**Supply of systematic evidence syntheses to inform the WHO Guidelines on management of chronic primary low back pain in adults**

**Request for Proposals (RFP)**

Bid Reference

2021/UHL/AAH/0001.

Country/Unit Name

**Switzerland/Ageing and Health Unit**

**Closing Date:**

8 November 2021

**Request for Proposals:** 2021/UHL/AAH/0001.

**Annex 7: Questions from Bidders** (Ref. Paragraph 4.6)

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| **No.** | **RFP Section reference** | **Question** | **WHO response** |
| 1 | 3.3 | The RFP refers to Cochrane reviews and we wish to know if it is the aim of the proposal to limit the reviews to only Cochrane reviews.  There is important literature which outside is not reflected in the Cochrane body of work | WHO acknowledges that some high-quality systematic reviews of randomized controlled trials (RCTs) of the listed interventions for chronic low back pain have been published previously, or are in preparation. In this context, existing high-quality systematic reviews may be updated with contemporary RCT evidence to derive the evidence syntheses for the interventions. WHO has identified and recommended which existing reviews should be used for this purpose, including Cochrane reviews and a non-Cochrane review for the intervention #5 ‘education/advice’. This information is outlined in Section 3.3 under ‘Interventions’. Specifically, bidders should navigate to the hyperlinks provided in Section 3.3, p.9 to identify the existing systematic reviews that are recommended by WHO.  Where no existing high-quality systematic review is available, a new evidence synthesis may be required.  Bidders may choose in their Proposal to deviate from WHO’s recommendations, however, this should be supported by a compelling reason for doing so. |
| 2 | 3.2 | Can we invite professionals from outside our institution to join the project team? | Yes. The project team may be assembled as deemed appropriate to ensure the composite mix of knowledge and skills aligns with the knowledge and skills requirements outlined in Section 3.2.3. Ultimate coordination and responsibility for the project team rests with the lead institution. Please refer to Section 4.5 for further details on consortia arrangements.  The lead institution should ensure its capacity to align with requirements outlined in sections 3.2.1-3.2.4. |
| 3 | 4.6 | Once the Nov 2 date has passed for questions, is there any way to communicate with your team?  When the project is under way, how will the successful candidate communicate with the WHO team: i.e. is there a specific “point person”? | Bidders are invited to communicate with WHO up to 2 November using the Annex 7 form.  Once Proposals have been evaluated and a supplier selected, a focal point in WHO will be established to ensure communication between WHO and the supplier. Specifically, please refer to Section 3.3.4, which outlines the requirements for formal monthly meetings between the supplier and WHO. |
| 4 | 3.3 | Is it correct that only one systematic review per area (e.g., exercise and low back pain) will be awarded or more systematic reviews can be funded, at the discretion of the WHO? | Yes this is correct. WHO will only seek one evidence synthesis for each of the interventions outlined in Section 3.3. Suppliers may choose to bid to undertake an evidence synthesis for one, several, or all nine intervention areas. |
| 5 | 3.3 | The systematic review proposal needs to update the most recently published Cochrane systematic reviews of the topic. For Exercise and low back pain there is one systematic review published in 2021 (Hayden et al. 2021, Cochrane) and an update is currently ongoing, as I can read from their paper | WHO has recommended which contemporary, high-quality systematic reviews should be used as evidence sources for the required evidence syntheses. Proposals should therefore outline how these existing reviews will be updated to deliver up-to-date evidence syntheses to inform the WHO Guideline.  For exercise, WHO has recommended an update to the current review by Hayden et al 2021 with results disaggregated by exercise modality (i.e. split not lumped). That review includes data for trials identified in searches up to 27 April 2018. Therefore, there is a need to update this synthesis to include trials in searches up to present day. |
| 6 | 3.3 | Is it possible to bid for an exercise systematic review with a different aim and methodology (e.g., individual patient meta-analysis) for exercise and low back pain? | WHO does not recommend this approach. However, a bidder may choose to propose a different method should the outcomes meet the requirements of WHO, as outlined in the RFP. A compelling argument for the alternative approach would be expected. |
| 7 | 3.3 | Is it possible to bid for a systematic review including only some of the Outcomes listed in section 3.3? | No. WHO considers outcomes listed in 3.3 as critical outcomes and asks the GRADE assessment for each critical outcome. Therefore, bidders should provide complete detail about the data for each outcome, including references.  Bidders should also report outcomes for which no evidence was found. |
| 8 | 3.3 | The section on interventions reports that specific categories of exercise will be considered separately. We interpret this to mean that separate GRADE profiles for each exercise category are required (i.e. 12 GRADE profiles for exercise). How should any additional exercise categories be considered in the analysis/GRADE?  Please confirm also whether the other 8 interventions are to be considered as a whole group or also separately, e.g. psychosocial therapies can be considered separately to mindfulness-based interventions. | WHO requires that evidence for the benefits and harms of exercise be disaggregated by exercise modality, i.e. ‘split’, rather than ‘lumped’. Therefore, separate GRADE evidence profiles are required for each of the exercise modalities (1a-i), which comprises 12 separate modalities and thus 12 GRADE evidence profiles.  If there are additional meaningful exercise categories beyond those listed (ie exercise types that cannot be grouped using the listed categories), the bidder may propose the additional category(ies) and these will be considered by WHO.  The other 8 intervention categories should be approached as separate groups of interventions with the following considerations:   * Psychosocial interventions including mindfulness-based stress reduction therapies. WHO suggests that a clinically useful categorization of psychosocial interventions be used, such as the framework used by [Henschke et al in the 2010 Cochrane Review](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002014.pub3/full). That review considered operant, cognitive, and respondent modalities. WHO also recommends that mindfulness-based stress reduction therapies be considered separately given the volume of research in this field. * Herbal medicines: each of the six medicines should be considered separately as outlined in the RFP. |
| 9 | 3.3 | It is not clear what interventions should be included in “local anaesthetic agents delivered to local soft tissues (excluding intra-spinal)”. Does this include both injections and topical application of anaesthetic agents to spinal muscles? Would intradiscal injections be classified as “intra-spinal”? Should we also include studies on local application of NSAIDS and patches that could have an anaesthetic effect? | This intervention should only consider subcutaneous or intra-muscular injection of anaesthetic agents into local soft tissues in the region of the low back (12th rib to gluteal fold). Intra-spinal interventions are not included, such as intra-discal, epidural, intra-facet, nerve root injections. Topical agents are not considered as injectable substances, so should not be included. |
| 10 | 3.3 | The comparators of interest are reported as placebo/sham, no intervention, and usual care.  We interpret this to mean that studies can be included if the effect of the intervention can be isolated e.g., we would include studies that compare exercise + usual care vs usual care alone. Please confirm if this is correct.  We also consider these three control interventions to be quite different to each other. Usual care is often poorly described or includes active interventions e.g., exercise or education. Should all three of these comparators be pooled together in the same analysis? If treated separately this would indicate three GRADE profiles for each intervention of interest. | Yes, studies should be included if the effect of the intervention can be isolated (e.g., studies that compare exercise + usual care vs usual care alone).  The three comparators are different and should be considered separately, i.e. they should not be pooled together in the same analysis, but analysed separately, requiring three GRADE profiles for each intervention of interest. |
| 11 | 3.3 | The between-trial sub-population evidence synthesis section reports that analyses should be considered for race/ethnicity. Please clarify how this analysis should be structured in a “between-trial” sense?  Our understanding of this request is that only within study subgroup analyses should be considered and not between-trial comparisons due to heterogeneity across trials. Is this in line with what is expected from the analysis? | All sub-population analyses are intended to be at the level of ‘between trials’, not ‘within trials’ as trial sub-groups.  Essentially, this sub-population analysis seeks to determine differences in outcomes that might be accounted for by a cultural/race/ethnicity difference (where evidence exists). For example, if an intervention was delivered in trials conducted in migrant populations in Europe (e.g. trial A in Germany, trial B in Greece) versus trials done in European residents in those same countries, then we may well expect different results due to culture/race/ethnicity even though the intervention and the country setting are the same. |
| 12 | 3.3 | For the sub-population evidence syntheses, it is requested that these appear as separate rows under the relevant outcome in the GRADE Evidence Profile table. However, these analyses will have a different PICO question, and result in a different guideline recommendation, than a comparison of intervention vs placebo/sham. How should GRADE be considered with respect to these analyses? Further clarification on this is required. | WHO requests that the GRADE Evidence Profile tables for each outcome include additional rows for the different sub-populations. For example, for the sub-population concerning regional economic development (high income vs low to middle-income), two additional rows would be added: one for high income and one for low to middle-income. Where there is no evidence, the additional rows should appear empty. |
| 13 | 4.12.6 | Is there a budget limit for the work requested in the RFP? It is difficult to put in a comprehensive proposal that covers all 9 review updates and subgroup analyses without knowing the limit. There is a substantial amount of work requested. | WHO does not disclose budgetary elements during the course of a competitive bidding process. Please also note that bidders may offer a Proposal that considers all nine interventions or a subset and the budget template (Appendix 2) seeks a quote by intervention. |
| 14 | 4.12.16 | Would the GDG consider using integrity criteria for inclusion of trials e.g. only considering registered trials, or trials at low risk of bias, or with a minimum follow-up time? This could reduce the budget implications and result in higher quality analyses. | WHO has not included integrity criteria as part of the inclusion criteria for evidence in this RFP. However, bidders may choose to offer this as an option in their Proposal for consideration by WHO. |
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