

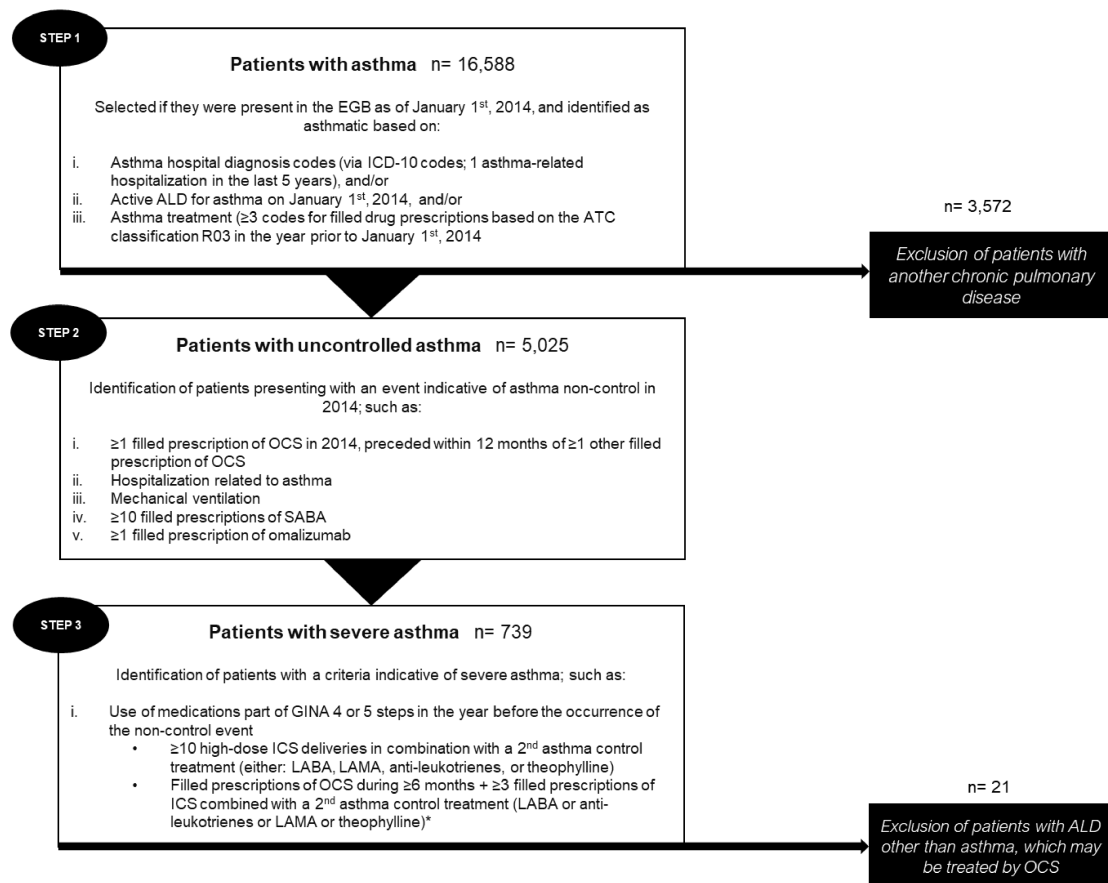
Real-life impact of uncontrolled severe asthma on mortality and healthcare use in adolescents and adults: findings from the retrospective observational RESONANCE study in France

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Supplementary materials

FIGURE S1. Patient selection algorithm

Key: ALD – affection de longue durée (long-term condition); ATC – Anatomical Therapeutic Chemical; COPD – chronic obstructive pulmonary disease; ICD-10 – International Classification of Diseases, 10th Revision; ICS – inhaled corticosteroid; LABA – long-acting β 2-agonist; LAMA – long-acting muscarinic antagonist; OCS – oral corticosteroid; SABA – short-acting β 2-agonist.



Footnote:

* Of note, these criteria did not apply to patients with an ALD other than asthma (i.e. rheumatoid arthritis, ulcerative colitis, Crohn's disease, cancer, etc) who can be treated by OCS identified by an exploratory analysis of ALD of patients from the target population meeting criterion.

Methods – Additional details on drugs of interest

Asthma treatments:

- short-acting beta2-agonists (SABA),
- long-acting beta2-agonists (LABA),
- long-acting anticholinergics (LAMA),
- antileukotriene receptor antagonists (LTRA),
- xanthines,
- inhaled and oral corticosteroids (ICS and OCS),
- combination treatments.

Other drug classes of interest:

- nasal antihistamines,
- antihistamines,
- nonsteroidal anti-inflammatory drugs (NSAIDs),
- antibiotics,
- proton pump inhibitors (PPIs),
- psychotropic drugs,
- topical corticosteroids,
- topical immunosuppressants.

Methods – ICD-10 codes used

For Asthma definition

- J45.0 Predominantly allergic asthma
- J45.1 Non-allergic asthma
- J45.8 Mixed asthma
- J45.9 Asthma, Unspecified
- J46 Status asthmaticus
- J96 Respiratory failure, not elsewhere classified

For Other chronic pulmonary disease definition

- J41 Simple and mucopurulent chronic bronchitis
- J42 Unspecified chronic bronchitis
- J43 Emphysema
- J44 Other chronic obstructive pulmonary disease
- J47 Bronchiectasis
- J61 Pneumoconiosis due to asbestos and other mineral fiber
- J62.8 Pneumoconiosis due to other dust containing silica
- J68.0 Bronchitis due to chemicals, gases, fumes and vapors
- E84 Mucoviscidosis
- J92.0 Pleural plaque with presence of asbestos
- J94.8 Other specified pleural conditions
- J96.1+0 Insuffisance respiratoire chronique obstructive

Methods – Variables defined for propensity score matching

1. nasal corticosteroid (Yes/No)
2. systemic antihistamine (Yes/No)
3. non-steroidal anti-inflammatory drugs (Yes/No)
4. antibiotic (Yes/No)
5. proton pump inhibitor (Yes/No)
6. dermocorticoids (Yes/No)
7. psychotropic drug (Yes/No)
8. age (years)
9. number of outpatient consultations
10. charlson's score
11. consultation with a nurse (Yes/No)
12. cardio-vascular diseases (Yes/No)
13. ocular antihistamine (Yes/No)
14. hypertension (Yes/No)
15. osteoporosis (Yes/No)
16. number of consultations with a physiotherapist
17. consultations with a physiotherapist (Yes/No)
18. depression (Yes/No)
19. psychiatric illness (Yes/No)
20. number of emergency room visits
21. hospitalization (Yes/No)
22. number of consultations with a nurse
23. emergency room visits (Yes/No)
24. number of hospitalizations
25. nasal antihistamine (Yes/No)
26. cataract (Yes/No)
27. nasal polyposis (Yes/No)
28. number of hospital consultations
29. gastroesophageal reflux (Yes/No)
30. dyslipidemia (Yes/No)
31. arrhythmia (Yes/No)
32. hospital consultations (Yes/No)
33. cerebrovascular diseases (Yes/No)
34. anxiety (Yes/No)
35. rhinosinusitis (Yes/No)
36. heart failure (Yes/No)
37. diabetes (Yes/No)
38. coronary heart disease (Yes/No)
39. sex
40. psychotic disorders (Yes/No)
41. outpatient consultation (Yes/No)
42. topical immunosuppressant (Yes/No)
43. CMU (Yes/No)
44. myocardial infarction (Yes/No)
45. atopic dermatitis (Yes/No)

TABLE S1. Quality of direct matching between cohort of patients with uncontrolled severe asthma and general population

<i>Matching variables</i>	<i>Before Matching</i>			<i>After Matching</i>		
	Uncontrolled severe asthma cohort (n=739)	General population (n=466,977)	Standardized mean differences	Uncontrolled severe asthma cohort (n=739)	General population (n=2,217)	Standardized mean differences*
Age (mean, SD)	62.0 (16.7)	48.5 (20.2)	0.7297	62.0 (16.7)	62.0 (16.7)	0.0000
Sex						
Male (n, %)	318 (43.0%)	228 841 (49.0%)	0.1201	318 (43.0%)	954 (43.0%)	0.0000
Female (n, %)	421 (57.0%)	238 136 (51.0%)		421 (57.0%)	1 263 (57.0%)	
Beneficiary of CMU-c (n, %)	74 (10.0%)	31 778 (6.8%)	0.1158	74 (10.0%)	222 (10.0%)	0.0000

* A standardized mean difference < 0,1 after matching is considered as acceptable.

TABLE S2. Quality of propensity score matching between cohort of patients with uncontrolled severe asthma and cohort of patients with asthma

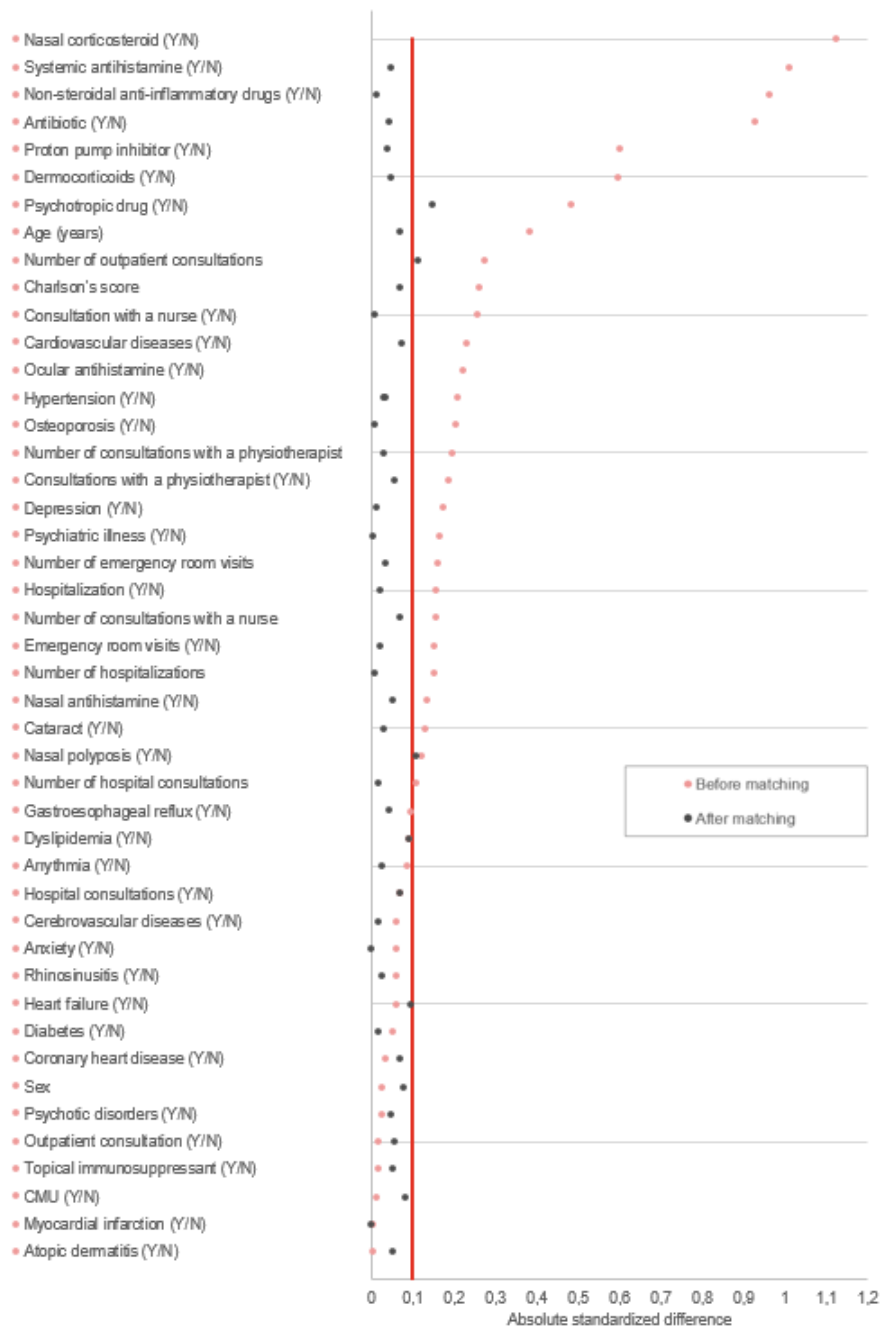
Matching variables	Before Matching			After Matching		
	Uncontrolled severe asthma cohort (n=739)	Asthma cohort (n=15,849)	Standardized mean differences	Uncontrolled severe asthma cohort (n=739)	Asthma cohort (n=739)	Standardized mean differences*
Age (mean, SD)	62.0 (16.7)	54.8 (20.9)	0.3826	62.0 (16.7)	63.2 (17.2)	-0.0688
Sex						
Male (n, %)	318 (43.0%)	7 010 (44.2%)	0.0242	318 (43.0%)	347 (47.0%)	0.0789
Female (n, %)	421 (57.0%)	8 839 (55.8%)		421 (57.0%)	392 (53.0%)	
Beneficiary of CMU-c (n, %)	74 (10.0%)	1 536 (9.7%)	0.0108	74 (10.0%)	57 (7.7%)	0.0810
Cardiovascular diseases (n, %)	405 (54.8%)	6 863 (43.3%)	0.2316	405 (54.8%)	431 (58.3%)	-0.0710
Coronary heart disease (n, %)	55 (7.4%)	1 036 (6.5%)	0.0355	55 (7.4%)	69 (9.3%)	-0.0684
Myocardial infarction (n, %)	8 (1.1%)	179 (1.1%)	-0.0045	8 (1.1%)	8 (1.1%)	0.0000
Arrhythmia (n, %)	60 (8.1%)	946 (6.0%)	0.0841	60 (8.1%)	65 (8.8%)	-0.0243
Heart failure (n, %)	33 (4.5%)	527 (3.3%)	0.0590	33 (4.5%)	49 (6.6%)	-0.0947
Hypertension (n, %)	364 (49.3%)	6 178 (39.0%)	0.2081	364 (49.3%)	375 (50.7%)	-0.0298
Cerebrovascular diseases (n, %)	27 (3.7%)	411 (2.6%)	0.0610	27 (3.7%)	29 (3.9%)	-0.0142
Dyslipidemia (n, %)	237 (32.1%)	4 439 (28.0%)	0.0887	237 (32.1%)	268 (36.3%)	-0.0885
Diabetes (n, %)	108 (14.6%)	2 047 (12.9%)	0.0493	108 (14.6%)	112 (15.2%)	-0.0152
Osteoporosis (n, %)	110 (14.9%)	1 325 (8.4%)	0.2046	110 (14.9%)	112 (15.2%)	-0.0076
Psychiatric illness** (n, %)	224 (30.3%)	3 671 (23.2%)	0.1621	224 (30.3%)	223 (30.2%)	0.0029
Cataract (n, %)	75 (10.1%)	1 049 (6.6%)	0.1276	75 (10.1%)	69 (9.3%)	0.0274
Rhinosinusitis (n, %)	3 (0.4%)	17 (0.1%)	0.0591	3 (0.4%)	2 (0.3%)	0.0233
Gastroesophageal reflux (n, %)	79 (10.7%)	1 261 (8.0%)	0.0941	79 (10.7%)	69 (9.3%)	0.0451
Atopic dermatitis (n, %)	1 (0.1%)	22 (0.1%)	-0.0009	1 (0.1%)	0 (0.0%)	0.0521
Nasal polyposis (n, %)	14 (1.9%)	91 (0.6%)	0.1198	14 (1.9%)	5 (0.7%)	0.1083
Nasal antihistamine (n, %)	1 (0.1%)	197 (1.2%)	-0.1342	1 (0.1%)	3 (0.4%)	-0.0521
Ocular antihistamine (n, %)	4 (0.5%)	589 (3.7%)	-0.2213	4 (0.5%)	6 (0.8%)	-0.0330
Systemic antihistamine (n, %)	65 (8.8%)	7 892 (49.8%)	-1.0090	65 (8.8%)	75 (10.1%)	-0.0462
Nasal corticosteroid (n, %)	10 (1.4%)	6 597 (41.6%)	-1.1249	10 (1.4%)	15 (2.0%)	-0.0525

Non-steroidal anti-inflammatory drugs (n, %)	70 (9.5%)	7 756 (48.9%)	-0.9634	70 (9.5%)	73 (9.9%)	-0.0137
Antibiotic (n, %)	170 (23.0%)	10 249 (64.7%)	-0.9251	170 (23.0%)	184 (24.9%)	-0.0444
Proton pump inhibitor (n, %)	122 (16.5%)	6 776 (42.8%)	-0.6001	122 (16.5%)	132 (17.9%)	-0.0359
Psychotropic drug (n, %)	128 (17.3%)	6 091 (38.4%)	-0.4844	128 (17.3%)	172 (23.3%)	-0.1484
Dermocorticoids (n, %)	19 (2.6%)	3 321 (21.0%)	-0.5954	19 (2.6%)	25 (3.4%)	-0.0478
Topical immunosuppressant (n, %)	1 (0.1%)	31 (0.2%)	-0.0148	1 (0.1%)	0 (0.0%)	0.0521
Outpatient consultation (n, %)	656 (88.8%)	14 159 (89.3%)	-0.0182	656 (88.8%)	668 (90.4%)	-0.0532
Hospital consultation (n, %)	193 (26.1%)	3 685 (23.3%)	0.0665	193 (26.1%)	171 (23.1%)	0.0691
Consultation with a nurse (n, %)	551 (74.6%)	9 941 (62.7%)	0.2572	551 (74.6%)	548 (74.2%)	0.0093
Consultation with a physiotherapist (n, %)	383 (51.8%)	6 754 (42.6%)	0.1853	383 (51.8%)	363 (49.1%)	0.0541
Hospitalization (n, %)	468 (63.3%)	8 834 (55.7%)	0.1551	468 (63.3%)	475 (64.3%)	-0.0197
Emergency room visits (n, %)	356 (48.2%)	6 442 (40.6%)	0.1519	356 (48.2%)	349 (47.2%)	0.0190
Number of outpatient consultations (mean, SD)	36.9 (30.0)	29.2 (25.9)	0.2724	36.9 (30.0)	33.7 (26.7)	0.1128
Number of hospital consultations (mean, SD)	3.4 (10.2)	2.4 (7.9)	0.1094	3.4 (10.2)	3.3 (10.0)	0.0175
Number of consultations with a nurse (mean, SD)	53.5 (195.3)	27.9 (132.7)	0.1535	53.5 (195.3)	41.6 (162.1)	0.0665
Number of consultations with a physiotherapist (mean, SD)	37.0 (98.8)	21.1 (62.3)	0.1935	37.0 (98.8)	34.1 (104.0)	0.0286
Number of hospitalizations (mean, SD)	2.3 (5.0)	1.6 (4.0)	0.1514	2.3 (5.0)	2.4 (5.0)	-0.0057
Number of emergency room visits (mean, SD)	1.2 (2.2)	0.9 (1.9)	0.1606	1.2 (2.2)	1.2 (1.9)	0.0340
Charlson's score (mean, SD)	3.6 (2.3)	3.0 (2.3)	0.2588	3.6 (2.3)	3.8 (2.4)	-0.0702

* A standardized mean difference < 0,1 after matching is considered as acceptable.

**Psychiatric illness includes depression, anxiety, and psychotic disorders.

FIGURE S2. Quality of propensity score matching between cohort of patients with uncontrolled severe asthma and cohort of patients with asthma



A standardized mean difference < 0,1 after matching is considered as acceptable.

FIGURE S3. Analysis of mortality by age group

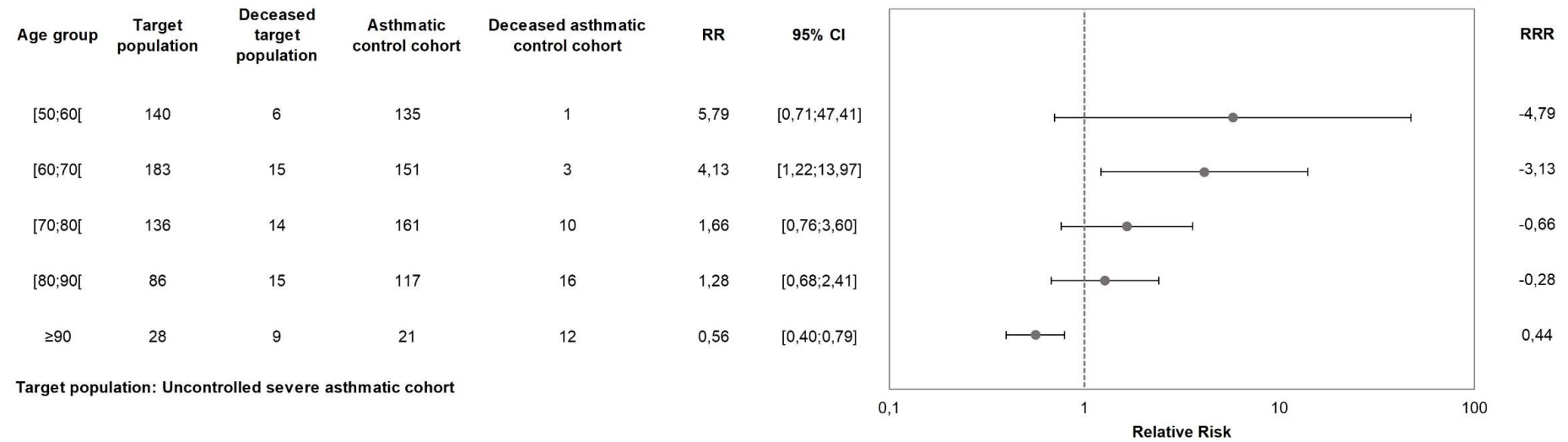


Table S3. Results of multivariate Cox model on mortality

Covariate	Hazard ratio	95% CI
Age (1-year increase)	1.07	1.05 - 1.09
History of cardiovascular diseases (with vs. without)	1.91	1.18 - 3.09
History of diabetes (with vs. without)	1.66	1.11 - 2.49
History of cancer (with vs. without)	2.40	1.64 - 3.50
Patients with uncontrolled severe asthma vs. general population in population with history of psychiatric disease	1.22	0.66 - 2.26
Patients with uncontrolled severe asthma vs. general population in population without history of psychiatric disease	3.25	2.14 - 4.92
History of psychiatric disease (with vs. without) in uncontrolled severe asthma cohort	0.93	0.52 - 1.65
History of psychiatric disease (with vs. without) in general population cohort	2.46	1.54 - 3.92

Key: CI – confidence interval.

FIGURE S4. 24-month survival for the uncontrolled severe asthmatic cohort versus general population among subjects without history of psychiatric disease

