**S3 Table. Risk of bias and sponsorship of included studies.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Trial name, year** | **Adequate sequence generation** | **Allocation concealment** | **Blinding** | **Incomplete outcome data addressed** | **Selective outcome reporting** | **Other bias** | **Overall risk of bias** | **Funding source** |
| Parving et al 19891,2 | Unclear risk | Unclear risk | High risk | Unclear risk | Low risk | Unclear risk | High risk | Not reported |
| Bauer et al 19923 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Unclear risk | Industry and nonindustry |
| Björck et al 19924 | Unclear risk | Unclear risk | High risk | Low risk | Unclear risk | Low risk | High risk | Industry and nonindustry |
| Chan et al 19925 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Lacourcière et al 19936 | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Unclear risk | Not reported |
| Lewis et al 19937 | Unclear risk | Unclear risk | Low risk | Low risk | Unclear risk | Low risk | Unclear risk | Industry and nonindustry |
| Ravid et al 19938 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |
| Elving et al 19949 | Unclear risk | Unclear risk | High risk | Low risk | Low risk | Low risk | High risk | Nonindustry |
| Sano et al 199410 | Unclear risk | Unclear risk | High risk | Low risk | Low risk | Low risk | High risk | Not reported |
| Laffel et al 199511 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Bakris et al 199612 | Unclear risk | Unclear risk | High risk | Low risk | Low risk | Low risk | High risk | Nonindustry |
| Viberti et al 199613 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Nielsen et al 199714,15 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Not reported |
| ABCD-Hypertension 199816,17 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| ABCD-normo 200218 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| Crepaldi et al 199819 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Not reported |
| FACET 199820 | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Nankervis et al 199821 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Not reported |
| Ravid et al 199822 | Low risk | Low risk | Low risk | Low risk | Unclear | Low risk | Unclear risk | Nonindustry |
| UKPDS-39  199823 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry and nonindustry |
| Fogari et al 199924 | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Not reported |
| ATLANTIS 200025 | Low risk | Low risk | Unclear risk | Unclear risk | Low risk | Low risk | Unclear risk | Industry |
| Tarnow et al 200026 | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Chan et al 200027 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Not reported |
| STOP HTN-2 200028 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Micro-HOPE 200029 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| J-MIND 200130 | Low risk | Low risk | High risk | Unclear risk | Unclear risk | Unclear risk | High risk | Not reported |
| IDNT 200131,32 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Unclear risk | Industry |
| IRMA-2 200133 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Unclear risk | Industry |
| Jerums et al 200134 | Unclear risk | Low risk | Low risk | Low risk | Unclear | Unclear | Unclear risk | Industry and nonindustry |
| RENAAL 200135,36 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| CAPPP 200137 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Val-HeFT 200138 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| Fogari et al 200239 | Low risk | Low risk | High risk | Low risk | Low risk | Low risk | High risk | Not reported |
| JAPAN-IDDM 200240 | Unclear risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |
| LIFE 200241 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| VALIANT 200342 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| VALUE 200443 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| BENEDICT 200444 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry and nonindustry |
| DETAIL 200445,46 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| DIABHYCAR 200447 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| NESTOR 200448 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| JMIC-B 200449 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |
| Ko et al 200550 | Unclear risk | Unclear risk | High risk | Unclear risk | Unclear risk | Unclear risk | High risk | Not reported |
| Schram et al 200551 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| PERSUADE 200552 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| ALLHAT 200553,54 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| SCOPE 200555 | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| ABCD-2V 200656 | Low risk | Low risk | High risk | Low risk | Low risk | Low risk | High risk | Industry |
| Tong et al 200657 | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| ADVANCE 200758,59 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| DIRECT-Prevent 1 200860,61 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| DIRECT-Protect 1 200860,61 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| DIRECT-Protect 2 200860,62,63 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| GUARD 200864 | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Industry |
| PRoFESS 200865 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| ONTARGET 200866-68 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| TRANSCEND 200869-71 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| Kohlmann Jr et al 200972 | Unclear risk | Low risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry |
| Mehdi et al 200973 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |
| RAAS 200974 | Low risk | Unclear risk | Low risk | Low risk | Low risk | Low risk | Unclear risk | Industry and nonindustry |
| CASE-J 201075 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry and nonindustry |
| ROADMAP 201176 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| ORIENT 201177,78 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| DEMAND 201179 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry and nonindustry |
| ALTITUDE 201280 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| NAGOYA HEART 201281,82 | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Industry and nonindustry |
| VA NEPHRON-D  201383 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Nonindustry |
| ASTRONAUT 201384,85 | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Low risk | Industry |
| COLM 201486 | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |
| OSCAR 201487,88 | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk | Unclear risk | Nonindustry |

\*Estimated by authors based on single components with available information. GRADE Working Group grades of evidence:

* High quality: further research is very unlikely to change our confidence in the estimate of effect
* Moderate: further research may change the estimate (and is likely to have an important influence on our confidence in the estimate of effect)
* Low: further research is likely to change the estimate (an is very likely to have an important influence on our confidence in the estimate of effect)
* Very low: any estimate of effect is very uncertain