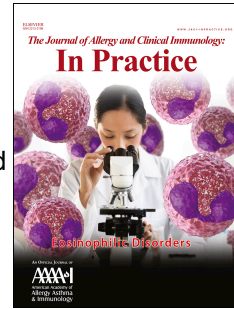# Journal Pre-proof

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

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Please cite this article as: Maa T, Scherzer D, Harwayne-Gidansky I, Capua T, Kessler DO, Trainor JL, Jani P, Damazo B, Abulebda K, Diaz MCG, Sharara-Chami R, Srinivasan S, Zurca A, Deutsch ES, Hunt EA, Auerbach M, PEAK Investigators of the International Network for Simulation-based Pediatric Innovation, Research and Education (INSPIRE), Prevalence of Errors in Anaphylaxis in Kids (PEAK): A Multi-Center Simulation-Based Study, *The Journal of Allergy and Clinical Immunology: In Practice* (2019), doi: https://doi.org/10.1016/j.jaip.2019.11.013.

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43 **Word count, abstract:** 272
44 **Word count, text:** 3154
45

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 (EAIs) 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

Introduction

83

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 soley 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.

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.

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

Discussion:

245

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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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

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

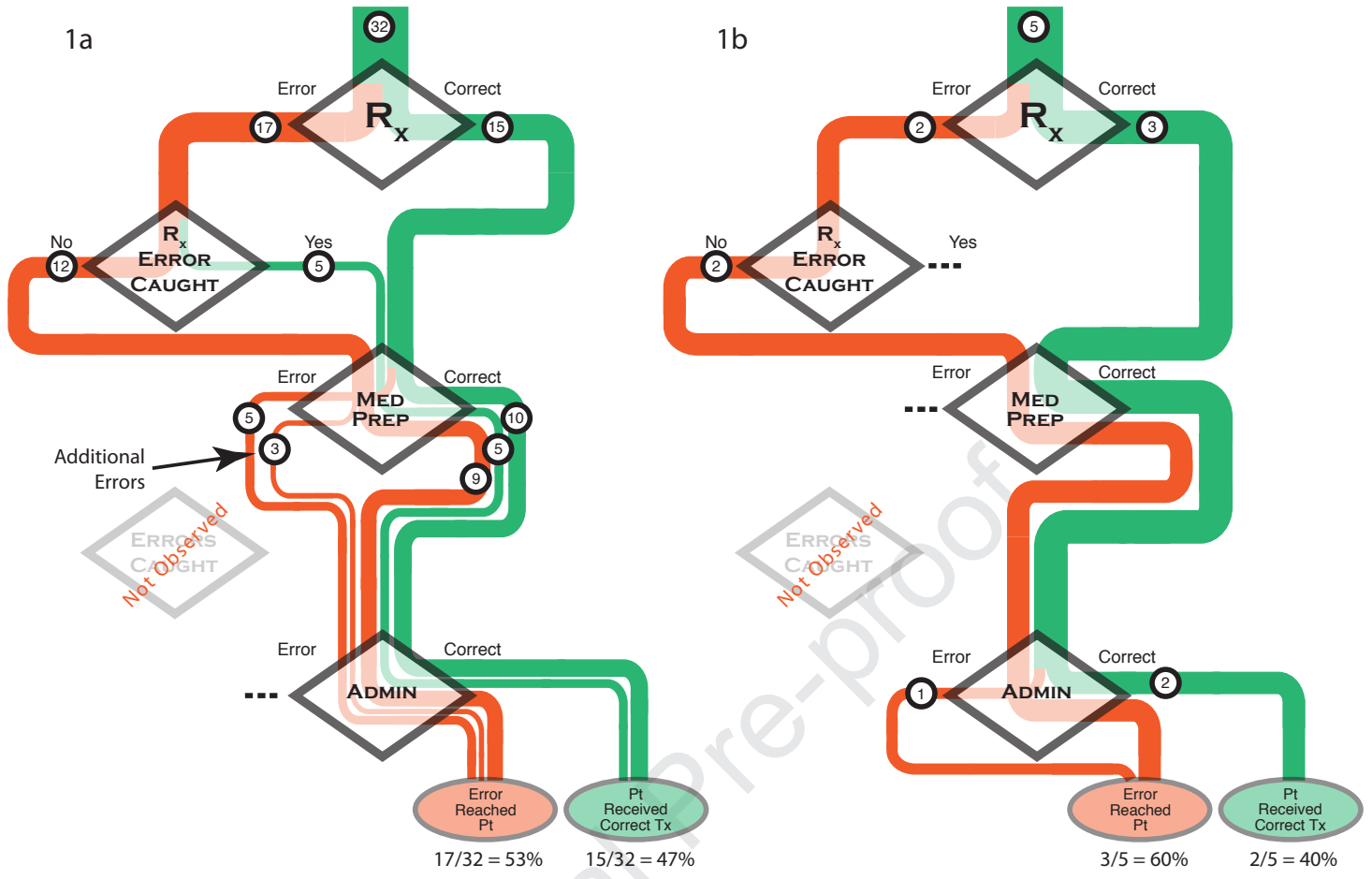| Risk Factor	Prescribing Error			Preparation Error			Administration Error		
	OR[a]	95% CI[b]	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Nursing with prior epinephrine administration for anaphylaxis	0.65	(0.15,2.78)	0.56	0.2	(0.04,0.93)	**0.04**	0.13	(0.03,0.62)	**.01**
Other Location vs. Intensive 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	(050,10.10)	.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   [a]OR = odds ratio, [b]CI = confidence interval. [c]Inexperienced team lead = still in residency

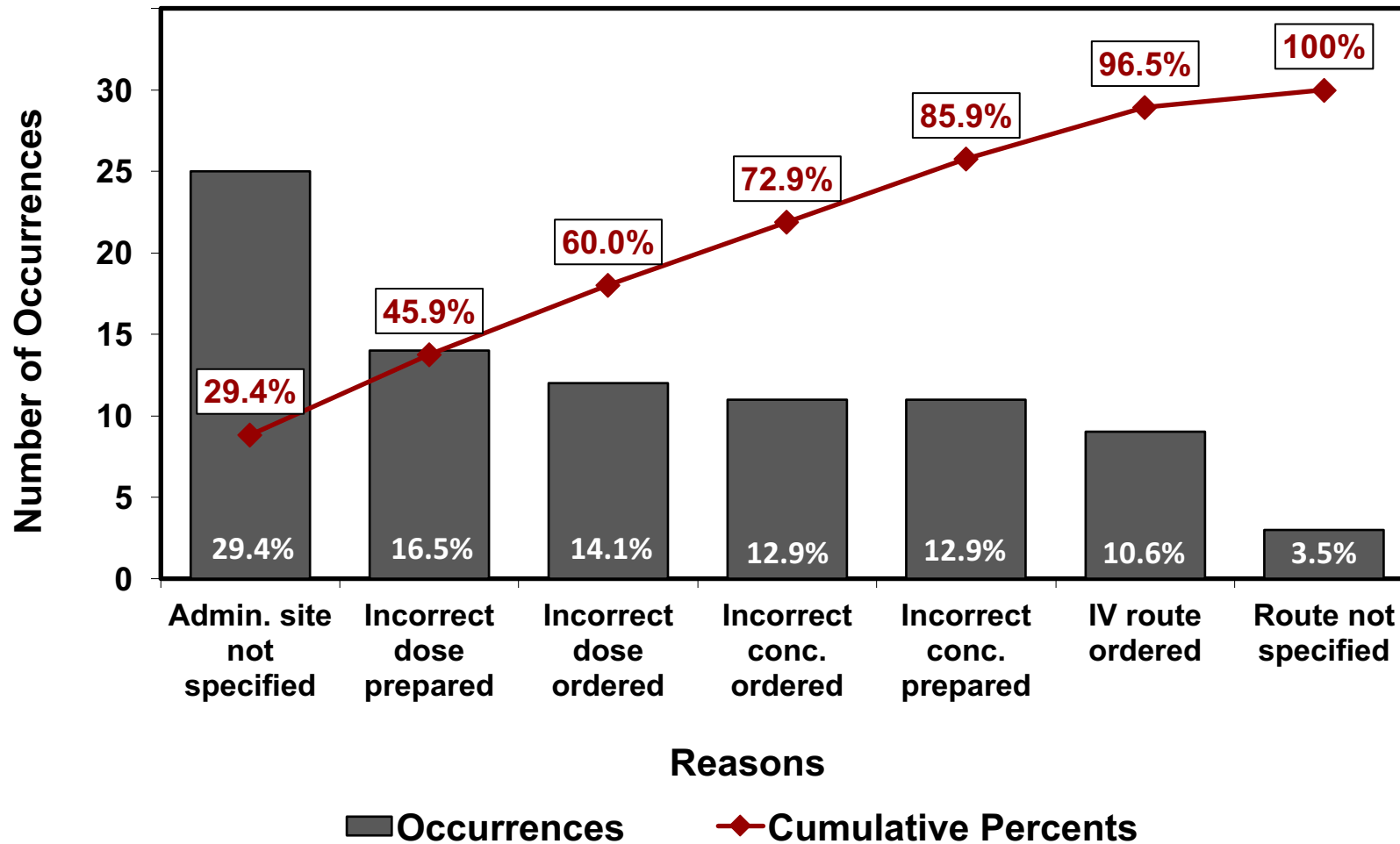479   training, EAI[d] = epinephrine auto injector

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Table III: Comparison of time (in seconds) by form of epinephrine used during simulation					
	Drawn up Epi[a] (n=32)		Epi[a] Auto injector (n=5)		
Time from	Median	IQR[b]	Median	IQR	p-value
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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482 Note: [a]Epi= epinephrine, [b]IQR= interquartile range, Start time = when the team engages in the
483 scenario, just after they are told the patient is in anaphylaxis from an intravenous medication.
484 [c]Start to order = the time to when the practitioner finishes verbally ordering the epinephrine
485 medication. [d]Start to administration = the time to when the epinephrine was administered,
486 includes medication preparation
487

488

1a

Error — (17) — **R$_X$** — (15) — Correct

(32)

No — (12) — **R$_X$ ERROR CAUGHT** — (5) — Yes

Error — (5) — **MED PREP** — (10) — Correct

Additional Errors → (3) — (5) — (9)

ERRORS CAUGHT Not Observed

Error — **ADMIN** — Correct

Error Reached Pt

Pt Received Correct Tx

17/32 = 53%   15/32 = 47%

1b

(5)

Error — (2) — **R$_X$** — (3) — Correct

No — (2) — **R$_X$ ERROR CAUGHT** — ... — Yes

Error — ... — **MED PREP** — Correct

ERRORS CAUGHT Not Observed

Error — (1) — **ADMIN** — (2) — Correct

Error Reached Pt

Pt Received Correct Tx

3/5 = 60%   2/5 = 40%

Reasons for Epinephrine Error

Number of Occurrences

Reason	Occurrences	Cumulative Percent
Admin. site not specified	29.4%	29.4%
Incorrect dose prepared	16.5%	45.9%
Incorrect dose ordered	14.1%	60.0%
Incorrect conc. ordered	12.9%	72.9%
Incorrect conc. prepared	12.9%	85.9%
IV route ordered	10.6%	96.5%
Route not specified	3.5%	100%

Reasons

■ Occurrences   ◆ Cumulative Percents

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.*

- o This time is for when the verbal order is given (not when it is entered into a computer).
  - o 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 being 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 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?

Table E2: Specific Latent Safety Threats	
General Process	• 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

	• 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	• 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	• 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	• 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.

	• 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	• Medical team was unable to find the Epi pen in timely manner.
	• Anaphylaxis kit had epinephrine ampule without filter needle, causing a significant delay in care.
	• 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.
	• Pediatric code cart (in a community ED) was not appropriately stocked. Supplies had been previously removed for other patients and not replaced.