Prediction models for exacerbations in patients with COPD: A systematic review

Online Material

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(Note: Along all this online material the labels m-Table and m-Figure refer, respectively, to a table and a figure included in the main text and reported for clarity in this online material as well. Their numbering will reflect the numbering of the main text and will be independent from the numbering of figures and tables of this online material. The numbering of the protocol of the systematic review is also independent form the numbering of the rest of the online material).
PROTOCOL FOR SYSTEMATIC REVIEW

The next pages contain the original protocol on which the systematic review relied. Each deviation from the original protocol is highlighted in red (the numbering of the figures, tables of this protocol reflects the ones of the original protocol and are independent form the numbering of the rest of this online material. The references are instead in line with the rest of the online material).

Background

A number of treatments for patients with COPD offer benefits but are associated with harms. For example, inhaled corticosteroids reduced the risk for exacerbations, in particular in patients with severe COPD, but are associated with fungal and bacterial infections of the oral cavity and respiratory tract, osteoporotic fractures and cataracts [1–4]. Or, the recently approved drug roflumilast also reduces exacerbations when added to standard inhaled therapy but comes with psychiatric and gastrointestinal harms [5].

Physicians face the challenging task of balancing these benefits and harms and discussing them with their patients. Ultimately, the treatment choice will depend on the patients' risk for benefit and harm outcomes and their preferences. If a COPD patient is at high risk for exacerbations, treatment with inhaled corticosteroids and even roflumilast may be justified because the potential benefits outweigh harms as benefit harm analyses shows [5]. A less harmful therapy (for instance more physical activity) would instead be implemented for patients at lower risk for exacerbations.

Another key challenge for physicians is to estimate outcome risks in individuals as a basis for balancing expected benefits and harms. Whereas the use of prediction models already has a tradition in some medical fields [6, 7], prediction of outcomes (e.g. BODE
and ADO index for mortality, DOSE for exacerbation, ICE COLD for quality of life) for COPD patients has been introduced relatively recently.

The first prominent example of an index predicting mortality in COPD patients was the BODE index [8]. Later a long list of indices (for instance, the ADO index [9, 10]) was developed in different cohorts and for different outcomes. In most indices non-lung related predictors like age, exercise capacity tests (e.g. the 6 minute walk or the sit to stand test [11]), dyspnoea, body-mass index were placed side by side to lung function tests (like FEV₁).

The clinically most helpful prediction models are arguably the ones predicting exacerbations, whose use could effectively drive risk-stratified treatment selection. A number of studies focusing on the prediction of exacerbations as outcome in COPD patients have been published in the last years [12, 13]. They refer to different populations and severity of the disease and to various definitions of exacerbation. It is currently unclear which of the existing prediction models have the best predictive performance. In addition, the potential of additional predictors needs to be evaluated. Particularly interesting is the possibility of “translational paths” that could help clinicians to integrate novel types of predictors into prognostic tools, such as biomarkers (e.g. arising from cell-biology, genomics and proteomics) that yield more complete profiles of patients with a potential to better predict exacerbations. Also, environmental factors (like indoor and outdoor air pollution or exposure to cold weather conditions) and monitoring data from smart devices (e.g. physical activity) could represent attractive predictors that add to existing prediction models and address some of the under-fitting that is likely to be present from some existing indices.

Therefore, our goal is to systematically review such models predicting exacerbations in COPD patients in order to evaluate their
comparative performances and set a basis for further development and updates of prediction models for exacerbations.

**Methods**

We will follow the standard systematic review methodology outlined in the handbook of the Centre for Reviews and Dissemination (York, UK).

**PROTOCOL EXTENSION:** We followed as well the PRISMA Statement for reporting of systematic reviews [14, 15]. We have adopted this extension, since it is the PRISMA statement is actually considered the gold standard for the reporting of systematic reviews.

The objective of the review is to identify and synthesize studies assessing the risk of exacerbation in COPD (Chronic Obstructive Pulmonary Disease) patients by means of a prediction model.

**Inclusion criteria**

- **Population**

Patients with moderate-to-very-severe COPD (Chronic Obstructive Pulmonary Disease), that according to the National Institute of Clinical Excellence, correspond to GOLD stage II to IV. The two spirometric measures associated to these conditions are FEV$_1$/FVC < 0.7 and FEV$_1$ < 80% of the predicted value (i.e. adjusted for age, sex, weight, height, etc). This choice constitutes a disease spectrum broad enough for prediction models that have the potential to be applicable to a broad range of COPD patients. We exclude GOLD I
patients (FEV$_1$ $\geq$ 80% predicted), though, since their likelihood of exacerbation is low.

- **Outcome**

  Exacerbation

  The definition of exacerbation is controversial [16]. We will accept both, the event-based definition and the symptom based definition. If prediction models predict hospitalisations because of COPD but do not explicitly refer to exacerbations we will also include them and consider them as prediction models for severe COPD exacerbations.

- **Types of study design**

  - Longitudinal observational studies: both prospective and retrospective.
  - Experimental studies: only control arm without active treatment.

- **Prognostic parameters, predictor acceptance framework and future validation strategy**

  Our goal is to find out which prediction models are able to predict exacerbations in COPD patients best. In principle, any possible available variable that could help in the prediction of the outcome
will be considered in this systematic review. Beside more traditional predictors such as lung function, age, previous exacerbations, etc. we also consider models that include non-lung related clinical predictors (e.g. physical activity, comorbidities) as well as novel type of predictors (e.g. biomarkers, environmental factors and smart devices data) that are becoming available.

Our choice of parameters could theoretically come from the three following sets of typical ways to associate an exposure with an outcome.

*Figure 1: Univariate and multivariate models with or without a focus on particular predictors*

| Univariate association | Multivariate Association with focus on a particular | Prediction model without focus on a particular |

We are aware of a number of prediction models for exacerbations (Table 1). We will aim to identify additional prediction models as part of this systematic review. However, there may be additional predictors not considered in the existing prediction models. We are interested in these predictors but are aware of the great number of studies that report on potential predictors of exacerbations. In principle and as shown above these predictors may have been assessed by uni- or multivariate models. We are not interested in univariate associations in this systematic review.
because their potential to predict exacerbations does not become apparent without considering other predictors in a multivariate model.

For potential predictors evaluated in multivariate models, that are not labeled as prediction models, investigators typically have a focus on a particular predictor (e.g. depression to predict exacerbations). The independent contribution of the predictor of interest is typically assessed while adjusting for other predictors (typically, age, sex, FEV₁, previous exacerbations). We are aware that such models are subject to biases, namely publication bias (only significant associations for the predictor of interest published). Nevertheless, we could potentially integrate these predictors into an already existing prediction model in future updates.

Figure 2 presents a framework for where we draw a line to distinguish between models that focus on particular predictors and models that are potentially valuable to improve prediction of exacerbations.
In order to judge the potential of predictors to add to already existing prediction models we will consider studies reporting on multivariate models with focus on a particular predictor if the association has been adjusted for predictors commonly included in existing prediction models.

**PROTOCOL DEVIATION:** given the great heterogeneity of the included studies, we deemed the models to be too heterogeneous to be compared (the reason why we did not perform a meta-analysis as well). Thus, for a concurrent comparison, we would need to start from scratch with a standard derivation and the same statistical approach for all the models. For these reasons, we considered this two categories (model in the green and yellow boxes in Figure 2) equivalent in the main text of the systematic review, being for our purposes equally informative, since they do not constitute final models that we can already concurrently compare, but they “only”

---

**Figure 2: Framework for evaluating prediction models and potentially new predictors**

| Models discarded | Predictors considered for new prognostic index | Indices to concurrently validate |
|------------------|-----------------------------------------------|---------------------------------|
| **Univariable association** | **Multivariable association with focus on a particular predictor (not adjusted for a set of typical predictors)** | **Multivariable association without focus on a particular predictor (a performance measure has to be provided)** |
| **Prediction model** | | |

---
provide us with an indication of which combination of predictors can be helpful for the prediction of exacerbations in patients with COPD.

Table 1 presents a summary of predictors in existing prediction models we are aware of. According to the most common predictors, we will consider the variables FEV$_1$ (or another lung function measure), age, current smoking status and previous exacerbation history predictors that have to be present in a multivariate model.

Table 1: Predictors used in different models predicting exacerbations for COPD patients

| Predictors | Dyspnea | FEV$_1$ % pred | Smoking | Previous Exacerbation | BMI | Age | Sex | Quality of Life | CVD History | Exercise Capacity | COPD duration | Cough | Drugs | Influenza | Other biomarkers | Race | Education |
|------------|---------|----------------|---------|-----------------------|-----|-----|-----|----------------|-------------|------------------|---------------|-------|-------|----------|-----------------|------|-----------|
| DOSE       | X       | X              | X       |                       |     |     |     |                |             |                  |               |       |       |          |                 |      |           |
| Briggs     | X       | X              | X       | X                     | X   |     |     |                |             |                  |               |       |       |          |                 |      |           |
| SAFE       | X       | X              | X       |                       |     |     |     |                |             |                  |               |       |       |          | X                |      |           |
| Niewoehner | X       | X              | X       |                       |     |     |     |                | X           | X                |               |       |       |          | X                |      |           |
| Schembri   | X       | X              | X       |                       | X   | X   |     | X              |             |                  |               |       |       |          | X                |      |           |
| Thomsen    | X       | X              | X       |                       | X   | X   | X   |                |             |                  |               |       | X    |          | X                |      |           |
| Omachi     | X       | X              | X       |                       | X   |     |     |                |             |                  |               |       | X    |          | X                |      |           |

Frequency 3 6 4 6 3 5 3 2 3 1 1 1 1 3 1 1 1 1

Thus in summary, in order to focus on existing prediction models and to identify potential new predictors that may improve existing prediction models, we will include:
- Studies reporting multivariate models that are explicitly labelled as prediction models for COPD exacerbations or hospitalisations.
- Studies reporting multivariate models that do not focus on any particular predictor
- Studies reporting multivariate models that focus on a particular predictor but where FEV₁ (absolute or in % predicted), age, current smoking status and previous exacerbation history were included.

PROTOCOL CLARIFICATION: we included as well indices already developed (as long as they were providing at least one performance measure), since it was a pretty common case where some variables were "forced" into a model. We accepted this case, since the whole model was "forced" and not only a predefined variable.

We will exclude:
- Studies reporting multivariate models where FEV₁ (absolute or in % predicted), age, current smoking status and previous exacerbation history (all four) were not included in the model.
- Studies reporting univariate models.
• **Information required to be reported in order to be considered in the systematic review**

  - For prediction models: all regression coefficients.

  **PROTOCOL DEVIATION:** In the end, we did not require the studies to provide the reader with regression coefficients, since we have realized that they were not meaningful for the purposes of our review, given the great heterogeneity of the literature. The statistical models were so different that comparing regression coefficients was not deemed to be relevant by the authors of this systematic review.

  - For multivariate associations with a focus on a specific predictor: at least regression coefficient for the predictor of interest
  - For prediction models and multivariate associations: at least one metric for fit performance out of: Goodness-of-fit, calibration (e.g. Hosmer-Lemeshow), discrimination (AUC), Brier score and other metrics of prediction model not based on generalised regression model

  **PROTOCOL CLARIFICATION:** R-square as well was considered enough alone for inclusion if it was referring to a predefined score).
Exclusion criteria

- Population

  Studies with patients with mild COPD (FEV₁ > 80% expected, GOLD grade I)

- Study Design

  Case-control studies and cross-sectional studies

- Statistical Analysis

  No regression analysis.

  PROTOCOL DEVIATION: as already previously explained in the text: in the end, no regression coefficients were required.

  No fit performances provided or no other statistical analysis provided

- Language restriction

  None

Search Strategy

  1. We will perform literature searches in the following electronic databases:

     - MEDLINE (1967 to December 2013)
     - EMBASE (1947 to December 2013)
     - SCOPUS

  The search strategy for the previous databases can be found in Appendix 1.
2. We will hand-search the bibliographies of reviews and of Conference proceedings and supplements (e.g. from ATS, ERS) to identify further relevant studies belonging to grey literature, like not published in peer reviewed journal or circulated as reports or discussion papers.

3. Title and abstract screening (duplicates will be removed).

4. Pub-med “related articles” search (first 50 studies sorted by ranking) for the so far included studies.

5. References of included articles

The selection process will provide us with the papers that will be further evaluated by full-text assessment.

*Management of references*

The bibliographic details of all retrieved articles will be stored in a Mendeley file. The source of identified articles (database, hand-search, Pub-med related articles) will be recorded in a field of the Mendeley file, as well.
**Study selection and data extraction strategy**

Abstracts and titles screening: Two members of the review team will independently assess the title and abstract of all identified papers (see Appendix 2). Decisions of the two reviewers will be recorded (0 = exclude; 1 = order for full text assessment) in the Mendeley file. We will order any full paper that is deemed potentially eligible by at least one of the reviewers.

Full text screening: two reviewers will evaluate the full text of all potentially eligible papers. Summary of the findings of individual studies will be performed by tabulating in a predefined Windows Excel form (Appendix 3) details about study design, severity of disease, outcome, as well as analysis performed (predictors, performance measures) and bibliographic details (such as authors, journal, year of publication). A small sample of studies with high likelihood for inclusion will serve to pretest the data forms. To obtain missing information, we will contact authors of primary studies. By means of the full text assessment, the two reviewers will make a decision whether to include or exclude each study, according to the specified inclusion and exclusion criteria (Appendix 4). Any disagreements will be resolved by consensus with close attention to the inclusion/exclusion criteria. If needed, a third reviewer will have a final decision. Final decisions on papers will then be recorded in the Mendeley file. All studies that do not fulfil all of the criteria will be excluded and the reasons for their exclusion
noted (see Appendix 5). A particular attention will be received by the “near misses” (studies that only narrowly failed to meet inclusion criteria and that some readers might have expected to be included). Even though knowledge of the authors, institutions, journals or the outcomes could affect the assessment, the reviewers will not be blind to them. Indeed, it was shown that the gain guaranteed by the blinding would not offset the effort required [17].

**Quality assessment**

Two reviewers will independently evaluate all included studies using a list of selected quality items (e.g. quality of the outcome assessment (i.e. exacerbation), follow-up length and completeness, ratio event per predictors, mathematical description provided; see Appendix 6. We will resolve discordant scores based on real differences in interpretation through consensus or third party arbitration.

PROTOCOL EXTENSION: we performed the quality assessment following the Cochrane guidelines [18] and the PROBAST manuscript, guidelines of quality assessment of prediction model (http://www.systematic-reviews.com/probast).
Expected Implications of the Systematic Review

- Identification of existing prediction models
- Judgment of their predictive performances
- Identification of new predictors that could be added to existing prediction indices.
- Basis for concurrent validation of the existing models and their further development
Appendix 1: Search strategy for Medline and Embase

Databases: MEDLINE, EMBASE, SCOPUS

Search Strategy: We will identify a few papers that fulfil the eligibility criteria for our study. We will, then, extract from them a few key words related to the three conceptual spheres:

- **Disease**: “COPD”, “Chronic Obstructive Pulmonary Disease”
- **Outcome**: “Exacerbation”, “Hospitalisation”
- **Risk**: “Risk”, “Prediction model”, “Probability”
Appendix 2: Selection criteria for title and abstract screening

Inclusion criteria

1. Study design: cohort studies or RCT (placebo arm).
2. Population: patients in COPD cohorts (medium-to-very-severe COPD, GOLD grade II, III, IV or GOLD grade B, C, D).
3. Outcome: Exacerbation (both symptom and event based). Also the terms “hospitalisazion”, “mechanical ventilation”, “worsening of symptoms”, “adverse outcome” will be accepted at this stage.
4. Prediction model or multivariable association.
5. Time range: any (from days to years)

Exclusion criteria:

1. Study design: case-control studies, cross-sectional studies.
2. Population: mild COPD patients (GOLD grade I or A), non COPD patients, COPD patients with comorbidities.
3. Outcome: “disability” will not constitute an accepted outcome.
4. No prediction of the risk of exacerbation or multivariable association with exacerbation.

Classification of title & abstract screening:

0 = exclude; 1 = include.
### Appendix 3: Excel form summarizing the findings of individual studies after full-text assessment

| Authors | Journal | Year | Study Design | Cases (Patients) | Severity | Follow up | Outcome | Predictors | Performance measures |
|---------|---------|------|--------------|------------------|----------|-----------|---------|------------|-----------------------|
|         |         |      |              |                  |          |           |         |            |                       |
|         |         |      |              |                  |          |           |         |            |                       |
|         |         |      |              |                  |          |           |         |            |                       |
|         |         |      |              |                  |          |           |         |            |                       |
|         |         |      |              |                  |          |           |         |            |                       |
Appendix 4: Selection criteria for full text assessment

Reviewer: Paper No: 1st Author: Year: Language:

**Inclusion criteria:**

1. Cohort or randomised control trial (placebo arm) Yes/No

2. Patients with COPD in a cohort Yes/No
   (medium-to-very-severe (GOLD score II to IV) COPD)

3. Outcome: Exacerbations Yes/No

4. Prediction model or Multivariable association Yes/No
   4.b. Multivariable association (focus on a particular predictor) Yes/No

5. Overall performance (e.g. Brier Score) or Discrimination (e.g. AUC) or Calibration (e.g. Hosmer-Lemeshow) measure reported Yes/No
   5.b Adjustment for previous exacerbations, age, FEV\textsubscript{1}, smoking status Yes/No

**Exclusion criteria:**

1. Study design: case-control or cross-sectional

2. Population: patients in COPD primary care (mild patients), non COPD patients
3. Outcome: no exacerbation

4. Neither prediction of risk nor multivariable association

If not included for other reasons, specify them below:
### Appendix 5: Reason for exclusion after full-text assessment and data extraction process

| Article | Reason for exclusion |
|---------|----------------------|
|         |                      |
|         |                      |
|         |                      |
## Appendix 6: Quality assessment

| Paper | Cohort | Outcome assessment | Follow up length | Follow up completeness | #Cases/ #Predictors | Performance measures | Quality |
|-------|--------|--------------------|------------------|------------------------|---------------------|----------------------|---------|
|       |        |                    |                  |                        |                     |                      |         |
|       |        |                    |                  |                        |                     |                      |         |
|       |        |                    |                  |                        |                     |                      |         |
|       |        |                    |                  |                        |                     |                      |         |
|       |        |                    |                  |                        |                     |                      |         |
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New section
SELECTION PROCESS (OVERVIEW)

Below in m-Figure 1 ("m" stays for main text) we report the flow diagram of the selection process.

![Flow diagram of the study selection process.](image)

m-Figure 1. Flow diagram of the study selection process.

The main steps concerning the selection process of the studies were:

- Search strategy
- Title and abstract screening
- Full-text assessment
- Data extraction and retrieval (the performance retrieval by asking the authors was needed for the inclusion of studies not providing any performance in the paper)

We carefully describe the different steps of the selection process in the next sections.
New section
SEARCH STRATEGY
We identified eligible papers through a search of the databases Medline (from 1949), Embase (from 1974) and Scopus (from 1996). The search was performed by an information specialist of the University of Zurich (Zurich, Switzerland).

We can summarize the results in Table 1.

|       | References | References after duplication |
|-------|------------|-----------------------------|
| Medline | 472        | 445                         |
| Embase | 355        | 171                         |
| Scopus | 1030       | 729                         |
| Pool   | 1857       | 1345                        |

Table 1. References coming from the different databases

We report in the next paragraphs the search strategies for the three databases.

MEDLINE
Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMED Present
Search Strategy:
# Searches Results
1 Lung Diseases/ 60324
2 chronic.tw. 828489
3 1 and 2 7277
4 lung diseases, obstructive/ or pulmonary disease, chronic obstructive/ or bronchitis, chronic/ 41959
5 (COPD or ‘chronic lung disease’ or ‘chronic obstructive lung disease’ or ‘chronic bronchitis’).tw. 41061
6 exp Pulmonary Emphysema/ 13841
7 emphysema.tw. 18546
8 emphysema/ or mediastinal emphysema/ or subcutaneous emphysema/ 8180
9 7 not 8 14574
10 3 or 4 or 5 or 6 or 9 80849
11 disease progression/ 106382
12 (exacerbation* or aggravation or worsening).ti,ab. 67536
13 ((COPD or respiratory) adj5 (hospitalisation or hospitalisation)).ti,ab. 1234
14 or/11-13 171248
15 10 and 14 8720
16 ((prediction or prognostic or prospective) adj3 (tool* or model* or score* or index* or validation or stratification)).ti,ab. 30013
17 (risk adj3 (estima* or score* or index* or assessment or stratification or validation)).ti,ab. 88825
18 (score* or index*).ti. 73231
19 16 or 17 or 18 181319
20 "severity of Illness Index"/ 172376
21 (severity adj3 (score or index or assessment or stratification or validation)).ti,ab. 21936
22 20 or 21 188090

Systematic Review, 10.01.17 - 31
1. Inflammatory biomarkers and exacerbations in chronic obstructive pulmonary disease.
Thomsen M. Ingebrigtsen TS. Marott JL. Dahl M. Lange P. Vestbo J. Nordestgaard BG.
JAMA. 309(22):2353-61, 2013 Jun 12.
[Journal Article. Research Support, Non-U.S. Govt]
UI: 23757083
Authors Full Name
Thomsen, Mette. Ingebrigtsen, Truls Sylvan. Marott, Jacob Louis. Dahl, Morten. Lange, Peter. Vestbo, Jorgen. Nordestgaard, Borge G.
Ovid: Search Results http://ovidsp.tx.ovid.com/sp-3.12.0b/ovidweb.cgi
1 von 2 21.08.2014 11:12
Ovid: Search Results http://ovidsp.tx.ovid.com/sp-3.12.0b/ovidweb.cgi
2 von 2 21.08.2014 11:12

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#27 #11 AND #24 AND [animals]/lim AND [humans]/lim 4
#26 #11 AND #24 AND [animals]/lim 4
#25 #11 AND #24 355
#24 #16 OR #23 259,505
#23 #19 AND #22 29,288
#22 #20 OR #21 803,070
#21 prediction:ti OR prognostic:ti OR prognosis:ti OR prospective:ti 272,216
#20 'prospective study'/exp OR 'prognosis'/de 671,247
#19 #17 OR #18 204,519
#18 (severity NEAR/3 (score OR index OR assessment OR stratification OR validation)):ab,ti 29,905
#17 'scoring system'/exp OR 'severity of illness index'/exp 179,790
#16 #12 OR #13 OR #14 OR #15 236,686
#15 score*:ti;OR index*:ti 91,892
#14 'international prognostic scoring system'/exp 907
#13 (risk NEAR/3 (estima* OR score* OR index* OR assessment OR stratification OR validation)):ab,ti 119,859
#12 ((prediction OR prognostic OR prospective) NEAR/3 (tool* OR model* OR score* OR index* OR validation OR stratification)):ab,ti
#11 #6 AND #10 13,148
#10 #7 OR #8 OR #9 127,303
#9 ((copd OR respiratory) NEAR/5 (hospitalisation OR hospitalisation)):ab,ti 1,667
#8 exacerbation*:ab,ti OR aggravation:ab,ti OR worsening:ab,ti 98,817
#7 'disease exacerbation'/exp 44,216
#6 #1 OR #2 OR #3 OR #4 OR #5 108,121
#5 'chronic pulmonary disease'/exp OR 'chronic obstructive pulmonary disease'/exp 78,965
#4 'copd'/exp OR 'chronic lung disease'/exp OR 'chronic obstructive lung disease'/exp OR 'chronic bronchitis':ab,ti
Auftragsrecherche zur Studie **Prediction modelling in COPD patients** Herr B. Guerra, ISPM

### Scopus Search History

(((TITLE-ABS-KEY(COPD or 'chronic lung disease' or 'chronic obstructive lung disease' or 'chronic bronchitis')) OR (TITLE-ABS-KEY(chronic W/3 "lung disease" or "bronchitis"))) AND ((TITLE-ABS-KEY(exacerbation* or aggravation or worsening)) OR (TITLE-ABS-KEY((COPD or respiratory) W/5 (hospitalisation or hospitalisation)))))) and ((TITLE-ABS-KEY((prediction or prognostic or prospective) W/3 (tool* or model* or score* or index* or validation or stratification)))) or (TITLE-ABS-KEY(risk W/3 (estima* or score* or index* or assessment or stratification or validation)))) or (TITLE(score* or index*)) or ((TITLE-ABS-KEY(severity W/3 (score or index or assessment or stratification or validation))))) and (TITLE(prediction or prognostic or prognosis or prospective)))
New section
TITLE AND ABSTRACT SCREENING
1345 studies were identified by the electronic search. They were screened by title and abstract according to the inclusion/exclusion criteria identified in the following sheet (already shown in the protocol section earlier in this document).

Selection criteria for title and abstract screening

Inclusion criteria
6. Study design: cohort studies or RCT (placebo arm).
7. Population: patients in COPD cohorts (medium-to-very-severe COPD, GOLD grade II, III, IV or GOLD grade B, C, D).
8. Outcome: Exacerbation (both symptom and event based). Also the terms “hospitalisation”, “mechanical ventilation”, “worsening of symptoms”, “adverse outcome” will be accepted at this stage.
9. Prediction model or multivariable association.
10. Time range: any (from days to years)

Exclusion criteria:
5. Study design: case-control studies, cross-sectional studies.
6. Population: mild COPD patients (GOLD grade I or A), non COPD patients, COPD patients with comorbidities.
7. Outcome: “disability” will not constitute an accepted outcome.
8. No prediction of the risk of exacerbation or multivariable association with exacerbation.

Classification of title & abstract screening:
0 = exclude; 1 = include.
New section
FULL-TEXT ASSESSMENT
The authors (BG and VG) have screened the full-text of the studies coming from two different source, as follows:

- **“Source 1 for full-text assessment”:** From title and abstract screening: **227 papers**

These are directly coming from the title and abstract screening of the initial 1345 studies (found by the electronic search).

- **“Source 2 for full-text assessment”:** From the references and Pubmed related search of the 20 papers definitively included from “source 1”) of full-text assessment or from grey literature or from suggestions of contacted authors or from reviews: **82 papers**

Table 2 and Table 3 show the reasons for exclusion for the two sets of papers.
| Reason for exclusion          | Number of studies | Details of the reason                                                                 | Number of studies |
|------------------------------|-------------------|--------------------------------------------------------------------------------------|-------------------|
| Not a prediction model       | 69                | Not a prediction model (neither prediction model nor multivariable association)      | 22                |
|                              |                   | Not a prediction model (focus on a particular predictor without the wanted adjustment) | 47                |
| Not the wanted outcome       | 43                |                                                                                      |                   |
| Not a primary study          | 35                | Not a primary study (abstract)                                                        | 3                 |
|                              |                   | Not a primary study (review)                                                           | 2                 |
|                              |                   | Not a primary study (editorial)                                                        | 23                |
|                              |                   | Not a primary study (commentary)                                                       | 3                 |
|                              |                   | Not a primary study (poster)                                                           | 4                 |
| Not the wanted study design  | 24                | Not the wanted study design (RCT, not only placebo arm)                               | 11                |
|                              |                   | Not the wanted study design (ecological study)                                         | 6                 |
|                              |                   | Not the wanted study design (case-control study)                                       | 3                 |
|                              |                   | Not the wanted study design (cross-sectional study)                                    | 1                 |
|                              |                   | Not the wanted study design (baseline assessment after the follow-up)                  | 2                 |
|                              |                   | Not the wanted study design (data partly collected after the outcome)                  | 1                 |
| Not a COPD cohort            | 12                |                                                                                      |                   |
| No performance measure provided |            |                                                                                      | 10                |
| No spirometry in the COPD definition |        |                                                                                      | 4                 |
| Duplicate*                   | 4                 |                                                                                      |                   |
| Not retrieved                | 4                 |                                                                                      |                   |
| Predictor and outcome not different in our definition | 2            |                                                                                      |                   |
| No GOLD standard for COPD definition |            |                                                                                      | 0                 |
| Included                     | 20                |                                                                                      |                   |
| TOTAL                        | 227               |                                                                                      |                   |

*Duplicates that passed the title initial removal of duplicates

Table 2. Distribution of the reasons for exclusion of the studies after full-text assessment of the 227 studies coming from what we have defined as “Source 1 for full-text assessment” (studies included after title and abstract screening)
| Reason for exclusion          | Number of studies | Details of the reason                                                                                      | Number of studies |
|------------------------------|-------------------|-----------------------------------------------------------------------------------------------------------|-------------------|
| Not a prediction model       | 27                | Not a prediction model (Not a prediction model (neither prediction model nor multivariable association)) | 5                 |
|                              |                   | Not a prediction model (Not a prediction model (focus on a particular predictor without the wanted adjustment)) | 22                |
| Not the wanted outcome       | 13                |                                                                                                           |                   |
| Not a primary study          | 7                 | Not a primary study (abstract)                                                                             | 0                 |
|                              |                   | Not a primary study (review)                                                                              | 6                 |
|                              |                   | Not a primary study (editorial)                                                                           | 1                 |
|                              |                   | Not a primary study (commentary)                                                                         | 0                 |
|                              |                   | Not a primary study (poster)                                                                             | 0                 |
| Not the wanted study design  | 8                 | Not the wanted study design (RCT, not only placebo arm)                                                  | 2                 |
|                              |                   | Not the wanted study design (ecological study)                                                           | 0                 |
|                              |                   | Not the wanted study design (case-control study)                                                          | 4                 |
|                              |                   | Not the wanted study design (cross-sectional study)                                                       | 2                 |
|                              |                   | Not the wanted study design (baseline assessment after the follow-up)                                     | 0                 |
|                              |                   | Not the wanted study design (data partly collected after the outcome)                                     | 0                 |
| Not a COPD cohort            | 2                 |                                                                                                           |                   |
| No performance measure provided | 12            |                                                                                                           |                   |
| No spirometry in the COPD definition | 1                      |                                                                                                           |                   |
| Duplicate*                   | 4                 |                                                                                                           |                   |
| Not retrieved                | 0                 |                                                                                                           |                   |
| Predictor and outcome not different in our definition | 2                      |                                                                                                           |                   |
| No GOLD standard for COPD definition | 1                      |                                                                                                           |                   |
| Included                     | 5                 |                                                                                                           |                   |
| TOTAL                        | 82                |                                                                                                           |                   |

*Duplicates that passed the title initial removal of duplicates
Table 3. Distribution of the reasons for exclusion of the studies after full-text assessment of the 82 studies coming from what we have defined as “Source 2 for full-text assessment” (From the references and Pubmed related search of the 20 papers definitively included from the set 1) of full-text assessment or from grey literature or from suggestions of contacted authors or from reviews on the topic)
In the following tables (Table 4 and Table 5) we report the reasons, paper by paper of the exclusion of each of the 227 + 82 papers included for full-text assessment. It is in general indicated only the main reason for exclusion but there could be other fundamental reasons not reported in the text to exclude each excluded paper.

**Reasons for exclusion: “source 1 for full-text assessment” (227 papers)**

|   | Reason for exclusion | Authors and Title |
|---|----------------------|--------------------|
| 1 | Not a prediction model (neither prediction model nor multivariable association) | Agüstí A, Edwards LD, Rennard SI, MacNee W, Tal-Singer R, Miller BE, Vestbo J, Lomas D a, Calverley PM a, Wouters E, Crim C, Yates JC, Silverman EK, Coxson HO, Bakke P, Mayer RJ, Celli B. Persistent systemic inflammation is associated with poor clinical outcomes in COPD: a novel phenotype. *PLoS One* [Internet] 2012 [cited 2014 May 27]; 7: e37483Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3356313&tool=pmcentrez&rendertype=abstract. |
| 2 | Not a prediction model (neither prediction model nor multivariable association) | Albert RK, Connett J, Curtis JL, Martinez FJ, Han MK, Lazarus SC, Woodruff PG. Mannose-binding lectin deficiency and acute exacerbations of chronic obstructive pulmonary disease. *Int. J. COPD* [Internet] Medicine Service, Denver Health and Department of Medicine, University of Colorado Denver, Denver, CO, United States Division of Biostatistics, School of Public Health, University of Minnesota, Minneapolis, MN, United States Pulmonary and Critical Care Me; 2012; 7: 767–777Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84872306384&partnerID=40&md5=9b2056ef587d547ff72052aece64347. |
| 3 | Not the wanted study design (cross-sectional study) | Alcázar B, García-Polo C, Herrejón A, Ruiz LA, de Miguel J, Ros JA, García-Sidro P, Tirado Conde G, López-Campos JL, Martínez C, Costán J, Bonnin M, Mayoralas S, Miravitlles M. Factors associated with hospital admission for exacerbation of chronic obstructive pulmonary disease. *Arch. Bronconeumol.* [Internet] Unidad de Gestión Clínica de Neumología, Complejo Hospitalario de Jaén, Jaén, Spain Unidad de Gestión Clínica de Neumología, Hospital Puerta del Mar, Cádiz, Spain Servicio de Neumología, Hospital Universitario Dr. Pesset, Valencia, Spain Servicio de Neumo; 2012; 48: 70–76Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84857191700&partnerID=40&md5=e1a9a8d2b9c347a132a2bbe575c96182. |
| 4 | Not a prediction model (neither prediction model nor multivariable association) | Almagro P, Cabrera FJ, Diez J, Boixeda R, Alonso Ortiz MB, Murio C, Soriano JB. Comorbidities and short-term prognosis in patients hospitalized for |
|   |   |   |
|---|---|---|
| **prediction model** nor multivariable association) | acute exacerbation of COPD: The EPOC en servicios de medicina interna (ESMI) study. *Chest* [Internet] P. Almagro, Hospital Mutua de Terrassa, Barcelona University, 08221 Terrassa, Barcelona, Spain; 2012; 142: 1126–1133Available from: [http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L366010474](http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L366010474) [http://dx.doi.org/10.1378/chest.11-2413](http://dx.doi.org/10.1378/chest.11-2413) [http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00123692&id=doi:10.1378/chest.11-2413&atitle=Comorbidities+and+short-term+progn.](http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00123692&id=doi:10.1378/chest.11-2413&atitle=Comorbidities+and+short-term+progn.) |   |
| 5 | Included | Almagro P, Soriano JB, Cabrera FJ, Boixeda R, Alonso-Ortiz MB, Barreiro B, Diez-Manglano J, Murio C, Heredia JL, Working Group on Copd SS of IM. Short- and medium-term prognosis in patients hospitalized for COPD exacerbation: the CODEX index. *Chest* [Internet] 2014; 145: 972–980Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24077342](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24077342) [http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24077342&id=doi:&issn=0012-3692&isbn=#volume=145&issue=5&spage=972&pages=972-80&date=2014&title=Chest&atitle=S.](http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24077342&id=doi:&issn=0012-3692&isbn=#volume=145&issue=5&spage=972&pages=972-80&date=2014&title=Chest&atitle=S.) |   |
| 6 | Included | Almagro P, Barreiro B, Ochoa de Echaguen A, Quintana S, Rodríguez Carballeira M, Heredia JL, Garau J. Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration*. [Internet] 2006 [cited 2014 Sep 8]; 73: 311–317Available from: [http://www.ncbi.nlm.nih.gov/pubmed/16155352.](http://www.ncbi.nlm.nih.gov/pubmed/16155352.) |   |
| 7 | Included | Amalakuhan B, Kiljanek L, Parvathaneni A, Hester M, Cheriyath P, Fischman D. A prediction model for COPD readmissions: catching up, catching our breath, and improving a national problem. *J. Community Hosp. Intern. Med. Perspect.*. [Internet] Department of Internal Medicine, Pinnacle Health System-Harrisburg Hospital, Harrisburg, PA, USA.; 2012; 2Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=23882354](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=23882354) [http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:23882354&id=doi:10.3402%2Fjchimp.v2i1.9915&issn=2000-9666&isbn=#volume=2&issue=1&page=&pages=&date=2012&title=Journal+of+Community+Hospital+Internal+Medicine+Perspectives+&atitle=A+prediction+model+for+COPD+readmissions%3A+catching+up%2C+catching+our+breath%2C+and+improving+a+national+problem.&aulast=Amalakuhan&pid=%3Cauthor%3EAmalakuhan+%3BKiljanek%3BL%3E.](http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:23882354&id=doi:10.3402%2Fjchimp.v2i1.9915&issn=2000-9666&isbn=#volume=2&issue=1&page=&pages=&date=2012&title=Journal+of+Community+Hospital+Internal+Medicine+Perspectives+&atitle=A+prediction+model+for+COPD+readmissions%3A+catching+up%2C+catching+our+breath%2C+and+improving+a+national+problem.&aulast=Amalakuhan&pid=%3Cauthor%3EAmalakuhan+%3BKiljanek%3BL%3E.) |   |
| 8 | Duplicate | Amalakuhan B, Kiljanic L, Hester M, Cheriyath P, Fischman D. A prediction model for COPD readmissions: Catching up, catching our breath and improving a national problem. *Am. J. Respir. Crit. Care Med.*. [Internet] B. Amalakuhan, PinnacleHealth Hospitals Network, Harriburg, United States; |   |
|   |   |   |
|---|---|---|
| 9 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Anderson B, Dominici F, Wang Y, Bell M, McCormack M, Peng R. Heat-related emergency hospitalizations for respiratory diseases in the medicare population. *Am. J. Epidemiol.* [Internet] B. Anderson, Johns Hopkins Bloomberg, School of Public Health, Baltimore, United States; 2013; 177: S64Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L71079377 http://dx.doi.org/10.1093/aje/kwt103 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00029262&id=doi:10.1093%2Faje%2Fkwt103&atitle=Heat-related+emergency+hospitalizations+for+respiratory+diseases+in+the+medicare+population&stitle=Am.+J.+Epidemiol.&title=American+Journal+of+Epidemiology&volume=177&issue=&spage=S64&epage=&aulast=Anderson&aufirst=Brooke&auinit=B.&aufull=Anderson+B.&coden=&isbn=&pages=S64-&date=2013. |
| 10 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD. Heat-related emergency hospitalizations for respiratory diseases in the medicare population. *Am. J. Respir. Crit. Care Med.* [Internet] R.D. Peng, Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205, United States; 2013; 187: 1098–1103Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L368940182 http://dx.doi.org/10.1164/rccm.201211-1969OC http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=1073449X&id=doi:10.1164%2Frccm.201211-1969OC&atitle=Heat-related+emergency+hospitalizations+for+respiratory+diseases+in+the+medicare+population&stitle=Am.+J.+Respir.+Crit.+Care+Med.&title=American+Journal+of+Respiratory+and+Critical+Care+Medicine&volume=187&issue=10&spage=1098&epage=1103&aulast=Anderson&aufirst=G.+Brooke. |
| 11 | Not the wanted outcome | Anon Elizalde JM, Garcia De Lorenzo Mateos A, Alvarez-Sala Walther R, Escuela Gerico MP. Treatment and prognosis of the severe exacerbation in the chronic obstructive pulmonary disease. *Rev. Clin. Esp.* [Internet] Servicio de Medicina Intensiva, Hospital Virgen de la Luz, Cuenca. elizalde@iponet.es; 2001; 201: 658–66Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext |
| No | Description                                                                 | Reference                                                                                                                                                                                                 |
|----|------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 12 | No spirometry in COPD definition                                              | Antonelli Incalzi R, Corsonello A, Masoti G, Rengo F, Grassi V, Bellia V, Airoldi G, Albo E, Allegra G, Andriolli A, Arzilli F, Ascione G, Attardo Parrinello G, Baldacchino A, Baldasseroni L, Ballini E, Barassi V, Bazzoni P, Benintende A, Bergamo O, Bernardi R, Bernardini M, Bertoni P, Bibbo P, Buizza M, Beatrice G, Cancian M, Cannao G, Caputo A, Catanese S, et al. The management of the elderly with COPD in Italy. The OLD-COPD study. G. Gerontol. [Internet] R. Antonelli Incalzi, CEMI, Universita Cattolica, 00168 Roma, Italy; 2003; 51: 463–475Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L38515128 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00170305&id=doi:&title=The+management+of+the+elderly+with+COPD+in+Italy.+The+OLD-COPD+study&stitle=G.+Gerontol.&title=Giornale+di+Gerontologia&volume=51&issue=5&spage=463&epage=475&aulast=Antonelli+Incalzi&aufirst=R.&auinit=R.&aufull=Antonelli+Incalzi+R.&coden=GIGEA&isbn=&pages=463-475&date=2003&auinit1=R&auinitm=. |
| 13 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Antoniu SA, Carone M. Hospitalizations for chronic obstructive pulmonary disease exacerbations and their impact on disease and subsequent morbidity and mortality. Expert Rev. Pharmacoeconomics Outcomes Res. [Internet] University of Medicine and Pharmacy Grigore T Popa, 16 Universităţii Str, Iasi 700115, Romania Division of Pulmonary Disease, Fondazione Salvatore Maugeri, IRCCS, 70020 Cassano Murge, Bari, Italy; 2013; 13: 187–189Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84876108392&partnerID=40&md5=41951af8b40330c2519cbbf221f36cb. |
| 14 | Not the wanted study design (RCT, not only placebo arm)                       | Anzueto A, Make BJ, Calverley PM, Jenkins C, Postma DS, Sciarfa F, Similowski T, Peterson S, Ostlund O, Eriksson GS. Effect of budesonide/formoterol treatment on dominant predictors of exacerbations in patients with COPD. Am. J. Respir. Crit. Care Med. [Internet] B.J. Make, National Jewish Health, Denver, United States; 2011; 183Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70849671 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=1073449X&id=doi:&a |
| Study Identification | Not the wanted study design (ecological study) | Arbex MA, De Souza Concepção GM, Cendon SP, Arbex FF, Lopes AC, Moysés EP, Santiago SL, Saldiva PHN, Pereira LAA, Braga ALF. Urban air pollution and chronic obstructive pulmonary disease-related emergency department visits. *J. Epidemiol. Community Health* [Internet] Internal Medicine Post-Graduate Programme, São Paulo Federal University, Medical School, São Paulo, Brazil Laboratory of Experimental Air Pollution, University of São Paulo, Faculty of Medical Sciences, São Paulo, Brazil Environmental Exposure and Risk An; 2009; 63: 777–783 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-70349456559&partnerID=40&md5=840b317dc0b8a6a01903a1fad5bb443d.

| Study Identification | No performance measure provided | Atis S, Kanik A, Ozgur ES, Eker S, Tumkaya M, Ozge C. How exactly can we predict the prognosis of COPD. *Tuberk. Toraks* [Internet] Department of Chest Diseases, Faculty of Medicine, Mersin University, Icel, Turkey. satis@mersin.edu.tr; 2009; 57: 289–297 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19787468 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:19787468&id=doi:&issn=049-1373&isbn=&volume=57&issue=3&spage=289&pages=289-97&date=2009&TITLE=Tuberkuloz+ve+Toraks&ATITLE=KOAH+hastalarinin+progresyonlarini+ne+olcude+tahmin+edebiliriz?&aulast=Atis&pid=<<author>Atis+S;Kanik+A;Ozgur+ES;Eker+S;Tumkaya+M;Ozge+C</author>&AN=19787468&DT=English+Abstract</DT>.

| Study Identification | Not the wanted study design (baseline assessment after the follow-up) | Azarisman MS, Fauzi MA, Faizal MP, Azami Z, Roslina AM, Roslan H. The SAFE (SGRQ score, air-flow limitation and exercise tolerance) Index: a new composite score for the stratification of severity in chronic obstructive pulmonary disease. *Postgrad. Med. J.* [Internet] Department of Medicine, International Islamic University Malaysia, Jalan Hospital Campus, Kuantan, Pahang, Malaysia. risman1973@hotmail.com; 2007; 83: 492–497 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=17621621 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:17621621&iddo:doi:&issn=0032-5473&isbn=&volume=83&issue=981&spage=492&pages=492-7&date=2007&TITLE=Postgraduate+Medical+Journal&ATITLE=The+SAFE+%28
| 18 | Not the wanted outcome | Bafadhel M, McKenna S, Terry S, Mistry V, Reid C, Haldar P, McCormick M, Haldar K, Kebadze T, Duvoix A, Lindblad K, Patel H, Rugman P, Dodson P, Jenkins M, Saunders M, Newbold P, Green RH, Venge P, Lomas DA, Barer MR, Johnston SL, Pavord ID, Brightling CE. Acute exacerbations of chronic obstructive pulmonary disease: identification of biologic clusters and their biomarkers. *Am. J. Respir. Crit. Care Med.* [Internet] Institute for Lung Health, University of Leicester, Leicester, United Kingdom.; 2011; 184: 662–671Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21680942
http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:21680942&id=doi:10.1164%2Frccm.201104-0597OC&issn=1073-449X&isbn=&volume=184&issue=6&page=662&pages=662-71&date=2011&title=American+Journal+of+Respiratory+Care+Medicine&atitle=Acute+exacerbations+of+chronic+obstructive+pulmonary+disease%3A+identification+of+biologic+clusters+and+their+biomarkers.&aulast=Bafadhel&pid=%3Cauteur%3EBafadhel+M%.

| 19 | Not the wanted outcome | Bahadori K, FitzGerald JM, Levy RD, Fera T, Swiston J. Risk factors and outcomes associated with chronic obstructive pulmonary disease exacerbations requiring hospitalization. *Can. Respir. J.* [Internet] Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute and Respiratory Medicine, Vancouver General Hospital, Vancouver, BC, Canada Division of Respiratory Medicine, University of British Columbia, 2775 Laurel Street.; 2009; 16: e43–e49Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-70350153392&partnerID=40&md5=7566b972ab278d5b560c23643b6c6e2.

| 20 | No performance measure provided | Baker CL, Zou KH, Su J. Risk assessment of readmissions following an initial COPD-related hospitalization. *Int. J. Coped* [Internet] Pfizer Inc, New York, NY, USA. Boehringer-Ingelheim Pharmaceuticals Inc, Ridgefield, CT, USA.; 2013; 8: 551–559Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24348031
http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24348031&id=doi:10.2147%2FCOPD.S51507&issn=1176-9106&isbn=&volume=8&issue=&spage=551&pages=551-9&date=2013&title=International+Journal+of+COPD&atitle=Risk+assessment+of+readmissions+following+initial+COPD-related+hospitalization.&aulast=Baker&pid=%3Cauteur%3EBaker+CL%3BZ
21) Not a prediction model (focus on a particular predictor without the wanted adjustment)

Bartziokas K, Papaioannou AI, Minas M, Kostikas K, Banya W, Daniil ZD, Haniotou A, Gourgoulianis KI. Statins and outcome after hospitalization for COPD exacerbation: a prospective study. *Pulm. Pharmacol. Ther.* [Internet] Respiratory Medicine Department, University of Thessaly Medical School, Larissa, Greece.; 2011; 24: 625–631 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21729761

22) Not a primary study (commentary)

Baselli LM, Oswald MA, Nashelsky JM. Do beta-blockers worsen respiratory status for patients with COPD? *J. Fam. Pract.* [Internet] West Jersey-Memorial Family Practice Residency at Virtua, Voorhees, NJ, United States Family Physicians Inquiries Network, Inc., Iowa City, IA, United States; 2005; 54: 472–473 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-20644460160&partnerID=40&md5=69933f5f618d62e0b01487641370dd28a

23) Not the wanted study design (RCT, not only placebo arm)

Beeh KM, Glaab T, Stowasser S, Schmidt H, Fabbri LM, Rabe KF, Vogelmeier CF. Characterisation of exacerbation risk and exacerbator phenotypes in the POET-COPD trial. *Respir. Res.* [Internet] University Medical Center Giessen and Marburg, Philippus-Universitat Marburg, Baldingerstrasse, D 35043 Marburg, Germany. claus.vogelmeier@med.uni-marburg.de.; 2013; 14: 116 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24168767

24) Not a prediction model (focus on a particular predictor without the wanted adjustment)

Benedik B, Farkas J, Kosnik M, Kadivec S, Lainscak M. Mini nutritional assessment score predicts rehospitalisations in patients with chronic
| Study Id | Status | Reference |
|----------|--------|-----------|
| 25       | Not the wanted study design (RCT, not only placebo arm) | Benzo RP, Chang CC, Farrell MH, Kaplan R, Ries A, Martinez FJ, Wise R, Make B, Sciurba F, Group NR. Physical activity, health status and risk of hospitalization in patients with severe chronic obstructive pulmonary disease. *Respiration* [Internet] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA. benzo.roberto@mayo.edu; 2010; 80: 10–18Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20234126 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:20234126&title=Respiration&atitle=Physical+activity%2C+health+status+and+risk+of+hospitalization+in+patients+with+severe+chronic+obstructive+pulmonary+disease.&aulast=Benzo&pid=%3Cauthor%3EBenzo+RP%3BChang+CC%3BFarrell+MH%3BKaplan+R%3BRies+A%3BMartinez+FJ%3BW. |
| 26       | Duplicate | Benzo R, Chang CCH, Farrell MH, Kaplan R, Ries A, Martinez FJ, Wise R, Make B, Sciurba F. Physical Activity, Health Status and Risk of Hospitalization in Patients with Severe Chronic Obstructive Pulmonary Disease. *Respiration* [Internet] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, Minn., USA; 2010; Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L50836950 http://dx.doi.org/10.1159/000296504 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00257931&id=doi:10.1159%2F000296504&atitle=Physical+activity%2C+health+status+and+risk+of+hospitalization+in+patients+with+severe+chronic+obstructive+pulmonary+disease.&aulast=Benzo&pid=%3Cauthor%3EBenzo+RP%3BChang+CC%3BFarrell+MH%3BKaplan+R%3BRies+A%3BMartinez+FJ%3BW. |
| 27       | Included | Bertens LC, Reitsma JB, Moons KG, van Mourik Y, Lammers JW, Broekhuizen BD, Hoes AW, Rutten FH. Development and validation of a particular predictor without the wanted adjustment) obstructive pulmonary disease. *J. Cachexia. Sarcopenia Muscle* [Internet] B. Benedik, University Clinic or Respiratory and Allergic Diseases Golnik, Golnik, Slovenia; 2011; 2: 248Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70808344 http://dx.doi.org/10.1007/s13539-011-0045-3 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=21905991&id=doi:10.1007%2Fs13539-011-0045-3&atitle=Mini+nutritional+assessment+score+predicts+rehospitalisations+in+patients+with+chronic+obstructive+pulmonary+disease&title=J.+Cachexia+Sarcopenia+Muscle&type=J&volume=2&issue=4&spage=248&epage=&aulast=Benedik&aufirst=Barbara&auinit. |
| 28 | Not a primary study (commentary) | Bertoletti L, Righini M. Adequate use of pulmonary embolism clinical prediction rule in COPD patients. *Eur. Respir. J.* [Internet] L. Bertoletti, Groupe de Recherche Sur la Thrombose, EA3065, Universite de Saint-Etienne Jean Monnet, 42000 Saint-Etienne, France; 2011; 37: 219–220. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=exp ort&id=L361187120 http://dx.doi.org/10.1183/09031936.00128410 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&id=pmid:20110309031936&iso=fr&date=2011&journal=Eur+Respir+J&volume=37&issue=1&spage=219&epage=220&title=Eur+Respir+J&atitle=Adequate+use+of+pulmonary+embolism+clinical+prediction+rule+in+COPD+patients&aulast=Bertoletti&aufirst=L.&auinit=L.&aufull=Bertoletti+L.&coden=ERJOE&isbn=&pages=219-220&date=2. |
| 29 | Not a primary study (commentary) | Bischoff M. COPD – Pseudomonas infections are risk factors for hospital treatment. *Pneumologie* [Internet] 2010; 64: 669. Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-78649249223&partnerID=40&md5=039fe624fcc60786a0773a1fae8797cc. |
| 30 | Not the wanted outcome | Blankenburg T, Guettel A, Busch C, Schuette W. Six-minute walk distance and dyspnoea scores to assess the course of COPD exacerbation in elderly patients. *Clin. Respir. J.* [Internet] Second Medical Clinic, Hospital Martha-Maria Halle-Doelau, Halle, Germany. th.blankenburg@gmx.de; 2013; 7: 261–267. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=medl&AN=22823008 http://sfx.metabib.ch/sfx_locator?sid=ovid_sp&pmid=22823008&id=doi:10.1111%2Fj.1752-699X.2012.00314.x&issn=1752-699X&isbn=&volume=7&issue=3&spage=261&pages=261-7&date=2013&title=The+clinical+respiratory+journal&atitle=Six-minute+walk+distance+and+dyspnoea+scores+to+assess+the+course+of+COPD+exacerbation+in+elderly+patients.&aulast=Blankenburg&pid=%3Cauthor%3EBBlankenburg+T%3BGGuettel+A%3BBusch+C%3BSchuett. |
| Study Design | Title                                                                 | Authors                                                                 |
|--------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------|
| 31           | Not the wanted study design (case-control study)                      | Boggon R, Hubbard R, Smeeth L, Gulliford M, Cassell J, Eaton S, Pirmohamed M, van Staa TP. Variability of antibiotic prescribing in patients with chronic obstructive pulmonary disease exacerbations: a cohort study. *BMC Pulm. Med.* [Internet] Clinical Practice Research Datalink, Medicines and Healthcare products Regulatory Agency, 151 Buckingham Palace Road, London SW1W 9SZ, UK.; 2013; 13: 32Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23724907 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23724907&i d=doi:10.1186%2F1471-2466-13-32&issn=1471-2466&isbn=&volume=13&issue=1&page=32&pages=32&date=2013&title =BMC+Pulmonary+Medicine&atitle=Variability+of+antibiotic+prescribing+in+patients+with+chronic+obstructive+pulmonary+disease+exacerbations%3A+a+cohort+study.&aulast=Boggon&pid=%3Cauthor%3EBoggon%3BHubbard%3BSmeeth%3BGulliford%3BCassell. |
| 32           | Not the wanted study design (case-control study)                      | Bourbeau J, Ernst P, Cockcroft D, Suissa S. Inhaled corticosteroids and hospitalisation due to exacerbation of COPD. *Eur. Respir. J.* [Internet] Respiratory Epidemiology Unit, Joints Department of Epidemiology, McGill University, Montreal, Que., Canada Division of Clinical Epidemiology, Pharmacoepidemiology Unit, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Que. H3A 1A1, Canada Respira; 2003; 22: 286–289Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0041525657&partnerID=40&md5=e6c18cc37845cca808c9bf78b5bed20. |
| 33           | Not the wanted outcome                                               | Bozinovski S, Hutchinson A, Thompson M, Macgregor L, Black J, Giannakis E, Karlsson AS, Silvestrini R, Smallwood D, Vlahos R, Irving LB, Anderson GP. Serum amyloid a is a biomarker of acute exacerbations of chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* [Internet] Department of Pharmacology, Medical Building (Level 8), University of Melbourne, Parkville, 3010 Australia. bozis@unimelb.edu.au; 2008; 177: 269–278Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=18006888 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18006888&i d=doi:&issn=1073-449X&isbn=&volume=177&issue=3&page=269&pages=269-78&date=2008&title=American+Journal+of+Respiratory+and+Critical+Care+Medicine&atitle=Serum+amyloid+a+is+a+biomarker+of+acute+exacerbations+of+chronic+obstructive+pulmonary+disease.&aulast=Bozinovski&pid= %3Cauthor%3EBozinovski%3BHutchinson%3BThompson%3BMacgregor%3BLBlack. |
| 34           | Not the wanted study design (RCT,                                    | Briggs A, Spencer M, Wang H, Mannino D, Sin DD. Development and validation of a prognostic index for health outcomes in chronic obstructive |
| Page | Included/Not the wanted outcome | Reference |
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| 35   | Included                        | Brusse-Keizer M, van der Palen J, van der Valk P, Hendrix R, Kerstjens H. Clinical predictors of exacerbation frequency in chronic obstructive pulmonary disease. *Clin. Respir. J.* [Internet] Department of Pulmonary Medicine, Medisch Spectrum Twente, Enschede, Netherlands Department of Research Methodology, Measurement, Data Analysis, University of Twente, Enschede, Netherlands Regional Laboratory of Public Health, Enschede, Netherlands Depart; 2011; 5: 227–234 Available from: [http://www.scopus.com/inward/record.url?eid=2-s2.0-80052992344&partnerID=40&md5=79d7e2f01445ae17b896ad0bba5169a7](http://www.scopus.com/inward/record.url?eid=2-s2.0-80052992344&partnerID=40&md5=79d7e2f01445ae17b896ad0bba5169a7) |
| 36   | Not the wanted outcome          | Bruyneel M, Jacob V, Sanida C, Ameye L, Sergysels R, Ninane V. Hoover’s sign is a predictor of airflow obstruction severity and is not related to hyperinflation in chronic obstructive pulmonary disease. *Eur. J. Intern. Med.* [Internet] Chest Service, Saint-Pierre University Hospital, Brussels, Belgium. Marie-Bruyneel@stpierre-bru.be; 2011; 22: e115–e118 Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22075295](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22075295) |
| 37   | Not the wanted outcome          | Calderon EJ, Rivero L, Respaldiza N, Morilla R, Montes-Cano MA, Friaza V, Munoz-Lobato F, Varela JM, Medrano FJ, Horra Cde L. Systemic inflammation in patients with chronic obstructive pulmonary disease who are colonized with Pneumocystis jiroveci. *Clin. Infect. Dis.* [Internet] Department of Internal Medicine, Virgen del Rocio University Hospital, |
| No. | Type of Study | Authors | Title | Journal and Details |
|-----|---------------|---------|-------|---------------------|
| 38 | No performance measure provided | Cao Z, Ong KC, Eng P, Tan WC, Ng TP. | Frequent hospital readmissions for acute exacerbation of COPD and their associated factors. | Respiratory Research, 2006; 11: 188–195 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-33644826174&partnerID=40&md5=357c20b73aa124748fba4daee6ef9fde0. |
| 39 | Not a primary study (editorial) | Casanova C, Celli BR. | Microalbuminuria as a potential novel cardiovascular biomarker in patients with COPD. | Eur. Respir. J., 2014; 43: 951–953 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84897389164&partnerID=40&md5=ed33ef1280264f6574da37d8f1382695. |
| 40 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Chailleux E, Laaban JP, Veale D. | Prognostic value of nutritional depletion in patients with COPD treated by long-term oxygen therapy: Data from the ANTADIR observatory. | Chest, 2003; 123: 1460–1466 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0037879078&partnerID=40&md5=9d3f3bc0835eeea748bee595277fccc6. |
| 41 | Predictor and outcome not different in our definition | Chandra D, Tsai CL, Camargo Jr CA. | Acute exacerbations of COPD: Delay in presentation and the risk of hospitalization. | COPD J. Chronic Obstr. Pulm. Dis., 2009; 6: 95–103 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-
| Page | Title | Authors | Abstract |
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| 42   | No performance measure provided | Chang SS, Chen S, McAvay GJ, Tinetti ME. Effect of coexisting chronic obstructive pulmonary disease and cognitive impairment on health outcomes in older adults. *J. Am. Geriatr. Soc.* [Internet] Department of Internal Medicine, School of Medicine, Yale University, 333 Cedar St., New Haven, CT 06520, United States Department of Chronic Disease Epidemiology, School of Public Health, Yale University, New Haven, CT, United States; 2012; 60: 1839–1846Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84867487392&partnerID=40&md5=69bcf8b37004e96e0f7d5eb8c5906515. |
| 43   | Not a primary study (editorial) | Chavannes NH, Jones RCM, Postma DS, Rennard S. Using COPD multidimensional indices in routine clinical practice: DOSE meets all criteria. *Prim. Care Respir. J.* [Internet] Department of Public Health and Primary Care, Leiden University Medical Center, Hippocratespad 21, Zone V0-P, PO Box 9600, 2300 RC Leiden, Netherlands Peninsula College of Medicine and Dentistry, Plymouth, United Kingdom Armada Surgery, Plymouth, United K; 2012; 21: 245–246Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84866410186&partnerID=40&md5=35fa7612e895b0ac76f65d0dea1. |
| 44   | Not the wanted study design (ecological study) | Chen Y, Yang Q, Krewski D, Shi Y, Burnett RT, McGrail K. Influence of relatively low level of particulate air pollution on hospitalization for COPD in elderly people. *Inhal. Toxicol.* [Internet] Department of Epidemiology and Community Medicine and McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, Ottawa, Ontario, Canada. ychen@uottawa.ca; 2004; 16: 21–25Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=14744661 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:14744661&did=doi:&issn=0895-8378&isbn=&volume=16&issue=1&page=21&pages=21-5&date=2004&title=Inhalation+Toxicology&atitle=Influence+of+relatively+low+level+of+particulate+air+pollution+on+hospitalization+for+COPD+in+elderly+people.&aulast=Chen&pid=%3Cauthor%3EChen+Y%3BYang+Q%3BKrewski+D%3BShi+Y%3BBurnett+RT%3BMcGrail+K%3C%2Fauthor%3E%3C%2FAuthor%3E%3C%2FC%3E%3E14744661%3C%2FC%3E%2F. |
| 45   | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Contoli M, Baraldo S, Marku B, Casolari P, Marwick JA, Turato G, Romagnoli M, Caramori G, Saetta M, Fabbrì LM, Papi A. Fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease: 5-year follow-up. *J. Allergy Clin. Immunol.* [Internet] A. Papi, Research Centre on Asthma, COPD, Department of Clinical and Experimental Medicine, Ferrara, Italy; 2010; 125: 830–837Available from: http://www.embase.com/search/results?subaction=viewrecord&from=exp |
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| 46 | Not the wanted outcome | Corbo GM, Di Marco Berardino A, Mancini A, Inchingolo R, Smargiassi A, Raimondo S, Valente S. Serum level of testosterone, dihydrotestosterone and IGF-1 during an acute exacerbation of COPD and their relationships with inflammatory and prognostic indices: a pilot study. *Minerva Med.* [Internet] Pulmonary Medicine Department Universita Cattolica del Sacro Cuore, Rome, Italy - horatio1983@libero.it.; 2014; 105: 289–294Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=24844347](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=24844347) |
| 47 | Not a primary study (editorial) | Cuvelier A. Assessment of prognosis and severity of COPD. Can we be satisfied with measurig of forced expiratory volume. *Rev. Mal. Respir.* [Internet] Serv. de Pneumologie/Soins Intensifs, Hôpital de Bois-Guillaume, CHU de Rouen, 76031 Rouen Cedex, France; 2002; 19: 4S21–S24Available from: [http://www.scopus.com/inward/record.url?eid=2-s2.0-0036818970&partnerID=40&md5=4770a02fc9a6300f3ba1eb56c21f701](http://www.scopus.com/inward/record.url?eid=2-s2.0-0036818970&partnerID=40&md5=4770a02fc9a6300f3ba1eb56c21f701) |
| 48 | Not a COPD cohort | Dahl M, Vestbo J, Lange P, Bojesen SE, Tybjærg-Hansen A, Nordestgaard BG. C-reactive protein as a predictor of prognosis in chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* [Internet] Department of Clinical Biochemistry, 54M1, Herlev University Hospital, Herlev Ringvej 75, Herlev DK-2730, Denmark; 2007; 175: 250–255Available from: [http://www.scopus.com/inward/record.url?eid=2-s2.0-33846785205&partnerID=40&md5=19e760d81a59996d48ad8d1f81dcd14e](http://www.scopus.com/inward/record.url?eid=2-s2.0-33846785205&partnerID=40&md5=19e760d81a59996d48ad8d1f81dcd14e) |
| 49 | Duplicate | Dahl M, Vestbo J, Zacho J, Lange P, Tybjærg-Hansen A, Nordestgaard BG. C reactive protein and chronic obstructive pulmonary disease: a Mendelian randomisation approach. *Thorax* [Internet] Department of Clinical |
50 Not the wanted outcome

Dal Negro RW, Micheletto C, Tognella S, Visconti M, Guerriero M, Sandri MF. A two-stage logistic model based on the measurement of pro-inflammatory cytokines in bronchial secretions for assessing bacterial, viral, and non-infectious origin of COPD exacerbations. *COPD J. Chronic Obstr. Pulm. Dis.* [Internet] Lung Department, “Orlandi” General Hospital, Bussolengo, Verona, Italy. rdalnegro@ulss22.ven.it; 2005; 2: 7–16Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=17136956

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Dalal AA, Shah MB, D’Souza AO, Dhamane AD, Crater GD. Outcomes associated with timing of maintenance treatment for COPD exacerbation. *Am. J. Manag. Care* [Internet] GlaxoSmithKline, Research Triangle Park, NC, United States Xcenda, Palm Harbor, FL, United States; 2012; 18: e338–e345Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84869228158&partnerID=40&md5=8a8e245edde7b5650ad0aa076a7a2a49.

52 Not a prediction model (neither prediction model nor multivariable association)

Dalal AA, Shah M, Lunacek O, Hanania NA. Clinical and economic burden of patients diagnosed with COPD with comorbid cardiovascular disease. *Respir. Med.* [Internet] Glaxo Smith Kline, 5 Moore Dr, Mail Stop 17.1355B, Research Triangle Park, North Carolina, Durham, NC 27709, United States Xcenda, Palm Harbor, 4114 Woodlands Parkway, Palm Harbor, FL 34685, United States Baylor College of Medicine, Houston, 1504 Taub Loo; 2011; 105: 1516–1522Available from:
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| 53 | Not a primary study (editorial) | Donaldson GC, Wedzicha JA. The codex index a collection or digest of laws: A code. *Chest* [Internet] G.C. Donaldson, Centre for Respiratory Medicine, University College London, Royal Free Hospital, London, NW3 2PF, United Kingdom; 2014; 145: 934–935Available from: [http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L373021260 http://dx.doi.org/10.1378/chest.13-2678 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=19313543&id=doi:10.1378/chest.13-2678]|
| 54 | Not retrieved | Dutta K, Bhadoria DP. Correlation of depression control (HAM-D score) with exacerbation of COPD in patients with co-morbid depression. *Indian J. Psychiatry* [Internet] K. Dutta, Maulana Azad Medical College, New Delhi, India; 2011; 53: S65Available from: [http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70733164 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00195545&id=doi:&atitle=Correlation+of+depression+control+(HAM-D+score)+with+exacerbation+of+COPD+in+patients+with+co-morbid+depression&stitle=Indian+J.+Psychiatry&title=Indian+Journal+of+Psychiatry&volume=53&issue=5&spage=S65&epage=&aulast=Dutta&aufirst=Koushik&auinit=K.&aufull=Dutta+K.&coden=&isbn=&pages=S65- &date=2011&auinit1=K&auinitm=.|
| 55 | Included | Echave-Sustaeta J, Comeche Casanova L, Garcia Lujan R, Sayas Catalan J, Gomez de la Camara A, Lopez Encuentra A. Prognosis following acute exacerbation of COPD treated with non-invasive mechanical ventilation. *Arch. Bronconeumol.* [Internet] Servicio de Neumologia, Hospital Universitario 12 de Octubre, Madrid, Espana. jmechave.mad@quiron.es; 2010; 46: 405–410Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=medl&AN=20451314 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:20451314&id=doi:10.1016%2Fj.arbres.2010.03.004&issn=0300- 2896&isbn=&volume=46&issue=8&spage=405&page=405-10&date=2010&title=Archivos+de+Bronconeumologia&atitle=Pronostico+tras+una+agudizacion+grav+e+de+la+EPOC+tratada+con+ventilacion+mecanica+no+invasiva.&aulast=Echave-Sustaeta&pid=%3CAuthor%3EEchave-Sustaeta%3BJ%3BComeche%3BCasanova%3BL%3BGarcia%3BLujan&R%3BSa. |
56. Not a prediction model (focus on a particular predictor without the wanted adjustment)

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57. No performance measure provided

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59. Not a prediction model (focus on a particular predictor without the wanted adjustment)

Escande W, Duva Pentiah A, Coisne A, Mouton S, Richardson M, Polge AS, Ennezat P V, Tillie-Leblond I, Montaigne D. Left ventricular myocardial performance index predicts poor outcome during COPD exacerbation. *Int. J. Cardiol.* [Internet] Department of Cardiovascular Medicine, Hopital Cardiologique, Lille University Hospital, Lille, France. Electronic address:
| 60 | Included | Faganello MM, Tanni SE, Sanchez FF, Pelegrino NR, Lucheta PA, Godoy I. BODE index and GOLD staging as predictors of 1-year exacerbation risk in chronic obstructive pulmonary disease. *Am. J. Med. Sci.* [Internet] Department of Physiotherapy, Centro Universitario Catolico Salesiano Auxilium-Unisalesiano, Sao Paulo, Brazil. marciafaganello@hotmail.com; 2010; 339: 10–14Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=19926966 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19926966&i d=doi:10.1097%2FMAJ.0b013e3181bb8111&issn=0002-9629&isbn=&volume=339&page=10&pages=10-4&date=2010&title=American+Journal+of+the+Medical+Sciences&atitle=BODE+index+and+GOLD+staging+as+predictors+of+1-year+exacerbation+risk+in+chronic+obstructive+pulmonary+disease.&aulast=Faganello&pid=%3Cauthor%3EFaganello+MM%3BTanni+SE%3BSanchez+FF%3B. |
| 61 | Not the wanted outcome | Falsey AR, Becker KL, Swinburne AJ, Nylen ES, Snider RH, Formica MA, Hennessey PA, Criddle MM, Peterson DR, Walsh EE. Utility of serum procalcitonin values in patients with acute exacerbations of chronic obstructive pulmonary disease: A cautionary note. *Int. J. COPD* [Internet] Department of Medicine, University of Rochester, Rochester, NY, United States Rochester General Hospital, Rochester, NY, United States Veterans Affairs Medical Center, George Washington University, Washington DC, United States Biostatistics and Computatio; 2012; 7: 127–135Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84860299080&partnerID=40&md5=33d5731adf3d8968967fab46831efe25. |
| 62 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Fan VS, Curtis JR, Tu SP, McDonell MB, Fihn SD. Using quality of life to predict hospitalization and mortality in patients with obstructive lung diseases. *Chest* [Internet] HSRandD (152), VA Puget Sound Health Care System, 1660 S Columbian Way, Seattle, WA 98108-1597, United States; 2002; 122: 429–436Available from: |
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| 63          | Not the wanted study design (RCT, not only placebo arm) | Fan VS, Ramsey SD, Giardino ND, Make BJ, Emery CF, Diaz PT, Benditt JO, Mosenifar Z, McKenna Jr R, Curtis JL, Fishman AP, Martinez FJ. Sex, depression, and risk of hospitalization and mortality in chronic obstructive pulmonary disease. *Arch. Intern. Med.* [Internet] Health Services Research and Development Center of Excellence, Veterans Affairs Puget Sound Health Care System, Seattle, WA, United States Cancer Technology Assessment Group, Fred Hutchinson Cancer Research Center, Seattle, WA, United States Department of; 2007; 167: 2345–2353 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-36549082823&partnerID=40&md5=3c48e437ba8dd9c4623b5a14c8a2afcf. |
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| 65          | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Farah R, Khamisy-Farah R, Arraf Z, Jacobson L, Makhoul N. Hypophosphatemia as a prognostic value in acute exacerbation of COPD. *Clin. Respir. J.* [Internet] Department of Internal Medicine B, Ziv Medical Center, Safed, Israel; Faculty of Medicine in the Galilee, Bar Ilan University, Safed, Israel.; 2013; 7: 407–415 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=23659185 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23659185&did=doi:10.1111%2Fcrj.12027&isbn=&volume=7&issue=4&page=407&pages=407-15&date=2013&title=Hypophosphatemia+as+a+prognostic+value+in+acute+exacerbation+of+COPD.&aulast=Farah&pid=%3Cauthor%3EFarah+R%3BKhamisy-Farah+R%3BArraf+Z%3BJacobson+L%3BMakhoul+N%3C%2Fauthor%3E%3CAN%3E23659185%3C%2FAN%3E. |
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| 66   | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Farkas J, Kosnik M, Flezar M, Suskovic S, Lainscak M. Self-rated health predicts acute exacerbations and hospitalizations in patients with COPD. *Chest* [Internet] Faculty of Medicine, University of Ljubljana, Zaloska cesta 4, SI-1000 Ljubljana, Slovenia Division of Cardiology, Golnik, Slovenia University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia Division of Applied Cachexia Research, Char; 2010; 138: 323–330Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-77955356188&partnerID=40&md5=c79f29dda3cbf060d2e0786d9a7c3a21. |
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| 68   | No performance measure provided | Foreman MG, DeMeo DL, Hersh CP, Reilly JJ, Silverman EK. Clinical determinants of exacerbations in severe, early-onset COPD. *Eur. Respir. J.* [Internet] Channing Laboratory, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, United States Dept. of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, United States Channing Laboratory, 181 Longwood Avenue, Boston, MA 02; 2007; 30: 1124–1130Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-38849132080&partnerID=40&md5=b7da97870e60363959b66991591dfbe6. |
| 69   | Not the wanted outcome | Frei A, Muggensturm P, Putcha N, Siebeling L, Zoller M, Boyd CM, ter Riet G, Puhan MA. Five comorbidities reflected the health status in patients with chronic obstructive pulmonary disease: the newly developed COMCOLD index. *J. Clin. Epidemiol.* [Internet] Institute of Social and Preventive Medicine, Department of Epidemiology, University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland; Institute of General Practice and Health Services Research, University of Zurich, Pestalozzistrasse 24, 8091 Zurich; 2014; 67: 904–911Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24786594 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24786594&doi=10.1016/j.jclinepi.2014.03.005&issn=0895- |
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| 71      | Not the wanted study design (data partly collected after the outcome) | Gaki E, Papatheodorou G, Pappa I, Papiris S, Loukides S. Correlation between frequency of hospitalization of patients with severe copd and severity indices. *Pneumon* [Internet] University of Athens Medical School, 2nd Respiratory Medicine Dept, Greece Clinical Research Unit, Athens Army General Hospital, Greece Department of Pneumonology, Veterans’ Hospital of Athens, Greece; 2011; 24: 164–171Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-79960313131&partnerID=40&md5=a724b705decbfd888e310a75d4317a53 . |
| 72      | Not a prediction model (neither prediction model nor multivariable association) | Garcia-Aymerich J, Gomez FP, Benet M, Farrero E, Basagana X, Gayete A, Pare C, Freixa X, Ferrer J, Ferrer A, Roca J, Galdiz JB, Sauled J, Monso E, Gea J, Barbera JA, Agusti A, Anto JM, Group P-CS. Identification and prospective validation of clinically relevant chronic obstructive pulmonary disease (COPD) subtypes. *Thorax* [Internet] Centre for Research in Environmental Epidemiology, Doctor Aiguader 88, 08003 Barcelona, Catalonia, Spain. jgarcia@creal.cat; 2011; 66: 430–437Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21177668 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:21177668&i d=doi:10.1136%2Fthx.2010.154484&issn=0040-6376&isbn=&volume=66&issue=5&page=430&pages=430-7&date=2011&title=Thorax&title=Identification+and+prospective+validation+of+clinically+relevant+chronic+obstructive+pulmonary+disease+%28COPD%29+subtypes.&aulast=Garcia-Aymerich&pid=%3Cauthor%3EGarcia-Aymerich+J%3B+Gomez+FP%3B+Benet+M%3B+Farrero+E%3B+Basaga . |
| 73      | Not the wanted study design (RCT, not only placebo arm) | Garcia-Aymerich J, Hernandez C, Alonso A, Casas A, Rodriguez-Roisin R, Anto JM, Roca J. Effects of an integrated care intervention on risk factors of COPD readmission. *Respir. Med.* [Internet] Centre for Research in Environmental Epidemiology (CREAL), Institut Municipal d’Investigació Mèdica (IMIM), Barcelona, Spain Department of Pneumology, Technology Innovation Unit, Hospital Clinic, Spain Department of Experimental and |
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Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: A population-based cohort study. Am. J. Respir. Crit. Care Med. [Internet] Centre for Research in Environmental Epidemiology (CREAL), Institut Municipal d’Investigació Mèdica (IMIM), Barcelona, Spain; Copenhagen City Heart Study, Epidemiological Research Unit, Bispebjerg University Hospital, Copenhagen, Denmark Department of Card; 2007; 175: 458–463Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-33847677739&partnerID=40&md5=5d722c818f9f581986357fb3a57d18bb.

75 Not a COPD cohort

Garcia-Aymerich J, Lange P, Serra I, Schnohr P, Antó JM. Time-Dependent Confounding in the Study of the Effects of Regular Physical Activity in Chronic Obstructive Pulmonary Disease: An Application of the Marginal Structural Model. Ann. Epidemiol. [Internet] Centre for Research in Environmental Epidemiology (CREAL) Municipal Institute of Medical Research (IMIM-Hospital del Mar) Department of Experimental and Health Sciences, Universitat Pompeu Fabra CIBER Epidemiologia y Salud Pública (CIBERESP), Barcelona, S; 2008; 18: 775–783Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-52049103409&partnerID=40&md5=0112fda890bb767aab5b03f1a9440ed8.

76 Not the wanted study design (case-control study)

Garcia-Aymerich J, Monso E, Marrades RM, Escarrabill J, Felez MA, Sunyer J, Anto JM, Investigators E. Risk factors for hospitalization for a chronic obstructive pulmonary disease exacerbation. EFRAM study. Am. J. Respir. Crit. Care Med. [Internet] Respiratory and Environmental Health Research Unit, Institut Municipal d’Investigacio Medica (IMIM), Barcelona, Spain.; 2001; 164: 1002–1007Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=11587986
http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:11587986&doi=1073-449X&isbn=&volume=164&issue=6&spage=1002&pagest=1002-7&date=2001&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Risk+factors+for+hospitalization+for+a+chronic+obstructive+pulmonary+disease+exacerbation.+EFRAM+study.&aulast=Garcia-Aymerich&pid=%3Cauthor%3EGarcia-Aymerich+J%3EMonso+E%3BMarrades+RM%3Escar.

77 Not a primary study

Garcia-Pachon E, Padilla-Navas I. Risk indexes for COPD exacerbations I.
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| 78 | Not the wanted study design (ecological study) | Gerke AK, Tang F, Yang M, Foster ED, Cavanaugh JE, Polgreen PM. Predicting chronic obstructive pulmonary disease hospitalizations based on concurrent influenza activity. *COPD J. Chronic Obstr. Pulm. Dis.* [Internet] University of Iowa, Department of Internal Medicine, 200 Hawkins Dr., Iowa City, IA 52242, United States University of Iowa, Department of Biostatistics, Iowa City, IA, United States Harvard School of Public Health, 651 Huntington Avenue, Boston, MA, Unite; 2013; 10: 573–580Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84884549524&partnerID=40&md5=3c2d75c88b2730a162b91c3cd541be7a . |
| 79 | Not a prediction model (neither prediction model nor multivariable association) | Giron R, Matesanz C, Garcia-Rio F, de Santiago E, Mancha A, Rodriguez-Salvanes F, Ancochea J. Nutritional state during COPD exacerbation: clinical and prognostic implications. *Ann. Nutr. Metab.* [Internet] Servicio de Neumologia, Hospital Universitario de la Princesa, Madrid, Spain.; 2009; 54: 52–58Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-78650225104&partnerID=40&md5=fd740033b0eff299d97f4f594ea1b2ee. |
| 80 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Gonzalez A V, Suissa S, Ernst P. Gender differences in survival following hospitalisation for COPD. *Thorax* [Internet] Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, McGill University Health Centre, Montreal, QC, Canada Center for Clinical Epidemiology, Sir Mortimer B Davis Jewish General Hospital, McGill University, Montreal, QC, Canada Pu; 2011; 66: 38–42Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-78650225104&partnerID=40&md5=fd740033b0eff299d97f4f594ea1b2ee. |
| ID | Title                                                                 | Authors                                                                 | Summary                                                                                      |
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| 81 | No performance measure provided                                     | Gonzalez C, Servera E, Ferris G, Blasco ML, Marin J.                    | Risk factors of readmission in acute exacerbation of moderate-to-severe chronic obstructive pulmonary disease. Arch. Bronconeumol. [Internet] Servicio de Neumologia, Hospital Clinico Universitario, Universidad de Valencia, Valencia, Spain. cruz.gonzalez@uv.es; 2004; 40: 502–507 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=15530342 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:15530342&iid=doi:&issn=0300-2896&isbn=&volume=40&issue=11&page=502|  |
| 82 | Not a primary study (editorial)                                      | Gonzalez GR.                                                            | Prognostic stratification in patients with exacerbated copd requiring hospitalization. Seeing through the smoke 2. Arch. Bronconeumol. [Internet] G.R. Gonzalez, Servicio de Medicina Interna, Hospital Universitario Dr. Gustavo Aldereguia Lima, Cienfuegos, Cuba; 2007; 43: 640 Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&i=1351041341 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=03002896&iid=doi:&a=Prognostic+stratification+in+patients+with+exacerbated+copd+requiring+hospitalization.+Seeing+through+the+smoke+2&atitle=Arch.+Bronconeumol.&title=Archivos+de+Bronconeumologia&volume=43&issue=11&spage=640&epage=&aulast=Gonzalez&aufirst=Gerardo+Rivero &auinit=G.R.&aufull=Gonzalez+G.R.&coden=ARBRD&isbn=&pages=640&date=2007&au. |
| 83 | Not a primary study (editorial)                                      | Gross NJ.                                                              | Managing acute exacerbations of COPD: a scorecard. Copd J. Chronic Obstr. Pulm. Dis. [Internet] 2010; 7: 81–82 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20397806 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:20397806&iid=doi:10.3109/15412551003719587&issn=1541-2563&isbn=7&issue=2&spage=81&epage=81&date=2010&title=Copd:+Journal+of+Chronic+Obstructive+Pulmonary+Disease&atitle=Managing+acute+exacerbations+of+COPD+a+scorecard.&aulast=Gross&pid=<author>Gross+NJ</author>&AN=20397806&DT=Editorial. |
| 84 | Not a primary study (poster)                                        | Gu W, Chen R.                                                           | Study of respiratory muscle strength, quality of life and bode index in patients with chronic obstructive pulmonary disease. |
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| 85   | Study of respiratory muscle strength, quality of life and body index in patients with chronic obstructive pulmonary disease | Respirology [Internet] W. Gu, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital, Guangzhou Medical College, Guangzhou, China; 2010; 15: 49Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70313291 http://dx.doi.org/10.1111/j.1400-1843.2010.01864.x http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=13237799&id=doi:10.1111%2Fj.1400-1843.2010.01864.x &atitle=Study+of+respiratory+muscle+strength%2C+quality+of+life+and+body+index+in+patients+with+chronic+obstructive+pulmonary+disease&title=Respirology&volume=15&issue=&spage=49&epage=&aulast=Gu&aufirst=Weili&auinit=W.&aufull=Gu+W.&c&isbn=&pa. |
| 86   | CODEX index and prognosis of patients with exacerbation of COPD | Hadda V, Madan K, Mohan A. CODEX index and prognosis of patients with exacerbation of COPD. Chest [Internet] 2014; 145: 1172Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24798848 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24798848&id=doi:10.1378/chest.13-2516&issn=0013-3692&isbn=&volume=145&issue=5&spage=1172&date=2014 &title=Chest&atitle=CODEX+index+and+prognosis+of+patients+with+exacerbation+of+COPD.&aulast=Hadda&pid=<author>Hadda+V;Madan+K;Mohan+A</author> &AN=24798848</AN>&DT=Comment|DT> |
| 87   | Nutritional status, dietary energy intake and the risk of exacerbations in patients with chronic obstructive pulmonary disease (COPD) | Hallin R, Koivisto-Hursti UK, Lindberg E, Janson C. Nutritional status, dietary energy intake and the risk of exacerbations in patients with chronic obstructive pulmonary disease (COPD). Respir. Med. [Internet] Department of Medical Sciences Respiratory Medicine and Allergology, Uppsala University, Akademiska Sjukhuset, Uppsala, Sweden Department of Public Health and Caring Sciences, Uppsala University, Uppsala Science Park, Uppsala, Sweden; 2006; 100: 561–567Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-32644452764&partnerID=40&md5=5c8007bcabc48b365b992d06a0bcd5ad |
| 88   | Clinical significance of radiologic characterizations in COPD | Han MK, Bartholmai B, Liu LX, Murray S, Curtis JL, Sciurba FC, Kazerooni EA, Thompson B, Frederick M, Li D, Schwarz M, Limper A, Freeman C, Landreneau RJ, Wise R, Martinez FJ. Clinical significance of radiologic characterizations in COPD. Copd J. Chronic Obstr. Pulm. Dis. [Internet] University of Michigan Health System, Ann Arbor, Michigan 48109-5360, USA. mrking@umich.edu; 2009; 6: 459–467Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=19938970 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:19938970&id=doi:10.3109%2F1541255090341513&issn=1541-2563&isbn=&volume=6&issue=6&spage=459&pages=459- |
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Theoretical model

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| 145 | Included                                     | Moy ML, Teylan M, Danilack VA, Gagnon DR, Garshick E. An index of daily step count and systemic inflammation predicts clinical outcomes in chronic obstructive pulmonary disease. *Ann. Am. Thorac. Soc.* [Internet] 1 Department of Veteran’s Affairs, Veterans Health Administration, Rehabilitation Research and Development Service; 2014; 11: 149–157Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext |
| ID  | Notation                                                                 | Title                                                                                     |
|-----|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| 146 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Moy ML, Teylan M, Weston NA, Gagnon DR, Garshick E. Daily Step Count Predicts Acute Exacerbations in a US Cohort with COPD. PLoS One [Internet] M. L. Moy, Department of Veteran Affairs, Veterans Health Administration, Rehabilitation Research and Development Service, Washington, DC, United States; 2013; 8Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L368686444 http://dx.doi.org/10.1371/journal.pone.0060400 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=19326203&id=doi:10.1371/journal.pone.0060400&atitle=Daily+Step+Predicts+Acute+Exacerbations+in+a+US+Cohort+with+COPD&stitle=PLoS+ONE&title=PLoS+ONE&volume=8&issue=4&page=&epage=&aulast=Moy&auinit=M.L.&aufirst=Marilyn+L.&auinit1=M&auinitm=L. |
| 147 | No spirometry in the COPD definition                                     | Nantsupawat T, Limsuwat C, Nugent K. Factors affecting chronic obstructive pulmonary disease early rehospitalization. Chron. Respir. Dis. [Internet] Department of Internal Medicine, Texas Tech Health Sciences Center, 3601 4th Street, Lubbock, TX 79430, United States; 2012; 9: 93–98Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84861833947&partnerID=40&md5=3b36a09c5a729784a9db14a932212176. |
| 148 | Not the wanted study design (RCT, not only placebo arm)                | Niewoehner DE, Lokhnygina Y, Rice K, Kuschner WG, Sharafkhaneh A, Sarosi GA, Krumpe P, Pieper K, Kesten S. Risk indexes for exacerbations and hospitalizations due to COPD. Chest [Internet] Department of Medicine at Veterans Affairs Medical Centers in Minneapolis, MN 55417, USA. niewo001@umn.edu; 2007; 131: 20–28Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=17218552 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:17218552&id=doi:&isbn=&volume=131&issue=1&page=20&pages=20-8&date=2007&title=Risk+indexes+for+exacerbations+and+hospitalizations+due+to+COPD.&aulast=Niewoehner&pid=%3Cauthor%3ENiewoehner+DE%3BLokhnygina+y%3BRice+k%3BKuschner+w%3Bsharpkahaneh+a%3BSarosi+g%3Bkrumpe+p%3Bpieper+k%3Bkesten+s%3C%2Fauthor%3E%3C2F%3E%3C%2F%3C%2F%3C%2F%3C%2F. |
Not the wanted outcome

Oga T, Tsukino M, Hajiro T, Ikeda A, Nishimura K. Predictive properties of different multidimensional staging systems in patients with chronic obstructive pulmonary disease. *Int. J. COPD* [Internet] Department of Respiratory Care and Sleep Control Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan. ogato@kuhp.kyoto-u.ac.jp; 2011; 6: 521–526 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22069363

http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:22069363&id=doi:10.2147%2FCOPD.204420&issn=1176-9106&isbn=&volume=6&issue=&spage=521&pages=521-6&date=2011&title=International+Journal+of+Copd&atitle=Predictive+properties+of+different+multidimensional+staging+systems+in+patients+with+chronic+obstructive+pulmonary+disease.&aulast=Oga&pid=%3Cauthor%3EOga+T%3BTsukino+M%3BHajiro+T%3BIkeda+A%3BNishimura+K%3D.

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Omachi TA, Katz PP, Yelin EH, Iribarren C, Knight SJ, Blanc PD, Eisner MD. The COPD Helplessness Index: a new tool to measure factors affecting patient self-management. *Chest* [Internet] University of California, San Francisco, Box 0111, 505 Parnassus Ave, San Francisco, CA 94143-0111, USA. omachi@ucsf.edu; 2010; 137: 823–830 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=19837823

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Omachi TA, Yelin EH, Katz PP, Blanc PD, Eisner MD. The COPD severity score: a dynamic prediction tool for health-care utilization. *COPD: Journal of Chronic Obstruct. Pulm. Dis.* [Internet] Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of California, San Francisco, California 94143-0111, USA. omachi@ucsf.edu; 2008; 5: 339–346 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19353347

http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:19353347&id=doi:10.1080%2F15412550802522700&issn=1541-2563&isbn=&volume=5&issue=&spage=339&pages=339-46&date=2008&title=Copd%3A+Journal+of+Chronic+Obstructive+Pulmonary+Disease&Disease&atitle=The+COPD+severity+score%3A+a+dynamic+prediction+tool+to+measure+factors+affecting+patient+self-management.&aulast=Omachi&pid=%3Cauthor%3EOmachi+TA%3BKatz+PP%3BYelin+EH%3BIribarren+C%3BKnight+SJ%3BBlanc+PD%3BEisner+MD%3C%2Fauthor%3E%3C
| **152** | Not a prediction model (focus on a particular predictor without the wanted adjustment) | O’Malley AS, Pham HH, Schrag D, Wu B, Bach PB. Potentially avoidable hospitalizations for COPD and pneumonia: The role of physician and practice characteristics. *Med. Care* [Internet] Center for Studying Health System Change, Washington, DC, United States Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, United States Social and Scientific Systems, Inc., Silver Spring, MD, United States Center for St; 2007; 45: 562–570Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-34249058051&partnerID=40&md5=dbe4e1a4e0c2820fc7c6176ac146a68b. |
| **153** | Not a prediction model (neither prediction model nor multivariable association) | Onadeko BO, Khadadah M, Abdella N, Mukhtar M, Mourou M, Qurtom M, Samad M, Al-Shayeb A. Prognostic factors in the management of exacerbation of chronic obstructive pulmonary disease in Kuwait. *Med. Princ. Pract.* [Internet] Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait. onadeko@hotmail.com; 2005; 14: 35–40Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=15608479http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:15608479&id=doi:1011-7571&isbn=&volume=14&issue=1&page=35&pages=35-40&date=2005&title=Medical+Principles+Practice&t=Prognostic+factors+in+management+of+exacerbation+of+chronic+obstructive+pulmonary+disease+in+Kuwait.&aulast=Onadeko&pid=%3Cauthor%3EOnadeko+BO%3B+Khadadah+M%3B+Abdella+N%3BMukhtar+M%3BMourou+M%3BSamad+M%3BSad+Sh. |
| **154** | Included | Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. *Chest* [Internet] Department of Respiratory Medicine, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433. kian_chung_ong@ttsh.com.sg; 2005; 128: 3810–3816Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16354849http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16354849&id=doi:1011-3692&isbn=&volume=128&issue=6&page=3810&pages=3810-6&date=2005&title=Chest+Practice+rsion+of+Multidimensional+Grading+System+(BODE+Index)+as+Predictor+of+Hospitalization+for+COPD.&aulast=Ong&pid=<author>Ong+KC;Earnest+A;Lu+SJ</author><AN>16354849</AN><DT>Compative+Study</DT>. |
| No. | Not the wanted study design (RCT, not only placebo arm) | Oostenbrink JB, Rutten-van Molken MP. Resource use and risk factors in high-cost exacerbations of COPD. *Respir. Med.* [Internet] Institute for Medical Technology Assessment, Erasmus Medical Centre Rotterdam, PO Box 1738, Rotterdam 3000 DR, The Netherlands. oostenbrink@bmg.eur.nl; 2004; 98: 883–891Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=15338802 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:15338802&i d=doi:&isbn=0954-6111&volume=98&issue=9&spage=883&pages=883-91&date=2004&title=Respiratory+Medicine&atitle=Resource+use+and+risk+factors+in+high-cost+exacerbations+of+COPD.&aulast=Oostenbrink&pid=<author>Oostenbrink+JB;Rutten-van+Molken+MP</author>&AN=15338802&D T=Journal+Article</DT>. |
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| 156 | Not the wanted outcome | Ou CY, Chen CZ, Yu CH, Shiu CH, Hsiue TR. Discriminative and predictive properties of multidimensional prognostic indices of chronic obstructive pulmonary disease: a validation study in Taiwanese patients. *Respirology* [Internet] Division of Chest Medicine, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan.; 2014; 19: 694–699Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=24797671 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24797671&i d=doi:10.1111%2Fresp.12313&issn=1323-7799&isbn=&volume=19&issue=5&spage=694&pages=694-9&date=2014&title=Respirology&atitle=Discriminative+and+predictive+properties+of+multidimensional+prognostic+indices+of+chronic+obstructive+pulmonary+disease%3A+a+validation+study+in+Taiwanese+patients.&aulast=Ou&pid=%3Cauthor%3EOu+CY%3BChen+CZ%3BShiue.& |
| 157 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Ozgur ES, Nayci SA, Ozge C, Tasdelen B. An integrated index combined by dynamic hyperinflation and exercise capacity in the prediction of morbidity and mortality in COPD. *Respir. Care* [Internet] Department of Chest Diseases, Mersin University School of Medicine, Mersin, Turkey. eyelemozgur@yahoo.com; 2012; 57: 1452–1459Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22348294 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:22348294&i d=doi:10.4187%2Frespcare.01440&issn=0020-1324&isbn=&volume=57&issue=9&spage=1452&pages=1452-9&date=2012&title=Respiratory+Care&atitle=An+integrated+index+combined+by+dynamics+hyperinflation+and+exercise+capacity+in+the+prediction+of+morbidity+and+mortality+in+COPD.&aulast=Ozgur&pid=%3Cauthor%3 EOzgur+ES%3BNayci+SA%3BOzge+C%3BTasdelen+B%3C%2FAuth. |
| Page | Title | Reference |
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| 158  | No performance measure provided | Ozyilmaz E, Kokturk N, Teksut G, Tatlicioglu T. Unsuspected risk factors of frequent exacerbations requiring hospital admission in chronic obstructive pulmonary disease. *Int. J. Clin. Pract.* [Internet] Department of Pulmonary Disease, Cukurova University, Balcali, Adana, Turkey Department of Pulmonary Disease, Gazi University, Faculty of Medicine, Ankara, Turkey; 2013; 67: 691–697 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84879116676&partnerID=40&md5=33086a1a0d081988e0b9c3510a43f126. |
| 159  | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Papaioannou AI, Bartziokas K, Tsikrika S, Karakontaki F, Kastanakis E, Banya W, Haniotou A, Papiris S, Loukides S, Polychronopoulos V, Kostikas K. The impact of depressive symptoms on recovery and outcome of hospitalised COPD exacerbations. *Eur. Respir. J.* [Internet] 3rd Respiratory Medicine Dept, Sismanogleion General Hospital, Athens, Greece Respiratory Medicine Dept, Amalia Fleming General Hospital, Athens, Greece 2nd Respiratory Medicine Dept, University of Athens Medical School, Athens, Greece Royal Brompton and; 2013; 41: 815–823 Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84875830105&partnerID=40&md5=4ca6e409ebb1fb05d57e7dfcdc84617b. |
| 160  | Not the wanted outcome | Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G, Fabbri LM, Johnston SL. Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. *Am. J. Respir. Crit. Care Med.* [Internet] Research Center on Asthma and COPD, Department of Respiratory Diseases, University of Modena and Reggio Emilia, Via del Pozzo 71, I-41100 Modena, Italy.; 2006; 173: 1114–1121 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16484677 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:16484677&id=doi:&issn=1073-449X&isbn=&volume=173&issue=10&page=1114-1114&date=2006&title=American+Journal+of+Respiratory+Care+Medicine&atitle=Infections+and+airway+inflammation+in+chronic+obstructive+pulmonary+disease+severe+exacerbations.&aulast=Papi&pid=%3Cauthor%3EPapi%A%3BBellettato+CM%3BBraccioni+F%3BRomagnoli+M%3BCasolari+P%3E. |
| 161  | Not a COPD cohort | Park TY, Kim KH, Koo HK, Lee JY, Lee SM, Yim JJ, Yoo CG, Kim YW, Han SK, Yang SC. Prognosis in patients having chronic obstructive pulmonary disease with significant coronary artery lesion angina. *Korean J. Intern. Med.* [Internet] Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine and Lung Institute, Seoul National University College of Medicine, Seoul, Korea.; 2012; 27: 189–196 Available from: |
| Reference                                                                                      | Type of Exclusion                                                                 |
|-----------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Parshall MB, Mapel DW, Rice L, Williams A, O’Reilly J. Predictive validity of short-form health survey 36 items scales for chronic obstructive pulmonary disease exacerbation. *Hear. Lung J. Acute Crit. Care* [Internet] M.B. Parshall, University of New Mexico College of Nursing, Albuquerque, NM, United States; 2008; 37: 356–365Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L352317047 http://dx.doi.org/10.1016/j.hrtlng.2007.09.007 | Included                                                                       |
| Patel IS, Vlahos I, Wilkinson TMA, Lloyd-Owen SJ, Donaldson GC, Wilks M, Reznek RH, Wedzicha JA. Bronchiectasis, exacerbation indices, and inflammation in chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* [Internet] Acad. Unit of Respiratory Medicine, Dominion House, St. Bartholomew’s Hospital, West Smithfield, London EC1A 7BE, United Kingdom; 2004; 170: 400–407Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-4544340201&partnerID=40&md5=221e5286f77bdc40e2ea36954e89d5c5. | 163 Not a prediction model (focus on a particular predictor without the wanted adjustment) |
| Pavlovic M, Simic D, Hrsak J. Emergency cases of chronic obstructive pulmonary disease (COPD) in adults and air pollution in Zagreb. *Arh. Hig. Rada Toksikol.* [Internet] Institute for Medical Research and Occupational Health Zagreb, Croatia.; 1997; 48: 365–371Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=9721455 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:9721455&id =doi:&issn=0004-1254&isbn=&volume=48&issue=4&page=365&pages=365-71&date=1997&title=Arhiv+Za+Higijenu+Rada+i+Toksikologiju&atitle=Emergency+cases+of+chronic+obstructive+pulmonary+disease+%28COPD%29+in+adults+and+air+pollution+in+Zagreb.&aulast=Pavlovic&pid=%3Cauthor%3EPavlovic+%3BSimic+%3B%3BHrsak+J%3C%2Fauthor%3E%3CAN%3E972 | 164 Not the wanted study design (ecological study) |
| 165 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Prescott E, Bjerg AM, Andersen PK, Lange P, Vestbo J. Gender difference in smoking effects on lung function and risk of hospitalization for COPD: Results from a Danish longitudinal population study. *Eur. Respir. J.* [Internet] Copenhagen Ctr. Prospective Pop. S., Institute of Preventive Medicine, Copenhagen Hospital Corporation, Copenhagen, Denmark Institute of Biostatistics, University of Copenhagen, Denmark Danish Epidemiology Science Center, State Serum Institute, Copenhagen; 1997; 10: 822–827Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0030990977&partnerID=40&md5=736d999970431dcd5aaa5eec88317548. |
| 166 | Not a prediction model (neither prediction model nor multivariable association) | Puhan MA, Siebeling L, Frei A, Zoller M, Bischoff-Ferrari H, Ter Riet G. No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD. *Chest* [Internet] Institute for Social and Preventive Medicine, University of Zurich, Hirschengraben 84, CH-8001 Zurich, Switzerland Horgen-Centre for Patient Oriented Research and Knowledge Transfer, University of Zurich, Zurich, Switzerland Institute of General Practice,; 2014; 145: 37–43Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84892636352&partnerID=40&md5=3285b20217912fac34b936b71aa07dbf. |
| 167 | Not a prediction model (neither prediction model nor multivariable association) | Puhan MA, Siebeling L, Zoller M, Muggensturm P, ter Riet G. Simple functional performance tests and mortality in COPD. *Eur. Respir. J.* [Internet] 2013 [cited 2014 Mar 28]; 42: 956–963Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3787814&tool=pmcentrez&rendertype=abstract. |
| 168 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Quint JK, Baghai-Ravary R, Donaldson GC, Wedzicha JA. Relationship between depression and exacerbations in COPD. *Eur. Respir. J.* [Internet] Academic Unit of Respiratory Medicine, University College London, Hampstead Campus, Rowland Hill Street, London NW3 2PF, UK.; 2008; 32: 53–60Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=18321938 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:18321938&i d=doi:10.1183%2F09031936.00120107&issn=0903-1936&isbn=&volume=32&issue=1&page=53&pages=53-60&date=2008&title=European+Respiratory+Journal&atitle=Relationship+between+depression+and+exacerbations+in+COPD.&aulast=Quint&pid=%3Cauthor%3EQ quint%3BBaghai-Ravary%3BDonaldson%3BCWedzicha%3A%3Cauthor%3E%3C%3E18321938%3C%2FAN%3E%3CDT%3EJourna.
| ID | Type of study | Authors | Title | Journal | Institution | Year | Volume | Issue | Pages | URL |
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| 169 | Not a primary study (editorial) | Rajagopalan S, Dellagrottaglie S, Sanz J. | Pulmonary arterial enlargement and COPD exacerbations. | N. Engl. J. Med. | Ohio State University, Wexner Medical Center, Columbus, OH, United States Ospedale Medico-Chirurgico Accreditato, Naples, Italy Mount Sinai School of Medicine, New York, NY, United States; 2012; 367: 2254 | Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84870484692&partnerID=40&md5=3fa84ee388bb3fe89b24e3505ed49ddb | |
| 170 | Not the wanted outcome | Roche N, Zureik M, Soussan D, Neukirch F, Perrotin D, Urgence BSC. | Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. | Eur. Respir. J. | Respiratory and Intensive Care Medicine, Hotel-Dieu, Paris, Descartes University, France. | 2008; 32: 953–961 | Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18508819 | |
| 171 | Not a primary study (editorial) | Rodriguez AME, Ioannis P. | A link of non-invasive ventilation in chronic hypercapnic COPD patients with pulmonary hypertension. A new index of prognosis. | Eur. Rev. Med. Pharmacol. Sci. | A.M.E. Rodriguez, International Fellow AARC, Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain; 2012; 16: 1133–1134 | Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L365924614 | |
| 172 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Rogha M, Behravesh B, Pourmoghaddas Z. | Association of gastroesophageal reflux disease symptoms with exacerbations of chronic obstructive pulmonary disease. | J. Gastrointest. Liver Dis. | Department of Internal Medicine, Islamic Azad University, Najafabad Branch, Najafabad, Iran Young Researchers Clubs, Islamic Azad University, Najafabad Branch, Najafabad, Iran; 2010; 19: 253–256 | Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-
| No. | Study Title and Authors | Table Link | Details |
|-----|------------------------|------------|---------|
| 173 | Using the DOSE index to predict changes in health status of patients with COPD: a prospective cohort study. Rolink M, van Dijk W, van den Haak-Rongen S, Pieters W, Schermer T, van den Bemt L. Prim. Care Respir. J. [Internet] Radboud University Nijmegen Medical Centre, Department of Primary and Community Care Nijmegen, The Netherlands.; 2013; 22: 169–174 | [Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23538702](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23538702) | Not the wanted outcome |
| 174 | A predictive model of hospitalisation and death from chronic obstructive pulmonary disease. Schembri S, Anderson W, Morant S, Winter J, Thompson P, Pettitt D, MacDonald TM, Winter JH. Respir. Med. [Internet] Department of Medicine and Therapeutics, University of Dundee, Dundee DD1 9SY, United Kingdom. sschembri@nhs.net; 2009; 103: 1461–1467 | [Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19515547](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19515547) | Not the wanted outcome |
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204 Not a prediction model (focus on a particular predictor without the wanted adjustment)

Vacca G, Schwabe K, Duck R, Hlawa HP, Westphal A, Pabst S, Grohe C, Gillissen A. Polymorphisms of the beta2 adrenoreceptor gene in chronic obstructive pulmonary disease. *Ther. Adv. Respir. Dis.* [Internet] St. Georg Medical Center, Robert-Koch-Hospital, Leipzig, Germany.; 2009; 3: 3–10Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19293197

http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19293197&id=doi:10.1177/2042263409345819&issn=2042-2634&isbn=&volume=3&issue=1&page=3&pages=3-10&date=2009&title=Therapeutic+Advances+in+Respiratory+Disease&atitle=Polymorphisms+of+the+beta2+adrenoreceptor+gene+in+chronic+obstructive+pulmonary+disease.&aulast=Vacca&pid=%3Cauthor%3EVacca+G%3BSchwabe+K%3BDuck+R%3BHlawa+HP%3BWestphal+A%3BPabst+S%3BGrohe.

205 Not a prediction model (focus on a particular predictor without the wanted adjustment)

Valvi D, Mannino DM, Mullerova H, Tal-Singer R. Fibrinogen, chronic obstructive pulmonary disease (COPD) and outcomes in two United States
| Page | Type | Title                                                                 | Authors                                                                                                                                                                                                 |
|------|------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 206  | Not a COPD cohort | Van Abeelen AFM, Elias SG, De Jong PA, Grobbee DE, Bossuyt PMM, Van Der Schouw VT, Roseboom TJ, Uiterwaal CSPM. Famine in the young and risk of later hospitalization for COPD and asthma. PLoS One [Internet] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands Dep; 2013; 8Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84893442985&partnerID=40&md5=9a6282c4d25938a333e9f7fbeb7339a. |
| 207  | Not a primary study (review) | van den Bemt L, Schermer TR. Multicomponent staging indices for chronic obstructive pulmonary disease in daily patient care: what’s the yield? Int. J. Clin. Pract. [Internet] Department of Primary and Community Care, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. l.vandenbemt@elg.umcn.nl; 2010; 64: 1475–1479Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medi&AN=20846194 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:20846194&iid=doi:10.1111%2Fj.1742-1241.2010.02434.x&issn=1368-5031&isbn=&volume=64&issue=11&spage=1475&pages=1475-9&date=2010&title=International+Journal+of+Clinical+Practice&atitle=Multicomponent+staging+indices+for+chronic+obstructive+pulmonary+disease+in+daily+patient+care%3A+what%27s+the+yield%3F.&aulast=van&pid=%3Cauthor%3EvandenBemt+L%3B.&aresult=40&md5=9a6282c4d25938a333e9f7fbeb7339a. |
| 208  | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Vaz Fragoso CA, Concato J, McAvay G, Van Ness PH, Gill TM. Respiratory impairment and COPD hospitalisation in older persons: A competing risk analysis. Eur. Respir. J. [Internet] Veterans Affairs Clinical Epidemiology Research Center, West Haven, CT, United States Dept. of Internal Medicine, Yale University School of Medicine, New Haven, CT, United States; 2012; 40: 37–44Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-
| 209 | Predictor and outcome not different in our definition | Vidal S, Gonzalez N, Barrio I, Rivas-Ruiz F, Bare M, Blasco JA, Ruiz-Frutos C, Quintana JM, Investigacion en Resultados y Servicios Sanitarios CG. Predictors of hospital admission in exacerbations of chronic obstructive pulmonary disease. *Int. J. Tuberc. Lung Dis.* [Internet] Unidad de Investigacion, Hospital Costa del Sol, Marbella, Spain.; 2013; 17: 1632–1637Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24200281 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:24200281&i d=doi:10.5588%2Fijtld.13.0177&issn=1027-3719&isbn=&volume=17&issue=12&spage=1632&pages=1632-7&date=2013&title=International+Journal+of+Tuberculosis+%26+Lung+Disease&Predictors+of+hospital+admission+in+exacerbations+of+chronic+obstructive+pulmonary+disease.&aulast=Vidal&pid=%3Cauthor%3EVidal+S%3BGonzalez+N%3BBario+I%3BRivas-Ruiz+F%3BBarri o+M%3BJRivas+Ruiz+C%3BQuintana+JM%3C%2Fauthor%3E%3C%2Ftitle%3E&atitle=Predictors+of+hospital+admission+in+exacerbations+of+chronic+obstructive+pulmonary+disease. | Exacerbation is predictor of hospitalization |
| 210 | Not the wanted outcome | Vitacca M, Clini E, Porta R, Foglio K, Ambrosino N. Acute exacerbations in patients with COPD: predictors of need for mechanical ventilation. *Eur. Respir. J.* [Internet] Salvatore Maugeri Foundation IRCCS, Respiratory Unit, Medical Center of Rehabilitation, Gussago (BS), Italy.; 1996; 9: 1487–1493Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=8836664 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:8836664&id =doi:&issn=0903-1936&isbn=&volume=9&issue=7&spage=1487&pages=1487-93&date=1996&title=European+Respiratory+Journal&atitle=Acute+exacerbations+in+patients+with+COPD%3A+predictors+of+need+for+mechanical +ventilation.&aulast=Vitacca&pid=%3Cauthor%3EVitacca+M%3BClini+E%3 BPorta+R%3BFoglio+K%3BAmbrosino+N%3C%2Fauthor%3E%3C%2Ftitle%3E%3C%2Fid%3E883 6664%3C%2Fdoi%3E&atitle=Acute+exacerbations+in+patients+with+COPD%3A+predictors+of+need+for+mechanical+ ventilation. | |
| 211 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Walters EH, Walters J, Wills KE, Robinson A, Wood-Baker R. Clinical diaries in COPD: Compliance and utility in predicting acute exacerbations. *Int. J. COPD* [Internet] Menzies Research Institute Tasmania, University of Tasmania, Hobart, Australia School of Nursing and Midwifery, University of Tasmania, Hobart, Australia; 2012; 7: 427–435Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84871679170&partnerID=40&md5=c241392cf672f4b853b50978fa9544d. | |
| 212 | Not a primary study (editorial) | Wedzicha JA. Winter forecasting of COPD exacerbations. *Prim. Care Respir. J.* [Internet] Academic Unit of Respiratory Medicine, UCL Medical School, Royal Free Campus, Rowland Hill Street, Hampstead, London NW3 2PF, United Kingdom; 2011; 20: 235–236Available from: | |
|   |   |
|---|---|
| 213 | Not a prediction model (neither prediction model nor multivariable association) |
|   | Witek Jr. TJ, Mahler DA. Minimal important difference of the transition dyspnoea index in a multinational clinical trial. *Eur. Respir. J.* [Internet] Respiratory Development and Operations, Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany. witek@ing.boehringer-ingelheim.com; 2003; 21: 267–272Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=12608440](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=12608440) [http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:12608440&id=doi:&issn=0903-1936&isbn=&volume=21&issue=2&spage=267&pages=267-72&date=2003&title=European+Respiratory+Journal&atitle=Minimal+important+difference+of+the+transition+dyspnoea+index+in+a+multinational+clinical+trial.&aulast=Witek+TJ.&pid=%3Cauthor%3EWitek+TJ+Jr%3B+Mahler+DA%3C%2Fauthor%3E%3CAN%3E12608440%3C%2FAN%3E%3CDT%3EJournal+Article%3C%2FD. |
| 214 | Not the wanted outcome |
|   | Witek Jr. TJ, Mahler DA. Meaningful effect size and patterns of response of the transition dyspnea index. *J. Clin. Epidemiol.* [Internet] Clinical and Scientific Affairs, Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, Ridgefield, CT 06877, USA. ted.witek@ing.boehringer-ingelheim.com; 2003; 56: 248–255Available from: [http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=12725879](http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=12725879) [http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:12725879&id=doi:&issn=0895-4356&isbn=&volume=56&issue=3&spage=248&pages=248-55&date=2003&title=Journal+of+Clinical+Epidemiology&atitle=Meaningful+effect+size+and+patterns+of+response+of+the+transition+dyspnea+index.&aulast=Witek+TJ.&pid=<author>Witek+TJ+Jr;Mahler+DA</author><AN>12725879</AN><DT>Clinical+Trial</DT>]. |
| 215 | Not a prediction model (focus on a particular predictor without the wanted adjustment) |
|   | Woodruff PG, Chatila W, Connett JE, Criner GJ, Curtis JL, Dransfield MT, Han MK, Lazarus SC, Marchetti N, Rogers TJ, Scanlon PD, Sin DD, Voelker H, Wendt C, Albert RK. Tumour necrosis factor receptor-75 and risk of COPD exacerbation in the azithromycin trial. *Eur. Respir. J.* [Internet] Cardiovascular Research Institute, University of California, 513 Parnassus Ave., San Francisco, CA 94143, United States Dept of Medicine, Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, CA, United States Division; 2014; 43: 295–298Available from: [http://www.scopus.com/inward/record.url?eid=2-s2.0-84891922037&partnerID=40&md5=4d6fc8ba79fc0daf6f0b04bd4db9904d](http://www.scopus.com/inward/record.url?eid=2-s2.0-84891922037&partnerID=40&md5=4d6fc8ba79fc0daf6f0b04bd4db9904d). |
| 216 | Not the wanted |
|   | Wu EQ, Birnbaum HG, Cifaldi M, Kang Y, Mallet D, Colice G. Development |
| outcome | No performance measure provided | Xu W, Collet JP, Shapiro S, Lin Y, Yang T, Platt RW, Wang C, Bourbeau J. Independent effect of depression and anxiety on chronic obstructive pulmonary disease exacerbations and hospitalizations. *Am. J. Respir. Crit. Care Med.* [Internet] Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada.; 2008; 178: 913–920Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18755925 &id=doi:10.1164%2Frrccm.200804-619OC&isbn=1073-449X&volume=178&issue=9&spage=913&pages=913-20&date=2008&title=American+Journal+of+Respiratory+Critical+Care+Medicine&atitle=Independent+effect+of+depression+and+anxiety+on+chronic+obstructive+pulmonary+disease+exacerbations+and+hospitalizations.&aulast=Xu&pid=%3Cauthor%3EXu+W%3BCollet+JP%3.|
| 218 | Not a prediction model (neither prediction model nor multivariable association) | Yanez AM, Guerrero D, Perez de Alejo R, Garcia-Rio F, Alvarez-Sala JL, Calle-Rubio M, Malo de Molina R, Valle Falcons M, Ussetti P, Sauleda J, Zamora Garcia E, Rodriguez-Gonzalez-Moro JM, Franco Gay M, Torrent M, Agusti A. Monitoring breathing rate at home allows early identification of COPD exacerbations. *Chest* [Internet] Fundacion de Investigacion Sanitaria Illles Balears, Edificio S. Hospital Universitario Son Espases, Palma de Mallorca, Spain. aina.yanez@caubet-cimera.es; 2012; 142: 1524–1529Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22797131 &id=http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:22797131&isbn=0012-3692&volume=142&issue=6&spage=1524&pages=1524-9&date=2012&title=Chest&atitle=Monitoring+breathing+rate+at+home+allows+early+identification+of+COPD+exacerbations.&aulast=Yanez&pid=%3EYanez+AM%3BGuerrero+D%3BPerez+de+Alejo+R%3BGarcia-Rio+F%3BAlvarez-Sala+JL%3BCalle-Rubio+M%3BMalo+de+Molina+R%3BValle+Falcones+M%3BU. |
| No performance measure provided | Yang H, Xiang P, Zhang E, Guo W, Shi Y, Zhang S, Tong Z. Predictors of exacerbation frequency in chronic obstructive pulmonary disease. *Eur. J. Med. Res.* [Internet] Department of Respiratory and Critical Care Medicine, Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital Beijing, Capital Medical University, No, 8 Gong Ti Southern Road, Chaoyang District, Beijing 100020, China. tongzhh2012@163.com.; 2014; 19: 18Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=24713440 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24713440&iid=doi:10.1186%2F2047-783X-19-18&issn=0949-2321&volume=19&issue=1&page=18&pages=18&date=2014&title=European+Journal+of+Medical+Research&atitle=Predictors+of+exacerbation+frequency+in+chronic+obstructive+pulmonary+disease.&aulast=Yang&pid=%3Cauthor%3EYang+H%3BXiang+P%3BZhang+E%3BGuo+W%3BShi+Y %3BZhang+S%3BTong+Z%3C%2Author%3E%3CAN%3E24713. |
| Not a prediction model (focus on a particular predictor without the wanted adjustment) | Yang Q, Chen Y, Krewski D, Burnett RT, Shi Y, McGrail KM. Effect of short-term exposure to low levels of gaseous pollutants on chronic obstructive pulmonary disease hospitalizations. *Environ. Res.* [Internet] McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, 1 Stewart Street, Ottawa, Ont. K1N 6N5, Canada Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, 451; 2005; 99: 99–105Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-22844434096&partnerID=40&md5=fdf71df548af19cd1021ea8ad3c971d. |
| Not the wanted outcome | Yeo J, Karimova G, Bansal S. Co-morbidity in older patients with COPD--its impact on health service utilisation and quality of life, a community study. *Age Ageing* [Internet] Education Centre, Wansbeck General Hospital, Woodhorn Lane, Ashington, Northumberland NE63 9JJ, UK. jennyyeo@doctors.org.uk; 2006; 35: 33–37Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16364931 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16364931&iid=doi:&issn=0002-0729&isbn=&volume=35&issue=1&page=33&pages=33-7&date=2006&title=Age%26%26Ageing&amp;atitle=Co-morbidity+in+older+patients+with+COPD--its+impact+on+health+service+utilisation+and+quality+of+life%2C+a+community+study.&aulast=Yeo&pid=%3Cauthor%3Eyoe+J%3BKarimova+G%3BBansal+S%3C%2Author%3E%3CAN%3E16364931%3C%2FAN%3E%3CDT%3EComparativ. |
| Not a primary study (editorial) | Yohannes AM. Depression and sleep disorders predict acute exacerbations and hospitalization in patients with chronic obstructive pulmonary disease.
|   |   |
|---|---|
| **Respirology** [Internet] Department Health Professions, Research Institute for Health and Social Change, Manchester Metropolitan University, Hathersage Road, Manchester, M13 0JA, United Kingdom; 2012; 17: 1278Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84867949021&partnerID=40&md5=4398c518065d4274ffdda559c584dabb. |   |
| 223 | Not a COPD cohort |
| Yoo JW, Hong Y, Seo JB, Chae EJ, Ra SW, Lee JH, Kim EK, Baek S, Kim TH, Kim WJ, Lee SM, Lee S, Lim SY, Shin TR, Yoon HI, Sheen SS, Lee JS, Huh JW, Oh YM, Lee SD. Comparison of clinico-physiologic and CT imaging risk factors for COPD exacerbation. *J. Korean Med. Sci.* [Internet] Department of Pulmonary and Critical Care Medicine, Clinical Research Center for Chronic Obstructive Airway Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea Department of Radiology, and Research Institute of Radio; 2011; 26: 1606–1612Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84863081713&partnerID=40&md5=f5f01846a62c3344025606d449c67720. |
| 224 | Not the wanted outcome |
| Yorgancioglu A, Havlucu Y, Celik P, Dinc G, Saka A. Relation between quality of life and morbidity and mortality in COPD patients: Two-year follow-up study. *COPD J. Chronic Obstr. Pulm. Dis.* [Internet] Department of Chest Disease, Medical Faculty, Celal Bayar University, 45020 Manisa, Turkey Department of Chest Disease, Dortyol State Hospital, Hatay, Turkey Department of Public Health, Medical Faculty, Celal Bayar University, Manisa, Turkey; 2010; 7: 248–253Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-77955182204&partnerID=40&md5=5bd88186aff801ee96685ae561e2d1cd. |
| 225 | Not a prediction model (neither prediction model nor multivariable association) |
| Zaman M, Mahmood S, Altayeh A. Low inspiratory capacity to total lung capacity ratio is a risk factor for chronic obstructive pulmonary disease exacerbation. *Am. J. Med. Sci.* [Internet] Department of Medicine, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV, United States Division of Pulmonary Medicine, Marshall University, Joan C. Edwards School of Medicine, Huntington, WV, United States; 2010; 339: 411–414Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-77952282161&partnerID=40&md5=e5e2e3d3d62edc63b9563c704437a321. |
| 226 | Not a prediction model (neither prediction model nor multivariable association) |
| Zhang JX, Hu JJ, Xu J, Zhao L, Bai C, Li Q. Relationship between chronic obstructive pulmonary disease (COPD) assessment test score and prognostic factors of COPD patients. *Acad. J. Second Mil. Med. Univ.* [Internet] Q. Li, Department of Respiratory Diseases, Shanghai Hospital, Second Military Medical University, Shanghai 200433, China; 2013; 34: 839–845Available from: http://www.embase.com/search/results?subaction=viewrecord&from=exp |
| 227 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Zhang R, Tan X, He Q, Chen Q, Gai J, Wei J, Wang Y. Comparison of symptom and risk assessment methods among patients with chronic obstructive pulmonary disease. *Chin. Med. J. (Engl).* [Internet] Department of Respiratory and Critical Care Medicine, Peking University People's Hospital, Beijing 100044, China. Department of Respiratory and Critical Care Medicine, Peking University People's Hospital, Beijing 100044, China. Email: hxk313@126.com.; 2014; 127: 2594–2598 Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=25043073 http://sfx.metabib.ch/sfx_locator?sid=OVID:medline&id=pmid:25043073&iid=doi:&issn=0366-6999&isbn=&volume=127&issue=14&spage=2594&pages=2594-8&date=2014&title=Chinese+Medical+Journal&atitle=Comparison+of+symptom+and+risk+assessment+methods+among+patients+with+chronic+obstructive+pulmonary+disease.&aulast=Zhang&pid=%3Cauthor%3EZhang+R%3BTan+X%3BHe+Q%3BChen+Q%3BGai+J%3BWei+J%3BWang+Y%3C%2Fauthor%3E%3CAN%3E25043073%. |

**Table 4. Reasons for exclusion after full-text assessment of each of the 227 studies coming from what we have defined as “Source 1 for full-text assessment” (studies included after title and abstract screening).**
| Paper coming from reviews identified during the title and abstract screening |
|---------------------------------|---------------------------------------------------------------------------------|
| **1** | Not a prediction model (focus on a particular predictor without the wanted adjustment) |
| | Connolly MJ, Lowe D, Anstey K, Hosker HSR, Pearson MG, Roberts CM. Admissions to hospital with exacerbations of chronic obstructive pulmonary disease: Effect of age related factors and service organisation. *Thorax* [Internet] 2006 [cited 2014 Dec 15]; 61: 843–848Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2104767&tool=pmc_entrez&rendertype=abstract. |
| **2** | Not the wanted outcome |
| | Gadoury M, Schwartzman K, Rouleau M, Maltais F, Julien M, Beaupré A, Renzi P, Bégin R, Nault D, Bourbeau J. Self-management reduces both short- and long-term hospitalisation in COPD. *Eur. Respir. J.* [Internet] 2005 [cited 2014 Dec 15]; 26: 853–857Available from: http://www.ncbi.nlm.nih.gov/pubmed/16264046. |
| **3** | Not the wanted outcome |
| | Groenewegen KH, Schols AM, Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. *Chest* [Internet] Department of Pulmonology, University Hospital Maastricht, Maastricht, The Netherlands. ewo@slon.azm.nl; 2003; 124: 459–467Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=12907529 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:12907529&id=doi: &issn=0012-3692&isbn=&volume=124&issue=2&spage=459&pages=459-67&date=2003&title=Chest&atitle=Mortality+and+mortality-related+factors+after+hospitalization+for+acute+exacerbation+of+COPD.&aulast =Groenewegen&pid=<author>Groenewegen+KH;Schols+AM;Wouters+EF</author><AN>12907529</AN><DT>Journal+Article</DT>. |
| **4** | Included |
| | Gudmundsson G, Gislason T, Janson C, Lindberg E, Hallin R, Ulrik CS, Brøndum E, Nieminen MM, Aine T, Bakke P. Risk factors for rehospitalisation in COPD: role of health status, anxiety and depression. *Eur. Respir. J.* [Internet] 2005 [cited 2014 Dec 15]; 26: 414–419Available from: http://www.ncbi.nlm.nih.gov/pubmed/16135721. |
| **5** | Included |
| | J Garcia-Aymerich, E Farrero, M A Félez, J Izquierdo, R M Marrades JMA. Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. 2003; . |
| **6** | Duplicate |
| | Kessler R, Faller M, Fourgaut G, Mennecier B, Weitzenblum E. Predictive Factors of Hospitalization for Acute Exacerbation in a Series of 64 Patients with pulmonary hypertension are predictive factors of hospitalization for acute exacerbation in COPD pa-. 1994; . |
| No. | Measure Provided | Reference |
|-----|-----------------|-----------|
| 7   | No performance provided | Lau a C, Yam LY, Poon E. Hospital re-admission in patients with acute exacerbation of chronic obstructive pulmonary disease. *Respir. Med.* [Internet] 2001 [cited 2014 Dec 15]; 95: 876–884Available from: http://www.ncbi.nlm.nih.gov/pubmed/11716201. |
| 8   | No performance provided | Wang Q, Bourbeau J. Outcomes and health-related quality of life following hospitalization for an acute exacerbation of COPD. *Respirology* [Internet] 2005; 10: 334–340Available from: http://www.ncbi.nlm.nih.gov/pubmed/15955146. |
| 9   | Not a prediction model (neither prediction model nor multivariable association) | Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* [Internet] Academic Unit of Respiratory Medicine, St Bartholomew’s Hospital, London, London, UK.; 2004; 169: 1298–1303Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med&AN=14990395 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:14990395&id=doi: &issn=1073-449X&isbn=&volume=169&issue=12&spage=1298&pages=1298-303&date=2004&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Early+therapy+improves+outcomes+of+exacerbations+of+chronic+obstructive+pulmonary+disease.&aulast=Wilkinson&pid=%3Cauthor%3EWilkinson+TM%3BDonaldson+GC%3BHurst+JR%3BSeemungal+TA%3BWedzicha+. |

Papers coming from grey literature, related articles PUBMED search, citations of included so far studies

| No. | Measure Provided | Reference |
|-----|-----------------|-----------|
| 10  | Not a primary study (review) | Bahadori K, FitzGerald JM. Risk factors of hospitalization and readmission of patients with COPD exacerbation--systematic review. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2007; 2: 241–251. |
| 11  | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Barba R, de Casasola GG, Marco J, Emilio Losa J, Plaza S, Canora J, Zapatero A. Anemia in chronic obstructive pulmonary disease: a readmission prognosis factor. *Curr. Med. Res. Opin.* [Internet] 2012 [cited 2014 Sep 17]; 28: 617–622Available from: http://www.ncbi.nlm.nih.gov/pubmed/22409165. |
| 12  | No performance measure provided | Berkius J, Nolin T, Mårdh C, Karlström G, Walther SM. Characteristics and long-term outcome of acute exacerbations in chronic obstructive pulmonary disease: An analysis of cases in the Swedish Intensive Care Registry during 2002-2006. *Acta Anaesthesiol. Scand.* 2008; 52: 759–765. |
| 13  | Not a prediction model (focus on a particular predictor without the) | Burgel PR, Nesme-Meyer P, Chanez P, Caillaud D, Carré P, Perez T, Roche N. Cough and sputum production are associated with frequent exacerbations and hospitalizations in COPD subjects. *Chest* 2009; 135: 975–982. |
|   |   |   |
|---|---|---|
| 14 | Not a COPD cohort | Cano NJM. C-Reactive Protein and Body Mass Index Predict Outcome in End-Stage Respiratory Failure<ref id="AFF1">*</ref>. CHEST J. 2004; 126: 540. |
| 15 | No performance measure provided | Chan FW, Wong FY, Yam CH, Cheung W-L, Wong EL, Leung MC, Goggins WB, Yeoh E-K. Risk factors of hospitalization and readmission of patients with COPD in Hong Kong population: Analysis of hospital admission records. BMC Health Serv. Res. [Internet] BioMed Central Ltd; 2011; 11: 186Available from: http://www.biomedcentral.com/1472-6963/11/186. |
| 16 | Not a primary study (editorial) | Chavannes NH, Jones RCM, Postma DS, Rennard S. Using COPD multidimensional indices in routine clinical practice: DOSE meets all criteria. Prim. Care Respir. J. [Internet] Primary Care Respiratory Society UK; 2012; 21: 245–246Available from: http://dx.doi.org/10.4104/pcrj.2012.00066. |
| 17 | Included | Chen Y. Readmission in Taiwan. 2015; : 105–124. |
| 18 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Connolly MJ, Lowe D, Anstey K, Hosker HSR, Pearson MG, Roberts CM. Admissions to hospital with exacerbations of chronic obstructive pulmonary disease: Effect of age related factors and service organisation. Thorax [Internet] 2006 [cited 2014 Dec 15]; 61: 843–848Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2104767&tool=pmceng&rendertype=abstract. |
| 19 | Not the wanted outcome | Connors AF, Dawson N V, Thomas C, Harrell FE, Desbiens N, Fulkerson WJ, Kussin P, Bellamy P, Goldman LEE. Outcomes Followin' of Acute Exacerbation of Severe Chronic Obstructive Lung Disease. 1998; . |
| 20 | No performance measure provided | Coventry P a, Gemmell I, Todd CJ. Psychosocial risk factors for hospital readmission in COPD patients on early discharge services: a cohort study. BMC Pulm. Med. [Internet] BioMed Central Ltd; 2011; 11: 49Available from: http://www.biomedcentral.com/1471-2466/11/49. |
| 21 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Dalal A a, Shah M, Lunacek O, Hanania N a. Clinical and Economic Burden of Depression/Anxiety in Chronic Obstructive Pulmonary Disease Patients within a Managed Care Population. COPD 2011; 8: 293–299. |
| 22 | No performance | De Oca MM, Tálamo C, Halbert RJ, Perez-Padilla R, Lopez MV, Muiño A, Jardim JRB, |
| Measure Provided | Reference |
|------------------|-----------|
| Valdivia G, Pertuzé J, Moreno D, Menezes AMB. Frequency of self-reported COPD exacerbation and airflow obstruction in five Latin American cities: The Proyecto Latinoamericano de Investigación en Obstrucción Pulmonar (PLATINO) study. *Chest* 2009; 136: 71–78. |
| 23 | Not the wanted outcome |
| de Torres JP, Cordoba-Lanus E, López-Aguilar C, Muros de Fuentes M, Montejo de García a., Aguirre-Jaime a., Celli BR, Casanova C. C-reactive protein levels and clinically important predictive outcomes in stable COPD patients. *Eur. Respir. J.* 2006; 27: 902–907. |
| 24 | Not the wanted outcome |
| Dev D, Wallace E, Sankaran R, Cunniffe J, Govan JR, Wathen CG, Emmanuel FX. Value of C-reactive protein measurements in exacerbations of chronic obstructive pulmonary disease. *Respir Med* 1998; 92: 664–667. ST – Value of C – reactive protein measurement. |
| 25 | Not the wanted outcome |
| Donaldson GC, Seemungal T a R, Bhowmik a, Wedzicha J a. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002; 57: 847–852. |
| 26 | Not a prediction model (focus on a particular predictor without the wanted adjustment) |
| Emerman CL, Effron D, Lukens TW. Spirometric criteria for hospital admission of patients with acute exacerbation of COPD. *Chest* 1991; 99: 595–599. |
| 27 | Not the wanted outcome |
| Esteban C, Quintana JM, Aburto M, Moraza J, Capelastegui a. A simple score for assessing stable chronic obstructive pulmonary disease. *QJM* 2006; 99: 751–759. |
| 28 | Not the wanted outcome |
| Gadoury M, Schwartzman K, Rouleau M, Maltais F, Julien M, Beaupré A, Renzi P, Bégir R, Nault D, Bourbeau J. Self-management reduces both short- and long-term hospitalisation in COPD. *Eur. Respir. J.* [Internet] 2005 [cited 2014 Dec 15]; 26: 853–857Available from: http://www.ncbi.nlm.nih.gov/pubmed/16264046. |
| 29 | Not the wanted study design (case-control study) |
| Garcia-Aymerich J, Monso E, Marrades RM E Al. Risk Factors for Hospitalization for a Chronic EFRAM STUDY. *Am J Respir Crit Med* 2001; 164: 1002–1007. |
| 30 | Not the wanted outcome |
| Garcia-Aymerich J, Barreiro E, Farrero E, Marrades RM, Morera J, Antó JM. Patients hospitalized for COPD have a high prevalence of modifiable risk factors for exacerbation (EFRAM study). *Eur. Respir. J.* 2000; 16: 1037–1042. |
| 31 | Duplicate |
| Garcia-Aymerich J, Farrero E, Félez M a, Izquierdo J, Marrades RM, Antó JM. Risk |
|   |   |   |
|---|---|---|
|   | **factors of readmission to hospital for a COPD exacerbation: a prospective study.** *Thorax* 2003; 58: 100–105. |   |
| 32 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | García-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006; 61: 772–778. |
| 33 | Not the wanted outcome | Goossens L, Baker C, Monz B, Zou K, Rutten-van MM. Prs46 Adjusting for Chronic Obstructive Pulmonary Disease (COPD) Severity in Database Research: Feasibility of Developing and Validating an Algorithm. *Value Heal.* 2010; 13: A327. |
| 34 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Groenewegen KH, Postma DS, Hop WCJ, Wielders PLML, Schlösser NJJ, Wouters EFM. Increased systemic inflammation is a risk factor for COPD exacerbations. *Chest* 2008; 133: 350–357. |
| 35 | Duplicate | Gudmundsson G, Gislasen T, Janson C, Lindberg E, Hallin R, Ulrik CS, Brøndum E, Nieminen MM, Aine T, Bakke P. Risk factors for rehospitalisation in COPD: role of health status, anxiety and depression. *Eur. Respir. J.* [Internet] 2005 [cited 2014 Dec 15]; 26: 414–419Available from: http://www.ncbi.nlm.nih.gov/pubmed/16135721. |
| 36 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Güerri R, Gayete A, Balcells E, Ramirez-Sarmiento A, Vollmer I, García-Aymerich J, Gea J, Orozco-Levi M. Mass of intercostal muscles associates with risk of multiple exacerbations in COPD. *Respir. Med.* 2010; 104: 378–388. |
| 37 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Han MK, Kazerooni E a., Lynch D a., Liu LX, Murray S, Curtis JL, Criner GJ, Kim V, Bowler RP, Hanania N a., Anzueto a. R, Make BJ, Hokanson JE, Crapo JD, Silverman EK, Martinez FJ, Washko GR. Chronic Obstructive Pulmonary Disease Exacerbations in the COPDGene Study: Associated Radiologic Phenotypes. *Radiology* 2011; 261: 274–282. |
| 38 | Not a prediction model (focus on | Hasford B, Fruhmann G. Air pollution and daily admissions for chronic obstructive pulmonary disease in six European cities: results from the APHEA project. Air |
|   |   |   |
|---|---|---|
| **a particular predictor without the wanted adjustment)** | Pollution and Health, a European Approach. *Eur. Respir. J. Off. J. Eur. Soc. Clin. Respir. Physiol.* 1998; 11: 992–993. |   |
| 39 | Not a primary study (review) | Hoogendoorn M, Feenstra TL, Hoogenveen RT, Al M, Mölken MR Van. Association between lung function and exacerbation frequency in patients with COPD. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2010; 5: 435–444. |
| 40 | Included | Hurst, Vestbo J, Anzueto A, Locantore N, Mullerova H, Tal-Singer R, Miller B, Lomas D, Agusti A, MacNee W, Calverley P, Rennard S, Wouters E, Wedzicha J, Longitudinally EC. Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease. 2010; Available from: http://discovery.ucl.ac.uk/1298728/. |
| 41 | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Ito K, Kawayama T, Shoji Y, Fukushima N, Matsunaga K, Edakuni N, Uchimura N, Hoshino T. Depression, but not sleep disorder, is an independent factor affecting exacerbations and hospitalization in patients with chronic obstructive pulmonary disease. *Respirology* [Internet] 2012; 17: 940–949Available from: http://www.ncbi.nlm.nih.gov/pubmed/22564039. |
| 42 | No performance measure provided | Jenkins CR, Celli B, Anderson J a., Ferguson GT, Jones PW, Vestbo J, Yates JC, Calverley PM a. Seasonality and determinants of moderate and severe COPD exacerbations in the TORCH study. *Eur. Respir. J.* 2012; 39: 38–45. |
| 43 | Not the wanted study design (RCT, not only placebo arm) | Jurado Gámez B, Feu Collado N, Jurado García JC, García Gil F, Muñoz Gomariz E, Jiménez Murillo L, Muñoz Cabrera L. Home intervention and predictor variables for rehospitalization in chronic obstructive pulmonary disease exacerbations. *Arch. Bronconeumol.* [Internet] 2013; 49: 10–14Available from: http://www.ncbi.nlm.nih.gov/pubmed/23089685. |
| 44 | Not a primary study (review) | Katon W, Lin EHB, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *Gen. Hosp. Psychiatry* 2007; 29: 147–155. |
| 45 | No performance measure provided | Kessler R, Faller M, Fourgaut G, Mennecier B, Weitzenblum E. Predictive factors of hospitalization for acute exacerbation in a series of 64 patients with chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* 1999; 159: 158–164. |
| 46 | No performance measure provided | Lau a C, Yam LY, Poon E. Hospital re-admission in patients with acute exacerbation of chronic obstructive pulmonary disease. *Respir. Med.* [Internet] 2001 [cited 2014 Dec 15]; 95: 876–884Available from: http://www.ncbi.nlm.nih.gov/pubmed/11716201. |
| No. | Note | Study Details |
|-----|------|---------------|
| 47  | Not a primary study (review) | Laurin C, Moullec G, Bacon SL, Lavoie KL. Impact of anxiety and depression on chronic obstructive pulmonary disease exacerbation risk. *Am. J. Respir. Crit. Care Med.* 2012; 185: 918–923. |
| 48  | Not the wanted study design (case-control study) | Liu S-F, Lin K-C, Chin C-H, Chen Y-C, Chang H-W, Wang C-C, Lin M-C. Factors influencing short-term re-admission and one-year mortality in patients with chronic obstructive pulmonary disease. *Respirology* 2007; 12: 560–565. |
| 49  | No performance measure provided | McGhan R, Radcliff T, Fish R, Sutherland ER, Welsh C, Make B. Predictors of rehospitalization and death after a severe exacerbation of COPD. *Chest* 2007; 132: 1748–1755. |
| 50  | Not the wanted study design (cross-sectional study) | Miravitlles M, Guerrero T, Mayordomo C, Sánchez-Agudo L, Nicolau F, Segú JL. Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis. The EOLO Study Group. *Respiration.* 2000; 67: 495–501. |
| 51  | Not a primary study (review) | Miravitlles M. Cough and sputum production as risk factors for poor outcomes in patients with COPD. *Respir. Med.* [Internet] Elsevier Ltd; 2011; 105: 1118–1128Available from: http://dx.doi.org/10.1016/j.rmed.2011.02.003. |
| 52  | Included | Müllerova H, Maselli DJ, Locantore N, Vestbo J, Hurst JR, Wedzicha J a., Bakke P, Agusti A, Anzueto A, Ivanov Y, Kostov K, Bourbeau J, Fitzgerald M, Hernández P, Killian K, Levy R, Malais F, O’Donnell D, Krepelka J, Vestbo J, Wouters EFM, Quinn D, Bakke P, Kosnik M, Agusti A, Feschenko Y, Gavrisyuk V, Yashina L, MacNee W, Singh SD, et al. Hospitalized Exacerbations of COPD. *CHEST J.* [Internet] 2015; 147: 999Available from: http://journal.publications.chestnet.org/article.aspx?doi=10.1378/chest.14-0655. |
| 53  | Predictor and outcome not different in our definition | Murata GH, Gorby MS, Kapsner CO, Chick TW, Halperin a K. A multivariate model for the prediction of relapse after outpatient treatment of decompensated chronic obstructive pulmonary disease. *Arch. Intern. Med.* 1992; 152: 73–77. |
| 54  | Predictor and outcome not different in our definition | Murata GH, Gorby MS, Kapsner CO, Chick TW, Halperin a K. A multivariate model for predicting hospital admissions for patients with decompensated chronic obstructive pulmonary disease. *Arch. Intern. Med.* 1992; 152: 82–86. |
| 55  | Not a prediction model (focus on a particular predictor) | Ng T, Mathew N, Tan W, Cao Z, Ong K, Eng P. Depressive Symptoms and Chronic Obstructive Pulmonary Disease. *Arch Intern Med* 2007; 167: 60–67. |
|   |   |
|---|---|
| 56 | Not a COPD cohort |
|   | Nichol KL, Baken L, Nelson a. Relation between influenza vaccination and outpatient visits, hospitalization, and mortality in elderly persons with chronic lung disease. *Ann. Intern. Med.* 1999; 130: 397–403. |
| 57 | Not the wanted outcome |
|   | Niewoehner DE, Collins D, Erbland ML. Relation of FEV 1 to Clinical Outcomes during Exacerbations of Chronic Obstructive. 2000; 161: 1201–1205. |
| 58 | Not the wanted outcome |
|   | Osman IM, Godden DJ, Friend J a, Legge JS, Douglas JG. Quality of life and hospital re-admission in patients with chronic obstructive pulmonary disease. *Thorax* 1997; 52: 67–71. |
| 59 | Not a prediction model (neither prediction model nor multivariable association) |
|   | Patel IS, Seemungal T a R, Wilks M, Lloyd-Owen SJ, Donaldson GC, Wedzicha J a. Relationship between bacterial colonisation and the frequency, character, and severity of COPD exacerbations. *Thorax* 2002; 57: 759–764. |
| 60 | Not a prediction model (focus on a particular predictor without the wanted adjustment) |
|   | Perera WR, Hurst JR, Wilkinson TM a, Sapsford RJ, Müllerova H, Donaldson GC, Wedzicha J a. Inflammatory changes, recovery and recurrence at COPD exacerbation. *Eur. Respir. J.* 2007; 29: 527–534. |
| 61 | Not a prediction model (focus on a particular predictor without the wanted adjustment) |
|   | Pitta F, Troosters T, Probst VS, Spruit M a., Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006; 129: 536–544. |
| 62 | Not a primary study (review) |
|   | Pooler A, Beech R. Examining the relationship between anxiety and depression and exacerbations of COPD which result in hospital admission: a systematic review. *Int. J. Chron. Obstruct. Pulmon. Dis.* [Internet] 2014; 9: 315–330Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3974694&tool=pmcentrez&rendertype=abstract. |
| 63 | Not the wanted outcome |
|   | Rabe KF, Fabbri LM, Vogelmeier C, Kögler H, Schmidt H, Beeh KM, Glaab T. Seasonal... |
| Study Design | Study Description | Reference |
|-------------|------------------|-----------|
| Not the wanted outcome | Not the wanted outcome | Seemungal T, Harper-Owen R, Bhowmik A, Moric I, Sanderson G, Message S, Maccallum P, Meade TW, Jeffries DJ, Johnston SL, Wedzicha J a. Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* 2001; 164: 1618–1623. |
| Not a prediction model (focus on a particular predictor without the wanted adjustment) | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Sharma G, Kuo Y-F, Freeman JL, Zhang DD, Goodwin JS. Outpatient follow-up visit and 30-day emergency department visit and readmission in patients hospitalized for chronic obstructive pulmonary disease. *Arch. Intern. Med.* 2010; 170: 1664–1670. |
| Not the wanted study design (cross-sectional study) | Not the wanted study design (cross-sectional study) | Rowe BH, Villa-Roel C, Guttman A, Ross S, Mackey D, Sivilotti ML a, Worster A, Stiell IG, Willis V, Borgundvaag B. Predictors of hospital admission for chronic obstructive pulmonary disease exacerbations in Canadian emergency departments. *Acad. Emerg. Med.* 2009; 16: 316–324. |
| Not a prediction model (focus on a particular predictor without the wanted adjustment) | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Rosell A, Monsó E, Soler N, Torres F, Angrill J, Riise G, Zalacaín R, Morera J, Torres A. Microbiologic determinants of exacerbation in chronic obstructive pulmonary disease. *Arch. Intern. Med.* 2005; 165: 891–897. |
| Not a prediction model (neither prediction model nor multivariable association) | Not a prediction model (neither prediction model nor multivariable association) | Roberts CM, Stone R a., Lowe D, Pursey N a., Buckingham RJ. Co-morbidities and 90-day Outcomes in Hospitalized COPD Exacerbations. *COPD J. Chronic Obstr. Pulm. Dis.* 2011; 8: 354–361. |
| **study design** (RCT, not only placebo arm) | **study design** (RCT, not only placebo arm) | distribution of COPD exacerbations in the prevention of exacerbations with tiotropium in COPD trial. *Chest* 2013; 143: 711–719. |
| Study Design (Case-Control Study) | Care and admissions in COPD patients with high consumption of health resources. *Respir. Med.* 2004; 98: 318–329. |
|----------------------------------|---------------------------------------------------------------------------------------------------------------|
| 71                               | Not a prediction model (focus on a particular predictor without the wanted adjustment) Stolz D, Christ-Crain M, Morgenthaler NG, Leuppi J, Miedinger D, Bingisser R, Müller C, Struck J, Müller B, Tamm M. Copeptin, C-reactive protein, and procalcitonin as prognostic biomarkers in acute exacerbation of COPD. *Chest* 2007; 131: 1058–1067. |
| 72                               | Not a prediction model (focus on a particular predictor without the wanted adjustment) Terada K, Muro S, Sato S, Ohara T, Haruna a, Marumo S, Kinose D, Ogawa E, Hoshino Y, Niimi a, Terada T, Mishima M. Impact of gastro-oesophageal reflux disease symptoms on COPD exacerbation. *Thorax* 2008; 63: 951–955. |
| 73                               | Not a prediction model (focus on a particular predictor without the wanted adjustment) Terada K, Muro S, Ohara T, Kudo M, Ogawa E, Hoshino Y, Hirai T, Niimi A, Chin K, Mishima M. Abnormal swallowing reflex and COPD exacerbations. *Chest* 2010; 137: 326–332. |
| 74                               | No performance measure provided Terzano C, Conti V, Di Stefano F, Petroianni A, Ceccarelli D, Graziani E, Mariotta S, Ricci A, Vitarelli A, Puglisi G, De Vito C, Villari P, Allegra L. Comorbidity, hospitalization, and mortality in COPD: Results from a longitudinal study. *Lung* 2010; 188: 321–329. |
| 75                               | No spirometry in the COPD definition Tsai C-L, Clark S, Cydulka RK, Rowe BH, Camargo C a. Factors associated with hospital admission among emergency department patients with chronic obstructive pulmonary disease exacerbation. *Acad. Emerg. Med.* 2007; 14: 6–14. |
| 76                               | Not a prediction model (neither prediction model nor multivariable association) Tumkaya M, Atis S, Ozge C, Delialioglu N, Polat G, Kanik A. Relationship between airway colonization, inflammation and exacerbation frequency in COPD. *Respir. Med.* 2007; 101: 729–737. |
| 77                               | No GOLD standard for Vega Reyes JA, Montero Pérez-Barquero M, Sánchez Guijo P. Factores pronósticos de reingreso en la enfermedad pulmonar obstructiva crónica. *Med. Clin. (Barc).* |
| COPD definition | 2004; 122: 293–297. |
|-----------------|---------------------|
| 78              | Not the wanted study design (case-control study) | Wan ES, DeMeeo DL, Hersh CP, Shapiro SD, Rosiello R a., Sama SR, Fuhlbrigge AL, Foreman MG, Silverman EK. Clinical predictors of frequent exacerbations in subjects with severe chronic obstructive pulmonary disease (COPD). *Respir. Med.* [Internet] Elsevier Ltd; 2011; 105: 588–594Available from: http://dx.doi.org/10.1016/j.rmed.2010.11.015. |
| 79              | Duplicate | Wang Q, Bourbeau J. Outcomes and health-related quality of life following hospitalization for an acute exacerbation of COPD. *Respirology* [Internet] 2005; 10: 334–340Available from: http://www.ncbi.nlm.nih.gov/pubmed/15955146. |
| 80              | Not a prediction model (focus on a particular predictor without the wanted adjustment) | Wong AWM, Gan WQ, Burns J, Sin DD, van Eeden SF. Acute exacerbation of chronic obstructive pulmonary disease: influence of social factors in determining length of hospital stay and readmission rates. *Can. Respir. J.* 2008; 15: 361–364. |
| 81              | Not a prediction model (neither prediction model nor multivariable association) | Yoshikawa M, Fujita Y, Yamamoto Y, Yamauchi M, Tomoda K, Koyama N, Kimura H. Mini Nutritional Assessment Short-Form predicts exacerbation frequency in patients with chronic obstructive pulmonary disease. *Respirology* [Internet] 2014; 19: 1198–1203Available from: http://doi.wiley.com/10.1111/resp.12380. |
| 82              | No performance measure provided | Zanoria SJT, ZuWallack R. Directly measured physical activity as a predictor of hospitalizations in patients with chronic obstructive pulmonary disease. *Chron. Respir. Dis.* [Internet] 2013; 10: 207–213Available from: http://www.ncbi.nlm.nih.gov/pubmed/24177682. |

Table 5. Reasons for exclusion after full-text assessment of each of the 82 studies coming from what we have defined as “Source 2 for full-text assessment” (from the references and Pubmed related search of the 20 papers definitively included from the “Source 1 for full-text assessment” or from grey literature or from suggestions of contacted authors or from reviews on the topic).
A list of the 25 studies after full-text assessment in alphabetical order follows:

| Study                                      | Year | Reference |
|--------------------------------------------|------|-----------|
| Almagro (2014)                             | 2014 | [19]      |
| Almagro (2006)                             | 2006 | [20]      |
| Amalakuhan (2012)                          | 2012 | [21]      |
| Bertens (2013)                             | 2013 | [22]      |
| Brusse-Keizer (2011)                       | 2011 | [23]      |
| Chen (2006)                                | 2006 | [24]      |
| Echave-Sustaeta (2010)                     | 2010 | [25]      |
| Faganello (2010)                           | 2010 | [26]      |
| Garcia-Aymerich (2003)                     | 2003 | [27]      |
| Gudmundusson (2005)                        | 2005 | [28]      |
| Hurst (2010)                               | 2010 | [29]      |
| Jakob (2013)                               | 2013 | [30]      |
| Jones (2009)                               | 2009 | [31]      |
| Ko (2011)                                  | 2011 | [32]      |
| Lee (2014)                                 | 2014 | [33]      |
| Marin (2009)                               | 2009 | [34]      |
| Moberg (2014)                              | 2014 | [35]      |
| Motegi (2013)                              | 2013 | [36]      |
| Moy (2014)                                 | 2014 | [37]      |
| Mülleroa (2015)                            | 2015 | [38]      |
| Ong (2005)                                 | 2005 | [39]      |
| Parshall (2008)                            | 2008 | [40]      |
| Suetomo (2014)                             | 2014 | [41]      |
| Takahashi (2012)                           | 2012 | [42]      |
| Thomsen (2013)                             | 2013 | [43]      |

Table 6. List of the 25 included papers
New section
QUALITY ASSESSMENT

The quality assessment concerned 6 categories of potential bias (participant selection as shown in the study flow, measurement of predictors, measurement of outcome (i.e. exacerbations), statistical analysis for model development, performance measures and validation) based on guidance from Cochrane [18], PROBAST guidelines (http://www.systematic-reviews.com/probast) and the needs of this particular systematic review. The final quality assessment of the 25 included studies is reported again in this online material (as in the main text) in m-Figure 2. Then, we report the quality assessment sheet that we have used for the quality assessment (Table 7) and a guideline for the criteria we have used to eventually downgrade the study quality per each bias category (Table 8).

| Study flow | Predictors | Outcome | Statistical analysis | Performance measures | Validation of prediction model |
|------------|------------|---------|----------------------|----------------------|-------------------------------|
| 🟢           | 🟢           | 🟢           | 🟢                      | 🟢                      | 🟢                               |
| 🟢           | 🟢           | 🟢           | 🟢                      | 🟢                      | 🟢                               |
| 🟢           | 🟢           | 🟢           | 🟢                      | 🟢                      | 🟢                               |
| 🟢           | 🟢           | 🟢           | 🟢                      | 🟢                      | 🟢                               |

+ Low risk of bias  🟢 Medium risk of bias  🟥 High risk of bias  ✗ Not performed

m-Figure 2. Quality Assessment

1) Study flow description from screening of the patients to patients included in the statistical analysis
2) Definition and measurement of the predictors
3) Definition and measurement of the outcome
4) Statistical model used and eventual procedure of predictors' selection
5) Separated evaluation of discrimination and calibration of the model
6) Validation in an external cohort
| STUDY |  |
|---|---|
| Flow | Setting and sampling: |
| | Inclusion criteria: |
| | Exclusion criteria: |
| | Ethical approval: |
| | Selection process: |
| Predictors |  |
| Outcome | Definition of exacerbation: |
| Statistical analysis | Ratio #events/#predictors: |
| | Predicted outcome: |
| | Statistical model: |
| | Missing data: |
| Performance Measures |  |
| Validation |  |

*Table 7. Quality assessment sheet*
| Study |  |
|---|---|
| **Flow** | Setting and sampling:  
Inclusion criteria:  
Exclusion criteria:  
DOWNGRADE if comorbidities allowed as main disease instead than COPD  
Ethical approval:  
Selection process: DOWNGRADE if selection bias is likely |
| **Predictors** | (Variables related to the prediction model and not to all the baseline assessment) Defined on the onset of the study? Standardized questionnaires were used? Predictors were evaluated by the standard procedures (explained or referring to some standard procedures)? Blinded to outcome? |
| **Outcome** | Definition of exacerbation: Symptom or event-based.  
DOWNGRADE the article only refers to generic respiratory symptoms; better with adjudication committee. |
| **Statistical analysis** | Ratio #events/#predictors: rule of thumb 10 events per initial predictors. Possibility of DOWNGRADE: if less than 10 events per predictor  
Predicted outcome: COPD exacerbation  
Statistical model: predefined or at most stepwise backward selection process  
DOWNGRADE if Univariate, bivariate (p<0.20) selectin process  
Missing data: |
| **Performance Measures** | Low risk of bias if performance of discrimination and calibration (e.g., respectively AUC and HL) are provided.  
DOWNGRADE if provided only r^2 or a correlation measure or a log-likelihood or only one between discrimination of calibration performance |
| **Validation** | External validation  
DOWNGRADE if no external validation was performes (internal validation was not deemed to be enough to have a low risk of bias in this category) |

Table 8. Criteria for the downgrading
Quality assessment paper by paper

We report below the quality assessment for the 25 included papers.
### Almagro (2014)

| Flow (Derivation cohort) | Settings and sampling: Spain 70 ED’s, 10 consecutive patients from each outpatients ED’s; previous ESMI cohort.  
| Inclusion criteria: | - age above 40 years  
| - admission for COPD exacerbation  
| - forced spirometry with a postbronchodilator FEV1 < 80% predicted and and FEV1/FVC < 0.70.  
| Exclusion criteria: | - a previous diagnosis of asthma or bronchiectasis as predominant disease, or other explainable cause of obstructive airflow limitation  
| - acute pulmonary edema or pneumonia upon admission  
| - inability to perform spirometry or noncompliance with spirometric criteria  
| - admission for reasons other than an exacerbation of COPD.  
| Ethical approval: the ESMI study and the studies used for the validation cohort were approved by the Clinical Investigation Ethics Committee of the Hospital Mútua de Terrassa (EO/0922_0709).  
| Selection process: Inconsistent. In the derivation cohort all the patients before follow-up (606) are analysed, instead, in the validation cohort all the patients with follow-up are analysed (377). No differences existed between included and excluded patients with respect to age, sex, smoking history, or dyspnoea measured by the mMRC scale (data not shown)  
| Predictors L | (Look at the supplementary material) The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome.  
| Outcome L | Definition of exacerbation: change in the symptoms of patients, beyond daily variations and requiring Emergency Room (ER) consultation with or without subsequent hospital admission  
| | Blinded to the predictors |
| Statistical analysis | Ratio #events/#predictors: more than 100 events vs less than 10 predictors.  
Predicted outcome: readmission to the hospital for the COPD exacerbation (derivation and validation cohort) at 3 months and 1 year after hospital discharge. Assessed by outpatient visits and when this was not possible, by reviewing medical records or through telephone calls to the patient or family.  
Statistical analysis: Cox regression model with indices as predictors.  
Missing data: handling missing data not described. |
| --- |
| Performance Measures | AUC (data obtained contacting the authors) |
| Validation | External validation. 3 previous cohorts in Spain University Hospital Mútua de Terrassa: 1997-1998; 1999-2000; 2003-2004.  
Inclusion/exclusion criteria’s –the same as in the derivation cohort. No performance measures for the validation data. |
### Almagro (2006)

| Flow | Setting and sampling: to any medical ward at this institution, an acute-care teaching referral centre, in the province of Barcelona, Spain. |
|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      | Inclusion criteria:                                                                                                             |
|      | • a clinical diagnosis of COPD                                                                                                   |
|      | • forced spirometry at discharge showing FEV 1<70% of their reference value and FEV 1/FVC < 0.7                                     |
|      | Exclusion criteria:                                                                                                             |
|      | • a history of asthma, pneumonia or pulmonary edema on admission, hospitalisation for causes other than COPD exacerbation or patient refusal to participate in the study. |
|      | Ethical approval: the study protocol was approved by the Hospital Research and Ethics Committee.                               |
|      | Selection process: consecutive                                                                                                  |

| Predictors | Detailed description of the measurements (clinical tests and questionnaires). The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

| Outcome | Definition of exacerbation: Reasons for hospital admission due to exacerbation were defined as worsening of breathlessness or change in the mental status due to hypercapnia. The need for readmission was decided by physicians in the Emergency Room unaware of the goals of the present study. Readmissions were assessed through revision of clinical records, and linkage was made with the database CMBD (Minimum Basic Dataset). Readmission was defined as one or more hospitalisations for COPD in the year following hospital discharge. If patients had been hospitalised in the Emergency Room for less than 24 h, they were not considered as readmissions. |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | Blinded to the predictors.                                                                                                          |
| Statistical analysis | Ratio #events/#predictors: more than 300 events vs less than 10 predictors. |
|----------------------|-------------------------------------------------------------------------|
|                      | Predicted outcome: readmission to the hospital for COPD exacerbation at 1 year after hospital discharge. Assessed from phone calls and clinical records. |
|                      | Statistical model: logistic regression; bivariate selection (p-value<=0.15); “Hypercapnia was retained in the final model because its exclusion changed the estimated coefficient of the two remaining variables >15%, an increase that was considered clinically significant” |
|                      | Missing data: handling missing data not described (data on subjects who died without readmission were considered as missing data) |
| Performance measures | R-square; Hosmer-Lemeshow (chi-square and p-value) (data in part obtained contacting the authors) |
| Validation           | X                                                                       |
| Amalakuhan (2012) |
|-------------------|
| **Flow** | Setting and sampling: unclear, retrospective |
| **Inclusion criteria:** | - Patients who were diagnosed with a COPD exacerbation between January, 2007 and September |
| **Exclusion criteria:** | - Age less than 18 years  
- Pregnancy |
| Ethical approval: | the selection of the study population, exclusion criteria, and sampling process were performed in compliance with standing policies and procedures of the Institutional Review Board |
| **Selection process:** | unclear; abstract and article data not consistent. |
| **Predictors** | Defined on the onset of the study (55-60 variables; abstract and article data is not consistent). |
| **Outcome** | Definition of exacerbation: unclear |
| **Statistical analysis** | Ratio #events/#predictors: more than 100 events vs more than 50 predictors. |
| | Predicted outcome: frequent or multiple COPD readmissions/exacerbations to the hospital for the COPD exacerbation (derivation and internal validation cohort) at 1 year. |
| | Statistical model: random forest model (200 simulation that divided randomly the data in 75% training data, 25% testing data). Crossing validation related to the random forest model |
| | Missing data: - |
| **Performance measures** | Mean AUC among the 200 simulation, sensitivity, specificity, PPV, NPV. |
| **Validation** | |
### Flow (Derivation cohort)

**Setting and sampling:** Primary care enlisted with a general practitioner’s (GP’s) diagnosis of COPD and aged 65 years or over were selected: 51 GP; Netherlands

**Inclusion criteria:**
- COPD was determined by an expert panel including a pulmonologist, applying the Global initiative for chronic Obstructive Lung Disease (GOLD) criteria.
- Aged 65 years or over, with a COPD diagnosis, who were followed up over 24 months (derivation)

**Exclusion criteria:**
- Pregnancy
- A history of lung cancer, tuberculosis, pulmonary fibrosis, asbestosis, organ transplantation, lung volume reduction surgery or previous lung resection

**Ethical approval:** University Medical Center Utrecht, Utrecht, the Netherlands, approved the study protocol, and all participants gave written informed consent.

**Selection process:** consecutive and detailed

### Predictors

The choice of the measured predictors is carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome.

### Outcome

**Definition of exacerbation:** “operational” - symptomatic deterioration requiring pulsed oral steroid use or hospitalisation.

### Statistical analysis

**Ratio #events/#predictors:** 70-222 events versus 6 predictors

Predicted outcome: binary outcome, patients with at least an exacerbation in the 2 years of follow-up. Blinded to the predictors. Well defined and assessed.

Statistical model: multivariable logistic regression with backward stepwise selection (p-value<0.20 from the log likelihood ratio test). Internal validation: bootstrapping, to correct for over fitting, the beta coefficients of the predictors in the final model were multiplied by
the shrinkage factor derived from the 500 bootstrap samples

Missing data: carefully described; multiple imputation used.

| Performance measures | AUC with 95% CI; Hosmer-Lemeshow test (chi-square and p-value); r-square (data in part obtained contacting the authors) |
|----------------------|---------------------------------------------------------------------------------------------------------------|
| Validation           | External validation: from the Utrecht General Practitioners Network database; Aged 50 years or over with a diagnosis of COPD based on available spirometric data ([FEV1]/FVC ,70%). dynamic cohort. Artificially set the study entry at January 2010 for 24 months from that period of time onwards. Performances: AUC 0.66 (0.62-0.71) in the validation cohort against AUC 0.75 (0.69-0.82) in the validation cohort |
Brusse-Keizer (2011)

| Flow                  | Setting and sampling: patients included in the control group of a self-management study in COPD, at the department of Pulmonology in Enschede study; Netherlands; prospectively |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Inclusion criteria:   | - clinical diagnosis of COPD, as defined by American Thoracic Society criteria  
                        - current or former smoker;  
                        - age between 40 and 75 years; baseline (FEV1) 25–80%; FEV1 / IVC 60%; |
| Exclusion criteria:   | - no history of asthma; no exacerbation in the month prior to enrollment  
                        - no maintenance treatment of oral steroids or antibiotics;  
                        - no medical condition with low survival or serious psychiatric morbidity; absence of any other active lung disease (e.g. sarcoidosis). |
| Ethical approval:     | this study has been reviewed and approved by the hospital’s medical ethical committee and has been performed in accordance with the ethical standards laid down in the Declaration of Helsinki. |
| Selection process:    | unclear |

| Predictors           | Clinical measurements and questionnaires carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |

| Outcome              | Definition of exacerbation: a worsening of respiratory symptoms that required treatment with a short course of oral corticosteroids and/or antibiotics as judged by the study physician. |
| Statistical analysis | Ratio #events/#predictors: >62 events (31 exacerbators*2) versus 15 predictors |
|----------------------|-----------------------------------------------------------------------------|
|                      | Predicted outcome: categorization presented: infrequent/frequent exacerbators (more than two exacerbations in the year of follow-up). Assessed by GP/ pharmaceutical records. Blinded to the predictors. |
| Statistical model:   | multivariable logistic regression; variables significant (p<0.15) were included in the multivariable analysis. Then, stepwise selection (log likelihood ratio test). To assess overfitting jackknife cross validation technique was applied to the prediction rule. |
| Missing data:        | unclear |
| Performance measures | AUC with 95% CI; Hosmer-Lemeshow test; r-square (COX & Snell, Negelkerke) |
|                      | (data in part obtained contacting the authors) |
Chen (2005)

Flow

Setting and sampling: A convenience, nonprobability sample of 145 patients with COPD scheduled for discharge from six regional hospitals in the Pingtung area in southern Taiwan was consecutively selected. Patients with COPD who were discharged were identified from general medical-surgical or thoracic wards in the hospitals.

Inclusion criteria: All participants (a) had been hospitalised with chronic bronchitis, emphysema, or COPD as the primary or secondary diagnosis based on the standard of the Taiwan Thoracic Medical Association; (b) had at least a 2-year history of COPD; (c) were alert, oriented, able to communicate in Mandarin or Taiwanese, and respond to questions and provide informed consent; and (d) were able to be followed up by phone or home visit after hospital discharge.

Exclusion criteria: if they had unstable health status (e.g., psychiatric illnesses, severe dementia, unstable myocardial infarction, or acute tuberculosis), were involved in another intervention study or protocol related to COPD, or were discharged to a nursing home setting.

Ethical approval: The study was approved by the protection of Human Subjects Committee at Case Western Reserve University (CASE).

Support statement: -

Selection process: there were 328 potential patients referred within the first 3 months; 199 met the inclusion-exclusion criteria; 49 refused to participate in the study or were lost to entry after discharge, and 150 agreed to participate and completed the study. At the 14 days after discharge, five participants were excluded from the study because two died before the 2-week follow-up, one was discharged to a nursing home, one committed suicide at home, and one could not be reached at home. Complete data sets were available for 143 participants at 2 weeks. Data were also completed by 140 participants at 90 days following discharge, two died early without readmission records and one was admitted to a nursing home.

Predictors

Defined on the onset of the study; were obtained from the standardized questionnaires/evaluated by the standard on the beginning defined procedures; Blinded to outcome.

Outcome

Definition of exacerbation: Event-based (Hospital readmission for exacerbation). Readmission was defined as an unplanned repeated hospitalisation or emergency medical care over 24 hours delivered at a hospital during the current study period related to a primary or secondary diagnosis of COPD. Readmission status at 14 days (short term) and 90 days (long term) following discharge were bivariate variables (yes or no) indicating whether the individual returned to the hospital after the hospitalisation in which the participant entered the study.
| Statistical analysis | Ratio #events/#predictors: 30 or 107 events (according to the follow-up period) vs 9 predictors |
|----------------------|-----------------------------------------------------------------------------------------------|
|                      | Predicted outcome: hospital readmission because exacerbation                                  |
|                      | Statistical model: Logistic regression                                                        |
|                      | Missing data: -                                                                               |
| Performance Measures | R-square Nagelkerke, -2LogLikelihood                                                          |
| Validation X         |                                                                                               |
### Echave-Sustaeta (2010)

#### Flow

**Setting and sampling:** prospective cohort- consecutive patients admitted to the pulmonology department with severe exacerbations of COPD, treated with NIMV, and successfully discharged were included in this study.

**Inclusion criteria:**

- severe exacerbations (no def. was found) of COPD (GOLD standard)
- treated with NIMV (pH < 7.35 and a PaCO2 > 45 mmHg.); (initiate NIMV after discharge was not random and on most occasions depended on tolerance to disconnection of NIV, the level of PaCO2, number and severity of previous admissions for exacerbation of COPD, especially previous episodes of respiratory acidosis, hypoventilation induced by oxygen; documented associated nocturnal hypoventilation, symptomatic hypercapnia, etc.)
- successfully discharged were included in this study.

**Exclusion criteria:**

- pneumonia, congestive heart failure, pneumothorax, and other specific causes of the exacerbation, inability to perform spirometry or noncompliance with spirometric criteria

**Ethical approval:** the study was approved by the local ethics committee, which decided that informed consent was not necessary.

**Selection process:** unclear

#### Predictors

- The baseline characteristics were evaluated at the start of the follow-up period, then, they were blinded to the outcome. Details of the clinical measurements not described

#### Outcome

- Definition of exacerbation: re-hospitalisations for respiratory causes

#### Statistical analysis

- Ratio #events/#predictors: >61 events versus 6 predictors
- Predicted outcome: re-hospitalisations for respiratory causes. Blinded to the predictors.
Statistical model: Cox proportional hazards regression, in which a final model is obtained by considering those risk factors with inferior outcome at $p < 0.15$ in the univariate analysis and selection criteria by stepwise selection were used.

Missing data: unclear

| Performance measures | AUC, r-square |
|----------------------|---------------|
| **H**                |               |
| **Validation**       | X             |
### Faganello (2010)

| Flow | Setting and sampling: consecutive patients with COPD with a wide range of disease severity were recruited from the outpatient clinic of a single institution |
|------|----------------------------------------------------------------------------------------------------------------------------------|
|      | Inclusion criteria:                                                                                                                |
|      | - COPD according to the criteria set out in GOLD 2003 and the Brazilian Thoracic Society (BTS)                                     |
|      | - age 40 years                                                                                                                     |
|      | - smoking history 10 pack-years, and a postbronchodilator FEV1/FVC ratio 70%.                                                      |
|      | - Disease severity was categorized according to BTS and GOLD stages, taking into consideration the values of FEV1 (% predicted) and arterial blood gases |
|      | Exclusion criteria:                                                                                                                |
|      | - history of asthma and/or FEV1>12% or 200 mL postbronchodilator, associated restrictive disorder;                                  |
|      | - other clinically significant concomitant respiratory diseases;                                                                     |
|      | - noncompliance with treatment;                                                                                                    |
|      | - myocardial infarction within the preceding 4 months; and unstable angina or congestive heart failure.                           |
|      | - Patients not considered clinically stable                                                                                         |
|      | Ethical approval: All procedures were approved by the Research Ethics Committee, Botucatu Medical School University Hospital+ written informed consent |
|      | Selection process: unclear                                                                                                         |

| Predictors | Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |

| Outcome | Definition of exacerbation: An increase in dyspnoea, sputum purulence, and increased sputum volume and classified as moderate (requiring a visit to a physician or the emergency department and treatment with antibiotics or systemic steroids or both) or severe type II (requiring hospital admission). Mild |
Exacerbations not requiring intervention were not included in the study.

| Statistical analysis | Ratio #events/#predictors: >95 events versus 1 predictor |
|----------------------|----------------------------------------------------------|
|                      | Predicted outcome: COPD exacerbation                      |
|                      | Statistical model: multivariable logistic regression, predefined combination of predictors (BODE, GOLD stages; multivariable regression not taken into account because of the lack of performance measure) |
|                      | Missing data: unclear                                    |
| Performance measures | AUC                                                       |
| Validation           |                                                           |
| Section | Description |
|---------|-------------|
| Setting and sampling: | A systematic sample of one out of every two patients admitted to hospital or remaining in the emergency room for at least 18 hours for a COPD exacerbation in four tertiary hospitals in the Barcelona area from 1 May 1997 to 30 April 1998 was identified, independently of whether they had previous COPD admissions or not. Six (1.7%) of the 346 patients recruited did not survive the recruitment admission; 340 patients were therefore followed from the day of discharge after the recruitment admission until 1 May 1999 or the day of death, if earlier. There were no losses to follow up as all patients were either contacted for telephone interview, registered as dead in the mortality registry, or visited in the outpatient clinics or hospitalised after 1 May 1999. Patients were allowed to enter the study as many times as they were hospitalised during the recruitment period, giving 346 individuals with 404 admissions. In patients with more than one admission during the recruitment period the first one was selected as the beginning of the follow up period. |
| Inclusion criteria: | x |
| Exclusion criteria (look at the references): | • mentally unable to answer a questionnaire; • severe comorbidities; • transtracheal catheter; • living outside of the province of Barcelona. Positive bronchodilator test (asthma) or pulmonary fibrosis. |
| Ethical approval: | The ethics committees of the participating hospitals. Approved the protocol and written informed consent was obtained from all patients. |
| Selection process: | A diagnosis of COPD was established by the ward pulmonologist based on medical history, current symptoms, and available pulmonary function tests, following the ERS guidelines. A systematic sample of one out of every two patients admitted to hospital or remaining in the emergency room for at least 18 hours for a COPD exacerbation. Twenty eight patients (8%) died without having a readmission during the follow up period and were excluded from the study of risk factors for a COPD readmission. |
| Predictors | Measurements carefully described (in references and online material). The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. A large number of |
A potential risk factors - including variables related to clinical status, characteristics of medical care, medical prescriptions, adherence to medication, lifestyle, quality of life, and social support - was identified and has been reported elsewhere. Most of the questionnaire content was obtained from previously validated instruments, while some questions were developed and pilot tested. Questions for usual physical activity were adapted from the Spanish validation of the Minnesota Leisure Time Physical Activity Questionnaire, a measure of physical activity in the general population.

| Outcome | Definition of exacerbation: An exacerbation was defined as an increase in dyspnoea, sputum production, or sputum purulence. |
|---------|---------------------------------------------------------------------------------------------------------------|
| Statistical analysis | Ratio #events/#predictors: >500 predictors vs 7 predictors |

Predicted outcome: Time to readmission to hospital for an exacerbation (It was the primary study outcome).

Statistical model: A multivariate model (COX) was then built including all relevant variables until the final most parsimonious model was fitted. Poisson regression was used as a complementary approach to obtain relative risks of readmission for COPD, modelling the individual number of readmissions and including the logarithm of the individual person-days at risk as the offset.

Missing data:

| Performance Measures | AUC |
|----------------------|-----|
| Validation           | X   |
| **Flow L** |
|---|
| **Setting and sampling:** This was a prospective study of patients hospitalised with acute exacerbations of obstructive airway disease in five university hospitals in the Nordic countries. The departments included were: Dept of Respiratory Medicine and Allergology, Akademiska sjukhuset, Uppsala, Sweden; Dept of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway; Dept of Respiratory Medicine, Tampere University Hospital, Tampere, Finland; Dept of Respiratory Medicine, Allergy and Sleep, Vifilstadir University Hospital, Gardabaer, Iceland; and Dept of Respiratory Medicine, Hvidovre Hospital, Copenhagen, Denmark.  

All information was collected by the same person in each country who had received basic training. The same person carried out the initial and follow-up information collection in each country  

**Inclusion criteria:** Consecutive patients from each of the participating hospitals were included provided that they had been admitted with acute exacerbations of obstructive lung disease. Only patients that were admitted for .24 h were included.  

**Exclusion criteria:** asthma  

**Ethical approval:** The study was approved by the Institute Review Board and/or an ethic committee for each institution or country. Informed consent was obtained from all the patients.  

**Support statement:** Financial support for the present study was provided by Boehringer Ingelheim in Denmark, Norway, Sweden and Finland, the Swedish Heart and Lung Association and the Swedish Heart Lung Foundation.  

**Selection process:** 10 out of 416 (2%) patients were lost to follow-up. Consecutive patients from each of the participating hospitals were included during the year 2000–2001. The reported data are only from those fulfilling criteria for COPD according to the Global initiative for chronic Obstructive Pulmonary Disease (GOLD) stage I or higher [15]. Codes from International classification of diseases-10 for COPD were used. All records were
| Predictors | Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. Defined on the onset of the study. All information was collected by the same person in each country who had received basic training. The same person carried out the initial and follow-up information collection in each country. |
|---|---|
| Outcome | Definition of exacerbation: An acute exacerbation was defined as a change in condition in a COPD patient from baseline of such a magnitude that it needed an acute hospital admission. |
| Statistical analysis | Ratio #events/#predictors: >246 events vs around 25 predictors |
| | Predicted outcome: Readmission for COPD exacerbation |
| | Statistical model: Cox regression |
| | Missing data: X |
| Performance Measures | Log-likelihood (provided after request) |
| Validation | |
### Flow L

Setting and sampling: (A detailed description of methods can be found in the Supplementary Appendix. The study was conducted in accordance with the protocol, which is available at NEJM.org.) This analysis was based on data collected as part of the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) observational study. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Inclusion criteria:
- age of 40 to 75 years
- a history of 10 more pack-years of smoking
- a forced expiratory volume in 1 second (FEV1) of less than 80% of predicted value after bronchodilator use
- a ratio of FEV1 to forced vital capacity (FVC) of 0.7 or less after bronchodilator use.

Exclusion criteria: X

Ethical approval: All patients provided written informed consent, and the study was approved by the relevant ethics and review boards.

Support statement: Supported by grants from GlaxoSmithKline (to Drs. Vestbo, Hurst, Anzueto, Lomas, Agusti, MacNee, Calverley, Rennard, Wouters, and Wedzicha).

Selection process: A total of 2164 patients were recruited for the study, and 2138 patients were enrolled and observed during follow-up.

### Predictors L

Measurements carefully described (see Supplementary Appendix as well). The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. Defined on the onset of the study.

### Outcome L

Definition of exacerbation: The case definition of an exacerbation was a functional one, based on the decision by a patient’s primary clinician or by study personnel to prescribe antibiotics or systemic corticosteroids, alone or in combination. Primary clinicians were not given a specific list of criteria that had to be met for an event to be classified as an...
exacerbation, but they were instructed to base their decision on common clinical criteria. This case definition therefore met the criteria for a definition of health care utilization, and the exacerbations we recorded would be classified as moderate or severe in intensity.

| Statistical analysis | Ratio #events/#predictors: >2500 events vs 31 predictors |
|----------------------|---------------------------------------------------------|
|                      | Predicted outcome: Exacerbation                         |
|                      | Statistical model: Multinomial logistic regression. A stepwise approach was used |
|                      | Missing data: X                                        |
| Performance Measures | R-square                                                |
| Validation           |                                                         |
### Setting and sampling:
A sub-analysis of a previous study assessing the impact of psychiatric disorders on the risk for COPD exacerbations. From the outpatient COPD clinics of two community hospitals in the Montreal (Quebec) area (Hôpital du Sacré-Coeur de Montréal and Hôpital de Saint-Eustache).

**Inclusion criteria:**
- <85 years of age
- have received a clinical diagnosis of COPD (confirmed by spirometry)
- have been hospitalised for an exacerbation in the past 24 months but be stable at the time of the recruitment (≥4 weeks without an exacerbation)
- have a smoking history of at least 10 pack-years

**Exclusion criteria:**
- a medical condition more severe than their COPD
- an apparent cognitive deficit (dementia).
- living in a long-term health care center.

**Ethical approval:** The human ethics committee of both study institutions approved the study and written informed consent was obtained from all participants.

**Selection process:** unclear

### Predictors
Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome.

### Outcome
Definition of exacerbation: event-based definition of exacerbations was used, which is characterized by any symptom deterioration requiring a change in usual treatment. A health care utilization definition (either requiring additional health care-prescribed corticosteroids or antibiotic treatment [outpatient] or requiring emergency department/hospital visit [inpatient]) of exacerbation was used. Exacerbation rates (dates, duration, and type of management) were assessed via monthly telephone interviews and medical chart review.

### Statistical analysis
Ratio #events/#predictors: around 680 events vs 7 predictors
| L | Predicted outcome: exacerbations (outpatient-treated, in-hospital treated, any exacerbations) |
|---|--------------------------------------------------------------------------------------------|
|   | Statistical model: Cox regression                                                           |
|   | Missing data: unclear                                                                       |
| Performance measures | -2 log Likelihood, AIC, SBC (data obtained contacting the authors)                          |
| H |                                                                                             |
| Validation | X                                                                                           |
| Setting and sampling: | Patients were recruited from the outpatient departments of the London Chest Hospital and the Royal Free Hospital. |
|-----------------------|--------------------------------------------------------------------------------------------------|
| Inclusion criteria:   | • COPD was defined as FEV1 <70% predicted for age, height, and sex; FEV1/FVC ratio < 70%;  
                        • At the start of the London COPD cohort the authors did require that patients had less than 15% or 200 ml reversibility in FEV1 but at some point relaxed this requirement when it was dropped from the BTS guidelines for the diagnosis of COPD. Reversibility was not an eligibility criteria for the DOSE study. |
| Exclusion criteria:   | • Patients with significant respiratory diseases other than COPD were not recruited. |
| Ethical approval:     | granted from East London and the City and Royal Free Hospital ethics committees. All patients provided written informed consent. |
| Selection process:    | No allowance has been made for patients withdrawing from the study or missing DOSE Index scores in any year. |

| Predictors | On the basis of theoretical clinical considerations a number of possible predictors of health status were selected. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |

| Outcome | Definition of exacerbation: symptom-based. All patients recorded daily, on diary cards, any increase in respiratory symptoms, which were classified as major (dyspnea, sputum purulence, and sputum volume) or minor (colds [nasal discharge/congestion], wheeze, sore throat, and cough). This daily recording of symptoms was used to precisely define the onset and recovery of exacerbations as described below. As in our previous work (1, 3), exacerbation onset was defined as the first of two or more days on which the patient recorded two or more new or worsening symptoms, with one of which being a major symptom. Symptoms were disregarded in identifying exacerbation onset if recorded continuously in the preceding 5 days. A small proportion (3.2%) of exacerbations for which |
no diary-card symptoms had been recorded was identified by hospital admission data or by questioning the patient at clinic visits. (See the reference Am J Respir Crit Care Med Vol 179, pp 369–374, 2009)

| Statistical analysis | Ratio #events/#predictors: 50 events vs 1 predefined predictor (MRC, FEV1% predicted, DOSE index) |
|----------------------|--------------------------------------------------------------------------------------------------|
|                      | Predicted outcome: hospital readmission because exacerbation                                      |
|                      | Statistical model: Correlation analysis                                                           |
|                      | Missing data: unclear                                                                             |
| Performance Measures | AUC                                                                                               |
| Validation           | X                                                                                                 |
**Ko (2011)**

**Flow**

Setting and sampling: This was a prospective study of patients who had been admitted to the Prince of Wales Hospital with acute exacerbations of COPD (AECOPD) between May 1, 2004, and April 30, 2005. Telephone follow-up to check for any hospital admissions or death was arranged for subjects who did not return for assessment. At the end of the 3 years, patients were contacted by phone to assess for readmissions and mortality involving 243 (208 males) COPD patients hospitalised for acute exacerbations of COPD [AECOPD].

Inclusion criteria: -

Exclusion criteria: -

Ethical approval: Written informed consent was obtained from each subject, and the study was approved by the Ethics Committee of the Chinese University of Hong Kong

Support statement: This study is supported by the Respiratory Research Fund of The Chinese University of Hong Kong

Selection process: -

**Predictors**

At the baseline assessment, the demographic characteristics and the medication usage of the subjects were recorded

**Outcome**

Definition of exacerbation: Event base. AECOPD was defined as occurring when a patient with background COPD,14 with FEV1/FVC ratio <70%, presented with at least two major symptoms (increased dyspnoea, increased sputum purulence, or increased sputum volume), or one major and one minor symptom (nasal discharge/congestion, wheeze, sore throat, or cough) for at least 2 consecutive days

**Statistical analysis**

Ratio #events/#predictors: at least 186 vs around 1 predictor (or index).

Predicted outcome: first readmission over 3 years
Statistical model: Cox proportional hazards regression. Furthermore, the predictive characteristics of the changes in serial BODE indices for survival and first readmission of AECOPD were assessed by Kaplan Meier analysis (serial change at a certain time point was classified as having decreasing [>1point], stable or increasing [>1point] BODE indices based on their absolute change from baseline) and statistical significance was evaluated with the use of the log-rank test.

Missing data: X

| Performance Measures | AUC |
|----------------------|-----|
| H                    |     |
| Validation           | X   |
### Lee (2014)

#### Flow

Setting and sampling: 19 hospitals in Australia, China, Korea and Taiwan, prospective cohort

Inclusion criteria:
- at least 40 years old
- with smoking history of more than 10 pack-years
- established diagnosis of COPD for at least six months
- FEV1/FVC <0.7
- history of at least one COPD exacerbation, which required additional treatment in the previous 12 months.

Exclusion criteria:
- asthma

Ethical approval: Written informed consent and the study was approved by the local ethics committees or review boards prior to the initiation of any study-related activities.

Selection process: unclear

#### Predictors

Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. Telephone calls/medical visits data.

#### Outcome

Definition of exacerbation: an exacerbation was defined as worsening of symptoms of COPD for at least two consecutive days and was classified as mild when patients did not require treatment with systemic corticosteroids and/or antibiotics; moderate when treatment with systemic corticosteroids and/or antibiotics were required; or severe when hospitalisation or visit to the emergency care unit was required.

#### Statistical analysis

Ratio #events/#predictors: unclear but >338 events versus 14-16 predictors

Predicted outcome: Time to first exacerbation, any exacerbations, moderate-severe exacerbations

Statistical model: Cox regression for the outcome time to first exacerbation, logistic regression for the outcomes any exacerbations and moderate-severe exacerbation.

Missing data: unclear

#### Performance Measures

AUC for all 6 measurements (3 outcomes and CAT categorized or not)

#### Validation
| **Marin (2009)**              |
|------------------------------|
| **Flow**                     |
| L                            |
| Setting and sampling: outpatient pulmonary clinics of two tertiary teaching hospitals in Tenerife and Zaragoza, both in Spain, prospective cohort. |
| Inclusion criteria:          |
|   • a history of smoking >20 pack-year, |
|   • a maximal ratio of FEV1/FVC<0.7 measured 20 min after the administration of inhaled salbutamol |
|   • a stable clinical condition for at least 8 weeks prior to enrolment |
| Exclusion criteria:          |
|   • uncontrolled co-morbidities likely to result in death |
|   • a history of asthma or an increase in the FEV1 greater than 15% or more than 200 ml from baseline after the administration of inhaled salbutamol |
|   • inability to perform the required tests. |
| Ethical approval: the study was approved by the human-research review board at each institution, and written informed consent. |
| Selection process: unclear   |
| **Predictors**               |
| L                            |
| Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
| **Outcome**                  |
| L                            |
| Definition of exacerbation: events characterized by a sustained worsening of baseline respiratory symptoms that lasted for at least 3 days and that required treatment intervention with antibiotics, and/or systemic corticosteroids. |
| **Statistical analysis**     |
| H                            |
| Ratio #events/#predictors: more than 500 events vs 1 predictor (BODE) |
| Predicted outcome: Primary care, Hospitalisation, Emergency Room visit |
| Statistical model: correlation with Rho Spearman coefficients and odds ratios used. |
| Missing data: unclear        |
| **Performance Measures**     |
| L                            |
| AUC, r-square, HL (p-value) (data obtained contacting the authors) |
| **Validation**               |
| X                            |
Moberg (2014)

### Flow

- **Setting and sampling:** All patients included in the present analyses participated in a 7-week pulmonary rehabilitation programme at Hvidovre Hospital, Copenhagen.

- **Inclusion criteria:**
  - stable COPD (FEV1%predicted < 80% and FEV1 / forced vital capacity < 0.70)
  - motivation
  - no previous participation in pulmonary rehabilitation

- **Exclusion criteria:**
  - significant musculo-skeletal, cardiac, or cognitive problems

- **Ethical approval:** not referred to any participation written consent or ethical board approval.

- **Selection process:** consecutive

### Predictors

- **Measurement:** carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome.

### Outcome

- **Definition of exacerbation:** unclear

### Statistical analysis

- **Ratio events/predictors:** unclear but > 421 events vs unclear but > 18 predictors

- **Predicted outcome:** Hospital admission for exacerbation. A primary diagnosis of COPD (J44.x), or a primary diagnosis of respiratory failure (J96.x) with a secondary diagnosis of COPD (J44.x) at discharge was recorded as an admission due to exacerbation in COPD.

- **Statistical model:** Multivariate Cox proportional hazard regression model starting from an uni-variable stepwise selection method (p<0.10). Assumption of linearity was assessed by
categorizing the variable into multiple dichotomous variables of equal units (quartiles) on the variable’s scale. The estimated coefficients of each dichotomous variable were compared.

Missing data: only a few missing data (no imputation used)

| Performance Measures | H                  |
|----------------------|--------------------|
|                      | AUC with CI (data obtained contacting the authors) |

| Validation X         |
|----------------------|
|                      |
**Motegi (2013)**

| Flow | Setting and sampling: Nippon Medical School, Tokyo, Japan; outpatient; prospective cohort, 1 time/month visit.  
Inclusion criteria:  
- A diagnosis of COPD by a chest physician  
- Current or former smoking history of at least 20 pack-years  
- Age of ≥40 years.  
Exclusion criteria:  
- A diagnosis of bronchial asthma, bronchiectasis, or bullous lung disease  
- Active tuberculosis or any history of pulmonary fibrosis  
- Withdrawal of consent  
- A diagnosis of any malignancy  
- A diagnosis of dementia  
Ethical approval: The study was approved by the ethics committee of the institution; written informed consent to participate was provided.  
Selection process: consecutive. Excluded from the final evaluation in the following cases: death or transfer to another clinic during the first year or lack of data. Patients who died during the second year were included |
| Predictors | (Look at the supplementary material as well) Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
| Outcome | Exacerbation:  
Agreement between  
- symptom-based definition, onset or worsening of more than two symptoms (dyspnoea, sputum purulence or volume, cough, or wheeze) for more than 2 consecutive days  
- medical definition. |
If the occurrence of an exacerbation was uncertain based on the diary descriptions, the patient’s chest physician decided whether an exacerbation had occurred. Any exacerbations occurring within 4 weeks of each other were considered a single exacerbation. Symptom based exacerbation evaluation. Each exacerbation recorded in a patient’s daily diary over the entire 2-year study period was thoroughly evaluated with accordance by three authors (TM, TI, and KK) and the research nurse. These episodes were confirmed by reviewing the medical and the hospital records. Blinded to the predictors.

| Statistical analysis | Ratio #events/#predictors: 193 events (105+88) vs unclear but 14 predictors |
|----------------------|--------------------------------------------------------------------------------|
|                      | Predicted outcome: exacerbation                                                  |
|                      | Statistical model: adjusted multiple logistic regression models including independent variables associated with exacerbation during univariate analysis were also constructed, and four models were tested |
|                      | Missing data: unclear but complete case analysis was used                       |

| Performance Measures | AUC; r-square (data in part obtained contacting the authors)                     |
|----------------------|--------------------------------------------------------------------------------|
|                      |                                                                                  |
|                      |                                                                                  |
|                      |                                                                                  |
|                      |                                                                                  |
|                      |                                                                                  |
|                      |                                                                                  |

| Validation | X |
|------------|---|
| Flow H | Setting and sampling: observational cohort; prospective, pulmonary clinic at VABoston Healthcare System (from reference 24) |
|---|---|
| Inclusion criteria: |
| • over 40 years of age |
| • COPD, defined as a smoking history of at least 10 pack-years and either a FEV1/FVC ratio of 0.70 or evidence of emphysema on chest computed tomography (CT). |
| • We included persons who required the assistance of a cane or walker to ambulate. |
| • Subjects were in stable clinical condition, and at least 4 weeks had elapsed since previous AEs. |
| Exclusion criteria: x |

Ethical approval: The protocol was approved by the VA Boston Healthcare System Committee on Human Research, and written informed consent obtained from each participant

Selection process: consecutive. One subject had < 90% SAM accuracy and was excluded from the final analysis. Participants were sent home to wear the SAM for 14 consecutive days. Days when a participant recorded less than 200 steps and less than 8 hours of wear time were considered no-wear days and were excluded from the analysis. Five of the 173 subjects were unable to complete 2 weeks of monitoring (having > 8 no-wear days) and were excluded from the final analysis.

| Predictors | Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, |
they were blinded to the outcome.

| Outcome | Definition of exacerbation: complex of respiratory symptoms (increased or new onset) of at least two of the following: cough, sputum, wheezing, dyspnoea, or chest tightness lasting 3 or more days, requiring a course of treatment with antibiotics or systemic steroids. COPD-related hospitalisations were due to AE and/or pneumonia. Hospitalisations due to other pulmonary or cardiac causes were excluded. |
|---|---|
| Statistical analysis | Ratio #events/#predictors: 263 events vs 4-5 predictors (according to the main predictor used)  
Predicted outcome: exacerbation and hospitalisation for exacerbation  
Statistical model: 3 negative binomial regression models (with the natural logarithm of observation time as an offset variable) with a predefined number of predictors (main predictor plus adjusting variables).  
Missing data: unclear |
| Performance Measures | AUC (data obtained contacting the authors) |
| Validation | X |
Müllerova (2015)

| Flow L | Setting and sampling: (The design of the ECLIPSE study (SCO104960, NCT00292552) has been published elsewhere.) This analysis was based on data collected as part of the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) observational study. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines. 

9 Subjects were followed-up at 3 months, 6 months, and every 6 months thereafter for a maximum of 3 years. All patients had their vital status confirmed 3 years after recruitment.

Inclusion criteria:
- age of 40 to 75 years
- a history of 10 more pack-years of smoking
- a forced expiratory volume in 1 second (FEV1) of less than 80% of predicted value after bronchodilator use
- a ratio of FEV1 to forced vital capacity (FVC) of 0.7 or less after bronchodilator use.

Exclusion criteria: X

Ethical approval: All patients provided written informed consent, and the study was approved by the relevant ethics and review boards

Support statement: Supported by grants from GlaxoSmithKline (to Drs. Vestbo, Hurst, Anzueto, Lomas, Agusti, MacNee, Calverley, Rennard, Wouters, and Wedzicha).

Selection process: A total of 2164 patients were recruited for the study, and 2138 patients were enrolled and observed during follow-up.

| Predictors | Measurements carefully described (see Supplementary Appendix of the paper as well). The baseline characteristics were obtained from the standardized |
| L | questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. Defined on the onset of the study. |
|---|---|
| Outcome | Definition of exacerbation: Information on COPD exacerbations was collected at scheduled visits by investigators using the case report forms and based on either subjects’ recall of exacerbation events or available medical records for exacerbation events, supplemented by monthly phone calls. For the purpose of the current analysis, we focused on those exacerbation episodes that required hospital admission (hospitalised exacerbation) |
| Statistical analysis | Ratio #events/#predictors: 1452 events vs around 10 predictors. Predicted outcome: episodes that required hospital admission (hospitalised exacerbation) Statistical model: Cox model Missing data: X |
| Performance Measures | AUC (with confidence interval), HL (chi-square and p-value), R^2 |
| Validation | X |
Setting and sampling: Between October 2002 and April 2004, patients with a wide range of severity of COPD, regardless of whether they had previous COPD hospital admissions or not, were recruited from a single institution and enrolled in the Health Service Development Program (HSDP) for COPD funded by the Ministry of Health, Singapore. This is a pilot service project. Patients were recruited from the outpatient clinic.

Inclusion criteria: clinically stable condition and receiving appropriate therapy.

Exclusion criteria: an illness other than COPD that was likely to result in death within 2 years; bronchial asthma, defined as an increase in the FEV1 >15% above the baseline value or 200 mL after the administration of a bronchodilator; an inability to perform the lung function and 6-min walk tests; myocardial infarction within the preceding 4 months; unstable angina; or congestive heart failure (New York Heart Association class III or IV).

Ethical approval: The study protocol was approved by the institutional ethics committee.

Selection process: Enrolment coming from a pilot service project (Health Service Development Program (HSDP) for COPD funded by the Ministry of Health, Singapore). This study involved the retrospective analysis of baseline variables on entry as well as outcomes during follow-up in the HSDP project for COPD.

**Predictors**
- Defined on the onset of the study; were obtained from the standardized questionnaires/evaluated by the standard on the beginning defined procedures; Blinded to outcome.

**Outcome**
- Definition of exacerbation: symptom-based. An exacerbation was defined as an increase in dyspnoea, sputum production, or sputum purulence.

**Statistical**
- Ratio #events/#predictors: >300 events vs 1 predictor
Predicted outcome: Hospital admission because exacerbation

Statistical model: Poisson regression analysis. The pseudo r^2 used quartiles for both indices (BODE and GOLD)

Missing data: There were no losses to follow-up, as all patients were contacted for telephone interview, registered as dead in the mortality registry, visited in the outpatient clinics, or hospitalised during the follow-up period.

| Performance Measures | Pseudo R^2               |
|----------------------|-------------------------|
| Validation X         |                         |
| Flow (Derivation cohort)                                      | Setting and sampling: The sampling frame for the study comprised all patients with COPD (with International Classification of Disease–9th Revision codes for COPD, emphysema, or chronic bronchitis) registered with general practitioners within the Wyre Primary Care Trust (WPCT; n = 848) in the United Kingdom.  
Inclusion criteria:  
- Confirmed COPD (Pauwels, Am J Respir Crit Care Med 2001;163:1256-76)  
- Diagnostic classification and spirometric data already available in administrative data for the WPCT. (FEV% and COPD criteria)  
Exclusion criteria:  
- Less than 80% of daily diary card entries during a 1-year period (>=292 days) completed  
Ethical approval: All study methods and documentation were reviewed and approved by the Blackpool, Wyre, and Fylde Local Research Ethics Committee  
Selection process: consecutive. A total of 309 patients in the WPCT with confirmed COPD agreed to participate in this observational study (36% of the sampling frame). At least 80% of daily diary card entries during a 1-year period (>=292 days) were completed by 127 patients  
Predictors Defined on the onset of the study; spirometric data already available in administrative data for the WPCT. For purposes of study entry, the most recently available spirometric data were used. The SF-36 was measured at baseline and at 3-month intervals throughout the study year. Questionnaire described in detail. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
**Outcome**

- **Definition of exacerbation:** Exacerbations were defined using two different methods. Symptom-defined exacerbations used criteria developed by Anthonisen et al., which included increased dyspnoea, sputum production, or sputum purulence, as noted on diary cards for at least 2 consecutive days. Health care resource use-defined exacerbations were based on taking oral corticosteroids or antibiotics, as reported on the diary cards.

**Statistical analysis**

- **Ratio #events/#predictors:** unclear but >98 events (patients with at least 1 exacerbation) vs 1 predictor (predefined indices used, coming from the SF-26 domain)

**Predicted outcome:** exacerbation (symptom-based) and exacerbation (event-based, health care-based)

**Statistical model:** correlation analysis between the different scores and the two outcomes (for domain scores that predicted exacerbation, it was conducted exploratory one-way analyses of variance (ANOVAs) by diary card status (> 80%, < 80%, none) to determine any effects of diary card adherence on scores).

**Missing data:** ROC analyses were limited to the group who completed at least 80% of diary card entries (n = 127) because exacerbation status could be determined most reliably for them without the need for imputation.

**Performance Measures**

- **AUC with CI, HL p-value, R^2, pseudo-R-square Cox & Snell, p-value for the model (data in part obtained contacting the authors)**
Flow (Derivation cohort)

Setting and sampling: Chest Disease Center of Kurume University Hospital (Kurume, Japan), the Chikugo City Hospital (Chikugo, Japan), and Nagata Hospital (Yanagawa, Japan) prospective observation

Inclusion criteria:

- Patients with COPD who had regularly attended each participating hospital for at least one year

Exclusion criteria:

- bronchiectasis, asthma, interstitial pneumonia and pneumoconiosis based on medical history and chest high-resolution computed tomography (HRCT);
- active malignancies;
- severe diseases of other organs such as dementia, cerebro or cardio-vascular disease, hepatitis and cirrhosis, chronic kidney disease, and psychological disease

Ethical approval: The study was conducted in accordance with the Good Clinical Practice guidelines and approved by the Ethics Committee of Kurume University and Chikugo City Hospital (Approval date: September 2011; Approved #: 11127). All of the study patients provided informed written consent.

Selection process: consecutive and displayed in details

Predictors

The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. Categorization presented for the three predictors (age, CAT, GOLD stage). Each patient self-reported his/ her own condition in a daily journal and visited the chief physician monthly.

Outcome

Definition of exacerbation: symptom-based diagnosis such as increased cough and sputum production, a change of sputum colour, and worsening of dyspnoea from a stable state and beyond-normal day-to-day variations, i.e., showing acute onset and necessitating a change in regular medication, in accordance with a previous report. Blinded to the predictors.

Statistical

Ratio #events/#predictors (outcome exacerbation): around 100 events vs 3 predictors; ratio
| analysis H | #events/#predictors (outcome hospitalisation): around 13 events vs 3 predictors |
| --- | --- |
| Predicted outcome: exacerbation (symptom-based) and hospitalisation (event-based, Assessed from daily journals) |
| Statistical model: Multivariate logistic regression analysis (with univariable selection for p<0.05). |
| Missing data: unclear |

| Performance Measures H | AUC |
| --- | --- |

| Validation X |  |
| **Flow (Derivation cohort)** | Setting and sampling: prospective cohort; an outpatient clinic at Kyoto University Hospital, Japan. |
|-------------------------------|--------------------------------------------------------------------------------------------------|
| **Inclusion criteria:**       | • COPD patients in stable conditions                                                            |
| **Exclusion criteria:**       | • female                                                                                                                                 |
|                               | • Brinkman index < 10 pack-years                                                                |
|                               | • respiratory diseases other than COPD                                                           |
|                               | • daily intake of systemic corticosteroids and complicated with malignant diseases within 5 years. |
| **Ethical approval:**         | Approved by the ethics committee of Kyoto University (approval No. E182), and written informed consent was obtained by all participants. |
| **Selection process:**        | consecutive                                                                                     |

| **Predictors**                | Measurements carefully described. The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
| **Outcome**                   | Definition of exacerbation: any two “major” symptoms (dyspnoea, sputum purulence and sputum quantity) or an increase in one “major” and one “minor” symptom (wheeze, sore throat, cough and nasal congestion/discharge) for at least two consecutive days (symptom based). |
| **Statistical analysis**      | Ratio #events/#predictors: around 90 events vs around 10 predictors                               |
|                               | Predicted outcome: patients with at least 2 exacerbations                                         |
|                               | Statistical model: Multivariable logistic regression (already predefined variables)               |
| Performance Measures | AUC, R^2, HL, model p-value model (data obtained contacting the authors) |
|-----------------------|-----------------------------------------------------------------------|
| Validation            | X                                                                     |
| Flow (Derivation cohort) | Setting and sampling: age-stratified, randomly selected white individuals from 2 similar general population studies, essentially conducted by the same investigators and using identical methods: the 2001-2003 examination of the Copenhagen City Heart Study and the 2003-2008 examination of the Copenhagen General Population Study. Prospective cohort study examining 61,650 participants with spirometry measurements.  
(The Copenhagen City Heart Study is a prospective cardiovascular study of the Danish general population initiated in 1976...Follow-up was 100% complete. The Copenhagen General Population Study is a cross-sectional study of persons selected from the population of the city of Copenhagen)  
Inclusion criteria:  
- COPD defined as ratio between FEV% predicted and FVC < 0.70. (The current study selected a subgroup of individuals with COPD for further studies. The participants with COPD in the 2 studies were analysed as 1 collective cohort to obtain maximal statistical power)  
Exclusion criteria:  
- Individuals with self-reported asthma (n=1198)  
- Individuals younger than 40 years of age (n=196)  
- Individuals with missing values for covariates (n=3)  
- Individuals with measurements of any of the 3 biomarkers (n=49)  
Ethical approval: Both studies were approved by Herlev Hospital and a Danish ethics committee and were conducted according to the Declaration of Helsinki. Written informed consent was obtained from all participants.  
Selection process: consecutive and detailed  
Measurements described (particularly carefully FEV1% predicted and biomarkers). The baseline characteristics were obtained from the standardized questionnaires/measurements at the start of the follow-up period, then, they were blinded to the outcome. |
| Outcome L | Definition of exacerbation: An exacerbation of COPD was defined as a short-course treatment with oral corticosteroids alone or in combination with an antibiotic or as a hospital admission due to COPD. This information was collected for each individual by linking our database to 2 national registries: the Danish Registry of Medicinal Product Statistics, which contains information on all prescriptions dispensed in all Danish pharmacies, and the Danish National Patient Registry covering all hospital contacts in Denmark. We identified treatment with oral corticosteroids (H02AB) and antibiotics (J01) using the Anatomic Therapeutic Chemical code22 and diagnoses of COPD (DJ41-44) using the World Health Organization International Classification of Diseases code. |
|---|---|
| Statistical analysis L | Ratio #events/#predictors: 3083 events vs around 10 predictors |
| | Predicted outcome: (with performance measures) frequent exacerbations (defined as at least 2 exacerbations more than 1 year apart) |
| | Statistical model: Multivariable logistic regression (with focus on the three tested biomarkers) for the first year of follow-up and for the maximum follow-up time. |
| | Missing data: individuals with missing values for covariates (n=3) or measurements of any of the 3 biomarkers (n=49) were excluded |
| Performance Measures H | AUC, Net Reclassification Index (used to evaluate the improvement of performances thanks to the predictors). |
| Validation X | --- |
New section
CLINICAL APPLICABILITY OF THE MODELS

The use of prediction models in practice needs to balance the clinical availability of predictors, i.e. the effort to obtain the information, the easiness with which doctors can obtain a risk for the individual patients and the predictive performance of the models. Ideally, predictors would be easily available, the model easy to obtain individual probabilities from, and the model would predict the risk of exacerbations accurately as shown by an external validation.

More in details, concerning the clinical availability, predictors’ data should be easy to obtain. Thus, the first step in this review was the categorization of each predictor across the 27 included prediction models, shown in Table 9, where the following legend is used:

- “1” refers to a simple test or simple questions or medical charts
- “2” refers to routine tests
- “3” refers to specialised tests.

We show 1 set of predictors per study, since we deemed all of the shown prediction models to be too similar among each other in terms of predictors used and performance to be considered separated models. The only exception is Almagro (2014) [19], where we considered the indices CODEX, ADO, BODEX to be three separated indices.
| Predictor                                                                 | Study | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|--------------------------------------------------------------------------|-------|---|---|---|---|---|---|---|---|---|----|----|----|----|
| Obstruction (FEV1% predicted or FEV1)                                    |       |   |   |   |   |   |   |   |   |   |    |    |    |    |
| Previous exacerbations                                                   |       | X | X |   |   |   | X |   |   |   |    |    |    |    |
| Age                                                                      |       |   |   |   |   |   |   | X |   |   |    |    |    |    |
| Smoking                                                                  |       | X |   |   |   |   | X |   |   |   |    |    |    |    |
| COPD specific HRQL (survey)                                             |       | X |   | X | X |   | X |   |   |   |    |    |    |    |
| Body-mass index                                                          |       |   |   |   |   |   |   |   | X |   |    |    |    |    |
| Sex                                                                      |       |   |   |   |   |   |   |   |   | X |    |    |    |    |
| BODE                                                                     |       |   |   |   |   |   |   |   |   |   |   | X  |    |    |
| Dyspnea                                                                  |       |   |   |   |   |   |   |   |   |   |   |   | X  |    |
| Comorbidities                                                            |       |   |   |   |   |   |   |   |   |   |   |   |   | X  |
| Long-term oxygen therapy (LTOT)                                         |       |   |   |   |   |   |   |   |   |   |   |   |   | X  |
| Duration of COPD                                                          |       |   |   |   |   |   |   |   |   |   |   |   |   | X  |
| ADO                                                                      |       |   |   |   |   |   |   |   |   | X |    |    |    |    |
| DOSE                                                                     |       |   |   |   |   |   |   |   |   |   |   |   |   | X  |
| Serum C-reactive protein (CRP)                                           |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| White Blood Cell count (WBC)                                             |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Hypercapnia at discharge                                                |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Physical activity                                                        |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Use of prednisone in the previous year                                   |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Oral corticosteroids                                                     |       |   |   |   |   |   |   |   |   |   |   |   |   | X  |
| Hospital stay                                                            |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Influenza vaccination                                                    |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Country                                                                  |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Inhaled corticosteroid (ICS)                                             |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Tiotropium                                                               |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Long-acting b2 agonists (LABA)                                           |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Employment status                                                        |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Administration of Azithromycin and                                     |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Inhaled medication                                                       |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Anticholinergics                                                         |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Control by Pulmonologist or GP                                           |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| History of reflux or heartburn                                          |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Education                                                                |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| CODEX                                                                    |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Health related quality of life (survey)                                 |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| BODEX                                                                    |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Oxygen saturation at rest                                                |       | X |   |   |   |   |   |   |   |   |   |   |   |    |
| Serum albumin on admission                                               |       |   | X |   |   |   |   |   |   |   |   |   |   |    |
| Depression                                                               |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Self-efficacy                                                            |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Perceived social support                                                 |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Hospital Anxiety and Depression scale                                   |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| y-globulin                                                               |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Plasma levels of fibrinogen                                              |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Whole blood leukocyte count                                              |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Exercise capacity                                                        |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| I-BODE                                                                   |       | X |   |   |   |   |   |   |   |   |   |   |   |    |
| Desaturation >4% during SWT                                              |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Partial pressure of oxygen (PO₂)                                        |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Normal IgG antibody titer against IL-6                                    |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Has emphysema>5% by radiology                                            |       |   |   |   |   |   |   |   |   |   |   |   |   |    |
| Plasma levels of high-sensitivity CRP                                    |       | X |   |   |   |   |   |   |   |   |   |   |   |    |
| Predictor                                      | Study | Frequency | Availability | Predictor                                      | Study | Frequency | Availability |
|-----------------------------------------------|-------|-----------|--------------|-----------------------------------------------|-------|-----------|--------------|
| Obstruction (FEV1% predicted or FEV1)         | x     |           |              | Previous exacerbations                        | x     |           |              |
|                                              |       |           |              |                                               |       |           |              |
|                                              |       |           |              | Age                                            | x     |           |              |
|                                              |       |           |              | Smoking                                        | x     |           |              |
|                                              |       |           |              | COPD specific HRQL (survey)                    | x     |           |              |
|                                              |       |           |              | Body-mass index                                | x     |           |              |
|                                              |       |           |              | Sex                                            | x     |           |              |
|                                              |       |           |              | BODE                                           | x     |           |              |
|                                              |       |           |              | Dyspnea                                        | x     |           |              |
|                                              |       |           |              | COPD comorbidities                              | x     |           |              |
|                                              |       |           |              | Long-term oxygen therapy (LTOT)                | x     |           |              |
|                                              |       |           |              | Duration of COPD                                | x     |           |              |
|                                              |       |           |              | ADO                                            | x     |           |              |
|                                              |       |           |              | DOSE                                           | x     |           |              |
|                                              |       |           |              | Serum C-reactive protein (CRP)                 | x     |           |              |
|                                              |       |           |              | White Blood Cell count (WBC)                   | x     |           |              |
|                                              |       |           |              | Hypercapnia at discharge                       | x     |           |              |
|                                              |       |           |              | Physical activity                               | x     |           |              |
|                                              |       |           |              | Use of prednisone in the previous year         | x     |           |              |
|                                              |       |           |              | Oral corticosteroids                            | x     |           |              |
|                                              |       |           |              | Hospital stay                                   | x     |           |              |
|                                              |       |           |              | Influenza vaccination                           | x     |           |              |
|                                              |       |           |              | Country                                         | x     |           |              |
|                                              |       |           |              | Inhaled corticosteroid (ICS)                   | x     |           |              |
|                                              |       |           |              | Tiotropium                                      | x     |           |              |
|                                              |       |           |              | Long-acting b2 agonists (LABA)                  | x     |           |              |
|                                              |       |           |              | Employment status                               | x     |           |              |
|                                              |       |           |              | Administration of Azithromycin and              | x     |           |              |
|                                              |       |           |              | Inhaled medication                              | x     |           |              |
|                                              |       |           |              | Anticholinergics                                | x     |           |              |
|                                              |       |           |              | Control by Pulmonologist or GP                  | x     |           |              |
|                                              |       |           |              | History of reflux or heartburn                 | x     |           |              |
|                                              |       |           |              | Education                                       | x     |           |              |
|                                              |       |           |              | CODEX                                          | x     |           |              |
|                                              |       |           |              | Health related quality of life (survey)         | x     |           |              |
|                                              |       |           |              | BODEX                                          | x     |           |              |
|                                              |       |           |              | Oxygen saturation at rest                       | x     |           |              |
|                                              |       |           |              | Serum albumin on admission                      | x     |           |              |
|                                              |       |           |              | Depression                                      | x     |           |              |
|                                              |       |           |              | Self-efficacy                                   | x     |           |              |
|                                              |       |           |              | Perceived social support                        | x     |           |              |
|                                              |       |           |              | Hospital Anxiety and Depression scale          | x     |           |              |
|                                              |       |           |              | y-globulin                                      | x     |           |              |
|                                              |       |           |              | Plasma levels of fibrinogen                     | x     |           |              |
|                                              |       |           |              | Whole blood leukocyte count                     | x     |           |              |
|                                              |       |           |              | Exercise capacity                               | x     |           |              |
|                                              |       |           |              | IL-BODE                                        | x     |           |              |
|                                              |       |           |              | Desaturation >4% during SWT                     | x     |           |              |
|                                              |       |           |              | Partial pressure of oxygen (PO2)               | x     |           |              |
|                                              |       |           |              | Normal IgG antibody titer against               | x     |           |              |
|                                              |       |           |              | IL-6                                           | x     |           |              |
|                                              |       |           |              | Has emphysema>5% by radiology                   | x     |           |              |
|                                              |       |           |              | Plasma levels of high-sensitivity CRP           | x     |           |              |
Legend:

| Simple tests or simple questions or medical charts |
|---------------------------------------------------|
| Routine tests                                      |
| Specialised tests                                  |

The colours of each predictor is just a visual help that correspond to the category of the availability of each predictor (1: simple test or simple questions or medical charts; 2: routine tests; 3: specialised tests).

Notes: 1. Gold stage; 2. Time between recruitment and previous exacerbation; 3. Both variables history of frequent exacerbations and time since most recent prior exacerbation are used in the model; 4. Pack-years; 5. Current smoking status; 6. St. George's Respiratory Questionnaire (SQRQ); 7. Pulmonary Functional Status Scale (PFSS); 8. COPD Assessment Test (CAT); 9. American Thoracic Society (ATS) Dyspnoea Scale; 10. MRC Dyspnoea Scale; 11. mMRC Dyspnoea Scale; 12. Number of previous surgeries; 13. History of vascular disease; 14. Charlson Comorbidities Index (CCI); 15. Measured in Kcal/day; 16. Daily step count (in the step_CRP index and step_IL-6 index); 17. Medical Outcomes Study short-form health survey [36 items] (SF-36); 18. Zung Self-Rating Depression Scale (SDS); 19. COPD Self-Efficacy Scale (CSES); 20. Personal Resource Questionnaires (PRQ2000); 21. Incremental shuttle walking test (ISWT); 22. BODE where the 6 Minute Walk Test (6MWT) is substituted by the Incremental Shuttle Walk Test (ISWT).

Table 9. Categorization of the predictors used in each study. The correspondence between number of study and study is shown below (for Almagro (2014) we show three models, since we deemed them to be independent).
A summary of the predictors included in the final models (ranked by frequency and further classified by their clinical availability) is shown in Table 10. More than 50 different predictors were used across the included prediction models. Airways obstruction (FEV1% predicted or FEV1 or GOLD stage) was the most common predictor (12 times out of 27 models). The next most common predictors were previous exacerbations (9 times), age (9 times), smoking (8 times) and health-related quality of life (8 times). More than half of the predictors were used only once.
| Predictor                                               | Frequency | Availability predictor |
|---------------------------------------------------------|-----------|------------------------|
| Obstruction (FEV1% predicted or FEV1 or GOLD stage)     | 12        | 2                      |
| Previous exacerbations                                  | 9         | 1                      |
| Age                                                     | 9         | 1                      |
| Smoking                                                 | 8         | 1                      |
| COPD specific HRQL (survey)                             | 8         | 2                      |
| Body-mass index                                         | 6         | 1                      |
| Sex                                                     | 6         | 1                      |
| BODE                                                    | 4         | 3                      |
| Dyspnoea                                                | 3         | 1                      |
| Comorbidities                                           | 3         | 1                      |
| Long-term oxygen therapy (LTOT)                         | 2         | 1                      |
| Duration of COPD                                         | 2         | 1                      |
| ADO                                                     | 2         | 1                      |
| DOSE                                                    | 2         | 2                      |
| Serum C-reactive protein (CRP)                          | 2         | 2                      |
| White Blood Cell count (WBC)                            | 2         | 2                      |
| Hypercapnia at discharge                                | 2         | 3                      |
| Physical activity                                       | 2         | 3                      |
| Use of prednisone in the previous year                  | 1         | 1                      |
| Oral corticosteroids                                    | 1         | 1                      |
| Hospital stay                                           | 1         | 1                      |
| Influenza vaccination                                   | 1         | 1                      |
| Country                                                 | 1         | 1                      |
| Inhaled corticosteroid (ICS)                            | 1         | 1                      |
| Tiotropium                                              | 1         | 1                      |
| Long-acting b2 agonists (LABA)                          | 1         | 1                      |
| Employment status                                       | 1         | 1                      |
| Administration of Azithromycin and Ceftriaxone in the admission period | 1         | 1                      |
| Inhaled medication                                      | 1         | 1                      |
| Anticholinergics                                        | 1         | 1                      |
| Control by Pulmonologist or GP                          | 1         | 1                      |
| History of reflux or heartburn                          | 1         | 1                      |
| Education                                               | 1         | 1                      |
| CODEX                                                   | 1         | 1                      |
| Health related quality of life (survey)                 | 1         | 2                      |
| BODEX                                                   | 1         | 2                      |
| Oxygen saturation at rest                                | 1         | 2                      |
| Serum albumin on admission                              | 1         | 2                      |
| Depression                                              | 1         | 2                      |
| Self-efficacy                                           | 1         | 2                      |
| Perceived social support                                | 1         | 2                      |
| Hospital Anxiety and Depression scale (HAD-total score) | 1         | 2                      |
| y-globulin                                              | 1         | 2                      |
| Plasma levels of fibrinogen                             | 1         | 2                      |
| Whole blood leukocyte count                             | 1         | 2                      |
| Exercise capacity                                       | 1         | 3                      |
| I-BODE<sup>2</sup>                                      | 1         | 3                      |
| Desaturation >4% during SWT                             | 1         | 3                      |
| Partial pressure of oxygen (PO<sub>2</sub>)             | 1         | 3                      |
| Normal IgG antibody titer against Porphyromonas gingivalis | 1         | 3                      |
| Interleukin 6 (IL-6)                                    | 1         | 3                      |
| Predictor                                      | Rank | Difficulty |
|------------------------------------------------|------|------------|
| Has emphysema >5% by radiology                 | 1    | E          |
| Plasma levels of high-sensitivity CRP          | 1    | D          |

Predictors are ranked according to how many studies used them in the final model. How clinically easy it is to obtain the data related to each predictor in clinical practice is also indicated (1: simple test or simple questions or medical charts; 2: routine tests; 3: specialised tests). Only one prediction model per study is considered, with exception of Almagro (2014), Moy (2014) and Motegi (2013), where different predefined indices or final models are shown. Single predictors used within the same study but in different models are considered only once. A detailed description of the predictors in each model is shown in the online material; FEV1: forced expiratory volume in 1 second; GOLD: global initiative for chronic obstructive lung disease; COPD: chronic obstructive pulmonary disease; HRQL: health-related quality of life; BODE: body mass index, airflow obstruction, dyspnoea and exercise capacity; ADO: age, dyspnoea, airflow obstruction; DOSE: Medical Research Council (MRC) Dyspnoea Scale, airflow obstruction, smoking status, and exacerbation frequency; CODEX: comorbidity, obstruction, dyspnoea, and previous severe exacerbations; BODEX: body mass index, airflow obstruction, dyspnoea and previous severe exacerbations; I-BODE: ISWT+BODE; ISWT: incremental shuttle walk test; SWT: shuttle walk test; PO2: partial pressure of oxygen; IgG: immunoglobulin G; CRP: C-reactive protein.

Table 10. Summary of the predictors included in the final models.

Table 11 shows the distribution of predictors’ availability for each model and how it results in an assessment of global clinical availability for each prediction model. We categorized as:

- with data easy to obtain (E) the models with only predictors of category one or at most one predictor of category “2” (in general this predictor was FEV1% predicted).
- with data moderately easy to obtain (M) the models including at least two predictors belonging to the category “2”, and no predictors of category “3”.
- with data difficult to obtain (D) the remaining models (constituted by at least 1 predictor of category “3”, i.e. specialised test).
### Studies

| Studies                                      | Availability predictors. Low (L), Medium (M), High (H) | Total variables in the model | Simple tests or simple questions or medical charts | Routine tests | Specialised tests |
|----------------------------------------------|--------------------------------------------------------|------------------------------|---------------------------------------------------|---------------|-------------------|
| 1 Almagro (2014) [19]                       | E                                                      | 4                            | 3                                                 | 1             | 0                 |
|                                              | E                                                      | 3                            | 2                                                 | 1             |                   |
|                                              | E                                                      | 4                            | 3                                                 | 1             |                   |
| 2 Almagro (2006) [20]                       | D                                                      | 3                            | 1                                                 | 1             |                   |
| 3 Amalakuhan (2012) [21]                     | E                                                      | 5                            | 4                                                 | 0             |                   |
| 4 Bertens (2013) [22]                        | E                                                      | 4                            | 3                                                 | 1             |                   |
| 5 Brusse-Keizer (2011) [23]                  | E                                                      | 2                            | 1                                                 | 0             |                   |
| 6 Chen (2006) [24]                           | M                                                      | 9                            | 5                                                 | 4             |                   |
| 7 Echave-Sustaeta (2010) [25]                | E                                                      | 2                            | 1                                                 | 1             |                   |
| 8 Faganello (2010) [26]                      | D                                                      | 4                            | 2                                                 | 1             | 1                 |
| 9 Garcia-Aymerich (2003) [27]                | D                                                      | 6                            | 3                                                 | 1             | 2                 |
| 10 Gudmundusson (2005) [28]                  | M                                                      | 5                            | 2                                                 | 3             | 0                 |
| 11 Hurst (2010) [29]                         | M                                                      | 5                            | 3                                                 | 2             | 0                 |
| 12 Jakob (2013) [30]                         | E                                                      | 7                            | 6                                                 | 1             | 0                 |
| 13 Jones (2009) [31]                         | E                                                      | 4                            | 3                                                 | 1             | 0                 |
| 14 Ko (2011) [32]                            | D                                                      | 4                            | 2                                                 | 1             | 1                 |
| 15 Lee (2014) [33]                           | E                                                      | 9                            | 8                                                 | 1             | 0                 |
| 16 Marin (2009) [34]                         | D                                                      | 4                            | 2                                                 | 1             | 1                 |
| 17 Moberg (2014) [35]                        | D                                                      | 11                           | 6                                                 | 2             | 3                 |
| 18 Motegi (2013) [36]                        | E                                                      | 5                            | 4                                                 | 1             | 0                 |
| 19 Moy (2014) [37]                           | D                                                      | 4                            | 1                                                 | 2             | 1                 |
| 20 Müllerova (2015) [38]                     | D                                                      | 8                            | 4                                                 | 3             | 1                 |
| 21 Ong (2005) [39]                           | D                                                      | 4                            | 2                                                 | 1             | 1                 |
| 22 Parshall (2008) [40]                      | E                                                      | 1                            | 0                                                 | 1             | 0                 |
| 23 Suetomo (2014) [41]                       | M                                                      | 3                            | 1                                                 | 2             | 0                 |
| 24 Takahashi (2012) [42]                     | D                                                      | 11                           | 7                                                 | 3             | 1                 |
| 25 Thomsen (2013) [43]                       | D                                                      | 11                           | 6                                                 | 3             | 2                 |

**Legend:**

- **E**: Data related to the predictors easy (E) to obtain: only predictors of category one or at most one predictor of category 2 (routine test, in general this predictor was FEV1% predicted)
- **M**: Data related to the predictors moderately easy (M) to obtain: including at least two predictors belonging to the category 2 (routine test), and no predictors of category “3”.
- **D**: Data related to the predictors difficult (D) to obtain: constituted by at least 1 predictor of category 3 (specialised test)

**Table 11.** Total number and distribution of the categorization of the predictors used in each study.
The assessment in Table 11 is reproduces in the column “Availability predictors” in m-Table 3.

| Study                        | Availability predictors | External validation | Practical applicability |
|------------------------------|-------------------------|----------------------|-------------------------|
| Bertens (2013) [22]          | E                       | Y                    | N                       |
| Almagro (2014) [19]          | E                       | Y                    | N                       |
| Almagro (2006) [20]          | D                       | N                    | Y¹                      |
| Brusse-Keizer (2011) [23]    | E                       | N²                   | N                       |
| Amalakuhan (2012) [21]       | E                       | N³                   | N                       |
| Jones (2009) [31]            | E                       | N                    | N                       |
| Echave-Sustaeta (2010) [25]  | E                       | N                    | N                       |
| Jakob (2013) [30]            | E                       | N                    | N                       |
| Motegi (2013) [36]           | E                       | N                    | N                       |
| Lee (2014) [33]              | E                       | N                    | N                       |
| Parshall (2008) [40]         | E                       | N                    | N                       |
| Chen (2006) [24]             | M                       | N                    | N                       |
| Gudmundusson (2005) [28]     | M                       | N                    | N                       |
| Hurst (2010) [29]            | M                       | N                    | N                       |
| Suetomo (2014) [41]          | M                       | N                    | N                       |
| Faganello (2010) [26]        | D                       | N                    | N                       |
| Ko (2011) [32]               | D                       | N                    | N                       |
| Ong (2005) [39]              | D                       | N                    | N                       |
| Garcia-Aymerich (2003) [27]  | D                       | N                    | N                       |
| Marin (2009) [34]            | D                       | N                    | N                       |
| Moberg (2014) [35]           | D                       | N                    | N                       |
| Moy (2014) [37]              | D                       | N                    | N                       |
| Müllerova (2015) [38]        | D                       | N                    | N                       |
| Takahashi (2012) [42]        | D                       | N                    | N                       |
| Thomsen (2013) [43]          | D                       | N                    | N                       |

The field “Availability predictors” refers to how easy is to obtain the data related to the predictors: E (easy), M (medium), D (difficult); the field “External validation” refers to the reliability of the model in terms of comparison of performance between derivation and eventual validation cohort: Y (yes), N (no). The field “Practical applicability” indicates if it is easy to extract individual likelihoods of exacerbation from the model: Y (yes), N (no). Studies presenting different models are considered only once, with exception of Almagro (2014) where different predefined indices are shown. ¹The paper explains how to you can obtain probabilities starting from the logistic regression equation and indicates how to calculate individual probabilities starting from the predictors; ²The jackknife cross validation was applied but no performance is indicated; ³Internal validation was applied but no performance is indicated; ⁴Validation is performed for other outcomes.
New section
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