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

Online Material

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Table of contents

(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 FEV_1).

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 >= 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
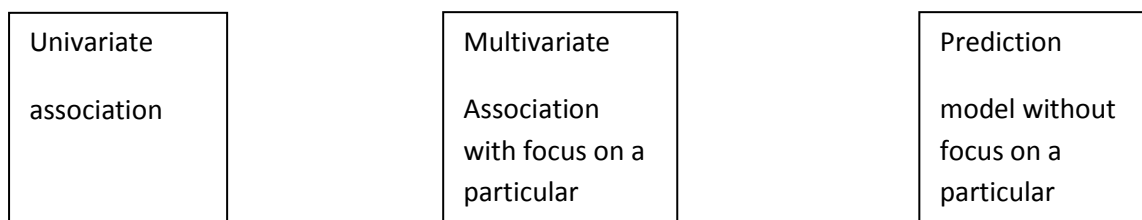
We are aware of a number of prediction models for exacerbations (Table 1). We will aim to identify additional prediction models as part of this systematic review. However, there may be additional predictors not considered in the existing prediction models. We are interested in these predictors but are 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, FEV_1, 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.

Figure 2: Framework for evaluating prediction models and potentially new predictors
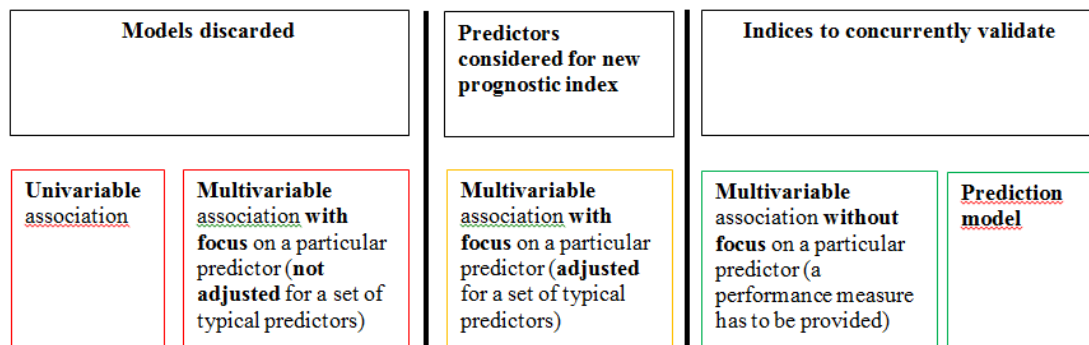
In order to judge the potential of predictors to add to already existing prediction models we will consider studies reporting on multivariate models with focus on a particular predictor if the association has been adjusted for predictors commonly included in existing prediction models.

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"

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

	Dyspnea	FEV1 % predi	Smoking	Previous Exace	BMI	Age	Sex	Quality of Life	CVD Histo	Exercise C	COPD dura	Cough	Drugs	Influenza	Other bio	Race	Education
DOSE	X	X	X	X													
Briggs		X	X	X	X	X	X	X	X								
SAFE		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				X			X	X
Frequency	3	6	4	6	3	5	3	2	3	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 FEV_1 (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 FEV_1 (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).

- **Population**

  Studies with patients with mild COPD (FEV_1>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

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

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   Outcome   Risk
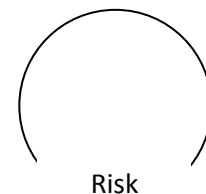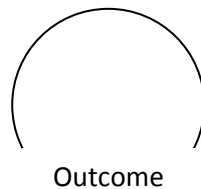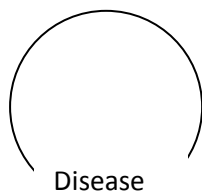
For instance, we will use the following words:

- Disease: "COPD", "Chronic Obstructive Pulmonary Disease"

- Outcome: "Exacerbation", "Hospitalisation"

- Risk: "Risk", "Prediction model", "Probability"

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

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_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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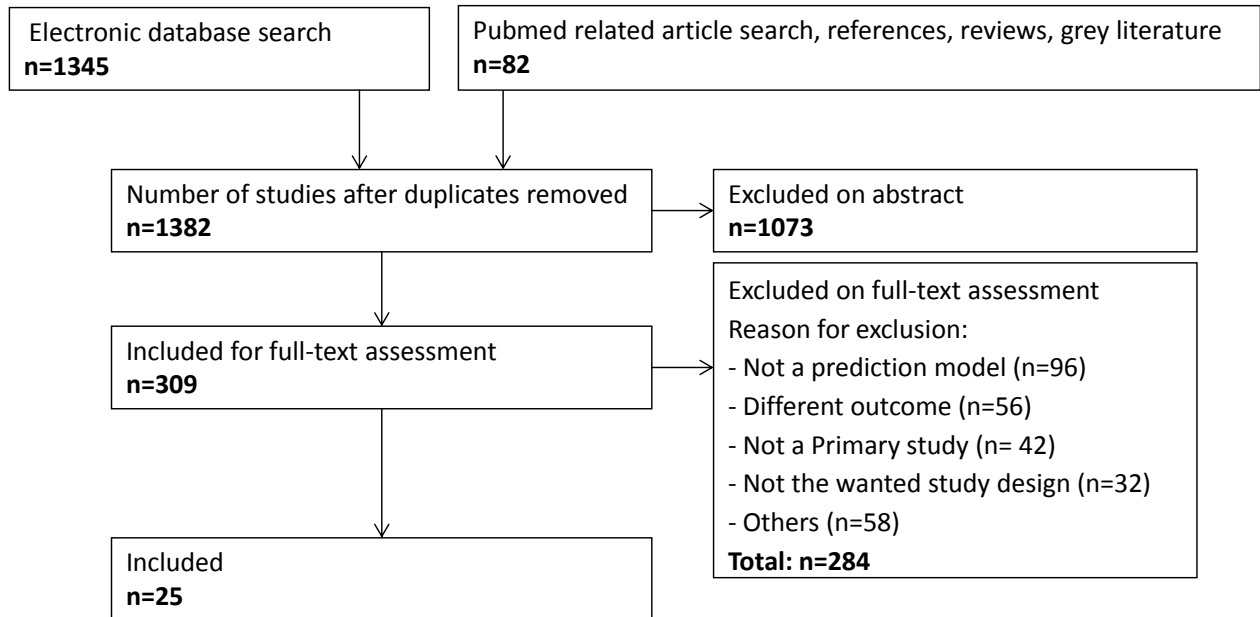
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New section

SELECTION PROCESS (OVERVIEW)

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

| Electronic database search **n=1345** | Pubmed related article search, references, reviews, grey literature **n=82** |

Number of studies after duplicates removed **n=1382** → Excluded on abstract **n=1073**

Included for full-text assessment **n=309** → Excluded on full-text assessment
Reason for exclusion:
- Not a prediction model (n=96)
- Different outcome (n=56)
- Not a Primary study (n= 42)
- Not the wanted study design (n=32)
- Others (n=58)
Total: n=284

Included **n=25**

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

23 Prospective Studies/ 377627
24 Prognosis/ 366590
25 (prediction or prognostic or prognosis or prospective).ti. 217572
26 23 or 24 or 25 789185
27 22 and 26 38568
28 19 or 27 215715
29 15 and 28 472
30 ("stage I" or "stage 1" or "grade I" or "grade 1").ti,ab. 58210
31 29 not 30 461
32 29 not 31 11
33 limit 29 to animals 2
34 limit 33 to humans 2
35 ("18195198" or "19797160" or "21177668" or "17218552" or "19353347" or "17621621" or "19515547" or "23757083").ui. 10
36 29 and 35 10

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. Gov't]
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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http://www.embase.com/search/results[21.08.2014 11:15:07]
No. Query Results

Embase Session Results

#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** 236,696
#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 41,070
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** 88,716
bronchitis':ab,ti

#3 'chronic obstructive lung disorder'/exp OR **'chronic obstructive lung disorder'** 72,701
#2 'chronic lung emphysema'/exp OR **'chronic lung emphysema'** 20,342
#1 'chronic lung disease'/exp OR **'chronic lung disease'** 9,818

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))))

Search history	
25 (((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 **hospitalization**))))) 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**))))	1,030 document results
18 (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**)))	989,200 document results
17 (TITLE-ABS-KEY(**severity** W/3 (**score** OR INDEX OR **assessment** OR **stratification** OR **validation**))) AND (TITLE(**prediction** OR **prognostic** OR **prognosis** OR **prospective**))	8,206 document results
15 TITLE(**prediction** OR **prognostic** OR **prognosis** OR **prospective**)	381,014 document results
14 TITLE-ABS-KEY(**severity** W/3 (**score** OR INDEX OR **assessment** OR **stratification** OR **validation**))	209,046 document results
12 TITLE(**score*** or **index***)	193,602 document results
11 TITLE-ABS-KEY(**risk W/3 (estima*** or **score*** or **index*** or **assessment** or **stratification** or **validation**))	594,917 document results

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)

1	Not a prediction model (neither prediction model nor multivariable association)	Agustí 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=9b2056ef587d547ff72052aeece64347.
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	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=L366010475 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.
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://sfx.metabib.ch/sfx_locater?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.
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://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23882354&id=doi:10.3402%2Fjchimp.v2i1.9915&issn=2000-9666&isbn=&volume=2&issue=1&spage=&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+B%3BKiljanek+L%.
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;

		2011; 183Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70851124 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=1073449X&id=doi:&atitle=A+prediction+model+for+COPD+readmissions%3A+Catching+up%2C+catching+our+breath+and+improving+a+national+problem&stitle=Am.+J.+Respir.+Crit.+Care+Med.&title=American+Journal+of+Respiratory+and+Critical+Care+Medicine&volume=183&issue=1&spage=&epage=&aulast=Amalakuhan&aufirst=B.&auinit=B.&aufull=Amalakuhan+B.&coden=&isbn=&pages=-&date=2011&auin.
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.+Brook.
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: 658–666Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext

		&D=med4&AN=11786136 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:11786136&id=doi:&issn=0014-2565&isbn=&volume=201&issue=11&spage=658&pages=658-66&date=2001&title=Revista+Clinica+Espanola&atitle=Tratamiento+y+pronostico+de+la+reagudizacion+grave+en+la+enfermedad+pulmonar+obstructiva+cronica.&aulast=Anon+Elizalde&pid=<author>Anon+Elizalde+JM;Garcia+De+Lorenzo+Mateos+A;Alvarez-Sala+Walther+R;Escuela+Gerico+MP</author><A.
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:&atitle=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=Raffaele&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=41951af8b40330c2519cbdfb221f36cb.
14	Not the wanted study design (RCT, not only placebo arm)	Anzueto A, Make BJ, Calverley PM, Jenkins C, Postma DS, Sciurba 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

		title=Effect+of+budesonide%2Fformoterol+treatment+on+dominant+predictors+of+exacerbations+in+patients+with+COPD&stitle=Am.+J.+Respir.+Crit.+Care+Med.&title=American+Journal+of+Respiratory+and+Critical+Care+Medicine&volume=183&issue=1&spage=&epage=&aulast=Anzueto&aufirst=A.&auinit=A.&aufull=Anzueto+A.&coden=&isbn=&pages=-&date=2011&auinit1=A&auinit.
15	Not the wanted study design (ecological study)	Arbex MA, De Souza Conceição 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: 777–783Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-70349456559&partnerID=40&md5=840b317dc0b8a6a01903a1fad5bb443d.
16	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: 289–297Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19787468 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19787468&id=doi:&issn=0494-1373&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</AN><DT>English+Abstract</DT>.
17	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: 492–497Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=17621621 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:17621621&id=doi:&issn=0032-5473&isbn=&volume=83&issue=981&spage=492&pages=492-7&date=2007&title=Postgraduate+Medical+Journal&atitle=The+SAFE+%28

		SGRQ+score%2C+air-flow+limitation+and+exercise+tolerance%29+Index%3A+a+new+composite+score+for+the+stratification+of+severity+in+chronic+obstructive+pulmonary+disease.&aulast=Azarisman&pid=%3Cauthor%3EAzarisman+.
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&spage=662&pages=662-71&date=2011&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Acute+exacerbations+of+chronic+obstructive+pulmonary+disease%3A+identification+of+biologic+clusters+and+their+biomarkers.&aulast=Bafadhel&pid=%3Cauthor%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=7566b972ab278d5bc560c23643b6c6e2.
20	No performance measure provided	Baker CL, Zou KH, Su J. Risk assessment of readmissions following an initial COPD-related hospitalization. *Int. J. Copd* [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+an+initial+COPD-related+hospitalization.&aulast=Baker&pid=%3Cauthor%3EBaker+CL%3BZ

		ou+KH%3BSu+J%3C%2Fauthor%3E%3CAN%3E24348031%3C%2FAN%3E%3CDT%3EJournal+Article%3C%.
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: 625–631Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21729761 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:21729761&id=doi:10.1016%2Fj.pupt.2011.06.003&issn=1094-5539&isbn=&volume=24&issue=5&spage=625&pages=625-31&date=2011&title=Pulmonary+Pharmacology+%26+Therapeutics&atitle=Statins+and+outcome+after+hospitalization+for+COPD+exacerbation%3A+a+prospective+study.&aulast=Bartziokas&pid=%3Cauthor%3EBartziokas+K%3BPapaioannou+AI%3BMinas+M%3BKostikas+K%3BBanya+W%.
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: 472–473Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-20644460160&partnerID=40&md5=6933f5f618d62e0b01487641370dd28a.
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, Philipps-Universitat Marburg, Baldingerstrasse, D 35043 Marburg, Germany. claus.vogelmeier@med.uni-marburg.de.; 2013; 14: 116Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24168767 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24168767&id=doi:10.1186%2F1465-9921-14-116&issn=1465-9921&isbn=&volume=14&issue=1&spage=116&pages=116&date=2013&title=Respiratory+Research&atitle=Characterisation+of+exacerbation+risk+and+exacerbator+phenotypes+in+the+POET-COPD+trial.&aulast=Beeh&pid=%3Cauthor%3EBeeh+KM%3BGlaab+T%3BStowasser+S%3BSchmidt+H%3BFabbri+LM%3BRabe+KF%3BVogelmeier+CF%3C%2Fautho.
24	Not a prediction model (focus on a	Benedik B, Farkas J, Kosnik M, Kadivec S, Lainscak M. Mini nutritional assessment score predicts rehospitalisations in patients with chronic

	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&stitle=J.+Cachexia+Sarcopenia+Muscle&title=Journal+of+Cachexia%2C+Sarcopenia+and+Muscle&volume=2&issue=4&spage=248&epage=&aulast=Benedik&aufirst=Barbara&au.
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_locater?sid=OVID:medline&id=pmid:20234126&id=doi:10.1159%2F000296504&issn=0025-7931&isbn=&volume=80&issue=1&spage=10&pages=10-8&date=2010&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%3B Chang+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&stitle=Respiration&title=Respiration&volume=&issue=&spage=&epage=&aulast=Benzo&aufirst=Roberto&auinit=R.&aufull=Benzo+R.&coden=RESPB&isbn=&pages=-&date=2010&auinit.
27	Included	Bertens LC, Reitsma JB, Moons KG, van Mourik Y, Lammers JW, Broekhuizen BD, Hoes AW, Rutten FH. Development and validation of a

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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: 219–220Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L361187120 http://dx.doi.org/10.1183/09031936.00128410 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=09031936&id=doi:10.1183%2F09031936.00128410&atitle=Adequate+use+of+pulmonary+embolism+clinical+prediction+rule+in+COPD+patients&stitle=Eur.+Respir.+J.&title=European+Respiratory+Journal&volume=37&issue=1&spage=219&epage=220&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: 669Available 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: 261–267Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22823008 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22823008&id=doi:10.1111%2Fj.1752-699X.2012.00314.x&issn=1752-6981&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%3EBlankenburg+T%3BGuettel+A%3BBusch+C%3BSchuett.

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&id=doi:10.1186%2F1471-2466-13-32&issn=1471-2466&isbn=&volume=13&issue=1&spage=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+R%3BHubbard+R%3BSmeeth+L%3BGulliford+M%3BCassel.
32	Not the wanted study design (case-control study)	Bourbeau J, Ernst P, Cockcoft 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=e6c18cc37845cca808c9b4f78b5bed20.
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&id=doi:&issn=1073-449X&isbn=&volume=177&issue=3&spage=269&pages=269-78&date=2008&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Serum+amyloid+a+is+a+biomarker+of+acute+exacerbations+of+chronic+obstructive+pulmonary+disease.&aulast=Bozinovski&pid=%3Cauthor%3EBozinovski+S%3BHutchinson+A%3BThompson+M%3BMacgregor+L%3BBlack+.
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

	not only placebo arm)	pulmonary disease. *Arch. Intern. Med.* [Internet] Section of Public Health and Health Policy, University of Glasgow, 1 Lilybank Gardens, Glasgow G12 8RZ, Scotland. a.briggs@clinmed.gla.ac.uk; 2008; 168: 71–79Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18195198 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18195198&id=doi:10.1001%2Farchinternmed.2007.37&issn=0003-9926&isbn=&volume=168&issue=1&spage=71&pages=71-9&date=2008&title=Archives+of+Internal+Medicine&atitle=Development+and+validation+of+a+prognostic+index+for+health+outcomes+in+chronic+obstructive+pulmonary+disease.&aulast=Briggs&pid=%3Cauthor%3EBriggs+A%3BSpencer+M%3BWang+H%3BMannino+D%3BSin+DD%3C.
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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–e118Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22075295 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22075295&id=doi:10.1016%2Fj.ejim.2011.08.020&issn=0953-6205&isbn=&volume=22&issue=6&spage=e115&pages=e115-8&date=2011&title=European+Journal+of+Internal+Medicine&atitle=Hoover%27s+sign+is+a+predictor+of+airflow+obstruction+severity+and+is+not+related+to+hyperinflation+in+chronic+obstructive+pulmonary+disease.&aulast=Bruyneel&pid=%3Cauthor%3EBruyneel+M%3.
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,

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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. *Respirology* [Internet] Gerontological Research Programme, Department of Psychological Medicine, National University of Singapore, Singapore, Singapore Department of Medicine, National University of Singapore, Singapore, Singapore Department of Respiratory Medicine, Tan Tock Sen; 2006; 11: 188–195Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-33644826174&partnerID=40&md5=357c20b73aa124748fba4dae6ef9fde0.
39	Not a primary study (editorial)	Casanova C, Celli BR. Microalbuminuria as a potential novel cardiovascular biomarker in patients with COPD. *Eur. Respir. J.* [Internet] Respiratory Research Unit, Pulmonary Dept., Hospital Universitario La Candelaria, Carretera del Rosario no. 145, 38010 Santa Cruz de Tenerife, Spain Respiratory Research Unit, Hospital Universitario La Candelaria, Tenerife, Spain Brigham and Women's Hospi; 2014; 43: 951–953Available 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* [Internet] ANTADIR Observatory, Paris, France ANTADIR, 66 Bd St Michel, 75006 Paris, France; 2003; 123: 1460–1466Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0037879078&partnerID=40&md5=9d3f3bc0835eeea748bee595277fccf6.
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.* [Internet] Department of Epidemiology, Harvard School of Public Health, United States Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States; 2009; 6: 95–103Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-

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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=35fa76122d5b1e895b0ac76f65d0dea1.
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 ar 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&id=doi:&issn=0895-8378&isbn=&volume=16&issue=1&spage=21&pages=21-5&date=2004&title=Inhalation+Toxicology&atitle=Influence+of+relatively+low+level+of+particulate+ar+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%3CAN%3E14744661%3C%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, Fabbri 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://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24844347&id=doi:&issn=0026-4806&isbn=&volume=105&issue=4&spage=289&pages=289-94&date=2014&title=Minerva+Medica&atitle=Serum+level+of+testosterone%2C+dihydrotestosterone+and+IGF-1+during+an+acute+exacerbation+of+COPD+and+their+relationships+with+inflammatory+and+prognostic+indices%3A+a+pilot+study.&aulast=Corbo&pid=%3Cauthor%3ECorbo+GM%3BDi+Marco+Berardi.
47	Not a primary study (editorial)	Cuvelier A. Assessment of prognosis and severity of COPD. Can we be satisfied with measurg 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–S24S25Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0036818970&partnerID=40&md5=4770a02fc9a6300f3ba1aeb56c21f701.
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.
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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 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:17136956&id=doi:&issn=1541-2555&isbn=&volume=2&issue=1&spage=7&pages=7-16&date=2005&title=Copd%3A+Journal+of+Chronic+Obstructive+Pulmonary+Disease&atitle=A+two-stage+logistic+model+based+on+the+measurement+of+pro-inflammatory+cytokines+in+bronchial+secretions+for+assessing+bacterial%2C+viral%2C+and+non-infectious+origin+of+COPD+exacerbations.&aulast=Dal.
51	Not a prediction model (neither prediction model nor multivariable association)	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, PalmHarbor, FL, United States; 2012; 18: e338–e345Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84869228158&partnerID=40&md5=8a8e245edde7b5650ad0aa076a7a2a49.
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52	Not a prediction model (neither prediction model nor multivariable association)	Dalal AA, Shah M, Lunacsek 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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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, Maualna 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&pages=405-10&date=2010&title=Archivos+de+Bronconeumologia&atitle=Pronostico+tras+una+agudizacion+grave+de+la+EPOC+tratada+con+ventilacion+mecanica+no+invasiva.&aulast=Echave-Sustaeta&pid=%3Cauthor%3EEchave-Sustaeta+J%3BComeche+Casanova+L%3BGarcia+Lujan+R%3BSa.

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57	No performance measure provided	Eisner MD, Iribarren C, Yelin EH, Sidney S, Katz PP, Sanchez G, Blanc PD. The impact of SHS exposure on health status and exacerbations among patients with COPD. *Int. J. Copd* [Internet] Division of Occupational and Environmental Medicine, University of California, San Francisco, CA 94143-0111, USA. mark.eisner@ucsf.edu; 2009; 4: 169–176Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=med5&AN=19516915 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19516915&i d=doi:&issn=1176-9106&isbn=&volume=4&issue=&spage=169&pages=169-76&date=2009&title=International+Journal+of+Copd&atitle=The+impact+o f+SHS+exposure+on+health+status+and+exacerbations+among+patients+ with+COPD.&aulast=Eisner&pid=%3Cauthor%3EEisner+MD%3BIribarren+C %3BYelin+EH%3BSidney+S%3BKatz+PP%3BSanchez+G%3BBlanc+PD%3C%2 Fauthor%3E%3CAN%3E195169.
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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:

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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.
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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: 2345–2353Available 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: 407–415Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23659185 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23659185&id=doi:10.1111%2Fcrj.12027&issn=1752-6981&isbn=&volume=7&issue=4&spage=407&pages=407-15&date=2013&title=The+clinical+respiratory+journal&atitle=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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67	Not a primary study (abstract)	Fernandez S, Rodriguez O, Ortin JA, Aibar J, Seijas N, Orquin A, Hernandez C. Hospital at home for acute exacerbations of chronic obstructive pulmonary disease (COPD). A series of 374 patients. *Eur. J. Intern. Med.* [Internet] S. Fernandez, Internal Medicine Department, Hospital Clinic Barcelona, Barcelona, Spain; 2013; 24: e60Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L71225791 http://dx.doi.org/10.1016/j.ejim.2013.08.146 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=09536205&id=doi:10.1016%2Fj.ejim.2013.08.146&atitle=Hospital+at+home+for+acute+exacerbations+of+chronic+obstructive+pulmonary+disease+%28COPD%29.+A+series+of+374+patients&stitle=Eur.+J.+Intern.+Med.&title=European+Journal+of+Internal+Medicine&volume=24&issue=&spage=e60&epage=&aulast=Fern%C3%A1ndez&aufirst=S.&auinit=S.&au.
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=b7da97870e60363959b66991591dffe6.
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_locater?sid=OVID:medline&id=pmid:24786594&id=doi:10.1016/j.jclinepi.2014.03.005&issn=0895-

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70	Not a COPD cohort	Fu JJ, Gibson PG, Simpson JL, McDonald VM. Longitudinal changes in clinical outcomes in older patients with asthma, COPD and asthma-COPD overlap syndrome. *Respiration* [Internet] Priority Research Centre for Asthma and Respiratory Diseases, School of Medicine and Public Health, Hunter Medical Research Institute, New Lambton Heights, NSW 2305, Australia School of Nursing and Midwifery, Faculty of Health, University of Newcastle, Ne; 2014; 87: 63–74Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84893317803&partnerID=40&md5=6a617d3ab08744c0550899f4b174e24e .
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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, Sauleda 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_locater?sid=OVID:medline&id=pmid:21177668&id=doi:10.1136%2Fthx.2010.154484&issn=0040-6376&isbn=&volume=66&issue=5&spage=430&pages=430-7&date=2011&title=Thorax&atitle=Identification+and+prospective+validation+of+clinically+relevant+chronic+obstructive+pulmonary+disease+%28COPD%29+subtypes.&aulast=Garcia-Aymerich&pid=%3Cauthor%3EGarcia-Aymerich+J%3BGomez+FP%3BBenet+M%3BFarrero+E%3BBasaga.
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 Clínic, Spain Department of Experimental and

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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: 640Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L351041341 http://sfx.metabib.ch/sfx_locater?sid=EMBASE&issn=03002896&id=doi:&atitle=Prognostic+stratification+in+patients+with+exacerbated+copd+requiring+hospitalization.+Seeing+through+the+smoke+%5B2%5D&stitle=Arch.+Bronconeumol.&title=Archivos+de+Bronconeumologia&volume=43&issue=11&spage=640&epage=&aulast=Gonz%C3%A1lez&aufirst=Gerardo+Rivero&auinit=G.R.&aufull=Gonz%C3%A1lez+G.R.&coden=ARBRD&isbn=&pages=640-&date=2007&aui.
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86	Not a prediction model (focus on a particular predictor without the wanted adjustment)	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.
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90	Not retrieved	Hijjawi S, Minshar MA, Wang Y, Sharma G. 30-Day readmissions in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. *Chest* [Internet] S. Hijjawi, UTMB, Galveston, United States; 2012; 142Available from: http://www.embase.com/search/results?subaction=viewrecord&from=exp ort&id=L71073075 http://dx.doi.org/10.1378/chest.1390319 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=00123692&id=doi:10. 1378/chest.1390319&atitle=30-Day+readmissions+in+patients+hospitalized+with+acute+exacerbation+of+ chronic+obstructive+pulmonary+disease&stitle=Chest&title=Chest&volum e=142&issue=4&spage=&epage=&aulast=Hijjawi&aufirst=Shadi&auinit=S. &aufull=Hijjawi+S.&coden=&isbn=&pages=-&date=2012&auinit1=S&auinitm=.
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94	Not a primary study (poster)	Hoyles KH, Sheehan AS, Forrester DLF, Johnson SJJ, Knox AJK, Bolton CEB. The Chronic obstructive pulmonary disease assessment tool (CAT) in patients admitted to hospital for exacerbation. *Thorax* [Internet] K.H. Hoyles, Respiratory Medicine, Nottingham University, Hospital Trust, Nottingham, United Kingdom; 2013; 68: A204Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L71367446 http://dx.doi.org/10.1136/thoraxjnl-2013-204457.432 http://sfx.metabib.ch/sfx_locater?sid=EMBASE&issn=00406376&id=doi:10.1136%2Fthoraxjnl-2013-204457.432&atitle=The+Chronic+obstructive+pulmonary+disease+assessment+tool+%28CAT%29+in+patients+admitted+to+hospital+for+exacerbation&stitle=Thorax&title=Thorax&volume=68&issue=&spage=A204&epage=&aulast=Hoyles&aufirst=K.H.&auinit=K.H.&aufull=Hoyles+K.H.&coden=&isbn=&pages.

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99	Duplicate	Jacob A, Laurin C, Lavoie KL, Moullec G, Boudreau M, Lemiere C, Bacon S. The impact of body mass index on inpatient- versus outpatient-treated chronic obstructive pulmonary disease exacerbations. *Can. Respir. J.* [Internet] Montreal Behavioural Medicine Centre, Hopital du Sacre-Coeur de Montreal, Quebec.; 2013; 20: 237–242Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23717822 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23717822&id=doi:&issn=1198-2241&isbn=&volume=20&issue=4&spage=237&pages=237-42&date=2013&title=Canadian+Respiratory+Journal&atitle=The+impact+of+body+mass+index+on+inpatient-+versus+outpatient-treated+chronic+obstructive+pulmonary+disease+exacerbations.&aulast=Jacob&pid=%3Cauthor%3EJacob+A%3BLaurin+C%3BLavoie+KL%3BMoullec+G%3BBoudreau+M%3BLemiere+C%3BBa.
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102	Not a prediction model (neither prediction model nor multivariable association)	Johnston NW, Lambert K, Hussack P, De Verdier MG, Higenbottam T, Lewis J, Newbold P, Jenkins M, Norman GR, Coyle P V, McIvor RA. Detection of COPD exacerbations and compliance with patient-reported daily symptom diaries. *Chest* [Internet] N.W. Johnston, Firestone Institute for Respiratory Health, McMaster University, Hamilton, ON, L8N 4A6, Canada; 2013; 144:

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103	Not a prediction model (neither prediction model nor multivariable association)	Johnston NW, McIvor A, Lambert K, Greene JM, Hussack P, De Verdier MG, Higenbottam T, Lewis J, Newbold P, Herath A, Jenkins M. The Christmas season as a risk factor for chronic obstructive pulmonary disease exacerbations. *Can. Respir. J.* [Internet] Firestone Institute for Respiratory Health, McMaster University, Hamilton, ON, Canada Respiratory and Inflammation Therapy Area, Astra Zeneca, Lund, Sweden Respiratory and Inflammation Therapy Area, Astra Zeneca Charnwood, Loughborough, United Kingdom Bio; 2010; 17: 275–281Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-78650639139&partnerID=40&md5=42725a4a288ed1adf4a0a66212cc4d0b.
104	Included	Jones RC, Donaldson GC, Chavannes NH, Kida K, Dickson-Spillmann M, Harding S, Wedzicha JA, Price D, Hyland ME. Derivation and validation of a composite index of severity in chronic obstructive pulmonary disease: the DOSE Index. *Am. J. Respir. Crit. Care Med.* [Internet] Respiratory Research Unit, Peninsula Medical School, University of Plymouth, Devon, UK. rupert.jones@pms.ac.uk; 2009; 180: 1189–1195Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medc&AN=19797160 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19797160&id=doi:10.1164%2Frccm.200902-0271OC&issn=1073-449X&isbn=&volume=180&issue=12&spage=1189&pages=1189-95&date=2009&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Derivation+and+validation+of+a+composite+index+of+severity+in+chronic+obstructive+pulmonary+disease%3A+the+DOSE+Index.&aulast=Jones&pid=%3Cauthor%3EJones+RC%3BDon.
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105	Not a primary study (review)	Junod AF. Chronic obstructive pulmonary disease: 2. Short-term prognostic scores for acute exacerbations. *Rev. Med. Suisse* [Internet] 2014; 10: 192–196Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=24624737 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24624737&i

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106	Not the wanted study design (RCT, not only placebo arm)	Jurado Gámez B, Feu Collado N, Jurado García JC, García Gíl 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] Servicio de Neumología, Hospital Universitario Reina Sofía, Córdoba, Spain Grado de Fisioterapia, Facultad de Ciencias de la Salud, Universidad Católica San Antonio, Murcia, Spain Unidad de Apoyo Metodológico, IMIBIC, Hospital Universitario Reina Sofía, C; 2013; 49: 10–14Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84871713309&partnerID=40&md5=47482f60b654ddca06ed61cba8e427fc.
107	Not the wanted outcome	Karadeniz G, Polat G, Senol G, Buyuksirin M. C-reactive protein measurements as a marker of the severity of chronic obstructive pulmonary disease exacerbations. *Inflammation* [Internet] Department of Chest Diseases, Izmir Chest Diseases and Thoracic Surgery Hospital, Izmir, Turkey.; 2013; 36: 948–953Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23547018 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23547018&id=doi:10.1007%2Fs10753-013-9625-z&issn=0360-3997&isbn=&volume=36&issue=4&spage=948&pages=948-53&date=2013&title=Inflammation&atitle=C-reactive+protein+measurements+as+a+marker+of+the+severity+of+chronic+obstructive+pulmonary+disease+exacerbations.&aulast=Karadeniz&pid=%3Cauthor%3EKaradeniz+G%3BPolat+G%3BSenol+G%3BBuyuksirin+M%3C%2Fauthor%3E%3C.
108	Not a prediction model (neither prediction model nor multivariable association)	Karwat K, Kosciuch J, Chazan R. Is microembolism present and is it important element of COPD exacerbation? *Pol. Merkur. Lek.* [Internet] Klinika i Katedra Chorob Wewnetrznych, Pneumonologii i Alergologii AM, Warszawie.; 2005; 18: 385–388Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16161916 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16161916&id=doi:&issn=1426-9686&isbn=&volume=18&issue=106&spage=385&pages=385-8&date=2005&title=Polski+Merkuriusz+Lekarski&atitle=Czy+mozna+rozpoznac+mikrozatorowosc+i+czy+jest+ona+istotnym+czynnikiem+wplywajacym+na+przebieg+zaostrzenia+POChP%3F&aulast=Karwat&pid=%3Cauthor%3E

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109	Not the wanted outcome	Kelly JL, Bamsey O, Smith C, Lord VM, Shrikrishna D, Jones PW, Polkey MI, Hopkinson NS. Health status assessment in routine clinical practice: the chronic obstructive pulmonary disease assessment test score in outpatients. *Respiration* [Internet] NIHR Respiratory Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust and Imperial College, London, UK.; 2012; 84: 193–199Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=medl&AN=22441322 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22441322&i d=doi:10.1159%2F000336549&issn=0025- 7931&isbn=&volume=84&issue=3&spage=193&pages=193- 9&date=2012&title=Respiration&atitle=Health+status+assessment+in+rout ine+clinical+practice%3A+the+chronic+obstructive+pulmonary+disease+ass essment+test+score+in+outpatients.&aulast=Kelly&pid=%3Cauthor%3EKell y+JL%3BBamsey+O%3BSmith+C%3BLord+VM%3BShrikrishna+D%3.
110	Not the wanted outcome	Kim C, Park YB, Park SY, Park S, Kim CH, Park SM, Lee MG, Hyun IG, Jung KS, Kim DG. COPD patients with exertional desaturation are at a higher risk of rapid decline in lung function. *Yonsei Med. J.* [Internet] Department of Pulmonary and Critical Care Medicine, Hallym University Kangdong Sacred Heart Hospital, Seoul, South Korea Lung Research Institute of Hallym University College of Medicine, Chuncheon, South Korea; 2014; 55: 732– 738Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0- 84898761679&partnerID=40&md5=bb1619f2a03755b4fda784af06817c31.
111	No spirometry in COPD definition	Kim S, Emerman CL, Cydulka RK, Rowe BH, Clark S, Camargo CA, Investigators M. Prospective multicenter study of relapse following emergency department treatment of COPD exacerbation. *Chest* [Internet] Department of Emergency Medicine, Massachusetts General Hospital, 55 Fruit Street, Clinics Building 397, Boston, MA 02114, USA.; 2004; 125: 473– 481Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=medc&AN=14769727 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:14769727&i d=doi:&issn=0012- 3692&isbn=&volume=125&issue=2&spage=473&pages=473- 81&date=2004&title=Chest&atitle=Prospective+multicenter+study+of+rela pse+following+emergency+department+treatment+of+COPD+exacerbation .&aulast=Kim&pid=%3Cauthor%3EKim+S%3BEmerman+CL%3BCydulka+RK %3BRowe+BH%3BClark+S%3BCamargo+CA%3BMARC+Investigators%3C%2 Fauthor%3E%3CAN%3E1476972.
112	Included	Ko FW, Tam W, Tung AH, Ngai J, Ng SS, Lai K, Au KF, Hui DS. A longitudinal

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113	Not a primary study (editorial)	Kocks JWH, Van Molen TD. Risk indexes for COPD exacerbations II 2. *Chest* [Internet] J.W.H. Kocks, Department of General Practice, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; 2007; 131: 1986–1987Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L46981666 http://dx.doi.org/10.1378/chest.07-0198 http://sfx.metabib.ch/sfx_locater?sid=EMBASE&issn=00123692&id=doi:10.1378/chest.07-0198&atitle=Risk+indexes+for+COPD+exacerbations+II+[2]&stitle=Chest&title=Chest&volume=131&issue=6&spage=1986&epage=1987&aulast=Kocks&aufirst=Jan+Willem+H.&auinit=J.W.H.&aufull=Kocks+J.W.H.&coden=CHETB&isbn=&pages=1986-1987&date=2007&auinit1=J&auinitm=W.H.
114	Not a primary study (editorial)	Kocks JW, van der Molen T. Risk indexes for COPD exacerbations II. *Chest* [Internet] 2007; 131: 1986–1987; author reply 1987Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=17644836 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:17644836&id=doi:&issn=0012-3692&isbn=&volume=131&issue=6&spage=1986&pages=1986-7;+author+reply+1987&date=2007&title=Chest&atitle=Risk+indexes+for+COPD+exacerbations+II.&aulast=Kocks&pid=<author>Kocks+JW;van+der+Molen+T</author><AN>17644836</AN><DT>Comment</DT>.
115	Not the wanted outcome	Krommidas G, Kostikas K, Papatheodorou G, Koutsokera A, Gourgoulianis KI, Roussos C, Koulouris NG, Loukides S. Plasma leptin and adiponectin in COPD exacerbations: associations with inflammatory biomarkers. *Respir. Med.* [Internet] 1st Respiratory Medicine Department, University of Athens Medical School, Mesogeion 152 15669 Athens Greece. geokrommidas@yahoo.gr; 2010; 104: 40–46Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext

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116	Not the wanted study design (RCT, not only placebo arm)	Kunisaki KM, Niewoehner DE, Connett JE. Vitamin D levels and risk of acute exacerbations of chronic obstructive pulmonary disease: A prospective cohort study. *Am. J. Respir. Crit. Care Med.* [Internet] Minneapolis Veterans Affairs Medical Center, Pulmonary, 111N, One Veterans Drive, Minneapolis, MN 55417, United States Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, School of Public Health, University of Minnesota, Minneapolis, MN, Uni; 2012; 185: 286–290Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84856802147&partnerID=40&md5=38ed82b8adcd5ebdc1fcbbf5d3ac9a45.
117	Not a prediction model (neither prediction model nor multivariable association)	Künzli N, Perez L, Lurmann F, Hricko A, Penfold B, McConnell R. An attributable risk model for exposures assumed to cause both chronic disease and its exacerbations. *Epidemiology* [Internet] Institucio Catalana de Recerca I Estudis Avancats-ICREA Center for Research in Environmental Epidemiology (CREAL), Municipal Institute for Medical Research-IMIM, Barcelona, Spain Keck School of Medicine, University of Southern California-USC, Los Angeles,; 2008; 19: 179–185Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-39149142814&partnerID=40&md5=2633accd3d9138bb1ccbe8a62b007c7c.
	Theoretical model	
118	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Lange P, Marott JL, Vestbo J, Nordestgaard BG. Prevalence of night-time dyspnoea in COPD and its implications for prognosis. *Eur. Respir. J.* [Internet] P. Lange, Section of Social Medicine, Dept of Public Health, University of Copenhagen, DK-1014 Copenhagen K, Denmark; 2014; 43: 1590–1598Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L373440457 http://dx.doi.org/10.1183/09031936.00196713 http://sfx.metabib.ch/sfx_locater?sid=EMBASE&issn=13993003&id=doi:10.1183%2F09031936.00196713&atitle=Prevalence+of+night-time+dyspnoea+in+COPD+and+its+implications+for+prognosis&stitle=Eur.+Respir.+J.&title=European+Respiratory+Journal&volume=43&issue=6&spage=1590&epage=1598&aulast=Lange&aufirst=Peter&auinit=P.&aufull=Lange+P.&coden=ERJOE&isbn=&pages=1590-1598&date=2014.
119	Not a prediction model (focus on a	Laurin C, Labrecque M, Dupuis G, Bacon SL, Cartier A, Lavoie KL. Chronic obstructive pulmonary disease patients with psychiatric disorders are at

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120	Not a primary study (editorial)	Laurin C, Lavoie KL, Bacon SL. Relationship between depression and exacerbations in COPD: a response. *Eur. Respir. J.* [Internet] 2008; 32: 1129–1130Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18827167 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18827167&id=doi:10.1183%2F09031936.00079808&issn=0903-1936&isbn=&volume=32&issue=4&spage=1129&pages=1129-30&date=2008&title=European+Respiratory+Journal&atitle=Relationship+between+depression+and+exacerbations+in+COPD%3A+a+response.&aulast=Laurin&pid=%3Cauthor%3ELaurin+C%3BLavoie+KL%3BBacon+SL%3C%2Fauthor%3E%3CAN%3E18827167%3C%2FAN%3E%3CDT%3EComment%3C%.
121	Not the wanted outcome	Lee JH, Oh SY, Hwang I, Kim O, Kim HK, Kim EK. The prognostic role of B-type natriuretic peptide in acute exacerbation of chronic obstructive pulmonary disease. *Tuberc. Respir. Dis. (Seoul).* [Internet] J.-H. Lee, Department of Internal Medicine, Bundang CHA Hospital, Pochon CHA University, Seongnam, Kyeonggi-do 463-712, South Korea; 2004; 56: 600–610Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L39164311 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=03780066&id=doi:&atitle=The+prognostic+role+of+B-type+natriuretic+peptide+in+acute+exacerbation+of+chronic+obstructive+pulmonary+disease&stitle=Tuberc.+Respir.+Dis.&title=Tuberculosis+and+Respiratory+Diseases&volume=56&issue=6&spage=600&epage=610&aulast=Lee&aufirst=Ji+Hyun&auinit=J.H.&aufull=Lee+J.H.&coden=KHCHA&isbn=&pages=600-610&date=2004&auinit1=J&auinitm=H.
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123	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Liang B, Wang M, Yi Q, Feng Y. Association of gastroesophageal reflux disease risk with exacerbations of chronic obstructive pulmonary disease. *Dis. Esophagus* [Internet] Department of Respiratory Medicine, West China Hospital of Sichuan University, Chengdu, Sichuan, China; 2013; 26: 557–560Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84881551199&partnerID=40&md5=773a361d7c899fdff6173b18d87742c0.
124	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Liu Z, Zhang W, Zhang J, Zhou X, Zhang L, Song Y, Wang Z. Oral hygiene, periodontal health and chronic obstructive pulmonary disease exacerbations. *J. Clin. Periodontol.* [Internet] Department of Stomatology, Beijing ChaoYang Hospital Affiliated to, Capital Medical University, Chao Yang District Beijing 100020, China Department of Stomatology, Beijing Hai Dian Hospital, Beijing, China Division of Preventive Medicine, Brigham and Wome; 2012; 39: 45–52Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-83555173361&partnerID=40&md5=73afa100db5c64b848ee755c08d77b6a.
125	Not the wanted outcome	Lode H, Allewelt M, Balk S, De Roux A, Mauch H, Niederman M, Schmidt-Ioanas M. A prediction model for bacterial etiology in acute exacerbations of COPD. *Infection* [Internet] Helios Klinikum Emil von Behring, affiliated Free University Berlin, Chest Hospital Heckeshorn (Infectious Disease and Immunology), Zum Heckeshorn 33, 14109, Berlin, Germany. haloheck@zedat.fu-berlin.de; 2007; 35: 143–149Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=17565454 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:17565454&id=doi:&issn=0300-8126&isbn=&volume=35&issue=3&spage=143&pages=143-9&date=2007&title=Infection&atitle=A+prediction+model+for+bacterial+etiology+in+acute+exacerbations+of+COPD.&aulast=Lode&pid=%3Cauthor%3ELode+H%3BAllewelt+M%3BBalk+S%3BDe+Roux+A%3BMauch+H%3BNiederman+M%3BSchmidt-Ioanas+M%3C%2Fauthor%3E%3CAN%3E17565454%3C%2FAN%3E%3CDT%3EJournal+A.

126	Not a prediction model (neither prediction model nor multivariable association)	Lusuardi M, Lucioni C, De Benedetto F, Mazzi S, Sanguinetti CM, Donner CF. GOLD severity stratification and risk of hospitalisation for COPD exacerbations. *Monaldi Arch. Chest Dis.* [Internet] Department of Pulmonary Rehabilitation, S. Sebastiano Hospital, AUSL RE, Correggio, RE, Italy. lusuardimi@ausl.re.it; 2008; 69: 164–169Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19350838 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19350838&id=doi:&issn=1122-0643&isbn=&volume=69&issue=4&spage=164&pages=164-9&date=2008&title=Monaldi+Archives+for+Chest+Disease&atitle=GOLD+severity+stratification+and+risk+of+hospitalisation+for+COPD+exacerbations.&aulast=Lusuardi&pid=%3Cauthor%3ELusuardi+M%3BLucioni+C%3BDe+Benedetto+F%3BMazzi+S%3BSanguinetti+CM%3BDonner+CF%3C%2Fauthor%3E%3CAN%3E19350.
127	Not a prediction model (neither prediction model nor multivariable association)	Lusuardi M, Lucioni C, De Benedetto F, Mazzi S, Sanguinetti CM, Donner CF. Severity stratification and hospitalization risk in COPD exacerbations: Clinical data from the ICE (Italian costs for exacerbations) study. *Multidiscip. Respir. Med.* [Internet] M. Lusuardi, UOC di Riabilitazione Respiratoria, Ospedale S. Sebastiano, 42015 Correggio (RE), Italy; 2009; 4: 197–202Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L355260340 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=1828695X&id=doi:&atitle=Severity+stratification+and+hospitalization+risk+in+COPD+exacerbations%3A+Clinical+data+from+the+ICE+%28Italian+costs+for+exacerbations%29+study&stitle=Multidiscip.+Resp.+Med.&title=Multidisciplinary+Respiratory+Medicine&volume=4&issue=3&spage=197&epage=202&aulast=Lusuardi&aufirst=Mirco&auinit=M.&aufull=Lusuardi+M.&coden=&isbn=&pages=197-20.
128	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Ma CI, Xiao J, Wang K, Xu ZB, Chen B, Yin C, Feng YL. Risk factors for acute exacerbation of chronic obstructive pulmonary disease in patients who survived the wenchuan earthquake. *J. Sichuan Univ. (Medical Sci. Ed.* [Internet] Department of Respiratory Medicine, West China Hospital, Sichuan University, Chengdu 610041, China Department of Respiratory Medicine, Second People's Hospital of Chengdu, Chengdu 610021, China Department of Respiratory Medicine, Mianyang Central Hospital; 2012; 43: 566–572Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84865025995&partnerID=40&md5=5c1b71b7df2c856a88c46ad95da967e6.
129	Not a primary study	Mador MJ, Sethi S. Systemic inflammation in predicting COPD

	(editorial)	exacerbations. *JAMA - J. Am. Med. Assoc.* [Internet] Department of Medicine, University at Buffalo, State University of New York, Buffalo, NY, United States VA Western New York Healthcare System, 3495 Bailey Ave, Buffalo, NY 14215, United States; 2013; 309: 2390–2391Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84878866743&partnerID=40&md5=4470f4debf9d74fb5bbc039754f4d80f.
130	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Makris D, Tzanakis N, Damianaki A, Ntaoukakis E, Neofytou E, Zervou M, Siafakas NM, Tzortzaki EG. Microsatellite DNA instability and COPD exacerbations. *Eur. Respir. J.* [Internet] Department of Thoracic Medicine, Medical School, University of Crete, 71110 Heraklion Crete, Greece.; 2008; 32: 612–618Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18508815 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18508815&id=doi:10.1183%2F09031936.00169307&issn=0903-1936&isbn=&volume=32&issue=3&spage=612&pages=612-8&date=2008&title=European+Respiratory+Journal&atitle=Microsatellite+DNA+instability+and+COPD+exacerbations.&aulast=Makris&pid=%3Cauthor%3EMakris+D%3BTzanakis+N%3BDamianaki+A%3BNtaoukakis+E%3BNeofytou+E%3BZervou+M%3BSiafakas+NM%3BTzortzaki+EG%3C%2Fauth.
131	Included	Marin JM, Carrizo SJ, Casanova C, Martinez-Camblor P, Soriano JB, Agusti AG, Celli BR. Prediction of risk of COPD exacerbations by the BODE index. *Respir. Med.* [Internet] Hospital Miguel Servet, Instituto Aragones de Ciencias de la Salud, Zaragoza, Spain. jmmarint@unizar.es; 2009; 103: 373–378Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19013781 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19013781&id=doi:10.1016%2Fj.rmed.2008.10.004&issn=0954-6111&isbn=&volume=103&issue=3&spage=373&pages=373-8&date=2009&title=Respiratory+Medicine&atitle=Prediction+of+risk+of+COPD+exacerbations+by+the+BODE+index.&aulast=Marin&pid=%3Cauthor%3EMarin+JM%3BCarrizo+SJ%3BCasanova+C%3BMartinez-Camblor+P%3BSoriano+JB%3BAgusti+AG%3BCelli+BR%3C%2Fauthor%3E%3CAN%3E1.
132	Not a COPD cohort	Marin JM, Soriano JB, Carrizo SJ, Boldova A, Celli BR. Outcomes in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: the overlap syndrome. *Am. J. Respir. Crit. Care Med.* [Internet] Respiratory Service, Hospital Universitario Miguel Servet, Zaragoza 50009, Spain. jmmarint@unizar.es; 2010; 182: 325–331Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20378728 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:20378728&i

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133	Not the wanted outcome	Martinez-Garcia MA, de la Rosa Carrillo D, Soler-Cataluna JJ, Donat-Sanz Y, Serra PC, Lerma MA, Ballestin J, Sanchez I V, Selma Ferrer MJ, Dalfo AR, Valdecillos MB. Prognostic value of bronchiectasis in patients with moderate-to-severe chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* [Internet] Pneumology Service, Polytechnic and University La Fe Hospital, Valencia, Spain. mianmartinezgarcia@gmail.com; 2013; 187: 823–831Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23392438 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23392438&id=doi:10.1164%2Frccm.201208-1518OC&issn=1073-449X&isbn=&volume=187&issue=8&spage=823&pages=823-31&date=2013&title=American+Journal+of+Respiratory+%26+Critical+Care+Medicine&atitle=Prognostic+value+of+bronchiectasis+in+patients+with+moderate-to-severe+chronic+obstructive+pulmonary+disease.&aulast=Martinez-Garcia&pid=%3Cauthor%3EMartinez-Garcia+.
134	Not the wanted outcome	Matkovic Z, Huerta A, Soler N, Domingo R, Gabarrus A, Torres A, Miravitlles M. Predictors of adverse outcome in patients hospitalised for exacerbation of chronic obstructive pulmonary disease. *Respiration* [Internet] Institut d'Investigacions Biomediques August Pi i Sunyer, Hospital Clinic, Ciber de Enfermedades Respiratorias, Barcelona, Spain.; 2012; 84: 17–26Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22327370 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22327370&id=doi:10.1159%2F000335467&issn=0025-7931&isbn=&volume=84&issue=1&spage=17&pages=17-26&date=2012&title=Respiration&atitle=Predictors+of+adverse+outcome+in+patients+hospitalised+for+exacerbation+of+chronic+obstructive+pulmonary+disease.&aulast=Matkovic&pid=%3Cauthor%3EMatkovic+Z%3BHuerta+A%3BSoler+N%3BDomingo+R%3BGabarrus+A%3BTorres+A%3BMiravitl.
135	Not the wanted study design (ecological study)	McAllister DA, Morling JR, Fischbacher CM, MacNee W, Wild SH. Socioeconomic deprivation increases the effect of winter on admissions to hospital with COPD: Retrospective analysis of 10 years of national hospitalisation data. *Prim. Care Respir. J.* [Internet] Centre for Population Health Sciences, The University of Edinburgh, Medical School, Edinburgh,

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136	Not a prediction model (neither prediction model nor multivariable association)	McKellar A, Cottrell WN, Whelan A. BODE score is a useful predictor of hospital admission in rural patients with chronic obstructive pulmonary disease. *Respirology* [Internet] Pharmacy Department, Golburn Base Hospital, Golburn, New South Wales, Australia. alice.mckellar@gsahs.health.nsw.gov.au; 2008; 13: 438–443Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18399869 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18399869&id=doi:10.1111%2Fj.1440-1843.2007.01169.x&issn=1323-7799&isbn=&volume=13&issue=3&spage=438&pages=438-43&date=2008&title=Respirology&atitle=BODE+score+is+a+useful+predictor+of+hospital+admission+in+rural+patients+with+chronic+obstructive+pulmonary+disease.&aulast=McKellar&pid=%3Cauthor%3EMcKellar+A%3BCottrell+WN%3BWhelan+A%3C%2Fauthor%3E%3CAN%3E.
137	Not the wanted outcome	Medina AM, Marteles MS, Saiz EB, Martinez SS, Laiglesia FR, Rodriguez JA, Perez-Calvo JI. Prognostic utility of NT-proBNP in acute exacerbations of chronic pulmonary diseases. *Eur. J. Intern. Med.* [Internet] Internal Medicine Service, Hospital Virgen de la Luz, Cuenca, Spain.; 2011; 22: 167–171Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21402247 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:21402247&id=doi:10.1016%2Fj.ejim.2010.12.002&issn=0953-6205&isbn=&volume=22&issue=2&spage=167&pages=167-71&date=2011&title=European+Journal+of+Internal+Medicine&atitle=Prognostic+utility+of+NT-proBNP+in+acute+exacerbations+of+chronic+pulmonary+diseases.&aulast=Medina&pid=%3Cauthor%3EMedina+AM%3BMarteles+MS%3BSaiz+EB%3BMartinez+SS%3BLaiglesia+FR%3BRodrig.
138	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Miravitlles M, Calle M, Alvarez-Gutierrez F, Gobartt E, López F, Martín A. Exacerbations, hospital admissions and impaired health status in chronic obstructive pulmonary disease. *Qual. Life Res.* [Internet] Servei de Pneumologia, Institut Clínic del Tòrax (IDIBAPS), Hospital Clinic, Barcelona, Spain Servicio de Neumología, Red Respira RTIC 03/11 ISCIII, Hospital Clínico San Carlos, Madrid, Spain Servicio de Neumología, Red Respira RTIC 03/11 ISCIII, Hospital; 2006; 15: 471–480Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-33645108515&partnerID=40&md5=d164a21bc840849ae4859d199dd9040

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139	Not a COPD cohort	Miravitlles M, Murio C, Guerrero T. Factors associated with relapse after ambulatory treatment of acute exacerbations of chronic bronchitis. DAFNE Study Group. *Eur. Respir. J.* [Internet] Dept of Pneumology, Vall d'Hebron General University Hospital, Barcelona, Spain.; 2001; 17: 928–933Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=med4&AN=11488328 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:11488328&i d=doi:&issn=0903- 1936&isbn=&volume=17&issue=5&spage=928&pages=928- 33&date=2001&title=European+Respiratory+Journal&atitle=Factors+associ ated+with+relapse+after+ambulatory+treatment+of+acute+exacerbations+ of+chronic+bronchitis.+DAFNE+Study+Group.&aulast=Miravitlles&pid=%3C author%3EMiravitlles+M%3BMurio+C%3BGuerrero+T%3C%2Fauthor%3E% 3CAN%3E114883.
140	Included	Moberg M, Vestbo J, Martinez G, Williams JE, Ladelund S, Lange P, Ringbaek T. Validation of the i-BODE index as a predictor of hospitalization and mortality in patients with COPD Participating in pulmonary rehabilitation. *Copd J. Chronic Obstr. Pulm. Dis.* [Internet] 1Section of Respiratory Medicine, Hvidovre University Hospital , Hvidovre , Denmark.; 2014; 11: 381–387Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=prem&AN=24111845 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:24111845&i d=doi:10.3109%2F15412555.2013.836171&issn=1541- 2563&isbn=&volume=11&issue=4&spage=381&pages=381- 7&date=2014&title=Copd%3A+Journal+of+Chronic+Obstructive+Pulmonar y+Disease&atitle=Validation+of+the+i- BODE+index+as+a+predictor+of+hospitalization+and+mortality+in+patient s+with+COPD+Participating+in+pulmonary+rehabilitation.&aulast=Moberg &pid=%3Cau.
141	Not a primary study (editorial)	Mohan A, Bhatt SP, Guleria R. Risk indexes for exacerbations due to COPD: need to validate using broader criteria. *Chest* [Internet] 2007; 132: 735; author reply 735–736Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=med5&AN=17699152 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:17699152&i d=doi:&issn=0012- 3692&isbn=&volume=132&issue=2&spage=735&pages=735;+author+reply +735- 6&date=2007&title=Chest&atitle=Risk+indexes+for+exacerbations+due+to +COPD:+need+to+validate+using+broader+criteria.&aulast=Mohan&pid=<

		author>Mohan+A;Bhatt+SP;Guleria+R</author><AN>17699152</AN><DT> Comment</DT>.
142	Not the wanted study design (ecological study)	Monteiro A, Carvalho V, Góis J, Sousa C. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): Case study in Porto. *Int. J. Biometeorol.* [Internet] ISPUP (Institute of Public Health from the University of Porto), CITTA, Department of Geography, University of Porto, Project FCT PTDC/SAU-ESA/73016/2006, Via Panoramica s/n, 4050-564 Porto, Portugal ISPUP (Institute of Public Health from the University o; 2013; 57: 857–870Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84886641308&partnerID=40&md5=e1fda9b4e3159e7c92198f61172a9027.
143	Not a COPD cohort	Moolgavkar SH, Luebeck EG, Anderson EL. Air pollution and hospital admissions for respiratory causes in Minneapolis-St. Paul and Birmingham. *Epidemiology* [Internet] Fred Hutchinson Cancer Res. Center, Seattle, WA, United States Sciences International, Inc., Alexandria, VA, United States Fred Hutchinson Cancer Res. Center, 1124 Columbia Street, MP-665, Seattle, WA 98104, United States; 1997; 8: 364–370Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-0030957688&partnerID=40&md5=158eb0fa893dbd6b7a7e88630885c4db.
144	Included	Motegi T, Jones RC, Ishii T, Hattori K, Kusunoki Y, Furutate R, Yamada K, Gemma A, Kida K. A comparison of three multidimensional indices of COPD severity as predictors of future exacerbations. *Int. J. Copd* [Internet] Division of Pulmonary Medicine, Department of Internal Medicine, Nippon Medical School, Tokyo, Japan. mo-dr@nms.ac.jp; 2013; 8: 259–271Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23754870 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23754870&id=doi:10.2147%2FCOPD.S42769&issn=1176-9106&isbn=&volume=8&issue=&spage=259&pages=259-71&date=2013&title=International+Journal+of+Copd&atitle=A+comparison+of+three+multidimensional+indices+of+COPD+severity+as+predictors+of+future+exacerbations.&aulast=Motegi&pid=%3Cauthor%3EMotegi+T%3BJones+RC%3BIshii+T%3BHattori+K%3BKusunoki+Y%3BFurutate+R%3BY.
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

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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+Count+Predicts+Acute+Exacerbations+in+a+US+Cohort+with+COPD&stitle=PLoS+ONE&title=PLoS+ONE&volume=8&issue=4&spage=&epage=&aulast=Moy&aufirst=Marilyn+L.&auinit=M.L.&aufull=Moy+M.L.&coden=&isbn=&pages=-&date=2013&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_locater?sid=OVID:medline&id=pmid:17218552&id=doi:&issn=0012-3692&isbn=&volume=131&issue=1&spage=20&pages=20-8&date=2007&title=Chest&atitle=Risk+indexes+for+exacerbations+and+hospitalizations+due+to+COPD.&aulast=Niewoehner&pid=%3Cauthor%3ENiewoehner+DE%3BLokhnygina+Y%3BRice+K%3BKuschner+WG%3BSharafkhaneh+A%3BSarosi+GA%3BKrumpe+P%3BPieper+K%3BKesten+S%3C%2Fauthor%3E%3CAN%3E17218552%3C%2F.

149	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: 521–526Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=22069363 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22069363&id=doi:10.2147%2FCOPD.S24420&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%3.
150	Not a prediction model (focus on a particular predictor without the wanted adjustment)	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: 823–830Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=19837823 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19837823&id=doi:10.1378%2Fchest.09-0764&issn=0012-3692&isbn=&volume=137&issue=4&spage=823&pages=823-30&date=2010&title=Chest&atitle=The+COPD+Helplessness+Index%3A+a+new+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.
151	Not the wanted outcome	Omachi TA, Yelin EH, Katz PP, Blanc PD, Eisner MD. The COPD severity score: a dynamic prediction tool for health-care utilization. *Copd J. Chronic Obstr. 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: 339–346Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19353347 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19353347&id=doi:10.1080%2F15412550802522700&issn=1541-2563&isbn=&volume=5&issue=6&spage=339&pages=339-46&date=2008&title=Copd%3A+Journal+of+Chronic+Obstructive+Pulmonary+Disease&atitle=The+COPD+severity+score%3A+a+dynamic+prediction+t

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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=15608479 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:15608479&id=doi:&issn=1011-7571&isbn=&volume=14&issue=1&spage=35&pages=35-40&date=2005&title=Medical+Principles+%26+Practice&atitle=Prognostic+factors+in+the+management+of+exacerbation+of+chronic+obstructive+pulmonary+disease+in+Kuwait.&aulast=Onadeko&pid=%3Cauthor%3EOnadeko+BO%3BKhadadah+M%3BAbdella+N%3BMukhtar+M%3BMourou+M%3BQurtom+M%3BSamad+M%3BAl-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=16354849 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16354849&id=doi:&issn=0012-3692&isbn=&volume=128&issue=6&spage=3810&pages=3810-6&date=2005&title=Chest&atitle=A+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>Comparative+Study</DT>.

155	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_locater?sid=OVID:medline&id=pmid:15338802&id=doi:&issn=0954-6111&isbn=&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</AN><DT>Journal+Article</DT>.
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_locater?sid=OVID:medline&id=pmid:24797671&id=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%3BYu+CH%3BShiu.
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. eylemozgur@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_locater?sid=OVID:medline&id=pmid:22348294&id=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+dynamic+hyperinflation+and+exercise+capacity+in+the+prediction+of+morbidity+and+mortality+in+COPD.&aulast=Ozgur&pid=%3Cauthor%3EOzgur+ES%3BNayci+SA%3BOzge+C%3BTasdelen+B%3C%2Fauth.

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: 691–697Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84879111667&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: 815–823Available 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: 1114–1121Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16484677 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16484677&id=doi:&issn=1073-449X&isbn=&volume=173&issue=10&spage=1114&pages=1114-21&date=2006&title=American+Journal+of+Respiratory+%26+Critical+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%.
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: 189–196Available from:

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162	Included	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 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=01479563&id=doi:10.1016%2Fj.hrtlng.2007.09.007&atitle=Predictive+validity+of+short-form+health+survey+%5B36+items%5D+scales+for+chronic+obstructive+pulmonary+disease+exacerbation&stitle=Heart+Lung+J.+Acute+Crit.+Care&title=Heart+and+Lung%3A+Journal+of+Acute+and+Critical+Care&volume=37&issue=5&spage=356&epage=365&aulas.
163	Not a prediction model (focus on a particular predictor without the wanted adjustment)	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.
164	Not the wanted study design (ecological study)	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&spage=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+M%3BSimic+D%3BHrsak+J%3C%2Fauthor%3E%3CAN%3E972

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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 front 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 Horten-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_locater?sid=OVID:medline&id=pmid:18321938&id=doi:10.1183%2F09031936.00120107&issn=0903-1936&isbn=&volume=32&issue=1&spage=53&pages=53-60&date=2008&title=European+Respiratory+Journal&atitle=Relationship+between+depression+and+exacerbations+in+COPD.&aulast=Quint&pid=%3Cauthor%3EQuint+JK%3BBaghai-Ravary+R%3BDonaldson+GC%3BWedzicha+JA%3C%2Fauthor%3E%3CAN%3E18321938%3C%2FAN%3E%3CDT%3EJourna.

169	Not a primary study (editorial)	Rajagopalan S, Dellagrottaglie S, Sanz J. Pulmonary arterial enlargement and COPD exacerbations. *N. Engl. J. Med.* [Internet] 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: 2254Available 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.* [Internet] Respiratory and Intensive Care Medicine, Hotel-Dieu, Paris, Descartes University, France. nicolas.roche@htd.aphp.fr; 2008; 32: 953–961Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=18508819 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18508819&id=doi:10.1183%2F09031936.00129507&issn=0903-1936&isbn=&volume=32&issue=4&spage=953&pages=953-61&date=2008&title=European+Respiratory+Journal&atitle=Predictors+of+outcomes+in+COPD+exacerbation+cases+presenting+to+the+emergency+department.&aulast=Roche&pid=%3Cauthor%3ERoche+N%3BZureik+M%3BSoussan+D%3BNeukirch+F%3BPerrotin+D%3BUrgence+BPCO+%28COP.
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.* [Internet] A.M.E. Rodriguez, International Fellow AARC, Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain; 2012; 16: 1133–1134Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L365924614 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=11283602&id=doi:&atitle=A+link+of+non-invasive+ventilation+in+chronic+hypercapnic+COPD+patients+with+pulmonary+hypertension.+A+new+index+of+prognosis&stitle=Eur.+Rev.+Med.+Pharmacol.+Sci.&title=European+Review+for+Medical+and+Pharmacological+Sciences&volume=16&issue=8&spage=1133&epage=1134&aulast=Rodriguez&aufirst=Antonio+M.+Esquinas&auinit=A.M.E.&aufull=Rodriguez.
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.* [Internet] Department of Internal Medicine, Islamic Azad University, Najafabad Branch, Najafabad, Iran Young Researchers Clubs, Islamic Azad University, Najafabad Branch, Najafabad, Iran; 2010; 19: 253–256Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-

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173	Not the wanted outcome	Rolink M, van Dijk W, van den Haak-Rongen S, Pieters W, Schermer T, van den Bemt L. Using the DOSE index to predict changes in health status of patients with COPD: a prospective cohort study. *Prim. Care Respir. J.* [Internet] Radboud University Nijmegen Medical Centre, Department of Primary and Community Care Nijmegen, The Netherlands.; 2013; 22: 169–174Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23538702 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:23538702&id=doi:10.4104%2Fpcrj.2013.00033&issn=1471-4418&isbn=&volume=22&issue=2&spage=169&pages=169-74&date=2013&title=Primary+Care+Respiratory+Journal&atitle=Using+the+DOSE+index+to+predict+changes+in+health+status+of+patients+with+COPD%3A+a+prospective+cohort+study.&aulast=Rolink&pid=%3Cauthor%3ERolink+M%3Bvan+Dijk+W%3Bvan+den+Haak-Rongen+S%3BPieters.
174	Not the wanted outcome	Schembri S, Anderson W, Morant S, Winter J, Thompson P, Pettitt D, MacDonald TM, Winter JH. A predictive model of hospitalisation and death from chronic obstructive pulmonary disease. *Respir. Med.* [Internet] Department of Medicine and Therapeutics, University of Dundee, Dundee DD1 9SY, United Kingdom. sschembri@nhs.net; 2009; 103: 1461–1467Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19515547 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19515547&id=doi:10.1016%2Fj.rmed.2009.04.021&issn=0954-6111&isbn=&volume=103&issue=10&spage=1461&pages=1461-7&date=2009&title=Respiratory+Medicine&atitle=A+predictive+model+of+hospitalisation+and+death+from+chronic+obstructive+pulmonary+disease.&aulast=Schembri&pid=%3Cauthor%3ESchembri+S%3BAnderson+W%3BMorant+S%3BWinter+J%3BThompson+P%3BPettitt+D%3BMacD.
175	Not a primary study (editorial)	Seemungal TAR, Wedzicha JA. Exacerbation frequency and FEV1 decline of COPD: Is it geographic? *Eur. Respir. J.* [Internet] Dept. of Clinical Medical Sciences, St Augustine Campus, University of the West Indies, St Augustine, Trinidad and Tobago National Heart and Lung Institute, Royal Brompton Campus, Imperial College London, London SW3 6LR, United Kingdom; 2014; 43: 1220–1222Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84899866541&partnerID=40&md5=6cb9045a5b543e0c881c2aca04d508bd.
176	Not a primary study	Shen S, Gershon A, To T. Can the air quality health index (aqhi) depict

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177	Not the wanted outcome	Shorr AF, Sun X, Johannes RS, Yaitanes A, Tabak YP. Validation of a novel risk score for severity of illness in acute exacerbations of COPD. *Chest* [Internet] Pulmonary and Critical Care Medicine, Washington Hospital Center, 110 Irving St, NW, Washington, DC 20010, USA. andrew.shorr@gmail.com; 2011; 140: 1177–1183Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21527510 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:21527510&id=doi:10.1378%2Fchest.10-3035&issn=0012-3692&isbn=&volume=140&issue=5&spage=1177&pages=1177-83&date=2011&title=Chest&atitle=Validation+of+a+novel+risk+score+for+severity+of+illness+in+acute+exacerbations+of+COPD.&aulast=Shorr&pid=%3Cauthor%3EShorr+AF%3BSun+X%3BJohannes+RS%3BYaitanes+A%3BTabak+YP%3C%2Fauthor%3E%3CAN%3E21527510%3C%2FAN%3E%3CDT%3.
178	Not a primary study (poster)	Shorr A, Sun X, Johannes R, Tabak Y. Novel BAP-65 score outperforms CURB-65 score for predicting outcomes in acute exacerbations of chronic obstructive disease. *Am. J. Respir. Crit. Care Med.* [Internet] A. Shorr, Potomac, United States; 2010; 181Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L70839860 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=1073449X&id=doi:&atitle=Novel+BAP-65+score+outperforms+CURB-65+score+for+predicting+outcomes+in+acute+exacerbations+of+chronic+obstructive+disease&stitle=Am.+J.+Respir.+Crit.+Care+Med.&title=American+Journal+of+Respiratory+and+Critical+Care+Medicine&volume=181&issue=1&spage=&epage=&aulast=Shorr&aufirst=A.&auinit=A.&aufull=Shorr+A.&coden=&isbn=&pages=-&date=2010&aui.
179	Not retrieved	Siddhuraj C, Srinivasan R, Shanmuganathan A, Thilagavathy G. To assess correlation of BODE index with AECOPD and pulmonary hypertension. *Lung India* [Internet] C. Siddhuraj, Department of TB and Chest Medicine, Meenakshi Medical College Hospital, Research Institute, Kanchipuram, Tamil Nadu, India; 2013; 30: S9–S10Available from:

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180	Not a primary study (editorial)	Simons S, van der Heijden E, Heijdra Y. The prevalence of pulmonary embolism in acute exacerbations of COPD. *Chest* [Internet] 2009; 136: 645; author reply 645–646Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=19666769 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:19666769&id=doi:10.1378%2Fchest.08-2644&issn=0012-3692&isbn=&volume=136&issue=2&spage=645&pages=645%3B+author+reply+645-6&date=2009&title=Chest&atitle=The+prevalence+of+pulmonary+embolism+in+acute+exacerbations+of+COPD.&aulast=Simons&pid=%3Cauthor%3ESimons+S%3Bvan+der+Heijden+E%3BHeijdra+Y%3C%2Fauthor%3E%3CAN%3E19666769%3C%2FAN%3E%3CDT%3EComment%3C%2FDT.
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183	Not retrieved	Stamatis P, Michalopoulou H, Stamatis D. N-terminal pro-brain natriuretic peptide as a prognostic marker in patients with exacerbation of chronic obstructive pulmonary disease. *Crit. Care* [Internet] P. Stamatis, Metaxa Hospital, Athens, Greece; 2013; 17: S50Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L71030431 http://dx.doi.org/10.1186/cc12071 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=13648535&id=doi:10.1186%2Fcc12071&atitle=N-terminal+pro-brain+natriuretic+peptide+as+a+prognostic+marker+in+patients+with+exacerbation+of+chronic+obstructive+pulmonary+disease&stitle=Crit.+Care&title=Critical+Care&volume=17&issue=&spage=S50&epage=&aulast=Stamatis&aufirst=P.&auinit=P.&aufull=Stamatis+P.&coden=&isbn=&pages=S50-&date=.
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195	Not a COPD cohort	Tata LJ, West J, Harrison T, Farrington P, Smith C, Hubbard R. Does influenza vaccination increase consultations, corticosteroid prescriptions, or exacerbations in subjects with asthma or chronic obstructive pulmonary disease? *Thorax* [Internet] Div. of Epidemiol. and Public Health, University of Nottingham, Nottingham, United Kingdom Division of Respiratory Medicine, Nottingham City Hospital, Nottingham, United Kingdom Statistics, Open University, Milton Keynes, United Kingdom; 2003; 58: 835–839Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-

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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%2F1753465809102553&issn=1753-4658&isbn=&volume=3&issue=1&spage=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	Valvi D, Mannino DM, Mullerova H, Tal-Singer R. Fibrinogen, chronic obstructive pulmonary disease (COPD) and outcomes in two United States

		cohorts. *Int. J. Copd* [Internet] Department of Preventive Medicine and Environmental Health, University of Kentucky College of Public Health, Lexington, KY 40536, USA.; 2012; 7: 173–182Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext &D=medl&AN=22419864 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22419864&i d=doi:10.2147%2FCOPD.S29892&issn=1176-9106&isbn=&volume=7&issue=&spage=173&pages=173-82&date=2012&title=International+Journal+of+Copd&atitle=Fibrinogen%2 C+chronic+obstructive+pulmonary+disease+%28COPD%29+and+outcomes +in+two+United+States+cohorts.&aulast=Valvi&pid=%3Cauthor%3EValvi+ D%3BMannino+DM%3BMullerova+H%3BTal-Singer+R%3C%2Fauthor%3E%3CAN.
206	Not a COPD cohort	Van Abeelen AFM, Elias SG, De Jong PA, Grobbee DE, Bossuyt PMM, Van Der Schouw YT, 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=9a6282c4d25938a333e9f7ffebd7339a.
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=medl&AN=20846194 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:20846194&i d=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=Mul ticomponent+staging+indices+for+chronic+obstructive+pulmonary+disease +in+daily+patient+care%3A+what%27s+the+yield%3F.&aulast=van+den+Be mt&pid=%3Cauthor%3Evan+den+Bemt+L%3B.
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-

		84863471807&partnerID=40&md5=cc46a9709cac1fd6fefa435182a724b9.
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_locater?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+Dis ease&atitle=Predictors+of+hospital+admission+in+exacerbations+of+chron ic+obstructive+pulmonary+disease.&aulast=Vidal&pid=%3Cauthor%3EVida l+S%3BGonzalez+N%3BBarrio+I%3BRivas-Ruiz+F%3BBar.
	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_locater?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+exacer bations+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%3CAN%3E883 6664%3C%2FAN%3E%3CDT%3.
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=c241392cf672f4b853b50978faf9544d.
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:

		http://www.scopus.com/inward/record.url?eid=2-s2.0-80052604375&partnerID=40&md5=cec55412be7a2c79702b3341c8a76c0c.
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://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%3BMahler+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://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.
216	Not the wanted	Wu EQ, Birnbaum HG, Cifaldi M, Kang Y, Mallet D, Colice G. Development

	outcome	of a COPD severity score. *Curr. Med. Res. Opin.* [Internet] Analysis Group, Inc., Boston, MA 02199, USA.; 2006; 22: 1679–1687Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&AN=16968571 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:16968571&id=doi:&issn=0300-7995&isbn=&volume=22&issue=9&spage=1679&pages=1679-87&date=2006&title=Current+Medical+Research+&+Opinion&atitle=Development+of+a+COPD+severity+score.&aulast=Wu&pid=<author>Wu+EQ;Birnbaum+HG;Cifaldi+M;Kang+Y;Mallet+D;Colice+G</author><AN>16968571</AN><DT>Journal+Article</DT>.
217	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 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:18755925&id=doi:10.1164%2Frccm.200804-619OC&issn=1073-449X&isbn=&volume=178&issue=9&spage=913&pages=913-20&date=2008&title=American+Journal+of+Respiratory+%26+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 Falcones 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 Illes 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 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:22797131&id=doi:&issn=0012-3692&isbn=&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=%3Cauthor%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.

219	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, Chao Yang 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&id=doi:10.1186%2F2047-783X-19-18&issn=0949-2321&isbn=&volume=19&issue=1&spage=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%2Fauthor%3E%3CAN%3E24713.
220	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=fdf71df548af19cdb1021ea8ad3c971d.
221	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&id=doi:&issn=0002-0729&isbn=&volume=35&issue=1&spage=33&pages=33-7&date=2006&title=Age+%26+Ageing&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%3EYeo+J%3BKarimova+G%3BBansal+S%3C%2Fauthor%3E%3CAN%3E16364931%3C%2FAN%3E%3CDT%3EComparativ.
222	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, Changhai Hospital, Second Military Medical University, Shanghai 200433, China; 2013; 34: 839–845Available from: http://www.embase.com/search/results?subaction=viewrecord&from=exp

		ort&id=L369677874 http://dx.doi.org/10.3724/SP.J.1008.2013.00839 http://sfx.metabib.ch/sfx_locator?sid=EMBASE&issn=0258879X&id=doi:10.3724%2FSP.J.1008.2013.00839&atitle=Relationship+between+chronic+obstructive+pulmonary+disease+%28COPD%29+assessment+test+score+and+prognostic+factors+of+COPD+patients&stitle=Acad.+J.+Second+Mil.+Med.+Univ.&title=Academic+Journal+of+Second+Military+Medical+University&volume=34&issue=8&spage=839&epage.
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: 2594–2598Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=25043073 http://sfx.metabib.ch/sfx_locater?sid=OVID:medline&id=pmid:25043073&id=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).

Reasons for exclusion: "source 2 for full-text assessement" (82 papers)

		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=pmcentrez&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; .

7	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.
8	No performance measure 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, UK.; 2004; 169: 1298–1303Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med5&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		
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.

	wanted adjustment)	
14	Not a COPD cohort	Cano NJM. C-Reactive Protein and Body Mass Index Predict Outcome in End-Stage Respiratory Failure<xref rid="AFF1">[*]</xref>. *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=pmcentrez&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 \ f Acute Exacerbation of Severe Chronic Obstrurtive 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, Lunacsek 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	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 Garcini 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 measuremen.
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, 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.
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)	Garcia-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, 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.
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, Garcia-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 Gíl 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.

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, Maltais 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.

	without the wanted adjustment)	
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	Rabe KF, Fabbri LM, Vogelmeier C, Kögler H, Schmidt H, Beeh KM, Glaab T. Seasonal

	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.
64	Not a prediction model (focus on a particular predictor without the wanted adjustment)	Rascon-Aguilar IE, Pamer M, Wludyka P, Cury J, Coultas D, Lambiase LR, Nahman NS, Vega KJ. Role of gastroesophageal reflux symptoms in exacerbations of COPD. *Chest* 2006; 130: 1096–1101.
65	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.
66	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.
67	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.
68	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.
69	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.
70	Not the wanted	Soler JJ, Sánchez L, Román P, Martínez MÁ, Perpiñá M. Risk factors of emergency

	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, DeMeo 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.
	, first 10 papers in this list	
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:

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

	Bertens	Almagro 2014	Takahashi	Müllerova	Brusse-Keizer	Marin	Garcia-Aymerich	Jakob	Faganello	Ong	Gudmundsson	Thomsen	Hurst	Ko	Lee	Jones	Chen	Motegi	Suetomo	Almagro 2006	Moy	Parshall	Moberg	Echave	Amalakuhan
Study flow[1]	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	−
Predictors[2]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	?
Outcome[3]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	−	?	
Statistical analysis[4]	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	−	−	−	−	−	+	−	−	−	−
Perfomance measures[5]	+	−	+	+	+	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−
Validation of prediction model[6]	+	+	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

(+) Low risk of bias (?) Medium risk of bias (−) High risk of bias (x) 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? Predcictors 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 pre initial predictors. Possiblity of DOWNGRADE: if less than 10 events per perdictor 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) H	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 L	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 H	AUC (data obtained contacting the authors)
Validation L	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 L	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 L	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 L	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 H	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 H	R-square; Hosmer-Lemeshow (chi-square and p-value) (data in part obtained contacting the authors)
Validation X	

	Amalakuhan (2012)
Flow H	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 U	Defined on the onset of the study (55-60 variables; abstract and article data is not consistent).
Outcome U	Definition of exacerbation: unclear
Statistical analysis H	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 H	Mean AUC among the 200 simulation, sensitivity, specificity, PPV, NPV.
Validation	

X	

		Bertens (2013)
Flow (Derivation cohort) L		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 L		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 L		Definition of exacerbation: "operational" - symptomatic deterioration requiring pulsed oral steroid use or hospitalisation.
Statistical analysis L		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 L	AUC with 95% CI; Hosmer-Lemeshow test (chi-square and p-value); r-square (data in part obtained contacting the authors)
Validation L	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 L	Setting and sampling: patients included in the control group of a self-management study in COPD, at the department of Pulmonology in Enschede study; Netherland; 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 L	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 L	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 H	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 L	AUC with 95% CI; Hosmer-Lemeshow test; r-square (COX & Snell, Negelkerke) (data in part obtained contacting the authors)
Validation X	

	Chen (2005)
Flow L	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 dis- charge.. 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 avail- able 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 L	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 L	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 H	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 H	R-square Negelkerke, -2LogLikelihood
Validation X	

	Echave-Sustaeta (2010)
Flow L	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 U	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 H	Definition of exacerbation: re-hospitalisations for respiratory causes
Statistical analysis H	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 H	AUC, r-square
Validation X	

	Faganello (2010)
Flow L	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 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: 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 L	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 H	AUC
Validation X	

	Garcia-Aymerich (2003)
Flow L	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 comorbities; - 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 L	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

	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 L	Definition of exacerbation: An exacerbation was defined as an increase in dyspnoea, sputum production, or sputum purulence.
Statistical analysis L	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 H	AUC
Validation	X

	Gudmundsson (2005)
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

	reviewed by the investigators to confirm the diagnosis
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. 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 L	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 L	Ratio #events/#predictors: >246 events vs around 25 predictors Predicted outcome: Readmission for COPD exacerbation Statistical model: Cox regression Missing data: X
Performance Measures H	Log-likelihood (provided after request)
Validation	

	Hurst (2010)
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 L	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 H	R-square
Validation	

	Jacob (2013)
Flow L	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 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: 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 H	-2 log Likelihood, AIC, SBC (data obtained contacting the authors)
Validation X	

	Jones (2009)
Flow L	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 L	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 L	Definition of exacerbation: symptom-based. All patients recorded daily, on diary cards, any increase in respiratory symptoms, which were classified as major (dysponea, 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 H	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 H	AUC
Validation X	

	Ko (2011)
Flow L	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(208males) 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 L	At the baseline assessment, the demographic characteristics and the medication usage of the subjects were recorded
Outcome L	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 L	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 Kaplane Meier analysis (serial change at a certain time point was classified as having decreasing [>1point], stable or increasing [>þ1point] 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 H	AUC
Validation X	

	Lee (2014)
Flow L	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 re- view boards prior to the initiation of any study-related activities. 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. Telephone calls/medical visits data.
Outcome L	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 L	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 H	AUC for all 6 measurements (3 outcomes and CAT categorized or not)
Validation	

X	

	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 L	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 L	(Look at the references) 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 U	Definition of exacerbation: unclear
Statistical analysis H	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 L	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 L	(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 L	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 H	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 H	AUC; r-square (data in part obtained contacting the authors)
Validation X	

	Moy (2014)
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,

L	they were blinded to the outcome.
Outcome L	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 L	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 H	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 L	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 L	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 L	AUC (with confidence interval), HL (chi-square and p-value), R^2
Validation X	

	Ong (2005)
Flow L	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. Support statement: - 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 L	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 L	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

analysis	
L	Predicted outcome: Hospital admission because exacerbation
	Statistical model: Poisson regression analysis. The pseudo r2 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 H	Pseudo R^2
Validation X	

	Parshall (2008)
Flow (Derivation cohort) H	Setting and sampling: The sampling frame for the study comprised all patients with COPD (with International Classification of Disease–9th Re- vision 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 L	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 L	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 H	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 L	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)
Validation X	

	Suetomo (2014)
Flow (Derivation cohort) L	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 L	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 L	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	

	Takahashi (2012)
Flow (Derivation cohort) L	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 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: 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 L	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)

	Missing data: unclear
Performance Measures L	AUC, R^2, HL, model p-value model (data obtained contacting the authors)
Validation X	

	Thomsen (2013)
Flow (Derivation cohort) L	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 61650 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 40years 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
Predictors L	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 perforamance 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						x			x		x	x	x	
Previous exacerbations				x		x					x		x	
Age								x				x		
Smoking						x[4]						x[5]		
COPD specific HRQL (survey)				x			x[6]	x[7]				x[6]	x[6]	
Body-mass index					x									
Sex								x						
BODE										x				
Dyspnea								x[9]						
Comorbidities					x[12]	x[13]		x[14]						
Long-term oxygen therapy (LTOT)														
Duration of COPD														
ADO		x												
DOSE														
Serum C-reactive protein (CRP)														
White Blood Cell count (WBC)												x		
Hypercapnia at discharge				x										
Physical activity											x[16]			
Use of prednisone in the previous year														
Oral corticosteroids							x							
Hospital stay									x					
Influenza vaccination														
Country														
Inhaled corticosteroid (ICS)														
Tiotropium														
Long-acting b2 agonists (LABA)														
Employment status					x									
Administration of Azithromycin and					x									
Inhaled medication														
Anticholinergics											x			
Control by Pulmonologist or GP											x			
History of reflux or heartburn													x	
Education								x						
CODEX	x													
Health related quality of life (survey)														
BODEX			x											
Oxygen saturation at rest														
Serum albumin on admission					x									
Depression								x[19]						
Self-efficacy								x[20]						
Perceived social support								x[21]						
Hospital Anxiety and Depression scale												x		
y-globulin														
Plasma levels of fibrinogen														
Whole blood leukocyte count														
Exercise capacity														
I-BODE[23]														
Desaturation >4% during SWT														
Partial pressure of oxygen (PO_2)											x			
Normal IgG antibody titer against														
IL-6														
Has emphysema>5% by radiology														
Plasma levels of high-sensitivity CRP														

Study / Predictor	...	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Frequency	Availability predictor
Obstruction (FEV1% predicted or FEV1 or		x					x		x	x			x^1	x	x	12	2
Previous exacerbations		x^2						x		x				x	x^3	9	1
Age		x			x		x			x			x	x	x	9	1
Smoking		x^4			x^5		x^4			x^5			x^4	x		8	1
COPD specific HRQL (survey)					x^8					x^6			x^8			8	2
Body-mass index		x			x		x							x	x	6	1
Sex		x			x		x			x					x	6	1
BODE				x		x					x					4	3
Dyspnea							x^{10}	x^{11}								3	1
Comorbidities					x^{15}											3	1
Long-term oxygen therapy (LTOT)									x	x						2	1
Duration of COPD		x			x											2	1
ADO								x								2	1
DOSE			x					x								2	2
Serum C-reactive protein (CRP)									x				x			2	2
White Blood Cell count (WBC)										x						2	2
Hypercapnia at discharge															x	2	3
Physical activity								x^{17}								2	3
Use of prednisone in the previous year									x							1	1
Oral corticosteroids																1	1
Hospital stay																1	1
Influenza vaccination					x											1	1
Country					x											1	1
Inhaled corticosteroid (ICS)													x			1	1
Tiotropium													x			1	1
Long-acting b2 agonists (LABA)													x			1	1
Employment status																1	1
Administration of Azithromycin and																1	1
Inhaled medication															x	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)												x^{18}				1	2
BODEX																1	2
Oxygen saturation at rest					x											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																1	2
y-globulin													x			1	2
Plasma levels of fibrinogen															x	1	2
Whole blood leukocyte count															x	1	2
Exercise capacity							x^{22}									1	3
I-BODE[23]							x									1	3
Desaturation >4% during SWT							x									1	3
Partial pressure of oxygen (PO_2)																1	3
Normal IgG antibody titer against													x			1	3
IL-6																1	3
Has emphysema>5% by radiology										x						1	3
Plasma levels of high-sensitivity CRP															x	1	3

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; [46]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); [16]Measured in Kcal/day; [17]Daily step count (in the step_CRP index and step_IL-6 index); [18]Medical Outcomes Study short-form health survey [36 items] (SF-36); [19]Zung Self-Rating Depression Scale (SDS); [20]COPD Self-Efficacy Scale (CSES); [21]Personal Resource Questionnaires (PRQ2000); [22]Incremental shuttle walking test (ISWT); [23]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).

	Studies
1	**Almagro (2014)** [19] CODEX
2	ADO
3	BODEX
4	**Almagro (2006)** [20]
5	**Amalakuhan (2012)** [21]
6	**Bertens (2013)** [22]
7	**Brusse-Keizer (2011)** [23]
8	**Chen (2006)** [24]
9	**Echave-Sustaeta (2010)** [25]
10	**Faganello (2010)** [26]
11	**Garcia-Aymerich (2003)** [27]
12	**Gudmundusson (2005)** [28]
13	**Hurst (2010)** [29]
14	**Jakob (2013)** [30]
15	**Jones (2009)** [31]
16	**Ko (2011)** [32]
17	**Lee (2014)** [33]
18	**Marin (2009)** [34]
19	**Moberg (2014)** [35]
20	**Motegi (2013)** [36]
21	**Moy (2014)** [37]
22	**Müllerova (2015)** [38]
23	**Ong (2005)** [39]
24	**Parshall (2008)** [40]
25	**Suetomo (2014)** [41]
26	**Takahashi (2012)** [42]
27	**Thomsen (2013)** [43]

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[23]	1	3
Desaturation >4% during SWT	1	3
Partial pressure of oxygen (PO_2)	1	3
Normal IgG antibody titer against Porphyromonas gingivalis	1	3
Interleukin 6 (IL-6)	1	3

Has emphysema>5% by radiology	1	3
Plasma levels of high-sensitivity CRP	1	3

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; PO_2: 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	Availability predictors. Low (L), Medium (M), High (M)	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	0
		E	4	3	1	0
2	Almagro (2006) [20]	D	3	1	1	1
3	Amalakuhan (2012) [21]	E	5	4	1	0
4	Bertens (2013) [22]	E	4	3	1	0
5	Brusse-Keizer (2011) [23]	E	2	1	1	0
6	Chen (2006) [24]	M	9	5	4	0
7	Echave-Sustaeta (2010) [25]	E	2	1	1	0
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:

Availability of predictors categories for each model:
- 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.

m-TABLE 3. Readiness of prediction models for clinical practice.

Study	Availability predictors	External validation	Practical applicability
Bertens (2013) [22]	E	Y	N
Almagro (2014) [19]	E	Y	N
	E	Y	N
	E	Y	N
Almagro (2006) [20]	D	N	Y[1]
Brusse-Keizer (2011) [23]	E	N[2]	N
Amalakuhan (2012) [21]	E	N[3]	N
Jones (2009) [31]	E	N[4]	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. [1]The 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; [2]The jackknife cross validation was applied but no performance is indicated; [3]Internal validation was applied but no performance is indicated; [4]Validation is performed for other outcomes

New section

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