

Systematic review

This record cannot be edited because it is being assessed by the editorial team

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

The effect of physical exercise on sex hormone binding globulin (SHBG) in adults: systematic review and meta-analysis

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

16/09/2019

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

30/11/2019

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: No

| Review stage | Started | Completed |
|---|---------|-----------|
| Preliminary searches | Yes | No |
| Piloting of the study selection process | No | No |
| Formal screening of search results against eligibility criteria | No | No |
| Data extraction | No | No |
| Risk of bias (quality) assessment | No | No |
| Data analysis | No | No |

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Gundula Behrens

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Dr Behrens

7. * Named contact email.

Give the electronic mail address of the named contact.

Gundula.Behrens@klinik.uni-regensburg.de

8. Named contact address

PLEASE NOTE this information will be published in the PROSPERO record so please do not enter private information

Give the full postal address for the named contact.

University of Regensburg, Department of Epidemiology and Preventive Medicine, Franz-Josef-Strauss-Allee 11, 93053 Regensburg

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

+49-941-944-5201

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Regensburg

Organisation web address:

11. * Review team members and their organisational affiliations.

Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.

Laura Rivera-Amézquita. Universidad del Rosario

Michael Leitzmann. University of Regensburg

Gundula Behrens. University of Regensburg

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

None.

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members.

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

Primary review questions:

1. What is the effect of 12 weeks or more of aerobic exercise on serum SHBG levels in adults?
2. What is the effect of 12 weeks or more of resistance exercise on serum SHBG levels in adults?

3. What is the effect of 12 weeks or more of combined aerobic and resistance exercise on serum SHBG levels in adults?

Secondary review questions:

Do any of the following variables modify the potential effects of physical exercise on serum SHBG:

1. Study design
2. Gender
3. Age
4. Hormonal status
5. Pre-intervention physical activity status
6. Pre-intervention adiposity status
7. Physical exercise intensity
8. Length of physical training period
9. Proportion of training sessions attended
10. Exercise-induced changes in anthropometric measures related to adiposity and muscle mass

16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

PubMed, Web of Science, EMBASE

17. URL to search strategy.

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy.

Do NOT provide links to your search results.

https://www.crd.york.ac.uk/PROSPEROFILES/151248_STRATEGY_20190920.pdf

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

We will examine the effects of physical exercise on serum sex hormone binding globulin (SHBG) in adults.

SHBG is a plasma glycoprotein that is primarily produced in the liver. It binds a variety of sex steroids including dihydrotestosterone, testosterone, and estradiol and transports them to target cells, thereby reducing the quantity of freely available steroid hormones in serum. Although SHBG is closely related to circulating levels of sex hormones and insulin, it potentially plays an independent preventive role in the etiology of major chronic diseases such as cancer and type 2 diabetes mellitus.

It is biologically plausible that physical exercise increases serum SHBG in part through reductions in hepatic and visceral fat stores and via decreases in insulin levels and insulin resistance. However, results from intervention studies examining the effect of physical exercise on SHBG have been inconsistent.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Included participants:

- Adults participating in intervention studies on the effect of aerobic or resistance exercise or the combination of aerobic and resistance exercise on serum sex-hormone binding globulin (SHBG) levels

Excluded participants:

- Participants with major chronic conditions
- Participants that used medications or exogenous hormones potentially affecting estrogen metabolism or physical exercise ability
- Participants that experienced substantial weight loss before the physical exercise intervention

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

Included studies:

- Intervention studies of aerobic or resistance exercise or the combination of aerobic and resistance exercise with a physical training period

of 12 weeks or longer

- Intervention studies with serum SHBG levels as outcome
- Intervention studies providing arithmetic or geometric serum SHBG means with 95% confidence levels or sufficient information to derive that information

Excluded studies:

- Intervention studies in which physical exercise was prescribed in combination with other interventions

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Main outcome:

Mean change score in serum SHBG levels =
mean post-intervention serum SHBG level - mean pre-intervention serum SHBG level

If the mean change scores in serum SHBG levels and their standard errors, standard deviations or 95% confidence intervals are directly reported, we will use the direct estimates; otherwise, we will use the available information on the pre- and post-intervention serum SHBG levels and on the within-person correlation coefficients of serum SHBG levels to impute the mean change scores in serum SHBG levels and their standard errors, standard deviations or 95% confidence intervals.

Comparator/control:

If a trial includes a no-intervention group or a group engaging in light stretching as control group, we will define the effect of the intervention as the difference of the mean serum SHBG change scores between the intervention and control group; otherwise, the effect of the intervention will be defined as the mean serum SHBG change score in the intervention group. In a sensitivity analysis, we will assess the difference between the effect estimates obtained from trials with and without control groups.

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

Included study designs:

- Intervention studies satisfying all the above defined inclusion criteria for participants and interventions

Excluded study designs:

- Intervention studies for which any of the above defined exclusion criteria for participants or interventions apply

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Main outcome:

Mean change score in serum SHBG levels =
mean post-intervention serum SHBG level - mean pre-intervention serum SHBG level

If the mean change scores in serum SHBG levels and their standard errors, standard deviations or 95% confidence intervals are directly reported, we will use the direct estimates; otherwise, we will use the available information on the pre- and post-intervention serum SHBG levels and on the within-person correlation coefficients of serum SHBG levels to impute the mean change scores in serum SHBG levels and their standard errors, standard deviations or 95% confidence intervals.

Comparator/control:

If a trial includes a no-intervention group or a group engaging in light stretching as control group, we will define the effect of the intervention as the difference of the mean serum SHBG change scores between the intervention and control group; otherwise, the effect of the intervention will be defined as the mean serum SHBG change score in the intervention group. In a sensitivity analysis, we will assess the

difference between the effect estimates obtained from trials with and without control groups.

Timing and effect measures

Mean change score in serum SHBG levels =

mean post-intervention serum SHBG level - mean pre-intervention serum SHBG level

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Not applicable

Timing and effect measures

Not applicable

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Study selection:

We will apply the inclusion/exclusion criteria for participants, interventions and exposures defined above (points 19 and 20).

Data extraction:

We will extract the following information for the physical exercise intervention and, if available, for the no-intervention or light stretching control groups as applicable:

- Type, frequency, intensity and duration of the physical exercise intervention
- Mean change score in serum SHBG levels with standard errors, standard deviations or 95% confidence intervals or any relevant information to derive that information
- Study design
- Gender
- Age
- Hormonal status
- Pre-intervention physical activity status
- Pre-intervention adiposity status
- Length of physical training period
- Proportion of training sessions attended
- Exercise-induced changes in anthropometric measures related to adiposity and muscle mass

27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

We will use the Cochrane Collaboration tool to assess the risk of bias induced by comparisons between exercise intervention and control groups (no-intervention or light stretching).

28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

We will use standard meta-analysis and meta-regression methods for data synthesis. In particular, we will summarize the mean effects of the physical exercise interventions on SHBG levels in random effects models using the inverse of the squared standard errors as weights. We will apply I^2 and χ^2 statistics to assess the between-study heterogeneity of the effects, and we will use funnel plots, Begg's test and Egger's test to detect potential publication bias. The influence of specific variables on the summary effect estimates will be examined in random effects meta-regression models. All statistical tests will be carried out two-sided, and the level of statistical significance will be set at 5%.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Subgroups:

- Aerobic exercise intervention
- Resistance exercise intervention

- Combined aerobic and resistance exercise intervention

Potential additional strata within subgroups:

- Study design (trials with/without a no-intervention or light stretching control group)
- Gender (men, women)
- Age (<50 years, >= 50 years)
- Hormonal status (premenopausal women, postmenopausal women, men aged <50 years, men aged >= 50 years)
- Pre-intervention physical activity status (sedentary, moderately active, vigorously active)
- Pre-intervention adiposity status (normal weight, overweight, obese)
- Physical exercise intensity (moderate, vigorous)
- Proportion of training sessions attended (<80%, 80-99%, 100%)

The influence of the following variables:

- Length of physical training period
 - Exercise-induced changes in anthropometric measures related to adiposity and muscle mass
- on the effect of the exercise intervention on serum SHBG will be examined using linear terms for those variables.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

Type of review

| | |
|---|-----|
| Cost effectiveness | No |
| Diagnostic | No |
| Epidemiologic | No |
| Individual patient data (IPD) meta-analysis | No |
| Intervention | Yes |
| Meta-analysis | Yes |
| Methodology | No |
| Narrative synthesis | No |
| Network meta-analysis | No |
| Pre-clinical | No |
| Prevention | No |
| Prognostic | No |
| Prospective meta-analysis (PMA) | No |
| Review of reviews | No |
| Service delivery | No |
| Synthesis of qualitative studies | No |
| Systematic review | Yes |
| Other | No |

Health area of the review

| | |
|--------------------------------|-----|
| Alcohol/substance misuse/abuse | No |
| Blood and immune system | No |
| Cancer | Yes |
| Cardiovascular | Yes |

| | |
|---|-----|
| Care of the elderly | No |
| Child health | No |
| Complementary therapies | No |
| Crime and justice | No |
| Dental | No |
| Digestive system | No |
| Ear, nose and throat | No |
| Education | No |
| Endocrine and metabolic disorders | No |
| Eye disorders | No |
| General interest | No |
| Genetics | No |
| Health inequalities/health equity | No |
| Infections and infestations | No |
| International development | No |
| Mental health and behavioural conditions | No |
| Musculoskeletal | No |
| Neurological | No |
| Nursing | No |
| Obstetrics and gynaecology | No |
| Oral health | No |
| Palliative care | No |
| Perioperative care | No |
| Physiotherapy | Yes |
| Pregnancy and childbirth | No |
| Public health (including social determinants of health) | Yes |
| Rehabilitation | No |
| Respiratory disorders | No |
| Service delivery | No |
| Skin disorders | No |
| Social care | No |
| Surgery | No |
| Tropical Medicine | No |
| Urological | No |

Wounds, injuries and accidents No

Violence and abuse No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Germany

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

No I do not make this file publicly available until the review is complete

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

Do you intend to publish the review on completion?

Yes

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38. * Current review status.

Review status should be updated when the review is completed and when it is published. For newregistrations the review must be Ongoing.

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

