International Severe Asthma Registry: A Real-life Data Capture Model

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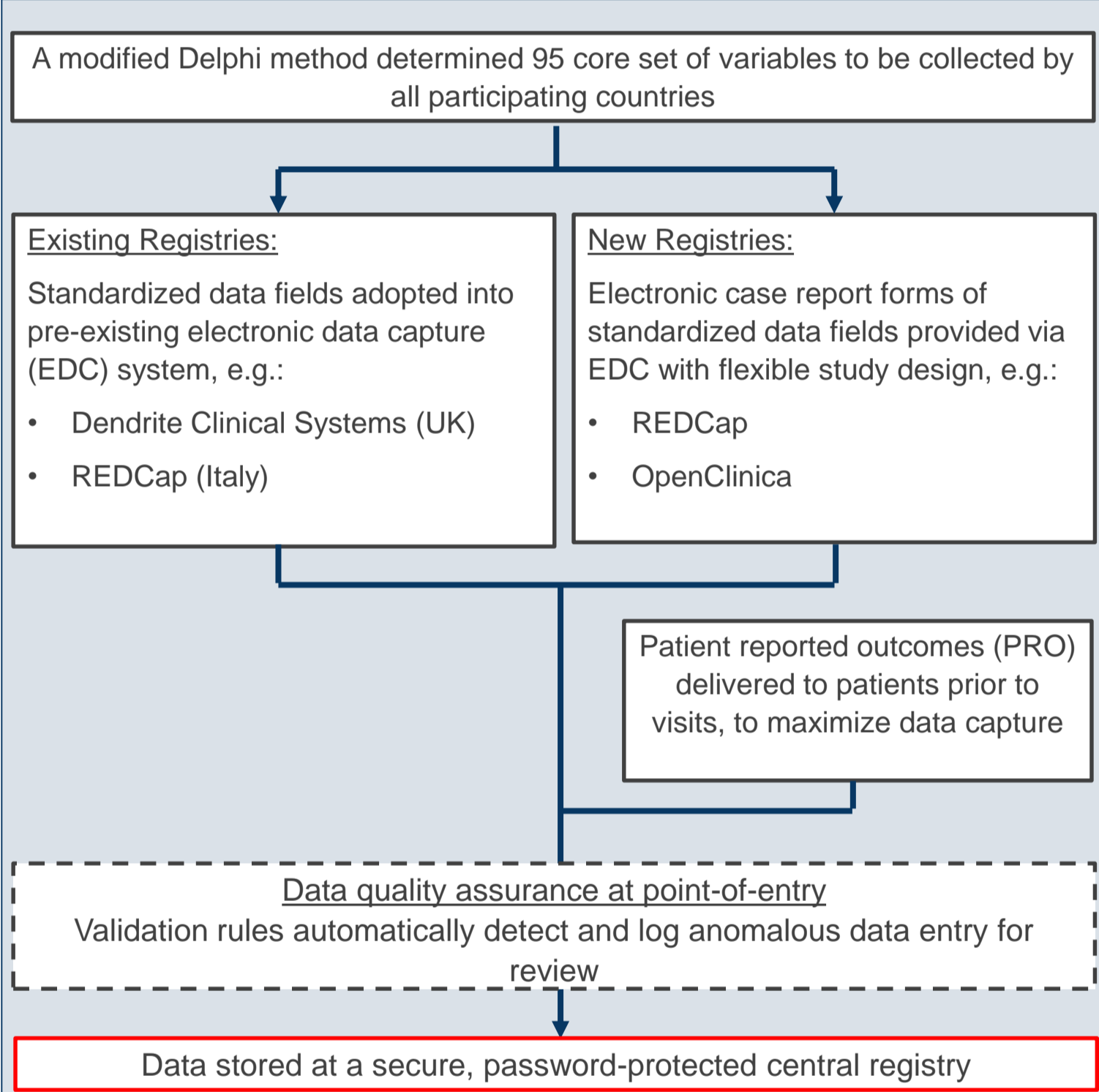
Introduction

- Severe asthma:
  - Defined by European Respiratory Society (ERS)/American Thoracic Society (ATS) Severe Asthma Guidelines as asthma requiring Global Initiative for Asthma (GINA) Step 4-5 treatment to control or that remains uncontrolled despite this treatment.[1]
  - Affects 5-10% of the asthma population[2] and carries a heavy health and socioeconomic burden.[3]
- Disease registries:
  - Provide valuable resources to study the natural history of diseases, diagnostic accuracy and effectiveness of therapies.[4]
  - Currently, severe asthma registries comprise of relatively small, locally administered databases with little interoperability and fundamental differences in data collection.
- A global registry for severe asthma with standardized data collection will aid the understanding and development of treatment for the disease.
- Aim: To describe the creation of a real-life data collection model for the **International Severe Asthma Registry (ISAR),** the first global severe asthma registry.

Methods

- ISAR Patient Inclusion Criteria:
  - Age 18 years or above.
  - Receiving treatment according to GINA Step 5 or uncontrolled at Step 4 as per ERS/ATS guidelines.[1]
- Data Collection Method:
  - Modified Delphi method was used to obtain expert consensus on a list of variables to be captured in the ISAR.[5]
  - Of initial 747 potential variables proposed, a panel of 27 severe asthma experts from 16 countries agreed on a core set 95 variables.
  - Optional variables are recorded at each participating countries' discretion.

### Figure 1. Data collection in ISAR

A modified Delphi method determined 95 core set of variables to be collected by all participating countries

Existing Registries:
Standardized data fields adopted into pre-existing electronic data capture (EDC) system, e.g.:
- Dendrite Clinical Systems (UK)
- REDCap (Italy)

New Registries:
Electronic case report forms of standardized data fields provided via EDC with flexible study design, e.g.:
- REDCap
- OpenClinica

Patient reported outcomes (PRO) delivered to patients prior to visits, to maximize data capture

Data quality assurance at point-of-entry
Validation rules automatically detect and log anomalous data entry for review

Data stored at a secure, password-protected central registry

Result – Modified Delphi Method

Table 1. List of variables captured in ISAR

Variable category	Description
Demographics	• Observation date, age, gender, ethnicity, body mass index, occupation
Medical History	• Current smoking status of patient, and number of pack years for smokers • Age of onset of asthma • Number and date of exacerbations requiring rescue steroids • Number of episodes of invasive ventilation ever • Number of emergency room attendances for asthma • Number of hospital admissions for asthma
Comorbidities	• Eczema • Cataract or Glaucoma • Allergic Rhinitis • Type-II Diabetes • Chronic Rhinosinusitis • Sleep Apnoea • Nasal Polyps • Renal Failure • Pneumonia • Depression • Osteoporosis • Anxiety • Circulatory System Disease • Peptic Ulcer
Biologic Safety	• Severe Infection • Malignancy • Anaphylactic Reaction
Blood/Sputum	• Blood eosinophil count measurements and dates • Highest sputum eosinophil count and date • Immunoglobulin E (IgE) count and date
Diagnostics	• Chest CT scan and date • Bone densitometry (DEXA) and date
Lung Function	• Pre- and Post-Bronchodilator spirometry • PC20 methacholine/histamine test date and result • Fractional Exhaled Nitric Oxide (FeNO) test date and result
Allergen Testing	• Serum allergy test: positive to allergen type, result and date • Skin prick test: Positive to allergen type, result and date
Asthma Control	• GINA assessment of asthma control
Asthma Medication	• Asthma medication • Medication start and end date • Maintenance Oral Corticosteroids (OCS) • Biologics • Macrolide antibiotic treatment • Other steroid sparing agents • Bronchial thermoplasty
Adherence	• Subjective and objective evidence of poor adherence
Medication Switch	• Reason for biologics switch
Management Plan	• Other factors contributing to severe asthma symptoms • Current Clinical Management Plan

Result – Current Progress of ISAR

Figure 2. Countries participating in ISAR as of September 2018
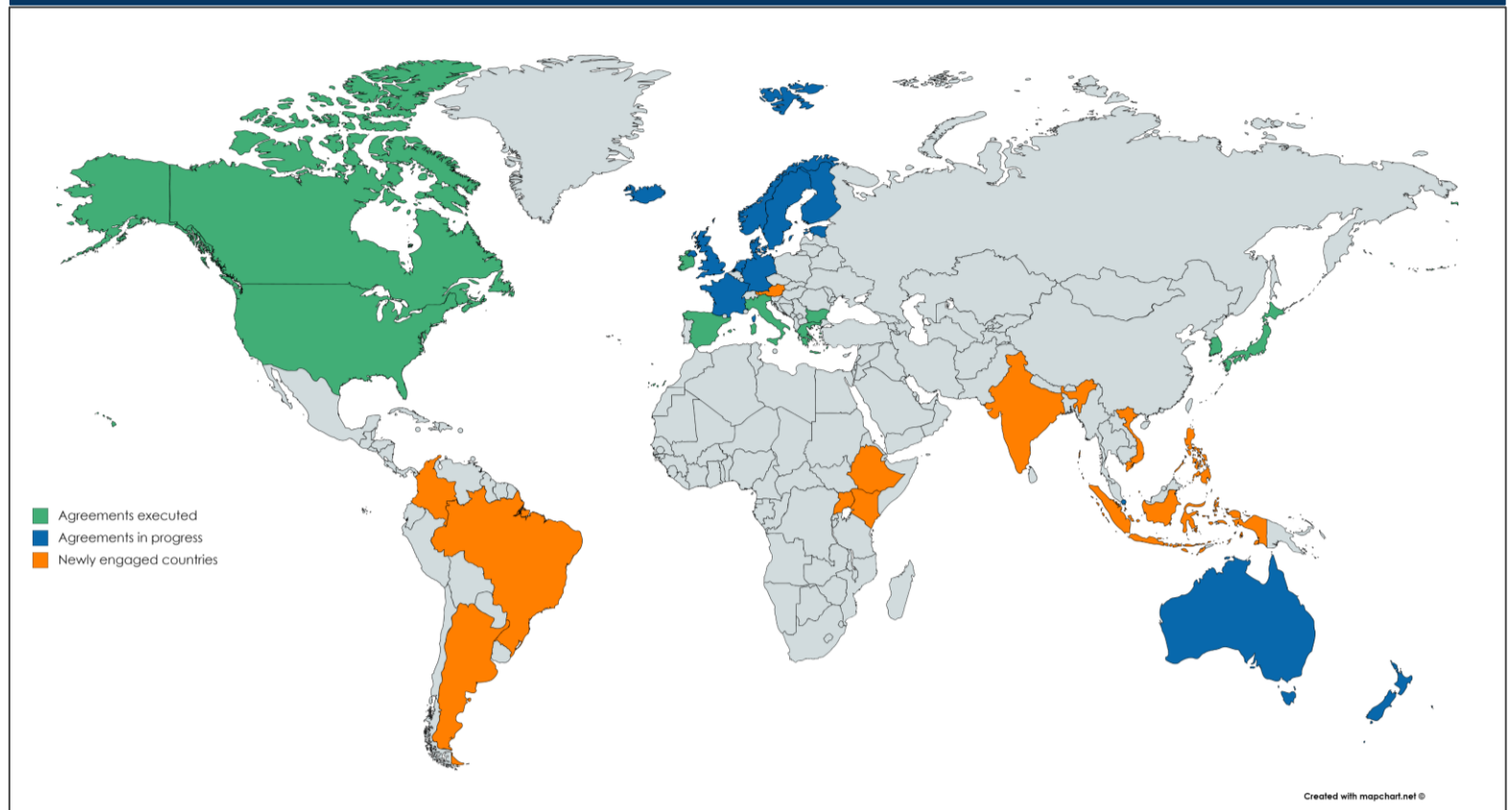
- **Nine** countries are currently participating in the ISAR, with an additional **nine** countries planned for participation

Table 2. Data Provided for ISAR Research as of September 2018

Country	Data provided by	Number of patients
Australia*	Severe Asthma Web-based Database (SAWD)	259
Italy	Severe Asthma Network Italy (SANI)	310
South Korea	Severe Asthma Registry by the Korean Academy of Asthma, Allergy and Clinical Immunology (KAAACI)	445
United Kingdom	UK Severe Asthma Registry	696
United States	National Jewish Health EMR Severe Asthma Cohort (NJH)	3,378
Ireland	Inhaler Adherence in Severe Unstable Asthma Cohort (INCA-SUN)	55
Greece	Attikon University Hospital, Athens, Greece	10
Total		5,153

*The SAWD also includes Singapore (n=16) and New Zealand (n=18).

Table 3. Active Research Projects

Demographic and Clinical Characteristics of Severe Asthma Patients Worldwide
Characterization and Comparison of Eosinophilic and Non-Eosinophilic Asthma Phenotypes
Outcomes of switching biologics
Hidden Severe Asthma Patients in Primary Care vs. ISAR Cohort
The Impact of Exacerbation Burden on Lung Function Trajectory in a Broad Asthma Population and Severe Asthma Population
Assess the Overlap (relatability) of Collected Biomarkers
Identify Predictors (e.g. biomarkers) of Response to Biologics
Hidden Chronic Asthma within the COPD/ACOS Population
Onset of Asthma in Severe Asthma patients
Relationship between Socioeconomic Status and Asthma Outcomes

Governance:
- All ISAR research must be approved by the ISAR steering committee and Anonymised Data Ethics & Protocol Transparency (ADEPT) committee of the Respiratory Effectiveness Group (REG).

Conclusions

- The ISAR captures a large volume of standardized data on severe asthma from multiple countries across the globe.
- The ISAR aims to compile data from 20 participating countries with over 10,500 patients to be reviewed annually.
- The ISAR is a platform that provides a basis to answer important research questions in severe asthma.

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Conflict of Interest:

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