Physical activity for primary dysmenorrhea: a systematic review and meta-analysis of randomized controlled trials

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Condensation: A systematic review and meta-analysis of randomized controlled trials of the effectiveness of physical activity as a treatment for primary dysmenorrhea

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Structured Abstract

Background: Primary dysmenorrhea is cramping abdominal pain associated with menses. It is prevalent, affects quality of life, and can cause absenteeism. Although evidence based medical treatment options exist, women may not tolerate these or may prefer to use non-medical treatments. Physical activity has been recommended by clinicians for primary dysmenorrhea since the 1930s, but its effectiveness is still unknown.

Objective: We sought to determine the effectiveness of physical activity for the treatment of primary dysmenorrhea

Data sources: Systematic literature searches of multiple databases were performed, including searches for grey literature, from database inception to 24th May 2017. Google searches and citation searching of previous reviews was also conducted.

Study eligibility criteria: Studies were selected using predefined selection criteria as specified in the registered protocol. Randomized controlled trials were included if they assessed physical activity interventions against any comparator over at least two menstrual cycles and assessed pain intensity or pain duration as an outcome. Study selection was performed by two independent reviewers at both the title/abstract and full text level.

Study appraisal and synthesis methods: Study quality was assessed by two independent reviewers using the Cochrane Risk of Bias Tool. Random effects meta-analyses for pain intensity and pain duration were conducted, with pre-specified subgroup analysis by type of physical activity intervention.

Results: Searches identified 15 eligible randomized controlled trials; totalling 1681 participants. Data from 11 studies was included in the meta-analyses. Pooled results demonstrated significant effect estimates for physical activity versus comparators for pain intensity (-1.89cm on Visual Analogue Scale, 95% confidence interval -2.96 to -1.09) and pain duration (-3.92 hours, 95% confidence interval -4.86, to -2.97). Heterogeneity for both these results was high and only partly mitigated by subgroup analysis. Primary studies were of low or moderate methodological quality but results for pain intensity remained stable during sensitivity analysis by study quality.

Conclusion: Clinicians can inform women that physical activity may be an effective treatment for primary dysmenorrhea but there is a need for high quality trials before this can be confirmed.

Key words: Exercise, Menstrual Pain, Physical Activity, Primary Dysmenorrhea

Main text

Introduction

Primary dysmenorrhea is pain occurring with menses in the absence of underlying pathology, commonly referred to as period pains or menstrual cramps by the lay press and public.[1-4] Women may consider primary dysmenorrhea to be a normal physiological state rather than a disorder.[5] However, studies consistently find it to be the most common gynaecological condition of adolescence,[6-8] with severe symptoms reported by 13 – 33%[9-11] of women and absenteeism by 24 – 43%.[11-13] Approximately one third of women with primary dysmenorrhea have seen a health professional because of this condition.[14,15]

Standard, evidence based treatment is with non-steroidal anti-inflammatory medications (NSAIDs)[16] or oral hormonal contraceptives.[17] However, some women may not be able to use medications, or may prefer to avoid them. There are plausible mechanisms by which physical activity may reduce pain in primary dysmenorrhea. Pain during menstruation is thought to be mediated by uterine prostaglandins, which stimulate myometrial contractions.[8] Pain sensitisation,[8] psychosocial[18,19] and cultural factors[20] may also play a role. Physical activity reduces stress,[21,22] has anti-nociceptive properties,[23-26] reduces levels of PGF2α[27,28] (the prostaglandin subtype most closely linked with primary dysmenorrhea),[8] and probably has hormonal effects on the menstrual cycle that are currently not fully understood.[29]

Physical activity has been recommended by clinicians for primary dysmenorrhea since the 1930s,[30,31] and this advice is reiterated on popular[1,3] and medical[4,32] websites, including guidelines from the American College of Obstetrics and Gynaecology.[33] However there is no clear evidence of effectiveness,[34-36] and even less is known

about which types of exercise might be beneficial or when these exercises should be performed. Three reviews of interventional studies of physical activity for primary dysmenorrhea have been performed (two narrative reviews in 1998[36] and 2008[34] and a systematic review in 2010).[35] Results from these reviews were inconclusive due to lack of primary studies, and the searches for the most recent review were performed almost a decade ago in 2009.[35] An unregistered systematic review was published in 2016[37] but this appears to have a number of shortcomings such as low return rates on the initial searches for potentially eligible studies, an unclear meta-analysis with no measure of heterogeneity reported, and discrepancies in the methodological descriptions of studies in different sections of the report. An updated review is therefore required.

Objective

We sought to systematically review the evidence from randomized controlled trials (RCTs) of the use of physical activity as treatment for primary dysmenorrhea. We also proposed subgroup analyses based on type of intervention, type of comparator, and whether participants were adolescents or adults.[38] We planned to perform sensitivity analysis according to study quality (not specified in the registered protocol).

Methods

A protocol for this review was registered on PROSPERO on 7th June 2017 prior to screening the studies (registration number 42017062202).[38] The search strategy was developed building on search strategies from previous similar reviews[18,22,23,34,35,39,40] by utilising common or unique but highly sensitive search terms. The following databases were used: Medline, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Science Citation Index, Social Sciences Citation Index, CINAHL, PsycINFO, SPORTDiscus, PEDro, AMED, Conference Proceedings

Citation Index, Social Sciences Conference Proceedings Citation Index, WHO International Clinical Trials Registry Platform, Clinicaltrials.gov and OpenGrey. Google searches and citation searching of previous reviews were also conducted.

Indexing terms (where possible) and text words (title, abstract, key words and text search) were used for "physical activity" and "dysmenorrhea" terms. Language, date or publication type restrictions were not applied. “Humans” filters were used on some databases with large return rates (e.g. Medline) to enable easier handling of search results. Validated RCT filters were used where required,[41-43] the inbuilt search filter was used for CINAHL. The Medline search strategy (see Appendix A) was piloted for sensitivity and specificity. Searches performed on other databases used the same text terms as the piloted Medline search, with index terms adapted for the specific database.

Eligibility criteria

Published and unpublished studies, in any language, were included where the following PICOS criteria were met:

- Participants: Non-athlete females with regular menstruation, experiencing primary dysmenorrhea, not using hormonal contraception
- Interventions: Physical activity interventions delivered over two or more menstrual cycles; as a single intervention or as a co-intervention, in any setting and via any mode of delivery
- Comparators: Any comparator that did not involve physical activity, including active comparators and usual care or no treatment
- Outcomes: Pain intensity measured by a validated tool or pain duration measured in hours

- Study type: RCTs

Title and abstract screening was performed independently by two reviewers and any discrepancies were resolved by consensus between the two reviewers. In cases of uncertainty or when discrepancies could not be resolved the article was obtained as a full text. Where the full text could not be located the study authors were contacted where possible. Two theses and one conference abstract could not be located by any method and were thus excluded at the full text stage. Full text screening for inclusion of eligible studies was completed by two independent reviewers; discrepancies were resolved by consensus between these reviewers. Study authors were contacted for missing information with a reminder sent after three weeks if there had been no reply. In total, 20 study authors were contacted for further information regarding 17 studies but only five replied.

Data extraction

The data extraction form was adapted from the Cochrane Good Practice Data Extraction form[44] and was piloted prior to use. Data from included studies was extracted for participants (setting, population, method of diagnosis, inclusion / exclusion criteria, sample size, age range), intervention (type of intervention, method, timing and frequency of delivery, duration), comparators (type of comparator, timing and duration), and outcomes (time point measured, measurement tool, mean, variance). Data extraction was completed by two independent reviewers using the full text copy and any supplementary information (protocols, correspondence from authors). The main publication was used as the reference and other sources were used to obtain any information that was not reported in the main study publication. Discrepancies were resolved by consensus between the two reviewers.

Assessment of risk of bias

The Cochrane Collaboration Risk of Bias Tool was used[45] with one adaption: "blinding of participants / personnel" was changed to "blinding to study purpose / group" as physical activity interventions do not allow complete blinding.[34,46] Studies could therefore still be rated to be of high methodological quality despite being at high risk of bias. The main biases considered in the "other bias" section were recall bias, interviewer bias, contamination, the Hawthorne effect and the effect of co-interventions. Studies were assessed for quality at the study level by two independent reviewers using the Cochrane guidance.[41] Discrepancies were resolved by consensus. Quality assessment was used for descriptive purposes and sensitivity analysis only.

Data synthesis

Review Manager 5.3 (Revman) was used for statistical analyses. Meta-analyses of pain intensity and duration were performed as specified in the review protocol.[38] Where trials compared two exercise interventions against one comparator, they were considered as two separate trials; the number of participants in the comparator group was evenly divided between the trials to avoid double-counting of comparators. The variance was adjusted accordingly where required. The final participant number (n) was not provided for three studies;[47-49] for these studies n was assumed to be the total randomized. Results for Ortiz 2015[50] were obtained from a graph; they did not specify the measure of variance so this was assumed to be standard deviation.

Results were combined using the weighted mean difference, as most studies reported pain intensity using a visual analogue scale (VAS) in centimetres and pain duration in hours. VAS is a 10cm, usually horizontal, line anchored by the phrases "no pain" and "worst pain imaginable" at each end. One study[51] used the McGill questionnaire,

which cannot be converted to VAS, so data from this trial could not be included in the meta-analysis. The remaining studies reported pain intensity using VAS in millimetres[50] and pain duration in days.[49,52] These results were converted to centimetres and hours respectively before analysis. A correlation coefficient of 0.6 was used to estimate the standard deviation of the mean difference where this was not provided, based on the result obtained in an RCT of a physical activity intervention in a similar population.[53] Inverse variance methods were used for weighting in the meta-analyses. The random effects model was used as it was anticipated there may be a high degree of heterogeneity. I^2 was used to assess heterogeneity; an I^2 value greater than 50% was considered to indicate substantial heterogeneity.[41] Funnel plots were produced to look for publication bias.

Cluster RCTs could not be included in the meta-analyses as no intra-cluster correlation coefficient was reported in the eligible trials. Separate pooling of cluster RCTs was performed for pain duration but only one cluster randomized study reported pain intensity in a format that could be used. Subgroup analysis was not possible for comparator type as specified in the protocol due to insufficient primary studies. Subgroup analysis by age, which was also specified in the protocol, was not possible as most included studies did not provide enough detail on age ranges.

Results

Searches were performed on 24th May 2017. The returns for individual databases are given in Appendix B. The PRISMA flow diagram, representing the flow of studies through the selection process, is shown in Figure 1. A list of studies excluded at the full text stage can be found in Appendix C with reasons for exclusion. Nine studies

were only found in Persian or Mandarin. These papers were assessed with the assistance of native Persian and Mandarin speakers.

Study characteristics

Fifteen RCTs, all published since 2011, met the review inclusion and exclusion criteria. This resulted in a total of 1681 participants across all included studies.[47-52,54-66] Details of these studies are presented in Table 1. Included studies were small or medium sized single-centre trials from a range of countries but primarily Iran or India. Most studies recruited university students. Diagnosis of primary dysmenorrhea was usually based on clinical history,[47-49,51,54-56,60-62,64-66] four studies performed a clinical examination for all participants,[50,52,57,58] and three used ultrasound[52,57,58] to exclude secondary causes. A range of physical activity interventions were used. These could be categorised into: aerobic exercise,[48,50,54,56,60,62,66] stretching exercises,[47,49-51,54,55,57,58,64,65] yoga[48,52,59,61] or Kegels exercises.[50,56,63,66] Ortiz 2015 used a mixed intervention.[50] The majority of studies asked participants to perform exercises throughout the menstrual cycle, but not during menstruation.[47,49,55,57,58,60,64] Reyhani 2013 asked participants to exercise by brisk walking for the first three days of menstruation.[62] Rakhshaee 2011 asked participants to perform yoga in the luteal phase of the menstrual cycle.[61]

Synthesis of results

Meta-analysis of pain intensity (Figure 3) produced a pooled effect estimate of -1.89cm (95% CI -2.96 to -1.09), representing a statistically significant reduction in pain intensity for those in the intervention (physical activity) group relative to comparators. Heterogeneity was high (I^2 = 95%).

Subgroup analysis by intervention demonstrated effect sizes of -1.29cm (95% CI -2.38 to -0.21, I^2 83%) for aerobic exercise interventions; -1.67cm (95% CI -2.70 to -0.63, I^2 94%) for stretching exercise interventions; -1.81cm (95% CI -2.37 to -1.61, I^2 0%) for yoga interventions; -1.68cm (95% CI -2.43 to -0.93, I^2 0%) for Kegels exercise interventions and -4.70cm (95% CI -5.15 to -4.25) for the single mixed intervention trial. Studies that could not be included in the meta-analysis demonstrated the same direction of treatment effect.[51,58,60,61,65]

Meta-analysis of pain duration (Figure 4) produced a pooled estimate of effect of -3.92 hours (95% CI -4.86 to -2.97), representing a reduction in pain duration for those in the intervention (physical activity) group relative to comparators. Heterogeneity was high (I^2 = 78%). Data from two cluster RCTs was combined with a similar pooled effect size of -3.34 hours (95% CI -4.15 to -2.53).

Subgroup analysis by intervention demonstrated effect sizes of -15.64 hours (95% CI -26.96 to -4.32, I^2 49%) for aerobic exercise interventions; -3.53 hours (95% CI -4.25 to -2.81, I^2 82%) for stretching exercise interventions; -6.74 hours (95% CI -13.4 to -0.03, I^2 32%) for yoga exercise interventions; and -21.00 hours (95% CI -38.70 to -3.30) for the single Kegels exercise intervention.

Sensitivity analysis was performed for type of comparator and timing of intervention, with no significant change in the combined estimate of treatment effect. Funnel plot asymmetry was seen for both outcomes. Pain intensity did not demonstrate the classical funnel shape, possibly due to the heterogeneity of primary studies. The funnel plot for pain duration suggested publication bias. This is potentially due to selective outcome reporting as five studies included in the pain intensity meta-analysis did not publish data on pain duration, and most studies were found to be at a high

risk of selective outcome reporting. However, results remained statistically significant when the smaller studies contributing to this asymmetry were removed.

Analysis of absenteeism was planned but this was only reported in one study with no measure of variance given.[49]

Risk of bias of included studies

Most included studies were at high risk of bias in multiple areas of study design, or did not report sufficiently in order for a conclusion to be made about the risk of bias (see Figure 2). The randomization process was not fully described for most studies[47-49,51,55,56,58,60,61,64-66] and allocation concealment was only performed in two studies.[50,59] No studies reported blinding participants to study purpose or group and only one study reported blinding outcome assessors.[50] Registered protocols were found for three studies,[49,51,56,64-66] of which two proposed outcomes that were not reported in the final study.[64,65] Selective outcome reporting is also suggested by the range of outcomes reported across studies. Results were sometimes reported incompletely;[50,51,55,65] for example, Aboushady 2016[55] did not report post-intervention pain intensity in the control group. Most studies had no loss to follow up,[49,51,52,55,56,58,59,62-66] the remaining studies did not use intention to treat analysis[50,57,61] or are unclear.[47,48,60]

Most biases would be expected to affect the results such that they increased the magnitude of the treatment effect. However, when low quality studies were removed (Score < 3 on risk of bias assessment in Figure 2), there was an increase in the pooled estimate of treatment effect for pain intensity (from -1.89cm (95% CI -2.96 to -1.09) to -2.87cm (95% CI -5.10 to -0.63)). Only one study of moderate quality assessed pain duration with a non-significant estimate of treatment effect of -2.64

hours (95% CI -11.58 to 6.30) suggesting that the evidence for the effect of physical activity on pain duration is less reliable.

Comment

Main findings

This systematic review and meta-analysis suggests that physical activity may be an effective intervention for primary dysmenorrhea. However, these results should be interpreted with caution, as heterogeneity was high and only partially mitigated by sub group analysis. Studies were of low or moderate quality, mainly due to performance bias and potential selective outcome reporting. Nevertheless, results for pain intensity remained stable when low quality studies were removed providing some reassurance of the treatment effect observed. All studies demonstrated an improvement in pain (intensity and / or duration) with intervention, including those that could not be included in the meta-analysis.

Strengths and limitations

Unlike previous reviews, this review was completed in conjunction with current guidelines for conducting and reporting systematic reviews.[41,67] A prospective protocol was registered on PROSPERO, ensuring methods were specified *a priori*.[38] Substantially more RCTs were found in this review than all previous reviews, mostly due to expansion in the primary literature. Searches used in this review were also more comprehensive than previous reviews; covering more databases, and identifying grey literature, such as theses and conference proceedings that were not identified in previous reviews. All eligible studies that were not published in English were translated so that they could be considered for inclusion. In compliance with current

best practice guidelines for systematic reviews, eligibility screening, data extraction and quality assessment were all performed by two independent reviewers. The meta-analyses for this review contain the largest number of RCTs to date, and assess both pain intensity and pain duration (only the former has been previously assessed by meta-analysis). Our review is also the first to include subgroup analysis by type of physical activity. Interrogation of the data using sensitivity analysis and Funnel plots was performed, which was not the case in previous reviews. This review is therefore the most complete, up to date and methodologically rigorous review of the effectiveness of physical activity interventions for primary dysmenorrhea.

Despite this the findings remain limited by the number of primary studies, trial sample size and the quality of included studies. No high quality trials were identified, and reporting of trial methodology was not always clear. The results of this review are subject to high levels of heterogeneity, introducing some uncertainty about the effectiveness of physical activity. Heterogeneity appeared to occur because studies evaluated a wide range of physical activity interventions. Attempts to resolve this by conducting subgroup analysis were somewhat limited because of insufficient primary studies. Insufficient data from primary studies also prevented reporting of one of the pre-specified outcomes (absenteeism) and two of the pre-specified subgroup analyses (adolescents and adults, comparator type).

Comparison with existing literature

Previous literature regarding the use of physical activity for primary dysmenorrhea is predominantly limited by insufficient primary studies. Consistent with our findings, increased physical activity was identified as a small protective factor against experiencing dysmenorrhea in a 2006 systematic review of observational studies (odds

ratio (OR) of 0.89, 95% CI 0.80 to 0.99).[18] A non-systematic review of controlled trials published in 1998 also found a beneficial effect, but noted there was a paucity of methodologically robust studies to confirm this.[36] Interestingly, it considered three trials to be randomized despite not being reported as such, and not being considered as such in other reviews.[34,35] Interventional studies were reviewed again in 2009 in a non-systematic review[34] and in 2010 as a Cochrane Library systematic review,[35] which included both primary and secondary dysmenorrhea in the same review. Both reviews identified just one small RCT which demonstrated a beneficial effect of treadmill running.[68] This trial had some methodological flaws and therefore the study authors concluded that there was insufficient evidence to recommend the intervention. The results of the current systematic review and meta-analyses are also consistent with those found in a systematic review published in 2016, which had potential methodological limitations mentioned previously.[37]

As well as considering the statistical significance and methodological quality of the results it is important to place these within a clinical context. No minimal clinically important difference (MCID) is available in the literature for pain intensity measured by VAS in primary dysmenorrhea, but the MCID in endometriosis is 1cm.[69] This suggests that the pooled estimate, at almost 2cm, is clinically significant. There are no reported values for the MCID for pain duration in primary dysmenorrhea or similar conditions.

Conclusions and Implications

This review provides evidence that physical activity may reduce pain intensity and duration in primary dysmenorrhea. However, although physical activity is currently recommended in clinical guidelines for primary dysmenorrhea, more high quality

studies are needed before this can be confirmed. Potential future trials should adhere to international reporting guidelines as well as attempting to minimise sources of bias. Trials that evaluate optimum type of physical activity intervention and timing for physical activity within the menstrual cycle are also required.

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Table 1 – Description of included studies

"Cycles" refers to menstrual cycles

Study	n	Participants	Intervention(s)	Comparator(s)	Outcome(s)	Results
Aboushady 2016 [55]	80	School / college students, Saudi Arabia (16–21yrs)	• Instructional sessions (Menstrual care, stretches); exercises at home, 20-30mins, 2x/day, 3d/w for 8wks	Menstrual care instructional session only	Pain duration Pain intensity via VAS	Statistically significant difference in pain duration Pain intensity only reported as pre/post-test
Behbahani 2016 [51,65]	120	Non-medical students, Iran (18–25yrs)	• 4wks educational classes (physiology, nutrition, exercises), "isometric exercises" at home for 4wks	Acupressure during pain Ibuprofen 400mg 3x/day	Pain intensity via McGill questionnaire	Statistically significant reduction in pain intensity in exercise / acupressure groups compared to ibuprofen
Kaur 2013a [63] Kaur 2013b	24	Hostel at Post-Graduate Institute, India (19–25yrs)	Slow Kegels group: • Hot pack, 90x Kegel exercises alt days, 5–10s hold; for 8wks Fast Kegels group as above, no hold	Hot pack over lower abdomen for 10mins	Pain intensity via VAS	No statistically significant difference in pain intensity between slow Kegels and control Statistically significant reduction in pain intensity in fast Kegels compared to control
Motahari-Tabari 2017 [49,64]	122	Medical students, Iran (Age range not reported)	• 15mins abdominal / pelvic stretching exercises, taught initially, 3x/wk; for 2 cycles	Mefenamic acid 250mg 3x/day	Pain intensity via VAS Pain duration	No statistically significant difference in pain intensity or pain duration
Nasri 2016a [56,66] Nasri 2016b	45	High school pupils, Iran ("Teenagers")	Aerobic group: • 45mins observed "aerobic exercise", 3x/wk; for 8wks Kegel group: • 15 mins Kegel exercises; 6s hold, 3x/day	Usual care - "no exercise", advised no salty / fatty foods, no medications	Pain intensity via VAS Pain duration	No statistically significant reduction in pain intensity / duration between exercise groups Statistically significant reduction in pain intensity / duration compared to control
Ortiz 2015 [50]	192	Uni students, Mexico (18–22yrs)	• Stretches (inc Billig / Kegel), jogging, relaxation led / monitored by instructors; 50mins, 3x/wk; for 3 cycles	Kept in courtyard; "walking, talking and standing"	Pain intensity via VAS	Statistically significant reduction in pain intensity
Patel 2015 [47]	120	Students, India (17–25yrs)	• 6 stretches; 2x/day, 3x/wk for 8wks	Usual care	Pain intensity via VAS	Statistically significant reduction in pain intensity

Study	n	Participants	Intervention(s)	Comparator(s)	Outcome(s)	Results
Rakhshaee 2011 [61]	120	Uni students, Iran (17–23yrs)	• 3 yoga poses / breathing techniques taught by booklet, for 20mins/day, luteal phase (14d) of 2 cycles	Usual care	Pain intensity via 0–3 scale Pain duration	Statistically significant reduction in pain intensity and pain duration
Reyhani 2013 [62]	90	Nursing/midwifery students, Iran (Age range not reported)	• 30mins brisk walking (one training session), 1st 3d of menstruation; for 3 cycles	Usual care	Pain intensity via VAS	Statistically significant reduction in pain intensity
Saleh 2016a [57] Saleh 2016b	150	Women from outpatient clinic, Egypt (Age range not reported)	Stretching group: • 4 stretches, 10mins, 3x/d, 3x/wk; for 8wks Core strengthening group: • 4 core strengthening exercises, 20mins, 4x/wk	Usual care	Pain intensity via VAS Pain duration	Statistically significant reduction in pain intensity / pain duration in both intervention groups when compared to control
Shahr-Jerdy 2012 [58]	179	High school pupils, Iran (15-17ys)	• 6 stretches taught initially, 10mins, 2x/d, 3x/wk; for 8wk	Usual care - exercises taught to controls after study	Pain intensity via VAS Pain duration	Statistically significant reduction in pain intensity and pain duration
Siahpour 2013a [48] Siahpour 2013b	60	Uni students, Iran (20–25yrs)	Aerobic group: • Aerobic dance for 60 mins, 3x/wk; for 8wks Yoga group: • 60 mins yoga, 3x/wk; "trained"	Usual care	Pain intensity via VAS Pain duration	Statistically significant reduction in pain intensity / pain duration between aerobic and yoga groups compared to control
Sutar 2016 [60]	100	Medical students, India (18–22yrs)	• Aerobic dance for 45mins, 3x/wk, for 8wks	Usual care	Pain intensity via VAS	Statistically significant reduction in pain intensity
Yang 2016[52]	140	Nursing students, S Korea (20–23yrs)	• 60mins guided yoga, 1x/wk (poses, sun salutations, relaxation); for 12wks	Usual care - told not to do yoga	Pain intensity via VAS Pain duration	Statistically significant reduction in pain intensity No statistically significant reduction in pain duration
Yonglitthip agon 2017 [59]	34	Uni students, Thailand (18–22yrs)	• 30mins yoga taught by booklet, 2x/wk; for 12wks • Diary / weekly phone calls to check adherence	Usual care	Pain intensity via VAS	Statistically significant reduction in pain intensity

Figure legends

Figure 1 – PRISMA flow diagram.

*PRISMA flow diagram demonstrating flow of studies through identification process and eligibility screening *See Appendix C for further details*

Figure 2 – Risk of Bias Summary

Summary of Risk of Bias of included studies

Figure 3 – Pain intensity meta-analysis

Random effects meta-analysis of pain intensity via VAS in cm

Figure 4 – Pain duration meta-analysis

Random effects meta-analysis of pain duration in hours

Appendix A – Sample search strategy (Medline / Medline in Process)

1 exp Dysmenorrhea/ 3600
2 dysmenorrh*.ti,ab. 4950
3 (menstrua* adj2 pain).ti,ab. 720
4 (menstrua* adj2 cramp).ti,ab. 7
5 (period* adj2 pain*).ti,ab. 1372
6 1 or 2 or 3 or 4 or 5 7684
7 exp Exercise/ or exp Exercise Therapy/ 184201
8 exp Physical Exertion/ or exp Physical Fitness/ 79696
9 exp running/ or exp swimming/ or exp walking/ 81381
10 exp tai ji/ or exp yoga/ 2941
11 exp dancing/ or exp gardening/ or exp sports/ 162811
12 exercis*.ti,ab. 245761
13 "physical activit*".ti,ab. 82503
14 sport*.ti,ab. 57350
15 stretch*.ti,ab. 62854
16 fitness.ti,ab. 55378
17 jog*.ti,ab. 2026
18 running.ti,ab. 49262
19 swim*.ti,ab. 32718
20 (cycl* adj2 train*).ti,ab. 2065
21 walk*.ti,ab. 93124
22 yoga.ti,ab. 3190
23 "tai ji".ti,ab. 25
24 "tai chi".ti,ab. 1249
25 pilates.ti,ab. 304
26 "physical training".ti,ab. 5245
27 "resistance training".ti,ab. 5278
28 (athlete* adj2 train*).ti,ab. 4489
29 "weight training".ti,ab. 914
30 isometric*.ti,ab. 30361
31 danc*.ti,ab. 5670
32 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 731463
33 6 and 32 312
34 randomized controlled trial.pt. 462560
35 controlled clinical trial.pt. 94063
36 randomized controlled trial.sh. 462560
37 random allocation.sh. 92576
38 double blind method.sh. 147085
39 single-blind method.sh. 24526
40 34 or 35 or 36 or 37 or 38 or 39 645852

41 (animals not human).sh. 6109803
42 40 not 41 571840
43 clinical trial.pt. 521341
44 exp clinical trial/ 803438
45 (clin$ adj25 trial$).ti,ab. 368228
46 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 161643
47 placebos.sh. 34931
48 placebo$.ti,ab. 192528
49 research design.sh. 96076
50 43 or 44 or 45 or 46 or 47 or 48 or 491211208
51 50 not 41 1110374
52 51 not 42 562047
53 comparative study.sh. 1809971
54 exp evaluation studies/ 232296
55 follow up studies.sh. 586124
56 prospective studies.sh. 456986
57 (control$ or 27thlete2727ve$ or volunteer$).ti,ab. 3751440
58 53 or 54 or 55 or 56 or 57 5717430
59 58 not 41 4252943
60 59 not (42 or 52) 3578680
61 42 or 52 or 60 4712567
62 33 and 61 136

Appendix B - Database search returns

Database	Interface	Returns
MEDLINE and MEDLINE In Process	Ovid	136
EMBASE	Ovid	243
PsycINFO	Ovid	23
Cochrane Database of Systematic Reviews (CDSR)	Cochrane Library	40 total*
Cochrane Central Register of Controlled Trials (CENTRAL)	Cochrane Library	
CINAHL	EBSCO	46
SPORTDiscus	EBSCO	53
AMED (Allied and Complimentary Medicine Database)	EBSCO	7
PEDro	NeuRA	41
Science Citation Index	Web of Science	231 total*
Conference Proceedings and Citation Index	Web of Science	
Social Sciences Citation Index	Web of Science	
Conference Proceedings and Citation Index – Social Sciences and Humanities	Web of Science	
Clinicaltrials.gov	National Institute of Health	13
WHO ICTRP	WHO	11
OpenGrey	SIGLE	21
Google	Google	42 new
Citation searching	N/A	1 new

All databases were searched from inception to 24/05/17. SCI/CPCI/SSCI/SS-CPCI and CDSR/CENTRAL were searched simultaneously; there is therefore no individual return numbers for these databases.

Appendix C – Excluded studies with reasons for exclusion

A reference list of excluded studies can be obtained from the study authors

Duplicate:

Azima 2015a– Two arm trial which is also reported as 3 arm trial - see Azima 2015b below
IRCT2013071013940N1 - Registered trial, results published in Behbahani 2016[51]

Unable to get full data:
Abbaspour 2006 - No inclusion / exclusion criteria, no reply from authors
ACTRN12613001195741 - Registered trial and feasibility study, contacted authors who have completed trial and are in process of publishing, however unwilling to share any of data
Arora 2014 - No inclusion / exclusion criteria, no reply from authors
Azima 2015b - No inclusion / exclusion criteria in either of papers reporting trial, protocol contains some inclusion / exclusion criteria but does not specify regarding secondary dysmenorrhoea, irregular menstruation or hormonal contraception
El Refaye 2007 - Thesis, no online abstract, unable to obtain full text
IRCT2016103119024N2 - Registered trial, unable to find published paper, contacted authors and no reply; probably still ongoing as only registered in 2016
Kang 2009 - Thesis, unable to obtain full text
Kumar 2013 - No inclusion / exclusion criteria, unable to find contact details for authors
Rezvani 2013 - Unclear whether women using hormonal contraception were excluded, no reply from authors
Rong 2013 - Unclear whether athletes or women using hormonal contraception were excluded, unable to find contact details for authors
Shah 2016 - No inclusion / exclusion criteria, no reply from authors
Yeknami 2015 - No inclusion / exclusion criteria, no reply from authors

Not RCT:
Anonymous 1945 – Letter
Anonymous 1960 - Letter
Anonymous 1993 - Review
Chien 2013 - Non-randomized controlled trial
Dehghanzadeh - Before and after trial
Golub 1960 - Non-randomized controlled trial
Golub 1963 – Before and after trial
Halder 2012 - Non-randomized controlled trial
Haman1945 – Before and after trial
Harris 1955 - Before and after trial

Hubbell 1949 - Non-randomized controlled trial
ISRCTN75567759 - Registered trial and published protocol, mixed-methods study with no randomization
Jahromi 2008 - Before and after trial
Locke 1999(1) – Review
Locke 1999(2) - Review
Lundquist 1947 - Non-randomized controlled trial
Mathur 1986 - Non-randomized controlled trial

Athlete population:
Chaudhuri 2013 - Some participants were athletes, also some had irregular periods (from correspondence with author)

Not primary dysmenorrhoea:
Heidarianpour 2016 - Menstrual characteristics, dysmenorrhoea considered but did not exclude secondary dysmenorrhoea
Kaur 2014 – No email address found. Unclear whether secondary causes excluded. Also mentions randomization in abstract but in text participants are "taken at random"
Pazoki 2013 - Pre-menstrual symptoms; dysmenorrhoea considered but did not exclude secondary dysmenorrhoea
Pazoki 2016 - Pre-menstrual symptoms; dysmenorrhoea considered but did not exclude secondary dysmenorrhoea
Roozbahani 2015 - Did not exclude secondary dysmenorrhoea
Steege 1993 - Pre-menstrual symptoms; dysmenorrhoea considered but did not exclude secondary dysmenorrhoea
Wilt 1976 - Not specified whether those with secondary cause excluded, unable to obtain information from authors as no contact details

Hormonal contraception not excluded:
DeWitt 1981 - Asked women about hormonal contraception but did not specify whether these women were excluded
Huang 2007 - No inclusion / exclusion criteria stated, unable to find contact details for authors
Israel 1985 - No inclusion / exclusion criteria stated, unable to find contact details for authors
Mahvash 2012 - No email address found. Unclear whether those on hormonal contraception or with irregular periods were excluded as no inclusion / exclusion criteria were given
Monika 2012 – Hormonal contraception specifically provided to the groups
Motesharee 2013 – Hormonal contraception / irregular periods not excluded
Nag 2013 - No email address found. Unclear whether athletes included (although have excluded those already practicing yoga), whether those on hormonal contraception or with irregular periods were excluded as no inclusion / exclusion criteria were given

Not physical activity intervention:

None

Intervention < 8 weeks:

Gamit 2014 - Four weeks
Kanwal 2016 - One month
Kashef 2014 - Four weeks
Khare 2016 - Three weeks
Mahishale 2013 - First two days of menstruation, only one cycle
Thomas 2010 - Three weeks

Pain not assessed:
Rani 2013 – Hormone profiles assessed as outcome
Vaziri 2015 – Menstrual symptoms assessed as outcome, unable to extract data about pain

Appendix D – Risk of Bias Assessment

	Risk of Bias	**Justification**
Random sequence generation	*Low / High / Unclear*	
Allocation concealment	*Low / High / Unclear*	
Blinding to study group / study purpose	*Low / High / Unclear*	Studies were considered at high risk of bias if they reported that no blinding was done, or blinding was not reported but the comparator group received no intervention.
Blinding of outcome assessment	*Low / High / Unclear*	
Incomplete outcome data	*Low / High / Unclear*	
Selective outcome reporting	*Low / High / Unclear*	
Other bias (observer bias, recall bias, contamination, co-interventions, Hawthorne effect)	*Low / High / Unclear*	Studies were considered at high risk of bias if one of these biases was present. If none of these biases were adequately described studies were considered at unclear risk of bias Interviewer bias - high risk if outcomes assessed during interview Recall bias – high risk if outcomes assessed more than one day after the end of menstruation Contamination – high risk if participants were from schools / colleges / individual courses unless cluster randomized Co-interventions – high risk if there was a co-intervention or physical activity was performed in a group Hawthorne effect – high risk if physical activity was performed in a group or closely monitored setting