|  |
| --- |
| **Supplemental Table 2**. Quality assessment of the included studies reporting candidate genes for Polycystic Ovary Syndrome (PCOS) |
| **Q-Genie Question**  | Rationale for study  | Selection and definition of outcome of interest  | Selection and comparability of comparison groups (if applicable)  | Technical classification of the exposure  | Non-technical classification of the exposure  | Other sources of bias  | Sample size and power  | A priori planning of analyses  | Statistical methods and control for confounding  | Testing of assumptions and inferences for genetic analyses  | Appropriateness of inferences drawn from results  | **TOTAL SCORE**  | Overall  |
| Heyes MG, et al. 2015  | 6 | 5 | 6 | 6 | 3 | 3 | 3 | 7 | 7 | 7 | 5 | 58 | Good |
| Day FR, et al. 2015 | 6 | 3  | 3 | 3  | 3 | 2 | 3 | 7 | 7 | 6 | 4 | 47 | Good |
| Tian Y, et al. 2016 | 6 | 4 | 6 | 6 | 3 | 3  | 7 | 7 | 7 | 6 | 5 | 60 | Good |
| Diao X, et al. 2014 | 6 | 3  | NA | 6 | 3 | 3 | 1 | 4 | 2  | 7 | 4 | 37 | Moderate |
| Ewens KG et al. 2010 | 5 | 5 | NA | 6 | 3 | 4 | 3 | 7 | 7 | 7 | 5 | 52 | Good |
| Gorsic LK et al. 2017 | 2 | 6 | 4  | 4 | 4 | 2 | 2 | 5 | 5 | 4 | 5 | 43 | Moderate  |
| Chen ZJ, et al. 2011 | 6 | 4  | 6 | 7 | 4 | 3 | 2 | 7 | 7 | 7 | 5 | 58 | Good |
| Shi Y et al. 2012 | 6 | 4  | 6 | 7 | 4 | 3 | 4 | 7 | 7 | 7 | 6 | 61 | Good |
| Zhao S et al. 2015 | 6 | 5 | NA | 6 | 3 | 4 | 2 | 5 | 2 | 6 | 5 | 44 | Good |
| Mutharasan P, et al. 2013 | 5 | 4 | 2 | 5 | 4 | 3 | 2 | 5 | 5 | 6 | 5 | 46 | Good |
| Du J et al. 2014 | 6 | 3  | NA | 6 | 4 | 3 | 1 | 4 | 2  | 5 | 4 | 36 | Moderate |
| Peng Y, et al. 2017 | 5 | 3 | 2 | 5 | 4 | 2 | 6 | 5 | 4 | 5 | 4 | 45 | Moderate |
| Song X et al. 2015 | 3 | 3 | NA | 5 | 3 | 4 | 1 | 4 | 2  | 6 | 4 | 35 | Moderate |
| Gorsic LK et al. 2019 | 3 | 6 | 4  | 4 | 4 | 2 | 2 | 5 | 5 | 6 | 5 | 46 | Good  |
| Louwers YV et al. 2013 | 6 | 3  | 2 | 2 | 5 | 3 | 6 | 5 | 3 | 3 | 3 | 42 | Moderate |
| Carey AH et al. 1994 | 5 | 3  | NA | 3 | 2 | 2 | 1 | 4 | 2 | 2 | 2 | 26 | Poor |
| Li T et al. 2013 | 5 | 3  | 5 | 6 | 3 | 3 | 6 | 7 | 3 | 5 | 5 | 51 | Good |
| Zhang B et al. 2012 | 5 | 3 | 2 | 5 | 4 | 2 | 6 | 5 | 3 | 5 | 4 | 44 | Moderate |
| Lee H et al. 2015 | 6 | 6 | 5 | 6 | 4 | 4 | 5 | 7 | 6 | 6 | 5 | 60  | Good |
| Zhao H et al. 2012 | 6 | 5 | NA | 6 | 3 | 4 | 1 | 5 | 2 | 6 | 5 | 43 | Good |
| Goodarzi, MO et al. 2012 | 5 | 3  | 4 | 5 | 3 | 2 | 5 | 5 | 3 | 5 | 5 | Moderate | Good |
| Dapas M et al. 2019 | 6 | 6 | NA | 6 | 4 | 4 | 1 | 5 | 5 | 6 | 5 | 48 | Good |
| Urbanek M. et al. 2005 | 5 | 6 | NA | 6 | 3 | 4 | 3 | 5 | 5 | 5 | 5 | 47 | Good |
| Zhang Y. et al. 2020 | 6 | 3 | 5 | 6 | 4 | 4 | 6 | 7 | 6 | 6 | 5 | 58  | Good |

NA: Not Applicable

**Data extraction and quality assessment of the included studies reporting candidate genes for PCOS**

The investigator (S.M.) extracted data associated with PCOS from OKdb including first author’s name, publication year, study design, location of the study, ethnicity of the participants, number of cases/controls, SNPs investigated, chromosome, candidate gene, genotyping platform used, set of diagnostic criteria used to diagnose PCOS, measure of association with corresponding 95% CI and P value obtained from the combined sample sets (GWAS). The candidate genes for PCOS derived from GWAS studies, family studies and their metanalysis were included. For case studies, only those with replication by more than one publication with adequate control groups were included.

To evaluate the quality of the included in the review, we used the Quality of Genetic Association Studies (Q-Genie) tool (Sohani et al., 2015)(22). The Q-Genie, developed and validated at the Population Genomics Program of McMaster University, contains 11 items assessing the following dimensions: i-ii) scientific basis for development of the research question, iii) ascertainment of comparison groups (ie, cases and controls), iv) technical and nontechnical classification of genetic variant tested, v) classification of the outcome, vi) discussion of sources of bias, vii) appropriateness of sample size, viii) description of planned statistical analyses, ix) statistical methods used, x) test of assumptions in the genetic studies (eg, agreement with the Hardy-Weinberg equilibrium), and xi) appropriate interpretation of results.

Each item is rated on a 7-point scale, where 1 is considered poor and 7 as excellent quality. The total scores ≤35 on the Q-Genie tool indicate poor quality studies, >35 and ≤45 indicate studies of moderate quality, and >45 indicate good quality studies. For the family studies by excluding the question number 3: a total score ≤32 on the Q-Genie tool indicate poor quality studies, >32 and ≤40 indicate studies of moderate quality, and >40 indicate good quality studies (Sohani et al., 2015)(22).

**Reference**

**22.** Sohani ZN, Meyre D, de Souza RJ, Joseph PG, Gandhi M, Dennis BB, Norman G, Anand SS. Assessing the quality of published genetic association studies in meta-analyses: the quality of genetic studies (Q-Genie) tool. *BMC genetics*.2015;16(1):50.