

Overview of registries for anaphylaxis: a scoping review protocol

Samantha L. Stiles¹ • Ingrid Roche² • Maria Said^{3,4} • Rhonda M. Clifford¹ • Frank M. Sanfilippo¹ • Richard Loh^{1,2,4,5} • Sandra M. Salter¹

¹The University of Western Australia, Perth, WA, Australia, ²Perth Children's Hospital, Perth, WA, Australia, ³Allergy and Anaphylaxis Australia, Sydney, NSW, Australia, ⁴National Allergy Strategy, Sydney, NSW, Australia, and ⁵Australasian Society of Clinical Immunology and Allergy (ASCIA), Sydney, NSW, Australia

ABSTRACT

Objective: This review will describe the scope and operational features of global registries for anaphylaxis and assess their contribution to improving knowledge and care of anaphylaxis by measuring their research output.

Introduction: The incidence of anaphylaxis is increasing around the world. Structured reporting systems, such as patient registries, are needed to better understand the burden of anaphylaxis and protect the growing number of allergic patients.

Inclusion criteria: The concept to be mapped is registries across the world that enroll patients who have experienced anaphylaxis. Published and gray literature sources will be considered if they describe the scope and operational features of anaphylaxis registries. Only full-text studies published in English will be included. There will be no date restriction.

Methods: The JBI methodology for scoping reviews will be followed. Embase, MEDLINE, Scopus, and CINAHL will be searched from inception date for relevant articles. Identified keyword and index terms will be adapted for searches of gray literature sources, using Google advanced search functions. The authors and developers of identified registries will be contacted, where possible, to obtain additional information about the development and structure of systems. Data will be extracted by two independent reviewers. Any discrepancies will be resolved by a third reviewer. Tables and a narrative summary will be used to describe and compare the scope and features of anaphylaxis registries and outline their output to assess their contribution to research, clinical practice, and public health policy for anaphylaxis.

Keywords: anaphylaxis; registries; reporting

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Introduction

There are increasing numbers of people living with allergies worldwide, with anaphylaxis posing a significant risk to health and quality of life.¹ Anaphylaxis is a severe and potentially life-threatening systemic allergic reaction, which occurs rapidly upon exposure to an allergen, typically food,

medication, or insect venom, by a person who is allergic.² Population-based studies have recorded an increase in incidence, mainly in hospital admissions and emergency department presentations for anaphylaxis.¹ Studies from Australia, the US, Europe, and the UK published after 2010 have reported incidence rates ranging from seven to 42 per 100,000 person-years, with extreme results exceeding 100 events per 100,000 person-years.^{3–9} Rates of fatal anaphylaxis have remained stable in the UK,³ US,¹⁰ and Canada,¹¹ however, an upward trend in anaphylaxis fatalities has been observed in Australia.¹² Much of this increase appears to be due to foods, with fatal food anaphylaxis rising by 9.7% per year,¹² with corresponding reports of

Corresponding: Samantha Stiles,
samantha.stiles@research.uwa.edu.au

MS and RL are affiliated with the National Allergy Strategy. A national reporting system in Australia for anaphylaxis is a goal of the National Allergy Strategy.

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increasing hospitalizations for food-related anaphylaxis⁵ and a high prevalence of food allergy¹³ in this population. Emerging studies from Asian regions also demonstrate a rising anaphylaxis incidence,¹⁴ highlighting a global public health problem.

Anaphylaxis events are generally poorly diagnosed and reported in morbidity and mortality records due to the unpredictable and multi-faceted clinical presentation and well-recognized limitations of the International Classification of Disease coding system to appropriately classify cases.¹⁵ Improved methods to capture valid, standardized data are needed globally to better understand the public health impact and improve management of anaphylaxis.^{1,16,17} Structured reporting systems that are purpose built, such as patient, disease, treatment, and clinical data registries, have increasingly been recognized as important tools in chronic disease care as they provide a real-world view of the natural course of disease.¹⁸ Gliklich¹⁸ defines a patient registry as “an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.”^(p.13) Data collected in registries can provide important information on the epidemiology and burden of disease; factors that influence morbidity, mortality and quality of life; disparities in clinical quality of care; and evaluations of safety and efficacy of patient care.¹⁸

Rich, real-world data collected through well-designed and executed registry systems have great potential to contribute to knowledge and management of anaphylaxis, which will benefit health professionals, policy makers, and researchers, and ultimately improve the care and quality of life of anaphylaxis sufferers.¹⁹ The ability to facilitate structured reporting of unexpected or adverse events makes registries particularly useful for active surveillance.¹⁸ With no identified cure, management of anaphylaxis risk relies on avoidance of known allergens.²⁰ Accidental allergic reactions to food are common and induce severe and fatal reactions.²¹ Issues around correct food labeling and the risk of cross-contamination are important to manage from a public health perspective to protect people with food allergies.^{20,21} Driven by a growing population

at risk of anaphylaxis and the desire to learn from tragic anaphylaxis deaths to improve management and prevention strategies, and to monitor novel or undeclared allergens in foods, there has been a burgeoning global effort to implement reporting systems for anaphylaxis.^{3,19,22,23} Beyond this, registries are increasingly seen as drivers of policy and decision-making.¹⁸ In the context of anaphylaxis, objective and accurate data relating to anaphylaxis fatalities, impact on quality of life, utilization and access to appropriate care, and cost to health care systems is essential to attract investment into this health condition from governments.^{16,24}

Establishing and maintaining registries requires a substantial resource commitment from funders, health care providers, administrative staff, and clinicians.¹⁸ To warrant such investment, there needs to be a clear and attainable purpose that can be achieved through the registry system design, with strong stakeholder participation.¹⁸ While still a relatively new area, a number of registries for anaphylaxis have been implemented around the world to collect epidemiological data, monitor quality of anaphylaxis care, facilitate notification/surveillance of anaphylaxis events, monitor fatal anaphylaxis, and conduct research.^{3,19,22,25} In order to inform future efforts to establish structured reporting systems, including anaphylaxis registries, it is important to learn from systems that currently exist. Important considerations are the purpose of registries and whether their scope and operational features are suitable in terms of: coverage; the health care setting in which they operate; mechanisms for data collection; data elements collected; whether they are mandatory or voluntary; governance structures; and mechanisms for feedback to other health care sectors, policy makers, food regulators, patients, research community, and the general population. Describing the collective utility of registries that exist for anaphylaxis aids understanding of barriers and enablers to implementation, which might inform new systems. An important goal highlighted by the community living with the risk of anaphylaxis is the need to harmonize global anaphylaxis data.¹⁷ There is a need to evaluate what data is being collected, and in which populations across registries, in order to harmonize public health understanding of anaphylaxis from a global perspective. Furthermore, anaphylaxis registries have provided infrastructure

for research projects that have informed clinical and public health understanding about anaphylaxis and contributed significantly to best practice guidelines and targeted educational programs.²⁶ There is a need to characterize the features and research output of these registries to better understand their value and support implementation of future reporting systems.

A preliminary search of Embase, MEDLINE, and the *JBIR Database of Systematic Reviews and Implementation Reports* was conducted and no current or in-progress scoping reviews on the topic were identified. Two reviews related to the topic were identified, including a 2010 discussion paper on the need for a European-wide registry that briefly described existing European anaphylaxis registries,²⁷ and a review published in 2016 on the usefulness of allergy registries, which included a brief section on those that exist for anaphylaxis.¹⁹ However, both of these papers were narrow in scope, so there is still a need for a more detailed description and evaluation of the value of current registries from a global perspective, using systematic methodology. This scoping review will identify and evaluate the literature on anaphylaxis registries that exist globally. The primary aim is to identify anaphylaxis registries and describe their scope and operational features. The secondary aim is to measure the research output of anaphylaxis registries to assess their contribution to improving knowledge and care of anaphylaxis.

Review questions

- i) What anaphylaxis registries exist around the world?
- ii) What is the purpose of anaphylaxis registries (eg, research, epidemiological data, monitor quality of care, notification/surveillance, monitor fatal outcomes)?
- iii) In which settings (primary care, emergency care, hospital, allergy specialists, coroners, general population) do anaphylaxis registries operate?
- iv) What data is collected by anaphylaxis registries and what are the mechanisms used for data collection?
- v) What mechanisms do registries use to feed information back to other health care sectors, policy makers, food regulators, research community, patients, and the general population; and what are their governance structures?
- vi) What research questions have been examined, and what outcomes have been published from registry data?

Inclusion criteria

Participants

This review will consider studies that include participants of any age or gender who have experienced anaphylaxis and had their event recorded in a registry as anaphylaxis or a severe allergic reaction. People recorded in reporting systems for asthma or other allergic conditions that are not consistent with anaphylaxis will be excluded.

Concept

For the purposes of this review, registries for anaphylaxis will be defined as an “organized system to collect uniform data on anaphylaxis, that serves one or more predefined scientific, clinical or policy purposes.”^{18(p.13)} Systems that collect general data on episodes of care from which anaphylaxis cases can be extracted, such as routinely collected hospital data, will be excluded as they are not set up for the express purpose of collecting anaphylaxis data; however, hospital-based anaphylaxis registries will be included. Systems that include patient-reported outcomes alone will be excluded. Preliminary review of the literature showed that some registries used “severe allergic reaction” to describe anaphylaxis, so any systems that indicate they have been set up to collect information on “anaphylaxis” or “severe allergic reactions,” including “food allergy,” “drug allergy,” or “insect allergy,” will be included.

Context

Registries established in all geographical locations and settings where anaphylaxis events occur will be included. Variations on the concept of registries will be included, such as reporting systems, notification systems, and surveillance systems, as long as they collect uniform data on anaphylaxis for a specific purpose.

Types of sources

This review will consider all quantitative and qualitative studies and gray literature pertaining to the scoping review aims that are published in English with no date restrictions. If English versions of relevant articles cannot be found they will be excluded, and their details reported as an appendix. Published

Table 1: Inclusion and exclusion criteria for screening

Criterion	Inclusion	Exclusion
Aim 1. To identify anaphylaxis registries and describe their scope and operational features		
Time period	No time limitation specified	N/A
Language	Published in English	Unavailable in English
Study design	Published and unpublished literature. All qualitative and quantitative studies of any design. Abstracts; official websites of identified registries; documents and reports written by key authors and system developers; news articles or documents published by allergy organizations and government websites; and coronial findings will be included	Other gray literature sources
Availability	Full-text or abstract version available	N/A
Focus of study	Any study describing the scope and operational features of registries established to collect information on patients with anaphylaxis	
Aim 2. To measure the research output of anaphylaxis registries to assess their contribution to improving knowledge and care of anaphylaxis and severe allergy		
Time period	No time limitation specified	N/A
Language	Published in English	Unavailable in English
Study design	Peer-reviewed; original research	Studies that are not peer-reviewed, literature reviews, letters, gray literature sources
Availability	Full-text version available	Full-text version not available (determined after title and abstract screening)
Focus of study	Any study presenting outputs obtained from a registry established to collect information on patients with anaphylaxis	

studies may either describe the scope and operational features of anaphylaxis registries or present the outputs obtained from identified systems. However, the type of sources that will be used to address aim 1 and aim 2 of this review will differ, as seen following and summarized in Table 1.

Aim 1. To identify anaphylaxis registries and describe their scope and operational features

Due to the expected limited published information on the scope and operational features of registries for anaphylaxis, both published and unpublished literature will be considered for inclusion. Qualitative and quantitative articles of any study type will be considered. Gray literature sources will include

relevant abstracts; information from official registry websites and associated links and documentation; documents written by key authors and system developers; news articles or documents published by allergy organizations and government websites; and coronial findings. Additional information will be gathered by contacting key authors of identified registries.

Aim 2. To measure the research output of anaphylaxis registries to assess their contribution to improving knowledge and care of anaphylaxis and severe allergy

Research output will be identified in full-text, peer-reviewed publications only.

Methods

A scoping review is considered the most suitable approach to address the broad aim of this study. Unlike systematic reviews, which address very precise questions, a scoping review maps the key concepts underpinning a topic. In this case, scoping review methodology can address multiple questions relating to the development of registries, scope, operation, and impact. This review follows the JBI methodology for scoping reviews²⁸ and will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) checklist.²⁹

Search strategy

To identify published studies, an initial limited search of Embase, MEDLINE, Scopus (through the Ovid database platform) and CINAHL (through the EBSCOhost database platform) will be undertaken using the following search terms: (/Anaphylaxis OR /Allergy) AND (/Register). The text words contained in the titles and abstracts of relevant articles and the index terms will be used to inform a full search strategy for the same databases (see Appendix I). Additional validation searches will be performed using the search term “[registry name]” as well as a combination of key terms used in the title of the registry. All databases will be searched from inception date with no language limitation used; however, if English versions of relevant articles cannot be found they will be excluded, and their details reported as an appendix. The reference list of included articles will be searched to identify further material. The search strategy, including all identified keywords and index terms, will be adapted for each included information source. Gray literature sources will be identified through Google, using the advanced search functions, with the name of the registry as the search term. Further searches will be conducted using the key terms “anaphylaxis” and “registry” in the advanced search function to identify any additional registries. Websites for identified registries will be searched in a systematic manner and additional research and/or publication links will be examined. Targeted searches of websites of relevant allergy organizations will also be conducted for information on anaphylaxis registries. The authors of identified registries will be contacted where possible to obtain additional information

about the development and structure of established systems that may not appear in published literature.

Several literature sources will be used, including published literature and unpublished literature. Published literature will be found by searching Embase (Ovid), MEDLINE (Ovid), Scopus (Elsevier), and CINAHL (EBSCOhost), as well as the reference lists of included literature. Unpublished literature sources will be found through electronic databases to identify abstracts and Google searches, which will include hand-searching key websites and relevant organizations, such as Allergy Anaphylaxis Australia; Australasian Society of Clinical Immunology and Allergy; European Academy of Allergy and Clinical Immunology; American Academy of Allergy, Asthma, and Immunology; and World Allergy Organization (amongst others). Global health organizations, such as the European Centre for Disease Prevention and Control, Centers for Disease Control and Prevention, and World Health Organization, will also be searched. Key authors of identified registries will be contacted where required.

Study selection

All publications will be exported to reference management software EndNote v.X8 (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts of articles will be screened by two independent reviewers, and those that do not meet the inclusion criteria will be discarded. The full text of selected articles will be retrieved and screened by the two reviewers to assess for eligibility, and those that meet the inclusion criteria will be included in the final analysis. Reasons for exclusion of full text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Screening of gray literature will also be conducted by two reviewers. A third investigator will resolve any discrepancies. The results of the search will be reported in full in the final scoping review and presented in a PRISMA-ScR flow diagram.³⁰

Data extraction

Data will be extracted from the included literature by two reviewers. Separate extraction pages for peer-reviewed publications and unpublished literature will be created. Important features of registry design and operation, guided by features highlighted in *Registries for evaluating patient outcomes: a user's guide*¹⁸ will be collected (see Appendix II). However,

mapping of information will follow an inductive approach, where additional key categories will be determined by the information found in the literature. Any discrepancies in the extra key categories added in this process will be discussed and resolved by reviewers or, where necessary, a third moderator. A Scopus citation index score will be recorded for each publication that relates to Aim 2 to indicate the impact of this research.

Data presentation

In line with JBI scoping review methodology,²⁸ data extracted from included studies and unpublished literature will be presented in one or more tables and/or figures with headings consistent with the items in the extraction tool (see Appendix II). A narrative summary will accompany the tabulated results to describe how the results relate to the key scope and operational features of identified reporting systems and their published research output.

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References

1. Turner PJ, Campbell DE, Motosue MS, Campbell RL. Global trends in anaphylaxis epidemiology and clinical implications. *J Allergy Clin Immunol* 2020;8(4):1169–76.
2. Reber LL, Hernandez JD, Galli SJ. The pathophysiology of anaphylaxis. *J Allergy Clin Immunol* 2017;140(2):335–48.
3. Turner P, Gowland M, Sharma V, Ierodiakonou D, Harper N, Garcez T, et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992–2012. *J Allergy Clin Immunol* 2015;135(4):956–63.
4. Harduar-Morano L, Simon M, Watkins S, Blackmore C. A population-based epidemiologic study of emergency department visits for anaphylaxis in Florida. *J Allergy Clin Immunol* 2011;128(3):594–600.
5. Mullins RJ, Dear KB, Tang ML. Time trends in Australian hospital anaphylaxis admissions in 1998–1999 to 2011–2012. *J Allergy Clin Immunol* 2015;136(2):367–75.
6. Motosue M, Bellolio M, Van Houten H, Shah N, Campbell R. Increasing emergency department visits for anaphylaxis, 2005–2014. *J Allergy Clin Immunol* 2016;5(1):171–5.
7. Kivisto J, Protudjer J, Karjalainen J, Wickman M, Bergstrom A, Mattila V. Hospitalizations due to allergic reactions in Finnish and Swedish children during 1999–2011. *Allergy* 2016;71(5):677–83.
8. Tejedor Alonso M, Moro Moro M, Mugica Garcia M, Esteban Hernandez J, Rosado Ingelmo A, Vila Albelda C, et al. Incidence of anaphylaxis in the city of Alcorcon (Spain): a population-based study. *Clin Exp Allergy* 2012;42(4):578–89.
9. Lee S, Hess E, Lohse C, Gilani W, Chamberlain A, Campbell R. Trends, characteristics, and incidence of anaphylaxis in 2001–2010: a population-based study. *J Allergy Clin Immunol* 2017;139(1):182–8.
10. Jerschow E, Lin RY, Scaperotti MM, McGinn AP. Fatal anaphylaxis in the United States, 1999–2010: temporal patterns and demographic associations. *J Allergy Clin Immunol* 2014;134(6):1318–28.
11. Xu YS, Kastner M, Harada L, Xu A, Salter J, Wasserman S. Anaphylaxis-related deaths in Ontario: a retrospective review of cases from 1986 to 2011. *Allergy Asthma Clin Immunol* 2014;10(1):38.
12. Mullins R, Wainstein B, Barnes E, Liew W, Campbell D. Increases in anaphylaxis fatalities in Australia from 1997 to 2013. *Clin Exp Allergy* 2016;46(8):1099–110.
13. Sasaki M, Koplin JJ, Dharmage SC, Field MJ, Sawyer SM, McWilliam V, et al. Prevalence of clinic-defined food allergy in early adolescence: The SchoolNuts study. *J Allergy Clin Immunol* 2018;141(1):391–8. e4.
14. Tham EH, Leung ASY, Pacharn P, Lee SY, Ebisawa M, Lee BW, et al. Anaphylaxis-lessons learnt when East meets West. *Pediatr Allergy Immunol* 2019;30(7):681–8.
15. Demoly P, Tanno L, Akdis C, Lau S, Calderon M, Santos A, et al. Global classification and coding of hypersensitivity diseases—An EAACI–WAO survey, strategic paper and review. *Allergy* 2014;69(5):559–70.
16. Turner P, Campbell D. Epidemiology of severe anaphylaxis: can we use population-based data to understand anaphylaxis? *Curr Opin Allergy Clin Immunol* 2016;16(5):441–50.
17. Tanno L, Bierrenbach A, Simons F, Cardona V, Thong B, Molinari N, et al. Critical view of anaphylaxis epidemiology: open questions and new perspectives. *Allergy Asthma Clin Immunol* 2018;14:12.
18. Gliklich RE, Dreyer NA, Leavy MB. Registries for evaluating patient outcomes: a user's guide. 3rd edn Rockville (MD): Agency for Healthcare Research and Quality Government (US); 2014.
19. Jares EJ, Badellino HA, Ensina LF. Registries as useful tools in characterization of allergic manifestations. *Curr Opin Allergy Clin Immunol* 2016;16(3):250–6.

20. Zurzolo GA, Allen KJ, Peters RL, Tang MLK, Dharmage S, de Courten M, *et al.* Anaphylaxis to packaged foods in Australasia. *J Paediatr Child Health* 2018;54(5):551–5.
21. Blom WM, Michelsen-Huisman AD, van Os-Medendorp H, van Duijn G, Versluis A, Castenmiller JJM, *et al.* Accidental food allergy reactions: products and undeclared ingredients. *J Allergy Clin Immunol* 2018;142(3):865–75.
22. Anaphylaxis notifications under the Public Health and Wellbeing Act 2008: a guide for Victorian hospitals [internet]. Victoria: Victorian State Government; 2018 [cited 2019 Oct 15]. Available from: http://www.victag.org.au/Anaphylaxis_notifications_guidance_Oct_18.pdf.
23. Worm M, Timmermans F, Moneret-Vautrin A, Muraro A, Malmheden Y, ILOvik M, *et al.* Towards a European registry of severe allergic reactions: current status of national registries and future needs. *Allergy* 2010;65(6):671–80.
24. Tanno LK, Simons FER, Sanchez-Borges M, Cardona V, Moon HB, Calderon MA, *et al.* Applying prevention concepts to anaphylaxis: a call for worldwide availability of adrenaline auto-injectors. *Clin Exp Allergy* 2017;47(9):1108–14.
25. Grabenhenrich LB, Dolle S, Moneret-Vautrin A, Kohli A, Lange L, Spindler T, *et al.* Anaphylaxis in children and adolescents: The European Anaphylaxis Registry. *J Allergy Clin Immunol* 2016;137(4):1128–37.
26. Pouessel G, Turner PJ, Worm M, Cardona V, Deschildre A, Beaudouin E, *et al.* Food-induced fatal anaphylaxis: From epidemiological data to general prevention strategies. *Clin Exp Allergy* 2018;48(12):1584–93.
27. Worm M, Timmermans F, Moneret-Vautrin A, Muraro A, Malmheden Yman I, Lövik M, *et al.* Towards a European registry of severe allergic reactions: current status of national registries and future needs. *Allergy* 2010;65(6):671–80.
28. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015;13(3):141–6.
29. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, *et al.* PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169(7):467–73.
30. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, *et al.* PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation. The PRISMA-ScR Statement. *Ann Intern Med* 2018;169(7):467–73.

Appendix I: Search strategy

Embase (Ovid)

Search conducted September 2019.

(A similar strategy will be used in other databases.)

1. register/ or regist*.mp.
2. mandatory reporting/ or mandatory reporting.mp.
3. disease surveillance/
4. notification.mp.
5. anaphylaxis/ or anaphylaxis.mp.
6. (severe adj3 allerg*).ti,ab.
7. 1 or 2 or 3 or 4
8. 5 or 6
9. 7 and 8

Search retrieved 1325 articles

Appendix II: Data extraction tool

General study details
Author
Year of publication
Features of reporting system (Aim 1)
Name
Start date
Main purpose
Geographical location
Regional, national, or international coverage
Number of sites/centers participating
Number of participants enrolled
Recruitment setting
Methods of data collection
Data elements collected
Governance
Mandatory or voluntary
Feedback mechanism (who receives information from registry? Is this in real-time?)
Funding
Additional scope and operational features identified in the iterative data extraction process
Research output (Aim 2)
<i>Extraction of research output information</i>
What is the research question?
What are the key findings?
What reporting system was used to collect data for the study?
What is the Scopus citation index score?