



HAL
open science

Association of Prehospital Time to In-Hospital Trauma Mortality in a Physician-Staffed Emergency Medicine System

Tobias Gauss, François-Xavier Ageron, Marie-Laure Devaud, Guillaume Debaty, Stéphane Travers, Delphine Garrigue, Mathieu Raux, Anatole Harrois, Pierre Bouzat

► To cite this version:

Tobias Gauss, François-Xavier Ageron, Marie-Laure Devaud, Guillaume Debaty, Stéphane Travers, et al.. Association of Prehospital Time to In-Hospital Trauma Mortality in a Physician-Staffed Emergency Medicine System. *JAMA Surgery*, 2019, 154 (12), pp.1117. 10.1001/jamasurg.2019.3475 . hal-04015102

HAL Id: hal-04015102

<https://hal.science/hal-04015102>

Submitted on 12 Mar 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **The relationship of pre-hospital time to in-hospital trauma mortality in a physician staffed**
2 **Emergency Medicine System**

3

4 Tobias Gauss, MD¹, François-Xavier Ageron, MD, PhD², Marie-Laure Devaud, MD³, Guillaume Debaty,
5 MD, PhD⁴, Stéphane Travers, MD⁵, Delphine Garrigue, MD⁶, Mathieu Raux, MD, PhD⁷, Anatole
6 Harrois, MD, PhD⁸, Pierre Bouzat, MD, PhD⁹
7 *for the French Trauma Research Initiative^a*

8

9 1 Department of Anaesthesia and Critical Care, Hôpital Beaujon, HUPNVS, AP-HP, Clichy, France

10 2 Trauma system of the Northern French Alps Emergency Network (TRENAU- RENAU), Hospital Annecy
11 Genevois, Annecy, France

12 3 Prehospital Emergency Medicine Service (SAMU 95), Centre Hospitalier René Dubos, Pontoise, France

13 4 Department of Emergency Medicine, SAMU 38, University Hospital of Grenoble Alps, Grenoble, France

14 5 Paris Fire Brigade Emergency Medical Department, French Military Health Service, Paris, France

15 6 Interdisciplinary Emergency Platform, Department of Anaesthesia and Critical Care, University Hospital, Lille,
16 France

17 7 Sorbonne University, INSERM, UMRS1158 Clinical and Experimental Respiratory Neurophysiology; AP-HP,
18 Trust Pitié-Salpêtrière Charles Foix, Department of Anaesthesia and Critical Care, Paris, France

19 8 University Paris Sud, University Paris Saclay, Department of Anesthesiology and Critical Care, AP-HP, Bicêtre
20 University Hospital Paris Sud, Le Kremlin Bicêtre, France

21 9 Department Anesthesia and Critical Care, University Hospital, Grenoble, France

22 APHP= Assistance Publique des Hôpitaux de Paris

23

24 ^aThe French Trauma Research Initiative is composed of: the Traumabase Group, Trauma system of the
25 Northern French Alps Emergency Network (TRENAU- RENAU), Pre-hospital Traumabase Group-Ile de France,
26 Committee for Acute Surgery, Emergency and Trauma (ACUTE, French Society Anesthesia and Critical Care).

27

28 A detailed list of all collaborators can be found at the end of the article

29

30 Corresponding Author

31 Tobias Gauss, Department of Anaesthesia and Critical Care, Hôpital Beaujon, HUPNVS, AP-HP, 100

32 Bld General Leclerc, 92110 Clichy, France; tgauss@protonmail.com

33

34 Conflict of Interest:

35 No Conflict of Interest to declare

36 Word count 3100

37

38 **Abstract**

39 **IMPORTANCE:** The relationship between total prehospital time and mortality in physician staffed trauma
40 systems remains uncertain.

41 **OBJECTIVE:** The objective was to describe the relationship of total pre-hospital time and in-hospital mortality in
42 a prehospital physician staffed trauma system in France with the hypothesis that total prehospital time is
43 associated with an increased mortality.

44 **DESIGN, SETTING, AND PARTICIPANTS:** Retrospective cohort study from 2011 to 2016. The relationship
45 between death and prehospital time was assessed with a multivariable model adjusted with confounders. Data
46 for this study were derived from two distinct regional trauma registries in France, one urban, one rural with
47 both having a physician staffed Emergency Service. A total of 10216 consecutive adult trauma patients
48 admitted to one of the regional trauma referral centers in the study period were included.

49 **MAIN OUTCOMES AND MEASURES:** Total Prehospital Time (TPT) was the primary exposure variable, recorded
50 as arrival of the physician-lead prehospital care-team on scene to arrival at the hospital. The main outcome of
51 interest was all cause in-hospital mortality.

52 **RESULTS:** Patients had a mean age of 41 years, were mostly men (78%) affected by predominantly non-
53 penetrating injury (91%) with a median ISS of 17. 67% of patients had at least one body region with an AIS

54 score ≥ 3 . 10% (n=406) presented in shock (systolic pressure < 90 mmHg) and 27% (n=1378) with severe head
55 injury AIS ≥ 3 . Unadjusted Increasing prehospital time 30-minute categories were associated with a markedly
56 and constant increase in the risk of in-hospital death. Odds of death increased of 9% for each ten-minute
57 increase in prehospital time (OR (95% CI) 1.09 (1.07-1.11). After adjustment the relationship between
58 prehospital time and in-hospital death was halved but still significant (OR (95% CI) 1.04 (1.01-1.07)).

59

60 **CONCLUSIONS AND RELEVANCE:** Increasing total pre-hospital time is associated with increasing in-hospital all-
61 cause mortality in trauma patients a physician staffed EMS after adjustment for case complexity. Pre-hospital
62 time is a management objective in analogy to physiological targets. These findings plaid for a further
63 streamlining of prehospital trauma care and the need to define the optimal *intervention to time-ratio*.

64

65

66

67

68 **Introduction**

69 The concept of time as essential determinant of outcome in the early care of trauma patients
70 is a prevailing doctrine ^{1,2}, symbolized in the catchphrase: the *Golden Hour* of Trauma ^{3,4}. The
71 concept of trauma as time-sensitive disease has guided education and policy for decades in the
72 international trauma community. Despite this cultural penetrance ⁵, evidence in favor remains
73 elusive and the concept controversial ⁶⁻¹⁰.

74 The concept of trauma as a time-sensitive disease was developed and nurtured in a specific
75 Emergency Medical System (EMS), mainly a paramedic-based system in North America. The
76 international trauma community transposed this concept to diverse specific settings, even if the
77 respective context was different from the North American system ¹¹. Data on system performance

78 from physician-staffed EMS are far less abundant than data from EMS systems. On the one side
79 physician-staffed-EMS (ps-EMS) are considered to add complexity to a complex situation, to perform
80 more interventions resulting in longer Total Pre-hospital Time (TPT).^{12,13}. On the other side,
81 proponents of the physician-led critical care team advocate a more tailored provision of advanced
82 pre-hospital critical care. The ensuing debate oscillates between dichotomist concepts such as *scoop*
83 *and run* or *stay and play*^{11,13,14}. The reality is probably less easy to frame.

84 Based on this rationale and considering the comparative lack of data for ps-EMS, it appeared
85 justified to reconsider the association of pre-hospital total time and in-hospital mortality in a
86 physician-staffed EMS. The objective was to describe the relationship of total pre-hospital time and
87 in-hospital mortality in a large and representative cohort of trauma patients from two regional and
88 geographically very distinct trauma systems in France, one urban and one rural-mountainous. We
89 hypothesized that total prehospital time is associated with a mortality increase in a physician staffed
90 EMS system.

91

92

93 **Material and Methods**

94 A strobe checklist for this retrospective cohort study is provided in the appendix.

95 **Ethical approval**

96 This is an observational study using data from two prospective multicenter regional trauma registries,
97 the TraumaBase[®](TB), from the Paris area, Ile-de-France, and TRENAU (TR), from the region Rhône-
98 Alpes. Both registries have obtained approval from the Institutional Review Board (Comité de
99 Protection des Personnes, Paris VI and Clermont-Ferrand) from the Advisory Committee for
100 Information Processing in Health Research (*Comite Consultatif Pour le Traitement de l'information en*
101 *matière de recherche dans le domaine de la santé* CCTIRS, 11.305bis and 15.038bis) and from the
102 National Data Protection Agency (*Commission Nationale de l'Informatique et des Libertés* CNIL,
103 911461 and CNIL 915372), waiving the need for informed consent. Both registries dispose of

104 algorithms for consistency and coherence and professional data monitoring. Datamonitoring for the
105 TraumaBase[®] is assured by the Biostatistics Laboratory of Paris 7, and for the TRENAU registry by
106 professional statisticians employed by the network.

107

108 **Setting**

109 The structure and triage in both trauma systems have been previously described ^{15,16}. In summary,
110 Physician-staffed Mobile Intensive Care Units (MICU) provide the prehospital care in both systems. A
111 MICU team provides the equivalent of ATLS-based pre-hospital interventions (sedation, prehospital
112 anesthesia, advanced airway management, chest decompression...). The TraumaBase[®] Ile-de France
113 covers an urban area of 12000 km² with a population of 12 million inhabitants and 15 million visitors
114 per year. Eight physician staffed EMS (SAMU, Service Aide Medicale Urgente) organized into 43
115 MICU (see above), 37 SAMU and 6 Brigade de Sapeurs de Pompiers (Paris Fire Brigade), and six
116 designated level-1 centers provide almost exclusively the trauma care; no lower care centers have
117 been designated. The TRENAU area covers an area of 18,000 Km² in the Northern French Alps with a
118 population of two million inhabitants and a high seasonal variation (8 million tourists each year).
119 Care in the TRENAU network is provided by three SAMUs and a total of 14 designated trauma
120 hospitals with two level-I, one level-II and eleven level-III centers. The TRENAU network disposes of
121 specific management and triage guidelines ¹⁵. Within the Paris network, national triage¹⁷ and
122 management guidelines apply such as those for shock¹⁸. At any given time, clinical management was
123 left to the discretion of the responsible physician (pre-hospital or in-hospital). Both networks and
124 registries are financially supported by the respective Regional Health Authorities Ile-de-France and
125 Rhône-Alpes (Agence Régionale de Santé, ARS).

126

127 **Study Populations**

128 All consecutive trauma patients triaged to one of the six regional, designated Paris level-1 trauma
129 centers or to one of the 14 centers participating in the TRENAU network were screened for inclusion.

130 Patients not managed by a physician-staffed mobile unit or not transported to a participating
131 hospital (death on scene or not transported) or transferred from a hospital outside of the respective
132 system were not included. Only patients directly admitted to level-1 or level-2 centers (TRENAU)
133 were included. The enhanced care teams in both systems are able to provide a full spectrum of ATLS
134 trauma care, including airway management with rapid sequence induction for intubation, sedation
135 and analgesia, fluid therapy, vasoactive medication, fracture and dislocation reduction, chest
136 decompression, hemorrhage control (tourniquets, splinting, compression...), red blood cell
137 concentrate transfusion, etc. They currently do not provide thoracotomy or blood component
138 therapy other than red blood cell concentrates occurring in less than 3% of cases in both systems.

139

140 We defined early critical pre-hospital trauma interventions as any of the following: pre-hospital
141 intubation, vasopressor use, osmotherapy and fluid resuscitation > 1000 mL. Shock was defined as a
142 systolic arterial pressure <90mmHg.

143

144 The eTable 1 provides the complete list of, epidemiological, clinical (pre-hospital and in-hospital),
145 physiological and biological variables that were recorded for each patient. In brief, both data
146 collection follow the style Utstein major trauma revised ¹⁹. Calculation of the following scores
147 completed this information, and 2005 version of Injury Severity Score (ISS).

148

149 **Exposure variable and outcome criteria**

150 Total Prehospital Time (TPT) was the primary exposure variable, recorded as arrival of the physician-
151 lead prehospital care-team on scene to arrival at the hospital. Arrival on scene, leaving scene and
152 arrival at the admitting hospital are systematically recorded in both registries, based on pre-hospital
153 intervention run sheets and/or dispatch center data; exact timing of injury is not recorded in both
154 registries.

155

156

157 The main outcome of interest was all cause in-hospital mortality. Patients who died within 24 hours
158 were retained in the analysis to minimize survivor bias. Cause-specific of death, “death from bleeding”
159 and death from “head injury” were considered as secondary end-points. The causes of death were
160 based on a judgment by a physician reviewing all evidence at routine case closure in both registries.
161 The physician performing case closure was not part of the working committee of this study.

162

163 **Statistical analysis**

164

165 **Sample size**

166 The retrospective nature of the study predetermines the sample size. A post-hoc power calculation
167 was performed to assess internal validity of the analysis. Internal validity was assessed in terms of
168 discrimination by the area under the curve and calibration by overall calibration, ratio
169 exposed/observed and calibration slope.

170

171 **Statistical methods**

172 Continuous variables were presented with mean and standard deviation or with median and
173 interquartile range when appropriate. Categorical variables were presented with frequency and
174 percentage.

175 The relationship between death and prehospital time was assessed graphically by plotting the risk of
176 death on prehospital time. A Generalized linear mixed model (GLM) with random effect by registry
177 and EMS system explored the relationship between death and prehospital time with a logit function.
178 We assessed graphically the departure of linearity in the relationship between death and time and
179 added the polynomial terms in the GLM if needed.

180 We fitted the best model according to likelihood ratio test and Akaike information criterion (AIC). In
181 addition, a Generalized additive model (GAM) assessed and explored the linearity of the relationship

182 between death and time. GAM is a flexible model of GLM with a link function based on smoothing
183 splines. The amount of smoothing is controlled by the number of equivalent degrees of freedom. We
184 assessed graphically the smooth function to fix the equivalent degrees of freedom for prehospital
185 time. We assessed the deviance variation that occurs depending on the use of the linear term or the
186 smoothing term in the equation.

187 To control for potential variables associated with case complexity, a GLM and GAM model was
188 applied in multivariable analysis to adjust for the confounders age, gender, severity of anatomic
189 injury pattern (ISS), systolic blood pressure (SBP) and Glasgow Coma Scale (GCS) in a parsimonious
190 method. These five variables are strongly correlated with prehospital interventions such as airway.
191 The more severely a patient is in shock (SBP), or likelihood of traumatic brain injury (GCS), the more
192 severely injured he is (ISS). The High injury load may trigger more interventions and longer
193 prehospital times. In consequence, for the sake of simplicity and to avoid collinearity, the models did
194 deliberately not include prehospital interventions.

195

196 Two-sided p values < 0.05 were considered significant. All statistical analyses were performed using
197 Stata SE, v.14.0 (StataCorp).

198

199

200

201 **Missing data**

202 Multiple imputation of missing values to predict total prehospital time was not feasible. Several
203 variables were not routinely collected in both registries (distance between scene of accident and
204 hospital, dispatching decision, etc.). Measurement errors in variables that are not routinely collected
205 could lead to inappropriate predictions when applied to multiple imputation. Data were unlikely to
206 be missing at random and this could lead to a bias towards the null when applying multiple
207 imputation. For this reason, a complete case analysis was performed. Patients with and without

208 missing data on TPT were compared to assess comparability between the groups in term of
209 demographic characteristics, prehospital condition, injury severity, in-hospital death.

210

211

212 **Results**

213 In total 6,441 patients were screened for inclusion from January 2011 to December 2016 in the
214 Traumabase database and 8,888 from the TRENAU database from January 2009 to December 2016.

215 The main reason to exclude patients were missing data (see flowchart, eFigure1, missing data eTable
216 2). In total 10,126 patients from both samples, 5,059 and 5,067 respectively, were retained for
217 complete case analysis.

218

219 Patients had a mean age of 41 years, most were men (78%) affected by predominantly non-
220 penetrating injury (91%) with a median ISS of 17, with 67% of patients with at least one body region
221 with an AIS score ≥ 3 . 10% (n=406) presented in shock (systolic pressure < 90 mmHg) and 27%
222 (n=1378) with severe head injury AIS ≥ 3 (detailed data, please refer to Table 1).


223

224 The median Total-Pre-hospital Time (TPT) was 73 [IQR, 54-100] minutes in the Traumabase cohort
225 and 60 [IQR, 45-80] in the TRENAU cohort (eTable 3). The median TPT was 65 [IQR, 49-90] for the
226 combined cohort with 43% cases presenting a TPT shorter than 60 minutes. Three quarters of
227 patients were transported by land and 90% were admitted to a designated trauma center. TPT
228 increased with the number of pre-hospital interventions performed Orotracheal intubation and
229 vasopressor use was more frequent in the Traumabase network, orotracheal intubation 23% versus
230 29%, fluid > 1000 ml 26% versus 38%, vasopressor 10% versus 13% (eTable 4).

231

232 Primary outcome

233 Unadjusted GLM and GAM showed a significant progressive increase of all-cause mortality with TPT

234 (figure 1 A and B). Increasing TPT 30-minute categories were associated with a markedly and
235 constant increase in the risk of in-hospital death (table 2). Odds of death increased by 9% for each
236 ten-minute increase in TPT (OR (95% CI) 1.09 (1.07-1.11), table 3). When adjusted for confounders,
237 the relationship between TPT and in-hospital death 4% (figure 2) but still significant (OR (95% CI) 1.04
238 (1.01-1.07), table 3) 

239

240 Secondary outcome

241 Increasing TPT 30-minute categories were associated with a progressive and constant increase in the
242 risk of death due to head injury (table 2). This relationship was also observed, though less marked,
243 when considering death from bleeding (table 2). Unadjusted odds of death due to head injury
244 increased by 9% for each ten-minute increase in TPT (OR (95% CI) 1.09 (1.07-1.11), table 3, while
245 unadjusted odds ratio of death due to bleeding increased by 4% (1.04 (1.01-07) respectively, table 3).
246 When adjusting for confounders, the relationship between TPT and in-hospital death due to head
247 and bleeding injury showed a non-significant increase (table 3).

248

249 **Discussion**

250 The main finding of this study is that longer TPT is independently associated with increasing all-cause
251 in-hospital mortality in a physician-staffed trauma system. To the best of our knowledge this is the
252 first study reporting such an association in a physician staffed EMS in Europe.

253 The increase of mortality with increasing TPT appears as common sense. However, existing
254 comparative data on TPT and mortality in physician staffed EMS are limited and conflicting ^{20,21}.
255 Although time would be considered as an independent exposure variable, it remains invariably
256 dependent on exposure variables such as physiology and severity and pre-hospital interventions.
257 Concordantly, it was justifiable to assume that TPT could only be the result of multifactorial
258 complexity thereby challenging its independent association with outcome. Nevertheless, by
259 accounting for complexity (age, ISS, GCS and shock), time remained an independent exposure

260 variable corroborating studies conducted in North America ²². Although other studies suggest that a
261 physician-led team exerts a positive impact on outcome ^{12,22} even when TPT is longer.

262

263 The association of TPT and mortality implies that time is an independent exposure that
264 should be a management objective. Observed TPT were comparable to other European physician
265 staffed EMS ^{13,23,24} but longer than in paramedic staffed EMS ²⁵. A propensity matched analysis
266 reported that critical prehospital interventions were associated with a decrease in mortality without
267 impacting TPT ¹⁴. Time needs to be kept as short as possible, maintaining a trade-off in favor of
268 critical interventions to be performed in the safest way possible. We suggest to call this the optimal
269 *intervention to time ratio*. This ratio implies, the time every pre-hospital intervention requires, must
270 be counterbalanced by a gain in survival it could generate. A recent cohort study of trunk trauma ⁵
271 revealed an increased mortality for shocked patients with incompressible trunk trauma, long before
272 any definitive hemorrhage control is possible, advocating eventually in favor of advanced pre-
273 hospital resuscitation-and hemorrhage control. However, TPT results from all elements constituting
274 the rescue chain: extrication, intervention²⁶, communication with command/dispatch and receiving
275 center and transport time. The whole process needs streamlining to keep TPT as short and safe as
276 possible to only address the targeted and individualized essential needs of each patient.

277

278 When looking at the specific causes of death, the adjusted model (Table 3, figure 2) showed a non-
279 significant effect of time on hemorrhage-associated mortality. The critical relationship of time and
280 trauma hemorrhage was recently observed, demonstrating peak mortality from hemorrhage at 37
281 minutes²⁷. This circumstance might have weakened the relationship with death by hemorrhage in the
282 model. Both registries only include patients that arrive alive at hospital. Ball et al. indicated that with
283 shorter TPT, more patients arrived alive, but then died subsequently ²⁸. Future studies need to
284 address this question and include all patients deceased on scene. In opposition to previous reports ²⁹,
285 the adjusted model did not show a significant association of TPT and TBI-induced mortality.

286 Affirmation of TBI as the cause of death is difficult since head injured patients commonly have other
287 confounding causes of death (hemorrhage, thoracic trauma). Moreover, a substantial proportion of
288 TBI patients ultimately die after withdrawal of treatment and are registered as such, which may have
289 biased the true proportion of death due to TBI.

290 This study has several strengths. Data were extracted from two established registries with
291 robust data management robust. Data were derived from two geographically and structurally distinct
292 regions with different trauma systems. The TRENAU system qualifies as *inclusive* with three
293 designated levels of care ¹⁶. The Paris system tends to be *exclusive* with six designated level-1
294 centers absorbing the most regional trauma cases ¹⁷. These characteristics apply to other European
295 EMS supporting the external validity and generalizability of the observations made. The present
296 model appears robust and generalizable. As eFigure 2 illustrates, mortality retains a coherent and
297 consistent relationship to well documented predictors and confounders.

298 This study carries a number of limitations linked to its design. Based on a prospective data collection
299 and with adequate control of potential confounders, it appeared however appropriate to examine
300 the hypothesis in a sufficiently large real-life cohort. A physician closing the case determined the
301 cause of death, a subjective bias cannot be excluded in analogy to most existing registries, unless
302 postmortem CT scans and/or systematic autopsies become standard. Only patients that arrived alive
303 in hospital were included in the study a feature shared with most established trauma registries and
304 as exposed may have weakened the relationship of hemorrhage induced mortality and time. The
305 choice of adjustment variables may seem arbitrary and the number of variables limited. However,
306 the adjustment aimed to compensate for case complexity and case-mix in a simple but robust way.
307 Cases with shock (SBP<90mmHg) and/or TBI (low GCS) and high injury load (ISS) and elderly patients
308 account for the greater part of this complexity, since they may require pre-hospital resuscitation.
309 Hence, the models did not include any specific prehospital interventions as they are well correlated
310 and share a high collinearity with any of the four adjustment variables in the model and are part of
311 the so-called causal pathway. Pre-hospital interventions in France focus on advanced airway

312 management, fluid and vasoactive therapy and simple hemostatic measures (eTable 4). At the time
313 of the study, blood product use was rare and advanced surgical techniques exceptional. We decided
314 to perform complete case analysis instead of performing multiple imputation. We cannot exclude
315 that exclusion of observations led to selection bias. Multiple imputation is not always superior to
316 complete case analysis, in particular if missing data are not missing at random; imputation may
317 generate a bias towards the null³⁰. In this study, it seems inappropriate to impute data on prehospital
318 time without precise geographical location as ambulances in France are currently not systematically
319 equipped with GPS systems. Missing data led to exclude 23% of patients from both registries.
320 However, apart from a slight difference in the mechanism of injury, excluded patients shared the
321 characteristics and severity of injury similar to the included patients. Finally, this study included cases
322 from a large urban and a rural-mountainous area, supporting the generalizability of the results to
323 most of Europe and mature trauma systems. These results may less apply to very remote isolated
324 regions and or systems with a high incidence of penetrating injury.

325

326 **Conclusion**

327 This study demonstrates an independent relationship of in-hospital all-cause mortality in trauma
328 with total prehospital time in a physician staffed EMS in France even after adjustment for case
329 complexity. These results imply that pre-hospital time management is to become a management
330 objective. Both findings plaid for further streamlining of prehospital trauma care and the need to
331 define the optimal *intervention to time-ratio*.

332

333 **The Traumabase Group®:**

334 **Paer Abback**, MD (*Beaujon University Hospital, Hôpitaux Universitaires Paris Nord-Val-De-Seine, Clichy AP-HP,*
335 *France*); **Arie Attias**, MD (*Department of Anaesthesiology and Critical Care, Hôpital Henri Mondor, APHP,*
336 *Créteil, France*); **Sylvain Ausset**, MD PhD (*Anaesthesiology and Critical Care, Hôpital Interarmées Percy, Clamart,*
337 *France*); **Mathieu Boutonnet** (*Anaesthesiology and Critical Care, Hôpital Interarmées Percy, Clamart, France*);

338 Fabrice Cook, MD (*Department of Anaesthesiology and Critical Care, Hôpital Henri Mondor, APHP, Créteil,*
339 *France*); **Gilles Dhonneur**, MD, PhD (*University Paris Est and Department of Anaesthesiology and Critical Care,*
340 *Hôpital Henri Mondor, APHP, Créteil, France*); **Jacques Duranteau**, MD, PhD (*University Paris Sud and*
341 *Department of Anaesthesiology and Critical Care, Hôpital Bicêtre, Hôpitaux Universitaires Paris Sud, AP-HP,*
342 *Kremlin Bicêtre, France*); **Sophie Hamada**, MD (*Department of Anaesthesiology and Critical Care, Hôpital*
343 *Bicêtre, Hôpitaux Universitaires Paris Sud, AP-HP, Kremlin Bicêtre, France*); **Olivier Langeron**, MD, PhD
344 (*Sorbonne University, UPMC Univ Paris 06 and Department of Anaesthesiology and Critical Care, Groupe*
345 *Hospitalier Pitié-Salpêtrière Charles Foix, AP-HP, Paris, France*); **Catherine Paugam-Burtz**, MD, PhD (*University*
346 *Denis Diderot and Department of Anaesthesiology and Critical Care, Beaujon University Hospital, Hôpitaux*
347 *Universitaires Paris Nord-Val-De-Seine, Clichy, AP-HP, France*); **Romain Pirracchio**, MD, PhD (*University Paris*
348 *Descartes and Department of Anaesthesiology and Critical Care, Hôpital Européen Georges Pompidou, APHP,*
349 *Paris, France*); **Bruno Riou**, MD, PhD (*Sorbonne University, UMRS 1166 and Department of Emergency*
350 *Medicine, Groupe Hospitalier Pitié-Salpêtrière Charles Foix, AP-HP, Paris, France*); **Guillaume de St Maurice**
351 (*Anaesthesiology and Critical Care, Hôpital Interarmées Percy, Clamart, France*); **Bernard Vigué**, MD
352 (*Department of Anaesthesiology and Critical Care, Hôpital Bicêtre, Hôpitaux Universitaires Paris Sud, AP-HP,*
353 *Kremlin Bicêtre, France*)

354

355 **TRENAU Network**

356 **François Albasini**, MD (*Emergency medical service, Saint Jean de Maurienne Hospital, Saint Jean de Maurienne,*
357 *France*); **Frederic Champly**, MD (*Emergency medical Department, Hopitaux du Mont-Blanc, Sallanches,*
358 *France*); **Laurent Chapiteau**, MD (*Emergency medical service, Albertville Hospital, Albertville, France*); **Etienne**
359 **Haller**, MD (*Emergency medical service, Saint Jean de Maurienne Hospital, Saint Jean de Maurienne, France*);
360 **Christophe Hoareau**, MD (*Emergency medical service, Bourg Saint Maurice Hospital, Bourg Saint Maurice,*
361 *France*); **Albrice Levrat**, MD (*Intensive care unit, Annecy Hospital, Annecy, France*); **Elisabeth Rancurel**, MD
362 (*Emergency medical service, Grenoble University Hospital, Hôpital Albert Michallon, Grenoble, France*);
363 **Dominique Savary**, MD (*Emergency medical service, Annecy Hospital, Annecy, France*); **Jean-Marc Thouret**, MD
364 (*Intensive Care Medicine, Chambéry Hospital, Chambéry, France*); **Pascal Useglio**, MD (*Emergency medical*
365 *service, Chambéry Hospital, Chambéry, France*); **Claire Vallenet**, MD (*Emergency medical service, Annemasse,*

366 *Centre Hospitalier Alpes Leman, France*); **Damien Venchiarutti**, MD (*Emergency medical service, Albertville*
367 *Hospital, Albertville, France*)

368

369 **The Prehospital Traumabase Group Ile de France :**

370 **Kilian Bertho** (*Brigade des Sapeurs de Pompiers Paris, Paris, France*); **Charlotte Chollet-Xemard** (*SAMU 94, Val*
371 *de Marne, Hôpital Henri-Mondor, AP-HP, Créteil, France*); **François Dolveck** (*SAMU 77, Seine et Marne, Melun,*
372 *France*); **Laurianne Michelland** (*SAMU 93, Seine-St-Denis, AP-HP, Bobigny, France*); **Paul-Georges Reuter**
373 (*SAMU 92, Hauts-De-Seine, Garches, AP-HP, France*); **Agnès Ricard-Hibon** (*SAMU 95, Val D'Oise, Pontoise,*
374 *France*); **Olivier Richard** (*SAMU 78, Yveslines, Versailles, France*); **David Sapir** (*SAMU 91, L'Essonne, Corbeil,*
375 *France*); **Benoît Vivien** (*SAMU 75, Paris, AP-HP, France*). SAMU= *Service d'Aide Médicale Urgente*

376

377 **Acknowledgments:**

378 We would like to thank and dedicate this work to the numerous dedicated and committed first aiders,
379 paramedics, pre- and intra-hospital physicians. Without their efforts this work would be not possible.
380 Without the tireless contribution, we would not dispose of the data to perform this analysis. TG and
381 FX had full access to all the data in the study and take responsibility for the integrity of the data and the
382 accuracy of the data analysis

383

384 **Funding:**

385 The study received no funding. Both trauma registries Traumabase and TRENAU are funded by the
386 respective Regional Health Authority Ile de France and Rhone-Alpes (Agence Regionale de Sante,
387 ARS)

388

389 **Bibliography**

390 1. Sampalis JS, Lavoie A, Williams JI, Mulder DS, Kalina M. Impact of on-site care, prehospital time,
391 and level of in-hospital care on survival in severely injured patients. *J Trauma*. 1993;34(2):252-
392 261.

- 393 2. Sampalis JS, Denis R, Lavoie A, et al. Trauma care regionalization: a process-outcome evaluation.
394 *J Trauma*. 1999;46(4):565-579; discussion 579-581.
- 395 3. Boyd DR, Cowley RA. Comprehensive regional trauma/emergency medical services (EMS)
396 delivery systems: the United States experience. *World J Surg*. 1983;7(1):149-157.
- 397 4. Rogers FB, Rittenhouse KJ, Gross BW. The golden hour in trauma: dogma or medical folklore?
398 *Injury*. 2015;46(4):525-527. doi:10.1016/j.injury.2014.08.043
- 399 5. Alarhayem AQ, Myers JG, Dent D, et al. Time is the enemy: Mortality in trauma patients with
400 hemorrhage from torso injury occurs long before the "golden hour." *The American Journal of*
401 *Surgery*. 2016;212(6):1101-1105. doi:10.1016/j.amjsurg.2016.08.018
- 402 6. Pepe PE, Wyatt CH, Bickell WH, Bailey ML, Mattox KL. The relationship between total
403 prehospital time and outcome in hypotensive victims of penetrating injuries. *Ann Emerg Med*.
404 1987;16(3):293-297.
- 405 7. Pons PT, Markovchick VJ. Eight minutes or less: does the ambulance response time guideline
406 impact trauma patient outcome? *The Journal of Emergency Medicine*. 2002;23(1):43-48.
407 doi:10.1016/S0736-4679(02)00460-2
- 408 8. Lerner EB, Billittier AJ, Dorn JM, Wu Y-WB. Is total out-of-hospital time a significant predictor of
409 trauma patient mortality? *Acad Emerg Med*. 2003;10(9):949-954.
- 410 9. Newgard CD, Meier EN, Bulger EM, et al. Revisiting the "Golden Hour": An Evaluation of Out-of-
411 Hospital Time in Shock and Traumatic Brain Injury. *Ann Emerg Med*. 2015;66(1):30-41, 41.e1-3.
412 doi:10.1016/j.annemergmed.2014.12.004

- 413 10. Kotwal RS, Howard JT, Orman JA, et al. The Effect of a Golden Hour Policy on the Morbidity and
414 Mortality of Combat Casualties. *JAMA Surg.* 2016;151(1):15-24.
415 doi:10.1001/jamasurg.2015.3104
- 416 11. Haas B, Nathens AB. Pro/con debate: is the scoop and run approach the best approach to
417 trauma services organization? *Crit Care.* 2008;12(5):224. doi:10.1186/cc6980
- 418 12. Yeguiayan J-M, Garrigue D, Binquet C, et al. Medical pre-hospital management reduces
419 mortality in severe blunt trauma: a prospective epidemiological study. *Crit Care.*
420 2011;15(1):R34. doi:10.1186/cc9982
- 421 13. Wyen H, Lefering R, Maegele M, et al. The golden hour of shock - how time is running out:
422 prehospital time intervals in Germany--a multivariate analysis of 15, 103 patients from the
423 TraumaRegister DGU(R). *Emerg Med J.* 2013;30(12):1048-1055. doi:10.1136/emered-2012-
424 201962
- 425 14. Meizoso JP, Valle EJ, Allen CJ, et al. Decreased mortality after prehospital interventions in
426 severely injured trauma patients. *J Trauma Acute Care Surg.* 2015;79(2):227-231.
427 doi:10.1097/TA.0000000000000748
- 428 15. Bouzat P, Ageron F-X, Brun J, et al. A regional trauma system to optimize the pre-hospital triage
429 of trauma patients. *Crit Care.* 2015;19:111. doi:10.1186/s13054-015-0835-7
- 430 16. Hamada SR, Gauss T, Duchateau F-X, et al. Evaluation of the performance of French physician-
431 staffed emergency medical service in the triage of major trauma patients. *J Trauma Acute Care*
432 *Surg.* 2014;76(6):1476-1483. doi:10.1097/TA.0000000000000239
- 433 17. Riou B, Thicoipe M, Atain-Kouadio P. Comment évaluer la gravité? *Actual En Réanimation*
434 *Préhospitalière Traumatisé Grave.* 2002:115-128.

- 435 18. Duranteau J, Asehnoune K, Pierre S, Ozier Y, Leone M, Lefrant J-Y. Recommandations sur la
436 réanimation du choc hémorragique. *Anesthésie & Réanimation*. 2015;1(1):62-74.
437 doi:10.1016/j.anrea.2014.12.007
- 438 19. Ringdal KG, Coats TJ, Lefering R, et al. The Utstein template for uniform reporting of data
439 following major trauma: a joint revision by SCANTEM, TARN, DGU-TR and RITG. *Scand J Trauma*
440 *Resusc Emerg Med*. 2008;16:7. doi:10.1186/1757-7241-16-7
- 441 20. Harmsen AMK, Giannakopoulos GF, Moerbeek PR, Jansma EP, Bonjer HJ, Bloemers FW. The
442 influence of prehospital time on trauma patients outcome: a systematic review. *Injury*.
443 2015;46(4):602-609. doi:10.1016/j.injury.2015.01.008
- 444 21. Jung K, Huh Y, Lee JC, et al. Reduced Mortality by Physician-Staffed HEMS Dispatch for Adult
445 Blunt Trauma Patients in Korea. *Journal of Korean Medical Science*. 2016;31(10):1656.
446 doi:10.3346/jkms.2016.31.10.1656
- 447 22. Fukuda T, Ohashi-Fukuda N, Kondo Y, Hayashida K, Kukita I. Association of Prehospital
448 Advanced Life Support by Physician With Survival After Out-of-Hospital Cardiac Arrest With
449 Blunt Trauma Following Traffic Collisions: Japanese Registry-Based Study. *JAMA Surg*.
450 2018;153(6):e180674. doi:10.1001/jamasurg.2018.0674
- 451 23. Funder KS, Petersen JA, Steinmetz J. On-scene time and outcome after penetrating trauma: an
452 observational study. *Emergency Medicine Journal*. 2011;28(9):797-801.
453 doi:10.1136/emj.2010.097535
- 454 24. Timm A, Maegele M, Lefering R, Wendt K, Wyen H. Pre-hospital rescue times and actions in
455 severe trauma. A comparison between two trauma systems: Germany and the Netherlands.
456 *Injury*. 2014;45:S43-S52. doi:10.1016/j.injury.2014.08.017

- 457 25. Ruelas OS, Tschautscher CF, Lohse CM, Sztajnkrzyer MD. Analysis of Prehospital Scene Times
458 and Interventions on Mortality Outcomes in a National Cohort of Penetrating and Blunt Trauma
459 Patients. *Prehospital Emergency Care*. April 2018;1-7. doi:10.1080/10903127.2018.1448494
- 460 26. Brown JB, Rosengart MR, Forsythe RM, et al. Not all prehospital time is equal: Influence of
461 scene time on mortality. *Journal of Trauma and Acute Care Surgery*. 2016;81(1):93-100.
462 doi:10.1097/TA.0000000000000999
- 463 27. Oyeniyi BT, Fox EE, Scerbo M, Tomasek JS, Wade CE, Holcomb JB. Trends in 1029 trauma deaths
464 at a level 1 trauma center: Impact of a bleeding control bundle of care. *Injury*. 2017;48(1):5-12.
465 doi:10.1016/j.injury.2016.10.037
- 466 28. Ball CG, Williams BH, Tallah C, Salomone JP, Feliciano DV. The impact of shorter prehospital
467 transport times on outcomes in patients with abdominal vascular injuries. *Journal of Trauma*
468 *Management & Outcomes*. 2013;7(1). doi:10.1186/1752-2897-7-11
- 469 29. Dinh MM, Bein K, Roncal S, Byrne CM, Petchell J, Brennan J. Redefining the golden hour for
470 severe head injury in an urban setting: The effect of prehospital arrival times on patient
471 outcomes. *Injury*. 2013;44(5):606-610. doi:10.1016/j.injury.2012.01.011
- 472 30. White IR¹, Carlin JB. Bias and efficiency of multiple imputation compared with complete-case
473 analysis for missing covariate values. *Stat Med*. 2010 Dec 10;29(28):2920-31. doi:10.1002/sim.3944.
474
475
476

477 **Table 1. Patient characteristics according to regional database.**

	Total	Paris_ Ile de France (TRAUMABASE)	Northern French Alps (TRENAU)
	N=10,126	N=5,067	N=5,059
Age, mean (sd)	41 (18)	38 (17)	42 (18)
Sex male, N (%)	7,937 (78)	3,998 (79)	3,939 (78)
Penetrating injury, N (%)	861 (9)	568 (11)	293 (6)
Circumstances, N (%)			
Road Traffic injury	5,598 (55)	3,014 (60)	2,549 (51)
Falls	3,053 (30)	1,231 (24)	1,805 (36)
Stabbing	605 (6)	399 (8)	201 (4)
Gun shot	250 (2)	169 (3)	80 (2)
Prehospital SBP, mean (sd)	117 (32)	109 (34)	126 (26)
Prehospital SBP <90 mmHg, N (%)	1,259 (13)	946 (19)	313 (7)
Prehospital GCS, N (%)			
3-8	1,518 (15)	889 (18)	629 (13)
9-13	963 (10)	517 (10)	446 (9)
13-15	7,453 (75)	3,648 (72)	3,805 (77)
ISS, mean (sd)	17 (14)	18 (15)	17 (13)
0-15, N (%)	5,313 (53)	2,679 (53)	2,634 (53)
16-24, N (%)	2,034 (20)	1,013 (20)	1,021 (20)
25-34, N (%)	1,757 (17)	818 (16)	939 (19)
≥35, N (%)	966 (10)	554 (11)	412 (8)
Overall AIS score ≥3, N (%)	6,737 (67)	3,302 (65)	3,435 (68)
Severe head injury (AIS Head ≥3), N (%)	2,724 (27)	1,346 (27)	1,378 (27)

Secondary transfer, N (%)			
In-hospital Mortality, N (%)	968 (10)	566 (11)	402 (8)

478 AIS=abbreviated injury scale, GCS=Glasgow Coma Scale, ISS=Injury severity score, SBP=systolic blood pressure

479

480 **Table 2. Primary and secondary outcome according to pre-hospital time.**

	Total	Overall in-hospital death		Death due to head injury		Death due to bleeding		
		N	% (95%CI)	N	% (95%CI)	N	% (95%CI)	
TPT ^a								
0-29 min	514	27	5.3 (3.6-7.6)	13	2.5 (1.5-4.3)	8	1.6 (0.8-3.1)	
30-59 min	3,535	244	6.9 (6.1-7.8)	129	3.7 (3.1-4.3)	53	1.5 (1.1-2.0)	
60-89 min	3,459	344	9.9 (9.0-11.0)	179	5.2 (4.5-6.0)	63	1.8 (1.4-2.3)	
90-119 min	1,624	208	12.8 (11.3-14.5)	109	6.7 (5.6-8.0)	36	2.2 (1.6-3.1)	
120-179min	870	121	13.9 (11.8-16.4)	55	6.3 (4.9-8.1)	19	2.2 (1.4-3.4)	
180 + min	124	24	19.4 (13.3-27.3)	16	12.9 (8.0-20.0)	3	2.4 (0.8-7.2)	
Total	10,126	968	9.6 (9.0-10.1)	501	5.0 (4.5-5.4)	182	1.8 (1.5-2.1)	
P value for Homogeneity test		<0.001		<0.001		0.467		

481 ^aTPT = Total Prehospital Time, arrival of the physician-lead prehospital care-team on scene to arrival at the
 482 hospital

483

484 **Table 3. Relationship between outcome and prehospital time.**

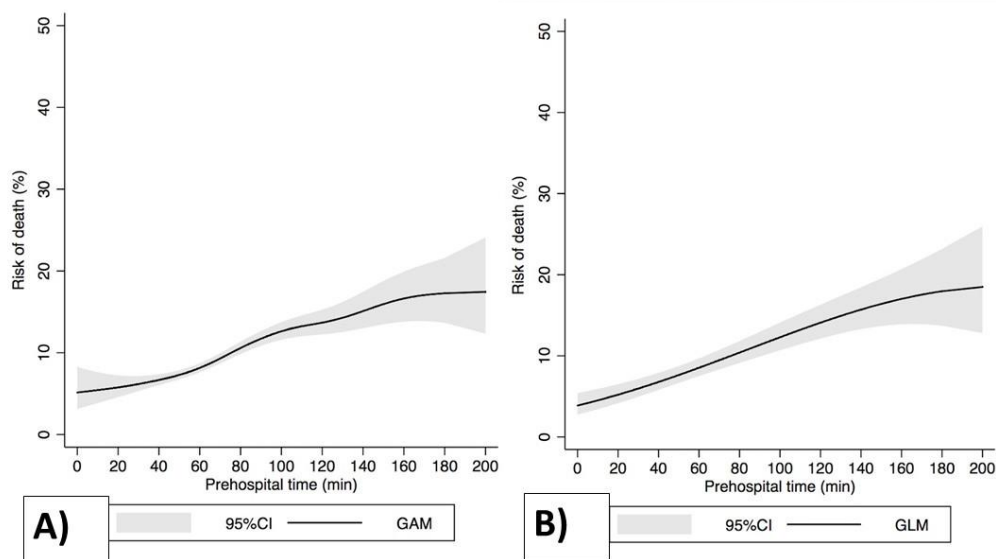
	GLM	P Value
	OR (95% CI) ^a	
Univariate analysis		

Overall death	1.09 (1.07-1.11)	<0.001
Death due to head injury	1.09 (1.06-1.11)	<0.001
Death due to bleeding	1.04 (1.00-1.09)	0.043
Multivariable analysis		
Overall death	1.04 (1.01-1.07)	0.007
Death due to head injury	1.03 (1.00-1.07)	0.153
Death due to bleeding	1.00 (0.99-1.02)	0.239

485 Generalized linear model with random effect by registry and EMS system

486 ^aOdds ratio for increase of 10 minutes in prehospital time.

487



488

489 **Figure 1: A) Unadjusted Generalized Additive Mixed Model representing the risk of death from all**

490 **cause according to prehospital time truncated at 200 minutes. Area Under the Curve: 0.59 (0.57-**

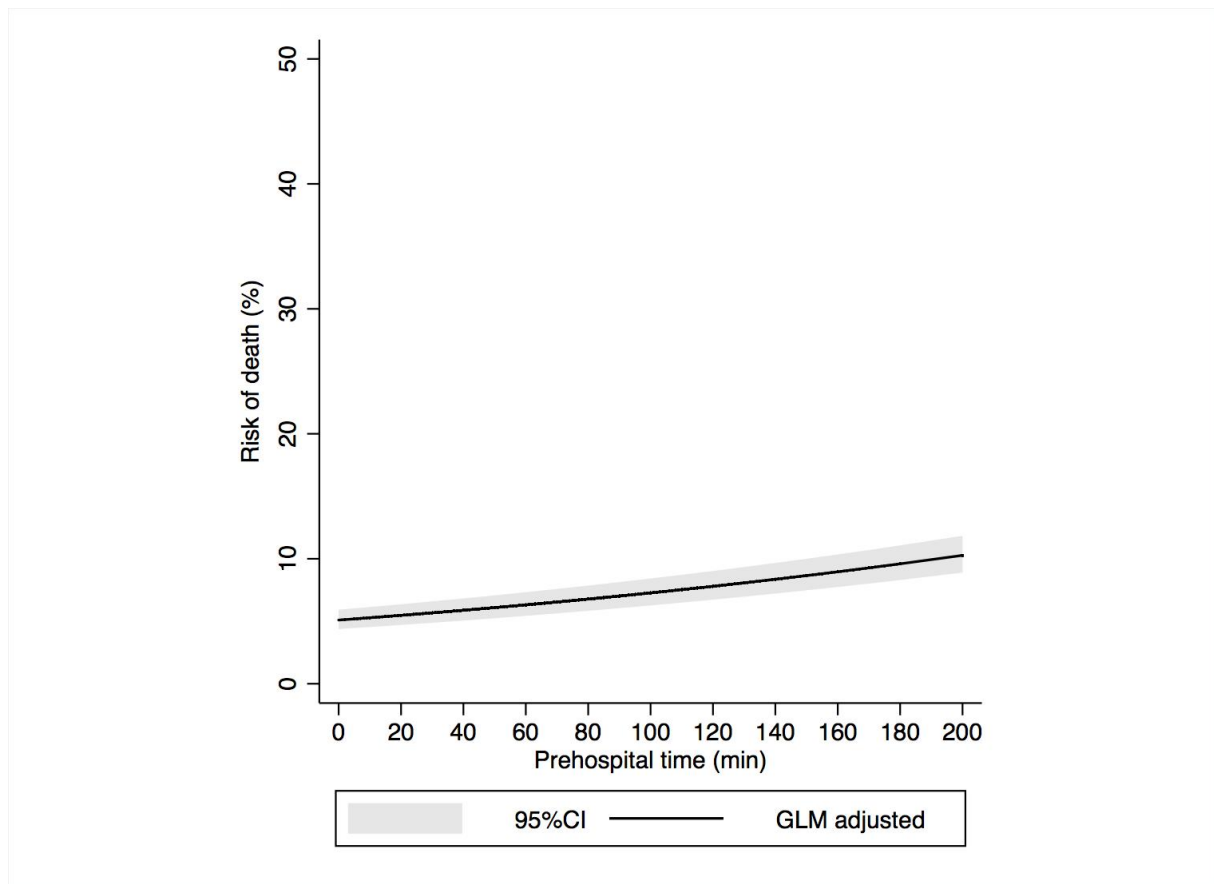
491 **0.61), Internal overall calibration E/O: 1.00 (0.94-1.06), Calibration slope: 1.03 (0.82-1.23).**

492 **B) Unadjusted Generalized Linear Mixed Model representing the risk of death from all cause**

493 **according to prehospital time truncated at 200 minutes. Area Under the Curve: 0.59 (0.57-0.61),**

494 **Internal overall calibration E/O: 1.01 (0.94-1.07), Calibration slope: 0.99 (0.79-1.19).**

495



496

497 **Figure 2. Adjusted relationship between death and prehospital time.**

498 Footnote: Multivariable Generalized Linear Mixed Model representing the risk of death from all
499 cause according to prehospital time adjusted for Age, Systolic blood pressure, GCS and Injury Severity
500 Score. Full model is presented in eTable 5. Area Under the Curve: 0.96 (0.95-0.96), Internal overall
501 calibration E/O: 1.00 (0.96-1.04), Calibration slope: 1.00 (0.94-1.06).

502

503

504

505

506

507

508

