**Supplementary Material**

Appendix A: The Search strategy which was used for the different electronic bibliographic databases:

### *Pubmed*

| Search | Query | Items found |
| --- | --- | --- |
| #3 | #1 AND #2 | 641 |
| #2 | "Pain"[Mesh] OR "Pain Measurement"[Mesh] OR "Hyperalgesia"[Mesh] OR "Pain Perception"[Mesh] OR pain\*[tiab] OR ache\*[tiab] OR nocicepti\*[tiab] OR neuralgia\*[tiab] OR hyperalgesi\*[tiab] OR analgesi\*[tiab] OR allodyni\*[tiab] OR vas[tiab] OR visual analog scale\*[tiab] OR formalin[tiab] OR "Quality of Life"[Mesh] OR "Health Status Indicators"[Mesh] OR SF-36\*[tiab] OR SF36[tiab] OR SF-12[tiab] OR SF12[tiab] OR SF-20[tiab] OR SF20[tiab] OR RAND-36[tiab] OR RAND36[tiab] OR EQ-5D\*[tiab] OR EQ5D\*[tiab] OR Health related Quality of Life[tiab] OR Qol[tiab] OR Hrql[tiab] OR hrqol[tiab] OR medical outcome stud\*[tiab] OR MOS[tiab] OR health utilities index[tiab] OR health utility index[tiab] OR hui[tiab] OR hui2[tiab] OR hui3[tiab] OR hui-2[tiab] or hui-3[tiab] OR health status indicator\*[tiab] OR health status inde\*[tiab] OR Nottingham Health Profile\*[tiab] OR Health Status Questionnaire[tiab] OR HSQ [tiab] OR Duke Health Profile[tiab] | 1245397 |
| #1 | "Huntington Disease"[Mesh] OR huntington\*[tiab] OR chronic progressive hereditary chorea[tiab] | 17148 |

### Embase

| Search | Query | Items found |
| --- | --- | --- |
| #3 | #1 AND #2 | 1404 |
| #2 | 'pain'/exp OR 'pain measurement'/exp OR 'pain assessment'/exp OR 'hyperalgesia'/exp OR 'nociception'/exp OR pain\*:ab,ti,kw OR ache\*:ab,ti,kw OR hyperalgesi\*:ab,ti,kw OR allodyni\*:ab,ti,kw OR nocicepti\*:ab,ti,kw OR vas:ab,ti,kw OR 'visual analog scale\*':ab,ti,kw OR formalin:ab,ti,kw OR 'quality of life'/exp OR 'health status indicator'/exp OR 'sf-36\*':ab,ti,kw OR sf36:ab,ti,kw OR 'sf-12':ab,ti,kw OR sf12:ab,ti,kw OR 'sf-20':ab,ti,kw OR sf20:ab,ti,kw OR 'rand-36':ab,ti,kw OR rand36:ab,ti,kw OR 'eq-5d\*':ab,ti,kw OR eq5d\*:ab,ti,kw OR 'health related quality of life':ab,ti,kw OR qol:ab,ti,kw OR hrql:ab,ti,kw OR hrqol:ab,ti,kw OR 'medical outcome stud\*':ab,ti,kw OR mos:ab,ti,kw OR 'health utilit\* index':ab,ti,kw OR hui:ab,ti,kw OR hui2:ab,ti,kw OR hui3:ab,ti,kw OR 'hui 2':ab,ti,kw OR 'hui 3':ab,ti,kw OR 'health status indicator\*':ab,ti,kw OR 'health status inde\*':ab,ti,kw OR 'nottingham health profile':ab,ti,kw OR 'health status questionnaire':ab,ti,kw OR 'duke health profile':ab,ti,kw  | 1928255 |
| #1 | 'huntington chorea'/exp OR huntington\*:ab,ti,kw OR 'chronic progressive hereditary chorea':ab,ti,kw | 27920 |

### PsycINFO

| Search | Query | Items found |
| --- | --- | --- |
| #3 | S1 AND S2 | 97 |
| 2 | DE ("Pain" OR "Aphagia" OR "Back Pain" OR "Chronic Pain" OR "Headache" OR "Myofascial Pain" OR "Neuralgia" OR "Neuropathic Pain" OR "Somatoform Pain Disorder" OR "Migraine Headache" OR "Muscle Contraction Headache" OR "Peripheral Neuropathy" OR "Trigeminal Neuralgia" OR "Complex Regional Pain Syndrome (Type I)" OR "Pain Management" OR "Pain Measurement" OR "Pain Perception" OR "Analgesia" OR "Pain Thresholds" OR "Somatosensory Disorders" OR "Nociceptors") OR ZM (pain OR “Quality of Life” OR “health status”) OR TI (pain\* OR ache\* OR nocicepti\* OR neuralgia\* OR hyperalgesi\* OR analgesi\* OR allodyni\* OR vas OR visual analog scale\* OR formalin OR “SF-36\*” OR SF36 OR “SF-12” OR SF12 OR “SF-20” OR SF20 OR “RAND-36” OR RAND36 OR “EQ-5D\*” OR EQ5D\* OR “Health related Quality of Life” OR Qol OR Hrql OR hrqol OR “medical outcome stud\*” OR MOS OR “health utilit\* index” OR hui OR hui2 OR hui3 OR hui-2 OR hui-3 OR “health status indicator\*” OR “health status inde\*” OR “Nottingham Health Profile\*” OR “Health Status Questionnaire” OR “Duke Health Profile”) OR AB (pain\* OR ache\* OR nocicepti\* OR neuralgia\* OR hyperalgesi\* OR analgesi\* OR allodyni\* OR vas OR visual analog scale\* OR formalin OR “SF-36\*” OR SF36 OR “SF-12” OR SF12 OR “SF-20” OR SF20 OR “RAND-36” OR RAND36 OR “EQ-5D\*” OR EQ5D\* OR “Health related Quality of Life” OR Qol OR Hrql OR hrqol OR “medical outcome stud\*” OR MOS OR “health utilit\* index” OR hui OR hui2 OR hui3 OR hui-2 OR hui-3 OR “health status indicator\*” OR “health status inde\*” OR “Nottingham Health Profile\*” OR “Health Status Questionnaire” OR “Duke Health Profile”) | 148673 |
| #1 | DE "Huntingtons Disease" OR TI (huntington\* OR chronic progressive hereditary chorea) OR AB (huntington\* OR chronic progressive hereditary chorea)  | 4498 |

### CINAHL

| Search | Query | Items found |
| --- | --- | --- |
| S3 | S1 AND S2 | 70 |
| S2 | MH ("Pain+" OR "Pain Measurement" OR "Pain Management" OR "Hyperalgesia" OR "Nociceptive Pain" OR "Allodynia" OR "Somatosensory Disorders+" OR "Visual Analog Scaling" OR "Quality of Life+" OR "Health Status Indicators" OR "Short Form-36 Health Survey (SF-36)") OR TI (pain\* OR ache\* OR nocicepti\* OR neuralgia\* OR hyperalgesi\* OR analgesi\* OR allodyni\* OR vas OR “isual analog scale\*” OR formalin OR “SF-36\*” OR SF36 OR “SF-12” OR SF12 OR “SF-20” OR SF20 OR “RAND-36” OR RAND36 OR “EQ-5D\*” OR EQ5D\* OR “Health related Quality of Life” OR Qol OR Hrql OR hrqol OR “medical outcome stud\*” OR MOS OR “health utilit\* index” OR hui OR hui2 OR hui3 OR hui-2 OR hui-3 OR “health status indicator\*” OR “health status inde\*” OR “Nottingham Health Profile\*” OR “Health Status Questionnaire” OR “Duke Health Profile”) OR AB (pain\* OR ache\* OR nocicepti\* OR neuralgia\* OR hyperalgesi\* OR analgesi\* OR allodyni\* OR vas OR “visual analog scale\*” OR formalin OR “SF-36\*” OR SF36 OR “SF-12” OR SF12 OR “SF-20” OR SF20 OR “RAND-36” OR RAND36 OR “EQ-5D\*” OR EQ5D\* OR “Health related Quality of Life” OR Qol OR Hrql OR hrqol OR “medical outcome stud\*” OR MOS OR “health utilit\* index” OR hui OR hui2 OR hui3 OR hui-2 OR hui-3 OR “health status indicator\*” OR “health status inde\*” OR “Nottingham Health Profile\*” OR “Health Status Questionnaire” OR “Duke Health Profile”) | 257947 |
| S1 | (MH "Huntington's Disease") OR TI (huntington\* OR “chronic progressive hereditary chorea”) OR AB (huntington\* OR “chronic progressive hereditary chorea”)  | 1152 |

### Cochrane Library

| Search | Query | Items found |
| --- | --- | --- |
| #3 | #1 AND #2 | 22 |
| #2 | pain\* OR ache\* OR nocicepti\* OR neuralgia\* OR hyperalgesi\* OR analgesi\* OR allodyni\* OR vas OR visual analog scale\* OR formalin OR “SF-36\*” OR SF36 OR “SF-12” OR SF12 OR “SF-20” OR SF20 OR “RAND-36” OR RAND36 OR “EQ-5D\*” OR EQ5D\* OR “Health related Quality of Life” OR Qol OR Hrql OR hrqol OR “medical outcome stud\*” OR MOS OR “health utilit\* index” OR hui OR hui2 OR hui3 OR “hui-2” OR “hui-3” OR “health status indicator\*” OR “health status inde\*” OR “Nottingham Health Profile\*” OR “Health Status Questionnaire” OR “Duke Health Profile”:ti,ab,kw (Word variations have been searched) | 150260 |
| #1 | huntington\* OR “chronic progressive hereditary chorea”:ti,ab,kw (Word variations have been searched) | 471 |

**Supplementary Material.**

Appendix B:The enhanced version (13-items) of the Research Triangle Institute (RTI) item bank, to assess the risk of biases.

|  |  |  |  |
| --- | --- | --- | --- |
| ***Question*** | ***Formulation question****Instructions for principal investigator (PI) and/or abstractor* | ***Modified version*** | ***Type of bias*** |
| Q1 | **Do the inclusion/exclusion criteria vary across the comparison groups of the****study?** [*PI: Drop question if not relevant to all included studies. To use this question for studies with one group, the focus of the question on comparison groups and related response categories would need to be changed to individuals.]* | **Are the inclusion and exclusion criteria clearly formulated?** | **Selection bias** |
| Q2 | **Does the strategy for recruiting participants into the study differ across groups?***[PI: Drop question if not relevant to all included studies. If the recruitment strategy results in pre-intervention differences in prognostic factors that could explain the selection of the intervention and the outcome, confounding can occur. If the strategy results in the selective and differential inclusion of patients (such as prevalent rather than new users), selection bias can occur. To use this question for studies with one group, the focus of the question on comparison groups and related response categories would need to be changed to individuals.]* | **Does the strategy for recruiting participants into the study differ across individuals? (For example from registry, hospital, specialized clinical setting).** | **Selection bias,****Confounding** |
| Q3 | **Is the selection of the comparison group inappropriate?***[PI: Provide instruction to the abstractor based on the type of study. Interventions with community components are likely to have contamination if all groups are drawn from the same community. Interventions without community components should select groups from the same source (e.g., community or hospital) to reduce baseline**differences across groups. For case-control studies, controls should represent the population from which cases arose; that is, controls should have met the case definition if they had the outcome.]* | **Is the selection of the comparison group inappropriate? (Only applicable if control group present)** Consider HD-clinic versus population based | **Selection bias, confounding** |
| Q4 | **Does the study fail to account for important variations in the execution of the****study from the proposed protocol?***[PI: Consider intensity, duration, frequency, route, setting, and timing of intervention/exposures. Drop if not relevant for body of literature.]* | **Not relevant for the included studies** | **Performance bias** |
| Q5 | **Was the assessor not blinded to the outcome, exposure, or intervention status of the participants?***[PI: Clinical assessors may not always be blinded to exposure/intervention as well as outcome status. For studies where patients are selected based on outcome (e.g., casecontrol), blinding to exposure or intervention status is particularly important. For designs where patients are selected based on exposure status (e.g., cohorts), blinding to outcomes is particularly important. Drop if not relevant to the body of literature.]* | **Not relevant for the included studies** | **Detection bias** |
| Q6 | **Were valid and reliable measures not used or not implemented consistently****across all study participants to assess inclusion/exclusion criteria,****intervention/exposure outcomes, participant benefits and harms, and potential****confounders?***[PI: Important measures should be identified for abstractors and if there is more than**one, they should be listed separately. PI may need to establish a threshold for what**would constitute acceptable measures based on study topic. When subjective or**objective measures could be collected, the PI will need to consider if subjective**measures based on self-report should be considered as being less reliable and valid**than objective measures such as clinical reports and lab findings. Some characteristics**may require that sources for establishing their validity and/or reliability be described or**referenced. If so, provide instruction to abstractors.]* | **Are valid and reliable measures implemented?*** Reliable and conventional ascertainment of HD?
* Reliable and conventional ascertainment of pain, depression and anxiety?
 | **Detecion bias, confoudnding** |
| Q7 | **Was the length of followup different across study groups?***[Abstractor: When followup was the same for all study participants, the answer is no. If**different lengths of followup were adjusted by statistical techniques, (e.g., survival**analysis), the answer is no. Studies in which differences in followup were ignored**should be answered yes.]* | **Is the length of follow-up the same across individuals or study group?**Only applicable in a follow-up study. | **Attrition bias** |
| Q8 | **In cases of missing data (e.g., overall or differential loss to followup for cohort****studies or missing exposure data for case-control studies), was the impact not****assessed (e.g., through sensitivity analysis or other adjustment method)?***[PI: For cohort studies, attrition is measured in relation to the time between baseline**(allocation in some instances) and outcome measurement for both retrospective and**prospective studies and could include data loss from switching. Attrition rates may**vary by outcome and time of measurement. Specify the criterion to meet relevant**standards for the topic. Specify measurement period of interest, if repeated measures.**For case-control studies, evaluate missing data in relation to exposure status.]* | **In case of missing data, was the impact not assessed?**

|  |  |
| --- | --- |
|  | Present |
| Described |  | Yes | No |
| Yes | + |  |
| No | - | ? |

 | **Attrition bias, detection bias** |
| Q9 | **Are any important primary outcomes missing from the results?***[PI: Identify all primary outcomes that one would expect to be reported in the study,**including timing of measurement.]* | **Are any important primary outcomes missing from the results?**The dependent variable has been mentioned in the introduction and presented in the result section (Table or text). | **Selective outcome reporting** |
| Q10 | **Are any important harms or adverse events that may be a consequence of the****intervention/exposure missing from the results?***[PI: Identify all important harms that one would expect be reported in the study,**including timing of measurement. Drop if not relevant to body of literature.]* | **Not relevant for the included studies** | **Selective outcome reporting** |
| Q11 | **Did the study fail to balance the allocation between the groups or match groups****(e.g., through stratification, matching, propensity scores)*?****[PI: Drop if not relevant to the body of evidence.]* | **Did the study fail to balance the allocation between groups or match group?** Only applicable if control group present**.** | **Confounding** |
| Q12 | **Were important confounding variables not taken into account in the design****and/or analysis (e.g., through matching, stratification, interaction terms,****multivariate analysis, or other statistical adjustment such as instrumental****variables)?***[PI: Provide instruction to abstractors on known confounding variables and inadequate**adjustment for confounding for each outcome.]* | **Were important confounding variables not taken into account in the design and/or analysis?** **Stratified by importance:**1. Genetic diagnosis HD, Stage of Disease, Years of onset disease, Gender
2. Psychiatric disturbances, drug treatment.
3. Calculation of group differences has been done.
 | **Confounding** |
| Q13 | **Are results believable taking study limitations into consideration?***[Abstractor: This question is intended to capture the overall quality of the study.Consider issues that may limit your ability to interpret the results of the study. Review responses to earlier questions for specific criteria.]* | **Are the result believable taking study limitations into consideration?** | **Overall assessment** |