RESEARCH ARTICLE

Sex and gender reporting in RCTs of internet and mobile-based interventions for depression and anxiety in chronic conditions: A secondary analysis of a systematic review

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Abstract

Mind-body internet- and mobile-based intervention (IMIs) are gaining traction as scalable and effective strategies to manage mental health symptoms experienced by people living with chronic physical conditions. Sex and gender have implications for mind-body IMI participation, adherence, and efficacy. The objective of this secondary analysis was to assess the extent and nature of reporting of sex and/or gender in randomized controlled trials retrieved by a primary systematic review of mind-body IMIs assessing depression and anxiety symptoms among adults living with chronic physical conditions. The collected information included whether sex and gender-based analyses were carried out and explored the role of sex and gender on mental health outcomes, attrition, and recruitment rates. The protocol was registered with PROSPERO. A comprehensive search of six electronic databases was completed from database inception to March 2023. Sex and gender terms were summarized according to a standardized, three-point criteria: (1) non-binary use (i.e., > 2 categories used for both sex and gender definitions) (2) use of appropriate categories (i.e., sex = male/female/intersex, gender = man/woman/gender-diverse) and (3) non-interchangeable use of sex or gender terms throughout the citation. The use of sex and gender terms was deemed correct if all three criteria were met. No studies met all three sex/gender criteria. Only one study provided stratified mental health scores by sex and/or gender throughout the citation. The use of sex and gender terms was deemed correct if all three criteria were met. The role of sex and gender on mental health outcomes, attrition, and recruitment rates. The protocol was registered with PROSPERO. A comprehensive search of six electronic databases was completed from database inception to March 2023. Sex and gender terms were summarized according to a standardized, three-point criteria: (1) non-binary use (i.e., > 2 categories used for both sex and gender definitions) (2) use of appropriate categories (i.e., sex = male/female/intersex, gender = man/woman/gender-diverse) and (3) non-interchangeable use of sex or gender terms throughout the citation. The use of sex and gender terms was deemed correct if all three criteria were met. No studies met all three sex/gender criteria. Only one study provided stratified mental health scores by sex and/or gender within the publication. Eleven (20%) studies reported sex or gender imbalance as being a potential reason for outcome differences, with 3 studies conducting an adjusted statistical analysis investigating sex/gender as a moderator. Findings highlight low
uptake of sex and gender considerations in the context of mind-body IMIs. Results underscore the need to incorporate guideline-based sex and gender terms and concepts, from data collection and analysis to reporting of evidence to inform mind-body IMI development and guide future research. Stratified sex and/or gender analyses are encouraged in future studies to assess intervention outcome differences.

1. Introduction

Globally, approximately 33% of adults live with at least one chronic physical condition (e.g., cardiac disease, chronic liver disease) [1]. Defined by the World Health Organization as “conditions requiring ongoing management and treatment over extended periods of time,” these conditions are closely linked to symptoms of depression and anxiety which in turn can decrease capacity for self-management [2, 3]. A 2020 qualitative systematic review of people living with chronic physical conditions highlighted that more steps must be taken to address unmet psychological and emotional needs of this patient population [4]. Sex and gender have garnered attention as critical factors in the experience of living with a chronic physical condition, and in the uptake and impact of clinical interventions [5, 6]. The Canadian Institute for Health Research (CIHR) defines sex as the classification of being biologically male, female, or intersex, including biological and/or physical characteristics such as reproductive anatomy and chromosomes [7]. The term gender is subject to change and exists on a continuum which includes identification as a man, woman or a gender-diverse identity. Gender also includes social constructs—such as identity, roles, relationships, and behaviours—and institutional-level factors—such as power relations and opportunities [7, 8].

Mental health conditions differ significantly across sex, with females developing depression, anxiety, and stress-related disorders more often than males [9, 10]. However, it is likely that this finding is complicated by gender-related factors such as stress, household responsibility, and societal pressures [11]. One qualitative study examined gender differences in the experiences of older adults with multimorbid conditions; despite gender similarities in mental health and quality of life, this study highlighted that men tended to discuss changes in personal power and control as a result of their chronic condition, whereas women reflected on the perceived impact of their chronic condition on their friends and family [12]. This highlights an important difference in how chronic conditions may be experienced differently due to gender roles and expectations. Emerging evidence also demonstrates worsened mental health outcomes among gender-diverse populations. Multiple studies have discussed the mental health burden that non-binary, transgender, and other gender-diverse populations may experience [13–15]. Gender-diverse populations may also experience higher rates of specific chronic conditions, such as depression, anxiety, and HIV compared to non-gender-diverse populations [16]. Overall, this presents a major point of discussion regarding health outcome research, as it highlights the importance of including expansive gender parameters and considering patient demographics beyond biological sex to fully examine the experience of individuals living with chronic conditions.

Mind-body interventions—which commonly include mindful movement (yoga, Tai-chi and qi gong), meditation, breathwork, and cognitive behavioural therapy (CBT)—have shown significant promise as non-pharmacological strategies to manage mental health symptoms and improve quality of life in individuals living with chronic physical conditions [17–20]. These interventions are amenable to digital delivery including by web and app-based platforms,
herein referred to as internet- and mobile-based interventions (IMIs). While IMIs offer the convenience of increased access to content and services from home environments and across geographic boundaries, the use of IMIs differs across sex and gender, with women being more likely to participate compared to men [21]. This may be related in part to gender socialization for young women being towards interdependence, sensitivity and connectedness, and for young men being towards independence [22]. Participant sex has been identified as a significant predictor of IMI attrition rates, with males at a higher risk of attrition compared to females [21, 23]. Previous research also reports that men are less likely to access mental health services compared to women [24–26]. These sex and gender differences have been noted across pharmacotherapeutic and interventional research responses [27, 28].

Sex- and gender-based adjustments to IMI format and delivery has been associated with increased engagement and adherence [24, 25]. One qualitative study found that female participants strongly preferred a self-help delivery style, whereas male participants preferred to have information delivered in a video game format [29]. Consideration of sex and gender differences in the development and facilitation phase of mind-body IMIs can influence whether the intervention is suited for its intended audience [26]. In the analysis phase of research trials, the opportunity to account for sex, gender, and other demographics may offer important insight into acceptability, feasibility, adoption, sustainability, patient outcomes, and generalizability of results [30].

While previous systematic reviews have demonstrated the benefit of mind-body IMIs on mental health symptoms [20, 31–33], given the growing prevalence and potential of mind-body IMIs for widespread delivery, more information is needed about the influence of sex and gender. Current research has demonstrated that while gender-based considerations in research are becoming more prevalent, this area requires more attention. In a review of over 768 papers for the treatment of depression, less than 1% reported an a priori intention to analyze results by gender [34]. Gender and its associated factors have long been omitted as important factors of consideration regarding the outcomes of randomized controlled trials (RCTs). Within the context of a primary systematic review of RCTs that evaluated the impact of select mind-body IMIs on depression and anxiety symptoms in individuals living with chronic physical conditions [35], the objectives of this secondary analysis were to: 1) describe how sex and gender were reported across included studies and compare these descriptions according to guideline-based classification criteria [7, 36, 37]; 2) report on the frequency of the author stratification of anxiety and depression outcomes by sex and/or gender; and 3) provide a summary of sex and/or gender considerations related to participant recruitment and attrition rates.

2. Methods

2.1 Protocol

A separate protocol for this secondary analysis was not registered. Instead, the registration protocol for the primary systematic review [35] (PROSPERO #CRD42022375606) included secondary questions assessing sex and gender. Specifically, this included the proportion of studies reporting differences in mental health outcomes and intervention adherence rates across different sexes and/or genders, as well as accuracy and consistency of sex and gender reporting. This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [38].

2.2 Literature search

Electronic searches were conducted on October 4, 2022 across MEDLINE, EMBASE, SCOPUS, PsycInfo, CINAHL, and Cochrane Central Register of Controlled Trials (CENTRAL).
Databases were searched from inception to present. Search results were updated on March 17, 2023. The complete search strategy for each database can be found in S1 Appendix. Keywords for this search include “mind-body therapies”, “cognitive behavioral therapy”, “wellness intervention”, “web based”, “remote”, “depression”, “anxiety” and “adult.” Records identified through database searches were exported in complete batches and duplicates were automatically removed upon import to the systematic review management software, Covidence [39]. In total 18,325 records were imported into Covidence from all databases and 7754 records were identified as duplicates, leaving 10,571 studies for title/abstract screening. In addition, hand searches were conducted among reference lists of relevant review articles [31, 40–42], though no studies were found for inclusion.

2.3 Eligibility criteria
The inclusion criteria of the primary systematic review has been published elsewhere and summarized in Table 1 [35].

Only studies written in English were included. The search and study selection and inclusion process results are reported using a PRISMA flow diagram in the primary systematic review [35]. Title/abstract as well as full-text screening were performed by two independent reviewers, with disagreements resolved through a third-party reviewer.

2.4 Data extraction

2.4.1 Sex and gender reporting. Data from the chosen articles were extracted independently using a form constructed in REDCap [43]. One author (SC) extracted data and another author (EJ) performed systematic verification checks. The primary objective was to summarize the reporting of sex and gender across studies and compare the reporting of sex and gender terms according to three-point evidence-based criteria previously published by Adisso et al. (2020), Gogovor et al. (2021), and developed with the CIHR framework and recommendations for defining sex and gender [7, 36, 37]. These guidelines take into account three criteria to assess accuracy of sex and gender reporting: (1) non-binary use (i.e., > 2 categories utilized for both sex and gender definitions) (2) use of appropriate categories (i.e., sex = male/female/intersex, gender = man/woman/gender-diverse/non-binary/gender-fluid) and (3) non-interchangeable use of sex or gender terms throughout the citation [36, 37]. The use of sex and gender terms was considered correct if all three criteria were met. All portions of the author’s Table 1. Inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>PICO-D Criteria</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Adults (≥ 18 years) living with a chronic physical condition</td>
<td>Adults with primarily chronic mental health conditions</td>
</tr>
<tr>
<td>Intervention</td>
<td>Delivered through an internet or mobile-based platform</td>
<td>DVD or teleconference delivery</td>
</tr>
<tr>
<td>Control</td>
<td>No intervention (treatment or care as usual)</td>
<td>Noninferiority trials</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Depression and/or anxiety outcomes utilizing psychometrically validated questionnaires</td>
<td>All other study designs</td>
</tr>
<tr>
<td>Design</td>
<td>Randomized controlled trials</td>
<td></td>
</tr>
</tbody>
</table>

https://doi.org/10.1371/journal.pmen.0000048.t001
manuscript were eligible for inclusion in this assessment and no adaptations were made to these criteria for the purpose of this analysis.

2.4.2 Sex and gender stratified data: Enrollment, attrition, and mental health outcomes. Secondary objectives were to report on the frequency of stratification of anxiety and depression outcomes according to sex and gender and to describe sex or gender differences related to participant enrollment and attrition rates. The proportion of studies that provided sex and/or gender-stratified data on participant enrollment and attrition rates was identified using a binary coding scheme (yes/no). A narrative review of the results and discussion of each study was also conducted to synthesize any commentary around sex and/or gender differences in recruitment rates, attrition rates, or any perceived differences in outcomes according to sex or gender-related factors. For each study that did not include the mean change scores and associated standard deviation for depression and/or anxiety scores stratified by sex and/or gender (n = 55 studies), one attempt was made to contact authors by email in April 2023.

2.5 Risk of bias assessment
The risk of bias of each study was assessed using the revised Cochrane risk-of-bias tool for RCTs (version 2.0) [44]. Each of the five risk domains was scored against a three-point rating scale, corresponding to a low, moderate, and high risk of bias. Studies were included regardless of methodological quality.

2.6 Data analysis and synthesis
A descriptive analysis was conducted and reported using text, tables, and figures.

3. Results
3.1 Study inclusion
A total of 18,325 titles were retrieved through database searching. Following removal of duplicates, 10,571 titles were screened for eligibility. Of the remaining articles, 276 full-text articles were retrieved and assessed for eligibility. Two hundred and twenty were excluded, with reasons for exclusion being ineligible population (n = 54), ineligible intervention (n = 46), not original research (n = 39), ineligible control group (n = 37), ineligible outcome (n = 22), non-RCT study (n = 15), or missing data (n = 7). The primary systematic review includes the full PRISMA flow diagram [35]. The included 56 texts were critically appraised.

3.2 Methodological quality
Four (7%) studies were appraised to be at low risk of bias, 7 (13%) studies were found to be at high risk of bias. Most studies (45, 80%) were appraised to have at least one methodological concern. The majority studies had missing or incomplete outcome data due to participant drop out (44, 79%) (see S2 Appendix).

3.3 Characteristics of included studies
Fifty-six RCTs involving a total of 7691 study participants (mean = 137). Participants were described as female or women (n = 4780 (62%)), male or men (n = 2751 (36%)), or intersex or gender diverse (n = 2 (0.03%)). One feasibility study consisting of 158 participants did not provide a breakdown of participant sex or gender [45]. Most studies were conducted in the United States (10, 18%), Sweden (9, 16%), Netherlands (8, 14%) and the United Kingdom (9, 16%) with the remaining 20 trials conducted in other countries. Twenty-four different chronic physical conditions were identified; for the purposes of this analysis, these conditions were divided
into four groupings: neurological conditions (17, 30%) (e.g., Parkinson’s disease) followed by cardiovascular conditions (e.g., heart failure) (7, 12%), cancer (6, 11%), and other (24, 43%) (e.g., HIV). Two (4%) trials enrolled participants living with multiple chronic conditions [46, 47] (Table 2). The most common mind-body IMIs were CBT (n = 28), followed by CBT with another mind-body technique (CBT+; n = 18), and non-CBT interventions (n = 10).

3.4 Sex and gender reporting
Two (4%) studies included a non-binary framework of assessing sex or gender. These studies were published in 2020, and 2022, respectively [46, 47] Twenty-eight (50%) studies categorized sex or gender using the appropriate category (sex = male/female/intersex, gender = man/woman/gender-diverse) [36, 37]. Twenty-five (45%) studies used sex and gender terms non-interchangeably. Studies fulfilling these two criteria ranged in publication year from 2009–2023. Twenty-one (38%) studies did not fulfill any of the sex or gender criteria. Of the studies that did exhibit sex or gender criteria, 13 (35%) fulfilled only one of the sex or gender criteria, and 21 (57%) fulfilled two. No studies fulfilled all three criteria. See Table 3 for more information.

3.5 Depression and anxiety outcomes
One study (2%) reported mean changes scores for anxiety stratified by sex or gender [92], with no authors reporting disaggregated sex/gender data for depression. As a result of email outreach to authors (n = 52), five authors responded with this data [46, 59, 61, 70, 92]; resulting in a total of four studies reporting sex/gender specific outcome data for depression, and three studies for anxiety. Two out of four studies reporting depression outcomes reported a greater decrease in mean scores for depression in females/women compared to males/men. For anxiety, all three studies reporting anxiety outcomes reported a greater decrease in mean change scores for females/women compared to males/men. Due to limited data availability, analysis of the stratified scores was not conducted. Of all studies included in the review, 11 (20%) studies discussed sex and/or gender as a potential reason for differences in anxiety and depression outcomes, the most common reason being attributed to differences in sex and/or gender ratios of participants within each study. Three studies included an adjusted analysis to investigate sex or gender as a moderator of anxiety or depression outcomes [53, 77, 87], with one out of three studies finding that sex was a significant moderator of treatment effects [77].

3.6 Sex and gender in recruitment and attrition rates
Six studies (11%) acknowledged that sex and/or gender imbalance within their participant pools served as a major limitation to their conclusions, with five of these studies citing greater females/women enrollment compared to males/men [53, 62, 70, 80, 90]. Kraepelien et al. further discussed this limitation of over-enrollment of females/women in mind-body IMIs within the context of disease incidence rates [70]. One (2%) study provided stratified sex or gender-based attrition data [92]. Authors of two studies (4%) also speculated on sex and gender differences regarding attrition rates [48, 79]. Authors reported discordant findings, with one reporting that females/women were more likely to drop out [48], and the other reporting that males/men were more likely to drop out [79]. Two studies discussed that gendered behaviours (e.g., willingness to reach out for support, reluctance to engage in discussion around mental health) could impact participation and attrition rates [46, 80]. Dear et al. suggested that gender-based adjustment trends to chronic illness are generally unknown, however, it was possible that emotional distress levels may be higher among women with chronic health conditions [46]. Migliorini et al. discussed that even though men were overrepresented in spinal cord injury
Table 2. Key study characteristics.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Intervention Type</th>
<th>Country</th>
<th>Sample Size</th>
<th>Condition Type</th>
<th>% Female or Women</th>
<th>Sex/Gender Criterion Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ainsworth (2019) [48]</td>
<td>Non-CBT</td>
<td>United Kingdom</td>
<td>88</td>
<td>Other (Asthma)</td>
<td>60</td>
<td>2, 3</td>
</tr>
<tr>
<td>Ainsworth (2022) [45]</td>
<td>Non-CBT</td>
<td>United Kingdom</td>
<td>158</td>
<td>Other (Asthma)</td>
<td>Not available</td>
<td>None</td>
</tr>
<tr>
<td>Bendig (2021) [50]</td>
<td>CBT</td>
<td>Germany</td>
<td>34</td>
<td>Cardiovascular</td>
<td>35</td>
<td>2, 3</td>
</tr>
<tr>
<td>Beukes (2018) [51]</td>
<td>CBT</td>
<td>United Kingdom</td>
<td>146</td>
<td>Neurological</td>
<td>43</td>
<td>None</td>
</tr>
<tr>
<td>Boeschoten (2017) [52]</td>
<td>CBT (Problem solving therapy)</td>
<td>Netherlands</td>
<td>171</td>
<td>Neurological</td>
<td>80</td>
<td>2, 3</td>
</tr>
<tr>
<td>Bromberg (2012) [53]</td>
<td>CBT+</td>
<td>United States of America</td>
<td>185</td>
<td>Neurological</td>
<td>89</td>
<td>None</td>
</tr>
<tr>
<td>Bundy (2013) [54]</td>
<td>CBT</td>
<td>United Kingdom</td>
<td>126</td>
<td>Other (Psoriasis)</td>
<td>53</td>
<td>2, 3</td>
</tr>
<tr>
<td>Burke (2019) [55]</td>
<td>CBT+</td>
<td>Ireland</td>
<td>69</td>
<td>Neurological</td>
<td>48</td>
<td>None</td>
</tr>
<tr>
<td>Cardol (2023) [56]</td>
<td>CBT</td>
<td>Netherlands</td>
<td>121</td>
<td>Other (Chronic kidney disease)</td>
<td>44</td>
<td>2, 3</td>
</tr>
<tr>
<td>Cooper (2011) [57]</td>
<td>CBT</td>
<td>United Kingdom</td>
<td>24</td>
<td>Neurological</td>
<td>73</td>
<td>None</td>
</tr>
<tr>
<td>Dear (2022) [46]</td>
<td>CBT</td>
<td>Australia</td>
<td>676</td>
<td>Multiple chronic conditions</td>
<td>89</td>
<td>1, 2</td>
</tr>
<tr>
<td>Devineni (2005) [58]</td>
<td>CBT+</td>
<td>United States of America</td>
<td>86</td>
<td>Neurological</td>
<td>89</td>
<td>None</td>
</tr>
<tr>
<td>Drozd (2014) [59]</td>
<td>Non-CBT</td>
<td>Norway</td>
<td>67</td>
<td>Other (HIV)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Ferwerda (2017) [60]</td>
<td>CBT</td>
<td>Netherlands</td>
<td>133</td>
<td>Other (Rheumatoid arthritis)</td>
<td>64</td>
<td>2, 3</td>
</tr>
<tr>
<td>Fischer (2015) [61]</td>
<td>CBT+</td>
<td>Germany</td>
<td>90</td>
<td>Neurological</td>
<td>78</td>
<td>None</td>
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<tr>
<td>Habibovic (2014) [62]</td>
<td>CBT</td>
<td>Netherlands</td>
<td>289</td>
<td>Cardiovascular</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Hauffman (2020) [63]</td>
<td>CBT</td>
<td>Sweden</td>
<td>245</td>
<td>Cancer</td>
<td>71</td>
<td>2, 3</td>
</tr>
<tr>
<td>Hesser (2012) [64]</td>
<td>CBT</td>
<td>Sweden</td>
<td>99</td>
<td>Neurological</td>
<td>43</td>
<td>None</td>
</tr>
<tr>
<td>Hilmarssdottir (2020) [65]</td>
<td>Non-CBT</td>
<td>Iceland</td>
<td>30</td>
<td>Other (Diabetes)</td>
<td>37</td>
<td>2, 3</td>
</tr>
<tr>
<td>Huberty (2019) [66]</td>
<td>Non-CBT</td>
<td>United States of America</td>
<td>48</td>
<td>Cancer</td>
<td>93</td>
<td>None</td>
</tr>
<tr>
<td>Hunt (2009) [67]</td>
<td>CBT+</td>
<td>United States of America</td>
<td>121</td>
<td>Other (Irritable bowel syndrome)</td>
<td>81</td>
<td>2, 3</td>
</tr>
<tr>
<td>Hunt (2021) [68]</td>
<td>CBT</td>
<td>United States of America</td>
<td>54</td>
<td>Other (Irritable bowel syndrome)</td>
<td>75</td>
<td>None</td>
</tr>
<tr>
<td>Johansson (2019) [69]</td>
<td>CBT</td>
<td>Sweden</td>
<td>144</td>
<td>Cardiovascular</td>
<td>38</td>
<td>2, 3</td>
</tr>
<tr>
<td>Kraepelien (2020) [70]</td>
<td>CBT</td>
<td>Sweden</td>
<td>77</td>
<td>Neurological</td>
<td>61</td>
<td>2, 3</td>
</tr>
<tr>
<td>Kubo (2019) [71]</td>
<td>Non-CBT</td>
<td>United States of America</td>
<td>97</td>
<td>Cancer</td>
<td>68</td>
<td>2, 3</td>
</tr>
<tr>
<td>Kubo (2020) [72]</td>
<td>Non-CBT</td>
<td>United States of America</td>
<td>103</td>
<td>Cancer</td>
<td>70</td>
<td>None</td>
</tr>
<tr>
<td>Lee (2019) [73]</td>
<td>CBT+</td>
<td>Taiwan</td>
<td>160</td>
<td>Other (Irritable bowel syndrome)</td>
<td>100%</td>
<td>None</td>
</tr>
<tr>
<td>Ljotsson (2010) [74]</td>
<td>CBT+</td>
<td>Sweden</td>
<td>61</td>
<td>Other (Irritable bowel syndrome)</td>
<td>85</td>
<td>2, 3</td>
</tr>
<tr>
<td>Ljotsson (2011) [75]</td>
<td>CBT+</td>
<td>Sweden</td>
<td>86</td>
<td>Other (Irritable bowel syndrome)</td>
<td>74</td>
<td>3</td>
</tr>
<tr>
<td>Lundgren (2016) [76]</td>
<td>CBT</td>
<td>Sweden</td>
<td>50</td>
<td>Cardiovascular</td>
<td>42</td>
<td>2</td>
</tr>
<tr>
<td>McCombie (2016) [77]</td>
<td>CBT+</td>
<td>New Zealand</td>
<td>231</td>
<td>Other (Inflammatory bowel disease)</td>
<td>64</td>
<td>2, 3</td>
</tr>
<tr>
<td>Mensorio (2019) [78]</td>
<td>CBT</td>
<td>Spain</td>
<td>106</td>
<td>Other (Obesity)</td>
<td>44</td>
<td>3</td>
</tr>
<tr>
<td>Meyer (2019) [79]</td>
<td>CBT</td>
<td>Germany</td>
<td>200</td>
<td>Neurological</td>
<td>63</td>
<td>None</td>
</tr>
<tr>
<td>Migliorini (2016) [80]</td>
<td>CBT</td>
<td>Australia</td>
<td>59</td>
<td>Neurological</td>
<td>29</td>
<td>None</td>
</tr>
<tr>
<td>Moss-Morris (2012) [81]</td>
<td>CBT</td>
<td>United Kingdom</td>
<td>45</td>
<td>Neurological</td>
<td>80</td>
<td>None</td>
</tr>
</tbody>
</table>

(Continued)
populations, their decreased participation in mind-body wellness interventions may be due to a gendered behavioral trend of reluctancy to seek support with emotional challenges [80].

4. Discussion

This secondary analysis assessed the reporting of sex and gender across 56 RCTs of mind-body IMIs on anxiety and depression symptoms in people living with a range of chronic physical conditions. Across studies, 4780 (62%) participants were described as female or women, 2751 (36%) were described as male or men, and 2 (0.03%) were described as intersex or gender

Table 3. Sex and gender reporting criteria and results.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Met Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-binary use (&gt; 2 categories utilized for sex and gender)</td>
<td>2/56 (4%)</td>
</tr>
<tr>
<td>Use of appropriate categories (e.g., sex = male/female/intersex, gender = man/woman/gender-diverse)</td>
<td>28/56 (50%)</td>
</tr>
<tr>
<td>Non-interchangeable use of sex or gender terms throughout the citation</td>
<td>25/56 (45%)</td>
</tr>
<tr>
<td>Did not meet any of the above criteria</td>
<td>21/56 (38%)</td>
</tr>
</tbody>
</table>

Abbreviations: Non-CBT = Non-Cognitive Behavioural Therapy; CBT = Cognitive Behavioural Therapy (CBT); CBT+ = Cognitive Behavioural Therapy + non-CBT technique

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diverse. None of the studies met all three criteria required to determine that sex and/or gender were accurately reported. Of the three criteria, half of the studies (n = 28, 50%) defined sex or gender using appropriate categories, less than half used sex and gender concepts non-interchangeably (n = 25, 45%). Very few (n = 2, 4%) defined sex or gender using a non-binary definition. Only one (2%) trial published sex or gender stratified data for anxiety outcomes within their report; no trials published sex or gender stratified data for depression outcomes, and 5 authors provided sex or gender-stratified data following an email request. Eleven studies described differences in recruitment or attrition trends by sex or gender within their reports, with five studies citing greater enrollment among females/women participants compared to male/men participants. Two studies that reported on sex and gender differences in attrition rates displayed disagreement, one suggesting that females/women were more likely to drop out and the other that males/men were more likely to drop out. These findings raise several points for discussion.

With 0% of studies using all three sex/gender criteria [36, 37], we have identified a low rate of detailed reporting on sex and gender within RCTs assessing anxiety and depression outcomes in participants exposed to mind-body IMIs. While our review represents the first evaluation of this data in mind-body IMIs, our findings are consistent with limited sex and/or gender reporting identified in several related reviews in the literature. A systematic evaluation of 133 Campbell reviews and 555 Cochrane reviews identified that less than 30% of series reported on sex and/or gender [100]. Others have come to similar conclusions regarding the low accuracy of sex and gender reporting, a meta-review assessing cardiovascular health interventions reporting that 0% of studies used sex and gender terms non-interchangeably [36, 101], and another systematic review of shared health care interventions for decision making reporting that 20% used these terms non-interchangeably [36].

Women and non-binary people, as well as females and intersex people have historically been neglected from health-related research. Repeated calls for greater attention to sex and gender within health-related research has made it imperative for studies to report their sex and gender demographics and analyses. When sex (male/female/intersex) and gender (man/woman/gender-diverse) are considered exclusively in binary terms (as occurred in 96% of our included studies), the generalizability of the study results are reduced to binary individuals and do not apply to individuals who are intersex or gender diverse [102]. This is of particular relevance with mental health initiatives as gender minorities face higher rates of mental health problems and unmet mental health needs compared to cisgender populations [13]. Unless focused recruitment strategies and data collection and reporting of diverse sexes and genders becomes a focus for research teams, it will remain a challenge to design effective mind-body IMIs that address these important drivers of mental distress [103–106].

Within our review, 45% of studies used sex and gender terms non-interchangeably. The high rates of interchangeable use (55%) and misclassification of sex and gender terms have important consequences, including confusion and inaccuracies in research and knowledge translation. Where sex is a biological difference, gender is a social construct. Reporting study results such as anxiety and depression symptoms which can so heavily be impacted by sex (e.g., hormones) [107] and gender (e.g., gender dysphoria, discrimination) risks inaccurately reporting the study results [108]. Additionally, when developing mind-body IMIs to manage anxiety and depression symptoms, accurately distinguishing between these two concepts is crucial for understanding health disparities and developing target mind-body IMIs [102]. Using these two terms interchangeably can lead to misleading or incomplete data and findings. Lastly, equating sex and gender can perpetuate societal norms and expectations related to gender roles and identities, hindering efforts to promote gender equality and inclusivity in health research and beyond.
Anxiety and depression data stratified by sex and/or gender was only reported in 1 (2%) study included in the current review, and for anxiety symptoms only. This presents a major limitation in determining how sex and gender may influence outcomes but is not uncommon. Consistent with our findings, in a 2017 review of Canadian RCTs involving human participants, only 6% of studies included any sex subgroup analysis, and only 4% reported sex-disaggregated data [30]. Without this data, we are unable to draw firm evidence-based conclusions about the sex and gender-specific impact of mind-body IMIs.

Despite the gaps in the previous literature, multiple measures are now being taken to improve sex and gender reporting in research. Targeted changes to common RCT practices can include more inclusivity of sex and gender considerations. First, the acknowledgement and distinction of sex and gender should be made within the RCT itself. Participants should be provided with multiple options to express both their biological sex as well as their gender. Current research is representing creative ways to capture participant gender quantitatively beyond gender identity, such as including targeted questions related to constructs such as gender roles, relations, and institutional factors that may influence study outcomes and experience [8]. Second, targeted recruitment of participants across genders is critical for promoting inclusivity within RCTs. Researchers hoping to champion gender diversity within their RCT sample can specify a targeted recruitment plan in their protocol, and pre-specify a post-hoc analysis of sex and gender [109]. Specific to examining mental health outcomes within RCTs, mixed methods approaches may also offer significant value in enhancing the assessment of participant gender and demographic factors on study outcomes [110]. Where possible, we recommend researchers incorporate both qualitative and quantitative measures to best incorporate the lived experiences and social determinants of participants within a sample. Some institutions such as the Canadian Institutes of Health Research have created measures to improve sex and gender-based outcomes by requiring research grant applicants to reflect on how they plan to include sex and gender within their proposed research [30, 111]. Other recommendations to increase sex and gender analysis within research include involving a “sex and gender champion” on each research team, which would either involve each team member taking a sex and gender in research course or having a team member become specialized in conducting sex and gender-based research [112]. This would ensure that trials have specialized methods and analysis protocols to improve the understanding of sex and gender-based differences. The consideration of sex as a biological variable is also a requirement in National Institutes of Health-funded research. Other initiatives have created standards for sex and gender reporting, including the criteria defined by Adisso et al. and Gogovor et al. [7, 36, 37] that were used in the current review, and the Sex and Gender Equity in Research (SAGER) guidelines [113]. While many journals have begun to include editorial policies for sex and gender analysis and guidelines such as SAGER, there are still opportunities to enhance and improve reporting policies [28, 113, 114]. A 2021 review of leading general medical and global health journals found that 5 out of 14 journals required a specific sex and gender analysis within the research, with the inclusion of sex and gender typically not extending beyond reporting the basic demographics of participants [115].

With nearly 2/3 of the participants in this secondary analysis reported as being female or women, the results highlight that recruitment of other sexes and genders living with chronic physical conditions into mind-body IMIs can be unequal. By accounting for the unique barriers that participants of different sexes and genders may experience in accessing mind-body IMIs, improved recruitment, attrition rates, and outcomes may be seen. For example, Young et al. developed a gender-based online eHealth intervention (“SHED-IT”) specifically for men living with obesity, recognizing the unique barriers that men may face in this space, such as gender-specific stigma around mental health and lower mental health access rates [98]. This
intervention was tailored to men at both the surface level (e.g., representation of men participating in wellness activities) and also at the core of the intervention, intentionally using more direct communication styles combined with light-hearted humor, which was intended to enhance program experiences based on evidence-based communication styles that men may respond more preferably towards [98, 116]. The program was found to be effective for participant depression and anxiety outcomes [98]. Lee et al. used a sex and gender-based approach when designing a mind-body IMI (“Mind Over Mood”) for female irritable bowel syndrome (IBS) patients [73]. This approach was taken with consideration of the 2:1 female-to-male incidence ratio for IBS and the recognition of greater levels of emotional distress present in female patients, which may contribute to the development and progression of IBS. Lee et al. tailored the intervention by incorporating mind-body practices that have been documented to be helpful in relieving emotional distress, such as expressive writing, and found statistically significant improvements in depression and anxiety outcomes [73]. Consequently, there may be significant value in tailoring interventions by sex and gender in terms of level of patient acceptability as well as mental health outcomes.

5. Limitations

This secondary analysis should be interpreted in the context of the underlying evidence base and analysis limitations. First, in the context of the evidence base, some studies were of low to moderate quality [44], and most required outreach to authors due to the limited availability of complete data. This may have affected the analysis by introducing sampling bias. Second, most evidence was extracted from studies conducted in higher-income countries, limiting the reflection of global heterogeneity in sex and gender definitions. Due to resource limitations for translation, analysis was limited to studies published in English. Third, the definition of gender used in this secondary analysis was largely limited to capturing the construct of gender identity; gender also includes constructs such as gender roles, relationships, and institution-level factors [8]. This data was not collected due to its limited availability in the included studies, but it should be considered in future studies. Fourth, in the broader published literature, there has been a steady rise of sex and gender-based analyses [117] and subsequent definitions for sex and gender [118]. It is recognized that definitions of sex and gender diversity may not have been as available (e.g., an option on a demographic survey) or deemed as important in clinical trials as it is in the present day [119]. As a result, while this secondary analysis can be used as a lens to interpret previous studies, it may more importantly be seen as a reference point for clinicians looking to conduct future mind-body IMI research amongst people living with chronic physical conditions.

6. Conclusion

With increasing access to internet and mobile tools, mind-body IMIs are anticipated to continue to rise in prevalence. In this context, it is essential that we equitably service the needs of the individuals using these interventions. This secondary analysis of a systematic review and meta-analysis of RCTs investigating mind-body IMIs reveals that no studies satisfied all three sex and gender-based reporting criteria, with 4% providing >2 categories for sex and gender, 45% using sex and gender categories non-interchangeably, and 50% using appropriate categories for sex and gender. To further our understanding of the impact of mind-body IMIs on symptoms of anxiety and depression, the interplay of biological sex, psychological, and social domains in the context of gender need to be prioritized both in intervention design and analysis. A sex and gender-sensitive approach holds promise to reduce health inequities, gain a better understanding of the effect of mind-body IMIs on anxiety and depression symptoms,
identify the characteristics of individuals who are likely to get the most benefit, and design interventions that are inclusive for the needs of diverse sexes and/or genders. Future studies investigating mind-body IMIs can use the findings of this secondary analysis to assist in intervention design and protocol development.

Supporting information

S1 Appendix. Full search strategy.
(DOCX)

S2 Appendix. Risk of bias assessment.
(DOCX)

S1 Data. Risk of bias data.
(XLSX)

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References


Sex and gender in internet and mobile-based interventions


