International Variation in Severe Exacerbation Rates in Patients with Severe Asthma

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Aim and Methods

Rationale

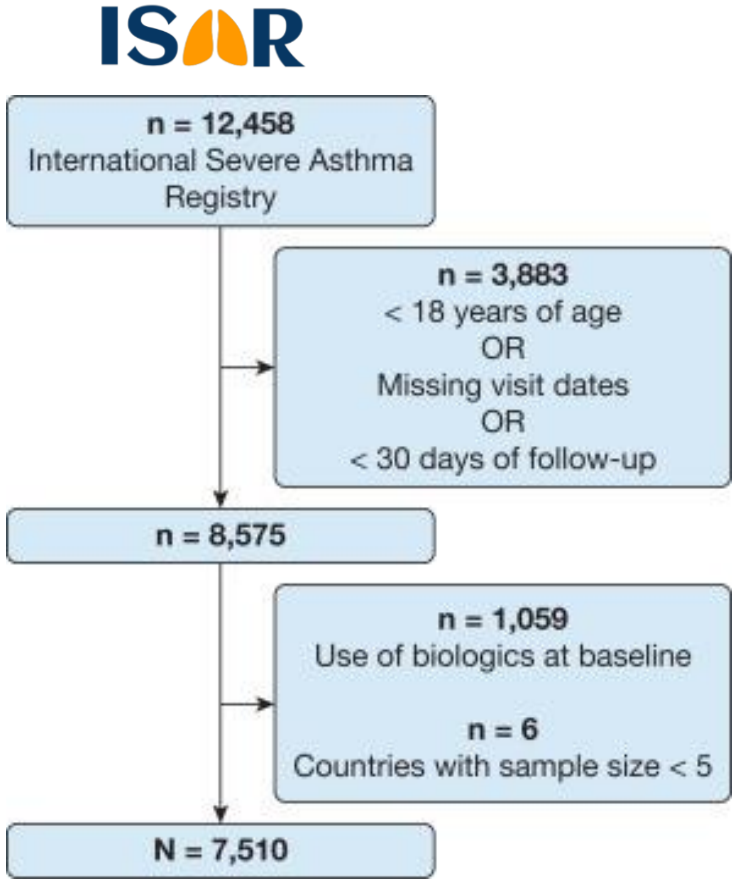
Exacerbation frequency strongly influences treatment choices in patients with severe asthma, but the rate of exacerbations varies across countries.

Aim

To examine the extent of the variability of exacerbations rate across countries and its implications in disease management.

Methods

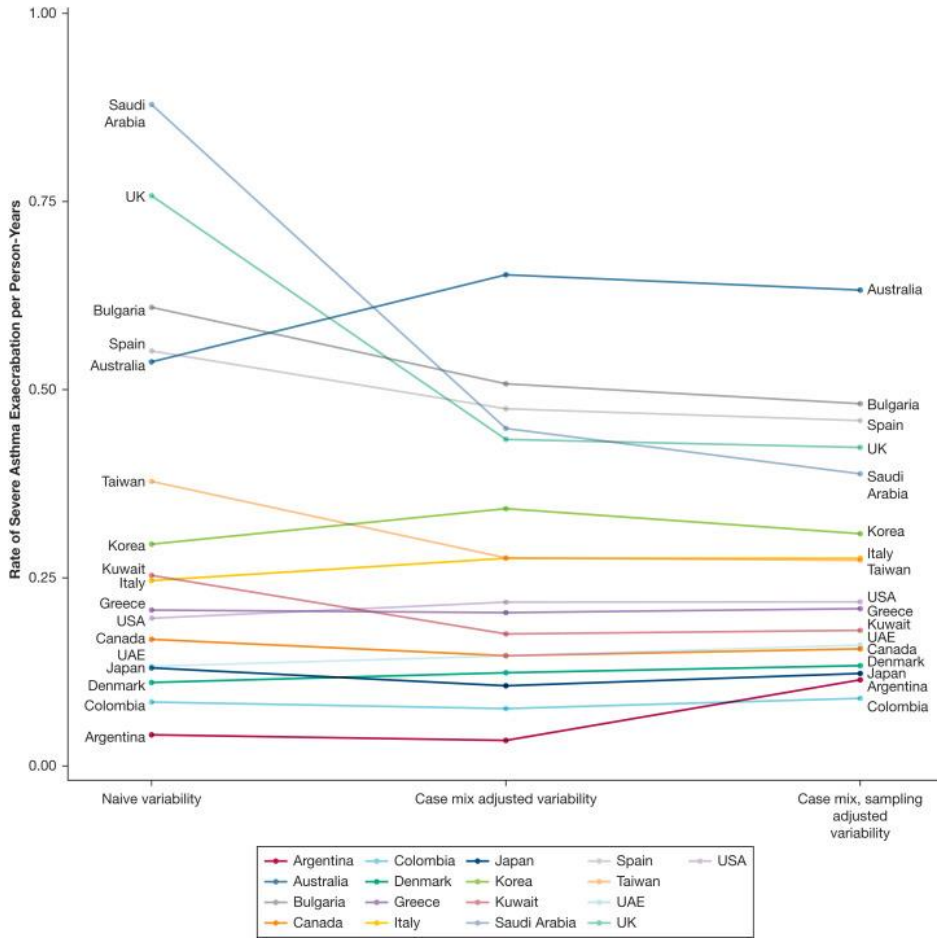
- **Data source:** The International Severe Asthma Registry (ISAR).
- **Study population:** Patients ≥ 18 years of age who did not initiate any biologics before baseline visit.
- **Statistical analyses:** Negative binomial models to estimate country-specific severe exacerbation rates during 365 days of follow-up in naïve and adjusted models.



Flow diagram of the International Severe Asthma Registry cohort

Large between-country variations of severe asthma exacerbation rates

Estimates of country-specific severe asthma exacerbation rates (per person-years) using the average marginal effect framework for naïve, case mix adjusted (fixed-effect), and case mix and sampling adjusted (random-effects) models.



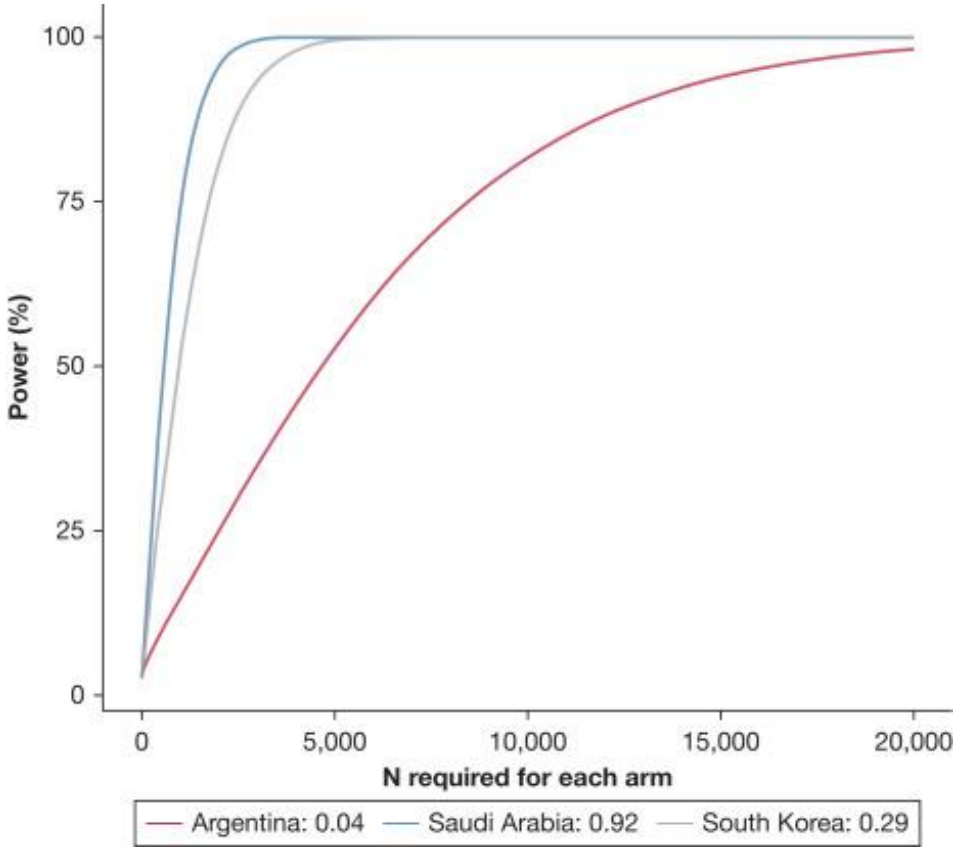
Findings

- **Large between-country variation** in observed severe exacerbation rate (minimum, 0.04 [Argentina]; maximum, 0.88 [Saudi Arabia]; interquartile range, 0.13-0.54).
- Remained substantial after adjusting for patient characteristics and sampling variability (interquartile range, 0.16-0.39).

UAE = United Arab Emirates; UK = United Kingdom; USA = United States.

Design of future severe asthma trials (desired sample sizes)

Power analysis for the lowest, median, and highest severe exacerbation rates (per person-years) observed in the International Severe Asthma Registry to detect a reduction of 20% in severe exacerbation rates from the comparator.



Findings

- To detect a **20% reduction in severe exacerbation rate** with 90% power
  - 12,699 patients per arm required in Argentina;
  - 2,503 patients in South Korea;
  - 1,432 patients in Saudi Arabia

- International clinical studies recruiting patients from specialty care should balance trial design's efficiency and representativeness of countries and regions.

Conclusions

- **Considerable heterogeneity** in severe exacerbation rates in patients with severe asthma across countries.

- Unidentified patient-specific factors and/or systemic intricacies contributing to the observed variations.

- Each country or jurisdiction should **adapt clinical recommendations for severe asthma to their setting** for optimal treatment escalation strategies.

- Risk prediction models **calibrated for each jurisdiction** will be needed to optimize treatment strategies.