Development of the International Severe Asthma Registry (ISAR): A Modified Delphi Study

Lakmini Bulathsinhala et al, *J Allergy Clin Immunol Pract* 2019;7(2):578-588.e2

Background and aims

Original Article

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Cambridge, London, Aberdeen, Manchester, UK; Belfast, Northern Ireland; Newcastle, New Lambton Heights, Sydney, Melbourne, Australia; Groningen, Amsterdam, The Netherlands; Tampere, Finland; Lyon, France; Madrid, Mallorca, Spain; Athens, Greece; Vancouver, Canada; Copenhagen, Denmark; Milan, Italy; Seoul, South Korea; Gent, Belgium; Mainz, Germany; Singapore; and Gaithersburg, Md

What is already known about this topic? All existing severe asthma registries in the world were either country or region specific. Most importantly, none shared a common set of variables for data collection. This impedes data sharing and subsequently disallows data pooling to conduct research with robust sample size.

What does this article add to our knowledge? This paper depicts a systematic method of soliciting group consensus on a topic that entails a spectrum of choices and viewpoints.

How does this study impact our current management guidelines? Using the standardized minimal list of variables identified by our study, we hope to achieve data interoperability between severe asthma registries across the globe and subsequently improve patient management guidelines in severe asthma.

BACKGROUND: The lack of centralized data on severe asthma has resulted in a scarcity of information about the disease and its management. The development of a common data collection tool for the International Severe Asthma Registry (ISAR) will enable standardized data collection, subsequently enabling data interoperability.

OBJECTIVES: To create a standardized list of variables for the first international registry for severe asthma via expert consensus.

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This study is cofunded by Optimum Patient Care Global and AstraZeneca.

Conflicts of interest: L. Bulathsinhala, N. Eleangovan, V. Carter, C. Price, T. Le, and M. S. d'Alcontres are employees of Optimum Patient Care, a cofunder of the International Severe Asthma Registry. L. G. Heaney has taken part in advisory boards and given lectures at meetings supported by GlaxoSmithKline, Respivert, Merck Sharpe & Dohme, Nycomed, Boehringer Ingelheim, Teva Pharmaceuticals, Vectura, Novartis, and AstraZeneca. He declares sponsorship for attending international scientific meetings from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Napp Pharmaceuticals; and speaker fees from AstraZeneca, Aerocrine, Hoffman-La Roche, and Teva Pharmaceuticals. A. Menzies-Gow declares grants from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Hoffman La Roche; consultancy agreements with AstraZeneca and Vectura;

Background

- Registries are well-established and valuable tools for disease surveillance, and the current registry landscape for severe asthma is viewed as a collection of **divergent, national and regional registries**.
- The **lack of centralized data on severe asthma** has resulted in a scarcity of information about the disease and its management.
  - Hence, the **development of a common data collection tool** for the International Severe Asthma Registry (ISAR) will **enable standardized data collection, subsequently enabling data interoperability**.

Aim

- To **create a standardised list of variables** for the first international registry for severe asthma via expert consensus.

Full Text available here.

ISAR: International Severe Asthma Registry

Methods:
Delphi panel, panel selection and consensus criteria

- Delphi panel
  - **27 international experts** in the field of severe asthma research, representing **16 countries.**

- Panel selection criteria – **2 or more** of the following:
  1. **Evidence of relevant asthma research** published in high-ranking peer-reviewed journals.
  2. A **history of participation** in:
     - The development and/or management of one or more severe asthma registries
     - Epidemiological databases, and
     - Scientific congress committees in a particular country and/or internationally.
  3. Experience as a medical provider with **interest in advancing asthma management** in clinical practice.

- Criteria for consensus
  - Variables receiving **≥66.6%** consensus were selected as **ISAR core variables**.
  - Variables receiving **50%-66.6%** consensus (“undecided”) were **circulated for another round of review**.
  - Variables receiving **<50%** consensus were **removed**.

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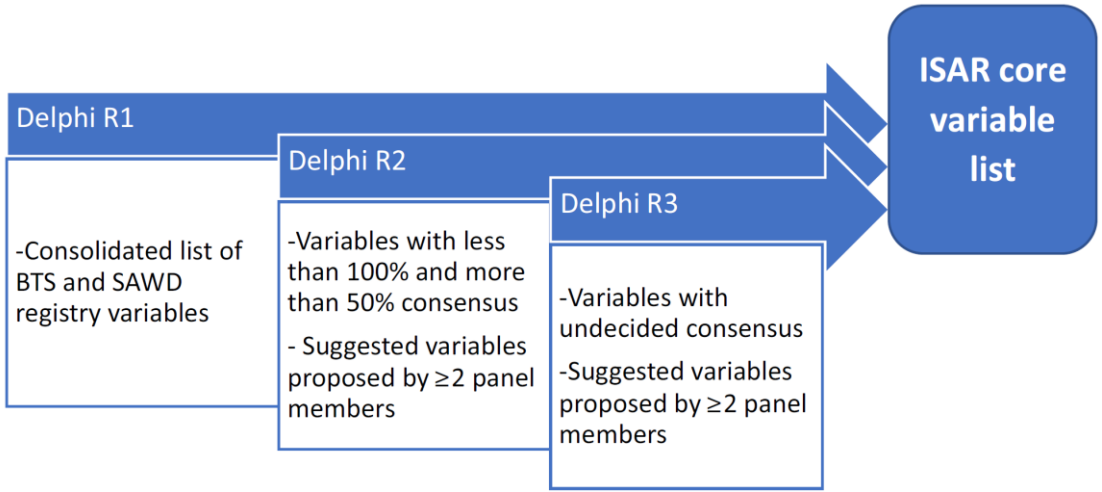
Methods: A 3-round modified Delphi process

- In each round:
  - Panel members were issued an **electronic ISAR Delphi workbook** to vote and comment for the inclusion of variables.
    - Experts were encouraged to **provide comments** for excluding or including variables, to **nominate variables** from the "suggest" variable list, and/or **propose new variables**.
  - These workbooks were returned to the ISAR Delphi administrator anonymously.
  - Variables with 'undecided' consensus for inclusion/exclusion → **submitted for evaluation in the subsequent round.**
  - Finalisation of the core variable list was facilitated by **2 face-to-face meetings**.



The modified Delphi process consisted of 3 iterative rounds (R1, R2, and R3).

BTS: British Thoracic Society; SAWD: Severe Asthma Web-based Database

ISAR: International Severe Asthma Registry

Methods:

Samples of the variable list from Delphi R1

Page	Potential core variables	Field format	Response option (where applicable)	Unit (where applicable)	Place in core list?	Reason for choice (if "no")
Patient details	Date of visit	Date		DDMMYY		
	Date of birth	Date		DDMMYY		
	Gender	Radio button	Female/Male			
	Ethnicity	Drop-down menu	Caucasian/South-East Asian/North-East Asian/African /Mixed/ Other			
	Height	Decimal		m		
	Weight	Number		kg		
	Bronchial thermo-plasty	Radio button				

Sample of the "Potential Core" variable list from the ISAR Delphi workbook R1.

Page	Suggest variables	Field format	Response option (where applicable)	Unit (where applicable)	Propose for core list?	Reason for choice (if "yes")
Sputum	Neutrophils	Decimal		%		
	Eosinophils	Decimal		%		
	Date of sputum	Date		DDMMYY		
	Sputum processing protocol	Text				
	Bronchial epithelial cells	Decimal		%		
	Bronchial epithelial cells	Decimal		109/L		
	Macrophages	Decimal				
	Lymphocytes	Decimal				
	Samples stored locally for biobanking	Radio button	No/Yes			

Sample of the "Suggest" variable list from the ISAR Delphi workbook R1.

R1: Round 1

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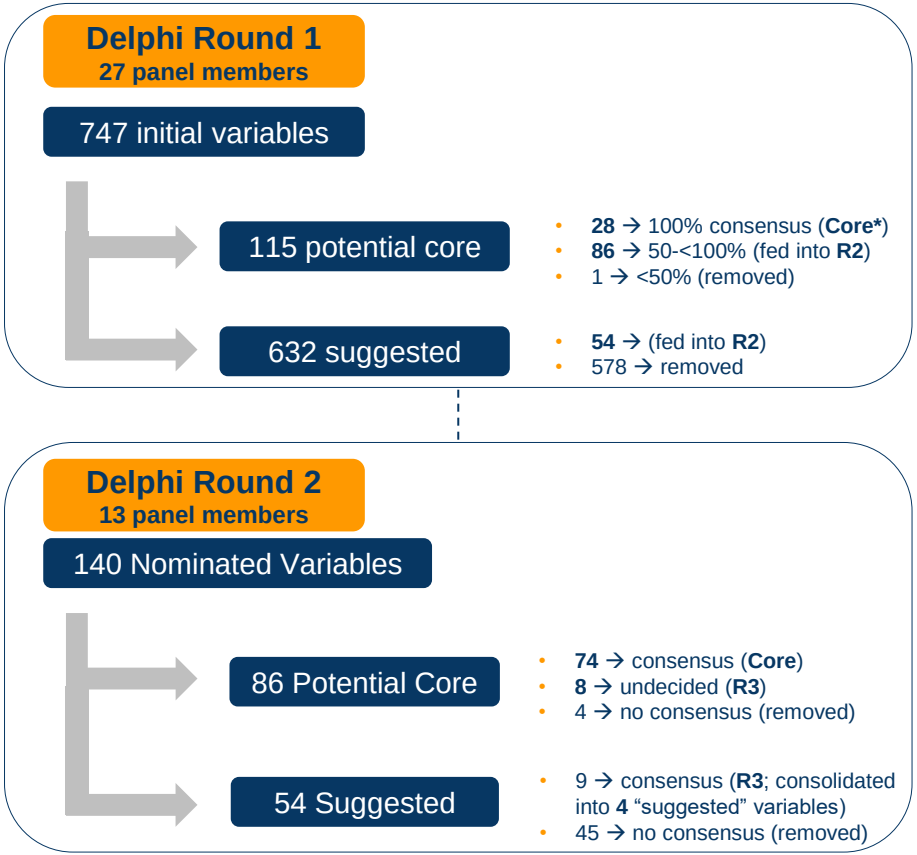
Results: Delphi R1 and R2

- A total of **747 variables** were identified and compiled from longstanding severe asthma registries (**UK** and **Australia**).
- The **Delphi workbook** comprises:
  - **115** potential core variables, **common** to UK and Australia, and
  - **632** suggested variables **unique** for either registry.



*Core Variable: Set of standardized variables that will be captured by ALL countries participating in the ISAR.

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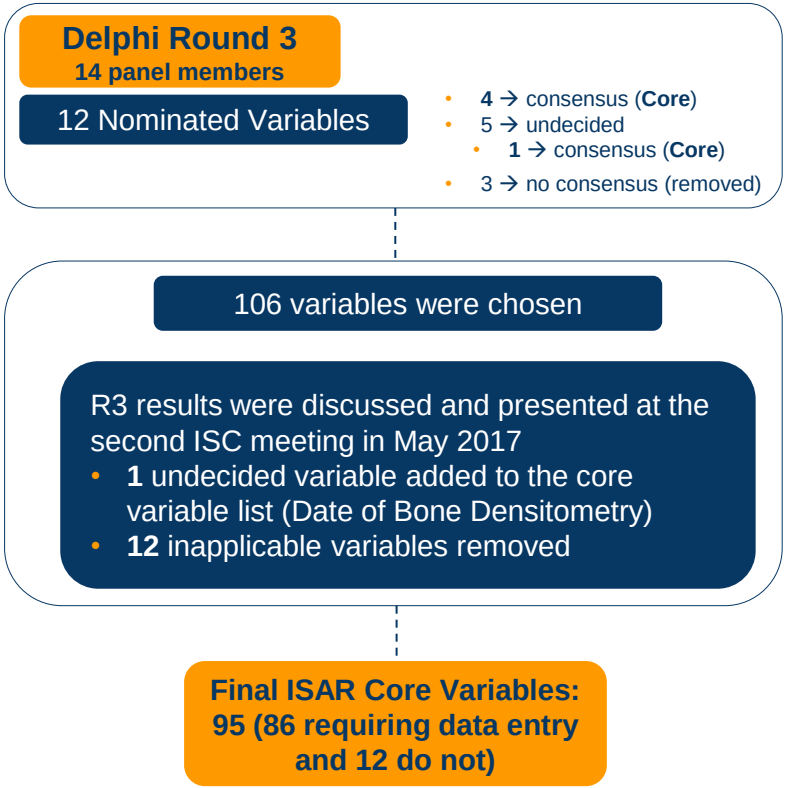
Results: Delphi R2 and R3



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Results: Consensus on 95 core variables

- Of the initial 747 selected variables, the Delphi panel **reached a consensus on 95**.
- The chosen variables will allow severe asthma to be assessed against:
  - Patient demographics
  - Medical history and diagnostics
  - Clinical characteristics
  - Patient-reported outcomes
- Physician-reported outcomes such as **nonadherence** and information about **treatment and management strategies** will also be recorded.

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Patient details and medical history

- Patient demographic and medical history data fields will allow patients to be **categorised**.
- The panel-approved variables were chosen to ensure that a **comprehensive set** of patient characteristics are collected for patient aggregation.
- Previous literature has shown that many patients **overestimate their level of asthma control** and **underestimate the severity of their condition**, indicating that they tolerate symptoms and lifestyle limitations.
- Thus, the **GINA Assessment for Asthma Control** was the preferred tool for this assessment because it:
  - does not overestimate the proportion of patients with controlled asthma, and
  - is therefore more likely to give a less exaggerated score compared with other available questionnaires.

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Diagnostics, adherence, and comorbidities

- The Delphi panel agreed to collect **screening and diagnostic results** to help identify the **care requirements** of individual patients.
- **Biomarkers** such as peripheral blood and sputum eosinophils, and fractional exhaled nitric oxide have been shown to be:
  - Useful for the **management of asthma**, and
  - May help identify specific subtypes of severe asthma **likely to benefit from treatment with novel biological agents**.
- Nonadherence to therapy is approximately **50%** in adults with severe asthma.
- Physicians need to ensure that patients are **satisfied** with their medication to increase adherence and optimise disease control.
- There is a potential for ISAR to investigate nonadherence across **different geographical regions**, which comes with different health care systems, availability of medications, access to specialists, and asthma education.

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Treatment management plan

- **Asthma patient management practices** among adults have been found to be **inadequate** in many practices in Europe.
- Along with the information that ISAR will collect on clinical outcomes and demographic characteristics, the **best treatment management plan by patient group** will be assessed.
- Moreover, the Delphi panel agreed to collect **broad treatment options** to ensure that all participating countries will be able to contribute without subjection to individual country specifications.

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Main strengths and weaknesses

Strengths

- Global panel of international severe asthma experts and professionals allowed **broad consensus** to be obtained
- Consistent number of experts participating in each Delphi round conserved possibility **of reaching consensus**
- **Efficient**, **economically viable**, and **rapid communication**
- Decreased bias and maximised diversity within the Delphi panel, resulting in a **decreased possibility of overlooking** the obvious facets of the questions

Weaknesses

- **Not fully representative** of the diversity amongst stakeholders of respiratory health
- Response rate was **not 100%**

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Conclusion, implications, and future work

- The Delphi process was utilised to **gain anonymized international consensus on 95 core variables** among **27 severe asthma experts** across **16 countries**.
  - **Less than 100 core variables** offers relatively **small data entry burden** for healthcare professionals.
- The first international severe asthma registry (ISAR) now allows for **exchange of data** across registries worldwide.
  - The international scientific community will have access to **larger databases** to conduct research with **improved power**, which further increases the **precision** of research results.
  - Ultimately, the ability to identify severe asthma **phenotypes** and **best clinical management** practices will be heightened.
- This is the first attempt to develop such a registry on a global scale within the severe asthma setting, using a **common set of core variables**, ensuring that data collected across all participating countries are **standardised**.
- The next step is to enroll patients and collect data that will allow **gaps in diagnosis and treatment** to be identified and **solutions to be found**, which will help bridge these gaps and thus bring us one step closer to controlling severe asthma.

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