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Systematic review

Biphasic anaphylaxis in children presenting to emergency departments: incidence, risk factors, timing, and implications for observation periods; a systematic review

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Abstract

Background: Biphasic anaphylaxis complicates observation decisions in pediatric emergency departments because of the variations in recurrence definitions, clinical severity, and timing. This review examined incidence, associated factors, recurrence timing, and implications for observation. **Methods:** PubMed, Scopus, and Web of Science were searched for studies published between 2000 and 2026. Two authors independently screened studies involving children with emergency department anaphylaxis. Findings were synthesized narratively according to PRISMA 2020; heterogeneity in definitions, denominators, and ascertainment precluded pooling. **Results:** Seven studies were included, five retrospective cohorts and two quality improvement studies. Reported recurrence proportions ranged from 1.7% to 14%, although the highest estimate included exacerbations after partial recovery. Clinically important recurrence requiring epinephrine occurred in 0.3% of one cohort. Delayed reactions reported up to 33 hours' after

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resolution, whereas one cohort recorded all treatment-requiring recurrences within four hours of treatment initiation. Lower systolic pressure, pallor or hypotonia, intravenous fluids, and greater initial severity were associated with recurrence in unadjusted comparisons. Observation pathways reduced hospitalization from 28.5% to 11.2% and low-risk admission from 49% to 7%, without increased recorded revisits. **Conclusions:** Findings support risk-stratified observation while distinguishing true biphasic anaphylaxis from persistent symptoms. Four-hour observation cannot exclude delayed recurrence. Standardized definitions, explicit timing origins, and active post-discharge follow-up are needed to clarify recurrence risk and evaluate observation strategies across pediatric age groups and clinical settings in children.

Keywords: Anaphylaxis; biphasic reaction; children; emergency department; epinephrine; observation period; systematic review.

Introduction

Anaphylaxis is an acute systemic hypersensitivity reaction that compromise the airway, breathing, or circulation. Intramuscular epinephrine is the first-line treatment, while antihistamines and corticosteroids must not delay epinephrine administration (1). Most children improve after initial treatment, and symptoms recur after apparent complete resolution without further allergen exposure. A multidisciplinary defined biphasic anaphylaxis as new or recurrent anaphylactic manifestations occurring between one and 48 hours after complete resolution of the initial reaction, in the absence of re-exposure (2).

Among 353 children hospitalized after pediatric emergency department presentation, six developed a biphasic reaction, corresponding to 1.7%; only one reaction, or 0.3% of the cohort, was clinically important and required epinephrine. The median interval from initial anaphylaxis to recurrence was 5.9 hours (3). A separate cohort of 292 epinephrine-treated children found ten biphasic reactions, representing 3.4%. Six occurred within 30-150 minutes of initial symptom resolution, whereas four occurred 10-33 hours after discharge (4).

A multicenter study reported treatment-requiring recurrence in 49 of 357 children who received intramuscular epinephrine and corticosteroids; all recorded recurrences requiring additional epinephrine occurred within four hours of treatment initiation (5). Treatment initiation is not equivalent to complete symptom resolution, and repeat epinephrine can indicate persistent or refractory disease rather than true biphasic anaphylaxis.

A 15-year cohort identified biphasic anaphylaxis in approximately 3.6% of children, with a median recurrence time of four hours; more complex anaphylaxis phenotypes were associated with greater severity and cardiovascular manifestations (6). In infants and toddlers presenting to a pediatric emergency department, biphasic anaphylaxis occurred in 11 of 239 evaluable episodes, or 4.6%. Recurrence occurred 70-330 minutes later, and lower systolic blood pressure, pallor or hypotonia, fluid resuscitation, and greater initial severity were associated with recurrence (7).

Observation recommendations range from short observation after rapid resolution to at least 6-12 hours for patients with severe reactions, multiple epinephrine doses, continuing symptoms, or barriers to emergency care. Guidance favors risk-

stratified observation rather than one duration for every patient (8). Pediatric quality-improvement studies also shown that structured pathways can reduce hospitalization without an observed increase in short-term revisits, although these studies do not by themselves establish the biological risk or timing of biphasic anaphylaxis (9,10).

It must separate true biphasic anaphylaxis from persistent symptoms, distinguish minor recurrence from clinically important recurrence, standardize the starting point used to measure observation, and consider the adequacy of post-discharge follow-up. In this study we aimed to synthesize the available pediatric emergency department literature on the incidence, clinical significance, timing, and risk factors of biphasic anaphylaxis and determine how these findings should inform risk-stratified observation after resolution of the initial reaction.

Methods

This systematic review examined the incidence, timing, clinical significance, and associated factors of biphasic anaphylaxis in children presenting to emergency departments with outcomes of post-treatment observation pathways. The manuscript was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 framework. PubMed, Scopus, and Web of Science were searched for studies published between 2000 and 2026. The search addressed pediatric anaphylaxis, biphasic or recurrent reactions, repeat epinephrine administration, emergency department observation, and post-discharge outcomes. Database-specific search strategies. Duplicate records were removed before screening.

Eligible studies included children younger than 18 years presenting to an emergency department with anaphylaxis; studies defining their pediatric population as including patients aged 18 years were also considered. Mixed adult and pediatric studies were eligible only when pediatric findings could be extracted separately. Original cohort, case-control, registry, surveillance, interventional, and relevant quality-improvement studies were considered when they reported biphasic reactions, recurrence timing, repeat epinephrine, observation outcomes, or subsequent emergency visits. Inclusion required a peer-reviewed report with freely accessible full text. Reviews, editorials, conference abstracts without complete data, case reports, and studies confined to oral food challenges, allergy clinics, or perioperative settings without separately extractable emergency department data were excluded.

Two authors independently screened titles and abstracts and subsequently assessed potentially eligible full texts against the predefined criteria. Disagreements were resolved through discussion between the two authors. Reasons for exclusion at the full-text stage were recorded, and the selection process was summarized in a PRISMA flow diagram (Fig 1).

The extraction framework covered study design, setting, recruitment period, population size, age criteria, anaphylaxis and recurrence definitions, observation practices, follow-up, recurrent-event frequency, timing, treatment, associated factors, hospitalization, and return visits. Recurrence following complete resolution was distinguished from persistence or exacerbation after partial recovery, while recurrent symptoms were considered separately from treatment-requiring or clinically important anaphylaxis. Timing origins and denominators were recorded explicitly, distinguishing patients, episodes, encounters, and selected subgroups.

Methodological quality was assessed using the JBI Critical Appraisal Checklist for Cohort Studies and the JBI Checklist for Quasi-Experimental Studies (2020 versions), according to study design, with domain-level judgments concerning participant selection, outcome measurement, confounding, follow-up, and statistical analysis summarized in Table 1.

Findings were synthesized narratively and presented in table 2 and 3. Cohort recurrence outcomes were considered separately from quality-improvement outcomes concerning observation and disposition. No pooled estimate was calculated because the selected studies differed in recurrence definitions, timing origins, denominators, and outcome ascertainment. Unadjusted associations were distinguished from independently adjusted predictors.

Table 1. Methodological quality assessment of the included studies

Study	Assessment tool	Selection and data collection	Outcome measurement and temporal classification	Confounding and comparison groups	Follow-up and missing information	Statistical analysis and interpretation
Ikegawa et al., 2021 (3)	JBICohort checklist	Defined hospital cohort and study period; all children presenting with anaphylaxis were admitted. Retrospective extraction depended on existing documentation.	Anaphylaxis criteria and clinically important recurrence were specified. However, the published symptom-free interval and inconsistent recurrence time origin introduce classification uncertainty.	No adjusted analysis of recurrence-associated factors. Treatment comparisons were descriptive and cannot establish a preventive effect.	Overnight inpatient observation supported detection of early recurrence, but complete ascertainment throughout the stated 72-hour window was not established.	Descriptive statistics were suitable for reporting the cohort. Only six recurrent events limited precision. Useful for descriptive incidence, with qualifications concerning definition, timing, and late-event ascertainment.
Short et al., 2024 (4)	JBICohort checklist	Eligibility, and setting were described. Selection required epinephrine treatment for presumed anaphylaxis; clinical confirmation against standardized criteria was not clearly documented for every case.	Persistence and recurrence were recorded separately. Nevertheless, no mandatory symptom-free interval or standardized severity classification was specified; some reported recurrences occurred within one hour of resolution.	Analyses were unadjusted; potential relationships between initial severity, treatment, and recurrence were not controlled jointly.	A 72-hour recurrence window was defined, but complete follow-up of every discharged patient was not documented. Caregiver recall and retrospective treatment timestamps could introduce measurement error.	Univariate comparisons were reported; ten recurrent events limited inference about predictors. Useful for observation patterns and recorded recurrence, with diagnostic and follow-up concerns.
Rueter et al., 2026 (7)	JBICohort checklist	Coding was checked by two independent allergists using standardized extraction forms; ASCIA criteria were applied. Four adrenaline-overdose cases were explicitly excluded from the recurrence comparison.	Complete resolution, absence of re-exposure, and a 1-48-hour recurrence window were specified. Recurrence required only one or more anaphylactic symptoms, rather than explicitly requiring the second episode to	Recurrence associations were based on unadjusted comparisons; independent effects of severity, cardiovascular findings, and treatment were not established.	Missing measurements were visible in variable-specific denominators. The authors acknowledged that post-discharge recurrence and loss to follow-up could not be excluded.	Distribution-appropriate tests and Fisher's exact test were described. Handling of repeated presentations within children was not reported. Detailed ascertainment strengthens the report, but predictor estimates remain exploratory and late-

Study	Assessment tool	Selection and data collection	Outcome measurement and temporal classification	Confounding and comparison groups	Follow-up and missing information	Statistical analysis and interpretation
			meet full anaphylaxis criteria.			event capture uncertain.
Uppala et al., 2021 (11)	JBICohort checklist	Defined ED cohort and recruitment period; diagnoses were reviewed by certified pediatricians. Data collection remained retrospective.	A detailed operational definition of biphasic anaphylaxis, minimum symptom-free interval, and standardized recurrent-event adjudication were not reported.	No adjusted model specifically examined biphasic recurrence. Reported regression analyses concerned other anaphylaxis associations.	Hospitalization allowed inpatient surveillance, but length of stay varied from 8 to 72 hours; systematic post-discharge ascertainment was not described.	Descriptive recurrence counts were interpretable, but only three events limited precision and predictor assessment. Substantial reporting limitations affect recurrence classification and completeness of ascertainment.
Bonadio et al., 2025 (5)	JBICohort checklist	Consecutive presentations in three EDs; templated documentation and an inter-rater agreement assessment were reported. Analysis selected episodes receiving both epinephrine and corticosteroids.	The definition allowed exacerbation after partial recovery, permitting persistent reactions to be classified as biphasic. Treatment initiation, rather than complete resolution, anchored timing.	No untreated corticosteroid comparator or confounder-adjusted treatment-effect analysis; steroid effectiveness cannot be inferred.	Electronic records were reviewed for subsequent visits, including other area facilities, but complete follow-up outside captured services was not established.	Fisher's exact testing was reported, but handling of repeated episodes within patients and comparison of successive observation windows was insufficiently explained. Substantial concerns for true biphasic incidence and causal treatment conclusions; broader treatment-requiring recurrence remains extractable.
Gaffney et al., 2022 (10)	JBICohort checklist	Intervention timing, eligibility, and comparison periods were clearly specified. Measured demographic characteristics were similar across phases; case identification relied on diagnosis codes.	Admission and ED length of stay were objectively recorded and measured consistently. Recurrence was not independently characterized as a separate outcome.	External hospital data and interrupted time-series analyses addressed national trends, but unmeasured local changes and the multiple intervention components limit causal attribution.	Admission outcomes were ascertainable from encounter records. Completeness of 72-hour revisit capture outside the hospital was not established.	Repeated measurements, statistical process control, and time-series analyses supported assessment of trends. Suitable for pathway-associated utilization changes, with residual confounding and

Study	Assessment tool	Selection and data collection	Outcome measurement and temporal classification	Confounding and comparison groups	Follow-up and missing information	Statistical analysis and interpretation
						revisit-ascertainment limitations.
Wolpert et al., 2022 (9)	QUIBI quasi-experimental checklist	Clearly defined intervention periods and low-risk criteria; baseline characteristics were compared. Estimated symptom timing and clinician judgment could influence low-risk classification.	Admission was recorded using consistent procedures. Return visits were assessed across the healthcare network; they were not equivalent to adjudicated biphasic events.	No independent concurrent control group. Before-after comparisons could not fully distinguish pathway effects from secular changes or other care processes.	Network-wide surveillance improved return-visit capture, but visits outside the network could be missed. Incomplete prehospital documentation was acknowledged.	Repeated measurements and a run chart were reported; the small low-risk sample limited assessment of uncommon safety outcomes. Suitable for descriptive pathway outcomes; causal effectiveness and discharge-safety conclusions require caution.

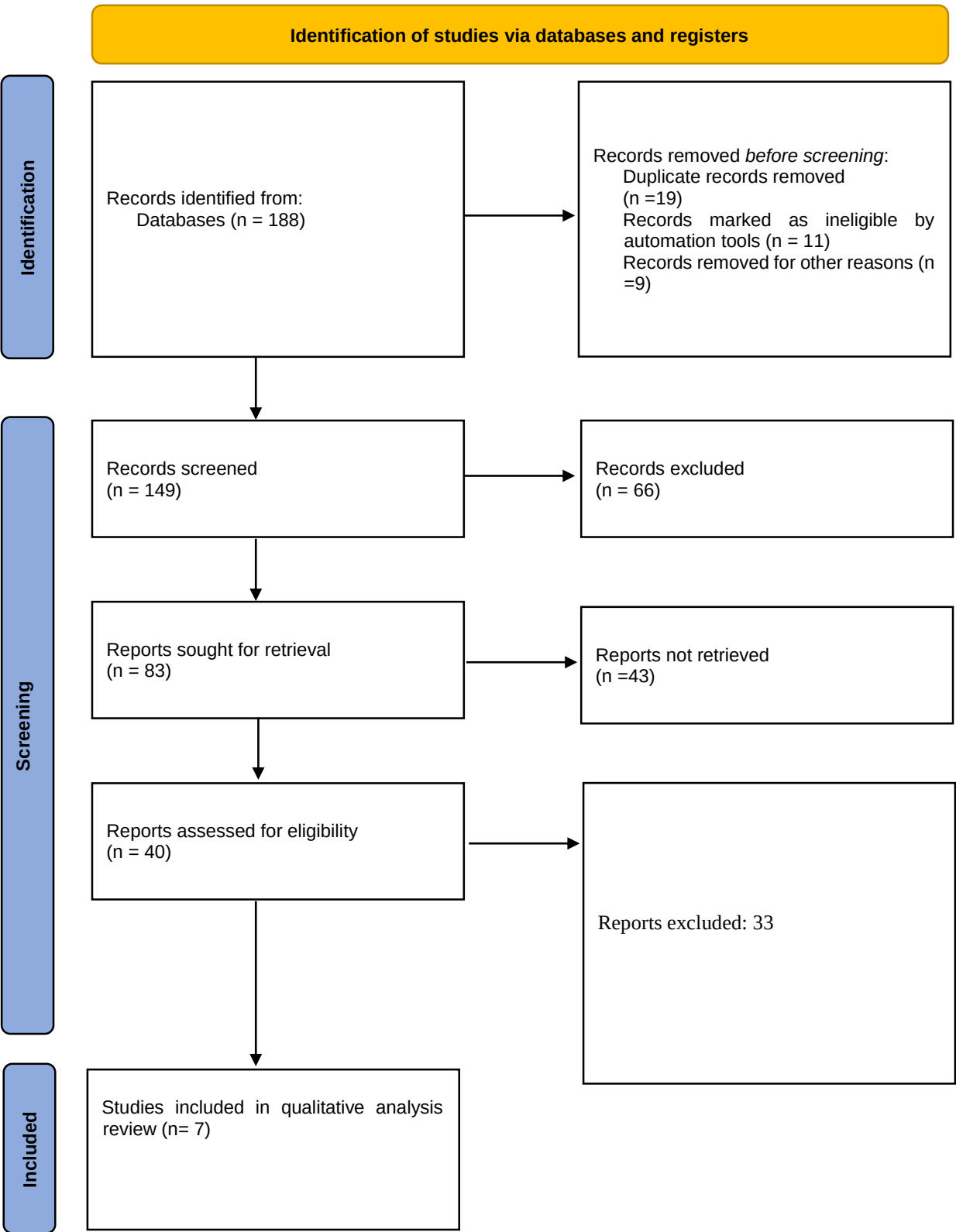


Figure 1: PRISMA flow chart

Results

The seven included studies comprised five retrospective cohorts and two quality improvement studies conducted in Japan, Australia, Thailand, and the United States. Five investigated recurrent reactions, whereas the two quality improvement studies examined observation pathways, hospitalization, and subsequent emergency visits. Study characteristics are summarized in Table 2, and recurrence, treatment, and disposition outcomes are presented in Table 3. Sample sizes represented different units, including individual patients, anaphylaxis episodes, encounters, and selected low-risk subgroups. The infant and toddler analysis excluded four adrenaline overdose cases from the recurrence comparison denominator.

Rueter et al. required recurrent symptoms between one and 48 hours after complete resolution without further exposure, while Short et al. used a 72-hour window following epinephrine administration. Ikegawa et al. additionally required treatment or extended hospitalization, although their published symptom-free interval differed from the protocol definition. Uppala et al. did not provide a detailed operational definition, and Bonadio et al. included exacerbations after partial recovery. Reported recurrence proportions ranged from 1.7% in the Japanese cohort to 14% in the treated subgroup studied by Bonadio et al. The other cohorts reported proportions between these values, including 3.4% in Short et al., 3.94% in Uppala et al., and 4.6% in Rueter et al. These estimates represented study-defined outcomes rather than a uniform endpoint, and the larger estimate from Bonadio et al. concerned recurrences sufficiently severe to require additional epinephrine.

Short et al. identified early emergency department events and delayed post-discharge events, with the latter occurring 10-33 hours after symptom resolution. Uppala et al. reported three later events at 10, 12, and 18 hours after the first episode.

Conversely, Bonadio et al. recorded all treatment-requiring recurrences within four hours of treatment initiation. Ikegawa et al. classified one recurrence as clinically important because epinephrine was required. All recurrent episodes in Uppala et al. received additional intramuscular adrenaline, while Rueter et al.'s patient-level descriptions recorded adrenaline treatment in ten recurrent cases and pediatric intensive care admission in one. Short et al. did not characterize recurrence severity sufficiently to estimate a comparable treatment-requiring endpoint. Recurrent symptoms and clinically important anaphylaxis remained distinct outcomes.

Associations with recurrence were most extensively described by Rueter et al., whose unadjusted comparisons identified lower systolic pressure, pallor or hypotonia, intravenous fluid administration, and greater initial severity. These comparisons did not establish independent predictors. Short et al. found no significant differences in observation duration or symptom-onset-to-epinephrine intervals between recurrence groups. Uppala et al.'s recurrent cases were all food-induced and adolescent, while Ikegawa et al. provided descriptive comparisons without an adjusted prediction model.

The observation-pathway studies reported changes in disposition rather than biphasic incidence. Gaffney et al. observed a hospitalization risk difference of -17.3 percentage points (95% confidence interval -21.4 to -13.2), accompanied by increased attainment of four-hour emergency department stays. Wolpert et al. reported an absolute admission reduction of 42 percentage points among low-risk patients, alongside longer emergency department stays and lower encounter costs. Post-discharge ascertainment relied on recorded return visits rather than uniform active follow-up. Gaffney et al. found no statistically significant change in 72-hour unplanned revisits, while Wolpert et al. recorded no anaphylaxis-

related returns in either comparison group. Bonadio et al. recorded no recurrence-related return within 48 hours.

Table 2. Characteristics, outcome definitions, and observation practices of the included studies

Study	Country, setting, and design	Study period	Study population	Definition or principal outcome	Observation and follow-up
Ikegawa et al., 2021 (3)	Japan; single pediatric ED; retrospective cohort	March 2010-March 2017	353 children hospitalized with anaphylaxis; median age 4.1 years (IQR 1.6-7.8)	Recurrence without allergen re-exposure within 72 hours, requiring treatment or prolonged hospitalization. Clinically important recurrence required epinephrine or resulted in death. ¹	All children presenting with anaphylaxis were admitted for at least one night; ascertainment relied on hospital records.
Short et al., 2024 (4)	United States; single tertiary academic pediatric ED; retrospective cohort	2017-2022	292 epinephrine-treated patients aged <18 years; mean age 8.8 years (SD 5.7)	Return of anaphylactic symptoms within 72 hours after epinephrine administration; persistent symptoms were recorded separately	Mean ED observation after epinephrine: 233.1 minutes (SD 78.9). Post-discharge reactions were identified through subsequent ED presentations.
Rueter et al., 2026 (7)	Australia; single tertiary pediatric ED in Perth; retrospective cohort	2003-2007 and 2013-2017	243 presentations among infants/toddlers aged 0-2 years; 239 included in the biphasic comparison after excluding four adrenaline overdoses	One or more anaphylactic symptoms recurring 1-48 hours after complete resolution, without further allergen exposure	ED and subsequent hospital care; ascertainment included return presentations for recurrence within the defined window.
Uppala et al., 2021 (11)	Thailand; single tertiary pediatric referral ED, Khon Kaen University; retrospective cohort	January 2016-December 2019	76 patients aged 5 months-18 years; median age 14.54 years (IQR 12.04-16.83)	Biphasic anaphylaxis reported; a detailed operational definition and minimum symptom-free interval were NR	All patients were hospitalized; mean hospital stay 29.89 hours (SD 14.57); median 24 hours, range 8-72 hours.
Bonadio et al., 2025 (5)	United States; three EDs in New York, including two pediatric EDs; retrospective cohort	January 2015-December 2022, according to Methods	371 episodes in 280 patients; analysis focused on 357 episodes treated with IM epinephrine and corticosteroids; median age 9.2 years. ²	Recurrence or exacerbation after partial or complete recovery, without re-exposure, requiring additional epinephrine	ED monitoring for 4-6 hours after treatment initiation; electronic records reviewed for subsequent visits within 48 hours after discharge.
Gaffney et al., 2022 (10)	United States; Boston Children's Hospital ED; quality-improvement study with before-after comparison	January 2014-December 2019; revised guideline introduced 23 May 2018	1,447 encounters: 1,055 prerevision and 392 implementation; eligibility ages 6 months-18 years; median age 6.99 years (IQR 2.59-13.3)	Hospitalization, ED length of stay, and unplanned revisits; a separate biphasic-incidence endpoint was not reported	Minimum four-hour observation from epinephrine administration; revised pathway also specified observation from symptom resolution when no ED treatment was given; 72-hour revisits monitored.
Wolpert et al., 2022 (9)	United States; single quaternary pediatric ED; quality-improvement study	Preintervention: November 2016-June 2018; postintervention: July 2018-December 2019	Low-risk subgroup: 53 preintervention and 43 postintervention; eligibility age ≤18 years; mean ages 7.0 (SD 5.5) and 6.6 (SD 5.3) years	Admission among low-risk patients, ED length of stay, costs, and anaphylaxis-related return visits	Updated decision tool recommended discharge after four-hour observation for low-risk patients; return visits within 72 hours were

Study	Country, setting, and design	Study period	Study population	Definition or principal outcome	Observation and follow-up
	with before-after comparison				assessed in the healthcare network.

Table 3. Biphasic-reaction frequency, recurrence timing, treatment, and observation outcomes

Study	Reported biphasic reactions	Timing of recurrence	Treatment or clinical importance of recurrence	Associations and observation outcomes
Ikegawa et al., 2021 (3)	6/353 (1.7%)	Median 5.9 hours (IQR 3.3-7.6); individual values 2.7-15.5 hours. ³	Clinically important recurrence: 1/353 (0.3%), requiring epinephrine	No adjusted predictor model reported. Initial epinephrine was administered in 3/6 biphasic cases versus 295/347 cases without recurrence; this descriptive comparison does not establish prevention.
Short et al., 2024 (4)	10/292 (3.4%)	Six recurred 30-150 minutes after initial resolution; four recurred 10-33 hours after resolution, following discharge	Treatment and severity of the recurrent episodes were not reported separately in sufficient detail	Observation duration ($p=0.98$) and symptom-onset-to-first-epinephrine interval ($p=0.90$) did not differ significantly between recurrence groups. Four post-discharge reactions required ED re-presentation.
Rueter et al., 2026 (7)	11/239 (4.6%)	Reported interval 70-330 minutes; one child experienced three distinct episodes	Patient-level Table 4 records adrenaline treatment for recurrence in 10/11 cases and PICU admission in one case	Unadjusted comparisons associated recurrence with lower systolic pressure ($p=0.011$), pallor/hypotonia ($p=0.046$), IV fluids ($p<0.001$), and greater initial severity ($p=0.014$). All recurrences occurred in the ED; no return presentations for biphasic anaphylaxis were recorded.
Uppala et al., 2021 (11)	3/76 (3.94%)	Individual recurrences occurred 10, 12, and 18 hours after the first episode	All three recurrent episodes received additional IM adrenaline	All three cases occurred in adolescents and were food-induced. No adjusted biphasic-predictor model reported. The authors recommended at least 24-hour hospital observation, particularly for adolescents.
Bonadio et al., 2025 (5)	49/357 (14%, as reported), using the study's broader recurrence definition	All 49 occurred within four hours of treatment initiation; none requiring additional epinephrine were recorded during hours 4-48	All 49 required additional IM epinephrine by definition	Median ED stay: 4.7 hours; 11 hospitalizations. No documented return for recurrent or exacerbated anaphylaxis within 48 hours after discharge. Inclusion of partial recovery prevents equating all events with recurrence after complete resolution.
Gaffney et al., 2022 (10)	Not reported as a separate incidence endpoint		Recurrent episodes were not separately characterized	Hospitalization decreased from 28.5% to 11.2% ($p<0.001$). Encounters with ED stay ≥ 240 minutes increased from 53.3% to 59.9% ($p=0.024$). Unplanned 72-hour revisit rates were 4.2% before versus 2.6% after revision ($p=0.23$).
Wolpert et al., 2022 (9)	Not reported as a separate incidence endpoint		Recurrent episodes were not separately characterized	Low-risk admissions decreased from 26/53 (49%) to 3/43 (7%). Anaphylaxis-related 72-hour returns were 0/53 and 0/43. Mean low-risk ED stay increased from 190 to 232 minutes; median encounter cost decreased from US\$826 to US\$449.

Discussion

This review found that a distinction between recurrent symptoms and consequential anaphylaxis which is consistent with an earlier pediatric cohort, in which six children experienced biphasic reactions but only three had significant episodes requiring additional respiratory or circulatory treatment (12). Our findings favor presenting symptom recurrence and treatment-requiring recurrence separately, while interpreting differences between cohorts through their definitions, patient selection, and ascertainment practices rather than assuming geographical variation alone.

The cardiovascular and severity associations identified in the included infant and toddler cohort correspond with previous pediatric research. Mehr et al. reported that children developing biphasic reactions more frequently required multiple adrenaline doses or fluid boluses during initial treatment and the positive predictive value of either characteristic was only 32% (13). This comparison indicate that these features can identify children warranting closer assessment without reliably predicting individual recurrence. Because treatment intensity reflects initial illness severity, our unadjusted associations with intravenous fluids should not be interpreted as indicating that fluid administration causes subsequent reactions.

The absence of significant associations with treatment delay in one included cohort does not establish that treatment timing is unimportant. A Canadian study identified delayed emergency presentation, widened pulse pressure, repeated epinephrine, and inhaled beta-agonist administration as independent predictors of biphasic reactions (14). Earlier pediatric research also associated delayed epinephrine administration with recurrence (15). delayed presentation and delayed drug administration represent different exposures, and retrospective documentation can

obscure their relationship. Our findings support extracting these intervals separately, while recognizing that small recurrence groups limit the ability to detect clinically relevant associations.

In a large multicenter pediatric cohort, repeat epinephrine beyond four hours was uncommon, although the endpoint included treatment for persistent as well as recurrent symptoms (16). Its findings complement our observation results without establishing that four hours excludes biphasic anaphylaxis. The comparison emphasizes that time measured from initial epinephrine administration cannot be substituted automatically for time following complete resolution. Observation decisions should consider the initial clinical course alongside access to rescue medication and prompt reassessment, rather than rely exclusively on elapsed time.

The reduction in admissions observed in our pathway studies is consistent with other pediatric improvement initiatives. Farbman et al. reduced hospitalizations from 54% to 36% without increasing recorded 72-hour revisits (17). Another pathway shortened recommended observation from eight to four hours and reduced admissions without a significant increase in returns (15). These comparisons suggest that structured discharge pathways can reduce hospitalization, but they do not establish equivalence between observation durations. Because education, medication access, and clinical processes changed simultaneously, the contribution of observation duration cannot be isolated, and longer emergency stays may accompany fewer inpatient admissions.

The treatment findings provide no basis for attributing reduced late recurrence to corticosteroids, because the relevant included cohort lacked an untreated comparator. The practice parameter similarly concluded that glucocorticoids and antihistamines do not reliably

prevent biphasic anaphylaxis (18). Interpretation is constrained by retrospective records, differing denominators, and incomplete capture of events managed elsewhere. Restricting inclusion to freely accessible reports may also omit relevant studies. Future prospective cohorts should document resolution and recurrence timestamps, apply explicit severity criteria, and actively ascertain post-discharge outcomes, while evaluating observation strategies alongside epinephrine availability and caregiver preparation. Investigators should distinguish multiple encounters from unique children and report outcomes within prespecified age strata, allowing reviews to compare incidence and treatment requirements using consistent denominators.

Conclusion

Reported recurrence ranged from 1.7% to 14% and definitions differed between cohorts. Clinically important recurrence occurred in 0.3% of the Japanese cohort, and delayed reactions occurred 10-33 hours after symptom resolution in one study, whereas all treatment-requiring recurrences occurred within four hours of treatment initiation in another. Lower systolic pressure, pallor or hypotonia, intravenous fluids, and greater initial severity were associated with recurrence in unadjusted comparisons. Observation pathways reduced hospitalization from 28.5% to 11.2% and low-risk admissions from 49% to 7%. 72-hour revisits decreased from 4.2% to 2.6%, without statistical significance.

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