Mass media representations of the evidence as a possible deterrent to recommending exercise for the treatment of depression: Lessons five years after the extraordinary case of TREAD-UK

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ABSTRACT

Exercise or physical activity are recommended options within stepped-care treatment models for depression. However, few physicians present these options to patients, in part because of the impression that the supporting evidence is weak or inconsistent. We speculate that the cooccurrence of “counter-messaging” and deficient critical appraisal may lead to such impressions. We focus on TREAD-UK (ISRCTN16900744), the largest trial to investigate “whether physical activity can be an effective treatment for depression within primary care”. In media statements, researchers declared that exercise was ineffective in lowering depression. We examined (a) the results of the trial, critiques, and rejoinders, (b) the impact on internet searches, and (c) whether TREAD-UK was critically appraised, as reflected in citing articles. We show that the results of TREAD-UK were misrepresented. The media campaign resulted in a fourfold increase in relevant internet searches. Of articles characterising the results, 57% adopted the interpretation that exercise failed to lower depression, whereas only 17% were critiques. We identify similarities to media portrayals of the OPERA (ISRCTN43769277), DEMO (NCT00103415), and DEMO-II trials (NCT00695552). We note a disconcerting trend of media campaigns that misrepresent the effects of exercise on depression and call for increased scrutiny in peer reviewing both pre- and post-publication.

The first decade of the 21st century marked a turning point in guidelines for the treatment of depression, with expert panels in several countries recommending “stepped care” or “stepped collaborative care” models. According to such models, the prescription of antidepressant drugs should be limited to individuals with severe symptoms. Two events probably precipitated this development. First, a comparison of data published in the medical literature to data held by the U.S. Food and Drug Administration revealed that the apparent therapeutic effect of antidepressant drugs had been manipulated by selective publication of results in order to appear considerably larger than it was (Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008). Second, meta-analyses showed that the therapeutic effect of antidepressant drugs is distinguishable from placebo only for individuals with severe initial levels of symptoms (Fournier et al., 2010; Khan, Leventhal, Khan, & Brown, 2002; Kirsch et al., 2008). According to stepped-care models, the clear majority of individuals requiring treatment for depression, whose symptoms are in the subthreshold or mild-to-moderate range, should be offered so-called “low-intensity” treatment options (i.e., widely accessible, nonpharmacological treatments that entail low economic cost and low patient burden, such as book-based or software-based self-help in accordance with the principles of cognitive behavioural therapy). Based on evidence from multiple randomised controlled trials (RCTs), exercise is one of the recommended low-intensity options in several countries (e.g., England, Scotland, Canada, Netherlands, Australia, New Zealand). While the effects of exercise on mental health have been questioned on both methodological (De Moor, Boomsma, Stubbe, Willemsen, & De Geus, 2008; Salmon, 2001) and practical grounds (Seime & Vickers, 2006), recent meta-analytic summaries indicate that the pooled effect of exercise interventions on depression is large and remains significant even when the analysis is restricted to trials that satisfy the criteria for high methodological quality (Ekkekakis, 2015; Schuch et al., 2016). Trials involving head-to-head comparisons of exercise to psychotherapy and antidepressant medication have shown no difference in efficacy (Cooney et al., 2013). While only two trials have compared the effects of exercise interventions against drug placebo, their pooled effect size is larger than the pooled effect sizes associated with trials of psychotherapy and antidepressants (Ekkekakis & Belvederi Murri, 2017).

Current practice in primary care overwhelmingly favors the use of antidepressants. For example, in France (Dumesnil et al., 2012), 82.6% of general practitioners prescribe pharmacotherapy, either alone (44.4%) or in combination with psychotherapy (38.2%). Given the radical change from current practice norms and the potential redistribution of the depression-treatment market that the transition to stepped-care models could entail, it is unsurprising that the new guidelines have sparked controversy. Authors have argued that “there is no scientific ground to deny mildly depressed patients the use of antidepressants” (p. 8), characterising the utilization of alternatives, such as exercise,
for individuals with mild and moderate symptoms as “mistaken” (Fountoulakis, Veroniki, Siamouli, & Möller, 2013, p. 1). This characterization follows claims that “the data on the efficacy of exercise . . . are either negative or do not exist” (Fountoulakis & Möller, 2012, p. 745). In its guideline, the American Psychiatric Association (Gelenberg et al., 2010) provides no systematic review of evidence pertaining to exercise and does not mention exercise among its “Recommended Modalities for Treatment” for any level of symptom severity. Physicians are only offered guidance for situations in which the option of exercise is raised by the patients themselves: “if a patient with mild depression wishes to try exercise alone for several weeks as a first intervention, there is little to argue against it” (Gelenberg et al., 2010, p. 30). This sentence has been interpreted as suggesting that “the clinician should not consider exercise as a first-line intervention even for mild depression” (Cosgrove et al., 2012, p. 187).

In apparent departure from the principle of evidence-based medicine, surveys in countries with stepped-care guidelines in place show that exercise has yet to enter clinical practice as antidepressant treatment. An analysis of patient records from the National Health Service (NHS) in England contains no mention of physical activity (Richards et al., 2012). Likewise, in the Netherlands, physicians report dispensing general advice regarding exercise but refrain from referring patients to exercise specifically for the treatment of depression (Hermens, Muntingh, Franx, van Splunteren, & Nuyen, 2014). The reasons behind this departure from the guidelines remain poorly understood. The few qualitative studies that have probed the causes of this phenomenon suggest that clinicians report being unaware of evidence supporting the use of exercise for the treatment of depression or express the belief that the evidence is weak or inconsistent (Searle et al., 2012; Stanton, Franck, Reaburn, & Happell, 2015).

In this review, we explore one mechanism that may fuel the apparent confusion surrounding the evidence on the antidepressant effects of exercise. Specifically, we focus on the combination of (a) “counter-messaging”, namely the dissemination by researchers, university communication offices, and journalists of information that runs counter to the bulk of the research evidence and thus appears to conflict with “conventional wisdom” on this topic, and (b) deficient critical appraisal by researchers, clinicians, and the public of the research cited as the source of the counter-message.

The power of “counter-messaging” or “counter-advertising” to influence public behaviour was broadly appreciated in the medical literature when the technique was used by the tobacco industry in its effort to neutralise evidence on the harmful effects of smoking. This method was used initially to counter information on the addictive effects of nicotine (Hurt & Robertson, 1998) and later to create doubt about the carcinogenic effect of secondhand smoke (Muggli, Hurt, & Becker, 2004). The effectiveness of counter-messaging relies on the intrigue or “attention-grabbing” potential of a message that seems to contradict what was believed to be common knowledge. This phenomenon is variously referred to as the “surprise effect” (Green, 1956), “isolation effect” (Hunt & Lamb, 2001), “distinctiveness effect” (Waddill & McDaniel, 1998), “expectation-violation effect” (Hirshman, 1988) or “bizarreness effect” (Macklin & McDaniel, 2005; McDaniel, Einstein, DeLosh, May, & Brady, 1995).

Counter-messaging assumes a necessary precondition, namely the absence of critical appraisal of the source of the counter-message. While physicians are strongly encouraged to base their treatment recommendations on research evidence, surveys reveal deficiencies in methodological and statistical knowledge that render the in-depth evaluation of published studies difficult (Godwin & Seguin, 2003; Shuval, Shachak, Linn, Brezis, & Reis, 2007; Young, Glasziou, & Ward, 2002). When asked, physicians report that they spend approximately 20 minutes reading each research article (Tenopir, King, Clarke, Na, & Zhou, 2007) but, when timed, this turns out to be closer to 3-to-5 minutes (Alper et al., 2004). In two thirds of the cases, physicians admit that they only read the abstracts (Saint et al., 2000).

The challenge of critical appraisal is presumably greater for members of the general public, who must rely on media reports to help them place research in proper context (Schwitzer et al., 2005). Media coverage of medical research is commonly criticised for being selective, oversimplifying, or sensationalised (Barbour et al., 2008; Bartlett, Sterne, & Egger, 2002), for the inability of journalists to “separate the wheat from the chaff” as manifested in the overemphasis on observational research, small experiments, or preliminary reports (Gonon, Konsman, Cohen, & Boraud, 2012; Robinson, Coutinho, Bryden, & McKee, 2013; Schwartz & Woloshin, 2004), the underreporting of study limitations (Kuriya, Schneid, & Bell, 2008; Woloshin & Schwartz, 2002; Woloshin, Schwartz, & Kramer, 2009), and the non-disclosure of financial interests (Campion, 2004). Analyses also suggest that “spin” in the original article typically finds its way into press releases (Yavchitz et al., 2012) and subsequently into news reports (Schwartz, Woloshin, Andrews, & Stukel, 2012). Press releases by university press offices are not immune to such problems (Woloshin, Schwartz, Casella, Kennedy, & Larson, 2009).

Making matters worse, evidence suggests that most people overlook the possibility of bias when interpreting research results (Strickland & Mercier, 2014) and retractions or corrections of misinformation are minimally effective (Lewandowsky, Ecker, Seifert, Schwarz, & Cook, 2012).

Here, we illustrate the cooccurrence of counter-messaging and deficient critical appraisal, focusing on the TREAD-UK trial (Chalder et al., 2012a, 2012b). We do so by examining media and academic sources from the five years since the publication of the results of this trial.

What makes the case of the TREAD-UK trial extraordinary?

With a sample of 361 patients diagnosed with depression, an eight-month intervention, and follow-up until the twelfth month post-randomisation, the TREAD-UK (Chalder et al., 2012a, 2012b) is the largest RCT on the effects of physical activity on depression ever conducted in primary care. According to its protocol, the purpose of the trial was to evaluate “whether physical activity can be an effective treatment for depression within primary care” (Baxter et al., 2010, p. 6). The TREAD-UK was designed as a two-arm, pragmatic multicentre study. Both arms received usual care for depression but the treatment arm received an additional “physical activity facilitation” intervention, encouraging participants to
raise their activity level. It was assumed that this additional intervention would manipulate the level of physical activity, thus permitting the trial to fulfill its purpose. Physical activity was treated as a dichotomous variable, indicating whether participants exceeded a rather high cutoff of 1000 MET-minutes per week from activities considered of “light” (e.g., yoga, bowling, golf), “moderate” (e.g., fast walking, tennis, badminton), and “vigorous” intensity (e.g., soccer, running, vigorous swimming), assessed by a seven-day recall questionnaire. For reference, the minimum threshold of health-promoting physical activity is 450 MET-minutes per week (Haskell et al., 2007).

As should be apparent to critical readers, the “A + B versus B” experimental design used in TREAD-UK could not fulfill the stated purpose of the trial (i.e., “whether physical activity can be an effective treatment for depression ”; Baxter et al., 2010, p. 6) since there was no arm that received only a “physical activity” intervention. Moreover, the “A + B versus B” design is generally considered biased since it tends to “generate only ‘positive’ results” (Ernst & Lee, 2008, p. 214) due to the added attention given to participants in the treatment group. However, one scenario that can lead to failure to demonstrate superiority in the treatment group is to provide the same or equivalent treatment to the “control” group, effectively turning the design into “A + B versus A + B”. This is what appears to have happened in TREAD-UK. According to the protocol (Baxter et al., 2010), the analytic plan called for the physical activity data to be analyzed by (a) an intergroup comparison at the primary outcome endpoint (4 months) and (b) a group by time analysis over the entire treatment and follow-up period (4, 8, 12 months). Both planned analyses yielded null results (see Chalder et al., 2012a, p. 5). The intergroup comparison at 4 months showed no significant difference in the percentage of participants classified as physically active (52% versus 43%, p = 0.08). Likewise, the group by time analysis showed no significant interaction (p = 0.71).

Given the failure to manipulate physical activity, the trial could not fulfill its original purpose of evaluating “whether physical activity can be an effective treatment for depression” (Baxter et al., 2010, p. 6). This led to certain unorthodox steps. First, in an analysis not explicitly specified in the trial protocol, the researchers collapsed the physical activity data from the three follow-up time points (4th, 8th, 12th month), including all participants who had provided at least one physical activity diary over the entire 12-month period. Due to the increased statistical power afforded by the larger sample, this analysis yielded a significant intergroup difference. The researchers interpreted this result as having demonstrated that “the intervention increased self-reported physical activity and this effect was sustained for 12 months” (Chalder et al., 2012a, p. 7). Arguably, however, this interpretation is unsupported by the analyses.

Second, on 10th April, 2012, after the final report (March 2012) to the funding agency (National Institute for Health Research) but before the publication of the results in the British Medical Journal (June 2012), the researchers revised the main study hypothesis in the trial registry (isrctn.com/ISRCTN16900744), changing the independent variable from “physical activity” (as specified in the protocol) to “facilitated physical activity”. This modification fundamentally changed the nature of the research question from whether participation versus non-participation in physical activity can lower depression to whether the provision versus non-provision of the “facilitated physical activity” intervention can lower depression.

On 6th June, the University of Bristol, as the coordinating center for this multicenter trial, issued a press release, in which a senior investigator was quoted as saying that “this carefully designed research study has shown that exercise does not appear to be effective in treating depression”. In response to a question by the host of a BBC Radio show, inquiring whether the effect of exercise was “absolutely zero”, the same senior investigator responded: “Yes, it was. It was an important study because it gave such a definite result. There was quite clearly no difference between the people who increased their activity and their exercise compared with the people who hadn’t actually had that opportunity” (also see Table 1). The British Medical Journal sent a promotional e-mail message to registered readers, titled “Exercise is good for depression, right? Wrong, according to this study”. The press release, and quotes therein, were cited extensively in media reports, identifying “exercise” or “physical activity” as the independent variable (e.g., “New study counters claim that exercise can ease depression”, “Exercise doesn’t ease depression, says experts”, “Exercise does not alleviate depression, says major study”, “Physical activity ’no benefit’ in alleviating symptoms of depression”; also see Table 2).

In the literature, the TREAD-UK trial has been discussed in strikingly discordant terms. In an invited editorial in the British Medical Journal, authors described it as a “large methodologically rigorous trial” that “tried to remedy the methodological concerns of previous trials and answer definitively whether or not physical activity is an effective treatment in patients diagnosed with depression” (Daley & Jolly, 2012, p. 1). The results were described as “negative” though “perhaps not surprising”. The authors also offered the following advice for clinicians, encouraging them to limit treatment to “usual drugs or psychological treatments (or both)” and even going well beyond the results of the trial to speculate on possible harms from exercise:

Table 1. Excerpts from an interview about the TREAD-UK trial to the BBC Radio 4 “Today” programme (>7 m listeners), on 6 June 2012, at 7:12 am (Host: Evan Davis, Guest: Professor John Campbell). Audio from: http://news.bbc.co.uk/today/hi/today/newsid_9726000/9726228.stm.

[Davis] Were you surprised by the results of this?
[Campbell] […] I think we did anticipate that exercise might have more of an effect than we actually saw for… for treating this very vulnerable group of patients.
[Davis] Was it really absolutely zero?
[Campbell] Yes, it was. It was… It was an important study because it gave such a definite result. There was quite clearly no difference between the people who were… who increased their activity and exercise compared with the people who hadn’t actually had that opportunity. […]
[Davis] […] you might have expected I suppose that there would be some beneficial effect on the mind. […] So, it is surprising that it seems to have none on people who are really depressed.
[Campbell] […] We know that exercise is very good for you. But it’s not good for treating people with what was actually quite severe depression. […]
[Davis] […] What remain then the clinically proven therapies, best clinically… best “evidence-based,” I suppose, therapies for depression?
[Campbell] And that’s exactly the right observation, Evan, because we are looking for evidence-based treatments. […] There are very good treatments available for depression. Drugs, obviously […] But also the talking therapies […] So, there are good treatments and, sadly, it appears that exercise as a treatment in its own right is probably not substantiated.


Table 2. Sample of news headlines related to the TREAD-UK trial on 6 June 2012 (Source: Lexis-Nexis®).

<table>
<thead>
<tr>
<th>Headline</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise “no help for depression”, research suggests</td>
<td>BBC News (bbc.co.uk)</td>
</tr>
<tr>
<td>Exercise doesn’t help depression, research concludes</td>
<td>The Guardian (London)</td>
</tr>
<tr>
<td>Exercise does little to help the symptoms of depression, new study finds</td>
<td>The Daily Mail (London)</td>
</tr>
<tr>
<td>Exercise does nothing to cure depression, says study</td>
<td>The Daily Telegraph (London)</td>
</tr>
<tr>
<td>Exercise “fails to lift clinical depression”; Exercise should not be “prescribed” to people with clinical depression, according to a study which found it did nothing to improve their moods</td>
<td>The Telegraph (telegraph.co.uk)</td>
</tr>
<tr>
<td>You can’t sweat off the blues</td>
<td>The Sun (London)</td>
</tr>
<tr>
<td>Exercise “is not effective in treating depression”</td>
<td>Metro (London)</td>
</tr>
<tr>
<td>New study counters claim that exercise can ease depression</td>
<td>The Bristol Post (Bristol)</td>
</tr>
<tr>
<td>Exercise doesn’t aid depressed, says study</td>
<td>The Western Mail (Cardiff)</td>
</tr>
<tr>
<td>Exercise doesn’t ease depression, say experts</td>
<td>Scotsman (Edinburgh)</td>
</tr>
<tr>
<td>Exercise does not benefit depressed people</td>
<td>The Herald (Glasgow)</td>
</tr>
<tr>
<td>Physical activity “no benefit” in alleviating symptoms of depression</td>
<td>Irish Examiner (Cork)</td>
</tr>
</tbody>
</table>

What should doctors advise their patients who present with depression? Within a clinical setting, for patients who are well managed on usual drugs or psychological treatments (or both), advice and support to be physically active does not seem to offer additional benefit and should not be given as standard. Indeed, recommending exercise to very depressed patients may worsen any thoughts of “failure” if they are unable to comply with the recommendation. (Daley & Jolly, 2012, p. 2)

Likewise, in a Clinical Opinion piece in the Journal of the Royal College of Physicians of Edinburgh, the author described the TREAD-UK as “a landmark trial”, a “methodologically robust” trial, and “substantially larger than previous trials” (Mead, 2012, p. 325). Echoing the editorial in the British Medical Journal, the author expressed the opinion that clinicians should disregard the guideline currently in effect (National Collaborating Centre for Mental Health and National Institute for Health and Clinical Excellence, 2010) and avoid presenting physical activity as a treatment option to their patients: “based on the results of this clinical trial, clinicians should not advise people with depression that physical activity will increase their chances of recovering from depression” (p. 325).

On the other hand, the TREAD-UK trial itself, and the manner in which the results were portrayed in the media, have also been strongly criticised. Authors have described the trial as having “several weaknesses” warranting that conclusions be “very cautiously interpreted” (Josefsson, Lindwall, & Archer, 2014, p. 270), “several methodological weaknesses [that] limit the interpretation of these results” (Rethorst & Trivedi, 2013, p. 204), and “severe methodological flaws that make its findings irrelevant to the originally stated purpose of the study” (Ekkekakis, 2013, p. 25). Davies, Larkin, Loosemore, and Montgomery (2012) expressed “dismay” at the media portrayal of the trial, pointing out that statements by the investigators, such as “exercise does not appear to be effective in treating depression” were not supported by the data. Pilling and Anderson (2012) argued that the trial “adds little to that evidence” and expressed concern that misleading statements to the press “could deprime patients of effective treatment” (p. 1). Donnelly (2012) characterised the conclusions of the trial as “misleading and ill considered”, the practice recommendations as “ill founded and unhelpful”, and the statements to the press as “not supported by the research” and creating “a misleading impression” (p. 1). Asmundson et al. (2013) stated that the statements by investigators to the press raise “questions whether there is a general resistance to the notion of using exercise as a treatment for mood or anxiety disorders” (p. 369).

Responding to the critics, the primary investigator conceded that “the headline that ‘exercise is no help for depression’ clearly goes beyond our findings and is not the conclusion given in our paper” (Lewis, 2012, p. 1). Two excerpts from the response warrant scrutiny. First, Lewis (2012) acknowledged that “statements on the press release and in interviews might have led to different conclusions” (p. 1). This statement raises interesting questions, especially in light of calls to redefine scientific misconduct as “distorted reporting” or a “mismatch between what was reported and what was done” (Fanelli, 2013, p. 149). Despite this acknowledgment, the press release was never edited or retracted and is still available from the news office of the University of Bristol (bristol.ac.uk/news/2012/8529.html). Second, Lewis (2012) urged “those confused by the headlines [to] please read our paper” (p. 1). Allegedly, the “confusion” was due to the failure of readers to recognise that the trial “did not evaluate ‘exercise’ or even ‘physical activity’ but the effect of our intervention on depression” (p. 1). This statement again raises intriguing questions considering that (a) the TREAD-UK trial was explicitly conceived as a test of “whether physical activity can be an effective treatment for depression” (Baxter et al., 2010, p. 6) and (b) the change of the independent variable in the trial registry from “physical activity” to “facilitated physical activity” was made only weeks earlier, after the trial had been completed.

What did the TREAD-UK find?

According to the abstract of the TREAD-UK article, there was no difference between “participants offered the physical activity intervention [note: not ‘the facilitated physical activity intervention’] … compared with those in the usual care group” in any of the depression-related outcomes, including scores on the Beck Depression Inventory, the proportion of recovered patients, or the use of antidepressants (Chalder et al., 2012a). What is not apparent from the abstract, however, is that both groups of participants exhibited large improvements in these outcomes. To illustrate, one can juxtapose the results of TREAD-UK to results from other depression-related RCTs conducted by overlapping groups of investigators within the NHS at approximately the same time. These examined various forms of cognitive-behavioural therapy (CBT), including CBT delivered via the internet (Kessler et al., 2009), via self-help books (Williams et al., 2013), and in face-to-face sessions (Wiles et al., 2013). These trials are comparable to TREAD-UK because they used the same experimental design (usual care versus usual care plus intervention), the same outcome measure of depression, the same definition of recovery (in 2 of 3 trials), and patients with similar baseline levels of depression (>50% on antidepressants).

As shown in Figure 1, while the treatment arm of TREAD-UK was at least as effective as the CBT arms of the other trials, the usual-care arm of TREAD-UK was considerably more effective than other usual-care arms. In fact, the effectiveness of the
usual-care arm of TREAD-UK was comparable to or better than the CBT interventions. This pattern of results suggests that the usual-care group of TREAD-UK received “unusual care” (Freedland, Mohr, Davidson, & Schwartz, 2011).

To identify possible reasons for this extraordinary effectiveness, one should consider ways in which “usual care” in TREAD-UK might have differed from NHS norms. Unlike other trials, in which the option of physical activity was probably not presented to patients (Richards et al., 2012), most participants in TREAD-UK enrolled after physicians discussed physical activity as a possible treatment for depression and gave them an informational brochure (Chalder et al., 2012b). Moreover, participants completed physical activity recall logs four times during a 12-month period. The measurement of physical activity through self-report, presumably acting as self-regulatory feedback, has been shown to produce changes in behaviour that approximate the effects of activity-promotion interventions (van Sluijs, van Poppel, Twisk, & van Mechelen, 2006).

Finally, physicians referred an unspecified number of participants allocated to “usual care” to exercise-on-prescription schemes “as ‘consolation’ for not being randomised to facilitated physical activity” (Chalder et al., 2012b, p. 63). Unlike the “facilitated physical activity” intervention, which entailed minimal contact and consisted of mere encouragement to be active, local exercise prescription schemes offer in-person supervision and support by certified exercise professionals.

At the end of the intervention, 49% of the participants in “usual-care” were classified as physically active. With the exception of the intervention group in TREAD-UK (63% classified as physically active), this is the highest rate of participation ever recorded in a physical activity promotion trial in primary-care settings among trials in which physical activity was reported as a dichotomous variable (Orrow, Kinmonth, Sanderson, & Sutton, 2012). What makes this observation even more remarkable is that the threshold for classifying participants as “physically active” in TREAD-UK (i.e., 1000 MET-minutes per week) was 222–370% higher than the threshold used in other trials (i.e., 270–450 MET-minutes per week).

A five-year retrospective analysis of impact

We conducted two analyses to illustrate that counter-messaging and deficient critical appraisal cooccurred in the case of TREAD-UK. For the first analysis, we used internet searches as a proxy measure of public interest in the subject of exercise for depression. Most patients use the internet as a source of health information (Diaz et al., 2002; Mc Mullan, 2006) and some discuss this information with their physicians (Schwartz et al., 2006). Search data from Google Trends (Google, Mountain View, California) show that the publicity surrounding the TREAD-UK trial was associated with a nearly fourfold (357% increase) increase in internet searches in the UK on “exercise” and “depression” in June 2012 compared to the average of the five-year period from February 2012 to February 2017 (see Figure 2).

In the second analysis, using Scopus (Elsevier BV, Amsterdam, Netherlands), we retrieved the 68 English-language articles in which the TREAD-UK article (Chalder et al., 2012a) had been cited until February 2017. Two investigators, working independently, read the articles and categorised them as citing the TREAD-UK in support of statements that (a) “exercise” or “physical activity” was found to lower depression, (b) failed to lower depression, (c) the results were inconclusive, or (d) the methodology and/or the conclusions of the trial were criticised. In addition, we identified articles that cited the TREAD-UK article (e) in reference to aspects of its

Figure 1. Google™ internet searches on “exercise” and “depression” in the United Kingdom from February 2012 to February 2017. Data are presented as percentages relative to the peak. Over 260 weeks, search activity showed no systematic change (slope of 0.000). However, in June 2012, when the results of the TREAD-UK trial were published, searches for these keywords nearly quadrupled (357% increase), illustrating the powerful effect of counter-messaging.
methodology without providing critical commentary or (e) for “other” reasons. The two evaluators agreed in all but four cases (94% agreement). These disagreements were resolved by consensus with the help of a third investigator.

This analysis showed that, in six articles (9%), the TREAD-UK was cited, erroneously, as having shown that “exercise” or “physical activity” lowered depression. Consistent with our prediction, in 27 articles (40%), the trial was cited, also erroneously, as having shown that “exercise” or “physical activity” failed to lower depression. In one example, the authors wrote that “after 8 months, physical activity was shown to be an ineffective and more costly strategy than conventional primary care assistance” (Schuch & de Almeida Fleck, 2013, p. 1). In another example, the authors noted that “a recent randomised trial failed to demonstrate efficacy as a treatment in depressed adults” (Fogelman & Zafonte, 2012, p. 910). The trial was characterised as having yielded “inconclusive” results in three articles (4%). For example, authors cited TREAD-UK as an example of research that had “yielded mixed results about the benefits of exercise for the brain” (Noakes & Spedding, 2012, p. 296) or was “inconclusive on the positive influences of exercise alone in improving depressive symptoms in patients” (Lall, Atkinson, Corlett, Broadbridge, & Bonsall, 2012, p. 1092). Only eight articles were critical of the methods and questioned the validity of the conclusions from TREAD-UK (12%). After removing the 21 articles in which the citations to TREAD-UK did not characterise the results (i.e., 17 articles referring to the methodology without making evaluative comments and 4 articles citing the trial for miscellaneous reasons), the majority (57%) of the remaining 47 articles cited the TREAD-UK as having shown that “exercise” or “physical activity” failed to lower depression. Only 17% were critiques.
Generalization to other exercise RCTs with “negative” results

The TREAD-UK is only one of a series of recent cases in which RCTs with considerable methodological limitations were portrayed by researchers to the media as having shown that exercise is an ineffective treatment for depression. A large cluster-randomised RCT, the OPERA trial (Underwood et al., 2013; ISRCTN43769277), aimed to investigate the effects of promoting physical activity and exercise as means of reducing depression in residents of nursing homes (N = 891, 21% of whom had depression at baseline). The researchers intended to implement an intervention that combined twice-weekly “moderate intensity strength and aerobic training” (p. 45) with a “whole-home approach” in which the care-home staff would be trained to encourage regular physical activity among the residents during the week. However, neither part of the programme could be implemented because the residents were much older and more frail than anticipated (mean age 86.5 years, range 65–107 years). The plan was to deliver “exercise classes [that] were designed to provide a moderate intensity strength and aerobic training stimulus” (p. 43). However, only 36% of eligible participants did one session per week and, importantly, the exercise was different from what was planned: “because of the poor physical health and abilities of participants in the exercise group, the exercises were largely done while seated, reducing the intensity of the exercises” (p. 48). Moreover, fewer than half of staff members attended training and the intended “whole-home approach” did not materialise.

In a subsequent process evaluation, the researchers conceded that the OPERA trial was plagued by poor planning: “the care home population is older and frailer than anticipated when the OPERA trial was planned” (Ellard, Thorogood, Underwood, Seale, & Taylor, 2014, p. 10). However, in the main report in the Lancet, the authors asserted that the trial was characterised by “robust methodology” and “a strong theoretical grounding” (Underwood et al., 2013, p. 48). Despite the fact that it was impossible to implement “regular moderately intense group exercise sessions”, the researchers concluded that “regular moderately intense group exercise sessions do not live up to their promise as a treatment for depression in elderly residents of care homes” (p. 48). In a scenario that resembles the TREAD-UK media campaign, the press release by the University of Warwick, extensively quoted in national media, was titled “Exercise proves to be ineffective against care home depression” (warwick.ac.uk/newsandevents/pressreleases/exercise_proves_to). In the DEMO, Krogh et al., 2012) and DEMO-II trials (Krogh, Videbech, Thomsen, Glud, & Nordentoft, 2012; NCT00695552), conducted in Denmark, aerobic or resistance exercise was compared to lower doses of exercise, leading to substantial decreases in depression but no intergroup differences. In DEMO, the “control” group, described as engaging in “relaxation”, performed various exercises, which were reportedly designed to “avoid muscular contractions or stimulation of the cardiovascular system” (Krogh et al., 2009, p. 792). However, contradicting this statement, the exercises consisted of “alternating muscle contraction and relaxation in different muscle groups” and participants were instructed that they could raise their perceived exertion up to “12 on the Borg scale” (p. 792). This level of exertion, between “Fairly light” and “Somewhat hard”, is within the range recommended for the improvement of cardiorespiratory fitness (Garber et al., 2011). Thus, after four months and one session per week on average (of the two scheduled), the “relaxation” group exhibited 6% improvement in aerobic capacity (comparable to 8% in the resistance-exercise group) and 10–14% improvement in muscular strength (larger than the 3–7% in the aerobic-exercise group). Having evidently received sufficient exercise to experience fitness gains, participants in the “relaxation” group reported a reduction of depression comparable to those found in the aerobic and resistance-exercise groups (see Figure 3). Overlooking the fitness gains in the “relaxation” group, the researchers concluded that their findings “do not support a biologically mediated effect of exercise on symptom severity in depressed patients” (Krogh et al., 2009, p. 790).

In DEMO-II, Krogh et al. (2012) increased the frequency to three planned sessions per week but shortened the duration of treatment to three months and increased the dose of exercise in the control group. Despite labeling the control group as an “attention control group” engaged in “stretching”, participants did 20 minutes of stretching and 25 minutes of aerobic activities, including riding a stationary cycle and throwing and catching balls. The “exercise” group rode stationary cycles for 45 minutes, including a 10-minute warm-up and a 5-minute cool-down. After an average of 13 of 36 planned sessions (approximately one session per week), both groups exhibited similar, clinically meaningful decreases in depression. The researchers concluded that “the DEMO-II trial does not support referring patients from general practices to a 3 month exercise programme to obtain antidepressant effects” (Krogh et al., 2012, p. 9). With a definitive tone reminiscent of the TREAD-UK and OPERA media campaigns, an article on the DEMO trials in the leading Danish newspaper Politiken stated: “Common perception that exercise works against depression is wrong” (Thomsen, 2015).

Concluding remarks

Confusion about the research evidence may be one of the factors that preclude the application of physical activity and exercise as options for the treatment of depression, even in countries in which they are explicitly recommended in stepped-care guidelines. We reviewed evidence suggesting that a media-disseminated counter-message can attract attention and be influential, especially if its original research source is not subjected to critical appraisal. The information we presented raises the possibility of an alternate, potentially powerful, pathway that can influence the behaviour of physicians and patients. This alternate pathway could be dubbed “press release-based medicine” (see Figure 4). In the idealised evidence-based medicine scenario, expert critical appraisal is present at each step of the process, from the peer reviewers of the original journal article, to the experts serving on guideline-development panels, and ultimately to physicians who...
have the knowledge, time, and inclination to scrutinise the methodological details of the numerous RCTs and systematic reviews published daily. In contrast, in the arguably more realistic "press release-based medicine" scenario, critical appraisal is mostly absent. The press release, along with any bias it contains, is likely to reach the public unmitigated. Commenting on tobacco industry strategies, De Camargo (2012) wrote that the research behind media communications "does not need to effectively produce an impact within the scientific community"; rather, the goal is to "provide ammunition for the battle that really counts: the one for public opinion, via the mass media" (p. 1234). A statement by a practice nurse on the impact of the TREAD-UK media campaign illustrates this point: "You know you are going to get patients saying 'This is rubbish. I'm not going to do it,' because they have heard the story too" (Trueland, 2012, p. 24).

Our review suggests that media portrayals of RCTs allegedly showing that exercise has no antidepressant effect tend to state this conclusion with a definitiveness that is unjustified by the methodological limitations of the trials. Our analysis of internet-search data suggests that, given sufficient media exposure, such messages can capture the attention of the public. Moreover, our analysis of citing articles suggests that, even in the case of TREAD-UK (i.e., the largest and most controversial trial in this research field), it is more likely for citing authors to adopt the media portrayal than to
criticise the methods. On the other hand, our review provides no evidence on the extent to which these media messages have influenced the opinion or attitude of physicians and patients, are discussed in physician-patient consultations, or have had an impact on clinical practice. The reasons why physical activity and exercise are still not presented as options within stepped-care models of treatment for depression warrant attention. We propose that confusion about the strength and consistency of the evidence should be considered as a possible culprit in future research on this important question.

Although the motivations of researchers and journalists are unknown, critical readers of this literature, including peer reviewers, journal editors, guideline developers, and policymakers, should take into account that the introduction of physical activity and exercise in clinical practice as antidepressant monotherapies could have considerable economic ramifications. As Ioannidis (2005) warned, “the greater the financial and other interests and prejudices in a scientific field, the less likely the research findings are to be true” (p. 698). In other words, the potential for motivated bias in this literature could be high and this element should not be overlooked when evaluating research on this topic. The potential for bias does not refer only to RCTs but also extends to systematic reviews and meta-analyses (Ekkekakis, 2015). For these reasons, we call for heightened scrutiny, both before and after publication, of methodological details and the extent to which conclusions are supported by the design and the data.

Despite rising attention to the topic of research bias across most scientific fields over the last decade (Ioannidis, 2005), no such trend is evident within exercise science. There have been no empirical analyses of bias, no special issues of journals dedicated to this topic, and no roundtable discussions on bias at conferences in the field of exercise science. It is also noteworthy that nearly all prior expressions of concern and critiques of the RCTs discussed here have come from disciplines outside of exercise science (e.g., primary care, psychology, psychiatry). The factors contributing to the apparent inattention to the topic of research bias within the field of exercise science are unclear. However, it is becoming apparent that a willingness to partake in scholarly critique and constructive debate could raise the sense of accountability and thus lead to an improvement of scientific standards in research that examines the effects of exercise and physical activity on health. Additionally, the trend we identified in the present analysis should provide the impetus for major scientific and professional organizations in exercise science to propose the establishment of critical appraisal as a central learning outcome in undergraduate and postgraduate curricula. Unlike other training programmes that prepare health practitioners (e.g., physiotherapy, community health, nursing), an ability to conduct critical appraisal as the basis for evidence-based practice has yet to be considered a core competence for a professional career in exercise science (Dallman et al., 2009; McCullagh & Wilson, 2007; Reeve, 2007) and this is reflected in training curricula (Amonette, English, & Ottenbacher, 2010; Elder, Pujol, & Barnes, 2003). As exercise scientists aspire to play a more active role in the domain of healthcare, the open acknowledgment of the problem of research bias and the systematic integration of critical-appraisal training in educational programmes is essential. Importantly, critical appraisal should be applied with equal scrutiny to empirical evidence portrayed as having shown exercise to be ineffective and evidence portrayed as having demonstrated that exercise benefits health.

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