RAPSODI

Annual report 2019

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12-12-2019

RAPSODI: Registry of adult patients with severe asthma for optimal disease management

1. Recruitment

Total in 12-12-2019: 610 included patients

Total included in 2019: 328

Patients included per site:

Academisch Medisch Centrum (AMC): 254

Medisch Centrum Leeuwarden: 104

St. Franciscus: 74

Deventer Ziekenhuis: 34

Catharina Ziekenhuis: 32

Isala: 32

Haga Ziekenhuis: 20

Rijnstate: 20

Medisch Spectrum Twente: 19

Ziekenhuis Gelderse Vallei: 11

Nederlands Astmacentrum Davos: 10

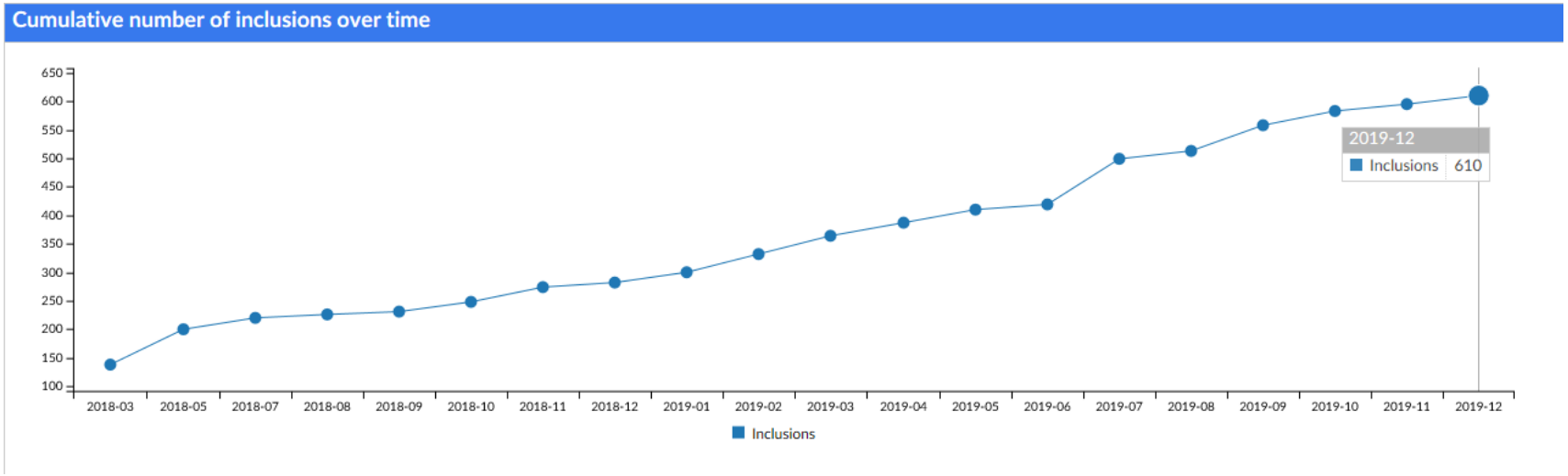

Fig. 1. Cumulative number of patients included in RAPSODI since the start of the register

2. Baseline demographics

	Total	Site 1	Site 2	Site 3	Site 4	Site 5
Age, mean (SD)	53.3 (±14.7)	53.7 (±14.4)	51.3 (±15.0)	50.6 (±14.5)	55.0 (±17.1)	59.1 (±11.1)
Female gender	290 (51.6)	121 (48.2)	56 (56)	43 (65.2)	12 (48.2)	12 (41.4)
BMI, mean (SD)	28.0 (±5.4)	28.3 (±5.7)	27.8 (±5.5)	28.3 (±5.5)	27.1 (±4.5)	26.7 (±4.2)
Weight in kg, mean (SD)	83.4 (±16.8)	84.1 (±17.5)	84.7 (±16.6)	81.9 (±17.4)	81.9 (±16.6)	81.1 (±14.9)
Onset of asthma	33.9 (±20.7)	34.3 (±19.6)	28.5 (±21.5)	40.6 (21.5)	40.1 (±20.6)	39.0 (±19.6)
- childhood onset <18 years	168 (36.3)	84 (36.5)	20 (36.4)	15 (38.5)	10 (37.0)	7 (24.1)
- adult-onset ≥18	295 (63.7)	146 (63.5)	35 (63.3)	24 (61.5)	17 (63.0)	22 (75.9)
- missing*	99 (17.6)	21 (8.3)	45 (45)	27 (40.9)	1 (3.5)	0 (0)

	Site 6	Site 7	Site 8	Site 9	Site 10	Site 11
Age, mean (SD)	50.1 (±18.4)	54.2 (±12.3)	57.1 (±17.4)	58.0 (±16.0)	55.8 (±14.3)	47.9 (±16.2)
Female gender	10 (58.8)	9 (50.0)	11 (64.7)	8 (53.3)	4 (36.4)	4 (40.0)
BMI, mean (SD)	28.0 (±3.17)	27.3 (±3.4)	28.9 (±5.9)	28.9 (±5.2)	27.3 (±5.14)	27.7 (±6.4)
Weight in kg, mean (SD)	84.2 (±10.5)	80.0 (±13.1)	83.6 (±16.8)	80.3 (±14.4)	81.4 (±19.2)	84.1 (±22.9)
Onset of asthma	28.9 (±19.3)	26.5 (±18.4)	39.9 (±28.5)	26.9 (±5.2)	36.1 (±21.9)	21.5 (17.1)
- childhood onset <18 years	6 (35.3)	8 (53.3)	6 (40.0)	5 (33.3)	3 (27.3)	4 (40.0)
- adult-onset ≥18	11 (64.7)	7 (46.7)	9 (60.0)	10 (66.7)	8 (72.7)	6 (60.0)
- missing	0 (0)	2 (11.1)	2 (11.7)	0 (0)	0 (0)	0 (0)

Data is presented as n (%) unless otherwise specified.

3. Baseline summary: n=562

Asthma History	
Ever admission to ICU - total number of admissions - ever intubated*	56 (10) 107 29 (5.2)
Pulmonary rehabilitation program at sea level - total number of participations	90 (16.1) 105
Pulmonary rehabilitation program at high altitude (Davos) - total number of participations	74 (13.2) 139
Bronchial thermoplasty	11 (2.0)
Smoking status	
Never smoked	331 (58.8)
Ex smoker	231 (41.0)
Current smoker	4 (0.7)
Number of pack years, median (IQR)	10 (4 – 20)

Lung Function	
Pre-bronchodilator	
FEV1 in L -missing/not measured	2.5 (±0.8) 45 (8.0)
FEV1 % -missing/not measured	78.4 (±0.2) 45 (8.0)
FVC in L -missing/not measured	3.8 (±1.1) 48 (8.5)
FVC in % -missing/not measured	98.4 (±18.6) 48 (8.5)
FEV1/FVC ratio in L -missing/not measured	0.6 (±0.1) 95 (16.9)
FEV1/FVC ratio in % -missing/not measured	78.2 (±16.9) 114 (20.2)

Post bronchodilator	
FEV1 in L -missing/not measured	2.6 (±0.8) 258 (45.9)
FEV1 in % -missing/not measured	83.1 (±20.7) 258 (45.9)
FVC in L -missing/not measured	4.0 (±1.1) 259 (46.1)
FVC in % -missing/not measured	102.2 (±17.3) 259 (46.1)
FEV1/FVC ratio in L -missing/not measured	0.6(±1.1) 268 (47.6)
FEV1/FVC ratio in % -missing/not measured	81.4 (±16.8) 268 (47.6)
CO-diffusion capacity ever measured, n (%) **-** DLCOc/HbVA in mmol/min/kPa/L - DLCOc/HbVA, % of predicted	212 (37.7) 1.6 (1.4 – 4.5) 97.7 (85.0 – 108.0)
Positive bronchial provocation test, n (%)	90 (16.5)
FeNO in ppb, median (IQR) -missing/not measured	32.0 (19 – 59) 58 (10.3)

Data is presented as n (%) unless otherwise specified.

Laboratory	
Leukocytes x10^9/L	8. 2 (6.9 – 10.2)
-missing	22 (3.9)
Neutrophils x10^9/L, median (IQR)	5.1 (3.8 – 7.0)
-missing	35 (6.2)
Eosinophils x10^9/L, median (IRQ)	0.2 (0.1 – 0.5)
-missing	29 (5.1)
Eosinophils percentage, median (IRQ)	2.3 (1.0 – 5.8)
-missing	
Highest eosinophil count x10^9/L ever measured	0.6 (0.4 – 1.1)
- missing	44 (7.8)
IgE kU/L, median (IQR)	186 (68.5 – 462.7)
-missing	46 (8.2)
Measurement of allergen specific IgE, n (%)	
- yes, positive	266 (48.5)
- yes, negative	191 (34.8)
- no	92 (16.8)
Test for aspergillus and/or molds, n (%)	
- yes, positive	83 (15.4)
- yes, negative	247 (45.9)
- no	208 (38.7)
Measurement of food allergies, n (%)	
- yes, positive	44 (8.2)
- yes, negative	58 (10.8)
- no	437 (81.1)
Sputum induction ever performed, n (%)	
- Yes	46 (8.4)
- Yes but inadequate sample, n(% of induction samples)	11 (2.0)
- Not performed	491 (89.6)
- % neutrophils, median (IQR)	46.0 (36.5 – 64.8)
- % eosinophils, median (IQR)	16.0 (5.6 – 32.3)

Sputum culture ever performed, n (%)	111 (21.0)
- Performed	35 (6.2)
- Performed, positive pathogen	28 (5.0)
- Performed, negative pathogen	61 (10.9)
- Performed, throat bacteria	

Imaging	
Chest X-ray ever performed	501 (89.1)
- with pathology associated with asthma	73 (13)
- with pathology not associated with asthma	67 (11.9)
- no pathology	358 (63.7)
Chest CT-scan ever performed	363 (65.9)
- bronchiectasis	75 (13.3)
- tree- in-bud configurations	14 (2.5)
- emphysema	17 (3.0)
- other pulmonary pathologies	174 (31.0)
- no pulmonary pathologies	127 (22.6)
DEXA-scan ever performed	127 (22.5)
- osteopenia/osteoporosis	63 (11.4)
- normal bone mineral density	64 (11.6)
Bronchoscopy ever performed	120 (21.4)
- with pathology associated with asthma	57 (10.1)
- with pathology not associated with asthma	15 (2.7)
- no pathology	37 (6.6)

Data is presented as n (%) unless otherwise specified.

Comorbidities diagnosed	
Atopic dermatitis	76 (13.9)
Allergic rhinoconjunctivitis	137 (25.0)
Chronic rhinosinusitis	323 (59.0)
Nasal polyps	229 (41.9)
Aspirin hypersensitivity	71 (12.9)
Vocal cord dysfunction	19 (3.5)
Hyperventilation/anxiety disorder	25 (4.5)
Depression disorder	56 (10.2)
Gastroesophageal reflux	98 (17.9)
Frequent (>2/year) respiratory infections treated with antibiotics	117 (21.6)
Bronchiectasis	84 (15.4)
Eosinophilic granulomatosis polyangiitis	18 (3.3)
Eosinophilic pneumonia	16 (3.0)
Allergic bronchopulmonary aspergillosis	12 (2.2)
Chronic congestive heart failure	9 (1.7)
Obstructive sleep apnea syndrome	59 (10.9)

Data is presented as n (%) unless otherwise specified.

Medication usage	
Total use of reliever/short-acting inhalers	429 (77.9)
SABA	363 (64.5)
- not daily	173 (47.6)
- <8 doses per day	158 (43.5)
- ≥8 doses per day	14 (3.8)
- missing	18 (4.9)
SAMA	47 (8.3)
- not daily	12 (25.5)
- <8 doses per day	28 (59.5)
- ≥8 doses per day	3 (6.3)
- missing	4 (8.5)
SAMA/LABA combination inhaler	20 (3.5)
- not daily	3 (15.0)
- <8 doses per day	11 (55.0)
- ≥8 doses per day	5 (25.0)
- missing	1 (5.0)
SAMA/SABA by nebulizer	65 (11.5)
- not daily	25 (38.4)
- <8 doses per day	24 (36.9)
- ≥8 doses per day	16 (24.6)
- missing	0 (0.0)

Data is presented as n (%) unless otherwise specified.

ICS single inhaler only	299 (53.2)
ICS single inhaler + LABA single inhaler	98 (17.4)
ICS/LABA combination inhaler only	416 (74.0)
LAMA single inhaler	184 (32.7)
LABA/LAMA combination inhaler	10 (1.8)
Triple therapy (ICS +lABA + LAMA)	4 (0.7)
Oral corticosteroid maintenance therapy - dosage in mg/day, pred equivalent, median (IQR) - tapering OCS	216 (38.4) 10 (5.0 – 15.0) 46 (18.1)
Antibiotics as maintenance therapy	50 (8.9)
Biologicals at time of inclusion - Omalizumab - 0malizumab (self administration) - Mepolizumab - Reslizumab - Benralizumab - Dupilumab	501 (89.1) 99 (17.6) 8 (252 (44.8) 75 (13.3) 63 (11.2) 13 (2.3)
Montelukast	134 (23.8)
Theophylline	19 (3.4)

Data is presented as n (%) unless otherwise specified.

Other medication	
Nasal corticosteroids	375 (66.7)
Antihistaminic drugs	192 (34.2)
Bisphosphonates	104 (18.5)
Calcium/vitamin D supplements	207 (36.8)
Proton pump inhibitors	235 (41.8)
Vitamine K antagonists	9 (1.6)
NSAIDs	14 (2.5)
Oral antidiabetic drugs	30 (5.3)

Data is presented as n (%) unless otherwise specified.

Previous therapy	
Omalizumab	83 (14.8)
Mepolizumab	73 (13.0)
Reslizumab	5 (0.9)
Benralizumab	4 (0.7)
Dupilumab	1 (0.2)
OCS maintenance therapy	75 (13.3)
antibiotics maintenance therapy	70 (12.5)
methotrexate	6 (1.1)
cyclosporine	2 (0.4)
azathioprine	8 (1.4)
cyclophosphamide	4 (0.7)
aspirin desensibilisation	0 (0.0)
anti-TNF alfa	1 (0.2)
other immunotherapy	22 (3.9)

Data is presented as n (%) unless otherwise specified.

Reason for cessation biologic	
Mepolizumab	n=73
Insufficient effect on OCS tapering	23
Adverse event	12
Insufficient effect on symptoms	44
Insufficient effect on lung function	8
Other reasons (logistics)	4
Reslizumab	n=5
Insufficient effect on OCS tapering	0
Adverse event	2
Insufficient effect on symptoms	3
Insufficient effect on lung function	1
Other reasons	1
Benralizumab	n=4
Insufficient effect on OCS tapering	0
Adverse event	2
Insufficient effect on symptoms	2
Insufficient effect on lung function	0
Other reasons	0
Dupilumab	n=1
Insufficient effect on OCS tapering	1
Adverse event	0
Insufficient effect on symptoms	0
Insufficient effect on lung function	0
Other reasons	1

Data is presented as n (%) unless otherwise specified.

Side effects chronic OCS usage	
Skin defects	67 (11.9)
Weight gain	178 (31.7)
Osteoporosis	70 (12.5)
Hypertension	30 (5.3)
Cataract	14 (2.5)
Diabetes mellitus	27 (4.8)
Depression	16 (2.8)
Adreno-cortical insufficiency	2 (0.4)

Data is presented as n (%) unless otherwise specified.
*percentages are based on the number of patients using reliever/short-acting inhalers. The frequency of use is according to the short-acting inhaler mentioned.
ICS=inhaled corticosteroids, LABA=long-acting β_2 adrenergic receptor agonist, LAMA= long-acting muscarinic receptor antagonist, NSAIDs=non-steroidal anti-inflammatory drugs, SABA=short-acting β_2 adrenergic receptor agonist, SAMA=short- muscarinic receptor antagonists

4. Follow-up 1: n= 233

Demographics	
Lost to follow-up	8 (3.4)
BMI, mean (SD)	28.7 (±5.7)
Weight in kg, mean (SD)	85.8 (± 17.3)

Asthma History previous 12 months	
Admission to ICU - total number of admissions - intubations	5 (2.1) 10 2 (0.9)
Pulmonary rehabilitation program at sea level - total number of participations	4 (1.7) 7
Pulmonary rehabilitation program at high altitude (Davos) - total number of participations	2 (0.9) 5
Bronchial thermoplasty	1 (0.4)

Data is presented as n (%) unless otherwise specified.

Lung Function previous 12 months	
Pre-bronchodilator	
FEV1 in L -missing/not measured	2.4 (±0.8) 11
FEV1 % -missing/not measured	79.3 (±22.1) 11
FVC in L -missing/not measured	3.8 (±1.1) 11
FVC in % -missing/not measured	100.0 (±20.4) 11
FEV1/FVC ratio in L -missing/not measured	0.6 (±0.1) 15
FEV1/FVC ratio in % -missing/not measured	79.1 (±16.4) 11
Post bronchodilator	
FEV1 in L -missing/not measured	2.7 (±0.8) 115
FEV1 in % -missing/not measured	82.4 (±22.2) 115
FVC in L -missing/not measured	4.1 (±1.0) 115
FVC in % -missing/not measured	102.7 (±20.0) 115
FEV1/FVC ratio in L -missing/not measured	0.6 (±0.1) 115
FEV1/FVC ratio in % -missing/not measured	81.2 (±16.8) 115

CO-diffusion capacity last 12 mths, n (%)	4
- DLCOc/HbVA in mmol/min/kPa/L	2.9 (±2.3)
- DLCOc/HbVA, % of predicted	88.2 (±60.0)

Positive bronchial provocation test, n (%)	2 (0.9)
FeNO in ppb, median (IQR) -missing/not measured	32 (20 - 47) 49 (21.0)

Laboratory	
Leukocytes x10^9/L, median (IQR) -missing	8.3 (6.9 – 10.2) 61
Neutrophils x10^9/L, median (IQR) -missing	5.1 (3.9 – 6.6) 65
Eosinophils x10^9/L, median (IRQ) -missing	0.1 (0.04 – 0.1) 60
Eosinophils percentage, median (IRQ) -missing	0.9 (0.3 – 2.4)
IgE kU/L, median (IQR) -missing	201.0 (40.5 – 541.0) 194
Measurement of allergen specific IgE, n (%) - yes, positive - yes, negative - no	 5 (2.2) 4 (1.7) 96.1
Test for aspergillus and/or molds, n (%) - yes, positive - yes, negative - no	 5 (2.2) 6 (2.6) 219 (95.2)
Measurement of food allergies, n (%) - yes, positive - yes, negative - no	 1 (0.4) 0 (0.0) 230 (99.6)

Data is presented as n (%) unless otherwise specified.

Sputum induction performed, n (%)	
- Yes	5 (2.2)
- Yes but inadequate sample, n(% of induction samples)	2 (0.9)
- Not performed	222 (96.9)
- % neutrophils, median (IQR)	28.0 (39.4 – 22.0)
- % eosinophils, median (IQR)	4.3 (0.8 – 18.3)
Sputum culture performed, n (%)	
- Performed	18 (8.1)
- Performed, positive pathogen	6 (2.6)
- Performed, negative pathogen	3 (1.3)
- Performed, throat bacteria	12 (5.2)

Imaging previous 12 months	
Chest X-ray performed	
- with pathology associated with asthma	8 (3.4)
- with pathology not associated with asthma	13 (5.6)
- no pathology	39 (16.7)
Chest CT-scan performed	21 (9.1)
- bronchiectasis	3 (1.3)
- tree- in-bud configurations	5 (2.1)
- emphysema	1 (0.4)
- other pulmonary pathologies	12 (5.2)
- no pulmonary pathologies	9 (3.9)
DEXA-scan performed	
- osteopenia/osteoporosis	4 (1.7)
- normal bone mineral density	3 (1.3)
Bronchoscopy performed	
- with pathology associated with asthma	1 (0.4)
- with pathology not associated with asthma	1 (0.4)
- no pathology	4 (1.7)

Data is presented as n (%) unless otherwise specified.

Comorbidities (diagnosed previous 12 months)	
Atopic dermatitis	2
Allergic rhinoconjunctivitis	13
Chronic rhinosinusitis	10
Nasal polyps	9
Aspirin hypersensitivity	1
Vocal cord dysfunction	1
Hyperventilation/anxiety disorder	2
Depression disorder	4
Gastroesophageal reflux	4
Frequent (>2/year) respiratory infections treated with antibiotics	3
Bronchiectasis	4
Eosinophilic granulomatosis polyangiitis	1
Eosinophilic pneumonia	1
Allergic bronchopulmonary aspergillosis	1
Chronic congestive heart failure	1
Obstructive sleep apnea syndrome	2

Data is presented as n (%) unless otherwise specified.

Medication usage	
Total use of reliever/short-acting inhalers	182 (78.1)
SABA	159 (68.2)
- not daily	92 (57.8)
- <8 doses per day	61 (38.3)
- ≥8 doses per day	6 (3.7)
- missing	0 (0.0)
SAMA/LABA combination inhaler	19 (8.1)
- not daily	4 (21.0)
- <8 doses per day	11 (57.8)
- ≥8 doses per day	2 (10.5)
- missing	2 (10.5)
SAMA/SABA by nebulizer	22
- not daily	4 (19)
- <4 doses per day	7 (33.3)
- ≥4 doses per day	10 (47.7
- missing	1

Data is presented as n (%) unless otherwise specified.

ICS single inhaler only	**129 (55.4)**
ICS single inhaler + LABA single inhaler	**34 (14.6)**
ICS/LABA combination inhaler only	**178 (76.4)**
LAMA single inhaler	**72 (30.9)**
LABA/LAMA combination inhaler	**4 (1.7)**
Triple therapy	**1 (0.4)**
Oral corticosteroid maintenance therapy - dosage in prednisone equivalent mg/day, median (IQR) - OCS tapering	**85 (36.5)** **7.5 (5.0 – 10.0)** **30 (35.3)**
Antibiotics as maintenance therapy	**11 (4.7)**
Biologicals - Omalizumab - Mepolizumab - Reslizumab - Benralizumab - Dupilumab	**205 (88.0)** **31 (13.3)** **91 (39.1)** **55 (23.6)** **26 (11.2)** **2 (0.9)**
Montelukast	**37 (15.9)**
Theophylline	**4 (1.7)**

Data is presented as n (%) unless otherwise specified.

Other medication	
Nasal corticosteroids	170 (73.0)
Antihistaminic drugs	67 (28.8)
Bisphosphonates	39 (16.7)
Calcium/vitamin D supplements	81 (34.8)
Proton pump inhibitors	91 (39.1)
Vitamine K antagonists	2 (0.9)
NSAIDs	9 (3.9)
Oral antidiabetic drugs	10 (4.3)

Data is presented as n (%) unless otherwise specified.

Previous therapy	
Omalizumab	11 (4.7)
Mepolizumab	55 (23.6)
Reslizumab	11 (4.7)
Benralizumab	4 (1.7)
Dupilumab	1 (0.4)
OCS maintenance therapy	16 (6.9)
antibiotics maintenance therapy	11 (4.7)
methotrexate	1 (0.4)
cyclosporine	0 (0.0)
azathioprine	1 (0.4)
cyclophosphamide	1 (0.4)
aspirin desensibilisation	0 (0.0)
anti-TNF alfa	0 (0.0)
other immunotherapy	1 (0.4)

Reason for cessation biologic	
Omalizumab	n=11
Insufficient effect on OCS tapering	1
Adverse event	1
Insufficient effect on symptoms	7
Insufficient effect on lung function	2
Other reasons (logistics)	1
Mepolizumab	n=55
Insufficient effect on OCS tapering	26
Adverse event	10
Insufficient effect on symptoms	43
Insufficient effect on lung function	11
Other reasons (logistics, pregnancy wishes)	3
Reslizumab	n=11
Insufficient effect on OCS tapering	3
Adverse event	3
Insufficient effect on symptoms	7
Insufficient effect on lung function	0
Other reasons (pregnancy wishes)	2
Benralizumab	n=4
Insufficient effect on OCS tapering	1
Adverse event	1
Insufficient effect on symptoms	1
Insufficient effect on lung function	1
Dupilumab	n=1
Insufficient effect on OCS tapering, Insufficient effect on symptoms	0
Adverse event, Insufficient effect on lung function	0
Other reasons	1

Side effects chronic OCS usage	
Skin defects	48 (20.6)
Weight gain	76 (32.6)
Osteoporosis	26 (11.2)
Hypertension	13 (5.6)
Cataract	6 (2.6)
Diabetes mellitus	13 (5.6)
Depression	9 (3.9)
Adreno-cortical insufficiency	1 (0.4)

Data is presented as n (%) unless otherwise specified.
ICS=inhaled corticosteroids, LABA=long-acting β_2 adrenergic receptor agonist, LAMA= long-acting muscarinic receptor antagonist, NSAIDs=non-steroidal anti-inflammatory drugs, SABA=short-acting β_2 adrenergic receptor agonist, SAMA=short- muscarinic receptor antagonists

5. PatientCoach questionnaires:

5.1. Availability of Asthma Control Questionnaire (ACQ): n= 508

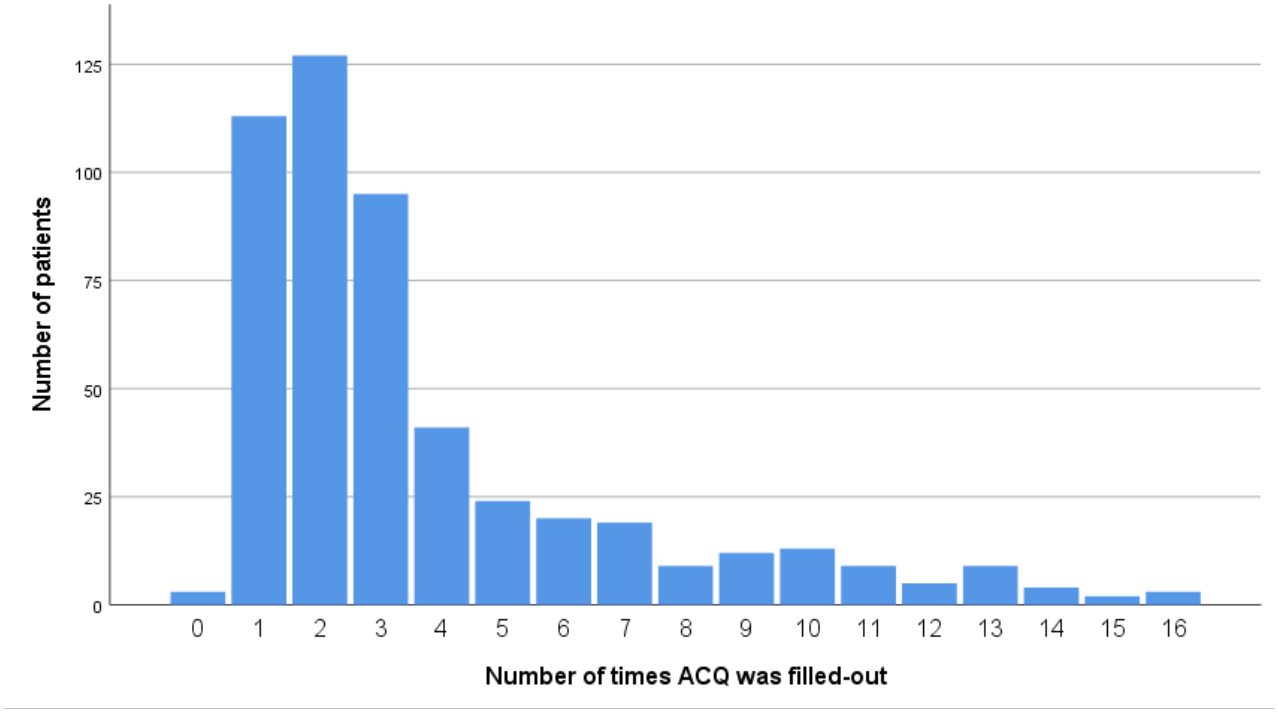

Fig. 2. Number of times that ACQ was completed by patients from RAPSODI, since the start of the register

5.2. Availability of Asthma related quality of life questionnaire (AQLQ): n= 508

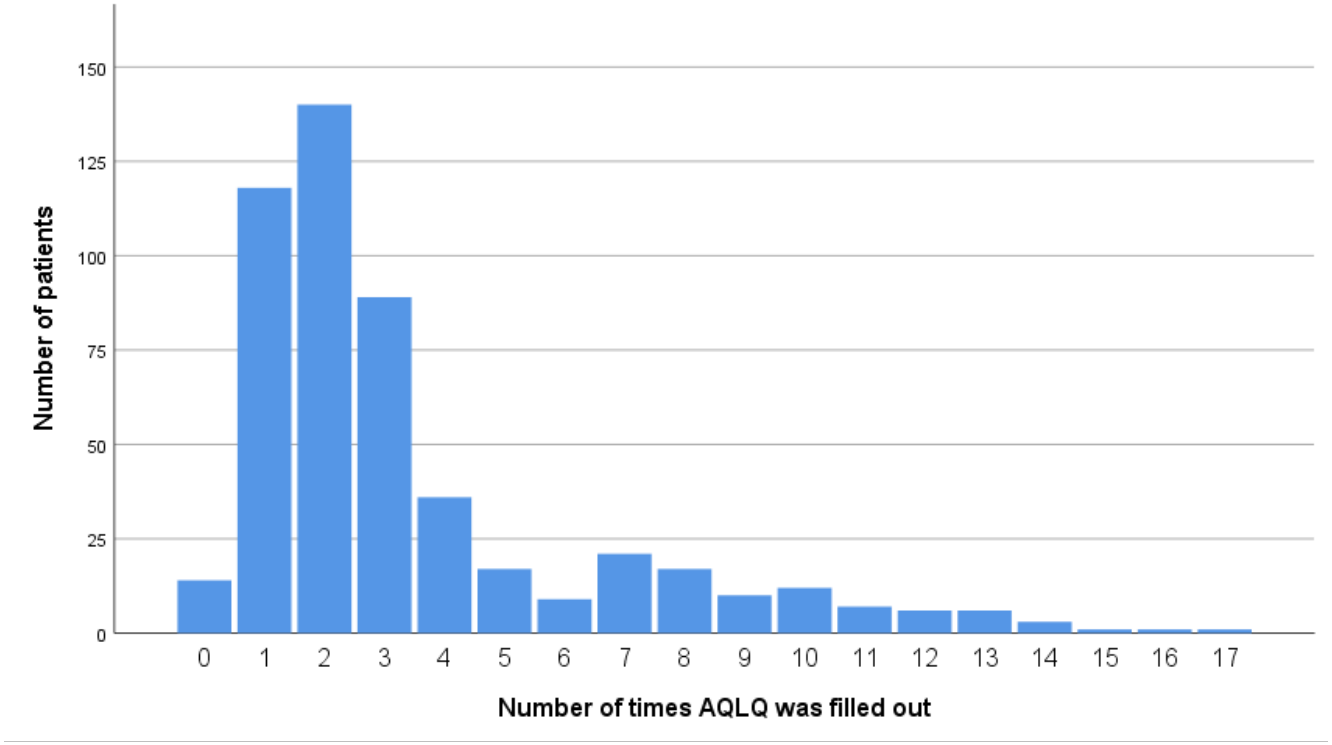

Fig. 3. Number of times that AQLQ was completed by patients from RAPSODI, since the start of the register

5.1. Availability of Checklist Individual Strength questionnaire, domain fatigue (CIS): n=508

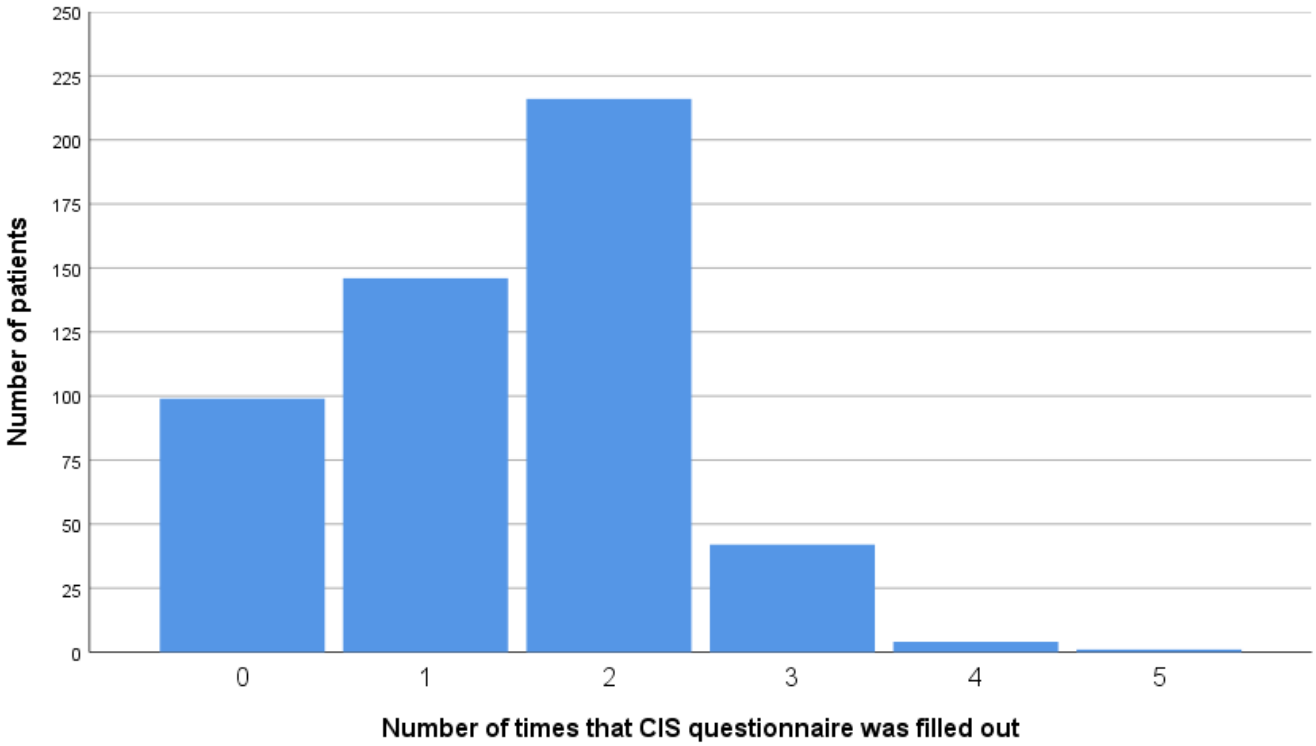

Fig. 4. Number of times that the Checklist Individual Strength questionnaire (CIS) was completed by patients from RAPSODI, since the start of the register