Systematic Identification and Mapping of Global Real-World DATA Sources for Atypical Hemolytic Uremic Syndrome (AHUS)

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Background

- Atypical hemolytic uremic syndrome (aHUS) is a disease characterized by thrombotic microangiopathy, thrombocytopenia and acute kidney injury as a result of abnormal activation of alternative complement pathway of the innate immune system.[1]
- aHUS occurs at any age, and approximately half of all patients are affected by this disease before the age of 18 without any difference between sexes.[2]

Objectives

- This systematic literature review (SLR) aims to procure in-depth information regarding the wealth of real-world data sources available in aHUS – the main goals are:
  - To identify as many data sources as possible (international, national, regional and local).
  - To describe the metadata of the data sources identified.
  - To identify variables which characterize aHUS.

Methodology

- A literature review was conducted to identify available data sources pertaining to aHUS based on the inclusion/exclusion criteria presented in **Table 1** below using MEDLINE and EMBASE from the time of inception until 21st July 2020.

Table 1. Inclusion/Exclusion criteria for screening the publications

| Inclusion criteria	Exclusion criteria
Patient population	Patients without aHUS
Any patient with aHUS	Non-human: Animal/In-vitro
Outcome	None
Any	
Study Design	Randomized controlled trials and Interventional studies
All real-world studies (observational)	Systematic reviews, meta-analysis
	Case series/Case reports
	Review/Editorial/Comments/Letters
Others	Data source not specified
Language scope: English only	

- Literature search was designed for the electronic databases reviewed; the search terms included keywords and medical subject headings (MeSH terms) and focused on disease and study design.
- Retrieved results were screened to compile a list of unique data sources and relevant meta-data was extracted (i.e., the type of data source, study design, population size, epidemiology, demographics, clinical, economic and humanistic burden, follow-up duration, and other variables).

- A metadata extraction tool in Excel format was also developed to record the information contained in these unique data sources.
- A random sample of 15% of the included/excluded citations were reviewed manually as quality control.

Results

- A total of 2,302 publications were retrieved during the literature search, out of which 148 unique RWD sources were identified, and information was extracted (**Figure 1**).
- Of these, 24 were aHUS specific data sources while remaining 124 data sources were generic (not exclusive to aHUS patients).

Figure 1. Flow of aHUS studies through SLR
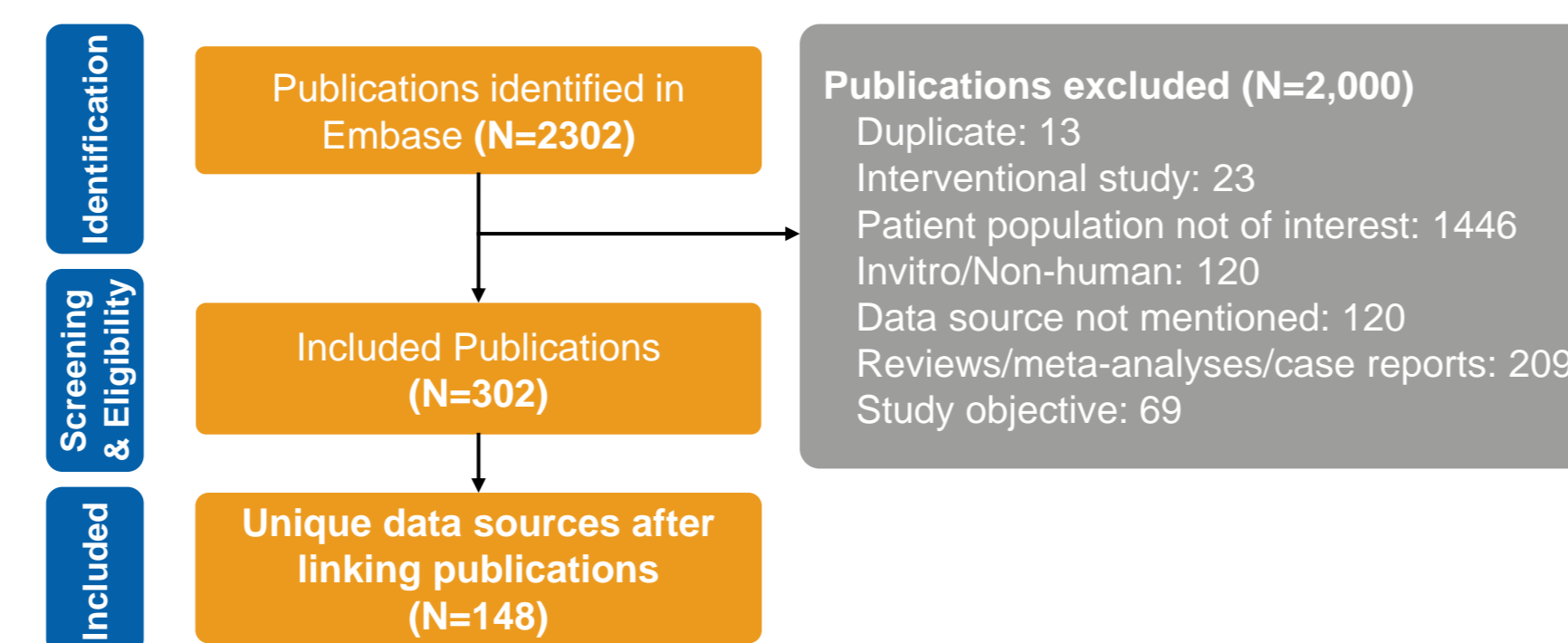
- More than one-third of the data sources came from Europe (36%), followed by Asia (29%), Americas (26%) and Oceania (5%), and 3% were multi-regional (**Figure 2**).
- As per the sample size distribution, nearly 60% of the data sources had a sample size of ≤ 50 patients.

Figure 2. Geographical and sample size distribution of data sources identified
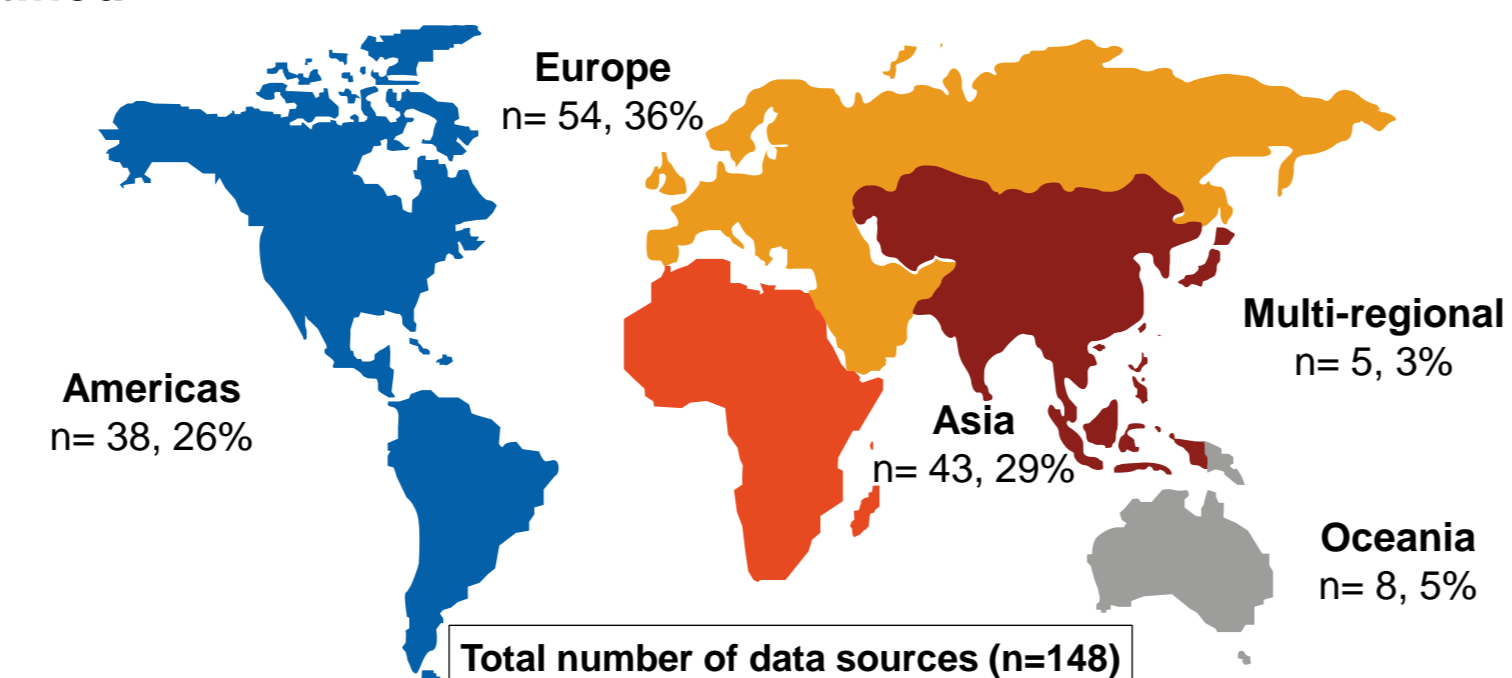
- As reported in the publications, administrative data sources were the most common (74%, n=110), followed by registries (17%, n=25) and surveys (6%, n=9). Observational studies (3%, n=4) were the least common source amongst the group.

- The majority of the identified sources (n=97) were from a single institution, followed by national multicentre (n=15) and international (n=10) data sources (**Figure 3**).

Figure 3. Distribution of data sources as per centre details
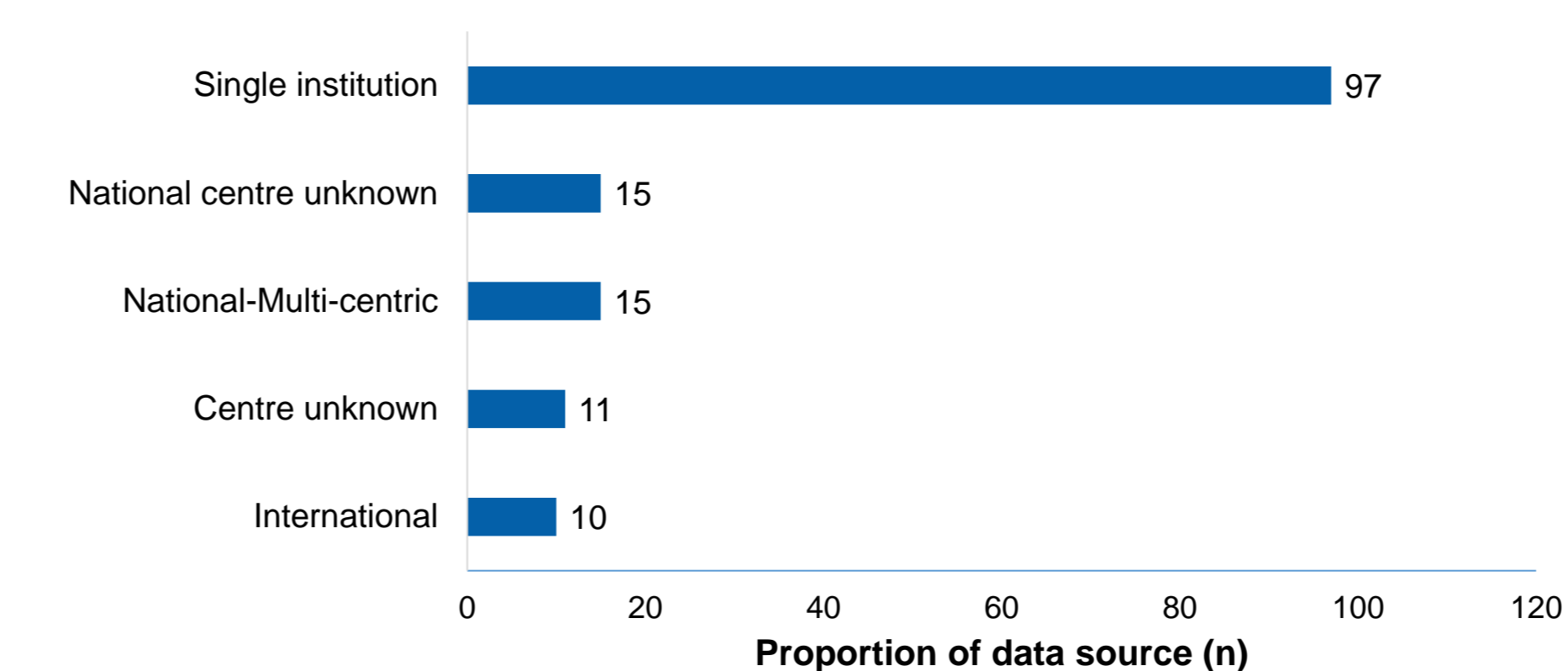
- The most widely reported parameters were age (91%) and gender (76%) along with clinical characteristics like platelet count (64%), serum creatinine (62%), hemoglobin levels (56%), dialysis (55%), all-cause mortality (55%), lactate dehydrogenase levels (LDH) (52%) and kidney transplant (41%).
- Some of the least reported parameters included hospital prescribed drugs (1%), healthcare resource utilization (1%) and quality of life (2%) (**Table 2**).

Figure 4. Distribution of variables as per data mapping
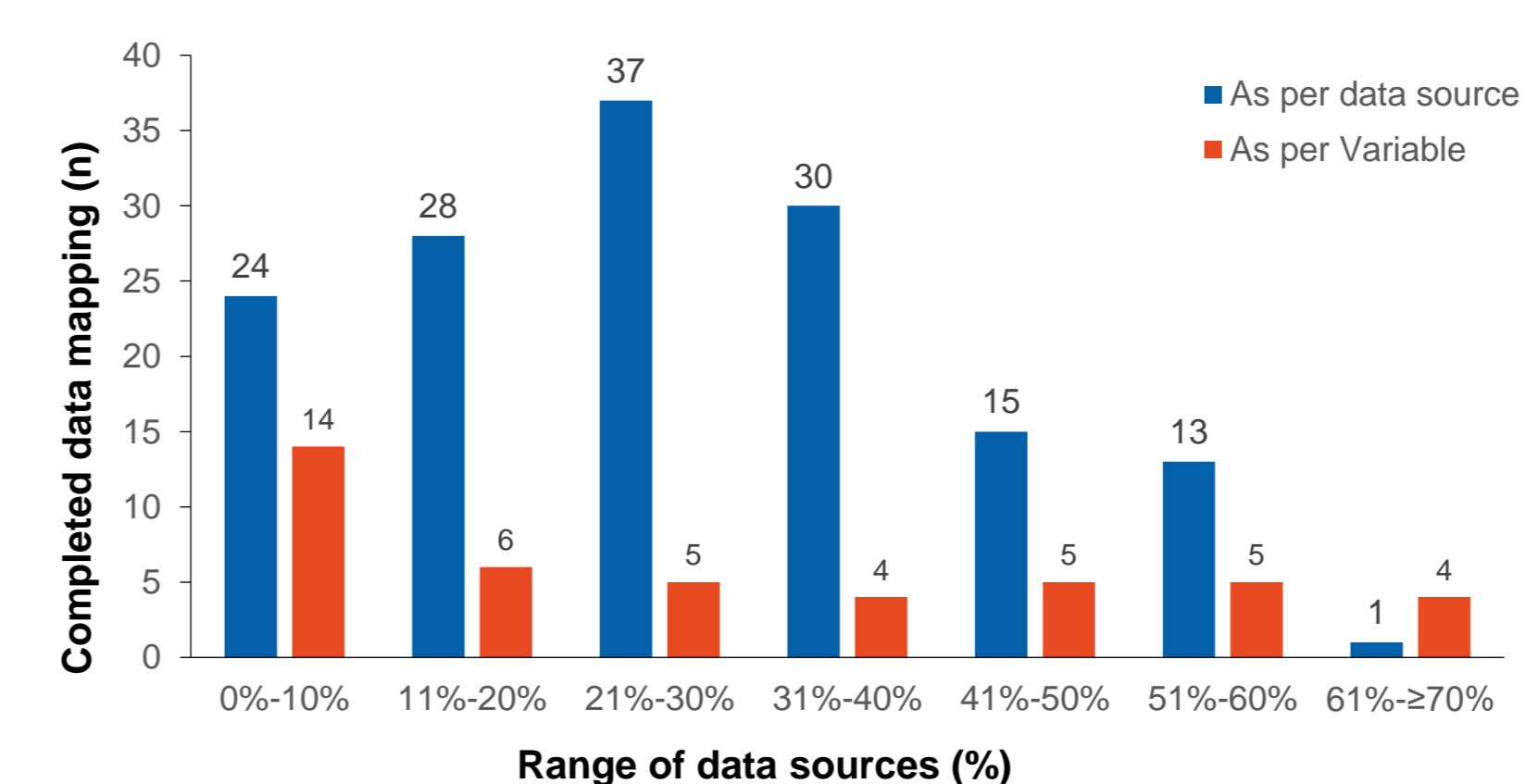
- A total of 43 variables were mapped.
- The degree of variable completeness varied from 2% to 72% across data sources.
- The range of data sources reporting variables varied from 2% to 91% (**Figure 4**) except for a few sources that did not report any variables (n=4).

Table 2. Variables reported in data sources considered in meta data

0% variables	≥1% to 10 variables	11% to 20% variables	21% to 30% variables
• Date of first diagnosis in the database	• Mode of diagnosis	• Race/ Ethnicity	• Age at onset of disease
• Hospital administrated drugs	• Duration between symptom onset and confirmed diagnosis	• Family history of aHUS	• Treatment duration
• Prescribed or dispatched drugs	• Urinary protein: creatinine	• Estimated GFR	• Infections
• Ravulizumab (Ultomiris)	• Drugs	• Proteinuria grade	• Genetic Mutation
	• Disease specific mortality	• Pregnancy	• Epidemiology
	• HCRU	• AEs	
	• QoL		

31% to 40% variables	41% to 50% variables	51% to 60% variables	>60% variables
• Symptoms	• Eculizumab (Soliris)	• Age range	• Age
• Antibodies (Factor H and Factor I)	• Kidney transplant	• Hemoglobin (Hb)	• The mean age
• Lactate dehydrogenase (LDH) at follow-up	• Clinical parameters	• Lactate dehydrogenase (LDH) at baseline	• Gender
• Dialysis status at follow-up	• Platelet count	• Dialysis at baseline	• % of females
	• Serum creatinine	• Therapeutic plasma exchange (TPE)/Therapeutic plasma infusion (TPI)	• Platelet count
		• All-cause mortality	• Serum creatinine

Note: Variables data reported at baseline and follow-up

Conclusions

- This overview presents a comprehensive list of published RWD sources for aHUS disease that can potentially support future research.
- There are still critical gaps in the existing data highlighting the importance of future collaborations to collect more granular and robust information to generate real-world evidence for better understanding of this rare disease.

References

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2. Sellier-Leclerc AL, Fremeaux-Bacchi V, Dragon-Durey MA, et al. Differential impact of complement mutations on clinical characteristics in atypical hemolytic uremic syndrome. *J Am Soc Nephrol.* 2007;18(8):2392-2400. doi:10.1681/ASN.2006080811

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