Step by step how to conduct evidence appraisal using Gradepro

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Problem:

" What is the quality of evidence of the effectiveness of mindfulness meditation for control of anxiety and depression for adults"?

Step by step

Step 1. Convert this question to a PICO formatted question and set up a PICO table

Descriptor	Description
P	Adults above 18 years both sex all ethnicity
I	Mindfulness based interventions
C	All other non-mindfulness based interventions
O	Stress (Depression and Anxiety)

Table 1: PICO table

Based on the PICO table, the pico formatted question for this topic is:

"Compared with non-mindfulness based approaches, what is the effectiveness of mindfulness meditation for stress (depression and anxiety

Step 2: Search literature databases and set up a table and identify an article.

This is the lengthiest part of the process. Accurately searching the databases and setting up or identification of the studies is the most critical aspect of this process.

From here, we will take two courses of action:

- We will identify a bunch of individual primary studies, synthesise the results of the studies and construct the evidence base (more work)

- We will identify a Cochrane Collaboration Review and use this to construct the evidence base (somewhat straightforward)

In this example, we will search Cochrane Database of Systematic Reviews and Pubmed. The following table returns the result of pubmed search:

Search and retrieval of results from Pubmed

Recent queries in pubmed

Search	Query	Items found	Time
#15	Search #7 AND #14	7	17:03:31
#14	Search #10 OR #12	92580	17:03:12
#13	Search #9 AND #12	0	17:02:37
#12	Search "meta analysis"[Title]	92580	17:02:15
#11	Search #9 AND #10	0	17:01:48
#10	Search meta-analysis[Title]	92580	17:01:31
#9	Search #7 AND #8	47	17:01:15
#8	Search "randomized controlled trial"[Title]	37883	17:00:55
#7	Search #2 AND #6	419	17:00:26
#6	Search #3 OR #4 OR #5	1071830	17:00:10
#5	Search stress[Title/Abstract]	705132	16:59:51
#4	Search depression[Title/Abstract]	320520	16:59:23
#3	Search anxiety[Title/Abstract]	179122	16:59:07
#2	Search mindfulness meditation[Title/Abstract]	792	

Steps to generate this table:

1. Run your query on pubmed (https://www.pubmed.gov)
2. Click on 'Advanced' and save all queries as 'Add to history'
3. Once you are done with the query, click on 'Download history'
4. This will create a 'history.csv' file on your local hard drive, save it and use it to generate a table like above.

If we click on item number 16, we see it lists 7 studies that are meta analyses on mindfulness meditation for adults on stress or anxiety or depression relief. Now based on the titles and abstract, let's see if any of them are any good. On closer inspection, no article was found to be suitable for our analyses.

We also conducted a search on the results of 47 studies we obtained (see search #9 on the table) and we narrowed down the list of studies to 9 based on the following criteria:

- Clinical trials (we would only select those that were randomised controlled trials)
- those that had free full text or full texts available
- those that were published within the last 10 years
- those that were conducted on humans
- those that were published in English language
- those that were published in adults

When we did that, we initially found that 9 studies qualified for this (see the screenshot):

Figure 1: Screenshot of qualified studies

On closer inspection, we read the titles and abstracts of each of these studies and found that based on our PICO criteria:

1. Barrett B, Hayney MS, Muller D, Rakel D, Brown R, Zgierska AE, Barlow S, Hayer S, Barnet JH, Torres ER, Coe CL. Meditation or exercise for preventing acute respiratory infection (MEPARI-2): A randomized controlled trial. PLoS One. 2018 Jun 22;13(6):e0197778. doi: 10.1371/journal.pone.0197778. eCollection 2018. PubMed PMID: 29933369; PubMed Central PMCID: PMC6014660.

2. Ho RTH, Wan AHY, Chan JSM, Ng SM, Chung KF, Chan CLW. Study protocol on comparative effectiveness of mindfulness meditation and qigong on psychophysiological outcomes for patients with colorectal cancer: a randomized controlled trial. BMC Complement Altern Med. 2017 Aug 8;17(1):390. doi: 10.1186/s12906-017-1898-6. PubMed PMID: 28789681; PubMed Central PMCID: PMC5549330.

3. van der Zwan JE, de Vente W, Huizink AC, Bögels SM, de Bruin EI. Physical activity, mindfulness meditation, or heart rate variability biofeedback for stress reduction: a randomized controlled trial. Appl Psychophysiol Biofeedback. 2015 Dec;40(4):257-68. doi: 10.1007/s10484-015-9293-x. PubMed PMID: 26111942; PubMed Central PMCID: PMC4648965.

4. Taren AA, Gianaros PJ, Greco CM, Lindsay EK, Fairgrieve A, Brown KW, Rosen RK, Ferris JL, Julson E, Marsland AL, Bursley JK, Ramsburg J, Creswell JD. Mindfulness meditation training alters stress-related amygdala resting state functional connectivity: a randomized controlled trial. Soc Cogn Affect Neurosci. 2015 Dec;10(12):1758-68. doi: 10.1093/scan/nsv066. Epub 2015 Jun 5. PubMed PMID: 26048176; PubMed Central PMCID: PMC4666115.

5. Bower JE, Crosswell AD, Stanton AL, Crespi CM, Winston D, Arevalo J, Ma J, Cole SW, Ganz PA. Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. Cancer. 2015 Apr 15;121(8):1231-40. doi: 10.1002/cncr.29194. Epub 2014 Dec 23. Erratum in: Cancer. 2015 Jun 1;121(11):1910. PubMed PMID: 25537522; PubMed Central PMCID: PMC4393338.

6. Ong JC, Manber R, Segal Z, Xia Y, Shapiro S, Wyatt JK. A randomized controlled trial of mindfulness meditation for chronic insomnia. Sleep. 2014 Sep 1;37(9):1553-63. doi: 10.5665/sleep.4010. PubMed PMID: 25142566; PubMed Central PMCID: PMC4153063.

7. Boettcher J, Aström V, Påhlsson D, Schenström O, Andersson G, Carlbring P. Internet-based mindfulness treatment for anxiety disorders: a randomized controlled trial. Behav Ther. 2014 Mar;45(2):241-53. doi: 10.1016/j.beth.2013.11.003. Epub 2013 Nov 25. PubMed PMID: 24491199.

8. Hoge EA, Bui E, Marques L, Metcalf CA, Morris LK, Robinaugh DJ, Worthington JJ, Pollack MH, Simon NM. Randomized controlled trial of mindfulness meditation for generalized anxiety disorder: effects on anxiety and stress reactivity. J Clin Psychiatry. 2013 Aug;74(8):786-92. doi: 10.4088/JCP.12m08083. PubMed PMID: 23541163; PubMed Central PMCID: PMC3772979.

9. Gross CR, Kreitzer MJ, Thomas W, Reilly-Spong M, Cramer-Bornemann M, Nyman JA, Frazier P, Ibrahim HN. Mindfulness-based stress reduction for solid organ transplant recipients: a randomized controlled trial. Altern Ther Health Med. 2010 Sep-Oct;16(5):30-8. PubMed PMID: 20882729; PubMed Central PMCID: PMC3076132.

As you will see,

- The first study does not meet our criteria, as the outcome is different from what we are planning to study
- The second study will not meet our criteria as we are not interested in any particular subgroup of patients or individuals, all adults, so it does not meet our 'P' criterion
- The third study 'may' meet our criterion, so we will select this study for the present
- The fourth study also may meet our criteria for selection from a more physiological perspective so we will keep this study for analysis
- The fifth study will not meet our criteria as it has breast cancer survivors for 'p', while we have decided to work for all adults, not just particular subgroups
- The sixth study will also not meet our requirement as we are not interested to study insomnia
- The seventh study may meet our criteria
- The eighth study may meet our criteria as well
- The ninth study will not meet our criteria as we are interested in all adults or patients, not a particular subgroup

So, based on our PICO criteria, we decide to include the following four studies for our analyses:

1. van der Zwan JE, de Vente W, Huizink AC, Bögels SM, de Bruin EI. Physical activity, mindfulness meditation, or heart rate variability biofeedback for stress reduction: a randomized controlled trial. Appl Psychophysiol Biofeedback. 2015 Dec;40(4):257-68. doi: 10.1007/s10484-015-9293-x. PubMed PMID: 26111942; PubMed Central PMCID: PMC4648965.

2. Taren AA, Gianaros PJ, Greco CM, Lindsay EK, Fairgrieve A, Brown KW, Rosen RK, Ferris JL, Julson E, Marsland AL, Bursley JK, Ramsburg J, Creswell JD. Mindfulness meditation training alters stress-related amygdala resting state functional connectivity: a randomized controlled trial. Soc Cogn Affect Neurosci. 2015 Dec;10(12):1758-68. doi: 10.1093/scan/nsv066. Epub 2015 Jun 5. PubMed PMID: 26048176; PubMed Central PMCID: PMC4666115.

3. Boettcher J, Aström V, Påhlsson D, Schenström O, Andersson G, Carlbring P. Internet-based mindfulness treatment for anxiety disorders: a randomized controlled trial. Behav Ther. 2014 Mar;45(2):241-53. doi: 10.1016/j.beth.2013.11.003. Epub 2013 Nov 25. PubMed PMID: 24491199.

4. Hoge EA, Bui E, Marques L, Metcalf CA, Morris LK, Robinaugh DJ, Worthington JJ, Pollack MH, Simon NM. Randomized controlled trial of mindfulness meditation for generalized anxiety disorder: effects on anxiety and stress reactivity. J Clin Psychiatry. 2013 Aug;74(8):786-92. doi: 10.4088/JCP.12m08083. PubMed PMID: 23541163; PubMed Central PMCID: PMC3772979.

We will obtain the full texts of these four studies and on the basis of reading the full texts of these four studies, we will now synthesise the evidence. We will input the methods section and the results section of these studies to a GRADEPro data sheet and then we will analyse the results.

Search and retrieval of results from Cochrane Database of Systematic Reviews

Alternatively, you can search and retrieve results from the Cochrane Database of Systematic Reviews. To do so, visit the following website,

https://www.cochranelibrary.com/advanced-search/search-manager

... and start searching. We used a similar set of search terms we used for pubmed and we came up with the following search results:

Search Name: mindfulness Date Run: 03/10/2019 00:23:32 Comment:

ID Search Hits #1 mindfulness meditation 1183 #2 anxiety 47635 #3 depression 70885 #4 #3 OR #2 94671 #5 #1 AND #4 586 #6 stress 54016 #7 #3 OR #2 OR #6 135490 #8 #7 AND #1 with Cochrane Library publication date Between Jan 2014 and Dec 2018, in Cochrane Reviews 34

You can produce this search result document by selecting "Print" and saving the printout of the search result to a text file from the list of Cochrane library search results.

We will now go through the 34 search results and see which ones will meet our needs. We will identify only ONE Cochrane Review out of the following list to meet our needs. You can identify more than one meta analysis and work on that basis, but to keep thing simple, we will work on only one of them. So, let's take a look at the list of 34 reviews we have identified so far (I have annotated in bold letters about whether they can be accepted or not):

Ali, A, Hall, I., Blickwedel, J., & Hassiotis, A. (2015). Behavioural and cognitive-behavioural interventions for outwardly-directed aggressive behaviour in people with intellectual disabilities. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD003406.pub4

Reject this as it does not have the right "P"

Bidonde, J, Busch, A., Webber, SC, Schachter, CL, Danyliw, A, Overend, TJ, Richards, RS, & Rader, T. (2014). Aquatic exercise training for fibromyalgia. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD011336 **Reject as it does not have the right Outcome or the population**

Broderick, J, & Vancampfort, D. (2017). Yoga as part of a package of care versus standard care for schizophrenia. Cochrane Database of Systematic Reviews, (9). https://doi.org/10.1002/14651858.CD012145.pub2 **Wrong intervention, we are not interested in yoga**

Cox, GR, Callahan, P., Churchill, R, Hunot, V, Merry, SN, Parker, AG, & Hetrick, S. (2014). Psychological therapies versus antidepressant medication, alone and in combination for depression in children and adolescents. Cochrane Database of Systematic Reviews, (11). https://doi.org/10.1002/14651858.CD008324.pub3 **Wrong population**

Cramer, H, Lauche, R., Klose, P, Lange, S, Langhorst, J., & Dobos, G. (2017). Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database of Systematic Reviews, (1). https://doi.org/10.1002/14651858.CD010802.pub2 **Wrong population and wrong outcome**

Eccleston, C, Hearn, L., & Williams, A. (2015). Psychological therapies for the management of chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD011259.pub2 **Wrong outcome**

Felbel, S, Meerpohl, J., Monsef, I, Engert, A., & Skoetz, N. (2014). Yoga in addition to standard care for patients with haematological malignancies. Cochrane Database of Systematic Reviews, (6). https://doi.org/10.1002/14651858.C
Gates, PJ, Sabioni, P., Copeland, J, Le Foll, B., & Gowing, L. (2016). Psychosocial interventions for cannabis use disorder. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD005336.pub4
Gendron, LM, Nyberg, A., Saey, D, Maltais, F., & Lacasse, Y. (2018). Active mind-body movement therapies as an adjunct to or in comparison with pulmonary rehabilitation for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD012290.pub2
Goldbeck, L, Fidika, A., Herle, M., & Quittner, A. (2014). Psychological interventions for individuals with cystic fibrosis and their families. Cochrane Database of Systematic Reviews, (6). https://doi.org/10.1002/14651858.CD003148
Hawton, K, Witt, K., Taylor Salisbury, TL, Arensman, E, Gunnell, D, Hazell, P, Townsend, E., & van Heeringen, K. (2016). Psychosocial interventions for self-harm in adults. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD012189 Hetrick, SE, Cox, G., Witt, KG, Bir, JJ, & Merry, S. (2016). Cognitive behavioural therapy (CBT), third-wave CBT and interpersonal therapy (IPT) based interventions for preventing depression in children and adolescents. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD003380.pub4 Imai, H, Tajika, A., Chen, P, Pompoli, A., & Furukawa, T. (2016). Psychological therapies versus pharmacological interventions for panic disorder with or without agoraphobia in adults. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD011170.pub2 Import errors found: Line 18, column 14: Expected "," or "=" but "d" found. (n.d.). Jackson, CF, Makin, S., & Baker, G. (2015). Neuropsychological and psychological interventions for people with newly diagnosed epilepsy. Cochrane Database of Systematic Reviews, (7). https://doi.org/10.1002/14651858.CD011311.pub2 Jassim, GA, Whitford, D., Hickey, A., & Carter, B. (2015). Psychological interventions for women with non-metastatic breast cancer. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD008729.pub2 Kew, KM, Nashed, M., Dulay, V., & Yorke, J. (2016). Cognitive behavioural therapy (CBT) for adults and adolescents with asthma. Cochrane Database of Systematic Reviews, (9). https://doi.org/10.1002/14651858.CD011818.pub2 Kuster, AT, Dalsbo, T., Luong Thanh, BY, Agarwal, A, Durand-Moreau, QV, & Kirkehei, I. (2017). Computer-based versus in-person interventions for preventing and reducing stress in workers. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD011899.pub2 Lawrence, M, Celestino Junior, F., Matozinho, HHS, Govan, L, Booth, J., & Beecher, J. (2017). Yoga for stroke rehabilitation. Cochrane Database

of Systematic Reviews, (12). https://doi.org/10.1002/14651858.CD011483.pub2 Levack, WMM, Weatherall, M., Hay-Smith, EJC, Dean, SG, McPherson, K., & Siegert, R. (2015). Goal setting and strategies to enhance goal pursuit for adults with acquired disability participating in rehabilitation. Cochrane Database of Systematic Reviews, (7). https://doi.org/10.1002/14651858.CD009727.pub2 Liu, Z, Sun, Y., & Zhong, B. (2018). Mindfulness-based stress reduction for family carers of people with dementia. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD012791.pub2 Madden, K, Middleton, P., Cyna, AM, Matthewson, M., & Jones, L. (2016). Hypnosis for pain management during labour and childbirth. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD009356.pub3 Martlew, J, Pulman, J., & Marson, A. (2014). Psychological and behavioural treatments for adults with non-epileptic attack disorder. Cochrane Database of Systematic Reviews, (2). https://doi.org/10.1002/14651858.CD006370.pub2 Michaelis, R, Tang, V., Wagner, JL, Modi, AC, LaFrance Jr, WC, Goldstein, LH, Lundgren, T., & Reuber, M. (2017). Psychological treatments for people with epilepsy. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD012081.pub2 Patel, N, Kellezi, B., & Williams, A. (2014). Psychological, social and welfare interventions for psychological health and well-being of torture survivors. Cochrane Database of Systematic Reviews, (11). https://doi.org/10.1002/14651858.CD009317.pub2 Pompoli, A, Furukawa, T., Imai, H, Tajika, A, Efthimiou, O., & Salanti, G. (2016). Psychological therapies for panic disorder with or without agoraphobia in adults: A network meta-analysis. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD011004.pub2 Ruotsalainen, JH, Verbeek, J., Marine, A., & Serra, C. (2015). Preventing occupational stress in healthcare workers. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD002892.pub5 Salhofer, I, Will, A., Monsef, I., & Skoetz, N. (2016). Meditation for adults with haematological malignancies. Cochrane Database of Systematic Reviews, (2). https://doi.org/10.1002/14651858.CD011157.pub2 Smith, CA, Levett, K., Collins, CT, Armour, M, Dahlen, HG, & Suganuma, M. (2018). Relaxation techniques for pain management in labour. Cochrane Database of Systematic Reviews, (3). https://doi.org/10.1002/14651858.CD009514.pub2 Thabrew, H, Stasiak, K., Hetrick, SE, Donkin, L, Huss, JH, Highlander, A, Wong, S., & Merry, S. (2018a). Psychological therapies for anxiety and depression in children and adolescents with long-term physical conditions. Cochrane Database of Systematic Reviews, (12). https://doi.org/10.1002/14651858.CD012488.pub2 Thabrew, H, Stasiak, K., Hetrick, SE, Wong, S, Huss, JH, & Merry, S. (2018b). E-Health interventions for anxiety and depression in children and adolescents with long-term physical conditions. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD012489.pub2 Theadom, A, Cropley, M., Smith, HE, Feigin, VL, & McPherson, K. (2015). Mind and body therapy for fibromyalgia. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD001980.pub3 Verkuijlen, J, Verhaak, C., Nelen, WLDM, Wilkinson, J., & Farquhar, C. (2016). Psychological and educational interventions for subfertile men and women. Cochrane Database of Systematic Reviews, (3). https://doi.org/10.1002/14651858.CD011034.pub2 Wilkinson, P, & Izmeth, Z. (2016). Continuation and maintenance treatments for depression in older people. Cochrane Database of Systematic Reviews, (9). https://doi.org/10.1002/14651858.CD006727.pub3

As you can see in this list, ***NONE*** of the titles match our requirements, so we need to search again. This time, we search with less restrictive terms to identify one or two reviews that will EXACTLY fit our criteria. Here is the list of search terms:

Date Run: 03/10/2019 01:13:04 Comment:

ID Search Hits #1 mindfulness meditation with Cochrane Library publication date Between Jan 2014 and Dec 2018, in Cochrane Reviews 34 #2 MBSR 646 #3 anxiety 47635 #4 depression 70885 #5 #4 OR #3 94671 #6 #1 AND #5 34 #7 stress 54016 #8 #4 OR #3 OR #7 135490 #9 #8 AND #1 with Cochrane Library publication date Between Jan 2014 and Dec 2018, in Cochrane Reviews 34 #10 #2 OR #1 677 #11 #10 AND #8 with Cochrane Library publication date Between Jan 2014 and Dec 2018, in Cochrane Reviews 35 #12 ("mindfulness meditation"):ti AND (stress):ti,ab,kw (Word variations have been searched) in Cochrane Reviews 0 #13 ("mindfulness meditation"):ti AND (anxiety):ti,ab,kw in Cochrane Reviews 0 #14 "MBSR":ti AND (anxiety):ti 16 #15 MBSR:ti in Cochrane Reviews 0 #16 MBSR:ti OR "mindfulness based stress reduction":ti in Cochrane Reviews 2 #17 MBSR:ti in Cochrane Reviews 0 #18 mindfulness:ti

in Cochrane Reviews 2 #19 "mindfulness":ti,ab in Cochrane Reviews 22 #20 meditation:ti,ab in Cochrane Reviews 20 #21 #19 OR #20 in Cochrane Reviews 37

And here is the list of 37 studies listed in #21

Ali, A, Hall, I., Blickwedel, J., & Hassiotis, A. (2015). Behavioural and cognitive-behavioural interventions for outwardly-directed aggressive behaviour in people with intellectual disabilities. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD003406.pub4 Bahar-Fuchs, A, Martyr, A., Goh, AMY, Sabates, J., & Clare, L. (2019). Cognitive training for people with mild to moderate dementia. Cochrane Database of Systematic Reviews, (3). https://doi.org/10.1002/14651858.CD013069.pub2 Candy, B, Jones, L., Varagunam, M, Speck, P, Tookman, A., & King, M. (2012). Spiritual and religious interventions for well-being of adults in the terminal phase of disease. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD007544.pub2 Cramer, H, Lauche, R., Klose, P, Lange, S, Langhorst, J., & Dobos, G. (2017). Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database of Systematic Reviews, (1). https://doi.org/10.1002/14651858.CD010802.pub2 Eccleston, C, Fisher, E., Thomas, KH, Hearn, L, Derry, S, Stannard, C, Knaggs, R., & Moore, R. (2017). Interventions for the reduction of prescribed opioid use in chronic non-cancer pain. Cochrane Database of Systematic Reviews, (11). https://doi.org/10.1002/14651858.CD010323.pub3 Felbel, S, Meerpohl, J., Monsef, I, Engert, A., & Skoetz, N. (2014). Yoga in addition to standard care for patients with haematological malignancies. Cochrane Database of Systematic Reviews, (6). https://doi.org/10.1002/14651858.CD010146.pub2 Forneris, CA, Nussbaumer-Streit, B., Morgan, LC, Greenblatt, A, Van Noord, MG, Gaynes, BN, Wipplinger, J, Lux, LJ, Winkler, D., & Gartlehner, G. (2019). Psychological therapies for preventing seasonal affective disorder. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD011270.pub3 Gates, PJ, Sabioni, P., Copeland, J, Le Foll, B., & Gowing, L. (2016). Psychosocial interventions for cannabis use disorder. Cochrane Database of Systematic Reviews, (5). https://doi.org/10.1002/14651858.CD005336.pub4 Gendron, LM, Nyberg, A., Saey, D, Maltais, F., & Lacasse, Y. (2018). Active mind-body movement therapies as an adjunct to or in comparison with pulmonary rehabilitation for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD012290.pub2 Gertler, P, Tate, R., & Cameron, I. (2015). Non-pharmacological interventions for depression in adults and children with traumatic brain injury. Cochrane Database of Systematic Reviews, (12). https://doi.org/10.1002/14651858.CD0 Grande, AJ, Reid, H., Thomas, EE, Nunan, D., & Foster, C. (2016). Exercise prior to influenza vaccination for limiting influenza incidence and its related complications in adults. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD011857.pub2 Gross, A, Kay, T., Paquin, JP, Blanchette, S, Lalonde, P, Christie, T, Dupont, G, Graham, N, Burnie, SJ, Gelley, G, Goldsmith, CH, Forget, M, Hoving, JL, Bronfort, G., & Santaguida, P. (2015). Exercises for mechanical neck disorders. Cochrane Database of Systematic Reviews, (1). https://doi.org/10.1002/14651858.CD004250.pub5 Hartley, L, Mavrodaris, A., Flowers, N, Ernst, E., & Rees, K. (2017). Transcendental meditation for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews, (11). https://doi.org/10.1002/14651858.CD010359.pub3 Haruna, M, Matsuzaki, M., Ota, E, Shiraishi, M, Hanada, N., & Mori, R. (2019). Guided imagery for treating hypertension in pregnancy. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD011337.pub Hillier, SL, Louw, Q., Morris, L, Uwimana, J., & Statham, S. (2010). Massage therapy for people with HIV/AIDS. Cochrane Database of Systematic Reviews, (1). https://doi.org/10.1002/14651858.CD007502.pub2 Import errors found: Line 182, column 14: Expected "," or "=" but "d" found.line 541, column 14: Expected "," or "=" but. (n.d.). Khianman, B, Pattanittum, P., Thinkhamrop, J., & Lumbiganon, P. (2012). Relaxation therapy for preventing and treating preterm labour. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD007426.pub2 Krisanaprakornkit, T, Ngamjarus, C., Witoonchart, C., & Piyavhatkul, N. (2010). Meditation therapies for attention-deficit/hyperactivity disorder (ADHD). Cochrane Database of Systematic Reviews, (6). https://doi.org/10.1002/14651858.CD006507.pub2 **Krisanaprakornkit, T, Sriraj, W., Piyavhatkul, N., & Laopaiboon, M. (2006). Meditation therapy for anxiety disorders. Cochrane Database of Systematic Reviews, (1)**. https://doi.org/10.1002/14651858.CD00

Kuster, AT, Dalsbo, T., Luong Thanh, BY, Agarwal, A, Durand-Moreau, QV, & Kirkehei, I. (2017). Computer-based versus in-person interventions for preventing and reducing stress in workers. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD011899.pub2 Liu, Z, Sun, Y., & Zhong, B. (2018). Mindfulness-based stress reduction for family carers of people with dementia. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD012791.pub2 Marc, I, Toureche, N., Ernst, E, Hodnett, ED, Blanchet, C, Dodin, S., & Njoya, M. (2011). Mind-body interventions during pregnancy for preventing or treating women's anxiety. Cochrane Database of Systematic Reviews, (7). https://doi.org/10.1002/14651858.CD007559.pub2 Martis, R, Crowther, C., Shepherd, E, Alsweiler, J, Downie, MR, & Brown, J. (2018). Treatments for women with gestational diabetes mellitus: An overview of Cochrane systematic reviews. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD012327.pu Michaelis, R, Tang, V., Wagner, JL, Modi, AC, LaFrance Jr, WC, Goldstein, LH, Lundgren, T., & Reuber, M. (2017). Psychological treatments for people with epilepsy. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD012081.pub2 Panebianco, M, Sridharan, K., & Ramaratnam, S. (2017). Yoga for epilepsy. Cochrane Database of Systematic Reviews, (10). https://doi.org/10.1002/14651858.CD001524.pub3 Ruotsalainen, JH, Verbeek, J., Marine, A., & Serra, C. (2015). Preventing occupational stress in healthcare workers. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD002892.pub5 Salhofer, I, Will, A., Monsef, I., & Skoetz, N. (2016). Meditation for adults with haematological malignancies. Cochrane Database of Systematic Reviews, (2). https://doi.org/10.1002/14651858.CD011157.pub2 Schell, LK, Monsef, I., Wockel, A., & Skoetz, N. (2019). Mindfulness-based stress reduction for women diagnosed with breast cancer. Cochrane Database of Systematic Reviews, (3). https://doi.org/10.1002/14651858.CD011518.pub2 Shrestha, N, Kukkonen-Harjula, K., Verbeek, JH, Ijaz, S, Hermans, V., & Pedisic, Z. (2018). Workplace interventions for reducing sitting at work. Cochrane Database of Systematic Reviews, (12). https://doi.org/10.1002/14651858.CD0 Smith, CA, Levett, K., Collins, CT, Armour, M, Dahlen, HG, & Suganuma, M. (2018). Relaxation techniques for pain management in labour. Cochrane Database of Systematic Reviews, (3). https://doi.org/10.1002/14651858.CD009514. Theadom, A, Cropley, M., Smith, HE, Feigin, VL, & McPherson, K. (2015). Mind and body therapy for fibromyalgia. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD001980.pub3 Treanor, CJ, McMenamin, U., O'Neill, RF, Cardwell, CR, Clarke, MJ, Cantwell, M., & Donnelly, M. (2016). Non-pharmacological interventions for cognitive impairment due to systemic cancer treatment. Cochrane Database of Systematic Reviews, (8). https://doi.org/10.1002/14651858.CD011325.pub2 Treanor, CJ, Santin, O., Prue, G, Coleman, H, Cardwell, CR, O'Halloran, P., & Donnelly, M. (2019). Psychosocial interventions for informal caregivers of people living with cancer. Cochrane Database of Systematic Reviews, (6). https://doi.org/10.1002/14651858.CD009912.pub2 Wieland, LS, Shrestha, N., Lassi, ZS, Panda, S, Chiaramonte, D., & Skoetz, N. (2019). Yoga for treating urinary incontinence in women. Cochrane Database of Systematic Reviews, (2). https://doi.org/10.1002/14651858.CD012668.pub2 Wu, S, Kutlubaev, M., Chun, HYY, Cowey, E, Pollock, A, Macleod, MR, Dennis, M, Keane, E, Sharpe, M., & Mead, G. (2015). Interventions for post-stroke fatigue. Cochrane Database of Systematic Reviews, (7). https://doi.org/10.1002/14651858.CD007030.pub3 Yang, ZY, Zhong, H., Mao, C, Yuan, JQ, Huang, YF, Wu, XY, Gao, YM, & Tang, J. (2016). Yoga for asthma. Cochrane Database of Systematic Reviews, (4). https://doi.org/10.1002/14651858.CD010346.pub2

Scanning the list of titles, we see that there is only one study or one review that has addressed our needs, that of addressing anxiety disorders using mindfulness based meditation therapy. So we will select this one Cochrane Review for our appraisal:

Krisanaprakornkit, T, Sriraj, W., Piyavhatkul, N., & Laopaiboon, M. (2006). Meditation therapy for anxiety disorders. *Cochrane Database of Systematic Reviews*, (1). https://doi.org/10.1002/14651858.

In the next step, we will show you how to use these four articles to conduct a meta-analysis and/or input them to GRADEpro GDT and work with the evidence. That would be step 3

Step 3. Input data from a Cochrane Review or a group of studies to Gradepro GDT

Now that you have either four randomised controlled trials or one large Cochrane Review, we will use BOTH to generate the evidence tables using Gradepro GDT. First, we will summarise the key points about Gradepro approach:

- Gradepro works on the basis of GRADE, which is used for developing guidelines. Here, however, we will only use GRADE for critical appraisal of a body of evidence
- GRADE is used to appraise a body of evidence specified for an outcome. For more information on GRADE, I recommend you read the article by Gordon Guyatt et al (2011) to learn about the principles of GRADE guidelines (Guyatt et al., 2011). This article has summarised the key principles of GRADE. In GRADE, an outcome can be studied by multiple studies, or multiple studies can study or report on a single outcome. As outcomes are key issues in clinical decision making and also for making guidelines for action, therefore, in evidence appraisal, how quality of studies affect appraising individual outcomes is important.
- The quality of this overall evidence is appraised on the basis of the strength of association, the risk of bias, whether the outcome was indirectly or directly measured, and whether the outcome was precise or in other words, whether the effect measure of the association was definitely in one direction. In our appraisal we would make these and other considerations as we will explain in the paragraphs below

How to use GRADEpro GDT

- First of all, access the following website: https://gdt.gradepro.org/app/
- If you have not created an account, create an account and log in with the email address you registered.

When you do that, it will look like this:

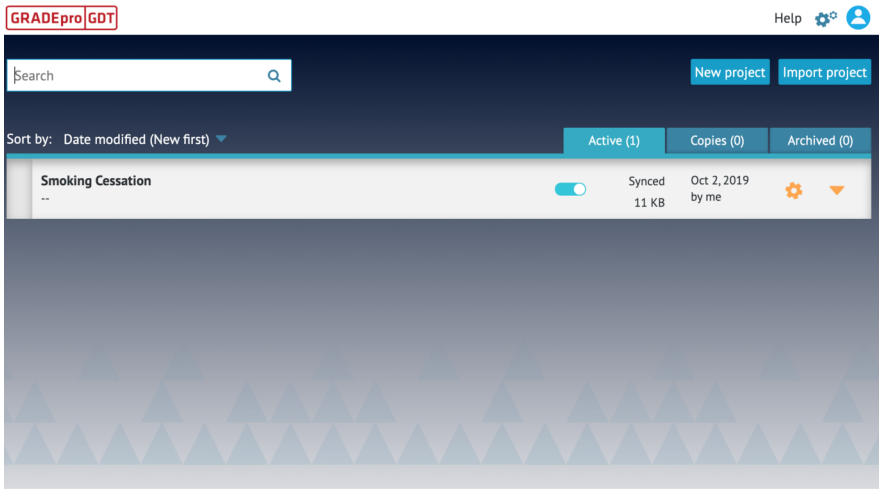

Figure 2: GRADEpro screen

Step by step:

1. Create a new project. Give the project a name and a type, select, “Grade evidence profile”

2. Click on the button labelled "Add management question"
3. Enter your PICO formatted question, in our case that would be: "Should mindfulness meditation vs. non-mindfulness based approaches be used for stress?"; if you wan to use for specific communities, mention that instead of the outcome. But I recommend you use 'stress' or another outcome based word or expression here. You can add up to 12 management questions
4. Then save the management question by clicking on the save icon that looks like a floppy disk.
5. Now click on "Add outcome"

Take a break: we will show you how to appraise individiual articles that are individual or results pooled AND abstraction of data from a Cochrane Review

How to add data from single studies

Let's start with the simplest of them all: take a SINGLE study and add data from a single study to the Gradepro table. The idea is not different for single as opposed to pooled studies. In each case you will need to specify the outcomes first, and then, based on your reading of the study, you will identify individual values and plug in those values in the individual cells. So let's get started with a single study and then we will build up the rest of the entries.We will use the vander Zwan article to put in data.

Judith van der Zwan and colleagues (2015) conducted a study on 76 participants and tested the effectiveness of physical activity (PA), mindfulness meditation (MM), or heart rate variability biofeedback (HRV-BF) for reducing stress. They randomly allocated these 76 individuals into the three modalities of treatment and conducted the study for 5 weeks. They obtained data on their stress levels using a questionnaire at the beginning of the study, during the study, and 6 weeks after conclusion of the study. If you want to follow along, open up the following webpage, download the PDF file and follow along

https://link.springer.com/content/pdf/10.1007%2Fs10484-015-9293-x.pdf

Follow the sequence.

First of all, fill in the outcomes information:

1. Log into gradepro, start a project or open your existing project, and set up the question till the step of "Add outcome"
2. We will start with adding the outcome. Here, we will include only ONE outcome (however, you are not restricted to one outcome, you can and should add as many outcomes that are relevant to your research question). We will select the 'anxiety' as an outcome. Let's fill in the entries
3. For the main outcome, we write, "Anxiety"
4. Short Name: 'Anxiety"
5. Assessed/measured with: "DASS"
6. Length of follow up group: We leave the first entry blank as it does not fit the proper unit (as they did a total of five weeks of study), in the middle box, we write '5' as they had five weeks of study, and in the third box, we select 'weeks'
7. In the 'Type', we select continuous as they used Cohen's "d", which is a measurement of standardised mean difference in the pre-study and post follow up scores; in the second box, we select 'single study'
8. For "Type of scale": "Ratio/interval measurement scale"
9. For conventional lower and upper limit of scale: note from the methods section of the paper that the DASS scale had three subscales; each subscale had seven items; each item had the lowest possible score of 0 and highest possible score of 3, therefore the theoretical lowest and highest scores would be 0 and 21. Enter these figures in the empty boxes

10. Then we click on the 'floppy disc' to save the entry. At this point, if you want to add another outcome, you can do so. For the sake of brevity, we will move on.

Second, fill in the 'Certainty Assessment' section next – work from left to right

1. Number of studies: 1, then click 'Apply'
2. Study design: Randomised trial
3. Risk of bias: You have three choices ("not serious", "serious", and "very serious"). This is a subjective choice but to make the decision, you must read the methods section of the study. This was a randomised controlled trial, but there were a few things that limited the scope of the study - first, they did not report 'how' exactly they 'randomised' the participants in their study. Second, this being a lifestyle intervention trial where they tested physical activity, meditation, device based assessment, it was impossible for them to 'blind' the participants or themselves to be agnostic of who received what interventions. Because of these limitations, we would rate this section as 'serious' and proceed to add explanations that we have provided here. If you add the explanations, and save it, the programme adds an 'a' to the box
4. Inconsistency: For a single study that has several outcomes, check the 'size' of the effect estimate and the 'direction' of the effect estimates. Check the results section of the paper. In this paper, study Table 2 and columns "pre-test-post-test' and 'pre-test-follow-up' and note the columns under 'd' ('d' = Cohen's 'd', or standardised mean difference). You will see that the numbers are similar for stress, anxiety, and deperession for DASS, with very little variablity. Based on this, we will decide that inconsistency is not a serious limitation here. On the other hand, there may be situations where for similar outcomes and using similar tests, the magnitude and direction of the effect estimates might differ at least by 20% or more (candidates for 'serious' inconsistencies). For pooled studies, we would refer to I-squared values to test for heterogeneity in the estimates plus variation around the point estimates. Here, we would come to the conclusion that inconsistency is 'not serious'. Select the drop down box to indicate that.
5. imprecision: In order to decide imprecision, study the associated p-value and where available 95% confidence interval around the point estimate. The authors in the present study did not report 95% confidence interval around the point estimate, but they did report p-values. On close inspection, you can see that while there were some drop in the scores of anxiety, the between group estimates did not meet statistical or clinical significance. This is the reason, we will rate this as imprecise.
6. Other considerations: We will consider four other considerations - publication bias (this is not an issue with single studies), large effect size (we did not find large effect size in this study), dose-response effect (the authors did not report dose-response effect and this was not an issue here), and whether plausible confounding could have impacted the effects (here, because we studied randomised trial, this was not an issue). Accordingly, we would have made these choices. Now you see that the 'certainty' box is labelled as 'low'. This indicates that we would have 'low' level of certainty or surety in interpreting the findings of this study

Third, fill in the summary of findings section next

1. Number of patients on the mindfulness meditation arm: 24
2. Number of patients on the non-mindfulness approach: 42
3. Note that the relative effect is now greyed out, so fill in the 'absolute effect' using the Cohen's d but note that you cannot fill in the 95% CI as this was not reported. The absolute effect is: -0.24 SD lower as we have decided to study standardised mean difference, and we have chosen to report the difference between pre-intervention and post intervention. If you want to report both pre-intervention and post intervention plus pre-intervention and post follow up, you will need to add another outcome and report it as such.

This completes reporting of one study, a single study. We will move on, and now we will fill in findings from a Cochrane review.

How to use Cochrane Review and add information to GRADEpro GDT

Now that we have added the findings from a single study, let us add findings from a Cochrane review. We will use the following Cochrane review to add the findings:

Krisanaprakornkit, T, Sriraj, W., Piyavhatkul, N., & Laopaiboon, M. (2006). Meditation therapy for anxiety disorders. *Cochrane Database of Systematic Reviews*, (1). https://doi.org/10.1002/14651858.

As before, download and open the PDF of the Cochrane review and remember to open the 'full text' of the review. As before, we will follow this in three steps:

- We will add the outcomes information
- We will next fill in the certainty assessment
- We will fill in the summary of findings information

To do this, as before, we will refer to the methods and results of the paper itself. To provide a brief overview of this paper, this is a fairly old paper (almost 13 years old at the time of writing this tutorial) and as you can see, this is a Cochrane meta analysis. We will use the following PDF to abstract information and fill the GDT

Step by step:

1. Add outcome (assuming that you have already set up your questions). Open up the full text and read the methods section. The outcome measure we will report here is 'clinical state of anxiety at the end of trial (continuous measure)'; so note we write:
2. Long name: 'Clinical state of anxiety'
3. Short name: 'Anxiety'
4. Measured with: ' different scales and inventories' (this is because in this meta-analysis the author mentioned a number of different scales and inventories rather than single instruments: in cases where the author would indicate that they used a single scale to measure anything, you can mention that)
5. Type: 'continuous'
6. Type: 'pooled'
7. Length of follow up: We leave it blank as different studies may have different lengths of follow up so we are not sure
8. Choose type of scale: 'Ratio/interval measurement scale' (but as different types of scales and instruments were used, we are not sure about the score range and we cannot fill in the rest of the boxes)

At this stage click on the save button and move to the next step.

Step 2: Fill in the certainty assessment

Number of studies: 2: Read the results section of this meta-analysis and you see that they have 2 studies

Study design: Randomised controlled trials

Risk of bias: Serious as the first study had issues with allocation concealment, and the second study did not describe how they randomised and both studies had issues with not being able to blind participants and uneven ratios of male:female. These would go into explanations

Inconsistency: Serious (you could also rate very serious if you want as one of these studies reported some measures but the other did not, so the findings were not consistent across the studies)

Indirectness: Serious (While the studies used direct measurement of anxiety states from participants using scales, none of the findings or measurements 'directly' reported anxiety state changes)

Imprecision: Not Serious (We have data from only one study and the point estimate relevant for anxiety according to the perceived stress scale is -7.57 (95%CI -13.06, -2.08 on 14 participants)

Other considerations: We found that this meta analysis was based on only two studies, one of which was low quality and did not report anything, the other had reported some measures. It is possible that other studies were conducted but the authors missed them, and being based on one study, they did not report or examine formal publication bias. However the effect size was reasonably large and as they had randomisatio, most confounding variables were adjusted for.

We now move to the Summary of findings but the notable thing here is that, for this outcome, the level of quality of evidence is very low. Let's move to the summary of findings:

Step 3: Fill in Summary of Findings

For this meta analysis , we will fill in the summary of findings tables from the following data:

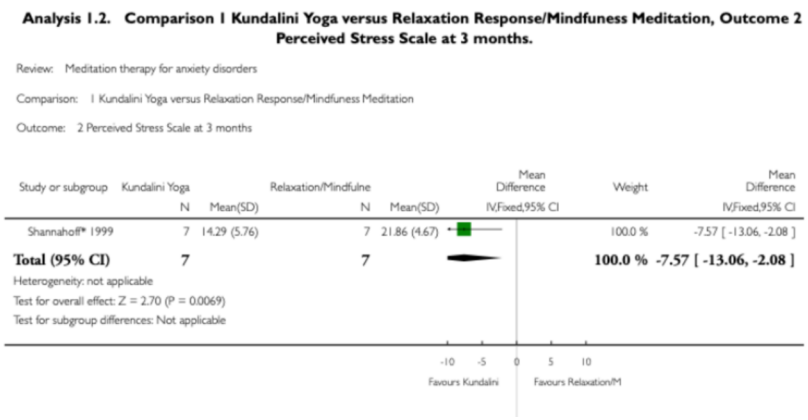

Figure 3: Data to fill in the summary of findings table

1. Number of patients on mindfulness meditation: 7
2. Number of patients on other treatment: 7
3. Absolute (95% CI)
4. Estimate of the effect: Mean Difference (MD), select from the dropdown box
5. of: -7.57
6. unit: 'points' (GRADE fills in 'lower', so we leave it at that)
7. 95% confidence intervals from and to: -13.06, -2.08

How to pool data from multiple studies and add to GRADEpro GDT

We will combine the Boettcher and Hoge study together to conduct a formal meta-analysis and repeate the processes we outlined above. The additional steps here will include:

- First, create a separate table of the data abstracted from the two studies
- Second, conduct a fixed effects and random effects meta-analysis and generate Forest Plot
- Third, put together a funnel plot to visually inspect study publication bias
- Fourth, fill in the three stages of Gradepro GDT: indicate outcomes, assess certainty, and fill in summary of findings

But before we did that and added this to our developing pool of summarised studies, let's export the existing table and examine this in the next section.

Step 4: How to use the Evidence Profile in Gradepro GDT for developing discussion on the topic

First, let's export the GRADEPRo table from GRADE. To do so,

- click on the 'export table' icon on the top right hand corner of the page.
- Select 'pdf' for format (you will see all the outcomes are already selected for you)
- Download the file (use landscape format)

The table looks like as follows:

Author(s):
Date:
Question: Mindfulness meditation compared to non-mindfulness based approached for stress
Setting: community
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mindfulness meditation	non-mindfulness based approached	Relative (95% CI)	Absolute (95% CI)		
Anxiety (follow up: 5 weeks; assessed with: DASS)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	24	42	-	SMD **0.24 SD lower** (0 to 0)	⨁⨁◯◯ LOW	
Clinical state of anxiety (assessed with: Different scales and inventories)												
2	randomised trials	serious [c]	serious [d]	serious [e]	not serious	publication bias strongly suspected strong association [f]	7	7	-	MD **7.57 points lower** (13.06 lower to 2.08 lower)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **SMD**: Standardised mean difference; **MD**: Mean difference

Explanations

a. The investigators were unable to provide details of randomisation; they also would not be able to provide for blinding given the type of intervention; hence this study would open up for biases
b. While there were some drop in the scores of anxiety, the between group estimates did not meet statistical or clinical significance
c. the first study had issues with allocation concealment, and the second study did not describe how they randomised and both studies had issues with not being able to blind participants and uneven ratios of male:female.
d. one of these studies reported some measures but the other did not, so the findings were not consistent across the studies
e. While the studies used direct measurement of anxiety states from participants using scales, none of the findings or measurements 'directly' reported anxiety state changes
f. This was based on only two published studies, and we do not know what other studies were conducted or what was missed.

Figure 4: Evidence profile table for mindfulness and anxiety

As you can see, the evidence profilel lists both the certainty assessment and the summary of findings. So what do you do with it?

Describe the table. What are the most striking feature of this table?

1. First, the certainty of the quality of evidence in support of whether mindfulness helps in relief of anxiety as from these two studies is low to very low. Hence, we would definitely need more evidence in

support of whether mindfulness helps or does not help in relieving anxiety; based on only these pieces of evidence will not help us in any way.

2. Second, overall, in general, the point estimates do seem to point that mindfulness meditation based approaches seem to reduce anxiety states. However, the absolute changes in anxiety scores seem to be low with large studies (expected) and some findings suggest the effect may even be large.

So overall, based only on these two pieces of evidence, we cannot say that mindfulness meditation has led to definite improvement in anxiety states, althought that may seem to be the case. More studies are needed that are of higher quality before a definite conclusion can be reached. Let's see what conclusions we reach when we supplement this evidence with addtional data of meta-analysis that we will conduct on the remaining three studies.

References

Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., ... deBeer, H. (2011). GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology*, *64*(4), 383–394. https://doi.org/10.1016/j.jclinepi.2010.04.026