

Appendix

Modifiable risk factors associated with progression to and extension of multimorbidity in people with COPD: a systematic review

Search 1: Embase Classic+Embase <1947 to 2021 July 26> (Updated February 2022)

- 1 exp multiple chronic conditions/ 4749
- 2 multimorbidity.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 6702
- 3 multimorbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 8228
- 4 multimorbidities.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 329
- 5 multi-morbidity.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 1141
- 6 multi-morbidities.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 151
- 7 multi-morbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 1584
- 8 multiple morbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 613
- 9 multiple comorbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 6860
- 10 polymorbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 634
- 11 polymorbid.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 317

- 12 poly-morbid\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 24
- 13 polymorbidity.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 333
- 14 polypath\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 420
- 15 pluralpath\$.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] 1
- 16 (Multiple adj2 disease\$.m_titl. 3873
- 17 (Multiple adj2 diagnos\$.m_titl. 4204
- 18 (Multiple adj2 illness\$.m_titl. 133
- 19 (multiple adj2 condition\$.m_titl. 780
- 20 (coexisting adj2 diseas\$.m_titl. 235
- 21 (coexisting adj2 illness\$.m_titl. 11
- 22 (coexisting adj2 diagnos\$.m_titl. 28
- 23 (coexisting adj2 condition\$.m_titl. 68
- 24 (coexisting adj2 morbid\$.m_titl. 3
- 25 (co-existing adj2 diseas\$.m_titl. 76
- 26 (co-existing adj2 illness\$.m_titl. 6
- 27 (co-existing adj2 diagnos\$.m_titl. 6
- 28 (co-existing adj2 morbid\$.m_titl. 2
- 29 (concurrent adj2 diseas\$.m_titl. 319
- 30 (concurrent adj2 illness\$.m_titl. 31
- 31 (concurrent adj2 diagnos\$.m_titl. 101
- 32 (concurrent adj2 condition\$.m_titl. 49
- 33 (concurrent adj2 morbid\$.m_titl. 9
- 34 (comorbid adj2 diseas\$.m_titl. 477
- 35 (comorbid adj2 illness\$.m_titl. 201
- 36 (comorbid adj2 diagnos\$.m_titl. 109
- 37 (comorbid adj2 condition\$.m_titl. 887

38	(comorbid adj2 morbid\$.m_titl.	4
39	(co-morbid adj2 diseas\$.m_titl.	71
40	(co-morbid adj2 illness\$.m_titl.	35
41	(co-morbid adj2 diagnos\$.m_titl.	16
42	(co-morbid adj2 condition\$.m_titl.	151
43	(co-morbid adj2 morbid\$.m_titl.	1264
44	(Polymorbid adj2 diseas\$.m_titl.	0
45	(Polymorbid adj2 diagnos\$.m_titl.	0
46	(Polymorbid adj2 illness\$.m_titl.	0
47	(Polymorbid adj2 condition\$.m_titl.	0
48	(Polymorbid adj2 morbid\$.m_titl.	0
49	(multiple adj2 comorbid\$.m_titl.	404
50	(Polymorbidity adj2 diseas\$.m_titl.	2
51	(Polymorbidity adj2 diagnos\$.m_titl.	0
52	(Polymorbidity adj2 illness\$.m_titl.	0
53	(Polymorbidity adj2 condition\$.m_titl.	0
54	(Polymorbidity adj2 morbid\$.m_titl.	0
55	(Simultaneous adj2 condition\$.m_titl.	62
56	(Simultaneous adj2 diagnos\$.m_titl.	170
57	(Simultaneous adj2 illness\$.m_titl.	2
58	(Simultaneous adj2 morbid\$.m_titl.	10
59	case-mix\$.m_titl.	1079
60	casemix\$.m_titl.	227
61	Health status indicator*.m_titl.	83
62	severity of illness index.m_titl.	16
63	diagnosis-related group.m_titl.	201
64	charlson.m_titl.	709
65	CIRS.m_titl.	138
66	CIRS-G.m_titl.	3
67	Adjusted Clinical Group\$.m_titl.	25
68	Ambulatory care group\$.m_titl.	17

69	Disease count.m_titl.	5	
70	DUSOI.m_titl.	4	
71	Duke severity of illness.m_titl.	4	
72	Duke case-mix system.m_titl.	1	
73	DUMIX.m_titl.	1	
74	ICED-DS.m_titl.	0	
75	ICED-FS.m_titl.	0	
76	Index of coexistent disease-disease severity.m_titl.	0	
77	Cornoni-Huntley index.m_titl.	0	
78	Liu index.m_titl.	0	
79	Shwartz index.m_titl.	0	
80	Kaplan index.m_titl.	0	
81	Kaplan-Feinstein index.m_titl.	2	
82	cumulative illness rating scale.ti,ab.	932	
83	Cornoni-Huntley index.ti,ab.	0	
84	Disease count.ti,ab.	79	
85	DUSOI.ti,ab.	22	
86	Duke severity of illness.ti,ab.	25	
87	Duke case-mix system.ti,ab.	1	
88	DUMIX.ti,ab.	1	
89	Liu index.ti,ab.	10	
90	Hurwitz index.ti,ab.	0	
91	Index of coexistent disease.ti,ab.	37	
92	ICED-DS.ti,ab.	0	
93	ICED-FS.ti,ab.	0	
94	Hallstrom index.ti,ab.	0	
95	Incalzi index.ti,ab.	0	
96	Shwartz index.ti,ab.	0	
97	Kaplan index.ti,ab.	2	
98	Kaplan-Feinstein index.ti,ab.	54	

99	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98	35343
100	exp chronic obstructive lung disease/	147726
101	exp chronic bronchitis/	15439
102	exp lung emphysema/	27851
103	obstructive airway disease/	2269
104	chronic obstructive pulmonary disease\$.ti,ab.	76884
105	chronic obstructive lung disease\$.ti,ab.	6932
106	chronic obstructive pulmonary disorder\$.ti,ab.	413
107	chronic lung disease\$.ti,ab.	12871
108	chronic pulmonary disease\$.ti,ab.	4191
109	chronic lung disorder\$.ti,ab.	160
110	chronic pulmonary disorder\$.ti,ab.	155
111	chronic airway disease\$.ti,ab.	1020
112	pulmonary emphysema.ti,ab.	5908
113	lung emphysema.ti,ab.	830
114	chronic emphysema.ti,ab.	151
115	COPD.ti,ab.	94690
116	chronic bronchitis.ti,ab.	16013
117	chronic airflow obstruction.ti,ab.	677
118	chronic airway obstruction.ti,ab.	530
119	chronic obstructive bronchitis.ti,ab.	895
120	chronic obstructive bronchopulmonary disease.ti,ab.	85
121	chronic obstructive lung disorder.ti,ab.	4
122	chronic obstructive respiratory disease.ti,ab.	177
123	lung chronic obstructive disease.ti,ab.	0
124	obstructive lung disease.m_titl.	2734
125	obstructive pulmonary disease.m_titl.	29199
126	obstructive respiratory disease.m_titl.	145

- 127 obstructive respiratory tract disease.ti,ab. 25
- 128 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 228620**
- 129 99 and 128 1979**

Search 2: Database: Ovid MEDLINE(R) ALL <1946 to February 10, 2022>

Search Strategy:

-
- 1 multimorbidity.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (6238)
- 2 multimorbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (7297)
- 3 multimorbidities.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (284)
- 4 multi-morbidity.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (773)
- 5 multi-morbidities.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (116)
- 6 multi-morbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (1066)
- 7 multiple morbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (470)
- 8 multiple comorbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
word, floating

- sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (4275)
9 polymorbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (410)
10 polymorbid.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (194)
11 poly-morbid\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (22)
12 polymorbidity.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (219)
13 polypath\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (245)
14 pluralpath\$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating
sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare
disease supplementary concept word, unique identifier, synonyms] (0)
15 (Multiple adj2 disease\$.m_titl. (2056)
16 (Multiple adj2 diagnos\$.m_titl. (2455)
17 (Multiple adj2 illness\$.m_titl. (69)
18 (multiple adj2 condition\$.m_titl. (696)
19 (coexisting adj2 diseas\$.m_titl. (188)
20 (coexisting adj2 illness\$.m_titl. (7)
21 (coexisting adj2 diagnos\$.m_titl. (22)
22 (coexisting adj2 condition\$.m_titl. (40)
23 (coexisting adj2 morbid\$.m_titl. (4)
24 (co-existing adj2 diseas\$.m_titl. (50)
25 (co-existing adj2 illness\$.m_titl. (3)
26 (co-existing adj2 diagnos\$.m_titl. (4)
27 (co-existing adj2 morbid\$.m_titl. (1)
28 (concurrent adj2 diseas\$.m_titl. (252)
29 (concurrent adj2 illness\$.m_titl. (27)

30 (concurrent adj2 diagnos\$.m_titl. (78)
31 (concurrent adj2 condition\$.m_titl. (41)
32 (concurrent adj2 morbid\$.m_titl. (8)
33 (comorbid adj2 diseas\$.m_titl. (317)
34 (comorbid adj2 illness\$.m_titl. (153)
35 (comorbid adj2 diagnos\$.m_titl. (79)
36 (comorbid adj2 condition\$.m_titl. (612)
37 (comorbid adj2 morbid\$.m_titl. (3)
38 (co-morbid adj2 diseas\$.m_titl. (40)
39 (co-morbid adj2 illness\$.m_titl. (23)
40 (co-morbid adj2 diagnos\$.m_titl. (6)
41 (co-morbid adj2 condition\$.m_titl. (86)
42 (co-morbid adj2 morbid\$.m_titl. (734)
43 (Polymorbid adj2 diseas\$.m_titl. (0)
44 (Polymorbid adj2 diagnos\$.m_titl. (0)
45 (Polymorbid adj2 illness\$.m_titl. (0)
46 (Polymorbid adj2 condition\$.m_titl. (0)
47 (Polymorbid adj2 morbid\$.m_titl. (0)
48 (multiple adj2 comorbid\$.m_titl. (259)
49 (Polymorbidity adj2 diseas\$.m_titl. (1)
50 (Polymorbidity adj2 diagnos\$.m_titl. (0)
51 (Polymorbidity adj2 illness\$.m_titl. (0)
52 (Polymorbidity adj2 condition\$.m_titl. (0)
53 (Polymorbidity adj2 morbid\$.m_titl. (0)
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55 (Simultaneous adj2 diagnos\$.m_titl. (135)
56 (Simultaneous adj2 illness\$.m_titl. (3)
57 (Simultaneous adj2 morbid\$.m_titl. (8)
58 case-mix\$.m_titl. (924)
59 casemix\$.m_titl. (214)
60 Health status indicator*.m_titl. (83)
61 severity of illness index.m_titl. (15)
62 diagnosis-related group.m_titl. (152)
63 charlson.m_titl. (447)
64 CIRS.m_titl. (93)
65 CIRS-G.m_titl. (0)
66 Adjusted Clinical Group\$.m_titl. (24)
67 Ambulatory care group\$.m_titl. (16)
68 Disease count.m_titl. (4)
69 DUSOI.m_titl. (3)
70 Duke severity of illness.m_titl. (3)
71 Duke case-mix system.m_titl. (1)
72 DUMIX.m_titl. (1)
73 ICED-DS.m_titl. (0)
74 ICED-FS.m_titl. (0)
75 Index of coexistent disease-disease severity.m_titl. (0)
76 Cornoni-Huntley index.m_titl. (0)
77 Liu index.m_titl. (0)

- 78 Shwartz index.m_titl. (0)
- 79 Kaplan index.m_titl. (0)
- 80 Kaplan-Feinstein index.m_titl. (1)
- 81 cumulative illness rating scale.ti,ab. (523)
- 82 Cornoni-Huntley index.ti,ab. (0)
- 83 Disease count.ti,ab. (56)
- 84 DUSOI.ti,ab. (17)
- 85 Duke severity of illness.ti,ab. (22)
- 86 Duke case-mix system.ti,ab. (1)
- 87 DUMIX.ti,ab. (1)
- 88 Liu index.ti,ab. (7)
- 89 Hurwitz index.ti,ab. (0)
- 90 Index of coexistent disease.ti,ab. (30)
- 91 ICD-DS.ti,ab. (0)
- 92 ICD-FS.ti,ab. (0)
- 93 Hallstrom index.ti,ab. (0)
- 94 Incalzi index.ti,ab. (0)
- 95 Shwartz index.ti,ab. (0)
- 96 Kaplan index.ti,ab. (2)
- 97 Kaplan-Feinstein index.ti,ab. (28)
- 98 chronic obstructive pulmonary disease\$.ti,ab. (54693)
- 99 chronic obstructive lung disease\$.ti,ab. (4715)
- 100 chronic obstructive pulmonary disorder\$.ti,ab. (271)
- 101 chronic lung disease\$.ti,ab. (8358)
- 102 chronic pulmonary disease\$.ti,ab. (2393)
- 103 chronic lung disorder\$.ti,ab. (117)
- 104 chronic pulmonary disorder\$.ti,ab. (99)
- 105 chronic airway disease\$.ti,ab. (700)
- 106 pulmonary emphysema.ti,ab. (4031)
- 107 lung emphysema.ti,ab. (447)
- 108 chronic emphysema.ti,ab. (66)
- 109 COPD.ti,ab. (51582)
- 110 chronic bronchitis.ti,ab. (10034)
- 111 chronic airflow obstruction.ti,ab. (571)
- 112 chronic airway obstruction.ti,ab. (349)
- 113 chronic obstructive bronchitis.ti,ab. (656)
- 114 chronic obstructive bronchopulmonary disease.ti,ab. (44)
- 115 chronic obstructive lung disorder.ti,ab. (4)
- 116 chronic obstructive respiratory disease.ti,ab. (87)
- 117 lung chronic obstructive disease.ti,ab. (0)
- 118 obstructive lung disease.m_titl. (1837)
- 119 obstructive pulmonary disease.m_titl. (21523)
- 120 obstructive respiratory disease.m_titl. (50)
- 121 obstructive respiratory tract disease.ti,ab. (21)
- 122 *Multimorbidity/ (1183)
- 123 exp Pulmonary Disease, Chronic Obstructive/ (62185)
- 124 exp Bronchitis, Chronic/ (1834)
- 125 exp Pulmonary Emphysema/ (16342)

126 Lung Diseases, Obstructive/ (18253)
 127 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 123 or 124 or 125 or 126 (122180)
 128 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 122 (23665)
 129 127 and 128 (899)

Results: 114

Search 3 Database: HMIC Health Management Information Consortium <1979 to November 2021>
 Search Strategy:

 1 [multimorbidity.mp](#). [mp=title, other title, abstract, heading words] (189)
 2 multimorbid\$.mp. [mp=title, other title, abstract, heading words] (205)
 3 [multimorbidities.mp](#). [mp=title, other title, abstract, heading words] (12)
 4 [multi-morbidity.mp](#). [mp=title, other title, abstract, heading words] (48)
 5 [multi-morbidities.mp](#). [mp=title, other title, abstract, heading words] (6)
 6 multi-morbid\$.mp. [mp=title, other title, abstract, heading words] (57)
 7 multiple morbid\$.mp. [mp=title, other title, abstract, heading words] (25)
 8 multiple comorbid\$.mp. [mp=title, other title, abstract, heading words] (17)
 9 polymorbid\$.mp. [mp=title, other title, abstract, heading words] (0)
 10 [polymorbid.mp](#). [mp=title, other title, abstract, heading words] (0)
 11 poly-morbid\$.mp. [mp=title, other title, abstract, heading words] (0)
 12 [polymorbidity.mp](#). [mp=title, other title, abstract, heading words] (0)
 13 polypath\$.mp. [mp=title, other title, abstract, heading words] (0)
 14 pluralpath\$.mp. [mp=title, other title, abstract, heading words] (0)
 15 (Multiple adj2 disease\$).m_titl. (6)
 16 (Multiple adj2 diagnos\$).m_titl. (2)
 17 (Multiple adj2 illness\$).m_titl. (1)
 18 (multiple adj2 condition\$).m_titl. (23)
 19 (coexisting adj2 diseas\$).m_titl. (0)
 20 (coexisting adj2 illness\$).m_titl. (0)
 21 (coexisting adj2 diagnos\$).m_titl. (0)
 22 (coexisting adj2 condition\$).m_titl. (0)
 23 (coexisting adj2 morbid\$).m_titl. (0)
 24 (co-existing adj2 diseas\$).m_titl. (2)
 25 (co-existing adj2 illness\$).m_titl. (0)
 26 (co-existing adj2 diagnos\$).m_titl. (0)

- 27 (co-existing adj2 morbid\$.m_titl. (0)
- 28 (concurrent adj2 diseas\$.m_titl. (1)
- 29 (concurrent adj2 illness\$.m_titl. (0)
- 30 (concurrent adj2 diagnos\$.m_titl. (0)
- 31 (concurrent adj2 condition\$.m_titl. (0)
- 32 (concurrent adj2 morbid\$.m_titl. (0)
- 33 (comorbid adj2 diseas\$.m_titl. (5)
- 34 (comorbid adj2 illness\$.m_titl. (5)
- 35 (comorbid adj2 diagnos\$.m_titl. (0)
- 36 (comorbid adj2 condition\$.m_titl. (4)
- 37 (comorbid adj2 morbid\$.m_titl. (0)
- 38 (co-morbid adj2 diseas\$.m_titl. (1)
- 39 (co-morbid adj2 illness\$.m_titl. (1)
- 40 (co-morbid adj2 diagnos\$.m_titl. (0)
- 41 (co-morbid adj2 condition\$.m_titl. (2)
- 42 (co-morbid adj2 morbid\$.m_titl. (14)
- 43 (Polymorbid adj2 diseas\$.m_titl. (0)
- 44 (Polymorbid adj2 diagnos\$.m_titl. (0)
- 45 (Polymorbid adj2 illness\$.m_titl. (0)
- 46 (Polymorbid adj2 condition\$.m_titl. (0)
- 47 (Polymorbid adj2 morbid\$.m_titl. (0)
- 48 (multiple adj2 comorbid\$.m_titl. (3)
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- 52 (Polymorbidity adj2 condition\$.m_titl. (0)
- 53 (Polymorbidity adj2 morbid\$.m_titl. (0)
- 54 (Simultaneous adj2 condition\$.m_titl. (0)
- 55 (Simultaneous adj2 diagnos\$.m_titl. (0)
- 56 (Simultaneous adj2 illness\$.m_titl. (0)
- 57 (Simultaneous adj2 morbid\$.m_titl. (0)
- 58 case-mix\$.m_titl. (118)
- 59 casemix\$.m_titl. (123)
- 60 Health status indicator*.m_titl. (2)
- 61 severity of illness index.m_titl. (0)
- 62 diagnosis-related group.m_titl. (10)
- 63 charlson.m_titl. (0)
- 64 CIRS.m_titl. (0)
- 65 CIRS-G.m_titl. (0)
- 66 Adjusted Clinical Group\$.m_titl. (1)
- 67 Ambulatory care group\$.m_titl. (0)
- 68 Disease count.m_titl. (0)
- 69 DUSOI.m_titl. (0)
- 70 Duke severity of illness.m_titl. (0)
- 71 Duke case-mix system.m_titl. (1)
- 72 DUMIX.m_titl. (1)
- 73 ICED-DS.m_titl. (0)
- 74 ICED-FS.m_titl. (0)

- 75 Index of coexistent disease-disease severity.m_titl. (0)
- 76 Corroni-Huntley index.m_titl. (0)
- 77 Liu index.m_titl. (0)
- 78 Shwartz index.m_titl. (0)
- 79 Kaplan index.m_titl. (0)
- 80 Kaplan-Feinstein index.m_titl. (0)
- 81 cumulative illness rating scale.ti,ab. (4)
- 82 Corroni-Huntley index.ti,ab. (0)
- 83 Disease count.ti,ab. (2)
- 84 DUSOI.ti,ab. (2)
- 85 Duke severity of illness.ti,ab. (0)
- 86 Duke case-mix system.ti,ab. (1)
- 87 DUMIX.ti,ab. (1)
- 88 Liu index.ti,ab. (0)
- 89 Hurwitz index.ti,ab. (0)
- 90 Index of coexistent disease.ti,ab. (0)
- 91 ICED-DS.ti,ab. (0)
- 92 ICED-FS.ti,ab. (0)
- 93 Hallstrom index.ti,ab. (0)
- 94 Incalzi index.ti,ab. (0)
- 95 Shwartz index.ti,ab. (0)
- 96 Kaplan index.ti,ab. (0)
- 97 Kaplan-Feinstein index.ti,ab. (0)
- 98 chronic obstructive pulmonary disease\$.ti,ab. (580)
- 99 chronic obstructive lung disease\$.ti,ab. (30)
- 100 chronic obstructive pulmonary disorder\$.ti,ab. (5)
- 101 chronic lung disease\$.ti,ab. (45)
- 102 chronic pulmonary disease\$.ti,ab. (11)
- 103 chronic lung disorder\$.ti,ab. (2)
- 104 chronic pulmonary disorder\$.ti,ab. (1)
- 105 chronic airway disease\$.ti,ab. (2)
- 106 pulmonary emphysema.ti,ab. (5)
- 107 lung emphysema.ti,ab. (0)
- 108 chronic emphysema.ti,ab. (0)
- 109 COPD.ti,ab. (466)
- 110 chronic bronchitis.ti,ab. (158)
- 111 chronic airflow obstruction.ti,ab. (8)
- 112 chronic airway obstruction.ti,ab. (4)
- 113 chronic obstructive bronchitis.ti,ab. (3)
- 114 chronic obstructive bronchopulmonary disease.ti,ab. (0)
- 115 chronic obstructive lung disorder.ti,ab. (1)
- 116 chronic obstructive respiratory disease.ti,ab. (1)
- 117 lung chronic obstructive disease.ti,ab. (0)
- 118 obstructive lung disease.m_titl. (8)
- 119 obstructive pulmonary disease.m_titl. (177)
- 120 obstructive respiratory disease.m_titl. (2)
- 121 obstructive respiratory tract disease.ti,ab. (0)
- 122 *Multimorbidity/ (0)

- 123 exp Pulmonary Disease, Chronic Obstructive/ (0)
 124 exp Bronchitis, Chronic/ (0)
 125 exp Pulmonary Emphysema/ (44)
 126 Lung Diseases, Obstructive/ (0)
 127 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 123 or 124 or 125 or 126 (973)
 128 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 122 (595)
 129 exp chronic obstructive pulmonary disease/ (390)
 130 exp chronic disease/ (2037)
 131 exp Bronchitis/ (178)
 132 exp Pulmonary emphysema/ (44)
 133 127 or 129 or 131 or 132 (1063)
 134 128 or 130 (2539)
 135 133 and 134 (114)

Search 4, 11 Feb 2022: Web of science

((((((((((((((((((((ALL=(chronic obstructive pulmonary disease\$)) OR TS=(chronic obstructive lung disease\$)) OR TS=(chronic obstructive pulmonary disorder\$)) OR TS=(chronic airway disease\$)) OR TS=(pulmonary emphysema)) OR TS=(lung emphysema)) OR TS=(chronic emphysema)) OR TS=(COPD)) OR TS=(chronic bronchitis)) OR TS=(chronic airflow obstruction)) OR TS=(chronic airway obstruction)) OR TS=(chronic obstructive bronchitis)) OR TS=(chronic obstructive bronchopulmonary disease)) OR TS=(chronic obstructive lung disorder)) OR TS=(chronic obstructive respiratory disease)) OR TS=(lung chronic obstructive disease)) OR TS=(obstructive lung disease)) OR TS=(obstructive pulmonary disease)) OR TS=(obstructive respiratory disease)) OR TS=(obstructive respiratory tract disease)

AND

((((((((TS=(multimorbidity)) OR TS=(multimorbid\$)) OR TS=(multimorbidities)) OR TS=(multimorbidity)) OR TS=(multi-morbidities)) OR TS=(multiple morbid\$)) OR TS=(polymorbid\$)) OR TS=(polypath\$)) OR TS=(plural path\$)

Search 5: Embase Classic+Embase <1947 to 2021 August 06>

1	hypertens\$.m_titl.	283154
2	high blood pressure.m_titl.	3735
3	depress\$.m_titl.	208336
4	Pain.m_titl.	271961
5	heart disease\$.m_titl.	85324
6	dyspep\$.m_titl.	7824
7	thyroid.m_titl.	153420
8	rheumat\$.m_titl.	166131
9	arthrit\$.m_titl.	162931
10	anxiety.m_titl.	72218
11	somatoform.m_titl.	1252
12	bowel.m_titl.	93115
13	stroke.m_titl.	173285
14	kidney.m_titl.	232486
15	transient isch?emic attack.m_titl.	3665
16	atrial fibrillation.m_titl.	73933
17	peripheral vascular disease.m_titl.	2517
18	heart failure.m_titl.	122577
19	coronary.m_titl.	295952
20	Prostate.m_titl.	180986
21	glaucoma.m_titl.	45134
22	epilep\$.m_titl.	124244
23	dementia\$.m_titl.	73067
24	schizophrenia.m_titl.	90443
25	psoria\$.m_titl.	56118
26	migraine\$.m_titl.	34609
27	bronchiectasis.m_titl.	6226
28	multiple sclerosis.m_titl.	80709

29	chronic liver disease.m_titl.	6146
30	parkinson\$.m_titl.	107064
31	learning disability.m_titl.	1352
32	risk factor/	1139460
33	risk\$.m_titl.	747136
34	predict\$.m_titl.	526687
35	copd.m_titl.	38867
36	chronic obstructive lung.m_titl.	2099
37	chronic obstructive pulmonary.m_titl.	29581
38	35 or 36 or 37	67530
39	32 or 33 or 34	2056980
40	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	2951991
41	38 and 39 and 40	641
42	41 not covid.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	637
43	42 not hospital\$.m_titl.	594
44	43 not exacerbat\$.m_titl.	544

Table 1: Articles included in the review

Reference	Country	Population	COPD definition	N #	Multimorbidity definition and risk factors
Ganga et al. 2013(36)	United States	Community based population of elderly patients aged 65-89 years with COPD/obstructive sleep apnoea (OSA) overlap syndrome. Data collected from the medical records of Mercy Medical Centre, Mason City, IA. Patients were alive throughout 2006 and had at least 2 years follow-up.	ICD-9 codes 491, 492, 494 and 496	Total: 2873 COPD: 416 Overlap syndrome: 28	<p>Risk factors for new-onset atrial fibrillation* in people with COPD and obstructive sleep apnoea vs COPD alone (logistic regression adjusted for other comorbidities):</p> <ul style="list-style-type: none"> Obstructive sleep apnoea (OR=3.66; 95%CI: 1.06, 6.9; p=0.007) <p>*Identified using ECG and hospital discharge diagnoses (including ICD code for AF or Atrial flutter)</p>
Asker et al. 2014(31)	Turkey	Patients diagnosed with COPD and pulmonary hypertension and undergone coronary angiography.	Not further defined	COPD: 95	<p>Risk factors for coronary artery disease* in people with COPD and pulmonary hypertension (multivariate logistic regression):</p> <ul style="list-style-type: none"> Male sex (Rs=0.224, p=0.029) Hypertension (Rs=0.227, p=0.07) FEV1/FVC ratio (Rs=-0.253, p=0.013) sPAP (Rs=-0.215, p=0.037) <p>*Defined as presence of >20% stenosis in coronary circulation</p>
Yusof et al. 2012(41)	UK	Patients with COPD and lung cancer attending an outpatient clinic in July 2011	Diagnosis of COPD – not further specified	COPD: 44	<p>Risk factors for depression* in people with COPD and lung cancer (stepwise logistic regression):</p> <p>Number of co-existing comorbidities (beta coefficient = 0.758, SE: 0.379, Wald: 3.998, df: 1, p: 0.046 and Exp (B): 2.134 (95%CI: 1.015, 4.485)</p> <p>*CES-D</p>
Silva Júnior et al. 2014(40)	Brazil	COPD patients aged 40 years and over with no exacerbation for the previous 4 weeks and mild hypoxemia. Demographically matched controls.	GOLD	COPD: 30 Control: 30	<p>Risk factors for major depression* in people with COPD with mild hypoxemia compared to demographically matched controls (adjusting for sleep parameters):</p> <p>Higher COPD assessment test (CAT) score (aOR=1.17; 95%CI: 1.00, 1.30; p=0.002)</p>

					*Diagnosed according to DSM IV criteria by a psychiatric evaluation and measured by the Beck Depression Inventory (BDI), second revision.
Phan et al. 2019(39)	Australia	Participants in a COPD outpatient database invited to take part in telephone or face-to-face interviews. Participants excluded if they had potential confounders of comorbidities or were unable to self-report.	Diagnosis confirmed by a physician	COPD: 242	<p>Risk factors for concomitant anxiety and depression* in patients with COPD (final multivariate model):</p> <ul style="list-style-type: none"> • Younger age (OR=0.88; 95%CI: 0.82, 0.94; p<0.001) • Having a carer (OR=4.83; 95%CI: 1.51, 15.48; p=0.008) • History of previous psychological illness (OR=9.67; 95%CI: 3.46, 27.05; p<0.001) • Increasing number of comorbidities (OR=1.48; 95%CI: 1.15, 1.90; p=0.002) • Increasing Impact SGRQ score (OR=1.07; 95%CI: 1.04, 1.10; p=0.001) <p>*Beck Anxiety Inventory (BAI) scores ≥8 and Beck Depression Inventory (BDI-II) scores ≥14</p>
Garneau-Picard et al. 2021(35)	Canada	Patients with Asthma-COPD overlap in the Quebec Heart and Lung Institute-Laval University asthma databank	Spirometry	COPD: 154	<p>Risk factors for multimorbidity* in patients with asthma and COPD:</p> <ul style="list-style-type: none"> • Smoking (for women only) (OR not stated) <p>*Not defined</p>
Spicuzza et al. 2019(37)	Italy	Retrospective observational study of consecutive patients with obstructive sleep apnoea or overlap syndrome (sleep apnoea + COPD) referred to a sleep laboratory.	Spirometry	OSA: 295 OS (OSA+COPD): 219	<p>Risk factors for three comorbidities* in people with sleep apnoea with/without COPD (multivariate logistic regression):</p> <ul style="list-style-type: none"> • Older age (OR=7.8; 95%CI: 4.86-11.39; p<0.001) • COPD (OR=6.17; 95%CI: 4.09-10.81; p<0.005) <p>*Hypertension, cardiovascular diseases (ischemic disease, heart failure, arrhythmias, etc), cerebrovascular diseases,</p>

					metabolic disorders (diabetes mellitus, thyroid disorders) and gastroesophageal reflux (GER)
Lacedonia et al. 2018(38)	Italy	Adults referred for sleep diagnostic testing to a sleep centre with obstructive sleep apnoea, overlap syndrome (COPD + sleep apnoea) and obesity hypoventilation syndrome.	Physician diagnosis	OSAS: 721 Overlap syndrome: 123 Obesity hypoventilation syndrome: 145.	Risk factor for 3 or more comorbidities in patients with overlap syndrome (COPD and obstructive sleep apnoea): Presence of self-reported sleepiness (ESS \geq 10) (OR=3.41; 95%CI: 0.97-11.93; p=0.049) ESS = Epworth Sleepiness Scale
Nesterovska et al. 2019(30)	Ukraine	Patients with asthma-COPD overlap syndrome (ACOS)	Not specified	ACOS: 86	Risk factors for new-onset AF in patients with asthma-COPD overlap syndrome: <ul style="list-style-type: none"> • Lower FEV1 (by 36.5%, p<0.05) • Hypoxemia (min% SpO2 12.3% higher; p<0.05) • Higher blood pressure (p<0.001) • Systemic inflammation (CRP levels 2.5 times higher in the group with AF than the group without rhythm disturbance, p=0.001)
Ingebrigtsen et al. 2020(32)	Denmark	Individuals representative of the general population of Copenhagen as collected in the Copenhagen General Population Study that met one of 8 different airway disease diagnoses (including asthma, COPD and asthma-COPD overlap syndrome). Patients aged 40 or above and those with previous cardiovascular admissions were excluded.	GOLD	54046	Risk factors for coronary artery disease or heart failure*: <ul style="list-style-type: none"> • Asthma COPD Overlap syndrome • Severity of lung function impairment. • Older age • Diabetes • Hypertension Protective factors for coronary artery disease or heart failure: physical activity in leisure time. *Hospital admission for coronary heart disease (ICD-8: 410–414 and ICD-10: I20–I25) and heart failure (ICD-8: 427.09–427.11 and ICD-10: I50)
Sánchez Castillo et al. 2020(42)	Spain	People completing the Spanish National Health Survey 2017. Participants were selected in a three-stage sampling. First, census	Self-reported diagnosis by a physician	Total: 23089 (17777 responding to physical activity questions)	Risk factors for multimorbidity in patients with asthma-COPD overlap (multivariable logistic regression analysis): <ul style="list-style-type: none"> • Low physical activity level (differences were not significant in the overall model).

		sections, then systematic sampling designated the family dwellings, then an adult (age 15 or over) was randomly selected from each dwelling. Analysis included people aged 15 to 69 who completed the International Physical Activity Questionnaire who had COPD diagnosed by a physician and asthma diagnosed by a physician.		Asthma-COPD overlap: 198	<p>Adjusted for presence of comorbidities and medication intake, lower levels of physical activities were associated with higher odds of osteoporosis and urinary incontinence in people with Asthma-COPD overlap.</p> <ul style="list-style-type: none"> Urinary incontinence (OR = 3.499; 95%CI: 1.369-8.944). <p>When considering those with ACO older than 50 years (n= 114), urinary incontinence was significant in all models, showing the highest odds in the fully adjusted model (OR = 3.906; 95%CI: 1.234-12.360; p=0.02), while osteoporosis was significant in the first and second model (Model 1: OR=2.866; 95%CI: 1.017-8.074; p= 0.046; Model 2: OR=3.187; 95%CI = 1.033-9.826; p=0.044), but not in the third model (p= 0.051).</p> <p><i>*Comorbidities were classified following the ICD in 12 different groups: (1) cardiovascular diseases; (2) musculoskeletal disorders; (3) immunological diseases; (4) digestive problems; (5) urogenital diseases; (6) eye problems; (7) dermatological problems; (8) mental health problems; (9) neurological disorders; (10) neoplasia; (11) endocrinal and metabolic diseases; (12) permanent injuries.</i></p>
Multimorbidity clusters (network/segmentation analysis)					
Hansen et al. 2020(33)	Denmark	Cluster/segmentation analysis of a nationwide cohort study including all individuals with COPD age 35 or older who lived in the Danish Capital Region on 1 January 2012. Participants were excluded from the regression analysis (but not the cluster analysis) if no information about their education was available.	Not specified	COPD: 70,274	<p>Three comorbidity clusters were selected based on 16 specific comorbid conditions*</p> <p>Cluster 1: (n = 11,300; 16.1%), individuals had high numbers of all comorbidities, including heart disease:</p> <ul style="list-style-type: none"> Highest proportion of individuals over 65 years old (77.6%) Lower secondary school or vocational education (81.4%) <p>Cluster 2: (n = 20,744; 29.5%), approximately one third suffered from allergies, whereas the rest had no comorbidities.</p>

					<ul style="list-style-type: none"> Highest proportion of individuals with undergraduate or postgraduate education (32.5%). <p>Cluster 3: (n= 38,230; 54.4%), individuals had all comorbidities except for heart disease.</p> <ul style="list-style-type: none"> Higher proportion of women (63.3%) <p>*Hypertension, allergies, high cholesterol, heart disease, diabetes, long-term use of antidepressants, osteoporosis, osteoarthritis, chronic back pain, cancer, stroke, schizophrenia, joint disease, dementia, and anxiety</p>
Triest et al. 2019(34)	Netherlands	Cross-sectional analysis of patients with COPD were recruited on admission to a tertiary care pulmonary rehabilitation centre or from the same southeastern region of the Netherlands. Smoking and never-smoking (<1 pack-year) non-COPD controls were also recruited from this region. Included patients were 45 to 75 years of age and clinically stable (no respiratory infection or exacerbation for 4 weeks before baseline). No malignancy within 5 years or other chronic lung diseases.	Spirometry	Total: 408 COPD: 208 Control: 200	<p>Cluster C1 (Less Comorbidity):</p> <ul style="list-style-type: none"> Less pack-years Less cardiovascular risk Better health-related quality of life. <p>Cluster C2 (Cardiovascular):</p> <ul style="list-style-type: none"> Older patients Less frequently active smokers. <p>Cluster C3 (Metabolic):</p> <ul style="list-style-type: none"> Lower degree of airflow limitation Static hyperinflation Better diffusion capacity Increased Framingham-defined cardiovascular risk <p>Cluster C4 (Psychologic):</p> <ul style="list-style-type: none"> Higher proportion of women Higher amount of pack-years Worse health status. <p>Cluster C5 (Cachectic):</p> <ul style="list-style-type: none"> More frequently active smokers Worse pulmonary function Higher degree of airflow limitation Static hyperinflation Lower Framingham-defined cardiovascular risk

Moore et al. 2014(18)	United States	Cross-sectional weighted sample from the National nursing home study (NNHS), including long-stay residents over 65 years of age. Patients in short-stay or specialty units were not included.	Not stated	11,734	<p>Risk factors for multimorbidity (2 or 3 disease combinations) in patients with COPD:</p> <ul style="list-style-type: none"> • Male sex (OR not stated) <p>Risk factors for multimorbidity (dementia, hypertension and vascular diseases) in patients with COPD:</p> <ul style="list-style-type: none"> • Increased age (OR not stated) <p>Risk factors for multimorbidity (hypertension, dementia, osteoporosis, depression, congestive heart failure, anaemia, arthritis) in patients with COPD:</p> <ul style="list-style-type: none"> • Female sex (OR not stated) <p>*No stats given</p>
Shen et al. 2021(19)	United States	Retrospective cohort study of adults with COPD diagnosed between January 2011 and September 2015.	ICD-9 491.XX, 492.XX, 493.2X, or 496 and one or more dispensed inhaler.	COPD: 91,453	<p>Patients in the low-morbidity profiles* tended to be (latent class analysis):</p> <ul style="list-style-type: none"> • younger (mean age, 68 vs 74 years; $p < 0.001$) • current smokers (20% vs 13%; $p < 0.001$) • more physically active (51% engaged in at least some moderate activity in a week vs 40% not engaged; $p < 0.001$) <p>*Based on Charlson Comorbidity index</p>
Jurevičienė et al. 2022(20)	Lithuania	Cross-sectional analysis of a nationwide health database. Included patients were age 40-79 with or without a diagnosis of COPD.	ICD-10-AM: J44.8 and six-month consumption of bronchodilators	Total: 321,297. COPD: 4834	<p>Hierarchical clustering algorithm identified comorbidity clusters for women and men with COPD:</p> <ul style="list-style-type: none"> • Cardiovascular cluster (COPD male) was the most prevalent, with the highest commonness of hypertension and ischemic heart disease. • Stroke-cancer-sensor cluster (COPD male) • Asthma-musculoskeletal and endocrine-metabolic clusters (COPD male) • Glaucoma and mental disorders (COPD females) • Dementia-stroke cluster (COPD females) • Cancer was linked to hypothyroidism, osteoporosis, and hearing loss.

					<ul style="list-style-type: none"> Anaemia cluster (COPD females).
Divo et al. 2015(21)	Spain and the United States	Observational prospective multi-centre cohort study. COPD defined by history of smoking and spirometric measures of lung function. Non-COPD controls were smokers and non-smoker individuals with no evidence of airway obstruction on spirometry. Clinical characteristics (age, degree of obstruction, walking, dyspnoea, body mass index) and 79 comorbidities were identified.	ATS/ERS	COPD: 1969 Control: 316	<p>Top 25th percentile of comorbidities with highest number of links (Network analysis):</p> <p>Systemic hypertension, hyperlipidaemia, coronary artery disease, degenerative joint disease, BPH: benign prostatic hypertrophy, diabetes mellitus (DM), gastro-oesophageal reflux</p> <p>Disease (GORD), depression, peripheral arterial diseases, congestive heart failure, substance abuse, atrial fibrillation/flutter, anxiety, cerebrovascular accident, erectile dysfunction, pulmonary hypertension, obstructive sleep apnoea (OSA), osteoporosis, bipolar/ schizophrenia, pulmonary fibrosis, gout, DM with neuropathy, dementia</p>
Divo et al. 2018(5)	Spain	COPD cases and controls age 40 years and older were selected from the EpiChron Cohort, which links, at the individual level, clinical and demographic information contained in the electronic medical records of the 1.3 million inhabitants of the Spanish autonomous community of Aragon.	ICD9 codes 490–492, 494, 496	COPD: 27,617 Controls: 27,617	<p>Risk factors for COPD plus at least one of 119 chronic conditions* (Network analysis):</p> <ul style="list-style-type: none"> Older age: “At every age category, the COPD Networks include more nodes, have a higher overall diseases prevalence and are much denser than the non-COPD, except for those older than 85 years old” <p>*Huntley AL et al. Measures of Multimorbidity and Morbidity Burden for Use in Primary Care and Community Settings: A Systematic Review and Guide. The Annals of Family Medicine. 2012; 10: 134–141. https://doi.org/10.1370/afm.1363 PMID: 22412005</p>
Carmona-Pérez et al. 2021(22)	Spain	Data from the EpiChron Cohort (as above). From all individuals aged 40 years and older on January 1, 2015 (n =673,059), selected those patients with a diagnosis of COPD and/or HF in their primary and/or hospital care EHRs. We stratified the study population by sex and as having COPD, HF, or COPD + HF.	ICD9 codes 490–492, 494, 496	COPD: 28,608 Heart Failure:13,414 COPD+HF: 3,952	<p>Risk factors for psychiatric diseases in women with COPD (Network analysis):</p> <ul style="list-style-type: none"> Behavioural risk disorders (in women) (No OR stated) <p>Risk factors for cancer in men with COPD (Network analysis):</p> <ul style="list-style-type: none"> Behavioural risk disorders (No OR stated) GERD (No OR stated) Obstructive sleep apnoea (No OR stated)

Zacarias-Pons et al. 2021(23)	Europe: Austria, Belgium, Czech Republic, Denmark, Estonia, France, Germany, Italy, Luxembourg, Slovenia, Spain, Sweden and Switzerland and Girona (in Spain)	Longitudinal cohort data from 3 times points in the Survey of Health, Ageing and Retirement Europe study. Included people aged 50 and older	Self-reported	Total: 25931	<p>Risk factors for multimorbidity* in male patients with COPD (sex-stratified latent transition analysis vs the healthy class):</p> <ul style="list-style-type: none"> • Age (OR=1.16; 95%CI: 1.15, 1.18; p<0.001) • Current smoker (OR=3.2; 95%CI: 2.38, 4.32; p<0.001) • Former smoker (OR=1.87; 95%CI: 1.44, 2.42; p<0.001) • Post-secondary education (OR=0.7; 95%CI: 0.53, 0.91; p<0.001) • Being separated or single (OR=1.66; 95%CI: 1.22, 2.26; p<0.001) • BMI Obese (OR=1.73; 95%CI: 1.25, 2.4; p<0.001) • Employed (OR=0.69; 95%CI: 0.49, 0.97) • 3rd quartile of material deprivation (OR=2.3; 95%CI: 1.61, 3.27; p<0.001) • 4th quartile of material deprivation (OR=3.28; 95%CI: 2.28, 4.73; p<0.001) <p>*Multimorbidity cluster including COPD, osteoarthritis, rheumatoid arthritis, ulcer and cataracts</p>
Multimorbidity regression analyses					
Ajmera et al. 2014(25)	United States	Observational retrospective cohort of Medicaid beneficiaries with COPD.	ICD-9-CM 491.xx, 492.xx, 496.xx	37,151	<p>Risk of inflammation-related multimorbidity* in patients with COPD (multinomial logistic regression):</p> <ul style="list-style-type: none"> • Women vs men (aOR=1.88; 95%CI: 1.75, 2.01) • Older adults (55-64 years) compared to younger adults (18-24 years) (aOR=6.14; 95%CI: 5.05, 7.04) • African Americans, Hispanics and Asians had lower likelihood of having IF_PHY/MI compared to Whites (aOR not specified) <p>*Cardiovascular disease, depression, diabetes mellitus, hypertension, hyperlipidaemia or musculoskeletal disorders</p>
Miller et al. 2010(26)	United States	People with COPD identified from a national sample of 134,401 US households from the Taylor Nelson Sofres household panel. Screened	Self-reported	COPD + CVD: 968 COPD alone: 757	Risk factors for multiple comorbidities* in patients with COPD:

		by postal survey for respiratory symptoms and physician-diagnosed conditions.			<ul style="list-style-type: none"> Heart disease. Patients with heart disease 50% to twice as likely to report multiple comorbidities and four times more likely to report diabetes <p>*Arthritis, sleep apnoea, chronic pain, depression, GERD, osteoporosis and overactive bladder</p>
Knorst et al. 2011(24)	Not specified	Patients who met GOLD spirometric criteria for COPD (post-bronchodilator FEV/FVC < 0.7)	GOLD	COPD: 470	<p>Risk factors for multimorbidity (number of comorbidities) in patients with COPD:</p> <ul style="list-style-type: none"> BMI (r = 0.323; p < 0.001) <p>Note: Obese patients had an average of 4.1 comorbidities, and underweight, normal-weight and overweight patients of 2.8, 2.5 and 3.1, respectively.</p>
Cunningham et al. 2015(27)	United States	State-based, random-digit-dialled telephone survey of noninstitutionalized, US adults aged 18 years or older, administered annually by state health departments with assistance from the US Centre for Disease Control and Prevention. Respondents with self-reported COPD and complete survey data in 2011 were selected.	Self-reported	Total: 405,856 COPD: 33,088	<p>Risk factors for any of 10 chronic conditions* in patients with COPD:</p> <ul style="list-style-type: none"> Smoking status (p < 0.001) for each of the chronic conditions. Among adults with COPD, current smokers had a higher likelihood of only cancer and depression compared to those who had never smoked after taking into account the covariates. <p>*Self-reported diagnosis of arthritis, asthma, cancer, coronary artery disease, depression, diabetes, high blood pressure, high cholesterol, kidney disease, and stroke</p>
Yu et al. 2017(43)	Netherlands and Switzerland	5-year prospective follow-up study of COPD patients aged 40 and over with GOLD stage II to IV and no exacerbations in the previous 4 years	GOLD	409	<p>Risk factors for multimorbidity* in patients with COPD:</p> <ul style="list-style-type: none"> Physical activity (lower), but not significantly so - except for depression and anxiety. <p>*Cardiovascular, neurological, endocrine, musculoskeletal, mental, malignant, or infectious diseases</p>
O'Kelly et al, 2011(28)	Ireland	A register of individuals with chronic respiratory disease and a sub-register of those with	International Classification of Primary	Chronic respiratory disease: 653	<p>Risk factors for multimorbidity in patients with COPD (univariate analysis) included:</p> <ul style="list-style-type: none"> Female sex (OR=1.67; 95%CI: 1.18-4.56) vs males

		multimorbidity were created in three general practice populations. Included diagnoses were chronic bronchitis, chronic obstructive pulmonary disease, asthma, or "respiratory disease other". Codes for acute respiratory events and lung cancer were not included.	Care (ICPC) codes.	of which 393 had multimorbidity (not further defined)	<ul style="list-style-type: none"> • low socio-economic status defined as poorest 30% of the population, entitled to a GMS card: OR=3.18; 95%CI: 2.23-4.56) • Increasing age <ul style="list-style-type: none"> ○ Age 30-39 (ref <30): (OR=1.98; 95%CI: 1.18-3.35) ○ Age 40-49 (ref <30): (OR=4.49; 95%CI: 2.53-8.13) ○ Age 50-59 (ref <30): (OR=7.62; 95%CI: 4.45-13.37) ○ Age 60-69: (OR=11.75; 95%CI: 6.48-22.21).
Ierodiakonou et al. 2021(44)	Greece	Convenience sample of patients attending primary care with a diagnosis of COPD. All patients with COPD invited for regular follow-up and renewal of prescriptions or chronic medications. No exclusion criteria.	Diagnosis by specialist with the use of spirometry	COPD: 245	<p>Risk factors for two or more comorbidities* in people with COPD:</p> <ul style="list-style-type: none"> • Polypharmacy (defined as taking five or more drugs per day) (p<0.05) <p><i>*Cardiometabolic diseases, prostate disorder, GERD-gastritis, cancer, depression, anxiety disorder and dementia</i></p>
Le et al. 2021(29)	United States	Retrospective cohort study using a nationally representative sample of Medicare fee-for-service beneficiaries. The COPD group included beneficiaries 65 years and older with a COPD diagnosis before January 1st, 2015. COPD beneficiaries were matched 1:1 on age, sex, and race with non-COPD controls. Diagnoses for COPD required at least one ICD-9-CM code in an inpatient, home health agency, hospice, or skilled nursing facility setting or at least two diagnosis codes in outpatient or physician visits. The date of the	ICD-9 codes 490, 491.1, 492.x, 494.x, and 496.x	COPD: 739118 Matched non-COPD: 739118	<p>Risk factors for multimorbidity* in patients with COPD included:</p> <ul style="list-style-type: none"> • Age over 85 years (except respiratory and tobacco use disorders) • Female sex (except cardiovascular diseases) <p><i>*Multimorbidity in patients with COPD and matched controls was defined as having at least one or more chronic conditions among the list of 40 chronic conditions. Our study considers COPD as an index disease to define other coexisting multimorbidity. Similar to the identification of COPD diagnoses, the initial diagnosis of these additional, chronic conditions identified by CMS using Medicare claims from January 1st, 1999, onward. Algorithms and ICD-9-CM codes utilized to identify these conditions are published by CMS.</i></p>

		initial COPD diagnosis was identified and confirmed by CMS using a one-year wash-out period, ensuring a lack of other prior COPD diagnoses.			
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