.mp Low Termperature.tw Thermoregulation.mp Thermoregulation.tw	29.	30.

	Oxidative Stress.mp Oxidative stress.tw Psychiatric Patients.mp Psychiatric Patients.tw Psychopathology.mp Psychopathology.tw	Whole Body.mp Whole Body.tw WBCT.mp WBCT.tw Whole Body Cryo Therapy.mp Whole Body Cryo Therapy.tw		
Limits	31. Last 36 years			

APPENDIX 2. Contra-indications whole body cryotherapy (WBC)

Condition	**Yes**	**No**
Moderately or seriously raised blood pressure		
Pregnancy		
Cancer		
Epileptic seizures		
Acute brain haemorrhage or brain haemorrhage in the past		
Reversible cerebral vasoconstriction syndrome		
Heat and vascular disease with symptoms		
Acute myocardial infarction or infarction in the past 6 months		
Unstable angina pectoris		

Cardiac arrhythmias		
Pacemaker		
Venous thrombosis		
Thromboembolic changes and venous inflammation		
Inflammation of the blood vessels		
Peripheral disease or claudicatio intermittens		
Bleeding disorders		
Raynaud disease		
Cold intolerance		
Cold utricaria		
Significant anaemia		
Organ disorders with manifest symptoms		
Thyroid disorders		
Acute kidney disorders and acute disorders of the urinary tract		
Open wounds		
Ulcers		
Fever		
Cryoglobulinaemia		

Cryofibrinogenemia		
Agammaglobulinemia		
Central nervous system disease		
Sympathetic neuropathy		
Local blood flow disturbances		
Emaciation and hypothermia		
Venous blood leaks in the lungs		
Acute respiratory diseases of various origin		
Serious substance abuse		
Claustrophobia		
BMI < 18		
Severe suicidal thoughts or recent suicidal behaviour		
Medication changes during the last six weeks		

FIGURE 1 Flowchart of the study inclusion/exclusion process

FIGURE 2 Within-group pre- to post effect sizes and forest plot for all WBC studies 59,6

FIGURE 3 Within-group pre- to post effect sizes and forest plot for depression studies (coded 1) versus other aspects of mental health (coded 0)

FIGURE 4 Within-group pre- to post effect sizes and forest plot for QOL-studies (coded 1) versus other aspects of mental health (coded 0)

FIGURE 5 Between-group effect sizes and forest plot of RCT-studies

TABLE 1 Study characteristics

Author and year of publication	**Intervention**	**Number of sessions**	**Dose (Frequency/duration and temperature)**	**Mental health aspect**	**Primary outcome measure**	***n* analysed WBC / control**	**Attrition percentage**	**Female/male ratio**	**Age (range and /or Mean ± SD)**	**Effect size Hegdes' *g***
Bettoni et al. (2013)	WBC*	15	5 days treatment, two days rest/ 30 sec.: -60˚C[†] + 180 sec.: -140˚C	Quality of life	MOS SF-36[≠] (mental)	50/50	0%	92/8	17-70	49.00
Happe et al. (2016)	WBC	10	5 days treatment, two days rest/ 180 sec.: -60˚C	Quality of life	RLS-QLI[§]	12/12/11	7,9%	28/7	18-75/ 60.9, ±12,5	0.40
Pawik et al. (2019)	WBC	10	5 days treatment, 2 days rest/ 180 sec.: -110˚C (first session) to -160˚C (last session)	Mental Health	PGWBI[¶]	20/20/20	0%	43/16	49.4, ± 12.2	0.48
Rymaszewska & Ramsey (2008)	WBC	15	5 days treatment, 2 days rest/ 120-180 sec: -110˚C (first session) to -160˚C (last session)	Depressive symptoms	HDRS[#]	26/34	0%	53/7	18-65/ 47.04, ±13.05 and 40.88, ±11.	2.70

									90	
Rymaszewska et al. (2003)	WBC	10	5 days treatment, 2 days rest/ 160 sec: -110˚C (first session) to -150˚C (last session)	Depressive symptoms	HDRS	23	0%	18/5	37-70	5.71
Rymaszewska et al. (2018)	WBC	10	5 days treatment, 2 days rest/ 30 sec.: -60˚C + 120 sec.: -110˚C (first session) to -130˚C (last session)	MCI[II]	DemTect	21	25%	14/7	65.38, ±7.2	0.68
Rymaszewska et al. (2019)	WBC	10	5 days treatment, 2 days rest/ 30 sec.: -60˚C + 120 sec.: -110˚C (first session) to -135˚C (last session)	Depressive symptoms	HDRS	21	8,7%	17/4	46.1, ±16.7	2.82
Rymaszewska et al. (2020)	WBC	10	5 days treatment, 2 days rest/ 30 sec.: -60 °C + 120 sec.: -110˚C (first session) to -135˚C (last session)	Depressive symptoms	HDRS	33/30	35%	21/9 and 19/7	46.57, ±14.87 and 48.23, ±16.34	2.89
Szczepańska-Gieracha et al. (2014)	WBC	10	5 days treatment, 2 days rest/ 60-120 sec.: -100˚C (2 first sessions), 180 sec.: -100˚C	Quality of life	PGWBI	55	0%	43/12	20-70/ 48.4, ±12.1	0.84

			(8 last sessions)							
Vitenet et al. (2018)	WBC	10	8 consecutive days: first 4 days en last 2 days once a day, day 5 and 6 2 times a day/ 180 sec.: -110˚C	Quality of life	MOS SF-36 (mental)	13/11	14,3%	20/4	55, ±10 and 50, ± 11	1.19

* Whole Body Cryotherapy

† Degrees Celsius

≠ Medical Outcome Study Short Form-36

§ Restless Legs Syndrome Quality of Life Index

¶ Psychological General Well-Being Index

Hamilton Depression Rating Scale

II Mild Cognitive Impairment

TABLE 2 Risk of bias included studies per article

Study (author, year)	**D1***	**D2†**	**D3≠**	**D4§**	**D5¶**	**D6#**	**D7II**
Bettoni et al. (2013)	Low	Low	Low	Moderate	Low	Low	Moderate
Happe et al. (2016)	Moderate	Low	Low	Low	Low	Low	Moderate
Pawik et al. (2019)	Low	Low	Low	Moderate	Low	Low	Moderate
Rymaszewska & Ramsey (2008)	Low	Low	Low	Moderate	Low	Low	Moderate
Rymaszewska et al. (2003)	Moderate	Low	Low	Moderate	Low	Low	Moderate

Rymaszewska et al. (2018)	Moderate	Low	Serious	Moderate	Low	Low	Serious
Rymaszewska et al. (2019)	Moderate	Low	Low	Moderate	Low	Low	Moderate
Rymaszewska et al. (2020)	Low	Low	Serious	Moderate	Low	Low	Serious
Szczepańska-Gieracha et al. (2014)	Moderate	Low	Low	Moderate	Low	Low	Moderate
Vitenet et al. (2018)	Low	Low	Moderate	Moderate	Low	Low	Moderate

* Bias arising form the randomization or selection process

† Bias due to deviations from intended interventions

≠ Bias due to missing outcome data

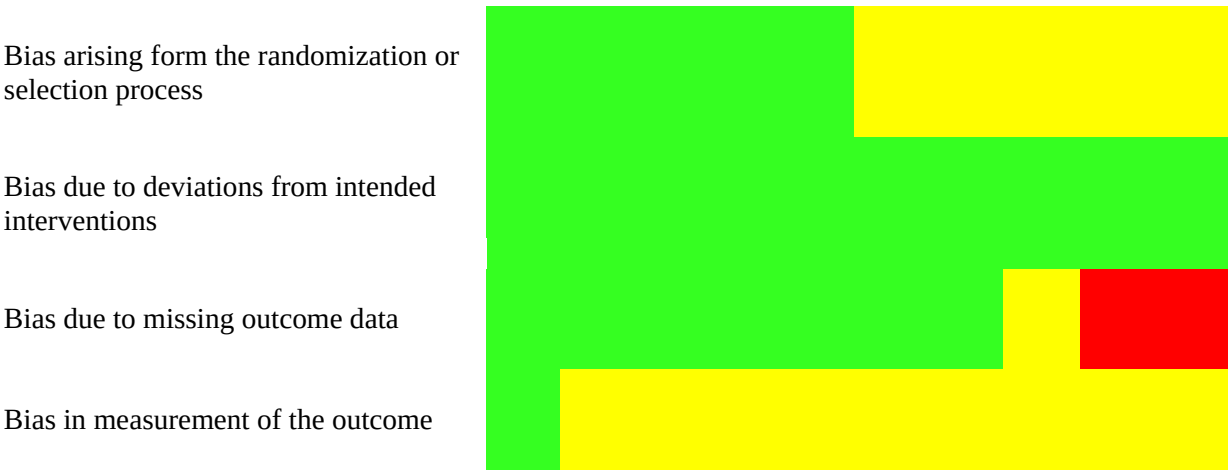
§ Bias in measurement of the outcome

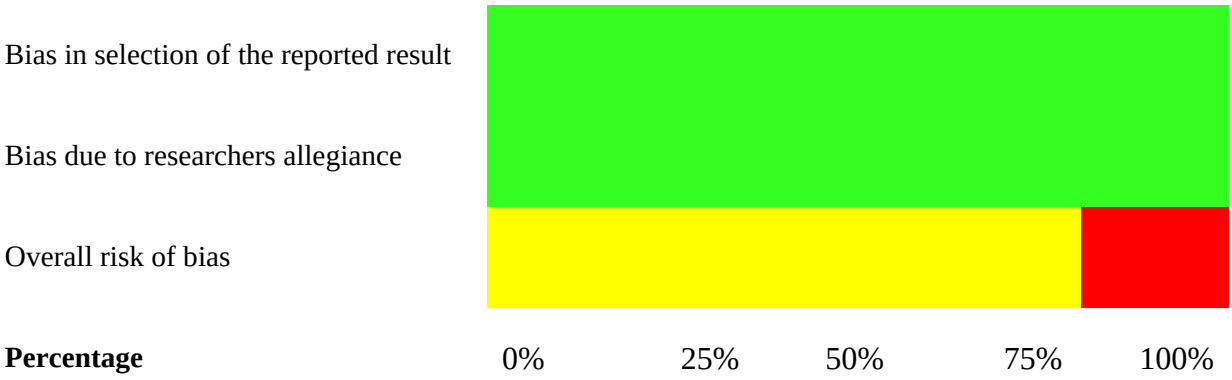
¶ Bias in selection of the reported result

Bias due to researchers allegiance

II Overall risk of bias

TABLE 3 Pooled risk of bias for all studies





Low risk of bias

Some concerns

High risk of bias

Declaration of interests

■ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

HIGHLIGHTS

• Whole body cryotherapy (WBC) is a procedure in which participants enter a cryo-cabin (enclosed space) with an air temperature of -110 degrees Celsius for approximately three minutes.

• In the professional world of sports WBC has been used for some decades. Research shows that WBC leads to better exercise capacity, more regular circadian rhythm, improved quality of sleep and less tiredness in athletes. These effects are also desired aims of treatment in people with certain psychiatric disorders.

• Recently studies appeared which measured the effect of WBC on mental health. So far, no meta-analysis was conducted on this subject.

• Currently there is a lack of low-cost, easily accessible treatment possibilities for most psychiatric disorders.

• This meta-analysis demonstrates that there is preliminary evidence for efficacy of WBC as an add-on intervention for mental health problems, especially where depressive symptoms are concerned.