

Table 1: Characteristics of the Included Studies Evaluating Barriers to Timely Intramuscular Epinephrine Administration for Anaphylaxis (n = 23)

Last name of first author, year	Study design, country	Study setting	Study period	Population type (Patients, physicians, nurses, residents, paramedics, mixed healthcare professionals)	Sample size	Patient age	Gender distribution (M/F)	Diagnostic criteria for anaphylaxis	Trigger of anaphylaxis	Comparator (if present)	Follow-up duration	Profession	Specialty	Year of experience	Level of training	Previous anaphylaxis education/training
Pape et al., 2025 ⁱ	Prospective, multicenter, randomized trial (single intervention team)	5 major European hospitals (neutral study locations not affiliated with authors)	January to June 2023	Physicians (doctors)	95	NA	NR	Video simulation of severe anaphylactic reaction (male actor with cutaneous reaction, itching, swelling around mouth, bronchospasm)	Iodinated contrast medium (IV administration during CT)	NA	NA	Physicians/Doctors	1. Radiology (n = 59) 2. Internal Medicine (n = 19) 3. Anesthesiology (n = 17) Total = 95	Detailed by Specialty & Level: - Radiologists: Board-certified avg 15 yrs (8–28); Residents avg 3 yrs (2–4.75). - Internists: Board-certified avg 13 yrs (10–20.5); Residents avg 2 yrs (1.5–2.5). - Anesthesiologists: Board-certified avg 25 yrs (21–32.5); Residents avg 7 yrs (5.5–7).	Residents (in-training): n = 45 (47.4%) - Radiology: 29 - Internal Medicine: 8 - Anesthesiology: 8	No formal data on previous anaphylaxis training/education
Bülbül et al., 2024 ⁱⁱ	Cross-sectional descriptive survey study (online questionnaire via Google Forms)	Türkiye (Nationwide; participants recruited via social media (WhatsApp) and e-mail)	June 2022 – August 2022	Physicians (Family Physicians actively working in primary healthcare)	207	NA	Physician study: 58.5% female, 41.5% male among respondents	NA	NA	NA	NA	Physicians (Family Physicians/Aile Hekimleri)	Family Medicine (Primary care)	Mean 8.5 ± 8.3 years (range: 1–43 years).	All participants were actively working Family Physicians.	40.6% (n=84) received post-graduate training on anaphylaxis. 24.6% (n=51) received specific training on Adrenaline Auto-Injector (AAI) use.
Hamadi & Casale, 2024 ⁱⁱⁱ	Mixed-methods descriptive study (Cross-sectional survey + Retrospective electronic medical record [EMR] review)	United States (National FARE Patient Registry + Tampa General Hospital [TGH] ER, Florida)	Survey: March 1, 2020 – January 31, 2022. ER Data: April 1, 2018 – March 31, 2022.	Patients (Survey respondents with food allergies) + ER patient records (patients with ICD-10 codes for anaphylaxis/allergic reaction)	190 survey responses + 4,358 ER patient records	All age groups included (NS further)	Females presented twice as often as males in the ER data (2,967 females vs. 1,391 males).	Survey: Self/parent-reported acute allergic reaction to food. ER: ICD-10 discharge diagnosis codes for anaphylaxis or allergic reaction (Z91.018, T78.40XA).	Survey: Food (Tree nuts 18%, Peanuts 14%, Egg 10%, Seafood 10%, Milk 8%). ER: Top ICD-10 code was "Allergy to other foods" (n=540).	Pre-pandemic (2018–2019) Pre-pandemic (2019–2020) Pandemic (2020–2021) Post-vaccine (2021–2022)	NA	NA	NA	NA	NA	
Kaya & Alaylar, 2024 ^{iv}	Cross-sectional descriptive survey (pretested structured questionnaire, face-to-face administration)	Tertiary care teaching hospital (Erzurum Training and Research Hospital), Türkiye	NS	Physicians (General practitioners, medical residency students, and specialist physicians from various surgical	85	NA	NA	NA	NA	NA	NA	Physicians (Doctors)	Mixed – 20 different branches	Categorized: 1–3 yrs (n=12), 4–10 yrs (n=37), 11–15 yrs (n=21), 16–20 yrs (n=7), Over 20 yrs (n=8).	- General Practitioners: 8 (9.4%) - Medical Residency Students (Residents): 26 (30.6%)	89.4% (n=76) stated they received training on anaphylaxis at some point. Sources: - Medical school only: 31 (36.5%)

				and internal medicine branches)										Mean age of participants: 42.6 years.	- Specialist Physicians: 51 (60.0%)	- Medical school + Residency: 25 (29.4%) - Residency only: 17 (20.0%) - Residency + Pharma meetings: 2 (2.4%) - Pharma meetings only: 1 (1.2%) No training: 9 (10.6%)
Ho et al., 2024 ^v	Retrospective observational cohort study (20-year analysis of electronic medical records)	2 emergency departments at the Linkou and Taipei branches of Chang Gung Memorial Hospital (largest tertiary hospital network in Taiwan)	January 1, 2001 – December 31, 2020	Patients with anaphylaxis presenting to emergency departments (not physicians)	771 patients with anaphylaxis	Mean 41.0 ± 22.2 years (range: children <18 to older adults ≥65)	55.0% male (n=424), 45.0% female	NIAID/FAAN criteria (National Institute of Allergy and Infectious Diseases / Food Allergy and Anaphylaxis Network)	Drugs (43.3%), Foods (34.5%), Insect venom (7.3%), Radiocontrast medium (4.8%), Other/unknown (10.1%)	Age groups: Children (<18 years, n=159), Adults (18–64 years, n=498), Older adults (≥65 years, n=114)	NA	NA	NA	NA	NA	NA
Price et al., 2023 ^{vi}	Prospective observational study (using in situ simulation [ISS] within a translational simulation [TS] program)	Tertiary Pediatric Emergency Department, Royal Children's Hospital Melbourne, Australia (annual census ~90,000)	March 2019 – June 2020 (16 months)	Multidisciplinary healthcare professionals (Doctors, Nurses, Nurse Practitioners, Students)	23 anaphylaxis simulations; 164 total staff participants (mean 8 per session)	NA	NA	NA	Simulated trigger: IM penicillin (for urinary tract infection)	NA	NA	Multidisciplinary ED Staff (Doctors, Nurses, Nurse Practitioners, Medical/Nursing Students)	Pediatric Emergency Department (Royal Children's Hospital Melbourne, Australia)	NR	Partially reported: - Doctors (Registrars, Residents): 83 participants (51%) - Nurses: 55 participants (33%) - Nurse Practitioners: 11 participants (7%) - Medical/Nursing Students: 15 participants (9%)	NR
Ateş & Sahiner, 2022 ^{vii}	Cross-sectional descriptive survey study (questionnaire-based)	Ankara City Hospital, Türkiye (COVID-19 vaccination centers within a tertiary hospital)	2021 (Ethics approval date: February 10, 2021; study conducted during COVID-19 vaccination campaign)	Health professionals (Specialist doctors, Assistant doctors, General practitioners, Nurses)	218	NA	NA	NA	NA	Training status (Received training vs. No training on adrenaline administration)	NA	Health Professionals (Physicians and Nurses)	- Specialist Doctors: 15 (6.9%) - Assistant Doctors (Residents): 107 (49.1%) - General Practitioners: 2 (0.9%) - Nurses: 94 (43.1%)	Not directly reported – Age and professional experience data not provided in the results. Only time since adrenaline training was reported: - ≤6 months: 20.2% - 6 months–2 years: 14.9% - 3–5 years: 22.5% - ≥6 years: 17.0%	- Specialist Doctors: 15 (6.9%) - Assistant Doctors (Residents): 107 (49.1%) - General Practitioners: 2 (0.9%) - Nurses: 94 (43.1%)	65.6% (n=143) had received prior training on adrenaline administration. 34.4% (n=75) had NOT received training.

Wijekoon et al., 2021 ^{viii}	Cross-sectional descriptive survey study (online questionnaire via Google Forms)	Three Sri Lankan universities (University 1 & 2 – Western Province; University 3 – Southern Province) – representing three different medical curricula types	2019 (April – September ; data collection within 4 months of final MBBS examinations)	Pre-intern medical graduates (doctors who passed MBBS 2019, awaiting internship)	385 (response rate 91.5% of 421 eligible)	NA	NA	NA	NA	University type/Curriculum type (University 1 vs. University 2 vs. University 3) and Final MBBS results category (class vs. no class)	NA	Physicians (Pre-intern medical graduates) – doctors who have completed MBBS and are awaiting internship appointment	General Medicine	Participants were fresh graduates. Mean duration from final MBBS examination to data collection was 2.7 ± 1 months. Mean age: 27.3 ± 1 years (range 23–29).	Pre-intern MBBS graduates (awaiting internship): First class: 4.9% Second-class upper: 26.0% Second-class lower: 40.5% Pass: 28.6%	Prior knowledge before university: 50.9% Knowledge gained during medical school: 99.0% Skills gained during medical school: 93.8% Main knowledge source: Paraclinical teaching (83.6%) Main skills source: Final-year clinical training (67.5%) Universities 2 & 3: Post-MBBS workshops/seminars
Francuzik et al., 2020 ^{ix}	Case-control study using registry data (European Anaphylaxis Registry)	Multicenter, international – 11 European countries (allergy centers and emergency departments)	Registry data until March 2019 (cases collected over approximately 12 years)	Patients with anaphylaxis (Venom-induced anaphylaxis [VIA] vs. non-VIA controls)	3,612 VIA cases + 3,605 non-VIA controls (age- and sex-matched)	All ages (bimodal distribution: children/young adults and older adults); matched by age	Matched by sex; overall majority male in VIA group (consistent with known epidemiology)	NIAID/FAAN criteria; severity graded by Ring and Messmer Scale (Grades II–IV)	Insect venom (Hymenoptera: yellowjacket, honeybee, hornet, etc.)	Non-VIA anaphylaxis (food, drug, other triggers), matched by age, sex, and severity.	NA	NA	NA	NA	NA	NA
Pimentel-Hayashi et al., 2020 ^x	Cross-sectional descriptive survey study (online questionnaire via SurveyMonkey)	Mexico City, Mexico – large hospitals (respondents working in the largest hospitals in Mexico City)	May 1 – June 10, 2020	Physicians	196 (after excluding 6 incomplete/out-of-range responses from 202 total)	NA	NA	NA	NA	Specialty groups (Group 1: Pediatrics; Group 2: Internal Medicine/Cardiology/Anesthesiology; Group 3: Surgery/Orthopedics/Gynecology)	NA	Physicians (Medical doctors)	Mixed specialties – categorized into 3 groups: - Group 1 (59.7%): Pediatricians and Pediatric Residents - Group 2 (28.1%): Internal Medicine Physicians, Cardiologists, Anesthesiologists - Group 3 (12.2%): General Surgeons, Orthopedic Doctors, Gynecologists	NR	Partially reported: Participants included residents and specialists. The survey was distributed to "pediatrics residents, pediatricians, internal medicine physicians, cardiologists, emergency medicine doctors, general surgeons, anesthesiologists, and gynecologists. " No breakdown by training level (resident vs. specialist) was provided beyond specialty groups.	NR
Krmpotic et al., 2019 ^{xi}	Retrospective cohort study (chart review of	Two Pediatric Intensive Care Units (PICUs) in Atlantic Canada:	January 1, 2006 – December 31, 2015 (10 years)	Patients (children with severe anaphylaxis requiring PICU	12 PICU admissions (unique patients)	Median 15 years (range 3–17 years)	58% female (7 females, 5 males)	Primary diagnosis of anaphylaxis (based on PICU	Identified in 6/12 (50%): - Allergy injection - Amoxicillin	NA	PICU length of stay: Median 2 days (range 2–9 days)	NA	NA	NA	NA	NA

	administrative databases)	- IWK Health Center, Halifax, Nova Scotia - Janeway Children's Health and Rehabilitation Center, St. John's, Newfoundland and Labrador		admission from outpatient setting)				administrative database admission diagnosis)	- Cashews - Dairy - Latex - Peanuts		Hospital length of stay (survivors): Median 3 days (range 2–10 days)					
Lauraa et al., 2019 ^{xii}	Cross-sectional descriptive survey study (self-administered anonymous survey)	Hospital de Pediatría "Prof. Dr. Juan P. Garrahan", Buenos Aires, Argentina (tertiary, 534-bed pediatric hospital; ~90,000 PED visits/year; 300 Intermediate and Moderate Care beds)	August 24, 2016 (single day, 8 consecutive hours)	Pediatricians (physicians with complete pediatric residency working shifts in IMC and PED units)	71 (of 100 eligible; 67 completed all questions)	NA	NA	NA	NA	Years of experience: <5 years vs. ≥5 years since completing residency	NA	Physicians (Pediatricians)	Pediatrics (Physicians with complete pediatric residency working in Intermediate Care [IMC] and Pediatric Emergency Department [PED] units)	Median 3 years since completing residency (range 0.1–24 years). Categorized for analysis: - <5 years: 48 participants (67.6%) - ≥5 years: 23 participants (32.4%)	Pediatricians with complete residency (excluded: PED fellows and staff physicians) – all participants had completed their pediatric residency training.	69% (49/71) reported having ever witnessed/treated an anaphylaxis episode in their daily practice.
Sharma et al., 2019 ^{xiii}	Randomized, double-blind, placebo-controlled trial (nested descriptive analysis of severe anaphylaxis cases)	Nepal – Bharatpur Hospital (tertiary referral hospital with ICU) and two snakebite treatment centers (Damak and Charali), with transfers to BPKIHS	April 2011 – March 2013	Patients with neurotoxic snakebite envenoming receiving VINS polyvalent antivenom	155 patients who received ≥1 dose of antivenom; 13 (8.4%) developed severe antivenom-related anaphylaxis (ARA)	Children: 5, 6, 11 years (n=3) Adults: 18–52 years (n=10)	Severe ARA patients: 5 males, 8 females (approximately 38% male, 62% female)	NIAID/FAAN criteria: "anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death"	VINS polyvalent antivenom	Antivenom dose: Low dose (6 vials, n=4 with severe ARA) vs. High dose (10+ vials, n=9 with severe ARA) Premedication: SC adrenaline premedication (n=6 with severe ARA) vs. no premedication (n=7 with severe ARA)	Hospital stay (until resolution/discharge/death) and follow-up at days 7, 21, and 6 months	NA	NA	NA	NA	NA
Xing et al., 2018 ^{xiv}	Retrospective cohort study (analysis of pharmacovigilance database records)	Beijing, China – Beijing Pharmacovigilance Database (BPD), including 94 participating hospitals	January 1, 2004 – December 31, 2014 (10 years)	Pediatric patients (age <18 years) with drug-induced anaphylaxis (DIA)	91 patients (from 9,425 hypersensitivity cases; 1,189 DIA cases total including adults)	0–5 years: 32 (35%) 6–12 years: 24 (26%) 13–17 years: 35 (39%)	62% male (n=56), 38% female (n=35)	NIAID/FAAN criteria; cases adjudicated by two physician/allergist reviewers; severity categorized as mild-moderate or severe	Drugs (antibiotics 53%, TCM injections 9%, biologics 8%, radiocontrast 4%, glucocorticoids 3%, chemotherapeutics 3%, anesthetics 3%)	Age groups: 0–5 years vs. 6–12 years vs. 13–17 years	NA	NA	NA	NA	NA	NA
Cohen et al., 2018 ^{xv}	Retrospective chart review (two chronological cohorts: 2013–2014 and 2015–2016)	Tel Aviv Sourasky Medical Center (TASMC), Israel – tertiary care, university-affiliated pediatric emergency department (PED)	January 2013 – December 2016 (4 years; compared 2013–2014 vs. 2015–2016)	Pediatric patients (aged 0–16 years) presenting to PED with anaphylaxis (based on NIAID/FAAN criteria) or allergic reaction	Total anaphylaxis cases meeting criteria: 193 - 2013–2014: 59 cases - 2015–2016: 134 cases Total PED visits: 113,067	Mean (range): - 2013–2014: 7.0 years (0.3–15.9) - 2015–2016: 6.7 years (0.1–15.2) - Overall mean: ~6.8 years	Male predominance: - 2013–2014: 66% male - 2015–2016: 65% male	NIAID/FAAN criteria (2005 Second Symposium); cases meeting criteria were included; severity graded by Brown classification	- Food: 91% (milk 27.6%, tree nuts 23.1%, peanut 8.2%, sesame 8.2%, egg 2.2%, fish/shellfish 4.5%) - Drugs: 2.9% - Insect venom: 1.5%	Time period: 2013–2014 (pre-guideline revision) vs. 2015–2016 (post-guideline revision)	NA	NA	NA	NA	NA	NA
Dubus et al., 2018 ^{xvi}	Retrospective cohort study (chart review of electronic emergency)	Two pediatric emergency departments (EDs) of the University Hospitals of	January 2010 – December 2015 (6 years)	Pediatric patients (aged 0–18 years) with anaphylaxis meeting	204 patients (from 422,483 total ED admissions; 235 coded as	Mean 7.9 years (range 2 months – 17.7 years)	55.9% male (n=114), 44.1% female	Sampson's criteria (NIAID/FAAN); severity graded by Ring and	- Food: 78.3% (nuts 32.5%, fruits 16.8%, milk 14.9%, egg 5.9%, others 16.3%)	Anaphylaxis severity: Grade II (moderate) vs. Grade III (severe) by Ring and Messmer classification	NA	NA	NA	NA	NA	NA

	department records)	Marseille, France (Assistance Publique-Hôpitaux de Marseille)		Sampson's criteria	anaphylaxis; 204 confirmed)			Messmer classification	- Drugs: 8.5% - Insect venom: 4.7% - Other: 8.5%							
Lee et al., 2018 ^{xvii}	Quality improvement (QI) initiative with retrospective cohort comparison (pre- vs. post-intervention)	Children's Hospital of Philadelphia (CHOP), USA – urban, tertiary, university-affiliated 527-bed children's teaching hospital; ED with ~90,000 visits/year	Baseline: April 20, 2013 – October 19, 2014 (18 months) Post-intervention: October 20, 2014 – April 20, 2016 (18 months)	Pediatric patients with anaphylaxis presenting to the ED (identified by ICD-9/ICD-10 codes)	- Baseline: 182 patients - Post-intervention: 257 patients	Median age: - Baseline: 6.5 years - Post-intervention: 6.6 years	NR	NIAID/FAAN criteria (expert consensus); clinical pathway included diagnostic criteria chart on main pathway screen	NR	Pre-intervention (baseline) vs. post-intervention (after clinical pathway revision)	72 hours for ED return visits; 1 and 3 months for Allergy clinic follow-up	NA	NA	NA	NA	NA
Wang et al., 2017 ^{xviii}	Retrospective cohort study (analysis of pharmacovigilance database records)	Beijing, China – Beijing Pharmacovigilance Database (BPD), including 94 hospitals (inpatient, outpatient, and ED settings)	January 1, 2004 – December 31, 2014 (10 years)	Patients with drug-induced anaphylaxis (DIA) – confirmed by physician adjudication using standard criteria	1,189 patients (from 9,425 hypersensitivity cases; 1,589 potential anaphylaxis; 1,189 confirmed)	Mean 47.6 ± 20.1 years - Children (<18 years): 91 (7.7%)	52.7% female (n=627), 47.3% male	Standard clinical diagnosis criteria [Sampson et al.]; severity categorized as grade 2 (mild-moderate) or grade 3 (severe); adjudicated by two physician reviewers	- Antibiotics: 38.4% - Radicontrast agents: 11.9% - TCM injections: 10.9% - Chemotherapeutic drugs: 10.3% - Biologics: 4.1% - Anesthetics: 2.1% - Plasma substitutes: 2.1%	Epinephrine group vs. Non-epinephrine group	NA	NA	NA	NA	NA	NA
Kawano et al., 2017 ^{xix}	Retrospective cohort study (chart review with robust methodology; inter-observer agreement κ > 0.9)	Two urban academic teaching hospitals in Vancouver, Canada	April 1, 2007 – March 31, 2012 (5 years)	Patients with anaphylaxis (aged ≥17 years) meeting pre-specified criteria adapted from NIAID/FAAN	492 patients (from 2,995 allergy-related visits; 665 patients ≥50 years screened)	- Older patients (≥50 years): 122 (24.8%), median 62 years (IQR 56–71) - Younger patients (<50 years): 370 (75.2%), median 31 years (IQR 25–41)	- Older: 46.7% female - Younger: 56.2% female	Adapted NIAID/FAAN criteria; cases adjudicated by trained abstractors	- Older patients: Drugs 39.3%, Food 25.4%, Other 11.5%, Unknown 23.7% - Younger patients: Drugs 17.8%, Food 51.1%, Other 10.5%, Unknown 20.5%	Older patients (≥50 years) vs. Younger patients (<50 years)	7 days – subsequent ED visits (allergy-related and non-allergy-related) and mortality via provincial vital statistics	NA	NA	NA	NA	NA
Campbell et al., 2016 ^{xx}	Cross-sectional survey study (Web-based survey via REDCap)	Mayo Clinic Hospital – Rochester, Saint Mary's Campus, Minnesota, USA – academic tertiary care ED with ~73,000 annual visits; ~20% pediatric patients	April 28 – June 16, 2011	ED Healthcare Providers (nurses, physicians, residents, pharmacists, advanced practice providers)	172 (79% response rate of 217 invited)	NA	NA	NA	NA	Autoinjector (EpiPen/EpiPenJr) vs. Manual IM injection (epinephrine drawn from 1:1000 ampule)	NA	Healthcare Professionals (Emergency Department providers)	Emergency Medicine	- 0–3 years: 24 (14%) - 4–9 years: 49 (28%) - 10–20 years: 52 (30%) - >20 years: 47 (27%)	- ED Nurses: 103 (60%) - EM Residents: 20 (12%) - EM Staff Physicians: 33 (19%) - ED Physician Assistants/Nurse Practitioners: 7 (4%) - ED Pharmacists: 8 (5%)	Estimated training time for safe administration: - Autoinjector: 88% estimated ≤10 minutes training needed - Manual IM injection: 57% estimated ≤10 minutes training needed

															- Not reported: 1 (<1%)	
Drupad & Nagabushan, 2015 ^{xxi}	Cross-sectional survey study (pretested structured questionnaire)	Tertiary care teaching hospital (India)	NR	Healthcare providers/students (Interns, MBBS Phase II students, Nursing students)	265 participants - Medical interns: 101 (38.1%) - MBBS Phase II students: 99 (37.4%) - Nursing students: 65 (24.5%)	NA	NA	NA	NA	Group comparison: Medical students vs. Interns vs. Nursing students	NA	Healthcare Providers/Students (Interns, Medical Students, Nursing Students)	NA	NR	- MBBS Phase II Students: 99 (37.4%) - Medical Interns: 101 (38.1%) - Final Year Nursing Students: 65 (24.5%)	NR
Özmen et al., 2015 ^{xxii}	Cross-sectional descriptive survey study (standardized questionnaire)	Dr. Sami Ulus Maternity and Children's Research and Training Hospital, Ankara, Türkiye (tertiary care children's hospital)	February 1 – March 15, 2014	Healthcare professionals (Specialist doctors, Resident doctors, Auxiliary health staff: nurses, health officers, emergency medical technicians)	166	NA	NA	NA	NA	Training status (received vs. did not receive anaphylaxis training); Professional group (specialist, resident, auxiliary staff)	NA	Healthcare Professionals (Physicians and auxiliary health staff)	Pediatrics (Specialist doctors and residents from a children's hospital; auxiliary staff: nurses, health officers, emergency medical technicians)	Mean 10.2 ± 9.0 years	- Specialist Doctors: 43 (25.9%) - Resident Doctors: 53 (31.9%) - Auxiliary Health Staff (nurses, health officers, emergency medical technicians): 70 (42.2%)	50.6% (84/166) reported having received previous training on anaphylaxis. - Time since training: - ≤2 years: 49 (58.3%) - 3–5 years: 17 (20.2%) - ≥6 years: 18 (21.5%)
Plumb et al., 2015 ^{xxiii}	Cross-sectional survey study (comparative with 2002 cohort using same methodology)	Southmead Hospital, Bristol, UK – large 850-bed teaching hospital with 107 Foundation trainees	Mid-2013	Foundation trainees (junior doctors): F1 (first year post-graduation) and F2 (second year post-graduation)	68 (64% response rate of 107 eligible Foundation trainees) - F1: 34 (50%) - F2: 34 (50%)	NA	NA	NA	NA	Historical comparator: 2002 cohort of Senior House Officers (SHOs) – 78 doctors using same methodology	NA	Junior Doctors (Foundation trainees)	NA	Not specifically reported.	- F1 doctors: 34 (50%) – no ALS training, no ED experience - F2 doctors: 34 (50%) – 97% had ALS training, 12% had ED experience	- ALS training completed: 33/34 (97%) of F2s; 0/34 (0%) of F1s - Specific anaphylaxis/allergy teaching: Not provided outside of ALS course. - Formal anaphylaxis training: Not reported; the study notes that "there is no specific anaphylaxis or allergy teaching outside of the ALS course at this level."
AAI: Adrenaline Auto-Injector; ALS: Advanced Life Support; BMI: Body Mass Index; BPD: Beijing Pharmacovigilance Database; CABG: Coronary Artery Bypass Graft; CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; COVID-19: Coronavirus Disease 2019; CT: Computed Tomography; ED: Emergency Department; EM: Emergency Medicine; EMR: Electronic Medical Record; EMS: Emergency Medical Services; ER: Emergency Room; ESI: Emergency Severity Index; F1: Foundation Year 1; F2: Foundation Year 2; FARE: Food Allergy Research and Education; GI: Gastrointestinal; ICD-9: International Classification of Diseases, Ninth Revision; ICD-10: International Classification of Diseases, Tenth Revision; ICU: Intensive Care Unit; IHD: Ischemic Heart Disease; IM: Intramuscular; IMC: Intermediate Care; IQR: Interquartile Range; ISS: In Situ Simulation; IV: Intravenous; MBBS: Bachelor of Medicine, Bachelor of Surgery; MET: Medical Emergency Team; MI: Myocardial Infarction; NA: Not Applicable; NIAID/FAAN: National Institute of Allergy and Infectious Diseases / Food Allergy and Anaphylaxis Network; NP: Nurse Practitioner; NR: Not Reported; NS: Not Specified; PA: Physician Assistant; PCI: Percutaneous Coronary Intervention; PED: Pediatric Emergency Department; PICU: Paediatric Intensive Care Unit; PRHO: Pre-Registration House Officer; QI: Quality Improvement; REDCap: Research Electronic Data Capture; RN: Registered Nurse; SAE: Serious Adverse Event; SC: Subcutaneous; SD: Standard Deviation; SHO: Senior House Officer; TASMC: Tel Aviv Sourasky Medical Centre; TCM: Traditional Chinese Medicine; TGH: Tampa General Hospital; TS: Translational Simulation; VIA: Venom-Induced Anaphylaxis; WHO-UMC: World Health Organization-Uppsala Monitoring Center.																

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Table 2: Characteristics of Patients Included in the Studies (n = 23)

Last name of first author, year	Number of patients	Mean age, SD	Cause of anaphylaxis	Severity of anaphylaxis	Respiratory involvement (%)	Cardiovascular involvement (%)	Cutaneous manifestations (%)	Gastrointestinal manifestations (%)	Previous history of anaphylaxis	Previous epinephrine auto-injector prescription	Arrival mode (EMS/self-transport)	Triage category	Comorbidities (asthma, cardiovascular disease, etc.)
Pape et al., 2025 ⁱ	NA												
Büllbül et al., 2024 ⁱⁱ													
Hamadi & Casale, 2024 ⁱⁱⁱ	190 (survey respondents) + 4,358 (ER patients)	NS	Food (Tree nuts 18%, Peanuts 14%, Egg 10%, Seafood 10%, Milk 8%) – others unspecified.	NS	NS	NS	NS	NS	NR	Inferred: 72 patients (38%) had epinephrine available but chose not to use it. 30 patients (16%) did not have it available.	NR	NR	NR
Kaya & Alaylar, 2024 ^{iv}	NA												
Ho et al., 2024 ^v	771 (Total) - Children (<18 yrs): 159 (20.6%) - Adults (18–64 yrs): 498 (64.6%) - Older adults (≥65 yrs): 114 (14.8%)	41.0 ± 22.2 years - Children: 9.2 ± 6.0 yrs - Adults: 43.6 ± 12.8 yrs - Older adults: 73.8 ± 6.5 yrs	Drugs (43.3%), Foods (34.5%), Insect venom (7.3%), Contrast medium (4.8%). Pattern varied by age: Foods were top in children (57.9%); Drugs were top in adults (47.0%) and older adults (63.2%)	Moderate (multivisceral signs): 271 (35.1%) Severe (hypoxia, hypotension, neurologic compromise): 500 (64.9%) Older adults had higher severe reaction rates (69.3%) vs children (40.9%).	78.0% (n=601) - Children: 81.8% - Adults: 77.3% - Older adults: 75.4%	76.1% (n=587) - Children: 51.6% - Adults: 82.9% - Older adults: 80.7%	91.7% (n=707) - Children: 98.1% - Adults: 90.8% - Older adults: 86.8%	23.2% (n=179) - Children: 34.0% - Adults: 20.7% - Older adults: 19.3%	8.6% (n=66) overall - Children: 8.8% - Adults: 8.2% - Older adults: 9.6%	NR	NR	NR	- Personal allergy history (asthma, AD, AR, food/drug allergy): 44.4% overall (57.2% in children, 42.8% in adults, 33.3% in older adults) - Hypertension: 16.7% (0% children, 14.7% adults, 49.1% older adults) - Diabetes mellitus: 10.4% (0% children, 9.6% adults, 28.1% older adults) - Cardiovascular disease: 4.5% (0% children, 2.6% adults, 19.3% older adults)
Price et al., 2023 ^{vi}	NA												

Ateş & Sahiner, 2022 ^{vii}														
Wijekoon et al., 2021 ^{viii}														
Francuzik et al., 2020 ^{ix}	3,612 VIA cases + 3,605 non-VIA controls (matched)	Bimodal distribution; cutoff age 22 years used for subgroup analysis	Venom (yellowjacket most common, followed by honeybee; regional variation with hornets in southern Europe)	Ring & Messmer Scale: - Grade II (mild): not separately reported - Grades III–IV (severe): proportion higher in VIA than non-VIA	Lower in VIA than non-VIA	82.8% in VIA vs. 62.2% in non-VIA (p < 0.001) – significantly higher in VIA	Lower in VIA: 68% vs. 70.4% in non-VIA (p = 0.031); Absence of skin symptoms in 54.4% of VIA patients with mastocytosis vs. 30.7% without mastocytosis	Lower in VIA than non-VIA; especially in younger patients (<22 years)	28.5% (n=940) of VIA patients had experienced venom anaphylaxis previously vs. 35.7% in non-VIA (p < 0.001)	Not directly reported; however, VIA patients received epinephrine less often (26.9% vs. 34.6% in non-VIA, p < 0.001), suggesting under-prescription/underuse	NR	NR	- Mastocytosis: significantly associated with VIA and severe reactions - Cardiovascular diseases: more prevalent in VIA (24.8% vs. 18.2%, p < 0.001) - Beta-blocker use: associated with higher severity and cardiac symptoms - ACE-I use: associated with cardiac arrest (5.8% vs. 1.9%, p < 0.001) - Baseline serum tryptase >8 ng/mL: associated with severe VIA	
Pimentel-Hayashi et al., 2020 ^x	NA													
Krmpotic et al., 2019 ^{xi}	12 admissions	NR	- Allergy injection (1) - Amoxicillin (1) - Cashews (1) - Dairy (1) - Latex (1) - Peanuts (1) - Unknown (6)	All patients experienced cardiovascular compromise, ranging from mild tachycardia to cardiovascular collapse. - 3 patients (25%) required continuous epinephrine infusion - 2 patients (17%) required intubation and mechanical ventilation - 2 patients (17%) had cardiorespiratory arrest	- Shortness of breath: 67% - Stridor/wheezing: 50%	100%	- Rash/hives: 58% - Facial/intraoral/perioral swelling: 83%	NS	5/12 (42%) had prior history of anaphylaxis	NR	NR	NR	Atopy history in 63% (8/12): - Allergy: 58% - Asthma: 50% - Allergic rhinitis: 25% - Atopic dermatitis: 17%	
Lauraa et al., 2019 ^{xii}	NA													
Sharma et al., 2019 ^{xiii}	13 patients with severe ARA (from 155 envenomed patients) – 3 children, 10 adults	Range: 5–52 years; median age not specified - Children: 5, 6, 11 years - Adults: 18–52 years	VINS polyvalent antivenom (Indian-manufactured equine antivenom)	Severe (life-threatening): - Hypotension/shock: n=3 - Respiratory/cardiorespiratory arrest: n=7 - Laryngeal edema: n=2 - Deaths: 8/13 (61.5% case fatality among severe ARA patients)	- Dyspnea alone: 5/13 (38.5%) - Dyspnea with wheezing: 3/13 (23.1%) - Gasping respirations: 2/13 (15.4%) - Respiratory/cardiorespiratory arrest: 7/13 (53.8%)	- Hypotension: 3/13 (23.1%) - Shock: 3/13 (23.1%) - Sinus bradycardia: present in multiple patients (preceding arrest) - Cardiac arrest: 7/13 (53.8%)	- Rash (urticaria/erythema/itchy rash): 10/13 (76.9%) – most common ARA manifestation	- Vomiting: 1/13 (7.7%) – reported in patient #8	NR	NA	NR	NR	- Neurotoxic envenoming (all patients): signs of bulbar/respiratory paralysis - Snake species identified: Naja naja (1), Bungarus caeruleus (3), Bungarus niger (1), unidentified (8)	

Xing et al., 2018 ^{xiv}	91 pediatric patients with drug-induced anaphylaxis	Categorized by age groups: - 0–5 years: 32 (35%) - 6–12 years: 24 (26%) - 13–17 years: 35 (39%)	- Antibiotics: 53% (cephalosporins 34%, macrolides 8%, penicillins 3%, others 8%) - TCM injections: 9% - Biologics: 8% - Radiocontrast agents: 4% - Glucocorticoids: 3% - Chemotherapeutic agents: 3% - Anesthetics: 3%	- Mild to moderate: 15/91 (17%) - Severe: 76/91 (84%) - 13–17 years group more likely to have severe anaphylaxis vs. 0–5 years (OR = 15.46, 95% CI 1.85–129.33, p = 0.002)	73% (n=66): - Cyanosis: 40% - Dyspnea: 24% - Wheezing: 23% - Hypoxemia: 9% - Respiratory arrest: 2%	78% (n=71): - Hypotension: 76% - Cardiac arrest: 1%	59% (n=54): - Diffuse urticaria: 36% - Flushing: 23% - Pruritus: 18% - Angioedema: 11% - Conjunctivitis: 10%	36% (n=33): - Emesis: 30% - Nausea: 13% - Abdominal cramping: 14%	39% (n=35): - Presyncope: 24% - Syncope: 17% - Convulsion: 4%	NR	NA	NR	- Infectious diseases: 54% (main admission diagnosis) - Stress/operation/trauma: 17% - Tumor: 11% - Gastrointestinal disease: 9% - Asthma: only 1 patient (1%)
Cohen et al., 2018 ^{xv}	193 patients meeting anaphylaxis criteria (59 in 2013–2014; 134 in 2015–2016)	Mean: 6.8 years (range 0.1–15.9)	- Food: 91% - Milk: 27.6% - Tree nuts: 23.1% - Peanut: 8.2% - Sesame: 8.2% - Egg: 2.2% - Fish/shellfish: 4.5% - Drugs: 2.9% - Bee sting: 1.5%	- Mild: ~14–15% - Moderate: ~83–85% - Severe: ~0.7–1.7% (1–2 patients) No significant change between periods.	88.2% overall (breathing difficulties). - Correctly diagnosed: 64.8% - Misdiagnosed: 47.8% (p = 0.03)	- Hypotension/circulatory collapse: Not reported (none had circulatory collapse) - Reduced BP: part of criteria but not quantified	- Urticaria: 90.7% overall - Correctly diagnosed: 59.4% - Misdiagnosed: 53.7% had urticaria - Angioedema: 40.5–45.3%	- Vomiting: 28.3–33.6% - Abdominal pain: 6.7–10%	NS	NR	NR	NR	Asthma: - 2013–2014: 8.4% - 2015–2016: 8.9% - Overall: ~8.7%
Dubus et al., 2018 ^{xvi}	204 patients meeting Sampson's anaphylaxis criteria	7.9 years (range 2 months – 17.7 years) - Grade II: 7.69 ± 4.86 years - Grade III: 9.03 ± 4.93 years (p = 0.12)	- Food: 78.3% (nuts 32.5%, fruits 16.8%, milk 14.9%, egg 5.9%) - Drugs: 8.5% - Insect venom: 4.7% - Other: 8.5% - Unknown: 36.8%	- Grade II (moderate, multivisceral): 170/204 (83.3%) - Grade III (severe, mono/multivisceral failure): 34/204 (16.7%) - Grade IV (cardiac arrest): 0	75.7% (n=154)	11.3% (n=23)	98.5% (n=200)	23% (n=47)	36.8% (n=75) – all had an epinephrine auto-injector available at home	36.8% had auto-injector at home (among those with prior anaphylaxis)	67.2% self-presented to ED; 32.8% via EMS (not explicitly stated but inferred)	- High severity (levels 1–2): 27.6% in Grade II; 67.6% in Grade III (p < 0.001) - Overall high severity: 34.3%	- Previous allergy: 60.8% (124/204) - Previous asthma: 35.1% (61/174) - Prophylactic daily asthma treatment: 39.3% (24/61) - Previous anaphylaxis: 36.8% (75/204)
Lee et al., 2018 ^{xvii}	- Baseline: 182 - Post-intervention: 257	Median: 6.5–6.6 years (range not specified)	NR	NR	NR	NR	NR	NR	NR	NR	NR	Emergency Severity Index (ESI) used; ESI level 1 (highest acuity) tracked for time-to-epinephrine metric	- Severe asthma history: listed as an admission "red flag" (risk factor for biphasic reaction) - Current asthma flare: listed as an admission "red flag"
Wang et al., 2017 ^{xviii}	1,189 patients with confirmed drug-induced anaphylaxis	47.6 ± 20.1 years (range not specified) - Children (<18 years): 91 (7.7%)	- Antibiotics: 38.4% - Radiocontrast agents: 11.9% - TCM injections: 10.9% - Chemotherapeutic drugs: 10.3% - Biologics: 4.1% - Anesthetics: 2.1% - Plasma substitutes: 2.1%	- Mild-to-moderate (grade 2): not separately reported - Severe (grade 3): higher proportion in epinephrine group - ICU admission: 73 (6.1%) - Death: 39 (3.3%)	55.4% overall: - Wheezing: 30.5% in epinephrine group vs. 18.9% in non-epinephrine group - Respiratory arrest: 9.6% vs. 3.3% - Cyanosis: 18.2% vs. 11.4% - Dyspnea: 19.5% vs. 21.8%	83.8% overall: - Hypotension: 82.8% - Cardiac arrest: 6.2% in epinephrine group vs. 1.9% in non-epinephrine group	47.4% overall: - Diffuse urticaria: 25.3% (epinephrine) vs. 20.0% (non-epinephrine) - Flushing: 16.9% vs. 20.8% - Pruritus: 19.4% vs. 18.3% - Angioedema: 9.9% vs. 7.1%	31.3% overall: - Emesis: 17.7–20.2% - Nausea: 19.5–23.5% - Abdominal cramping: 5.8–6.7%	NR	NA	NA	NR	- Cardiovascular disease: 14.5% (epinephrine) vs. 13.3% (non-epinephrine) - Hypertension: 5.4% vs. 4.6% - Asthma/COPD: 2.0% vs. 1.0%
Kawano et al., 2017 ^{xix}	492 total: - Older (≥50 years):	- Older: median 62 years (IQR 56–71) - Younger: median 31 years (IQR 25–41)	- Older: Drugs 39.3%, Food 25.4%, Other 11.5%, Unknown 23.7%	- Severe anaphylaxis: Older 27.1% vs. Younger 21.4% (p = NS)	- Respiratory compromise: Older 85.3% vs. Younger 86.5%	- Lowest sBP (median): Older 115 mmHg vs.	- Skin involvement: Older 88.5% vs. Younger 89.5%	- Gastrointestinal symptoms: Older 5.7% vs. Younger 14.9%	- History of allergies: Older 68.0% vs. Younger 73.8%	NR	- Ambulance arrival: Older 32.8% vs. Younger 31.9%	NR	- Cardiac risk factors: Older 6.5% (8 patients)

	122 (24.8%) - Younger (<50 years): 370 (75.2%)		- Younger: Drugs 17.8%, Food 51.1%, Other 10.5%, Unknown 20.5%	- Hypotension (sBP <90 mmHg): Older 13.8% vs. Younger 12.2% - Neurological symptoms: Older 12.3% vs. Younger 4.1%	- Respiratory rate >22: Older 39.6% vs. Younger 49.4% - Oxygen saturation <95%: Older 45.5% vs. Younger 26.5%	Younger 110 mmHg - sBP <90 mmHg: Older 13.8% vs. Younger 12.2%	- Mucosal tissue involvement: Older 27.1% vs. Younger 28.9%		- History of asthma: Older 13.9% vs. Younger 29.3%				vs. Younger 0.3% (1 patient) - History of MI: Older 4.1% vs. Younger 0% - History of CABG: Older 1.7% vs. Younger 0% - History of angina: Older 0.8% vs. Younger 0.3%
Campbell et al., 2016 ^{xx}	NA												
Drupad & Nagabushan , 2015 ^{xxi}	NA												
Özmen et al., 2015 ^{xxii}	NA												
Plumb et al., 2015 ^{xxiii}	NA												
ACE-I: Angiotensin-Converting Enzyme Inhibitor; AD: Atopic Dermatitis; AR: Allergic Rhinitis; ARA: Antivenom-Related Anaphylaxis; BMI: Body Mass Index; BST: Baseline Serum Tryptase; CABG: Coronary Artery Bypass Graft; CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; COVID-19: Coronavirus Disease 2019; CVS: Cardiovascular System; DIA: Drug-Induced Anaphylaxis; EAI: Epinephrine Autoinjector; ED: Emergency Department; EMS: Emergency Medical Services; ER: Emergency Room; ESI: Emergency Severity Index; FARE: Food Allergy Research and Education; GI: Gastrointestinal; HIV: Human Immunodeficiency Virus; ICD-10: International Classification of Diseases, Tenth Revision; ICU: Intensive Care Unit; IHD: Ischaemic Heart Disease; IM: Intramuscular; IQR: Interquartile Range; IV: Intravenous; MI: Myocardial Infarction; NA: Not Applicable; NIAID/FAAN: National Institute of Allergy and Infectious Diseases / Food Allergy and Anaphylaxis Network; NR: Not Reported; NS: Not Specified; PCI: Percutaneous Coronary Intervention; PICU: Paediatric Intensive Care Unit; QI: Quality Improvement; RN: Registered Nurse; SC: Subcutaneous; SD: Standard Deviation; sBP: Systolic Blood Pressure; SpO2: Oxygen Saturation; TCM: Traditional Chinese Medicine; TGH: Tampa General Hospital; VIA: Venom-Induced Anaphylaxis.													

Table 3: Identified Barriers and Predictors of Delayed or Omitted Intramuscular Epinephrine Administration

Last name of first author, year	Outcome evaluated (Delayed epinephrine, omitted epinephrine, inappropriate route, guideline adherence)	Definition of delay	Time to IM epinephrine (mean, median, or minutes)	IM epinephrine administered (n, %)	Delayed administration (n, %)	Omitted administration (n, %)	Barrier category (Clinician-related, patient-related, healthcare system-related)	Specific barrier identified (exact barrier reported)	Predictor investigated (Variable entered regression analysis)	Statistical method	Effect estimate, OR, RR, HR, β coefficient 95% Confidence interval, p-value	Significant predictor (y/n)
Pape et al., 2025 ⁱ	Incorrect treatment selection (failure to recommend IM adrenaline as first-line therapy) and incorrect autoinjector use (failure to operate adrenaline autoinjector correctly)	NA	Median 18 seconds (range 5–100 seconds) among physicians who used the autoinjector correctly	32/95 (33.7%) recommended correct IM adrenaline therapy	NR	63/95 (66.3%) did not recommend correct IM adrenaline therapy	Clinician-related (knowledge deficit, lack of training, experience-related factors)	- Uncertainty regarding appropriate first-line therapy (66%) - Inability to correctly operate autoinjectors (68%) - Accidental self-injection into thumb (31.6%) - Failure to trigger injector (20%) - Insufficient injection duration (14.7%) - Incorrect anatomical site (1.1%) - Broke the device (1.1%)	- Medical specialty (radiology, internal medicine, anesthesiology) - Level of qualification (board-certified vs. resident) - Years of experience	- Chi-square test - Logistic regression	OR 0.21 (79% decrease) for board-certified vs. residents selecting correct treatment (P < 0.001)	Yes – Board certification (more experienced physicians were significantly less likely to select correct therapy) No – Medical specialty (P = 0.64)
Bülbul et al., 2024 ⁱⁱ	Incorrect knowledge of anaphylaxis treatment (failure to know first-line drug, correct route, correct site, correct dose) and lack of AAI knowledge/prescription	NA	NR	93.7% (n=194) knew that IM adrenaline is the first-line treatment (knowledge rate, not actual administration).	NR	61.8% knew adult dose; 75.4% knew pediatric dose (indicating a knowledge gap in dosing, which could lead to omission/error).	Clinician-related (Knowledge deficit, lack of training, experience-related decay)	- Lack of postgraduate training (only 40.6% had training; those without training scored significantly lower). - More years of experience (senior physicians performed worse, likely due to outdated guidelines recommending subcutaneous adrenaline). - Inability to use AAI: 51.2% stated they did not know how to use AAI. - Low prescription rates: 44.4% do not prescribe AAI to at-risk patients.	- Professional experience (years) - Post-graduate education (Yes/No) - Previous involvement in treating anaphylaxis - Age	- Mann-Whitney U test (for continuous variables: age, professional years) - Chi-square (χ^2) test (for categorical variables: education, treatment experience)	p-values provided (no OR/RR calculated): - Correct first-line drug vs. professional years: p = 0.031 - Correct route vs. professional years: p < 0.001 - Correct site vs. professional years: p < 0.001	Yes – Less professional experience (p<0.05) and having received post-graduate training (p<0.05) were significantly associated with better knowledge.

											- Knowing AAI use vs. professional years: p = 0.041 - Post-graduate training vs. knowing first-line drug: p = 0.013	
Hamadi & Casale, 2024 ⁱⁱⁱ	Omitted/delayed epinephrine (at home and in the ER) and avoidance of seeking ER care during the COVID-19 pandemic.	Self-reported delayed use of medication (survey)/not receiving epinephrine in the ER.	NR	Survey (home): 87 events (46%) treated with epinephrine. ER: 718 out of 4,358 patients (16%) received epinephrine in the ER.	Survey: 14% (of the 63 patients who changed their behavior) delayed their medication use.	Survey: 72 patients (38%) had epinephrine available but did NOT use it. ER: 3,640 patients (84%) did NOT receive epinephrine in the ER.	Patient-related (fear of COVID, avoidance of healthcare, hesitancy to use epinephrine) and Healthcare system-related (low ER administration rates).	- Fear of COVID-19: 71% avoided seeking medical care outside the home. - 30% used self-medication more quickly (not necessarily a barrier, but changed behavior). - 14% delayed medication use. - 38% had epinephrine but chose not to use it. - 16% did not have epinephrine available.	Time period relative to the COVID-19 pandemic (pre-pandemic vs. during pandemic vs. post-COVID vaccine availability).	Descriptive statistics only (percentages, counts). No regression analysis (OR/RR) was performed.	NA (no regression). Observed trend: ER visits increased from 867 (1 year pre-pandemic) to 1,833 (1 year post-vaccine availability).	Trend noted, but no statistical significance testing (p-values) was reported in the results.
Kaya & Alaylar, 2024 ^{iv}	Incorrect diagnosis (failure to correctly identify all anaphylaxis diagnostic criteria) and incorrect treatment selection (failure to choose IM adrenaline as first-line therapy)	NA	NR	65/85 (76.5%) knew to administer IM adrenaline (55 chose IM adrenaline alone; 10 chose IM adrenaline + fluid replacement) (knowledge rate).	NR	20/85 (23.5%) did NOT select IM adrenaline as first-line therapy (chose antihistamines, steroids, IV adrenaline, or fluids instead).	Clinician-related (Knowledge deficit, insufficient retention of training, failure to recognize full diagnostic criteria)	- Failure to recognize full diagnostic criteria: Only 4 participants (4.7%) correctly marked all criteria. - Missing CVS/GI symptoms: 85% marked skin+respiratory, but only 15% included cardiovascular and gastrointestinal symptoms. - Incorrect first-line treatment: 23.5% did not choose IM adrenaline (8 chose IV adrenaline, others chose antihistamines/steroids/fluids). - Low retention of training: Despite 89.4% claiming prior training, knowledge was poor.	- Professional experience (years) - Medical specialty/branch - Previous encounter with anaphylaxis - Previous anaphylaxis training	Chi-square (χ^2) test	Diagnosis vs. experience: p = 0.92 (NS) Diagnosis vs. specialty: p = 0.03 (Significant) Diagnosis vs. prior anaphylaxis encounter: p = 0.48 (NS) Treatment vs. experience: p = 0.39 (NS) Treatment vs. specialty: p = 0.19 (NS) Encounter rate vs. experience: p = 0.76	Yes – Specialty/branch was significantly associated with correct diagnosis (p = 0.03). No – Professional experience was NOT a significant predictor for diagnosis (p=0.92) or treatment (p=0.39).
Ho et al., 2024 ^v	Guideline adherence – specifically: (1) IM epinephrine administration in the ED, (2) Allergist referral, (3) Education on trigger avoidance, (4) Education on alarm symptoms	Not defined.	NR	294/771 (38.1%) overall - Children: 74/159 (46.5%) - Adults: 186/498 (37.3%) - Older adults: 34/114 (29.8%)	Not specifically measured.	477/771 (61.9%) did NOT receive IM epinephrine. - Children: 85/159 (53.5%) - Adults: 312/498 (62.7%) - Older adults: 80/114 (70.2%)	Clinician-related (emergency physician practice patterns) and Patient-related (age-specific factors, comorbidity concerns)	- Underutilization of IM epinephrine, particularly in older adults (only 29.8% received IM epi). - Severity-based hesitancy: Among moderate reactions, only 14.3% of older adults received IM epi vs 55.3% of children (p<0.001). - Overuse of alternative therapies: H1-antihistamines (89.5%) and corticosteroids (82.5%) were used more frequently than epinephrine. - Low allergist referral: 15.3% overall (1.8% in older adults). - Low patient education rates: Trigger avoidance (12.5%) and alarm symptoms (16.1%). - No epinephrine autoinjector prescriptions upon discharge (not available/prescribed).	- Age group (children vs adults vs older adults) - Severity (moderate vs severe) - Time period (2001–2020 trend)	- ANOVA (continuous variables) - Pearson's χ^2 test (categorical comparisons) - Cochran-Armitage trend test (age-group differences and 20-year trends)	p-values only (no OR/RR reported): - IM epi administration by age group: P trend = 0.004 - IM epi in moderate reactions by age: P trend < 0.001 - IM epi in severe reactions by age: P trend = 0.76 - 20-year trend for epi use: P trend < 0.001	Yes – Age group was a significant predictor of IM epinephrine administration (p=0.004), particularly driven by lower use in older adults. Yes – Severity modified this effect (moderate reactions showed significant age disparity, p<0.001; severe reactions did not). Yes – Time period showed significant improvement over 20 years (p<0.001).
Price et al., 2023 ^{vi}	- IM adrenaline medication errors (administration errors and 'near misses')	NA	Median 2:57 (IQR 2:30–3:40). All 23 simulations achieved	23/23 (100%) simulations – adrenaline was administered	NR	0/23 (0%) – adrenaline was administered in every simulation.	Clinician-related (verbal order errors, failure to use cognitive aids, lack of	Medication errors: 30% (7/23) of simulations. Administration errors: 13% (wrong dose or IV instead of IM).	- Use of weight-based cognitive aid (Monash Pediatric	Descriptive statistics only (medians, interquartile	- 3/3 administration errors occurred when the cognitive aid was NOT used.	Yes (implied) – Use of the cognitive aid was associated with prevention of

	- Time to IM adrenaline administration - Identification of latent safety threats (LSTs)		adrenaline administration within 5 minutes.	within the 5-minute scenario.			familiarity) and Healthcare system-related (latent safety threats: missing equipment, unfamiliarity with MET trolley contents).	Near misses: 17% (incorrect concentration or IV orders). Cognitive aid underused: Used in 56%; absent in all administration errors. Inconsistent adrenaline orders: Variable dose/concentration/route reporting. Latent safety threats: unfamiliarity with equipment and poor situational awareness.	Emergency Medication Book) - MET trolley arrival time (faster arrival did not always correlate with faster adrenaline administration)	ranges, percentages, content analysis of debrief themes). No regression/ORs calculated.	- 3/4 near misses were avoided because staff used the cognitive aid (i.e., it caught the error before administration).	medication errors (all actual errors occurred when it was not used; 3 of 4 near misses were intercepted when it was used). No – Faster MET trolley arrival did not predict faster adrenaline administration (on 4 occasions, trolley arrived faster than median, but adrenaline was given slower than median).
Ateş & Sahiner, 2022 ^{vii}	Incorrect knowledge of anaphylaxis treatment (failure to know adrenaline is first-line, incorrect route/site/dose of IM adrenaline)	NA	NR	78.9% (n=172) knew adrenaline is the first-line drug for anaphylaxis (knowledge rate, not actual administration).	NR	21.1% (n=46) did NOT know adrenaline is first-line (chose antihistamines, corticosteroids, or fluid replacement instead).	Clinician-related (Knowledge deficit, lack of/outdated training)	- Incorrect first-line drug: 21.1% did not select adrenaline. - Incorrect route: 33.5% did NOT choose intramuscular administration. - Incorrect site: 24.3% did NOT identify vastus lateralis as the correct IM site. - Incorrect adult dose: 17% did NOT know the correct 0.3–0.5 mg dose. - Time since training: Nearly 40% of trained participants had their training ≥3 years ago, suggesting knowledge decay.	- Profession (specialist doctor, assistant doctor, practitioner, nurse) - Training status (Received vs. did not receive training on adrenaline)	- ANOVA test (for comparing groups) - p-values reported (no OR/RR)	First-line drug vs. profession: p = 0.002 Route vs. profession: p < 0.001 Injection site vs. profession: p < 0.001 Dose vs. profession: p = 0.264 Route vs. training: p = 0.001 First-line drug vs. training: p = 0.296	Yes – Profession was significantly associated with knowledge of first-line drug, route, and site (p < 0.05). Yes – Training status was significantly associated with knowledge of the correct route (p = 0.001). No – Training status was NOT significantly associated with knowledge of first-line drug, site, dose, or repeat interval.
Wijekoon et al., 2021 ^{viii}	Knowledge deficits in: (1) Case diagnosis (ability to correctly diagnose anaphylaxis vs. non-anaphylaxis from 10 scenarios) (2) Management (20 questions on acute and long-term management) (3) Knowledge of triggers (4) Self-confidence in diagnosis and management	NA	NR	98.2% knew adrenaline is the first-line drug (knowledge rate, not actual administration). 97.9% knew the correct route is intramuscular. 79.2% knew the correct adult dose. 55.6% knew the correct pediatric dose.	NR	1.8% did NOT know adrenaline is first-line. 2.1% did NOT know IM route. 20.8% did NOT know adult dose. 44.4% did NOT know pediatric dose. 9.9% would incorrectly use IV adrenaline if access available.	Clinician-related (knowledge deficits in diagnosis, trigger recognition, dosing, long-term management, low self-confidence) and Educational (inadequate training, lack of hands-on experience)	Poor diagnosis: 7.3% identified all scenarios; 34.5% identified all anaphylaxis cases. Poor trigger knowledge: Only 16.4% identified all triggers; ≤40% for several local triggers. Case misdiagnosis: 49.1% misdiagnosed isolated wheezing as anaphylaxis. Dosing errors: 20.8% (adult) and 44.4% (pediatric). Incorrect route: 9.9% preferred IV over IM adrenaline. Misconceptions: Some considered IHD, hypertension, tachycardia, or pregnancy contraindications. Follow-up gap: 50% were unaware of required follow-up. Low confidence: 62.1% felt confident; lack of hands-on experience was the main reason.	- Final MBBS results category (first-class, second upper, second lower, pass) - University (curriculum type) - Personal history of allergy - Family history of allergy - Gender	- Chi-square test (categorical variables) - Independent sample t-test (two-group comparisons) - One-way ANOVA with Tukey post-hoc (multiple group comparisons) - Multiple linear regression (predictors of scores) - Point-biserial correlation (confidence vs. scores)	Regression coefficients (B) with 95% CI: - Case diagnosis: - First-class vs. no first-class: B = 0.887 (95% CI 0.261–1.514), p = 0.006 - Class vs. no class: B = 0.662 (95% CI 0.347–0.978), p < 0.001 - Management score: - University 2 vs. others: B = 1.568 (95% CI 1.182–1.953), p < 0.001 - Class vs. no class: B = 0.716 (95% CI 0.319–1.113), p < 0.001	Yes – Higher MBBS classification (class vs. no class) significantly predicted better case diagnosis (p < 0.001) and management scores (p < 0.001). Yes – University 2 graduation significantly predicted better management score (p < 0.001). Yes – Personal history of allergy significantly associated with higher management score (p = 0.049).

											- Correlation: - Case diagnosis score & self-confidence: $r_{pb} = 0.111$, $p = 0.03$ - Management score & self-confidence: $r_{pb} = 0.164$, $p = 0.001$	No – gender and family history of allergy are not significant predictors.
Francuzik et al., 2020*	- Epinephrine administration (any route) in VIA vs. non-VIA - Severity of anaphylaxis (Ring & Messmer III–IV vs. II) - Absence of skin symptoms as predictor of severe reactions	Not directly measured; "underutilization" defined as failure to administer epinephrine during anaphylaxis episode	NR	- VIA patients: 597/2,219 (26.9%) received epinephrine - Non-VIA patients: 738/2,132 (34.6%) received epinephrine	NR	VIA: 73.1% did NOT receive epinephrine Non-VIA: 65.4% did NOT receive epinephrine Difference significant ($p < 0.001$)	Clinician-related (failure to recognize VIA, especially without skin symptoms; hesitancy to use epinephrine in milder cases) and Patient-related (first-time reactions less likely to receive epinephrine)	- VIA patients received epinephrine significantly less often than non-VIA patients ($p < 0.001$), even after severity adjustment. - First-time VIA: epinephrine given less often than first-time non-VIA ($p < 0.001$); no difference if previous history of anaphylaxis ($p = 0.438$). - Moderate VIA: epinephrine used significantly less than moderate non-VIA ($p < 0.001$). - Absence of skin symptoms: associated with underuse of epinephrine. - Clinicians may misattribute VIA symptoms to anxiety rather than anaphylaxis. - High blood pressure/tachycardia at initial phase may make clinicians reluctant to use epinephrine.	- Elicitor type (VIA vs. non-VIA) - Previous history of anaphylaxis - Presence of skin symptoms - Severity (mild/moderate vs. severe) - Baseline serum tryptase (BST) levels - Comorbidities (mastocytosis, cardiovascular disease) - Medications (beta-blockers, ACE-I)	- Chi-square test/Fisher's exact test - Mann-Whitney U test (continuous variables) - Factorial ANOVA / Generalized Linear Models - Random Forest classifier (Gini importance) - Logistic regression	Epinephrine use in VIA: $p < 0.001$ First-time VIA vs. epinephrine use: $p < 0.001$ β -blockers vs. severe cardiovascular symptoms: $p = 0.144$ (NS) ACE inhibitors vs. cardiac arrest: $p < 0.001$ BST (8–11.5 ng/mL) $\times$ severe VIA: $p = 0.006$ Elicitor $\times$ skin symptoms (severity): $OR = 0.585$, $p < 0.001$	Yes: VIA associated with lower epinephrine use ($p < 0.001$). Yes: Absence of skin symptoms predicted severe VIA ($p < 0.001$). Yes: BST > 8 ng/mL predicted severe VIA ($p = 0.006$). Yes: Cardiovascular disease predicted severe VIA ($p < 0.001$). Yes: First-time anaphylaxis predicted lower epinephrine use ($p < 0.001$). No: β -blocker use was not a significant predictor ($p = 0.144$).
Pimentel-Hayashi et al., 2020*	Knowledge deficits in: (1) Diagnosis of anaphylaxis (with and without cutaneous symptoms) (2) Epinephrine as first-line treatment (3) Route of administration (IM vs. IV vs. SC) (4) Correct dose of epinephrine (5) Contraindications to epinephrine use (6) Prescription of autoinjector/epinephrine ampule at discharge	NA	NR	72.4% knew epinephrine is first-line treatment. 63.4% knew the correct route is intramuscular. 49.5% would have used IM epinephrine as first-line (correct bundle: first-line + IM route). (Knowledge rates).	NR	- 27.6% did NOT know epinephrine is first-line. - 36.6% did NOT know IM route. - 50.5% would NOT have used IM epinephrine as first-line. - 50% did NOT know the correct dose. - 57.7% believed there is a contraindication or didn't know. - 61.7% would NOT prescribe an autoinjector/ampule at discharge.	Clinician-related (knowledge deficits in diagnosis, dosing, route, contraindications, discharge planning)	Diagnostic gap: 96.4% diagnosed anaphylaxis with skin symptoms vs. 59.2% without. First-line treatment: 72.4% identified epinephrine; 27.6% chose other drugs. Route errors: Only 63.4% chose IM; 22.4% SC, 12.8% IV. Dosing errors: Only 50% knew the correct dose. Contraindication misconceptions: Only 42.3% knew there are no absolute contraindications. Discharge gap: Only 38.3% would prescribe epinephrine on discharge. Low competence: 2.6% answered all questions correctly; 7.1% answered the key management bundle correctly. Limited autoinjector availability: Autoinjectors were not widely available in Mexico.	Specialty group	- Measures of central tendency (frequencies, percentages, 95% CI) - Chi-square test for comparing groups	p-values only (no OR/RR calculated): - No statistically significant differences among the 3 specialty groups for any knowledge item ($p > 0.05$ for all comparisons). - Correct anaphylaxis with cutaneous symptoms: $p > 0.05$ - Correct anaphylaxis without cutaneous symptoms: $p > 0.05$ - Epinephrine first-line: $p > 0.05$ - IM route: $p > 0.05$ - Contraindication: $p > 0.05$ - Correct dose: $p > 0.05$	No – Specialty group was NOT a significant predictor of any knowledge outcome ($p > 0.05$ for all comparisons). Knowledge gaps were consistent across all specialties.

											- Autoinjector prescription: p > 0.05	
Krmpotic et al., 2019 ^{vi}	Delayed/omitted IM epinephrine administration leading to mortality in severe anaphylaxis cases requiring PICU admission	IM epinephrine not administered until after cardiorespiratory arrest occurred (i.e., delayed beyond the point of potentially preventing arrest)	Not specifically measured; in both fatal cases, epinephrine was not administered until after cardiorespiratory arrest.	NR overall. Both fatal cases had immediate access to epinephrine (i.e., it was available), but it was not administered until after arrest.	2/12 (17%) – both deaths occurred in patients who had immediate access to epinephrine, but it was not administered until after cardiorespiratory arrest.	2/12 (17%) – epinephrine was not administered until after cardiorespiratory arrest in both fatal cases.	Clinician-related (failure to administer available epinephrine promptly despite recognition of anaphylaxis) and Patient/Caregiver-related (possible failure to use AAI at home)	- Delayed epinephrine administration despite availability: Both patients who died had: (1) Witnessed anaphylaxis event (2) Immediate recognition of anaphylaxis after exposure to known allergen (3) Immediate access to IM epinephrine (4) Epinephrine NOT administered until after cardiorespiratory arrest	NA	Descriptive statistics only (medians, ranges, proportions)	No regression/ORs calculated. Mortality rate: 2/12 (17%) – both deaths associated with delayed epinephrine administration until after arrest.	Not tested – small sample size precluded regression analysis. However, the study strongly suggests that delayed epinephrine administration is a key factor contributing to mortality.
Lauraa et al., 2019 ^{vii}	Knowledge deficits in: (1) Recognition of anaphylaxis clinical criteria (NIH/NIAID-FAAN) (2) Epinephrine as first-line treatment (3) Route of administration (IM vs. IV vs. SC) (4) Correct dose (0.01 mg/kg)	NA	NR	- 99% (70/71) knew epinephrine is first-line treatment - 73% (52/71) knew the correct route is IM - 55% (39/71) knew correct dose (0.01 mg/kg) - 48% (34/71) knew both correct dose and route (Knowledge rates).	NR	- 1% did NOT know epinephrine is first-line - 27% did NOT know IM route - 45% did NOT know correct dose - 52% did NOT know both dose and route - 79% did NOT correctly identify anaphylaxis AND use epinephrine correctly	Clinician-related (knowledge deficits in diagnosis, dosing, route) and Educational (lack of familiarity with NIH criteria)	Poor diagnosis: Only 35% recognized all anaphylaxis criteria. Misdiagnosis: 52% recognized skin + GI symptoms; 14% misclassified isolated mucocutaneous symptoms. Route errors: 19% chose IV; 7% chose SC instead of IM. Dosing errors: Only 55% knew the correct dose. Experience-related gaps: ≥5 years of experience performed worse on IM route (52% vs. 83%, p=0.006) and GI symptom recognition (35% vs. 60%, p=0.043). Overall competence: Only 21% correctly diagnosed anaphylaxis and appropriately managed it.	Years of experience (<5 years vs. ≥5 years since completing residency)	- Measures of central tendency (median, range, frequencies) - Chi-square test for comparison between experience groups	p-values only (no OR/RR): - IM route: <5 yrs 83% vs. ≥5 yrs 52%, p = 0.006 - GI symptom recognition: <5 yrs 60% vs. ≥5 yrs 35%, p = 0.043 - Recognition of NIH criteria: <5 yrs 85% vs. ≥5 yrs 83%, p = 0.762 (NS) - Epinephrine first-line: <5 yrs 42% vs. ≥5 yrs 22%, p = 0.14 (NS) - Correct dose: <5 yrs 65% vs. ≥5 yrs 35%, p = 0.128 (NS) - Correct dose + route: <5 yrs 58% vs. ≥5 yrs 26%, p = 0.024	Yes – Fewer years of experience (<5 years) significantly predicted better knowledge of: - IM route (p = 0.006) - GI symptom recognition (p = 0.043) - Correct dose + route combination (p = 0.024)
Sharma et al., 2019 ^{viii}	Delayed/omitted IM adrenaline administration in severe antivenom-related anaphylaxis (ARA)	- Failure to give IM adrenaline at the first sign/s of ARA - Delay in giving IM adrenaline (given after IV hydrocortisone instead of immediately) - Use of SC adrenaline (ineffective) instead of IM adrenaline	Not precisely measured; documented delays: - Patient #5: IMAd given 6 minutes after IV hydrocortisone - Patient #10: IMAd given 15 minutes after first ARA signs (when rash appeared) - Patients #6, #8, #9: received no IM adrenaline for suspected ARA	- IMAd given appropriately: 4/13 (30.8%) - IMAd given with delay: 2/13 (15.4%) - IMAd NOT given (subcutaneous or IV adrenaline used instead, or no adrenaline): 7/13 (53.8%)	2/13 (15.4%) – IMAd given after IV hydrocortisone or after initial signs had progressed	7/13 (53.8%) – patients did NOT receive IM adrenaline: - Patient #6: treated for ARA but no IMAd documented - Patient #7: received IV adrenaline (not IM) during resuscitation - Patient #8: received nebulized salbutamol but no IMAd for initial ARA - Patient #11: received SC adrenaline (not IM) - Patient #12: received SC adrenaline (not IM) - Patients #2, #3: received IV adrenaline (not IM)	Clinician-related (failure to recognize ARA when symptoms overlap with envenoming; use of incorrect route [SC/IV] instead of IM; delayed treatment) and Healthcare system-related (limited resources, lack of surgical airway equipment, transfers to distant hospitals)	Diagnostic confusion: ARA often mistaken for worsening snakebite. Incorrect adrenaline route: SC or IV used instead of IM. Delayed IM adrenaline: Given after IV hydrocortisone (6–15 min delay). Missed early treatment: Mild ARA not treated promptly; one patient died. Airway management failures: Severe laryngeal edema with failed intubation. Protocol gaps: No surgical airway training or equipment. Transfer delays: Three patients died during hospital transfer.	- Premedication with SC adrenaline (introduced in second year) - Antivenom dose (low dose vs. high dose) - Timing of antivenom administration (IV push vs. infusion)	Descriptive statistics (no regression/ORs). - Mann-Whitney U test for continuous data comparisons (times to ARA events).	- SCAd premedication vs. no SCAd: Median time to first ARA event: 17 min vs. 30 min (p = 0.5, NS) - Low dose vs. High dose: Median time to first ARA event: 14.5 min vs. 28 min (p = 0.4, NS) - Severe ARA incidence: 13/155 (8.4%, 95% CI 4.9–13.8%) - Case fatality rate: 8/155 (5.16%, 95% CI 2.25–9.9%)	No – Neither SCAd premedication nor antivenom dose significantly predicted time to ARA or severity.

Xing et al., 2018 ^{xiv}	Epinephrine use (receipt, timing, route, dosing) in pediatric drug-induced anaphylaxis	NS	NR	- Any epinephrine: 62/91 (68%) - Epinephrine as initial treatment: 49/91 (54%) - Among those with documented route: IM route = 11/48 (23%); SC route = 16/48 (33%); IV bolus = 15/48 (31%); IV infusion = 6/48 (13%)	37/91 (41%) – received epinephrine but NOT as initial treatment (i.e., delayed).	29/91 (32%) – did NOT receive any epinephrine.	Clinician-related (failure to recognize anaphylaxis, misuse of IV route, supratherapeutic dosing, preference for corticosteroids over epinephrine)	Epinephrine underuse: 54% received initial epinephrine; 32% received none. Incorrect route: Only 23% received IM; 31% received IV bolus. Overdosing: 54% received supratherapeutic doses; IV bolus strongly associated (92% vs. 36% for IM/SC; $p = 0.005$). Corticosteroid overuse: 80% received corticosteroids; 37% received them as sole initial therapy. Age-related presentation differences: Younger children more often had cyanosis (OR = 5.14); adolescents more often had hypotension (OR = 11.79) and neurological symptoms (OR = 3.56).	- Age group (0–5, 6–12, 13–17 years) - Route of epinephrine administration (IM, SC, IV bolus)	- Pearson's chi-square test / Fisher's exact test - Kruskal-Wallis test (dosing data) - Bonferroni correction for multiple comparisons	Odds ratios (OR) with 95% CI, p-values: - Cyanosis (0–5 vs. 13–17): OR = 5.14 (1.74–15.20), $p = 0.002$ - Hypotension (13–17 vs. 6–12): OR = 11.79 (2.28–60.87), $p = 0.002$ - Neurological symptoms (13–17 vs. 0–5): OR = 3.56 (1.26–10.08), $p = 0.015$ - Severe anaphylaxis (13–17 vs. 0–5): OR = 15.46 (1.85–129.33), $p = 0.002$ - Supratherapeutic dosing (IV bolus vs. IM): OR = 19.25 (1.77–209.55), $p = 0.009$ - Supratherapeutic dosing (IV bolus vs. SC): OR = 19.80 (1.94–201.63), $p = 0.005$	Yes – Age group significantly predicted symptom patterns and severity. Yes – IV bolus route significantly predicted supratherapeutic dosing.
Cohen et al., 2018 ^{xv}	Correct diagnosis of anaphylaxis and IM epinephrine administration (pre-hospital, in-PED, total)	Not defined as a time interval; assessed as "epinephrine administered" vs. not	NR	- 2013–2014: 33/59 (56%) - 2015–2016: 72/134 (54%) - Overall: 105/193 (54%) - In PED (2015–2016): 47/134 (35%) - Pre-hospital (2015–2016): 28/134 (21%)	Not specifically measured; some patients received epinephrine pre-hospital or in PED	- 2013–2014: 26/59 (44%) - 2015–2016: 62/134 (46%) - Overall: 88/193 (46%)	Clinician-related (misdiagnosis, reluctance to label mild cases as anaphylaxis, coding issues) and Healthcare system-related (limited coding options, lack of computerized decision support)	Low diagnosis rate: Only 37–39% are correctly diagnosed as anaphylaxis. Misdiagnosis: Less respiratory symptoms (breathing difficulty $p = 0.03$; wheezing $p = 0.001$). Reluctance to diagnose mild cases: Often coded as allergic reaction. Coding limitation: No dedicated code for mild/moderate anaphylaxis. Epinephrine underuse: Only 54% received IM epinephrine. No improvement over time: Diagnosis and epinephrine use remained unchanged. Improved discharge care: Allergist referrals increased (68%→90%; $p = 0.0002$); autoinjector prescriptions increased (64%→73%).	- Time period (2013–2014 vs. 2015–2016) - Clinical features (breathing difficulties, wheezing, urticaria, angioedema, etc.) - Asthma history	- Fisher exact test (categorical variables) - Two-sided t-test (continuous variables)	Diagnosis rate (2015–16 vs. 2013–14): 39% vs. 37%, $p = 0.87$ IM epinephrine use: 54% vs. 56%, $p = 0.88$ Breathing difficulty (diagnosed vs. misdiagnosed): $p = 0.03$ Wheezing (diagnosed vs. misdiagnosed): $p = 0.001$ Allergist referral: 90% vs. 68%, $p = 0.0002$	Yes – Presence of breathing difficulties and wheezing significantly predicted correct diagnosis of anaphylaxis. No – Time period (guideline revision) did NOT significantly improve correct diagnosis or epinephrine use.
Dubus et al., 2018 ^{xvi}	IM epinephrine administration (pre-hospital and in-ED) and association with anaphylaxis severity	Not specifically defined; assessed as "epinephrine administered" vs. "not administered"	NR	- Pre-hospital: 23/201 (11.4%) - In ED: 45/202 (22.3%) - Overall (pre-hospital or ED): 65/199 (32.7%)	Not specifically measured	- Pre-hospital: 178/201 (88.6%) - In ED: 157/202 (77.7%) - Overall: 134/199 (67.3%)	Clinician-related (intuitive adaptation of epinephrine use to severity; fear of side effects; underestimation of mild-moderate anaphylaxis) and Healthcare system-related (delay between symptom	Severity-driven epinephrine use: Grade III vs. II, 84.8% vs. 22.3% (OR = 19.05, $p < 0.001$). Reserved for severe cases: Epinephrine often withheld in moderate anaphylaxis. Low prehospital use: 11.4% received epinephrine before ED arrival. Hospital underuse: 47.3% received no epinephrine.	- Anaphylaxis severity (Grade II vs. Grade III by Ring and Messmer) - Triage severity (nurse triage scale levels 1–2 vs. others) - Previous anaphylaxis history - Asthma history	- Simple logistic regression for qualitative variables (unadjusted OR with 95% CI) - Student t-test or Fisher's exact test (quantitative variables) - SPSS v20.0	Grade III vs. II epinephrine use: OR = 19.05 (95% CI 7.05–54.10), $p < 0.001$ High vs. low triage severity: OR = 2.81 (95% CI 1.51–5.21), $p < 0.001$ Previous anaphylaxis vs.	Yes – Anaphylaxis severity (Grade III vs. Grade II) was a highly significant predictor of epinephrine use (OR = 19.05, $p < 0.001$). Yes – High triage severity was a significant

							onset and ED presentation; lack of auto-injector availability)	Delayed presentation: Symptom improvement before ED may have reduced epinephrine use. Fear of side effects: Concern over cardiovascular effects limited use. Poor discharge care: AAI prescribed in 31.7%; allergist referral in 44.2%.			prehospital epinephrine: 21.3% vs. 5.6%, p < 0.001 Asthma (Grade III vs. II): 50.0% vs. 25.9%, p = 0.005	predictor of epinephrine use (OR = 2.81, p < 0.001).
Lee et al., 2018 ^{vii}	- Admission rate (primary outcome) - Time to first epinephrine administration (for ESI level 1 patients) - Rate of discharge with epinephrine autoinjector (EAI) in hand - ED return visits within 72 hours (balancing measure)	Time from ED arrival to first epinephrine administration; target ≤20 minutes (later reduced to ≤10 minutes)	- Post-intervention median: 10 minutes (for ESI level 1 patients) - Baseline median: 15 minutes (p = 0.87, NS) - Target achieved: consistently <20 minutes	NR for overall cohort; tracked for ESI level 1 patients only	Not specifically reported; time-to-epinephrine metric tracked	Not specifically reported	Healthcare system-related (prolonged observation leading to unnecessary admissions; lack of standardized discharge practices; lack of EAI in hand at discharge) and Clinician-related (variation in recognition and treatment)	- Prolonged observation (8 hours) led to high admission rates: 58.2% baseline. - Variable observation periods: 4–24 hours recommended in literature, leading to inconsistent practice. - Low discharge with EAI in hand: prior practice likely relied on prescriptions that may not have been filled. - Delayed epinephrine administration: median 15 minutes at baseline; target set at ≤20 minutes. - Low Allergy follow-up: only 20.3% seen within 1 month at baseline.	- Intervention: revised clinical pathway (4-hour observation vs. 8-hour; EAI in hand; provider education) - Time period (pre- vs. post-intervention)	- Fisher's exact test (proportions: admission rate, return visits, Allergy referrals) - Mann-Whitney U test (median time to epinephrine) - Run chart (admission rate over time)	p-values, proportions: - Admission rate: 58.2% baseline vs. 25.3% post-intervention, p < 0.0001 - ED return visits: 1.3% baseline vs. 2.6% post-intervention, p = 0.99 (NS) - Allergy referral: 62.1% baseline vs. 64.6% post-intervention, p = 0.62 (NS) - Allergy visit within 1 month: 20.3% baseline vs. 31.1% post-intervention, p = 0.01 - Allergy visit within 3 months: 30.2% baseline vs. 40.1% post-intervention, p = 0.03	Yes – Clinical pathway revision (4-hour observation, EAI in hand, education) significantly predicted: - Lower admission rate (p < 0.0001) - Higher Allergy follow-up (p = 0.01, 0.03) No – No significant difference in ED return visits (p = 0.99) or time to epinephrine (p = 0.87)
Wang et al., 2017 ^{viii}	Epinephrine use (receipt, timing, route, dosing, and adverse events) in drug-induced anaphylaxis	Epinephrine use vs. non-use; "initial treatment" (first medication administered) vs. not initial	NR	- Any epinephrine: 708/1,189 (59.5%) - Epinephrine as initial treatment: 518/699 (74.1%) of those with documentation - Among those with documented route: - IM route: 83/518 (16.9%) - SC route: 155/518 (31.5%) - IV bolus: 214/518 (43.5%) - IV infusion: 40/518 (8.1%)	- 181/699 (25.9%) – received epinephrine but NOT as initial treatment (i.e., delayed)	481/1,189 (40.5%) – did NOT receive any epinephrine	Clinician-related (failure to use epinephrine, incorrect route [IV bolus overuse], overdose, use of SC instead of IM, preference for corticosteroids over epinephrine)	Epinephrine underuse: 59.5% received epinephrine; 40.5% received none. Incorrect route: IM 16.9%, SC 31.5%, IV bolus 43.5%, IV infusion 8.1%. Overdosing: IV bolus strongly associated with supratherapeutic dosing (p < 0.001). Corticosteroid overuse: 82.2% received corticosteroids; 92.5% as initial therapy. Predictors of epinephrine use: Wheezing (OR 1.96), respiratory arrest (OR 3.67), diffuse urticaria (OR 1.43), younger age (OR 0.91 per 10-year increase). Cardiovascular adverse events: Mainly associated with IV bolus overdosing (9.62% vs. 0% IM; 1.64% SC).	- Clinical features (symptoms, signs) - Route of epinephrine administration (IM, SC, IV bolus, IV infusion) - Age - Current diseases	- Pearson χ^2 test / Fisher's exact test (categorical variables) - Independent samples t-test (continuous variables) - Bivariate and multivariate logistic regression (forward stepwise selection)	Age (per 10 years): OR = 0.91, p = 0.003 Flushing: OR = 0.70, p = 0.024 Diffuse urticaria: OR = 1.43, p = 0.018 Wheezing: OR = 1.96, p < 0.001 Respiratory arrest: OR = 3.67, p < 0.001 Corticosteroid use: OR = 2.02, p < 0.001 Bronchodilator use: OR = 0.44, p = 0.013 IV bolus vs. IM/SC (overdosing): p < 0.001 IV bolus vs. IM (cardiovascular adverse events): p = 0.016 IV bolus vs. SC (cardiovascular adverse events): p = 0.006	Yes – Wheezing, respiratory arrest, diffuse urticaria, younger age, and corticosteroid use significantly predicted epinephrine receipt. Yes – IV bolus route significantly predicted supratherapeutic dosing and cardiovascular adverse events.

Kawano et al., 2017 ^{xi}	- Epinephrine administration (overall, IM, IV, self-administered) - Excessive dosing (>0.5 mg IM or >100 µg IV) - Cardiovascular complications post-epinephrine	Not defined as time interval; assessed as "received epinephrine" vs. "did not receive epinephrine"	NR	- Overall epinephrine: 269/492 (54.7%) - Older patients: 44/122 (36.1%) - Younger patients: 225/370 (60.8%) - IM epinephrine: Older 31/122 (25.4%) vs. Younger 186/370 (50.3%) - IV epinephrine: Older 5/122 (4.1%) vs. Younger 2/370 (0.5%) - Self-administered: Older 9/122 (7.4%) vs. Younger 43/370 (11.6%)	Not specifically measured	- Overall: 223/492 (45.3%) - Older patients: 78/122 (63.9%) - Younger patients: 145/370 (39.2%)	Clinician-related (reluctance to use epinephrine in older patients due to fear of cardiovascular complications; use of IV instead of IM route) and Patient-related (older patients more likely to have cardiac risk factors)	Age-related decline in epinephrine use: 57.9% (17–29 years) vs. 16.0% (>70 years), $p < 0.01$. Older patients less likely to receive epinephrine: OR = 0.30 (95% CI 0.2–0.5). Older patients more likely to receive IV epinephrine: OR = 14.1 (95% CI 2.2–152.6). Excessive dosing: Higher in older patients (OR = 20.7); all cases involved IV epinephrine. Cardiovascular complications: Higher in older patients (OR = 22.4). IM epinephrine remained safe: No significant increase in complications.	- Age group (older ≥50 years vs. younger <50 years) - Route of epinephrine administration (IM vs. IV)	- Mann-Whitney U test (continuous variables) - Univariate logistic regression / Fisher exact test - Exact logistic regression (for rare events) - Cochran-Armitage test (trend across age categories)	Epinephrine use (older vs. younger): OR = 0.30 (95% CI 0.2–0.5) IM epinephrine use: OR = 0.30 (95% CI 0.2–0.5) IV epinephrine use: OR = 14.1 (95% CI 2.2–152.6) Excessive dosing: OR = 20.7 (95% CI 3.8–211.7) Cardiovascular complications: OR = 22.4 (95% CI 2.1–1129.8) IV vs. IM cardiovascular complications: OR = 99.6 (95% CI 7.4–∞) IM complications (older vs. younger): OR = 1.09.	Yes – Older age significantly predicted lower epinephrine use ($p < 0.01$ trend), higher IV use, excessive dosing, and cardiovascular complications. Yes – IV route significantly predicted cardiovascular complications. No – IM epinephrine in older patients did NOT significantly predict cardiovascular complications (OR 1.09).
Campbell et al., 2016 ^{xv}	Provider perceptions and preferences regarding IM epinephrine administration methods (autoinjector vs. manual injection).	NA	NR	NR	NR	NR	Clinician-related (fear of dosing errors, lack of familiarity, need for training) and Healthcare system-related (cost of autoinjectors, risk of self-injury)	Higher dosing error risk: Manual injection vs. autoinjector ($p < 0.001$). More training required: ≤10 min adequate for 57% (manual) vs. 88% (autoinjector). Lower cost: Manual injection favored ($p < 0.001$). Lower self-injury risk: Manual injection favored; 2% reported autoinjector finger-stick injuries. Limited weight-based dosing: Autoinjectors available only in 0.15 mg and 0.30 mg. Needle length concerns: May result in SC rather than IM delivery in patients with higher BMI.	- Occupation (nurses, physicians, residents, pharmacists, advanced practice providers) - Experience with both autoinjector and manual injection methods - Years in practice	- Wilcoxon signed rank test (paired comparisons of ratings for autoinjector vs. manual injection) - Kruskal-Wallis test (comparisons by occupation) - Fisher exact test (categorical variables)	Ease of use: 85.5 vs. 49.6, $p < 0.001$ Convenience: 88.7 vs. 38.2, $p < 0.001$ Weight-based dosing: 68.3 vs. 56.7, $p < 0.001$ Dosing error risk: 20.1 vs. 67.8, $p < 0.001$ Patient cost: 58.2 vs. 40.6, $p < 0.001$ Administration speed: 84.1 vs. 45.7, $p < 0.001$ Self-injury risk: 52.6 vs. 38.4, $p < 0.001$ Overall preference: 82% preferred the autoinjector.	Yes – Autoinjector significantly preferred for ease of use, convenience, dosing error risk, speed, and training time. Yes – Manual injection significantly preferred for cost and self-injury risk. No – Occupation did not significantly affect preference patterns.
Drupad & Nagabushan, 2015 ^{xvi}	Knowledge deficits in: (1) First-line drug for anaphylaxis (adrenaline) (2) Correct dose of adrenaline (3) Route of administration (IM vs. SC vs. IV) (4) Site of administration (5) Concentration of adrenaline for IV, IM, and SC routes (6) Pediatric dose	NA	NR	NA	NR	NR	Clinician-related / Educational (lack of knowledge of dose, route, site, and concentration)	First-line adrenaline knowledge: 56.9%. Among those aware: Correct dose 26.4%; correct IM route 16.5%. Overall correct management: Only 9.4% identified the first-line drug, dose, and IM route. Very poor concentration knowledge: IV 0.4%; IM 0%; SC 1.5%; pediatric dose 0%. Medical students outperformed interns and nursing students on dose, route, and injection site ($p < 0.001$).	- Level of training (medical students vs. interns vs. nursing students)	- Chi-square test (comparing responses between groups) - Descriptive statistics (numbers and percentages)	p-values only (no OR/RR): - Question 2 (first-line drug): $p < 0.001$ (significant difference between groups) - Question 4 (route of administration): $p < 0.001$ - Question 5 (site of administration): $p < 0.001$ - Medical students performed better than interns and nursing students.	Yes – Level of training (medical students vs. nursing students) was a significant predictor of knowledge of first-line drug, route, and site ($p < 0.001$).

Özmen et al., 2015 ^{xxii}	Knowledge deficits in: (1) Route of adrenaline administration (IM vs. SC vs. IV) (2) Awareness of epinephrine auto-injector (EAI) (3) Prescription of EAI (report) (4) Prior training on anaphylaxis	NA	NR	NA	NR	NR	Clinician-related / Educational (lack of training, knowledge decay, poor awareness of auto-injector, low prescription rates)	Anaphylaxis training: 50.6% received training. Correct IM route knowledge: 46.4%; higher in trained participants (73.8% vs. 39%, p < 0.001). Lowest knowledge: Auxiliary staff (21.4% vs. 51.2% specialists, 75.5% residents). EAI awareness: 48.8%. EAI prescribing: Only 3.0% had ever prescribed an EAI. Knowledge decay: 41.7% trained >2 years previously. Specialists: Highest EAI awareness but lowest recent training.	- Training status (received vs. did not receive anaphylaxis training) - Professional group (specialist, resident, auxiliary staff) - Time since training	- Chi-square test (categorical variables) - Student's t-test (continuous variables)	p-values: - Correct IM route vs. training status: p = 0.000 - Correct IM route vs. professional group: p = 0.000 - EAI awareness vs. training status: p = 0.000 - EAI awareness vs. professional group: p = 0.000 - Anaphylaxis training vs. professional group: p = 0.002	Yes – Training status significantly predicted knowledge of IM route (p = 0.000) and EAI awareness (p = 0.000). Yes – Professional group significantly predicted knowledge of IM route (p = 0.000) and EAI awareness (p = 0.000).
Plumb et al., 2015 ^{xxiii}	Knowledge deficits in: (1) Recognition of anaphylaxis vs. non-anaphylactic presentations (5 case scenarios) (2) Correct dose and route of adrenaline (0.5 mL of 1:1000 IM)	NA	NR	NA	NR	NR	Clinician-related / Educational (lack of recognition of anaphylaxis vs. other conditions; incorrect route [IV] and dosing; inappropriate use of adrenaline in non-anaphylactic cases)	Correct dose + IM route: Only 34%. Incorrect IV adrenaline: 25% for true anaphylaxis. Adrenaline overuse: 82% (foreign body), 21% (urticaria), 22% (rash + asthma), 69% (angioedema + IHD). Inappropriate use in non-anaphylaxis: 49% (vs. 32% in 2002; p < 0.0001). F2 vs. F1: Better IM route knowledge (79% vs. 68%; NS). Improved since 2002: Correct IM route (45%→74%), correct dose + route (13%→34%), IV adrenaline use decreased (42%→25%). Overuse worsened: More adrenaline given for non-anaphylactic cases (49% vs. 32%; p < 0.0001).	- Training level (F1 vs. F2) - Historical era (2013 vs. 2002 cohort) - ALS training (F2s had ALS training, F1s did not) - ED experience (only 4/68 had worked in ED)	- Two-tailed Fisher's exact test (comparisons between 2002 and 2013 cohorts) - Descriptive statistics (percentages)	p-values: - Correct IM route (2013 vs. 2002): 74% vs. 45%, p = 0.0007 - Correct dose + route (2013 vs. 2002): 34% vs. 13%, p = 0.0029 - Inappropriate IV adrenaline (2013 vs. 2002): 25% vs. 42%, p = 0.0359 - Inappropriate adrenaline for non-anaphylactic cases (2013 vs. 2002): 49% vs. 32%, p < 0.0001 - F1 vs. F2 correct route: 68% vs. 79%, p = 0.41.	Yes – Historical era (2013 vs. 2002) significantly predicted improved dose and route knowledge but also predicted worse recognition of non-anaphylactic cases. No – F1 vs. F2 training level did not significantly predict correct route knowledge (p = 0.41).
AAI: Adrenaline Auto-Injector; ACE-I: Angiotensin-Converting Enzyme Inhibitor; ALS: Advanced Life Support; ANOVA: Analysis of Variance; ARA: Antivenom-Related Anaphylaxis; β: Beta Coefficient; BMI: Body Mass Index; BPD: Beijing Pharmacovigilance Database; BST: Baseline Serum Tryptase; CABG: Coronary Artery Bypass Graft; CAE: Cardiovascular Adverse Events; CI: Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; COVID-19: Coronavirus Disease 2019; CVS: Cardiovascular System; DIA: Drug-Induced Anaphylaxis; EAI: Epinephrine Autoinjector; ED: Emergency Department; EMR: Electronic Medical Record; EMS: Emergency Medical Services; ER: Emergency Room; ESI: Emergency Severity Index; F1: Foundation Year 1; F2: Foundation Year 2; FARE: Food Allergy Research and Education; GI: Gastrointestinal; HR: Hazard Ratio; ICD-10: International Classification of Diseases, Tenth Revision; ICU: Intensive Care Unit; IHD: Ischemic Heart Disease; IM: Intramuscular; IQR: Interquartile Range; ISS: In Situ Simulation; IV: Intravenous; LST: Latent Safety Threat; MBBS: Bachelor of Medicine, Bachelor of Surgery; MET: Medical Emergency Team; MI: Myocardial Infarction; NA: Not Applicable; NIAID/FAAN: National Institute of Allergy and Infectious Diseases / Food Allergy and Anaphylaxis Network; NR: Not Reported; NS: Not Specified; OR: Odds Ratio; PED: Pediatric Emergency Department; PICU: Pediatric Intensive Care Unit; QI: Quality Improvement; REDCap: Research Electronic Data Capture; RR: Relative Risk; SAE: Serious Adverse Event; SC: Subcutaneous; SD: Standard Deviation; sBP: Systolic Blood Pressure; SHO: Senior House Officer; SpO2: Oxygen Saturation; TSMC: Tel Aviv Sourasky Medical Centre; TCM: Traditional Chinese Medicine; TGH: Tampa General Hospital; TS: Translational Simulation; VIA: Venom-Induced Anaphylaxis; WHO-UMC: World Health Organization-Uppsala Monitoring Center.												

Table 4: Detailed Summary of Reported Barriers to Timely Intramuscular Epinephrine Administration

Last name of first author, year	Specific barrier	Description of barrier	Measurement method	Frequency/prevalence (%)	Associated outcome	Significant association (y/n)	Authors' recommendation
Pape et al., 2025 ⁱ	Uncertainty regarding appropriate first-line therapy	Physicians did not recommend IM adrenaline as first-line treatment for severe anaphylaxis; instead, recommended antihistamines/corticosteroids, IV adrenaline, or other incorrect treatments	Structured interview after viewing video simulation	63/95 (66.3%)	Incorrect treatment selection	Yes (P < 0.001 for board-certified vs. residents)	Periodic refresher training; short self-learning modules or micro-learning approaches; training videos (YouTube)
Bülbül et al., 2024 ⁱⁱ	Knowledge decay / Outdated training among senior physicians	Physicians with more years of professional experience were significantly less likely to know adrenaline is first line, the correct IM route, and the correct lateral thigh site. This is likely due to older guidelines recommending subcutaneous administration.	Online questionnaire comparing correct answers against self-reported professional years.	- Those who didn't know the correct route had a mean experience of 16.3 years vs. 7.1 years for those who knew (p<0.001). - Those who didn't know the correct site had a mean experience of 18.6 years vs. 7.1 years (p<0.001).	Incorrect treatment selection (choosing the wrong route/site/dose) can lead to treatment failure.	Yes (p < 0.001 for route/site; p = 0.031 for first-line drug)	Periodic in-service postgraduate training and refresher courses are essential to update senior physicians on current guidelines.

Hamadi & Casale, 2024 ⁱⁱⁱ	Fear of COVID-19 leading to healthcare avoidance	Patients experiencing acute allergic reactions at home avoided going to the ER or doctor's office during the pandemic out of fear of contracting COVID-19.	Self-reported survey question: "Did the COVID-19 pandemic change how you responded to an allergic reaction?"	63 patients reported behavioral changes; of those: 71% (n=45) avoided seeking medical care outside the home.	Delayed/omitted professional medical treatment for anaphylaxis.	Not statistically tested (descriptive only).	Increased patient education on when to seek care despite external fears (pandemics).
Kaya & Alaylar, 2024 ^{iv}	Inadequate knowledge of anaphylaxis diagnostic criteria	Physicians failed to recognize that anaphylaxis can involve multiple systems simultaneously. While most recognized skin and respiratory involvement, they frequently missed cardiovascular and gastrointestinal symptoms as part of the diagnostic criteria.	Face-to-face questionnaire asking participants to select which signs/symptoms meet the diagnostic criteria for anaphylaxis (based on the Turkish National Guideline 2018).	- Only 4/85 (4.7%) correctly marked all diagnostic criteria. - 85% marked skin + respiratory, but only 15% included cardiovascular and gastrointestinal signs.	Underdiagnosis of anaphylaxis (missing atypical or non-cutaneous presentations, particularly cardiovascular collapse or GI symptoms), leading to failure to initiate life-saving treatment.	Yes for specialty branch (p = 0.03). No for professional experience (p = 0.92) or prior encounter with anaphylaxis (p = 0.48).	In-service training programs for all physicians, regardless of specialty or experience, to improve recognition of the full spectrum of anaphylactic symptoms.
Ho et al., 2024 ^v	Underutilization of intramuscular epinephrine in older adults	Emergency physicians were significantly less likely to administer IM epinephrine to older adult patients (≥65 years) compared to children and younger adults. This disparity was most pronounced in patients with moderate (non-severe) anaphylactic reactions, where only 14.3% of older adults received IM epi vs 55.3% of children.	Retrospective EMR review; epinephrine administration documented in medication records; age groups compared using trend tests.	- Overall IM epi: 38.1% - Older adults IM epi: 29.8% - Moderate reactions in older adults: 14.3% received IM epi (vs 35.2% adults, 55.3% children)	Omission of first-line life-saving therapy, increased risk of progression to severe/biphasic reactions, and potentially higher mortality in a vulnerable population with comorbidities.	Yes – Age-group difference significant (P trend = 0.004 for overall; P trend < 0.001 for moderate reactions).	Intensified medical care targeting older adult patients; physician continuing education to address age-based biases and emphasize that IM epinephrine is indicated for all anaphylaxis, regardless of severity or age.
Price et al., 2023 ^{vi}	Failure to utilize weight-based cognitive aids for adrenaline dosing	Staff were either unaware of the Monash Pediatric Emergency Medication Book, could not locate it on the MET trolley, or chose not to use it during the emergency. This led to dosing/route/concentration errors. All three actual administration errors (wrong dose, wrong route) occurred in simulations where the cognitive aid was NOT used.	Direct observation and documentation on the audit tool during ISS.	- Cognitive aid used in only 56% (13/23) of simulations. - 44% (10/23) of teams did NOT use the cognitive aid. - 100% (3/3) of administration errors occurred when it was not used.	Medication errors (wrong dose, wrong route) leading to potential patient harm (underdosing or overdose).	Yes – All administration errors were associated with non-use of the aid.	Improve accessibility of cognitive aids (labeled dosing boxes in cubicles), promote awareness during orientation, and continue ISS education to reinforce their use.
Ateş & Sahiner, 2022 ^{vii}	Insufficient/outdated training on adrenaline administration	Only 65.6% of health professionals had received training on adrenaline. Among those trained, nearly 40% had their training ≥3 years ago, suggesting knowledge decay over time. Those with training were significantly more likely to know the correct IM route (74.1% vs 52%, p=0.001), but training did not significantly improve knowledge of first-line drug, site, dose, or repeat interval.	Self-reported questionnaire: "Have you received training on adrenaline application?" and "If yes, how much time has passed since the training?"	- No training: 34.4% (n=75) - Training ≥3 years ago: ~39.5% of trained participants (22.5% at 3–5 years, 17% at ≥6 years) - Training ≤6 months: only 20.2%	Lower knowledge of correct adrenaline administration, particularly route of administration.	Yes – Training was significantly associated with knowing the correct route (p = 0.001).	Frequent, repetitive training on anaphylaxis and the use of adrenaline is essential. Since anaphylaxis is rare, knowledge is easily forgotten; therefore, refresher courses should be conducted regularly for all health personnel involved in vaccination and drug administration.
Wijekoon et al., 2021 ^{viii}	Poor diagnostic accuracy – inability to differentiate anaphylaxis from simple allergic reactions	Pre-interns struggled to diagnose anaphylaxis from case scenarios correctly. Only 7.3% correctly diagnosed all 10 cases; 65.5% failed to identify all 7 anaphylaxis cases. The most problematic case was Case 9 (isolated wheezing after diclofenac – simple allergy), in which 49.1% were incorrectly diagnosed with anaphylaxis. This reflects a fundamental gap in the application of diagnostic criteria.	10 case scenarios; respondents selected the most likely diagnosis (anaphylaxis, allergy, or other).	- 7.3% correctly diagnosed all 10 case scenarios - 34.5% correctly diagnosed all 7 anaphylaxis cases - 49.1% misdiagnosed isolated wheezing as anaphylaxis (Case 9) - 42.1% failed to diagnose hypotension with GI symptoms as anaphylaxis (Case 4) - 10.7% unaware anaphylaxis can occur without hypotension - 6.3% unaware anaphylaxis can occur without skin manifestations - 16% unaware that criteria exist for diagnosing anaphylaxis	Over-diagnosis (treating simple allergy as anaphylaxis) leading to unnecessary treatment and adverse effects; Under-diagnosis (missing true anaphylaxis) leading to delayed/omitted life-saving adrenaline.	Yes – Higher MBBS classification (class vs. no class) was a significant predictor of better diagnosis scores (p < 0.001).	Structured educational programs focusing on criteria-based diagnosis using case scenarios; teaching should emphasize both typical and atypical presentations of anaphylaxis.
Francuzik et al., 2020 ^x	Under-recognition/under-treatment of venom-induced anaphylaxis (VIA)	Patients with VIA received epinephrine significantly less often than patients with anaphylaxis from other triggers (food, drugs), even after matching for age, sex, and severity. This suggests clinicians may not recognize VIA as promptly or may be hesitant to treat it with epinephrine. The barrier was most pronounced in: (1) First-time VIA episodes (no previous history) (2) Moderate (non-severe) VIA reactions (3) VIA cases without skin symptoms	Registry data analysis comparing documented epinephrine administration (any route) between VIA and non-VIA cases, matched by age, sex, and severity.	- VIA: 26.9% received epinephrine - Non-VIA: 34.6% received epinephrine - Difference: 7.7% absolute reduction in VIA (p < 0.001) - First-time VIA: epinephrine use significantly lower than first-time non-VIA (p < 0.001)	Delayed/omitted administration of life-saving first-line therapy, increasing risk of progression to severe/biphasic reactions and mortality.	Yes – VIA was significantly associated with lower epinephrine use (p < 0.001), even after controlling for severity, age, and sex.	Clinicians should not underestimate VIA, even in milder cases, and should treat all diagnosed anaphylaxis with intramuscular epinephrine as first-line therapy. Education should emphasize that transient hypertension/tachycardia is not a contraindication to epinephrine in anaphylaxis.
Pimentel-Hayashi et al., 2020 ^x	Difficulty recognizing anaphylaxis without cutaneous symptoms	While 96.4% of physicians correctly diagnosed anaphylaxis with cutaneous, respiratory, and cardiovascular symptoms, only 59.2% correctly	Two clinical case scenarios: one with cutaneous symptoms, one	- Correct diagnosis with cutaneous symptoms: 96.4%	Missed diagnosis of anaphylaxis leading to delayed or omitted	Not tested as a separate predictor; no significant differences between specialty groups.	Reinforce education that anaphylaxis can present without cutaneous symptoms; emphasize that

		diagnosed anaphylaxis when skin symptoms were absent. This is a critical gap because VIA and some drug-induced anaphylaxis can present without skin involvement.	without. Respondents selected the diagnosis.	- Correct diagnosis without cutaneous symptoms: 59.2% - Knowledge gap: 40.8% failed to diagnose anaphylaxis without skin symptoms	epinephrine administration; increased risk of fatal outcomes.		cardiovascular and respiratory symptoms alone (especially in the context of known allergen exposure) are sufficient for diagnosis.
Krmpotic et al., 2019 ^{xi}	Delayed epinephrine administration despite immediate recognition and access	Both patients who died had witnessed anaphylaxis events that were immediately recognized as anaphylaxis after exposure to known allergens. They had immediate access to IM epinephrine (implying AAI availability). However, epinephrine was not administered until after cardiorespiratory arrest occurred, suggesting failure to act promptly even when the diagnosis was clear and the medication was available.	Retrospective chart review; data extracted from PICU admission records and death reviews.	- 2/12 (17%) of PICU admissions resulted in death - Both deaths (100%) were associated with delayed epinephrine administration until after arrest - Patients who died represent 2/2 (100%) of cases where epinephrine was available but not administered promptly	Cardiorespiratory arrest, severe global hypoxic ischemic brain injury, and death. Both patients had return of spontaneous circulation (ROSC) and achieved hemodynamic stability post-arrest but suffered irreversible brain injury and died.	Not statistically tested; however, the association between delayed epinephrine and mortality is strongly implied by the case descriptions.	This study highlights the high mortality associated with severe anaphylaxis and the ongoing need for education surrounding the early administration of intramuscular epinephrine. Continued strategies are needed to increase awareness regarding the need for early IM epinephrine administration immediately after the onset of symptoms consistent with anaphylaxis.
Lauraa et al., 2019 ^{xii}	Inadequate recognition of anaphylaxis clinical criteria	Only 35% of pediatricians recognized all NIH/NIAID-FAAN diagnostic criteria. While 85% recognized skin+respiratory symptoms, only 52% recognized skin+gastrointestinal symptoms. Isolated mucocutaneous symptoms were incorrectly identified as anaphylaxis by 14% of respondents. This reflects a lack of familiarity with the full spectrum of anaphylaxis presentations.	Survey questions assessing knowledge of NIH/NIAID-FAAN clinical criteria for anaphylaxis diagnosis.	- 35% recognized all NIH criteria - 85% recognized skin + respiratory (Criterion 1) - 52% recognized skin + gastrointestinal (Criterion 2) - 14% incorrectly identified isolated mucocutaneous symptoms as anaphylaxis	Underdiagnosis of anaphylaxis, particularly in cases without skin symptoms or with atypical presentations (isolated gastrointestinal symptoms); delayed or omitted epinephrine administration.	Yes – Physicians with <5 years of experience were significantly better at recognizing gastrointestinal symptoms (60% vs. 35%, p = 0.043).	Enhanced dissemination of standardized diagnostic criteria; educational strategies to improve recognition of less common presentations (gastrointestinal involvement without skin symptoms).
Sharma et al., 2019 ^{xiii}	Diagnostic confusion: overlapping signs of anaphylaxis and neurotoxic envenoming	Patients with neurotoxic snakebite envenoming and antivenom-related anaphylaxis can present with similar clinical features: dyspnea, restlessness, hypoxia, and respiratory failure. This made it difficult for clinicians to determine whether deterioration was due to worsening envenoming (requiring more antivenom) or anaphylaxis (requiring IM adrenaline and stopping antivenom). In several patients (#s 6, 8, 9, 13), symptoms were initially attributed to envenoming, leading to delayed or omitted adrenaline treatment.	Clinical case review of SAE forms and associated communications; reconstruction of clinical events by senior author.	- 6/13 (46.2%) patients had clinical features consistent with both severe ARA and severe neurotoxic envenoming. - 5 patients developed dyspnea without wheezing – a feature of both anaphylaxis and envenoming. - 2 patients developed restlessness with increasing neurotoxicity scores.	Failure to recognize ARA led to continued antivenom administration (which can exacerbate ARA), delayed adrenaline treatment, and death in multiple patients.	Not statistically tested; identified as a major clinical challenge by authors.	Clinicians should have a low threshold for treating ARA when the clinical picture is not clear-cut, and anaphylaxis cannot be excluded. "Danger signs" requiring urgent assessment include sinus bradycardia, relative bradycardia and hypotension, dyspnea alone or with wheezing, hoarse voice, restlessness, and non-specific acute clinical deterioration.
Xing et al., 2018 ^{xiv}	Epinephrine underuse and delayed administration	Only 68% of pediatric DIA patients received epinephrine at all, and only 54% received it as initial therapy. This suggests that a significant proportion of children with anaphylaxis either did not receive the first-line drug or received it after other treatments were given (corticosteroids). Delayed epinephrine is associated with poorer outcomes.	Database review of documented treatments; comparison of initial vs. non-initial epinephrine administration.	- Any epinephrine: 68% - Epinephrine as initial therapy: 54% - No epinephrine at all: 32% - Epinephrine but NOT initial (delayed): 41% of all cases	Delayed epinephrine is associated with increased risk of hospitalization and poorer outcomes (cited from literature).	Not statistically tested for outcome; however, the authors note the discrepancy between guidelines and practice.	"Clinicians should use epinephrine as a first-line therapy as soon as they make a diagnosis of anaphylaxis since delayed epinephrine administration is associated with a risk of hospitalization and poor outcomes."
Cohen et al., 2018 ^{xv}	Misdiagnosis of anaphylaxis (especially in patients without prominent respiratory symptoms)	Despite using NIAID/FAAN criteria, 61% of patients who met the criteria for anaphylaxis were not correctly diagnosed. Misdiagnosed patients had significantly lower rates of breathing difficulties (47.8% vs. 64.8%) and wheezing (11.7% vs. 31%). Physicians appear to rely heavily on respiratory symptoms to diagnose anaphylaxis, missing cases in which gastrointestinal or cutaneous symptoms predominate.	Comparison of clinical features between patients correctly diagnosed as anaphylaxis vs. those misdiagnosed (based on NIAID/FAAN criteria applied retrospectively).	- Overall correct diagnosis rate: 38% (74/193) - Misdiagnosis rate: 62% (119/193) - Breathing difficulties: correctly diagnosed 64.8% vs. misdiagnosed 47.8% (p = 0.03) - Wheezing: correctly diagnosed 31% vs. misdiagnosed 11.7% (p = 0.001)	Delayed or omitted IM epinephrine; failure to provide appropriate discharge instructions (allergist referral, AAI prescription).	Yes – Breathing difficulties (p = 0.03) and wheezing (p = 0.001) were significantly associated with correct diagnosis.	"Physicians must be familiar with the definitions of anaphylaxis and updated treatment guidelines to avoid misdiagnosis. Computerized support should be planned to assist them." Emphasis on recognizing anaphylaxis even in the absence of prominent respiratory symptoms.
Dubus et al., 2018 ^{xvi}	Intuitive adaptation of epinephrine use to anaphylaxis severity	Pediatricians were significantly more likely to administer epinephrine to patients with severe anaphylaxis (Grade III) than to those with moderate anaphylaxis (Grade II). Only 22.3% of Grade II patients received epinephrine, compared to 84.8% of Grade III patients (OR = 19.05). This suggests that clinicians reserve epinephrine for the most severe cases, contrary to guidelines that	Retrospective chart review; anaphylaxis severity classified by Ring and Messmer grade; comparison of epinephrine use between grades.	- Grade II (moderate): 22.3% received epinephrine - Grade III (severe): 84.8% received epinephrine - Grade II (moderate): 77.7% did NOT receive epinephrine - Grade III (severe): 15.2% did NOT receive epinephrine	Underuse of epinephrine in moderate anaphylaxis, potentially leading to progression to more severe reactions, biphasic reactions, and poorer outcomes.	Yes – Grade III vs. Grade II: OR = 19.05 (7.05–54.10), p < 0.001.	"This medical behavior ascertainment may be in part explained by the delay between the ED admission/management and the anaphylactic episode onset, and maybe also by a relative fear of the epinephrine side effects." Education should emphasize that epinephrine is indicated for ALL anaphylaxis, not just

		recommend IM epinephrine for all cases of anaphylaxis, regardless of severity.					severe cases. Auto-injector devices may enhance epinephrine use.
Lee et al., 2018 ^{xvii}	Prolonged recommended observation period (8 hours) leading to high admission rates	The initial 2011 clinical pathway recommended 8 hours of observation after anaphylaxis, resulting in the majority of patients (58.2%) being admitted to the ED observation unit or the inpatient unit. This was based on variable literature recommendations (4–24 hours) and a conservative approach. Prolonged observation contributed to unnecessary hospitalizations, increased costs, missed school/work, and caregiver burden.	Comparison of admission rates before and after pathway revision using ICD-coded anaphylaxis cases.	- Baseline admission rate: 58.2% (106/182) - Post-intervention admission rate: 25.3% (65/257) - Reduction: ~60% (p < 0.0001)	Unnecessary hospitalizations, increased healthcare costs, social/family burden, and use of inpatient resources.	Yes – Pathway revision (4-hour observation) significantly reduced admission rate (p < 0.0001).	"Decreasing the recommended length of observation from 8 to 4 hours resulted in a near 60% reduction in the average rate of admission... A similar pathway could be used at other organizations to promote the efficient care of anaphylaxis patients and help prevent unnecessary hospitalizations."
Wang et al., 2017 ^{xviii}	Epinephrine underuse and delayed administration	Only 59.5% of DIA patients received epinephrine at all, and only 74.1% of those received it as initial therapy. This means 40.5% received no epinephrine, and 25.9% received it after other treatments (i.e., delayed). Clinicians were more likely to administer epinephrine to patients with respiratory symptoms (wheezing, respiratory arrest), suggesting that epinephrine is reserved for more severe presentations rather than used for all anaphylaxis.	Database review of documented treatments; comparison of epinephrine and non-epinephrine groups.	- Any epinephrine: 59.5% - Epinephrine as initial therapy: 74.1% (of those receiving epinephrine) - No epinephrine at all: 40.5% - Epinephrine but NOT initial (delayed): 25.9%	Delayed epinephrine is associated with poor outcomes and fatality. Among death cases in the epinephrine group, 55.9% experienced respiratory/cardiac arrest before epinephrine administration, and 44.1% did not receive it as initial treatment.	Yes – Wheezing (OR 1.96), respiratory arrest (OR 3.67), and diffuse urticaria (OR 1.43) significantly predicted epinephrine receipt.	"The importance of a timely administration of epinephrine should be stressed in DIA management." "Educational training for health care professionals on the appropriate use of epinephrine in managing anaphylactic reactions is suggested."
Kawano et al., 2017 ^{xix}	Clinician reluctance to use epinephrine in older patients (underuse)	Older patients with anaphylaxis were significantly less likely to receive epinephrine than younger patients (36.1% vs. 60.8%, OR 0.3). This trend was most pronounced among the oldest patients (only 16% of those >70 years received epi vs. 57.9% of those 17–29 years). Clinicians may be reluctant due to fear of cardiovascular complications in older patients with cardiac risk factors.	Retrospective chart review; comparison of epinephrine administration rates between age groups.	- Epinephrine use: Older 36.1% vs. Younger 60.8% - Age trend: 17–29 yrs 57.9%, 30–39 yrs 50.0%, 40–49 yrs 38.9%, 50–59 yrs 22.4%, 60–69 yrs 29.6%, >70 yrs 16.0% (p < 0.01) - Omission: Older 63.9% vs. Younger 39.2%	Missed opportunity for life-saving treatment; older patients had higher hospitalization rates (4.1% vs. 0.5%) and higher 7-day allergy-related ED revisits (10.7% vs. 3.2%), which may be related to under-treatment.	Yes – Age was significantly associated with lower epinephrine use (p < 0.01 for trend; OR 0.3).	"These data assist clinicians by highlighting missed opportunities for epi administration in older patients with anaphylaxis, as well as supporting the safety of intramuscular epi. Our data support current recommendations for administration of IM epi to anaphylactic patients including those who are older ages."
Campbell et al., 2016 ^{xx}	Fear of dosing errors with manual epinephrine administration	Providers rated manual IM injection as having significantly higher risk of dosing errors compared to autoinjectors. Factors contributing to this perception include: unfamiliarity with appropriate doses, miscalculation of weight-based doses, confusion between 1:1000 and 1:10,000 formulations, miscommunication between the ordering provider and the administering nurse, and the high-stress context of anaphylaxis management. Epinephrine use in the ED is relatively infrequent, leading to lack of familiarity.	Survey question: "Rate the risk of dosing errors" on a 0–100 scale for each method.	- Autoinjector mean risk score: 20.1 (SD 19.8) - Manual injection mean risk score: 67.8 (SD 22.0) - p < 0.001 - 87% of respondents had experience with epinephrine administration in the ED	Dosing errors can lead to under-treatment (ineffective response) or overdose (cardiovascular complications, arrhythmias, hypertension). Fatalities associated with epinephrine are often due to improper dosages.	Yes – Manual injection rated significantly higher for risk of dosing errors (p < 0.001).	"Autoinjector use may reduce the risk of dosing errors... and reduce barriers to epinephrine administration for anaphylaxis management in the ED." Manual dosing training should be reinforced for providers who prefer that method.
Drupad & Nagabushan, 2015 ^{xxi}	Poor knowledge of adrenaline as first-line treatment for anaphylaxis	Only 56.9% of healthcare providers/students identified adrenaline as the first-line drug for anaphylaxis. This knowledge gap was most pronounced in nursing students (35.3% correct) compared to medical students (67.6%) and interns (60.3%).	Questionnaire (question #2: "What is the first line of drug for anaphylaxis?")	- Total correct: 56.9% (151/265) - Medical students: 67.6% (67/99) - Interns: 60.3% (61/101) - Nursing students: 35.3% (23/65) - Knowledge gap: 43.1% did NOT know adrenaline is first-line	Failure to administer life-saving first-line therapy in anaphylaxis; reliance on suboptimal treatments.	Yes – Significant difference between groups (p < 0.001).	"Proper initial training and periodic review and reinforcement of the steps in the treatment of anaphylaxis is necessary for all health care providers to achieve better patient care."
Özmen et al., 2015 ^{xxii}	Insufficient anaphylaxis training and knowledge decay	Only 50.6% of healthcare providers had received training on anaphylaxis. Among those trained, 41.7% had training more than 2 years ago. Knowledge decay over time was evident: those who correctly identified the IM route had a mean time since training of 2.8 ± 3.5 years, while those who did not had longer intervals. Residents had the most recent training (53% ≤2 years), while specialists and auxiliary staff had older training.	Self-reported training history and time since training; comparison with knowledge of IM route.	- Any anaphylaxis training: 50.6% - Training ≤2 years: 58.3% (of trained) - Training 3–5 years: 20.2% (of trained) - Training ≥6 years: 21.5% (of trained) - Correct IM route in trained group: 73.8% - Correct IM route in untrained group: 39.0% (p = 0.000)	Poor knowledge of the correct route of adrenaline administration; delayed or incorrect treatment of anaphylaxis.	Yes – Training significantly associated with correct IM route knowledge (p = 0.000).	"Post-graduate training is required for the treatment of anaphylaxis... All healthcare providers should be trained on the use of epinephrine and prescribing epinephrine auto-injector." Regular refresher training is essential due to knowledge decay.
Plumb et al., 2015 ^{xxiii}	Poor knowledge of correct dose and route of adrenaline in anaphylaxis	Despite 100% of junior doctors recognizing the need for adrenaline in true anaphylaxis, only 34% knew the correct dose (0.5 mg of 1:1000) AND route (IM). A dangerous 25% would use IV	Case scenario (Case 1: true anaphylaxis) with answer grid for dose/route of adrenaline.	- Correct dose + route: 34% (23/68) - Correct IM route (any dose): 74% (50/68) - Inappropriate IV route: 25% (17/68) - Incorrect route (SC/nebulized): 1% (1/68)	Incorrect dosing (underdosing/overdosing) and incorrect route (IV instead of IM) can lead to ineffective treatment or life-	Yes – Significant improvement from 2002 (13% to 34%, p = 0.0029), but still unacceptably low.	"Remedial action to improve knowledge regarding the recognition and management of anaphylaxis needs to be provided through Foundation

		adrenaline, which is associated with iatrogenic deaths. This represents a significant knowledge gap in the practical administration of the life-saving drug.			threatening complications (arrhythmias, severe hypertension).		Program training and at medical school."
AAI: Adrenaline Auto-Injector; ACE-I: Angiotensin-Converting Enzyme Inhibitor; ALS: Advanced Life Support; ARA: Antivenom-Related Anaphylaxis; BPD: Beijing Pharmacovigilance Database; BST: Baseline Serum Tryptase; CAE: Cardiovascular Adverse Events; CI: Confidence Interval; COVID-19: Coronavirus Disease 2019; CVS: Cardiovascular System; DIA: Drug-Induced Anaphylaxis; EAI: Epinephrine Autoinjector; ED: Emergency Department; EMR: Electronic Medical Record; EMS: Emergency Medical Services; ER: Emergency Room; ESI: Emergency Severity Index; F1: Foundation Year 1; F2: Foundation Year 2; FARE: Food Allergy Research and Education; GI: Gastrointestinal; ICD-10: International Classification of Diseases, Tenth Revision; ICU: Intensive Care Unit; IHD: Ischemic Heart Disease; IM: Intramuscular; ISS: In Situ Simulation; IV: Intravenous; LST: Latent Safety Threat; MBBS: Bachelor of Medicine, Bachelor of Surgery; MET: Medical Emergency Team; NA: Not Applicable; NIAID/FAAN: National Institute of Allergy and Infectious Diseases / Food Allergy and Anaphylaxis Network; NR: Not Reported; NS: Not Specified; OR: Odds Ratio; PED: Pediatric Emergency Department; PICU: Pediatric Intensive Care Unit; QI: Quality Improvement; SAE: Serious Adverse Event; SC: Subcutaneous; SD: Standard Deviation; SHO: Senior House Officer; TASMCI: Tel Aviv Sourasky Medical Centre; TCM: Traditional Chinese Medicine; TGH: Tampa General Hospital; TS: Translational Simulation; VIA: Venom-Induced Anaphylaxis.							

Table 5: JBI Checklist for Analytical Cross-Sectional Studies (n = 10)

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Bülbul et al., 2024	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Kaya & Alaylar, 2024	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Ateş & Sahiner, 2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Wijekoon et al., 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pimentel-Hayashi et al., 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Lauraa et al., 2019	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Campbell et al., 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Drupad & Nagabushan, 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Özmen et al., 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Plumb et al., 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Q1: Were the criteria for inclusion in the sample clearly defined?; Q2: Were objective, standard criteria used for measurement of the condition?; Q3: Was the exposure measured in a valid and reliable way?; Q4: Were the outcomes measured in a valid and reliable way?; Q5: Were confounding factors identified?; Q6: Were strategies to deal with confounding factors stated?; Q7: Was appropriate statistical analysis used?; Q8: Were the study subjects and the setting described in detail?								

Table 6: Risk of bias evaluation using the Newcastle-Ottawa Scale (NOS) (n = 8)

Studies	Selection				Comparability	Outcome			Total Score
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
Ho et al., 2024	✓	✓	✓	✓	*	✓	✓	✓	8/9
Xing et al., 2018	✓	✓	✓	✓	*	✓	✓	✓	8/9
Wang et al., 2017	✓	✓	✓	✓	✓✓	✓	✓	✓	9/9
Dubus et al., 2018	✓	✓	✓	✓	*	✓	✓	✓	8/9
Cohen et al., 2018	✓	✓	✓	✓	*	✓	✓	✓	8/9

Krmpotic et al., 2019	✓	NA	✓	✓	NA	✓	✓	✓	6/9
Francuzik et al., 2020*	✓	✓	✓	✓	✓✓	✓	✓	✓	9/9
Kawano et al., 2017	✓	NA	✓	✓	NA	✓	✓	✓	6/9
Domains and questions: Selection: Q1: Representativeness of the exposed cohort, Q2: Selection of the non-exposed cohort, Q3: Ascertainment of exposure, Q4: Outcome was not present as baseline. Comparability: Q5: Control for the most important factor and Control for any additional factor. (* = control for one factor, ✓✓ = control for two or more factors). Outcome: Q6: Assessment of outcome. Q7: Adequate follow-up period for outcome, Q8: Adequacy of follow-up of cohorts.									
*Case-control study (Francuzik et al., 2020) – NOS for case-control studies assesses Selection, Comparability, and Exposure domains. Note: NA = Not applicable (single-arm descriptive cohort with no comparator group).									

Table 7: MMAT Assessment of Quality Improvement Study (n = 1)

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	✓			
	S2. Do the collected data allow to address the research questions?	✓			
	<i>Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.</i>				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				

4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?	✓			
	4.2. Is the sample representative of the target population?		✓		
	4.3. Are the measurements appropriate?	✓			
	4.4. Is the risk of nonresponse bias low?		✓		
	4.5. Is the statistical analysis appropriate to answer the research question?	✓			
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	✓			
	5.2. Are the different components of the study effectively integrated to answer the research question?		✓		
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?		✓		
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?		✓		
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	✓			