| Section/topic | #  | Checklist item                                                                                                                                                                                                 | Reported on section |
|---------------|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| TITLE         |    |                                                                                                                                                                                                             |TITLE               |
| Title         | 1  | Identify the report as a systematic review, meta-analysis, or both.                                                                                                                                        |                    |
| ABSTRACT      |    |                                                                                                                                                                                                             |ABSTRACT            |
| Structured summary | 2  | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. |                    |
| INTRODUCTION  |    |                                                                                                                                                                                                             |INTRODUCTION        |
| Rationale     | 3  | Describe the rationale for the review in the context of what is already known.                                                                                                                              |                    |
| Objectives    | 4  | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).                                                            |                    |
| METHODS       |    |                                                                                                                                                                                                             |METHODS             |
| Protocol and registration | 5  | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.                                      |                    |
| Eligibility criteria | 6  | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | Selection Criteria |
| Section/topic                          | # | Checklist item                                                                 | Reported on section |
|---------------------------------------|---|-------------------------------------------------------------------------------|---------------------|
| Information sources                   | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | Search Strategy     |
| Search                                | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Search Strategy     |
| Study selection                       | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Selection Criteria  |
| Data collection process               | 10| Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | Data Extraction     |
| Data items                            | 11| List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Data Extraction     |
| Risk of bias in individual studies    | 12| Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | Statistical Analysis|
| Summary measures                      | 13| State the principal summary measures (e.g., risk ratio, difference in means), | Statistical Analysis|
| Synthesis of results                  | 14| Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis. | Statistical Analysis|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). |
|-----------------------------|----|----------------------------------------------------------------------------------------------------------------------------------|
| Additional analyses         | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. |

**RESULTS**

| Study selection             | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. |
|                            |    |                                                                                                                                  |
| Study characteristics       | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. |
|                            |    |                                                                                                                                  |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).                             |
|                            |    |                                                                                                                                  |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. |
|                            |    |                                                                                                                                  |
| Synthesis of results        | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.                             |

**Statistical Analysis**
| Topic                                      | Item | Description                                                                                           | Section          |
|-------------------------------------------|------|-------------------------------------------------------------------------------------------------------|------------------|
| Risk of bias across studies               | 22   | Present results of any assessment of risk of bias across studies (see Item 15).                         | Figure 2         |
| Additional analysis                       | 23   | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | I/D Polymorphism and COPD risk: Meta-Regression Analysis |
| DISCUSSION                                |      |                                                                                                       |                  |
| Summary of evidence                       | 24   | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | DISCUSSION       |
| Limitations                               | 25   | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | DISCUSSION       |
| Conclusions                               | 26   | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | DISCUSSION       |
| FUNDING                                   |      |                                                                                                       |                  |
| Funding                                   | 27   | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Not available    |
Supplementary Table 2. Baseline characteristics of eligible studies for the changes of FEV1, FEV1/FVC and circulating ACE across genotypes of ACE gene I/D polymorphism.

| First author | Year | Subjects | Sample size | FEV1 (%predicted FEV1) | FEV1/FVC (%) | Circulating ACE (U/L) |
|--------------|------|----------|-------------|------------------------|--------------|-----------------------|
| Kon          | 2017 | Patients | 168         | DD 50.40               | DD 48.00     | DD n.a.               |
|              |      |          |             | ID 52.80               | ID 48.70     | ID n.a.               |
|              |      |          |             | II 50.10               | II 46.20     | II n.a.               |
| Lee          | 2009 | All      | 9034        | DD 89.00               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 89.00               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 89.00               | II n.a.     | II n.a.               |
| Lee          | 2009 | Patients | 1259        | DD 76.00               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 74.00               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 75.00               | II n.a.     | II n.a.               |
| Lee          | 2009 | Controls | 717         | DD n.a.                | DD 34.00    | DD 36.00              |
|              |      |          |             | ID n.a.                | ID 27.00    | ID 22.00              |
|              |      |          |             | II n.a.                | II 21.00    | II n.a.               |
| Zhang        | 2008 | Controls | 57          | DD 102.10              | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 93.50               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 99.40               | II n.a.     | II n.a.               |
| Zhang        | 2008 | Patients | 61          | DD 46.10               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 48.50               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 44.40               | II n.a.     | II n.a.               |
| Tkacova      | 2005 | Patients | 66          | DD 45.80               | DD 53.90    | DD n.a.               |
|              |      |          |             | ID 45.90               | ID 52.10    | ID n.a.               |
|              |      |          |             | II 47.40               | II 54.20    | II n.a.               |
| Kanazawa     | 2004 | Patients | 33          | DD 49.00               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 53.00               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 52.00               | II n.a.     | II n.a.               |
| Ahsan        | 2004 | Controls | 40          | DD n.a.                | DD 56.13    | DD 56.09              |
|              |      |          |             | ID n.a.                | ID 36.09    | ID 30.75              |
| Ahsan        | 2004 | Controls | 24          | DD n.a.                | DD 53.43    | DD 42.70              |
|              |      |          |             | ID n.a.                | ID 42.92    | ID n.a.               |
| Ahsan        | 2004 | Patients | 18          | DD n.a.                | DD 79.24    | DD 79.93              |
|              |      |          |             | ID n.a.                | ID 69.93    | ID 54.00              |
| Kanazawa     | 2003 | Patients | 43          | DD 50.00               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID 49.00               | ID n.a.     | ID n.a.               |
|              |      |          |             | II 48.00               | II n.a.     | II n.a.               |
| van Suylen   | 1999 | Patients | 27          | DD 38.20               | DD n.a.     | DD n.a.               |
|              |      |          |             | ID n.a.                | ID n.a.     | ID n.a.               |
|              |      |          |             | II n.a.                | II n.a.     | II n.a.               |

Abbreviations: FEV1, forced expiratory volume in one second; FVC, forced vital capacity; ACE, angiotensin converting enzyme; DD, deletion/deletion genotype; ID, insertion/deletion; II, insertion/insertion genotype; n.a., not available.
Supplementary Figure 1. PRISMA flow diagram

Records identified through database searching (n = 97) → Additional records identified through other sources (n = 2) → Records after duplicates removed (n = 53) → Records screened (n = 46) → Records excluded (n = 7) → Full-text articles assessed for eligibility (n = 42) → Full-text articles excluded, without published in English, or lacked the control group (n = 4) → Studies included in qualitative synthesis (n = 16) → Studies included in quantitative synthesis (meta-analysis) (n = 16)

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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