**Supplementary table**

**Table S1 PubMed search strategy**

|  |  |
| --- | --- |
| **Number** | **Search items** |
| #1 | "Hepatolenticular Degeneration"[Mesh] OR Hepatolenticular Degeneration\*[tw] OR Pseudosclerosis[tw] OR "Wilson Disease\*"[tw] OR "Wilson's Disease\*"[tw] OR "Wilsons Disease\*"[tw] OR "Westphal-Strumpell Syndrome\*"[tw] OR "Copper Storage Disease\*"[tw] OR "Progressive Lenticular Degeneration\*"[tw] OR Neurohepatic Degeneration\*[tw] |
| #2 | "Zinc Compounds"[Mesh] OR Zincteral[tw] OR Zinc[tw] |
| #3 | "Penicillamine"[Mesh] OR Penicillamin\*[tw] OR Mercaptovaline[tw] OR Dimethylcysteine[tw] OR Metalcaptase[tw] OR Cuprimine[tw] OR Cuprenil[tw] OR Acetylpenicillamine[tw] OR "S-NONAP"[tw] OR atamir[tw] OR pendramine[tw] |
| #4 | #4. "Trientine"[Mesh] OR Trientine[tw] OR Triethylenetetramine[tw] OR Trien[tw] OR Syprine[tw] OR teta[tw] |
| #5 | #1 AND (#2 OR #3 OR #4) |
| #6 | ("controlled clinical trial"[pt] OR "Controlled Clinical Trials as Topic"[MeSH] OR "Random Allocation"[MeSH] OR "Double-Blind Method"[MeSH] OR "single-blind method"[MeSH] OR "Control Groups"[MeSH] OR "cross-over studies"[MeSH] OR random\*[tiab] OR placebo[tiab] OR trial[tiab] OR groups[tiab] OR crossover[tiab] OR cross-over[tiab]) NOT ("Animals"[Mesh] NOT ("Humans"[Mesh] AND "Animals"[Mesh])) |
| #7 | #5AND #6 |

**Table S2 Evaluation of the quality of cohort studies included in the meta analysis (assessed by Newcastle-Ottawa scale)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author | Year | Study population selection | Comparability between groups | Outcome measurement | Total score(9) |
| Representativeness of the sample（1） | Determination of treatment（1） | Make sure that the research started withoutOutcome indicators to be observed（1） | Identify patients in the non-exposed group（1） | Subjects are comparable in design and statistical analysis（2） | Result evaluation（2） | Adequacy of follow-up time after the results occurred（1） |
| Merle | 2007 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
| Zhang | 2020 | 1 | 1 | 0 | 0 | 2 | 2 | 1 | 7 |
| Medici | 2006 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
| Członkowska | 2014 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
| Litwin | 2015 | 0 | 1 | 0 | 0 | 2 | 2 | 1 | 6 |
| Czlonkowska  | 1996 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 7 |
| Sini | 2013 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
|  Zhou | 2020 | 1 | 1 | 1 | 1 | 1 | 2 | 0 | 7 |
| Mayr | 2020 | 1 | 0 | 1 | 0 | 1 | 2 | 1 | 6 |
| Couchonnal | 2021 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
|  Masebas | 2010 | 1 | 0 | 0 | 0 | 2 | 2 | 1 | 6 |
| Kalita | 2015 | 1 | 1 | 0 | 0 | 2 | 2 | 1 | 7 |
| Yokoyama | 2010 | 1 | 1 | 1 | 0 | 2 | 2 | 1 | 8 |
| Bruha | 2010 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 7 |
| Weiss | 2011 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 7 |
| Rodriguez | 2012 | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 7 |

**Supplementary figure**

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**Figure S1. Forest plot of the WD patients treated with penicillamine compared with zinc salts.**

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**Figure S2. Forest plot of the pooled improved rate for hepatic WD patients.**

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**Figure S3. Meta-analysis of treatment effectiveness in hepatic WD patients treated with penicillamine compared with zinc salts.**

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**Figure S4. Forest plot of the pooled improved rate for neurological WD patients.**

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**Figure S5. Meta-analysis of treatment effectiveness in neurological WD patients treated with penicillamine compared with zinc salts.**

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**Figure S6. Sensitivity analysis of the treatment effectiveness included studies**

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**Figure S7. Egger chart of the treatment effectiveness included studies**

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**Figure S8. Funnel plot of the treatment effectiveness included studies**

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**Figure S9. Meta-analysis of adverse effects in WD patients treated with penicillamine compared with trientine**