

GENERAL MEDICINE/ORIGINAL RESEARCH

Incidence of Clinically Important Biphasic Reactions in Emergency Department Patients With Allergic Reactions or Anaphylaxis

Brian E. Grunau, MD*; Jennifer Li, BSc; Tae Won Yi; Robert Stenstrom, MD, PhD; Eric Grafstein, MD;
Matthew O. Wiens, PharmD; R. Robert Schellenberg, MD; Frank Xavier Scheuermeyer, MD, MHSc

**Corresponding Author. E-mail: briangrunau@gmail.com.*

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INTRODUCTION :

Allergic reactions are common presentations to the emergency department (ED).

An unknown proportion of patients will develop biphasic reactions

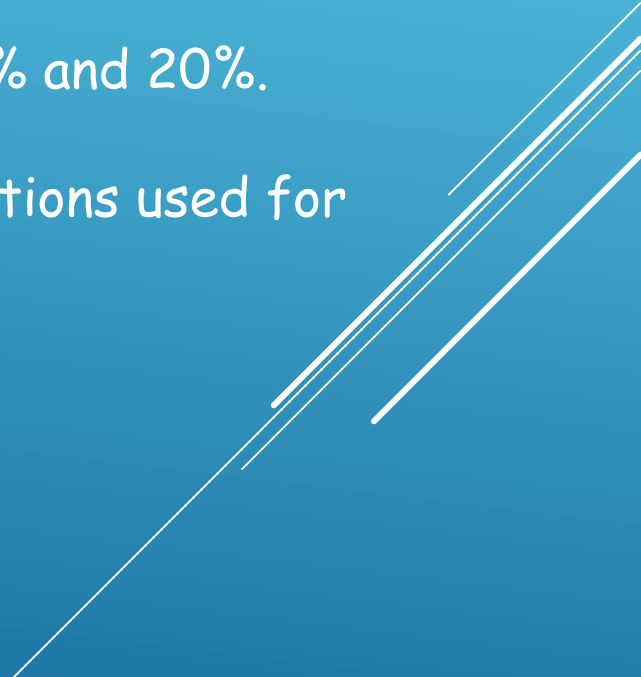
Because of this concerns , patients are often observed in a monitored setting for 6 hours or longer

However, the benefit of this prolonged ED stay has not been demonstrated to decrease complications of biphasic reactions and incurs significant ED cost and patient inconvenience.

We seek to determine the incidence of clinically important biphasic reactions.

Importance

Although several studies have examined the incidence of biphasic reactions in ED patients, conclusions about their incidence have varied significantly, between 0.5% and 20%. Reasons for this heterogeneity are likely due to a wide variety of definitions used for anaphylaxis and biphasic reactions

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MATERIALS AND METHODS :

This retrospective cohort study took place at 2 urban academic teaching hospitals in Vancouver, British Columbia, Canada.

The 2 study hospitals use a common comprehensive electronic medical record.

All consecutive ED visits between April 1, 2007, and March 31, 2012, were examined.

Adult patients presenting with allergic reactions were identified.

Regional and provincial databases were linked to identify subsequent ED visits and deaths within a 7-day period.

The primary outcome was the proportion of patients with a clinically important biphasic reaction, and the secondary outcome was mortality

Encounters were dichotomized as "anaphylaxis" or "allergic reaction" with an explicit algorithm.

Selection of Participants

Patient encounters were identified from the electronic medical database if the ED discharge diagnosis code of "allergic reaction" was used.

Patient were excluded if any of the following criteria were met:

- the patient was younger than 17 years,

- the primary diagnosis (as coded by the treating physician) was asthma with allergic reaction coded as a secondary diagnosis,

- the patient left the ED immediately after registration (was not assessed by nursing staff or a physician),

- or the patient had a preexisting condition that was known to cause nonallergic angioedema.

We divided patients into 2 groups: "anaphylaxis" included those satisfying the definition for anaphylaxis, and "allergic reaction" included those not satisfying it (Figure 1).

The definition for anaphylaxis was adapted from the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network criteria developed at the Second Symposium on the Definition and Management of Anaphylaxis.

Anaphylaxis: Any of the following three numbered criteria must be satisfied:

1. Both of the following must be satisfied:
 - a. Skin or mucosal tissue involvement
 - b. One of the following:
 - i. Respiratory compromise
 - ii. Systolic blood pressure < 90 mmHg or syncope
2. Two of the following must be satisfied after exposure to a likely allergen:
 - a. Skin or mucosal tissue involvement
 - b. Respiratory compromise
 - c. Systolic blood pressure < 90 mmHg or syncope
 - d. Gastrointestinal symptoms
3. Systolic Blood Pressure < 90 mmHg after exposure to a known allergen.

Skin Involvement: Urticaria, rash, pruritus, and swelling of the face or ears. Localized pruritus or rash which were deemed secondary to trauma or an obvious insect bite were not considered as fulfilling the definition of "skin involvement."

Mucosal tissue involvement: Swelling of lips, tongue, or pharynx.

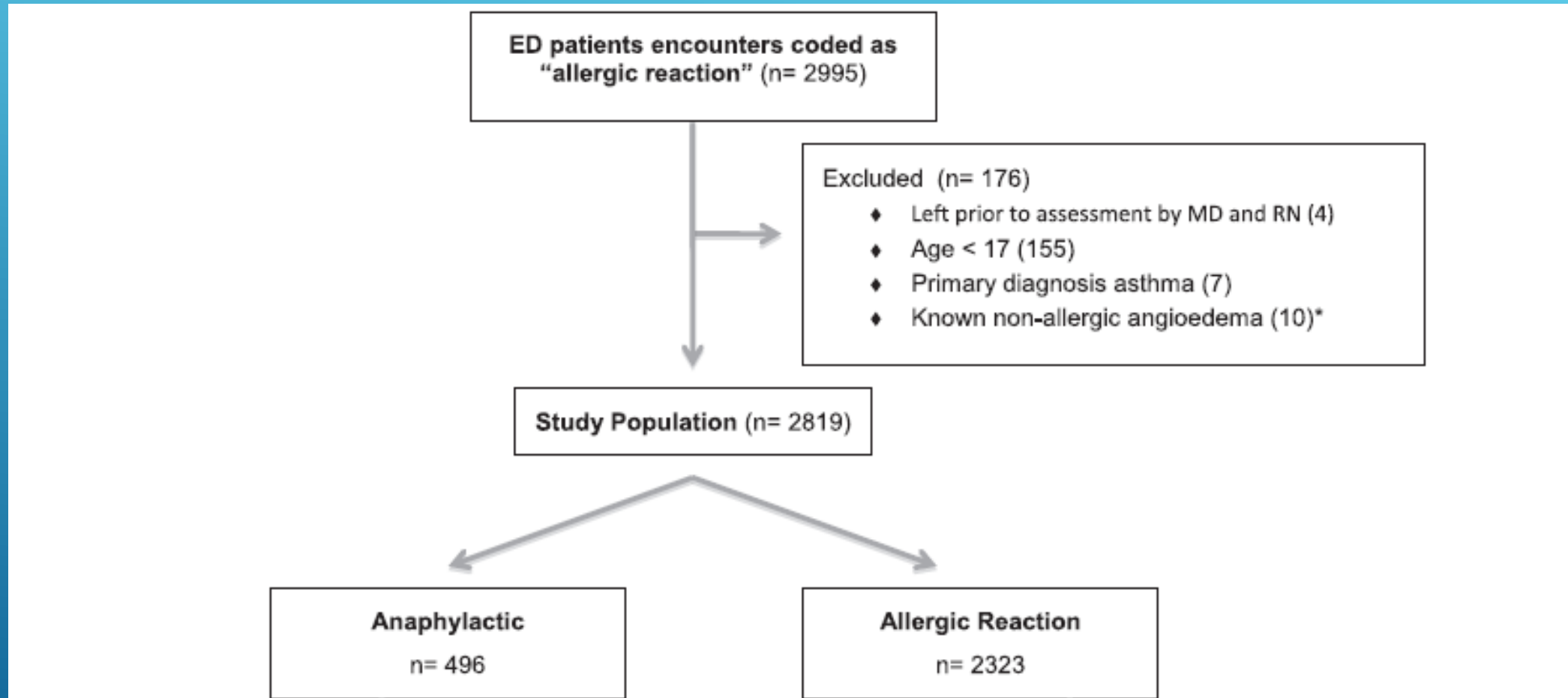
Respiratory Compromise: Wheeze or stridor on auscultation, hypoxemia (oxygen saturation < 95%), or respiratory rate >22.

Gastrointestinal Symptoms: Abdominal pain or vomiting which is present in the ED.

Allergic Reaction: A clinical patient presentation in which the criteria for anaphylaxis was not met, however the attending physician deemed the etiology of the signs and/or symptoms secondary to allergic processes (as demonstrated by the discharge diagnosis code).

Clinically Important Biphasic Reaction: Recurrent or new signs or symptoms occurring after an initial allergy-related presentation, which satisfy the definition for anaphylaxis, without any obvious further exposure to an offending allergen. If certain signs or symptoms were present on the index visit and did not resolve or improve prior to the subsequent visit, these signs or symptoms were not considered "recurrent" or "new" and thus were not used in the classification of biphasic reaction in subsequent visits.

RESULTS:



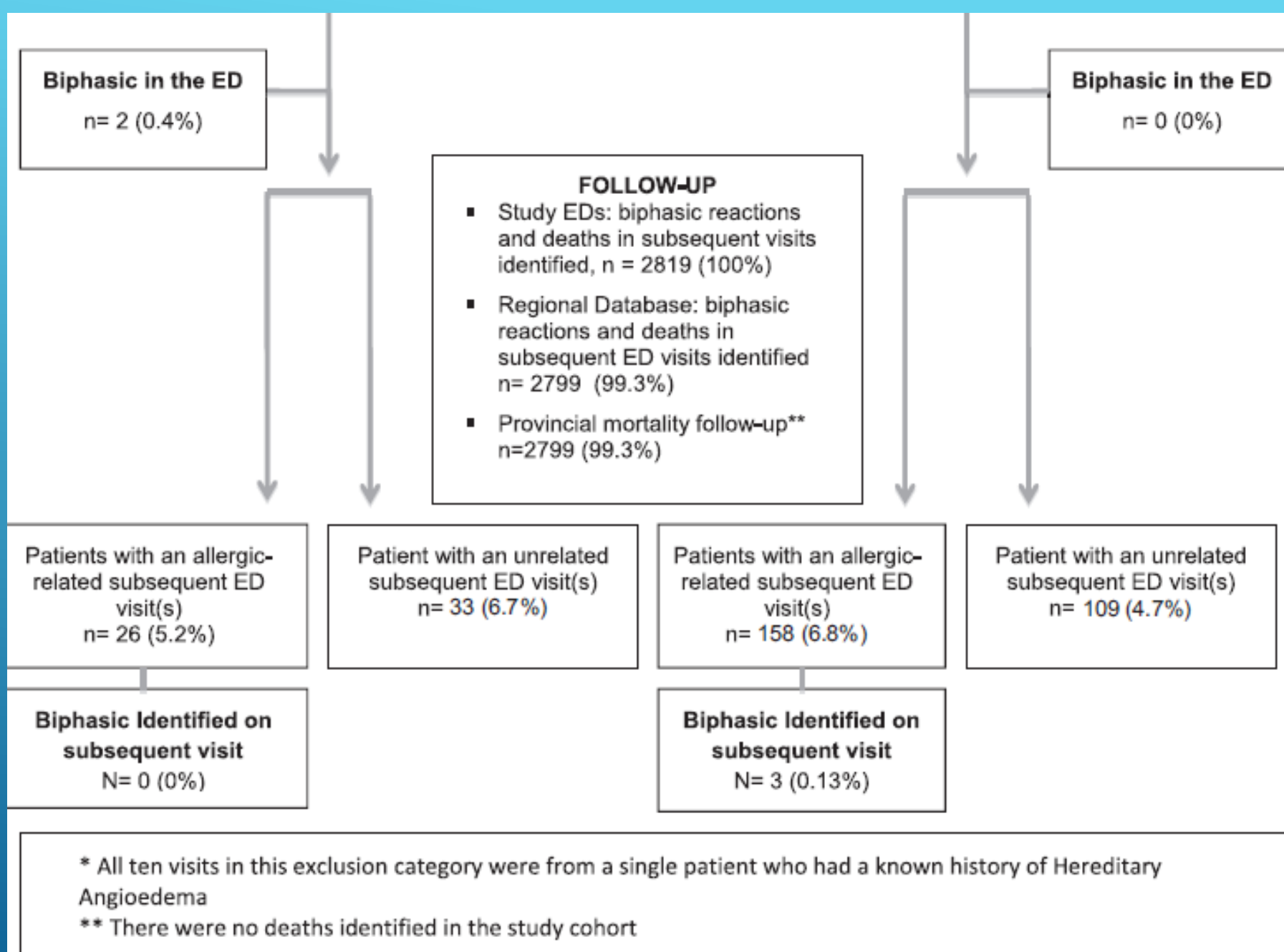


Figure 2. Flow diagram.

Table. Subject characteristics and outcomes.*

Subject characteristics and outcomes	Anaphylaxis, n = 496			Allergic Reactions, n = 2,323		
	No. (IQR or %)	95% CI	Missing (%)	No. (IQR or %)	95% CI	Missing (%)
Demographics						
Age	38 (27–51)		0	34 (26–48)		0
Female	264 (53)		0	1,456 (63)		0
Medical history						
History of allergies	358 (72)		1 (0.2)	1,350 (58)		5 (0.2)
Medications						
Epinephrine [†]	266 (54)		0	483 (21)		0
Steroids [‡]	362 (73)		0	985 (42)		0
ED index visit, %						
Biphasic in ED	2 (0.40)	0.07–1.6	0	0	0–0.21	0
Admit	7 (1.4)	0.60–3.0	0	13 (0.6)	0.31–0.98	0
7-Day follow-up, %						
Biphasic post-ED discharge	0	0–0.96	0	3 (0.13)	0.03–0.41	0
Death in 7 days	0	0–0.96	0	0	0–0.21	0
Biphasic reactions, %						
Total	2 (0.40)	0.07–1.6	0	3 (0.13)	0.03–0.41	0

IQR, Interquartile range.

*Categorical variables are presented as number followed by percentage in parentheses. Continuous variables are represented as the median with IQR in parentheses.

[†]Includes intramuscular, subcutaneous, or intravenous administration by patient, EMS, or in ED.[‡]Includes oral or intravenous routes administered in the ED or prescribed on discharge.

LIMITATIONS

This is a retrospective medical record review and is subject to several limitations.

The study sites were 2 urban Canadian EDs, and treatments and disposition may vary in different settings.

There was no defined protocol for allergic reactions, and physicians managed patients in an unstructured, individualized manner, including ED treatment, investigations, length of stay, disposition, outpatient prescriptions, and follow-up.

It is possible that treatment of one or various medications or other unmeasured cofounders influenced the incidence of biphasic reactions.

Patients who presented only to a primary care physician within the region or an ED out of the region within 7 days would not have been identified as having a subsequent visit or potential clinically important biphasic reaction.

The diagnosis of allergic reactions is based on clinical impression, which is a potential source of error.

Patients with true allergic-related presentations may have been coded as other entities such "shock not otherwise specified" or "rash."

Missing clinical variables relevant to the definition of anaphylaxis may have also contributed to misclassified patient encounters

DISCUSSION

To our knowledge, this is the largest study to date examining ED allergic reactions, anaphylaxis, biphasic reactions, and allergy-related mortality.

We identified 2,819 patient encounters during a 5-year period, which composed 0.66% of all ED patients.

We applied an objective and reproducible definition for anaphylaxis to each study patient and identified 496 patient encounters with anaphylaxis.

Clinically important biphasic reactions, which satisfied the definition for anaphylaxis with recurrent or new signs or symptoms without reexposure to an allergen, were identified through a comprehensive strategy, revealing an incidence of 0.18%.

This assists clinicians by demonstrating that few patients with allergic reactions or anaphylaxis have subsequent clinically important biphasic reactions.

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Allergic reactions and anaphylaxis are diagnoses that are made on clinical grounds in the acute phase because there are no reliable laboratory or other objective markers on which to rely.

Objective and reproducible definitions are essential in the identification and study of anaphylaxis.

Several studies have examined the incidence of anaphylaxis; however, the definitions used have been subjective, variable, and lacking in assessments of inter rater reliability.

Little is known of the pathophysiology of biphasic reactions and, similar to issues with defining true anaphylaxis, there is no criterion standard for diagnosis. Furthermore, the time frame in which biphasic reactions may occur is unknown.

In conclusion

clinically important biphasic reactions and fatalities are rare among ED patients with allergic reactions or anaphylaxis.

Our data suggest that prolonged routine ED monitoring of patients whose symptoms have resolved is likely unnecessary for patient safety.

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Editor's Capsule Summary

What is already known on this topic

There are reports of delayed, so-called biphasic reactions after the emergency department (ED) treatment of allergy and anaphylaxis, prompting some emergency physicians to retain patients for multiple hours of monitoring.

What question this study addressed

How often do clinically important biphasic reactions occur?

What this study adds to our knowledge

In this retrospective review of 2,819 consecutive adults with allergic reaction or anaphylaxis, there were just 5 with clinically important biphasic reactions. There were no deaths or serious morbidity.

How this is relevant to clinical practice

Extended monitoring after ED treatment of allergy or anaphylaxis appears unnecessary for the majority of patients whose symptoms have resolved.