

Prevalence of Errors in Anaphylaxis in Kids (PEAK): A Multi-Center Simulation-Based Study

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No financial support was obtained for this study. The authors have no conflicts of interest relevant to this manuscript to disclose.

Word count, abstract: 272

Word count, text: 3154

46 **Abstract**

47 **Background:** Multi-institutional, international practice variation of pediatric anaphylaxis
48 management by healthcare providers has not been reported.

49 **Objective:** Characterize variability in epinephrine administration for pediatric anaphylaxis
50 across institutions, including frequency and types of medication errors.

51 **Methods:** A prospective, observational, study using a standardized in situ simulated anaphylaxis
52 scenario was performed across 28 healthcare institutions in six countries. The on-duty
53 healthcare team was called for a child (patient simulator) in anaphylaxis. Real medications and
54 supplies were obtained from their actual locations. Demographic data about team members,
55 institutional protocols for anaphylaxis, timing of epinephrine delivery, medication errors, and
56 systems safety issues discovered during the simulation were collected.

57 **Results:** Thirty-seven in situ simulations were performed. Anaphylaxis guidelines existed in 41%
58 (15/37) of institutions. Teams used a cognitive aid for medication dosing 41% (15/37) of the
59 time and 32% (12/37) for preparation. Epinephrine auto injectors (EAI) were not available in
60 54% (20/37) of institutions and were used in only 14% (5/37) simulations. Median time to
61 epinephrine administration was 95 seconds (IQR 77, 252) for EAI and 263 seconds (IQR 146,
62 407.5) for manually prepared epinephrine ($p=.12$). At least one medication error occurred in
63 68% (25/37) of simulations. Prior nursing experience with epinephrine administration for
64 anaphylaxis was associated with fewer preparation ($p=.04$) and administration ($p=.01$) errors.
65 Latent safety threats (LSTs) were reported by 30% (11/37) of institutions, more than half of
66 these (6/11) involved a cognitive aid.

67 **Conclusion and Relevance:** A multicenter, international study of simulated pediatric
68 anaphylaxis reveals: 1) variation in management between institutions in usage of protocols,

69 cognitive aids, and medication formularies, 2) frequent errors involving epinephrine, 3) LSTs
70 related to cognitive aids among multiple sites.

71 **Highlights box: (35 words)**

72 What is already known about this topic? Factors impacting patient safety in pediatric
73 anaphylaxis management across healthcare institutions are unknown.

74 What does this article add to our knowledge? Preventable medication errors involving
75 epinephrine are more prevalent than previously recognized.

76 How does this study impact current management guidelines? Variability for use of protocols,
77 cognitive aids, and medication formularies exist.

78 **Keywords:** simulation, anaphylaxis, medication error, autoinjector, epinephrine

79 **Abbreviations:** EAI (Epinephrine auto injector), EI (Epinephrine injection), IM (Intramuscular), IV
80 (Intravenous), ED (Emergency department), ICU (Intensive care unit), LST (Latent safety threat),
81 PI (Principal investigator), IQR (Interquartile range), WAO (World Allergy Organization)

82

83 **Introduction**

84 Anaphylaxis is a severe, life threatening, systemic allergic reaction that is rapidly
85 progressive and potentially fatal.(1) In the United States, estimated lifetime prevalence is at
86 least 1.6% with an increasing incidence globally and in children. (2) Rapid deterioration and
87 death can occur within minutes from the onset of symptoms, and prompt reversal can occur
88 after administration of intramuscular (IM) epinephrine.(3-4) Delays in epinephrine treatment
89 increase the risk of adverse outcomes including mortality.(5,6) The recommended dose and
90 route for treating pediatric anaphylaxis is 0.01 mg/kg administered IM in the vastus lateralis
91 muscle.(1) IM epinephrine is given via an epinephrine injection (EI) or an epinephrine auto-
92 injector (EAI). EI requires that the epinephrine dose be calculated and drawn up from a vial into
93 a syringe whereas EAIs deliver a single dose of epinephrine via a disposable, pre-filled,
94 automatic injection device.

95 A review of the literature from 1990-2015 by Cohen et al. found an extensive list of
96 hazards involving epinephrine use for anaphylaxis.(7) However, only a small number of single-
97 center, observational and descriptive studies have reported on errors by healthcare providers
98 associated with EI compared to EAI delivery.(8, 9) Knowledge and skill gaps in the use of the EAI
99 among healthcare providers have been identified. (8,10) There is no published multi-center
100 overview of clinical or simulation research comparing the prevalence of errors with EI versus
101 EAI in the management of anaphylaxis by healthcare providers.(8)

102 Randomized controlled trials of anaphylaxis management are currently not feasible
103 given the life-threatening nature of this condition. Additionally, anaphylaxis has an
104 unpredictable incidence with varied presentations across different clinical disciplines

105 throughout healthcare systems. Standardized in situ simulation-based assessments have been
106 used to investigate quality of care across a spectrum of healthcare systems without the
107 unpredictability, variability and higher stakes inherent to studying care delivered to actual
108 patients.(11,12) In situ simulation research involves bringing the simulator into the clinical
109 environment to assess the quality of care delivered by intact care teams using real-world
110 equipment.(13) Potential safety concerns, or latent safety threats (LSTs), are often exposed. We
111 utilized simulation-based assessments to examine management of anaphylaxis in pediatric
112 patients across different healthcare institutions.

113 Our primary objective was to characterize variability in practices across institutions
114 related to epinephrine administration, the frequency and types of epinephrine medication
115 errors, and to explore factors associated with errors. We hypothesized that errors would be
116 more likely to occur with EI than with EAI and sought to investigate the point prevalence of
117 errors in anaphylaxis management in children during in situ simulation.

118

119 **Methods**

120 *Study Design*

121 This was a prospective, multicenter, international simulation-based study of the
122 management of pediatric anaphylaxis at various patient care locations in healthcare
123 institutions. We report our study in accordance with reporting guidelines for simulation-based
124 research extensions for the STROBE statement.⁽¹⁴⁾ Recruitment of a convenience sample
125 began March 2018 via email and social media (Twitter) advertisement directed to members of
126 the International Network for Simulation-based Pediatric Innovation, Research and Education
127 (INSPIRE), the Pediatrics section of the Society for Simulation in Healthcare (SSH) and the
128 International Pediatric Simulation Society (IPSS). Healthcare institutions that care for pediatric
129 patients capable of performing a single in situ anaphylaxis simulation scenario within a six-
130 month period were included. Multiple simulations from a single institution were allowed if they
131 were performed on different clinical units with unique healthcare teams. Each site principal
132 investigator (PI) obtained local institutional review board approval for exempt status.
133 Institutions unable to obtain approval and accomplish the simulation within the specified time
134 were excluded. As these simulations were performed in the real work environment, feasibility
135 depended on competing clinical demands, thus, a six-month period allowed flexibility in
136 scheduling the simulation.

137 *Setting*

138 Twenty-eight institutions from six countries (Israel, Spain, Lebanon, Germany, New
139 Zealand, and 16 states in the United States) submitted data from 37 simulated events that
140 occurred May 4 through November 20, 2018. Almost all simulations (n=36) were performed in

141 tertiary or quaternary care academic children's hospitals, ranging in size from 30 to over 300
142 pediatric beds, and 81% (n=30) cared solely for pediatric patients. Only one simulation was
143 performed in the emergency department (ED) of a community hospital. Three institutions (11%)
144 performed the scenario in more than one clinical location. Simulations took place most often in
145 the ED (38%), followed by the inpatient non-oncology floor (30%) and the intensive care unit
146 (ICU) (16%). Other locations included an infusion center, procedural sedation unit and oncology
147 clinic (see Table I).

148 *Simulation Scenario*

149 The scenario, created by a multidisciplinary group of simulation experts, involved a five
150 year-old, 20 kilogram (kg) child with a history of peanut and drug allergies who has an
151 anaphylactic reaction after receiving an intravenous (IV) medication. The human patient
152 simulator manikin had an IV catheter in place at the start of the simulation and demonstrated
153 clinical symptoms of anaphylaxis as allowed by the individual simulator. The scenario ended
154 after epinephrine was administered. The procedures for selection of the in situ environment
155 and delivery of the simulation (including pre-simulation script and post-simulation debriefing)
156 were standardized (see eMethods in the Online Repository). The following components of the
157 simulation were site specific and not standardized: brand of simulator, IV medication causing
158 the allergic reaction, use of video recording, pre-announcement of the simulation to
159 participants, team composition, and team leader.

160 Site PIs were directed to choose an in situ environment that would allow the on duty
161 healthcare team to respond. The scenario started with calling the team for help with a patient
162 in anaphylaxis, thus obviating the need to recognize and diagnose an allergic drug reaction.

163 Participants managed the anaphylaxis scenario as they would in real life. Real medications and
164 supplies for the administration of epinephrine were obtained from their authentic locations in
165 the clinical space. Immediately after the simulation, the team participated in a post-
166 performance debriefing focused on adherence to anaphylaxis guidelines, drug dosing and
167 administration errors, as well as the identification of systems, patient or staff safety concerns.

168 *Data collection*

169 Demographic data were obtained to characterize the simulation team and understand
170 the local standards for anaphylaxis and epinephrine administration. Data collected using a
171 standardized form included: site demographics (availability of EAI and in which locations,
172 existence of local anaphylaxis guidelines), dose, concentration, route, correct site of
173 administration and the timing of epinephrine delivery. This data was provided by the site PI.
174 Time dependent metrics were verified after reviewing video recordings when available. Data
175 was entered into a central server, associated with the SSH International Simulation Data
176 Registry, over a web-based, password protected collection tool.

177 Published anaphylaxis guidelines for dosing were used to define correct dose, and for a
178 20 kg child this is the 0.15 milligram (mg) autoinjector or 0.01 mg/kg, i.e. 0.2 mg.(1) The correct
179 concentration is 1:1000 or 1 mg/milliliter (ml) for EI. The correct route is IM. It was also
180 considered a separate error if specifics on dose, concentration or route were not prescribed
181 (i.e. the practitioner only said "Let's give epi."). The site PI was instructed to position
182 themselves so they could observe the medication preparation process to ensure correct volume
183 and concentration was drawn up. An administration error for EAI use was recorded if the device
184 was not held in place for 3 seconds. (15) Medication errors in prescribing (dose, concentration,

185 route), preparation (dose and concentration) or administration (route or location), as well as
186 safety issues discovered during the simulation were collected. An error in prescribing that was
187 prepared and given as incorrectly prescribed could potentially be counted as 3 separate errors
188 (one for prescribing, one for preparation and one for administration). This was because there
189 was opportunity for the error to be caught and corrected at each of those time points.

190 *Statistical Analysis*

191 Data were summarized using frequency and percentage for categorical variables and
192 medians with interquartile range (IQR) for continuous. Demographic and simulation team
193 factors associated with medication errors were evaluated using odds ratio (OR) and 95%
194 confidence intervals (CI) were assessed using univariate logistic regression with Firth's
195 penalized likelihood for small sample size. Differences in time to order and time to
196 administration of epinephrine were assessed using Wilcoxon rank sum tests. Primary analysis
197 includes all simulation events from each site. Within-site correlation was not accounted for due
198 to limitations of sample size. Sensitivity analysis using one simulation event per site was
199 performed and results were substantively similar (not shown). All analyses were conducted
200 using SAS 9.4 (SAS Institute, Cary, NC) with two-sided p-values <0.05 considered statistically
201 significant.

202

203 **Results**

204 Table I lists simulation site and team characteristics. Teams included at least one nurse and
205 practitioner (physician or advanced practice nurse/physician assistant) for all simulations. An
206 EAI was used in five (14%) simulations. Only 46% (17/37) of simulations reported having an EAI
207 available somewhere in their institution, not necessarily throughout all locations. The sites in
208 Israel, Lebanon and New Zealand do not have any epinephrine autoinjectors available in their
209 hospitals. The sites in Spain used Jext[®] and the United States and Germany used EpiPen[®].
210 Institutions using EAI as first-line therapy in some, but not all, areas of the hospital stocked
211 them mostly within medication dispensing units (47%) and in radiology (41%). Table E1 in the
212 online repository has specifics about which locations EAI are available as first line therapy and
213 how they are stored.

214 *Epinephrine errors*

215 At least one error was made in 68% (25/37) of simulations. Of the five events using EAI:
216 40% (n=2) of errors were due to over-dosing, 20% (n=1) included an error in administration (i.e.
217 injection duration less than 3 seconds per recommendations).(15) Of the 32 events utilizing EI:
218 53% (n=17) involved an error only in prescribing, 16% (n=5) had an error only in preparation
219 and 9% (n=3) had separate errors made during both prescribing and preparation. Figure 1
220 shows the progression and propagation of EI and EAI errors. In two events, the medication
221 dose, concentration, and route (i.e., all 3 parameters) were not specified. Epinephrine was
222 ordered to be administered IV in 24% (n=9). A specific intramuscular location for giving
223 epinephrine was not specified in 43% (16/37), although we did not count this as an error.
224 Figure 2 is a Pareto chart showing types of errors in descending order of frequency. There were

225 five “near miss” events involving a prescribing error that was caught and did not reach the
226 patient.

227 *System-level safety hazards*

228 Nearly one-third of sites (n=11) discovered one or more safety hazards during
229 simulations. More than half of these (n=6, 54%) involved problems with usability or design of a
230 cognitive aid, such as missing anaphylaxis dosing, dosing only listed in milligrams and not
231 milliliters, cardiac arrest dosing used, and conflicting dosing recommendations. Table E2 in the
232 Online Repository contains additional details related to latent safety threats.

233 *Risk factors for errors*

234 Estimated odds ratios for presence of at least one medication error by site and team
235 characteristics are shown in Table II. Teams that had a nurse with prior experience giving
236 epinephrine for anaphylaxis were significantly associated with events without medication
237 preparation errors (OR = 0.2, 95% CI = [0.04, 0.93], p = .04) and with events without
238 administration errors (OR = 0.13, 95% CI = [0.03, 0.62], p = .01). There were an insufficient
239 number of sites using EAI to compare error rates with EI in a meaningful way.

240 Table III compares times from medication ordering to administration for EI to EAI use.

241 Although the difference was not statistically significant, the median time to administration
242 between the two forms of epinephrine was over 2.5 minutes longer for EI. Time to prepare the
243 EAI dose was significantly shorter (p=.02) than for EI.

244

245 **Discussion:**

246 This is the first, multi-center prospective, observational study to investigate the
247 variability and vulnerabilities of pediatric anaphylaxis management in healthcare institutions,
248 many of which are academic, pediatric medical centers. The primary objective was to
249 characterize variability in practices across institutions related to epinephrine administration,
250 the frequency and types of epinephrine medication errors, and to explore factors associated
251 with errors. The key results of this study are that, in this cohort, errors in anaphylaxis
252 management are common in clinical sites specialized in pediatric acute or critical care. High
253 rates of both prescribing errors and IV administration were observed during the management
254 of a simulated child with anaphylaxis. The use of an EAI and the presence of an anaphylaxis
255 guideline have the potential to improve safety but both were uncommon in this cohort and not
256 associated with reduced error. (7,16) Prior nursing experience giving epinephrine for
257 anaphylaxis was the only protective factor against preparation and administration errors.

258 At least one medication error was made in 68% of events. Medication dosing in
259 pediatrics is weight-based and more complex than for adults, thus most pediatric medication
260 errors occur during the prescribing stage and are related to dosing errors (17,18). In this study,
261 the most common errors centered on incorrect prescribing of epinephrine, which occurred with
262 both EAI and EI, followed by errors in EI preparation. Prescribing errors that were not caught
263 resulted in the administration of epinephrine via the IV route in 24% of cases that used EI. The
264 errors noted in this cohort pose a significant potential for harm due to the narrow therapeutic
265 index and systemic cardiovascular side effects of epinephrine.(19) Variations in indications for
266 epinephrine use, concentration, routes of administration, commercial delivery devices and

267 nomenclature to express dosages and concentrations all contribute to potential for error. (20-
268 22)

269 Standardization of the administration of epinephrine through the use of EAI or storing
270 pre-filled syringes of epinephrine specifically designated for IM use in anaphylaxis have the
271 potential to reduce errors.(7,21) Only two sites reported EAI as first line therapy throughout
272 their institution whereas an additional 15 sites have EAI available in select locations. Only 29%
273 (5/17) of teams with access to an EAI chose to use one to respond to a simulated case of
274 anaphylaxis. Fifty-four percent of sites do not have EAI available at their institution at all. The
275 small number of institutions using EAI precluded identification of a statistically significant
276 difference in error rates compared with EI. We observed that EAI use was associated with an
277 almost 3-minute reduction in the median time to administer epinephrine compared to the
278 median time of 4.4 minutes to administration of EI. This delay in treatment is concerning as
279 anaphylaxis can lead to death in less than five minutes. (3) Increased costs, drug shortages and
280 device recalls can be barriers to the standardization of EAI use for anaphylaxis within healthcare
281 systems.(23) As these barriers may not change quickly, it is important to have a mechanism to
282 examine prevalence of epinephrine errors across institutions, understand their causes, and
283 share successful risk mitigation plans in order to prevent patient harm.

284 Fewer than half the sites identified having an anaphylaxis protocol. The World Allergy
285 Organization (WAO) guidelines recommend having a written protocol for management of
286 anaphylaxis.(16) A clinical guideline is of particular use for anaphylaxis, an event that is low
287 frequency per practitioner, and may cause confusion to practitioners about appropriate

288 practice.(24,25) The presence of an identified guideline was not significantly associated with
289 decreased frequency of errors in this study.

290 There was low overall use of cognitive aids in this study with only 41% of simulation
291 teams utilizing aids for prescribing and 32% for preparing medication doses. Cognitive aids,
292 which may include checklists, flowcharts, and posters, can improve the speed and accuracy of
293 task completion, including improving outcomes and decreasing the number of errors in
294 emergency situations.(26) There was no significant association between cognitive aid use and
295 decreased frequency of error in our study.

296 Cognitive aids are widely underused as they require good design, easy access, and a
297 supportive systemic environment.(27) More than half of the latent safety threats reported in
298 this study involved errors found in institutional cognitive aids themselves. Hazards included
299 missing anaphylaxis dosing on the aids, dosages listed in milligrams but not milliliters (thus
300 requiring hand-calculation of the volume), practitioners selecting cardiac arrest instead of
301 anaphylaxis dosages, conflicting dosage recommendations, and an outdated cognitive aid with
302 the incorrect suggested route (subcutaneous) of administration. In these instances, the design
303 of the cognitive aid itself created a vulnerability for errors.

304 Prior nursing experience administering epinephrine for anaphylaxis was significantly
305 associated with simulations that were free of medication preparation and administration
306 errors. In emergent situations, nurses are the ones who typically prepare and administer
307 medications and thus play a key role in catching and preventing prescribing errors. (28)
308 Previously reported knowledge and experience gaps of the prescribing practitioner as well as

309 the medication nurse may be important contributors to error during management of
310 anaphylaxis and key targets for intervention.(29,30)

311 We have several recommendations to improve anaphylaxis management and patient
312 safety based on our findings. Systems-based interventions could include establishment,
313 dissemination and education of a written guideline or protocol for anaphylaxis management as
314 recommended by the WAO. Additionally, institutions should regularly review their cognitive
315 aids to ensure accessibility, clarity and accuracy. Less than one third of institutions with EAI
316 available used them during these simulations. Use of an EAI, or having an experienced nurse on
317 site might result in decreased error rates and more timely preparation and appropriate
318 administration of epinephrine for anaphylaxis. Additional training using interprofessional
319 anaphylaxis simulations could focus on 1) awareness of the high risk of medication errors, 2)
320 familiarization with cognitive aids 3) use of aids for preparation and administration of
321 epinephrine and 4) exploration of barriers to EAI use in institutions with EAI available.

322 This study has several limitations. Limitations intrinsic to simulation-based studies
323 include the fact that simulated scenarios may not fully mimic real life, which may impact the
324 speed and efficiency of health care providers' actions. To mitigate this, we used an in situ
325 simulation and instructed sites to approximate an authentic response as much as possible,
326 including use of real medications and equipment. Simulation studies run the risk of potential
327 unmeasured confounders including deviations in conducting the scenario, differences in team
328 composition, and practice variation over time. We attempted to mitigate these by using a very
329 simple, standardized scenario and limiting the time period for its performance. Generalizability
330 may be limited as this study was performed mostly in academic pediatric institutions with

331 simulation programs in North America and may not be as relevant in institutions with different
332 attributes.

333 These preliminary results should be confirmed with a larger sample. Our study was
334 underpowered to detect statistically significant differences in errors between EAI and EI.
335 However, it provides preliminary pilot data on the proportion of EAI use at institutions and the
336 error rate with EI to understand what sample size is needed for an appropriately powered
337 study.

338 **Conclusion**

339 This multicenter, international, prospective observational study of simulated pediatric
340 anaphylaxis confirms wide variability among healthcare institutions for usage of protocols,
341 cognitive aids, and medication formularies, timing of epinephrine dose delivery, and types of
342 medication errors made. Prior nursing experience with giving epinephrine for anaphylaxis was
343 significantly associated with fewer preparation and administration errors. There was an
344 unexpectedly low rate of EAI use, and not all teams with access to EAIs used them.

345

346 **Acknowledgements**

347 The authors would like to acknowledge the contributions of the International Network for
348 Simulation-Based Pediatric Innovation, Research, & Education (INSPIRE) who have helped to
349 shape this project and the International Meeting for Simulation in Healthcare for providing
350 conference meeting space.

351

352 Group information: The International Network for Simulation-Based Pediatric Innovation,
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Journal Pre-proof

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460 Figure 1: Pathways for error propagation during 32 simulation events using manually drawn up
461 epinephrine (1a) and five events with epinephrine autoinjectors (1b). Simulation-discoverable
462 medication errors and opportunities for correction differ between these formulations. Rx =
463 prescribed, Med Prep= medication preparation, Admin = administration, Pt = patient, Tx =
464 treatment

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466 Figure 2: Pareto chart with decreasing frequency of epinephrine errors from 37 simulations.
467 Some had more than one error. Prescribing of concentration and route and preparation errors
468 are not applicable for epinephrine autoinjectors. Admin = administration, conc = concentration,
469 IV = intravenous.

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Table I: Simulation and Site Characteristics (n=37)

	N	%
Institution Specialty		
Pediatric	30	81
Mixed (adult and pediatric)	7	19
Anaphylaxis protocol/guideline		
No/Unsure	22	59
Yes	15	41
Institution allows use of patient's EAI^a		
No/Unsure	21	57
Yes	16	43
EAI^a available somewhere in institution		
No/Unsure	20	54
Yes	17	46
EAI^a as first line therapy throughout institution (n=17)		
No	15	88
Yes	2	12
EAI^a as first line therapy in some areas of hospital (n=15)		
No/Unsure	4	27
Yes	11	73
Simulation Location		
Emergency Department	14	38
ICU ^b	6	16
Inpatient floor (Non-Oncology)	11	30
Other	6	16
Team composition:		
Resident	27	73
Fellow	9	24
Attending	11	30
Advance Practice Nurse/Physician Assistant	6	16
Pharmacist	3	8
Experience of team leader		
5 or more years of clinical experience (after residency)	7	19
Less than 5 years of clinical experience (after residency)	9	24
trainee (resident)	21	57
Nursing experience		
Never given epinephrine for anaphylaxis	12	32
Given EI ^c for anaphylaxis at least once	17	46
Given EAI ^a for anaphylaxis at least once	8	22
Cognitive aid used for prescribing	15	41

Cognitive aid used for preparation	12	32
^a EAI = Epinephrine auto injector, ^b ICU = Intensive care unit ^c EI = Epinephrine injection		

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477 Table II: Odds ratio estimates for risk factors associated with epinephrine error

Risk Factor	Prescribing Error			Preparation Error			Administration Error		
	OR ^a	95% CI ^b	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Nursing with prior epinephrine administration for anaphylaxis	0.65	(0.15,2.78)	0.56	0.2	(0.04,0.93)	0.04	0.13	(0.03,0.62)	.01
Other Location vs. Intensive Care Unit	3.18	(0.46,22.22)	.24	5.13	(0.58,45.45)	.14	1.02	(0.15,7.09)	.99
Other Location vs. Emergency Department	1.77	(0.42,7.46)	.44	2.42	(0.57,10.31)	.23	1.32	(0.29,5.99)	.72
Inexperienced team lead ^c	2.01	(0.50,8.13)	.33	2.93	(0.66,13.11)	.16	2.84	(0.55,14.71)	.21
Less than 3 anaphylaxis simulations/year	1.8	(0.47,6.90)	.39	1.11	(0.29,4.26)	.88	2.25	(0.50,10.10)	.29
No attending on team	2.62	(0.61,11.24)	.19	1.44	(0.34,6.10)	.63	2.42	(0.46,12.66)	.30
No pharmacist on team	2.1	(0.18,23.91)	.55	1.32	(0.12,15.09)	.82	3.89	(0.12,127.78)	.44
Institution has EAI ^d	3.89	(0.33,45.61)	.28	1.4	(0.12,16.43)	.79	0.41	(0.04,4.33)	.46
EAI used	0.61	(0.17,2.22)	.46	0.36	(0.09,1.41)	.14	0.79	(0.20,3.15)	.74
Cognitive aid used for dosing	1.73	(0.44,6.81)	.44	0.91	(0.24,3.51)	.89	0.87	(0.21,3.77)	.87
Cognitive aid used for preparation	0.94	(0.23,3.90)	.93	1.07	(0.28,4.44)	.92	0.21	(0.03,1.50)	.12
Protocol/Guideline	2.27	(0.59,8.82)	.24	1.93	(0.51,7.34)	.33	1.74	(0.43,6.95)	.43
Pediatric (vs mixed) institution	1.67	(0.32,8.75)	.55	0.53	(0.10,2.77)	.45	1.13	(0.19,6.61)	.89

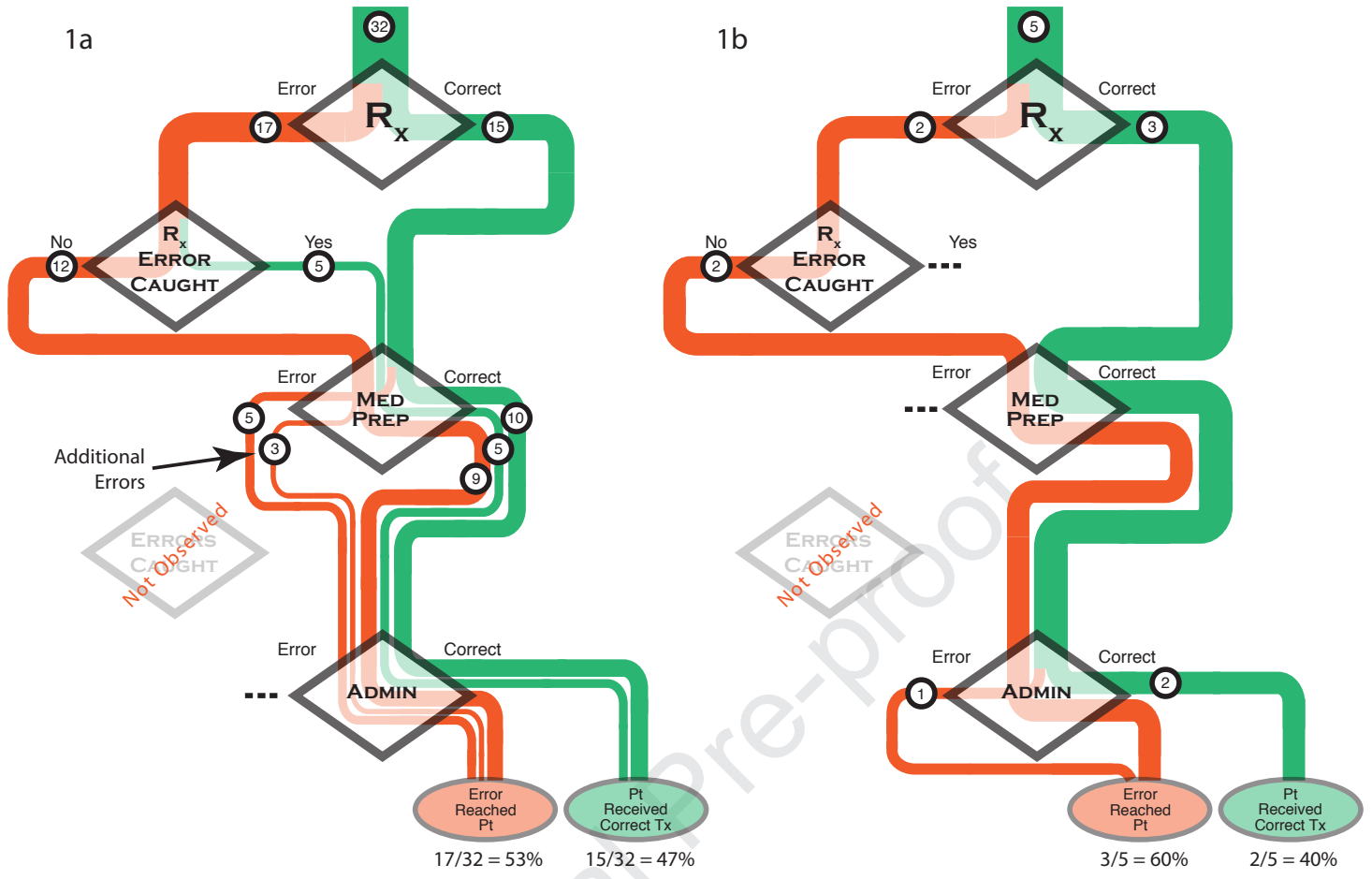
478 ^aOR = odds ratio, ^bCI = confidence interval. ^cInexperienced team lead = still in residency479 training, EAI^d = epinephrine auto injector

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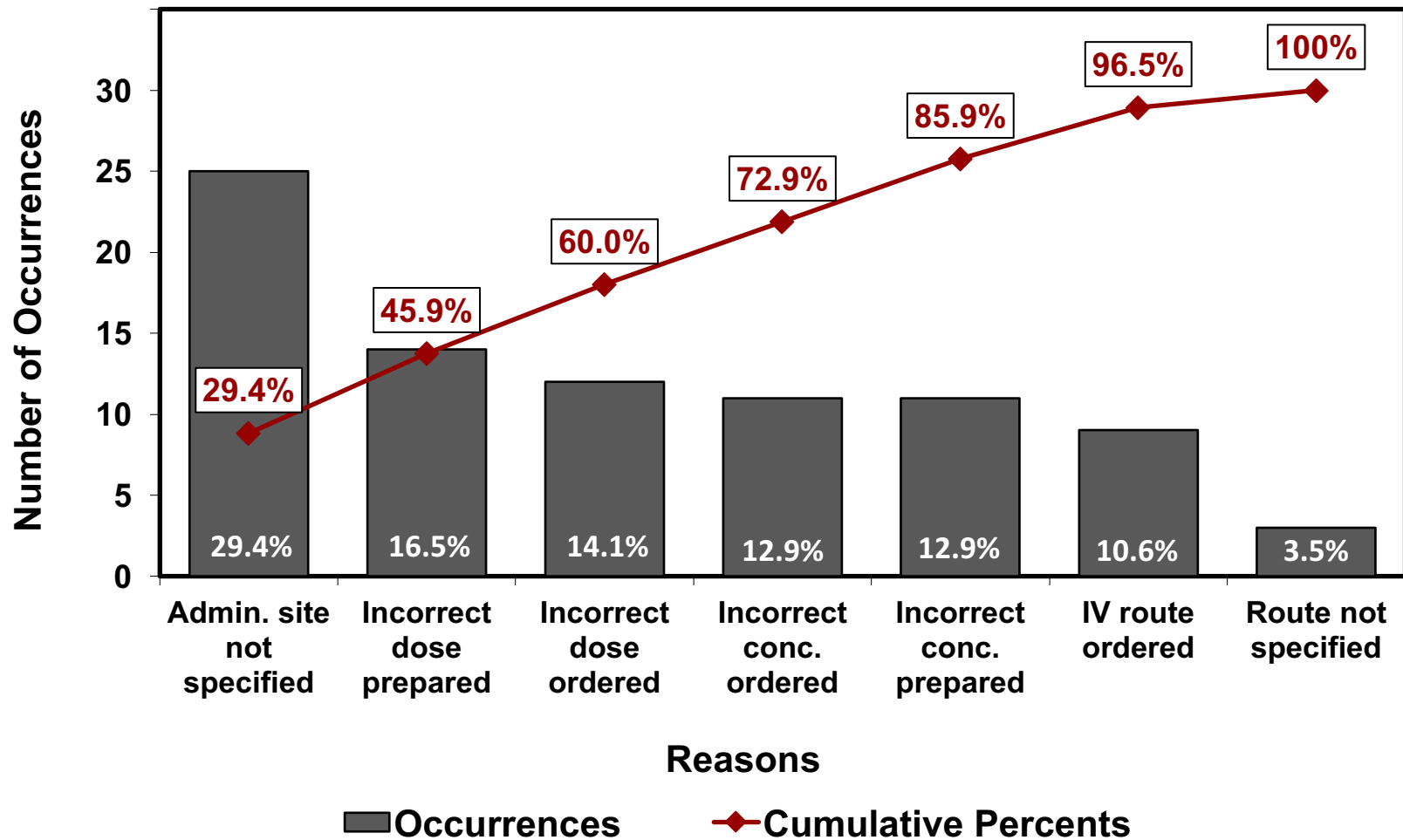
Time from	Drawn up Epi ^a (n=32)		Epi ^a Auto injector (n=5)		p-value
	Median	IQR ^b	Median	IQR	
Start to order ^c	91.5	(37.5, 227.5)	49	(38, 184)	.74
Order to administration	114	(62, 174.5)	28	(26, 68)	.02
Start to administration ^d	262.5	(146, 407.5)	95	(77, 252)	.12

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Note: ^aEpi= epinephrine, ^bIQR= interquartile range, Start time = when the team engages in the scenario, just after they are told the patient is in anaphylaxis from an intravenous medication. ^cStart to order = the time to when the practitioner finishes verbally ordering the epinephrine medication. ^dStart to administration = the time to when the epinephrine was administered, includes medication preparation



Reasons for Epinephrine Error



eMethods: Simulation scenario instructions

Choosing which clinical site to perform your simulation

We ask that the scenario be performed “in situ”, and not in a simulation center, because we are interested in recreating and capturing what happens in real life. You can choose which clinical environment to perform the scenario- the ED, ICU, radiology, inpatient floor, etc. I would base your choice on which location will be most receptive to you coming to run a simulation that meets these requirements:

1) We would like to use a healthcare team that is “on duty” and most representative of the team that would normally respond and manage a patient in anaphylaxis on that unit. This will depend on your location. For my hospital, typically a resident, nurse practitioner or fellow and a nurse would manage such a patient. Perhaps an attending would also be involved. I would not want a team of just medical students because that is not a realistic representation for my institution.

There may be some sites that are less accustomed to running a simulation in the real clinical environment. If this is the case, you may want to recruit a healthcare team to participate or provide a prebrief so that the team knows to behave as they would in real life. There will be a question on the data collection survey that asks if this simulation was partially announced or unannounced.

2) We would like to use real medications. So, the staff participating in the simulation should go to where epinephrine is stored on the unit and obtain it from there for med preparation. On some units, this may be an epi auto-injector that is kept in the medication room. Other units may open the crash cart to obtain the epinephrine and manually draw up the drug from a vial. We know that epi auto-injectors are quite expensive, so if you would like to substitute either an expired one or a trainer, that is ok. Just switch it out at the last minute.

Preparing for data collection during the simulation

Please review the data collection form and demographics form so you will know what to look for as you observe the simulation.

- 1) Timed metrics that we are interested in:
- Time 0 = when the healthcare team starts the simulation (typically when the nurse or practitioner goes to assess the patient) after they have been given the starting prompt by the simulation team.
 - Time elapsed for the epinephrine to be ordered, *even if the dose is not specified*.

- This time is for when the verbal order is given (not when it is entered into a computer).
- Some practitioners may just ask for “a dose of epi for anaphylaxis” but not give the dose until later when asked. Please record the earlier time but make a note that the dose was not specified. This will be a question in the online data collection tool.
- Time elapsed before the epinephrine is administered in relation to the start of the simulation.

It would be best if you can video record the simulation to ensure accuracy of these times. It does not have to be super high tech. I am planning on just using my iPhone to record this. For some of you, it may be that you use a stopwatch as your timer. After you have collected the timed metrics, you can delete the video. I do not need it for this study.

2) Try to position yourself close to the medication preparation area so that you can watch for any mistakes that are made. Did they choose the right dose and concentration of epi? Did they use the correct route of administration? If an auto-injector is used, did they know how to use the auto-injector correctly? The drug should be administered IM in the anterolateral thigh. For the auto-injectors, they should be held in place for at least 3 secs if not longer. (Please know that some healthcare staff have accidentally injected themselves when using auto-injectors. If you see that is about to happen, it would be ok to stop them.)

The simulation scenario

We purposely chose a very simple scenario because we wanted to make sure we could standardize it across sites. No confederate or parent needs to be involved or trained. We are not testing to see if participants can diagnose anaphylaxis. We want to see what they do to treat anaphylaxis.

Equipment/Set Up

1. 5 year old manikin (high of low fidelity) *with a PIV in place.*
2. Cardiorespiratory monitor for manikin.
Starting vitals: HR 155, CR flash, BP 88/30, RR 26, saturations 94%, wheezing and increased WOB, normal mental status
Weight - 20 kg
3. Epinephrine supplies that your institution would normally have available such as an Epi Auto-injector, code cart, drug tray, syringes and needles for IV, subcutaneous, and intramuscular dosing, etc. Try to use the equipment that is already present in the real clinical setting.

4. Institutional reference or medication dosing cognitive aid, as particular to each site.
5. Smart phone or video recording device to capture timed metrics.

Script to tell participants:

“Please come evaluate this patient. He just received an IV antibiotic and is now covered in hives and is having trouble breathing. He has a history of anaphylaxis and he is in anaphylaxis now. He weighs 20 kg.”

Remember to start video recording, or start your stop watch once you finish telling the simulation participants this and they begin the simulation = Time 0.

Scenario End: Right after the epinephrine is administered, the *vitals can return to a normal state.*

Debriefing

You can use whatever debriefing style you prefer. Any obvious errors (ex. medication error) should be debriefed.

Let the team know what the objectives of the scenario were and give them the option of not participating in the study. This was the statement included in the IRB application:

“The anaphylaxis scenario you just participated in is an attempt to gain a better understanding of how pediatric anaphylaxis is managed both in our institution and at others. Information regarding epinephrine dosing, preparation and administration was collected. Any video recording performed was to ensure accuracy of timed metrics and drug preparation. The video will be destroyed immediately after this data is obtained. Results will be analyzed as research data. No identifying information will be included in any report, abstract, or publication originating from this data. This study is voluntary, and you may choose to not participate at any time by simply notifying the simulation team.”

Examples of questions you could use if relevant to their performance:

1. Tell me more about the strategies you used that helped you to administer the correct dose of epinephrine for anaphylaxis so quickly.
2. Is there anything you would do differently the next time this happens?
3. Did anything surprise you about this scenario? Were there any non-routine events? How were those managed?

4. Epinephrine is a high-risk medication and there have been errors made by multiple healthcare providers because of confusion over the correct concentration/ dosing/ route of administration. For example, the 1:1000 concentration for anaphylaxis has been given via the IV route. This has resulted in significant patient side effects including arrhythmias and hypertension.
 - a. What do you think could have gone wrong in that case?
 - b. Have any of you had a similar experience with epinephrine before? Perhaps a near-miss where the error was caught before it reached the patient?

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Table E2: Specific Latent Safety Threats	
General Process	<ul style="list-style-type: none"> No Standard Operating Procedure is available for Epinephrine use in our ED's anaphylaxis response.

Table E1: Characteristics of sites (n=17) with epinephrine auto injectors (EAI)

	N	%
Locations where EAI is first line therapy (% of sites with EAI available)		
Emergency Department	5	29
Oncology inpatient unit	5	29
Inpatient unit (Non-Oncology)	2	12
Intensive Care Unit	0	0
Operating Room	0	0
Radiology	7	41
Outpatient clinic	3	18
High reaction areas	2	12
Where EAIs are stored (% of sites with EAI available)		
Code cart	1	6
Medication dispensing unit	8	47
Code Go bag	1	6
Unit-specific medication box	7	41

	<ul style="list-style-type: none"> • There are delays in administering Epi because nursing is unable to draw up medications for a patient until the patient is registered in our 2 computer systems. • Outdated anaphylaxis protocol exists involving use of Epi Pen, but autoinjectors are no longer available at the hospital.
Specific Process: Cognitive Aid	<ul style="list-style-type: none"> • There is no anaphylaxis dosing of epinephrine on the code sheet. • Dosing on anaphylaxis sheet is written in mg (not mL), which caused a delay in administration because nursing needed to calculate the volume to be administered. • Nursing staff was not familiar with the dosing book available at every crash cart. The nurse almost drew up the arrest dose of epinephrine but at the last minute saw the heading entitled "anaphylaxis." • Inappropriate labelling of Epi for anaphylaxis on the code sheet. • Our pre-made code sheets do not have an anaphylaxis dose, so our team saw the 1:1000 Epinephrine dose listed for ETT administration and used this inappropriate dosing. • IM dosing of epinephrine not on code sheets. • Outdated cognitive aid recommending subcutaneous route. • Two cognitive aids present in same room but with different doses listed for anaphylaxis. • The fellow used a PALS card which lists both IM and IV dosing (IV use for hypotension) and he inappropriately chose IV.
Knowledge Gap	<ul style="list-style-type: none"> • Dosing for anaphylaxis was unknown. The wrong volume and concentration were asked for making the order a correct 'dose' but incorrect concentration and route of epinephrine administration. • There was inadequate knowledge of our hospital process for anaphylaxis. • Due to a recent shortage of epinephrine, the nursing staff has been diluting 1:1,000 epinephrine to the 1:10,000 concentration for cardiac arrest. So they inadvertently diluted the anaphylaxis dose as well. • Staff not aware that Epi Pens were stocked in our PYXIS
Specific Process Pyxis	<ul style="list-style-type: none"> • Epi Pen and Epi Pen Jr. should be stocked in the PYXIS for all units. However, not all units had Epi Pen Jr stocked and when stocked it was not available for override in case of emergency.

	<ul style="list-style-type: none">• There was a several minute delay in administration of Epinephrine because the team did not know how to obtain the anaphylaxis kit from the PYXIS.
Equipment/ Human Factors Related	<ul style="list-style-type: none">• Medical team was unable to find the Epi pen in timely manner.
	<ul style="list-style-type: none">• Anaphylaxis kit had epinephrine ampule without filter needle, causing a significant delay in care.
	<ul style="list-style-type: none">• The two different concentrations of epi are in bags with warning stickers. However, the bags look exactly the same which caused the wrong concentration to be utilized.
	<ul style="list-style-type: none">• Pediatric code cart (in a community ED) was not appropriately stocked. Supplies had been previously removed for other patients and not replaced.

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