Cross-Country Comparison of Demographic and Clinical Characteristics of Patients Managed in Severe Asthma Services across UK, USA, Australia, South Korea, and Italy

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Background

Rationale

- Severe asthma carries a high morbidity and socio-economic burden.[1,2]

- Regional and national severe asthma registries have been actively collecting locally-relevant demographic and clinical data. However, there is a lack of inter-registry interoperability due to diverse severe asthma definitions and different variables collected.

- Inter-country characteristics of severe asthma patients have not previously been described.

- The International Severe Asthma Registry (ISAR; http://isaregistries.org/) is the first global adult severe asthma registry; a multicountry, multicenter, observational real-life initiative

- ISAR combines data from the regional and national severe asthma registries into a single large database, and standardizes the variables collected.

Objective

- To describe and compare the clinical and demographic characteristics of adult severe asthma patients across the initial five registries collaborating with ISAR.

Methods

Data Capture

- Data for this study were collected from secondary and tertiary severe asthma centers for the time period December 2014 to December 2017.

- Patients included in ISAR are:
  - ≥18 years old,
  - Receiving treatment at Global Initiative for Asthma (GINA) Step 5 or had uncontrolled asthma (i.e. severe symptoms or frequent exacerbations) at GINA Step 4.

- Baseline patient-level data were collected from 4 registries and shared with ISAR as summarized statistics via pre-specified tables (Figure 1):
  - The Severe Asthma Web-Database (SAWD, comprising data from Australia, Singapore and New Zealand),
  - The UK Severe Asthma Registry,
  - The Severe Asthma Network in Italy (SANI),
  - The Korean Academy of Asthma Allergy & Clinical Immunology (KAAACI) registry.

- Baseline patient-level data were collected and shared from 1 database:
  - National Jewish Health Electronic Medical Record Severe Asthma Cohort in Colorado, USA.
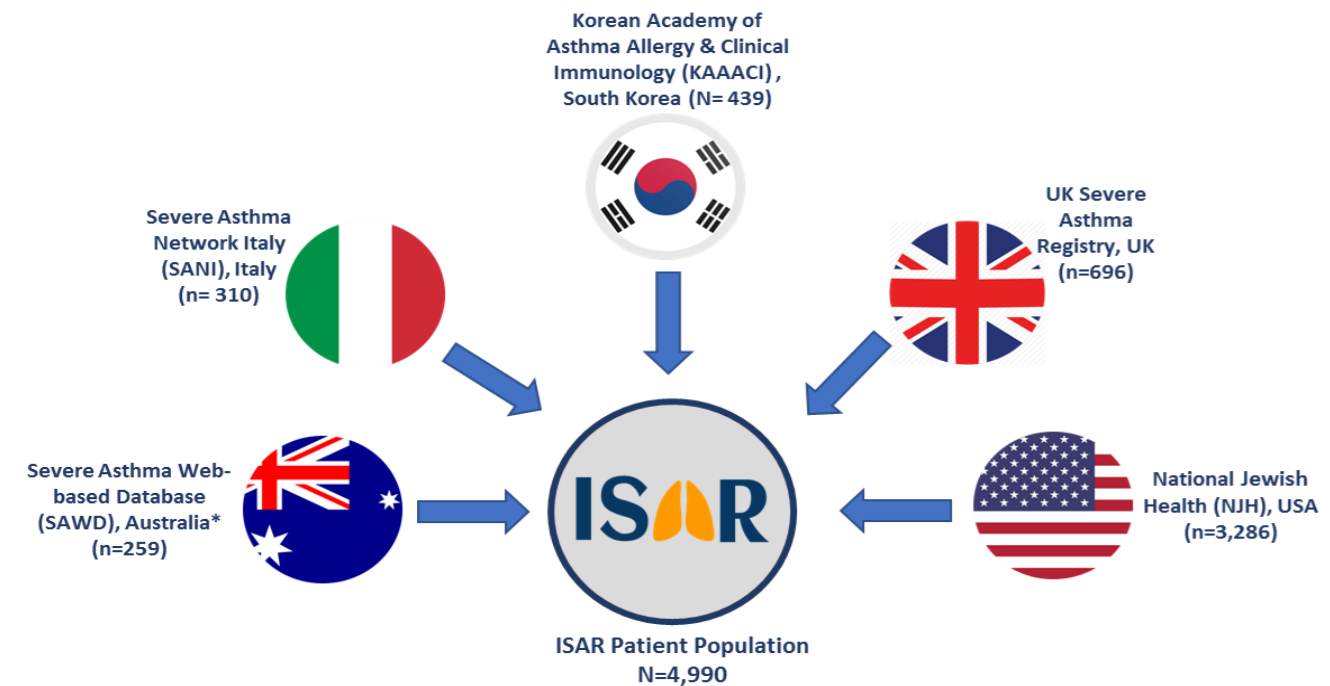

Figure 1: The initial five registries collaborating with ISAR

Analysis

- Descriptive statistics for demographic and clinical characteristics are summarized.

Results

- A total of 4,990 patients are included in the study.

Demographic and Clinical Characteristics

Table 1: Demographic and Clinical characteristics for all patients and according to country/registry

	Age (mean [SD])	Female (%)	Ever Smoked* (%)	Overweight/Obese (BMI≥25) (%)	Age of Asthma Onset (mean [SD])	Post-bronchodilator % Predicted FEV$_1$ (Mean [SD])
All (n=4,990)	55.0 (15.9)	59.3	39.5	70.4	30.7 (17.7)	75.8 (17.1)
USA (n=3,286)	55.5 (16.7)	59.7	43.0	74.2	Not captured	75.7 (14.4)
UK (n=696)	48.3 (14.1)	62.6	27.9	78.2	25.4 (18.7)	72.5 (22.2)
South Korea (n=439)	62.4 (14.1)	54.2	46.0	35.1	41.0 (17.1)	73.4 (21.2)
Italy (n=310)	54.5 (13.8)	56.1	23.2	54.6	34.4 (17.1)	83.2 (20.5)
SAWD (n=259)	55.1 (15.3)	58.3	32.8	80.6	22.7 (17.1)	Not available

*includes current and ex-smokers. SD: standard deviation; BMI: body mass index; SAWD: Severe Asthma Web-based Database; FEV$_1$: forced expiratory volume in 1sec

- Patients were predominantly female.

- The mean (SD) age was 55 (15.9) years; the oldest patients were in South Korea and the youngest in the UK.

- Overall, 39.5% patients had a history of smoking, with the highest proportion of current or previous smokers in South Korea and USA.

- Most patients in each of the registries were overweight/obese, except in South Korea (35.1%).

- The mean age at onset was 30.7 (SD:17.7 years).
  - 77.5% of patients developed asthma after the age of 12 years, and 34.4% developed asthma after the age of 40 years.
  - Patients from the UK and SAWD developed asthma slightly earlier than overall average, while South Korea and Italy slightly later.

- Severe asthma patients from Italy had the highest mean (SD) post-bronchodilator percent predicted FEV$_1$.

- 35% of the patients were on GINA Step-5; a large majority of patients from the UK (81.8%), followed by Italy. In contrast, the USA and South Korea had the lowest proportion of GINA Step 5 patients (Figure 2A).

- The majority of patients had poorly-controlled asthma globally (57.2%). Poor asthma control was reported in majority of UK patients and in the SAWD registry (Figure 2B).

- The mean (SD) number of exacerbations within the last 12 months for the total population was 1.7 (2.7).
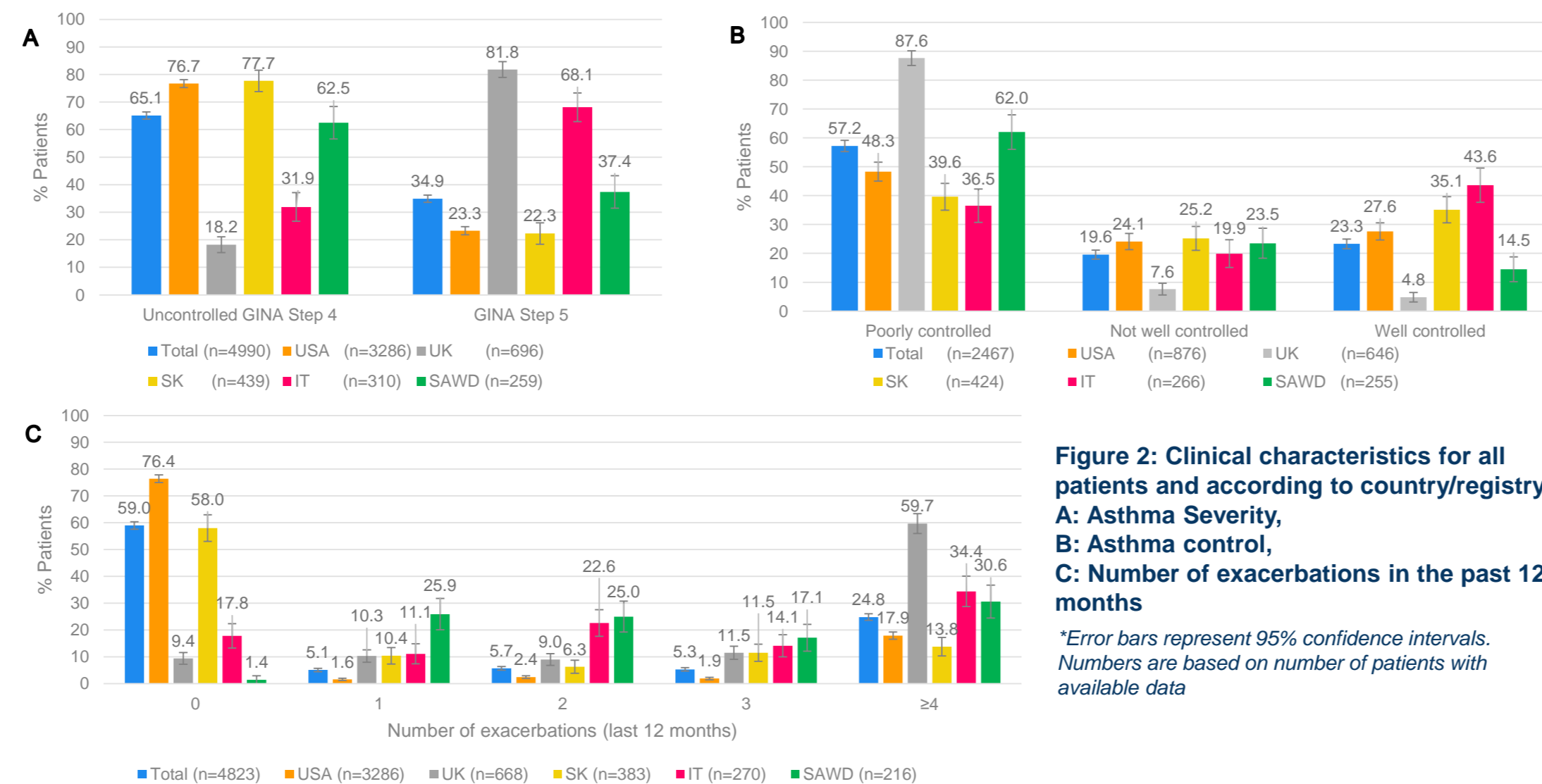 - The mean number of exacerbations was lowest in the USA and the highest in the UK (Figure 2C).

Figure 2: Clinical characteristics for all patients and according to country/registry.*
A: Asthma Severity,
B: Asthma control,
C: Number of exacerbations in the past 12 months

*Error bars represent 95% confidence intervals. Numbers are based on number of patients with available data
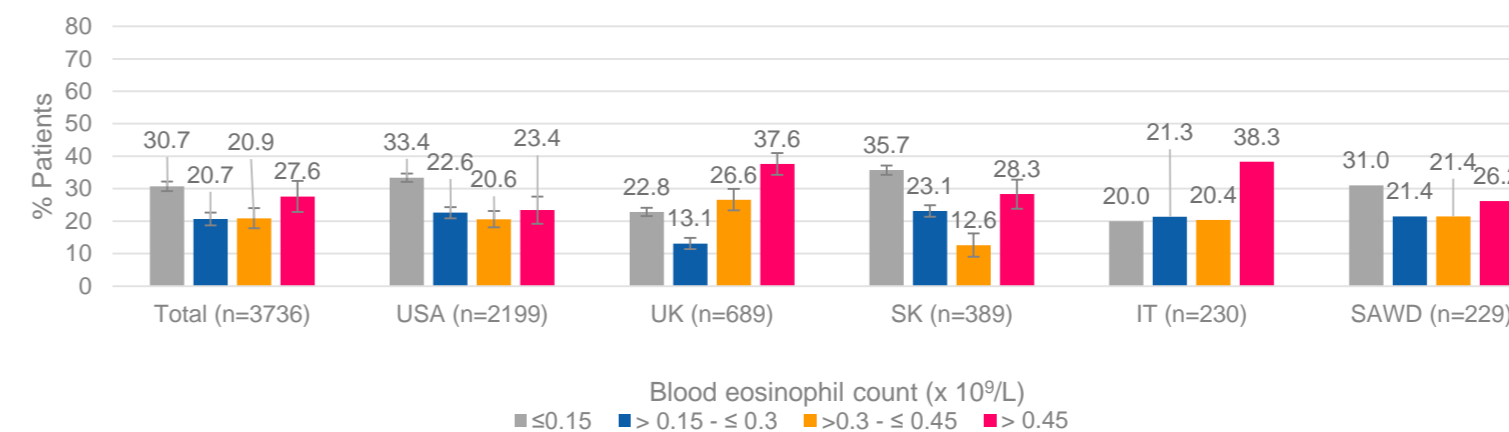
Results

Key Biomarkers

Medication

Figure 3: Blood eosinophil count according to county/registry

- In the overall population, 51.4% of patients had a BEC ≤0.3 (x 10^9 cells/L).

- The majority of patients in USA (56.0%), South Korea (58.8%), and the SAWD registries (52.4%) had BEC ≤0.3.
  - The majority of patients from the UK (64.2%) and Italy (58.7%) had BE ≥0.3.

- A significant proportion of severe asthma patients in Italy (38.3%) and the UK (37.6%) had BEC >0.45.

- Around one-third of the patients in South Korea (35.7%), USA (33.4%) and the SAWD (31.0%) had BEC level ≤0.15.
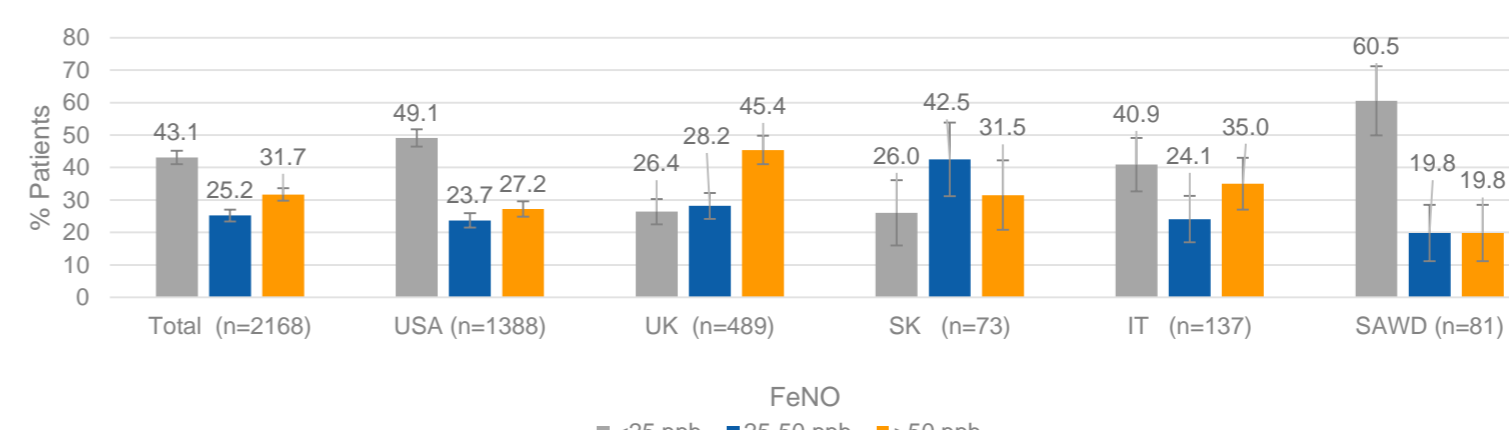
Figure 4: FeNO measurement according to county/registry

- Overall, 43.1% of severe asthma patients had FeNO concentrations <25 ppb and 56.9% had a concentration ≥25 ppb.

- In USA, a similar proportion of patients had FeNO concentration <25 ppb (49.1%) and ≥25 ppb (50.9%).

- Most patients from the UK (73.6%), South Korea (74.0%) and Italy (59.1%) had FeNO concentrations ≥25 ppb. However, most SAWD patients (60.5%) had FeNO concentrations <25 ppb.
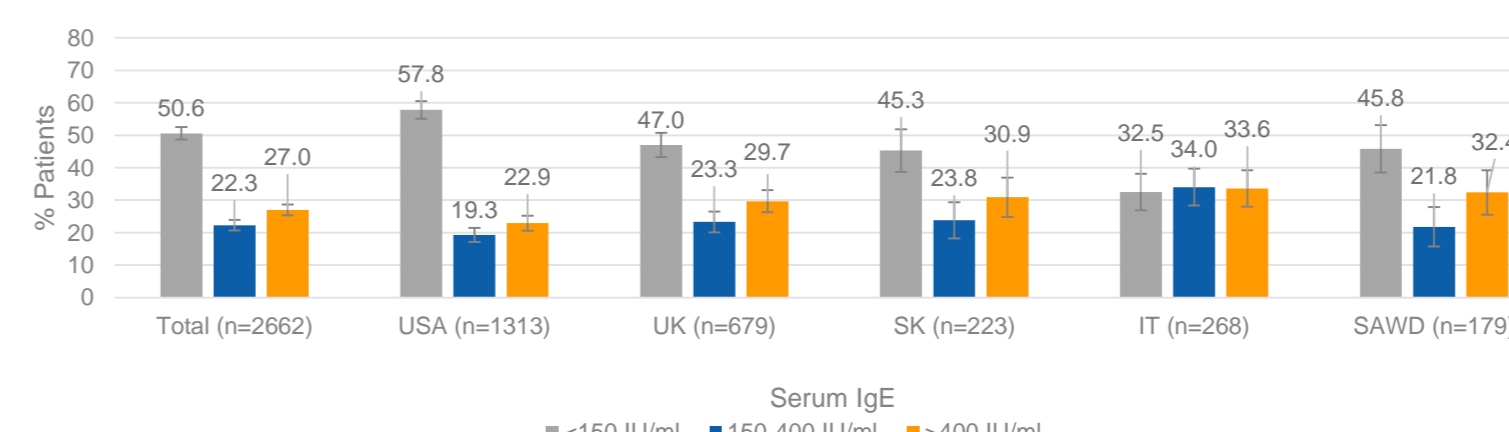
Figure 5: Serum IgE measurement according to county/registry

- Serum IgE distribution across countries were similar.

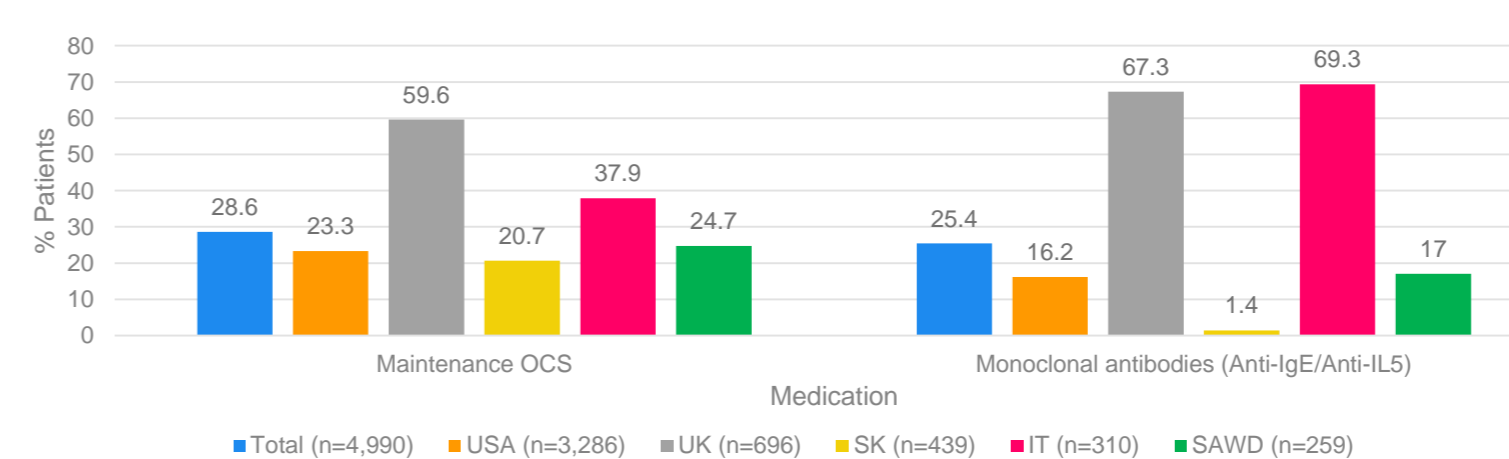- Most severe asthma patients had IgE concentration of <150IU/mL for all countries, except Italy.

Figure 6: Medication usage across countries

- Overall, 28.6% patients were prescribed maintenance oral corticosteroid with the highest prescriptions in the UK.

- Prescription of monoclonal antibodies (Anti-IgE and Anti-IL5) was predominantly high in Italy and the UK and the lowest in South Korea

Conclusions

- Using a common dataset and definitions, this study is the first to describe severe asthma characteristics of a large cohort of patients included in national severe asthma registries

- We observed a substantial variation in demographic and clinical characteristics of severe asthma patients across countries.

- This may reflect the differences in the organization of severe asthma referral centers, associated referral patterns and requirements for reimbursement of new asthma therapies.

- The difference in biomarker profiles across regions and countries may indicate the heterogeneity of asthma phenotypes across regions or countries and impact of treatment.

- Future studies will contextualize the results within country-specific health systems and use the prospectively collected patient-level data.

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Conflict of interest statement: