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ORIGINAL RESEARCH

Clinical Predictive Models of Sudden Cardiac Arrest: A Survey of the Current Science and Analysis of Model Performances

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BACKGROUND: More than 500 000 sudden cardiac arrests (SCAs) occur annually in the United States. Clinical predictive models (CPMs) may be helpful tools to differentiate between patients who are likely to survive or have good neurologic recovery and those who are not. However, which CPMs are most reliable for discriminating between outcomes in SCA is not known.

METHODS AND RESULTS: We performed a systematic review of the literature using the Tufts PACE (Predictive Analytics and Comparative Effectiveness) CPM Registry through February 1, 2020, and identified 81 unique CPMs of SCA and 62 subsequent external validation studies. Initial cardiac rhythm, age, and duration of cardiopulmonary resuscitation were the 3 most commonly used predictive variables. Only 33 of the 81 novel SCA CPMs (41%) were validated at least once. Of 81 novel SCA CPMs, 56 (69%) and 61 of 62 validation studies (98%) reported discrimination, with median c-statistics of 0.84 and 0.81, respectively. Calibration was reported in only 29 of 62 validation studies (41.9%). For those novel models that both reported discrimination and were validated (26 models), the median percentage change in discrimination was –1.6%. We identified 3 CPMs that had undergone at least 3 external validation studies: the out-of-hospital cardiac arrest score (9 validations; median c-statistic, 0.79), the cardiac arrest hospital prognosis score (6 validations; median c-statistic, 0.83), and the good outcome following attempted resuscitation score (6 validations; median c-statistic, 0.76).

CONCLUSIONS: Although only a small number of SCA CPMs have been rigorously validated, the ones that have been demonstrate good discrimination.

Key Words: cardiac arrest ■ prediction ■ sudden cardiac death

Sudden cardiac arrest (SCA) is the abrupt cessation of cardiac activity such that an individual becomes unresponsive, without breathing or signs of circulation.[1] In the United States, there are ≈360 000 out-of-hospital cardiac arrest (OHCA) events and 210 000 in-hospital cardiac arrest (IHCA) events annually.[2] Prognosis after an SCA is dismal, with survival from OHCA and IHCA estimated to be ≈10%[3] and 25%,[4] respectively; rates of good neurologic outcome are even lower. Because of the often-precipitous nature of SCA, surrogate decision makers may find themselves in the position of having to make unexpected, difficult choices about care for these patients. Critical decisions, such as withdrawal of care, tracheostomy or percutaneous gastrostomy tube placement, and subsequent changes in code status, are particularly difficult when overall prognosis is unclear. Effectively differentiating patients who are likely to do well after an SCA event from those who are unlikely to do well may help to guide these decisions. Unfortunately, this task

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CLINICAL PERSPECTIVE

What Is New?

- Sudden cardiac arrest (SCA) is a common but disastrous event that can leave both physicians and surrogate decision makers in the difficult position of determining treatment plans in the setting of unclear prognosis; clinical predictive models represent objective, quantitative tools for guiding this type of decision on the behalf of critically ill victims of SCA.
- There are many unique clinical predictive models available for use in SCA, and these tools generally have excellent ability to discriminate between those patients who are likely and those who are unlikely to survive with good neurologic outcome following SCA; only a few of these models have been rigorously validated.

What Are the Clinical Implications?

- The out-of-hospital cardiac arrest score, the cardiac arrest hospital prognosis score, and the good outcome following attempted resusciation score are the 3 most rigorously validated tools for predicting the prognosis of SCA victims; however, the predictions made using these tools should be interpreted cautiously and in the context of an individual patient's clinical picture to avoid inappropriate early withdrawal of life-sustaining treatment.

Nonstandard Abbreviations and Acronyms

SCA	sudden cardiac arrest
CPM	clinical predictive model
OHCA	out-of-hospital cardiac arrest
IHCA	in-hospital cardiac arrest
IQR	interquartile range

is made more difficult by a lack of clear criteria or published guidelines on when and from whom care should be withdrawn after an SCA.

Clinical predictive models (CPMs) can help stratify patients by outcome risk. These models use patient-specific data to make personalized clinical predictions. However, although some CPMs have been validated rigorously and incorporated into clinical practice guidelines, there is currently no CPM related to SCA outcome that has gained widespread use. In the present study, we assessed currently available SCA CPMs with special attention to how rigorously models have been validated and which variables emerge as being consistently important for predicting outcomes.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Model and Validation Identification

We performed a systematic review of novel SCA CPMs and their validations (Figure 1). We included previously identified SCA CPMs from the Tufts PACE (Predictive Analytics and Comparative Effectiveness) CPM Registry. The registry, which is free and available to the public at http://pace.tuftsmedicalcenter.org/com, contains a field synopsis of CPMs in cardiovascular disease, including SCA, published between January 1990 and December 2015. These methods have been previously reported.[5] We identified additional English-language abstracts containing potential SCA CPMs via a targeted PubMed search (Figure S1) of the OVID Medline database extending through February 1, 2020. Two independent reviewers screened potential abstracts using *Abstrackr*, a semiautomated online screening program. Discrepancies were discussed until consensus was achieved. We then selected abstracts for full-text review if they met the following inclusion criteria: (1) made specific mention of multivariate modeling, (2) specified SCA as the index condition, and (3) were based on data from a primarily adult population. We then doubly screened full-text publications and included them for further analysis if, in addition to meeting the inclusion criteria, they contained a novel, useable (meaning that an end user could generate an outcome prediction given knowledge of the appropriate set of patient variables) SCA CPM. We identified CPM validation studies by performing a Scopus citation search on all novel SCA CPMs identified as above. Two independent reviewers screened abstracts and full-text publications in the same manner as for novel models. We included validation studies for further analysis if they assessed a previously published SCA CPM in a population temporally and/or spatially distinct from the population used in the initial development of that model. Novel models that were incidentally identified during validation search were also included, and the cycle of validation search was repeated until no further novel models were identified.

Data Extraction and Statistical Analysis

We extracted data on the studied population, the proposed model, and SCA outcomes from both novel model and validation studies in accordance

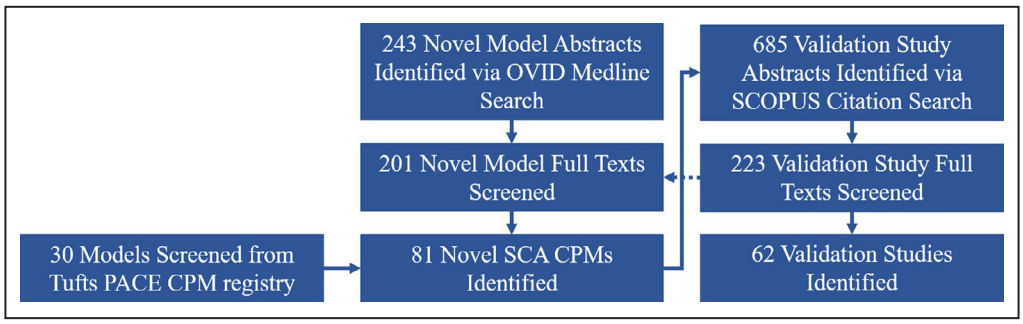

Figure 1. A flowchart showing methods by which both novel sudden cardiac arrest clinical predictive models and their validations were identified.
CPM indicates clinical predictive model; PACE, Predictive Analytics and Comparative Effectiveness; and SCA, sudden cardiac arrest.

with the checklist for systematic reviews of prediction modeling studies.[6] Collected fields included location of data origin, whether data were collected prospectively or retrospectively, the approach to and amount of missingness in the data set, time frame of the predicted outcome, sample size, number of SCA events and whether the arrest occurred out of hospital or in hospital, model discrimination, and calibration. A modified version of the Prediction Model Risk of Bias Assessment Tool[7,8] was used to assess the risk of bias in model development and applicability of the models by a trained research assistant. The simplified version, Prediction Model Risk of Bias Assessment Tool Short Form, is a structured judgment system focusing on the analytic items in Prediction Model Risk of Bias Assessment Tool. It was collaboratively developed by clinicians and modeling experts for use and tested for agreement with the complete Prediction Model Risk of Bias Assessment Tool on models included in the Tufts PACE Center CPM Registry; the results are currently pending publication. We categorized the time frame of predicted outcome into 3 categories: (1) early, through 1 day after SCA, (2) intermediate, >1 day post-SCA to hospital discharge, and (3) long-term, beyond hospital discharge. We used the c-statistic (or area under the curve of the receiver operator curve) to assess model discrimination. Because the c-statistic is bounded between 0.5 and 1.0, we used percentage change in discrimination (equation 1) to make direct comparisons between discrimination of novel models and validation studies.

$$\text{Percent change in discrimination} = \left(\text{c-statistic}_{\text{Validation}} - \text{c-statistic}_{\text{Novel}}\right) / \left(\text{c-statistic}_{\text{Novel}} - 0.5\right) \times 100. \quad (1)$$

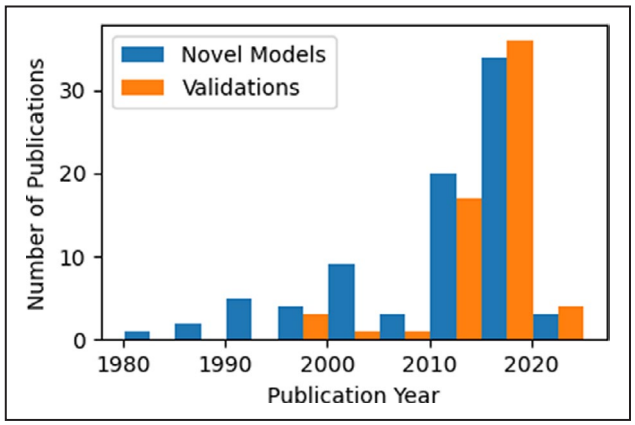

Figure 2. Histogram showing the number of both novel sudden cardiac arrest clinical predictive models (blue) and validation (orange) studies that were published per 5-year interval between January 1980 and February 2020.

RESULTS

Novel SCA CPMs

We identified 81 unique CPMs of SCA published between July 1981 and February 2020 (Figure 2). Table 1 summarizes characteristics of the populations used in these novel SCA CPMs, and Table 2[9–71] presents detailed information on the complete set of identified models. Herein, models are identified using PubMed identification numbers; a model identification number further differentiates between multiple

Table 1. Characteristics of the SCA CPM Derivation and Validation Populations

Characteristic	Novel Model	Validation Study
No. of models	81	62
Average age, y	65 (61–67)	65 (62–70)
Men, %	66 (60–75)	63 (58–70)
Sample size	591 (140–1028)	430 (212–1657)

Data are given as median (interquartile range), unless otherwise indicated.
CPM indicates clinical predictive model; and SCA, sudden cardiac arrest.

Table 2. List of the Identified SCA CPMs With Information Detailing the Derivation Population, Including Whether These Models Were Derived for a More Specific Index Condition (eg, in Patients Undergoing ECPR or TTM), Associated Model Outcomes, Discrimination if Investigated, and Number of External Validation Studies

PMID	Model No.	Population Size	OHCA vs IHCA	Specific Index Condition	Outcome Type	Outcome Time Frame	% Good Outcome	C-Statistic	No. of External Validations
1315072[9]	1	112	Mixed	None	Survival	Intermediate	55	0.83	0
1578040[10]	1	6179	Mixed	None	Survival	Intermediate	11	NR	0
1661018[11]	1	710	IHCA	None	Survival	Short-term	28	0.78	0
1661018[11]	2	198	IHCA	None	Survival	Intermediate	47	0.8	0
2246419[12]	1	347	OHCA	None	Neurologic	Intermediate	11	NR	0
2551011[13]	1	2235	Mixed	None	Survival	Intermediate	16	NR	1
2741977[14]	1	140	IHCA	None	Survival	Intermediate	24	NR	2
7241728[15]	1	611	OHCA	None	Survival	Intermediate	19	NR	2
9396421[16]	1	1872	OHCA	None	Survival	Intermediate	31	0.65	0
9462599[17]	1	127	OHCA	Witnessed arrest; cardiac cause	Survival	Intermediate	42	0.81	1
9462599[17]	2	127	OHCA	Witnessed arrest; cardiac cause	Neurologic	Intermediate	39	0.89	1
9547842[18]	1	100	OHCA	Cardiac cause; ventricular fibrillation	Survival	Intermediate	29	NR	0
12533358[19]	1	741	IHCA	None	Survival	Short-term	10	NR	1
12533358[19]	2	707	IHCA	None	Survival	Short-term	9	NR	0
12626988[20]	1	34	Mixed	None	Neurologic	Intermediate	47	NR	0
15246581[21]	1	219	IHCA	None	Survival	Intermediate	15	NR	0
15246581[21]	2	219	IHCA	None	Survival	Long-term	14	NR	0
15246581[21]	3	219	IHCA	None	Survival	Long-term	11	NR	0
15531065[22]	1	754	OHCA	None	Survival	Intermediate	1	NR	0
15531065[22]	2	754	OHCA	None	Neurologic	Intermediate	2	NR	0
15531065[22]	3	754	OHCA	None	Neurologic	Intermediate	2	NR	0
17082207[23]	1	130	OHCA	None	Neurologic	Intermediate	22	0.82	9
18573589[24]	1	1028	OHCA	Cardiac cause; shockable rhythm	Survival	Long-term	20	0.74	0
18584503[25]	1	748	OHCA	Ventricular fibrillation	Survival	Short-term	NR	NR	0
20655699[26]	1	591	OHCA	None	Survival	Short-term	21	0.83	0
20655699[26]	2	591	OHCA	None	Survival	Intermediate	13	0.88	0
20655699[26]	3	591	OHCA	None	Survival	Long-term	10	0.91	0
21482007[27]	1	285	OHCA	Shockable rhythm	Neurologic	Long-term	32	0.85	1
21482007[27]	2	577	OHCA	Nonshockable rhythm	Neurologic	Long-term	6	0.89	1
21515626[28]	1	5471	OHCA	None	Survival	Intermediate	43	0.71	4
21756969[29]	1	457	Mixed	None	Survival	Long-term	47	NR	2
22281226[30]	1	66	OHCA	TTM	Neurologic	Intermediate	61	0.95	0
22641228[31]	1	28 629	IHCA	None	Neurologic	Intermediate	25	0.8	2
23844724[32]	1	307 896	OHCA	None	Survival	Long-term	4	0.79	1
23844724[32]	2	307 896	OHCA	None	Neurologic	Long-term	2	0.85	1
24018585[33]	1	22 626	IHCA	None	Neurologic	Long-term	11	0.78	6
24107638[34]	1	38 092	IHCA	None	Neurologic	Long-term	10	0.76	2

(*Continued*)

Table 2. Continued

PMID	Model No.	Population Size	OHCA vs IHCA	Specific Index Condition	Outcome Type	Outcome Time Frame	% Good Outcome	C-Statistic	No. of External Validations
24107638[34]	2	38 092	IHCA	None	Neurologic	Long-term	10	0.73	2
24309445[35]	1	750	OHCA	None	Survival	Long-term	6	NR	0
24830872[36]	1	14 688	IHCA	None	Survival	Short-term	45	0.73	2
24830872[36]	2	14 688	IHCA	None	Survival	Intermediate	20	0.81	2
24960427[37]	1	1068	OHCA	None	Survival	Long-term	40	NR	1
25443259[38]	1	152	IHCA	ECPR	Survival	Intermediate	32	0.86	1
25828128[39]	1	32	Mixed	TTM; ventricular fibrillation	Neurologic	Long-term	47	0.98	1
25911585[40]	1	92	OHCA	TTM	Survival	Long-term	54	0.82	0
25911585[40]	2	66	OHCA	TTM	Survival	Long-term	67	0.88	0
26322336[41]	1	96	OHCA	None	Neurologic	Intermediate	20	0.84	0
26497161[42]	1	819	OHCA	None	Neurologic	Intermediate	27	0.93	6
26689743[43]	1	207	OHCA	Cardiac cause	Survival	Intermediate	65	0.81	1
28410590[44]	1	933	OHCA	Cardiac cause; TTM	Neurologic	Long-term	47	0.84	0
28490379[45]	1	151	OHCA	TTM	Neurologic	Intermediate	42	0.96	0
28528323[46]	1	122	OHCA	TTM	Neurologic	Intermediate	27	0.82	1
28629472[47]	1	687	OHCA	Cardiac cause; TTM	Neurologic	Long-term	51	0.84	0
28647407[48]	1	547	OHCA	None	Survival	Short-term	59	0.66	0
28856660[49]	1	111	Mixed	ECPR	Survival	Intermediate	19	0.88	0
29074504[50]	1	638	OHCA	None	Survival	Intermediate	81	0.73	0
29317350[51]	1	420 959	OHCA	None	Neurologic	Intermediate	1	NR	0
29481910[52]	1	286	OHCA	Hypothermic arrest; ECPR	Survival	Intermediate	37	0.9	1
29580960[53]	1	658	OHCA	Hypothermic arrest; ECPR	Neurologic	Continuous	40	NR	0
29677083[54]	1	81	OHCA	Hanging-induced arrest; TTM	Survival	Intermediate	25	0.91	0
29677083[54]	2	81	OHCA	Hanging-induced arrest; TTM	Neurologic	Intermediate	20	0.86	0
29942359[55]	1	129	OHCA	None	Neurologic	Intermediate	30	0.84	1
30001950[56]	1	153	OHCA	TTM	Neurologic	Long-term	43	0.9	1
30261969[57]	1	198	OHCA	Patients undergoing angiography	Survival	Long-term	53	NR	1
30292802[58]	1	456	OHCA	None	Neurologic	Long-term	19	0.82	0
30345531[59]	1	768	Mixed	None	Survival	Continuous	52	NR	0
30413210[60]	1	107	OHCA	Cardiac cause; TTM	Neurologic	Long-term	47	0.92	0
30601816[61]	1	19 609	OHCA	None	Survival	Short-term	41	NR	0
30650128[62]	1	40	OHCA	None	Survival	Long-term	30%	0.94	0
30650128[62]	2	40	OHCA	None	Survival	Long-term	30	0.95	0
30650128[62]	3	40	OHCA	None	Survival	Long-term	30	0.99	0
30807816[63]	1	580	Mixed	None	Neurologic	Intermediate	37	0.88	0
30819521[64]	1	852	OHCA	None	Neurologic	Intermediate	4	0.82	1
30848327[65]	1	3855	OHCA	None	Neurologic	Intermediate	34	NR	0
31153943[66]	1	460	OHCA	TTM	Neurologic	Long-term	38	0.89	1
31153943[66]	2	460	OHCA	TTM	Neurologic	Long-term	29	0.9	0

(*Continued*)

Table 2. Continued

PMID	Model No.	Population Size	OHCA vs IHCA	Specific Index Condition	Outcome Type	Outcome Time Frame	% Good Outcome	C-Statistic	No. of External Validations
31412292[67]	1	628	IHCA	None	Neurologic	Intermediate	28	0.81	0
31539610[68]	1	2685	OHCA	None	Survival	Intermediate	34	0.72	0
31730900[69]	1	7985	OHCA	None	Neurologic	Intermediate	23	0.88	1
31821836[70]	1	23 713	IHCA	None	Neurologic	Intermediate	22	0.7	0
31980268[71]	1	1962	OHCA	None	Survival	Short-term	22	0.83	1

CPM indicates clinical predictive model; ECPR, extracorporeal cardiopulmonary resuscitation; IHCA, in-hospital cardiac arrest; NR, not reported; OHCA, out-of-hospital cardiac arrest; PMID, PubMed identification; SCA, sudden cardiac arrest; and TTM, targeted temperature management.

models contained within a single publication. Fifty-five of those models (68%) predicted outcomes following OHCA, 17 (21%) following IHCA, and 9 (11%) following a mixture of both. Nine (11%) models predicted early outcomes, 42 (52%) predicted intermediate time frame outcomes, and 28 (35%) predicted long-term outcomes. Thirty-one (38%) models used European populations during derivation, 24 (30%) used North American populations, and 17 (21%) used Asian populations. Thirty-one (38%) models were developed with prospective cohort data, and 49 (61%) models were developed using retrospective cohort data. Thirty-three (41%) models reported their approach to missingness, and 27 (33%) models reported amount of missingness in the derivation cohort. Models took various forms, with point score-based models constituting 35 (43%) models, logistic regression constituting 29 (36%) models, and characteristic decision trees constituting 16 (20%) models. The median sample size of derivation populations was 591 (interquartile range [IQR], 140–1028). The number of studies at low risk of bias was 6 (7%); the remaining 75 (93%) were high risk of bias. The median number of predictive covariates was 5 (IQR, 3–6), and the 3 most commonly used covariates were initial rhythm (n=51, 63%), age (n=42, 52%), and the duration of cardiopulmonary resuscitation (n=31, 38%) (Figure 3). Of models that reported discrimination (n=56, 69%), the median c-statistic was 0.84 (IQR, 0.80–0.89) (Figure 4A).

Validation Studies

We identified 62 SCA CPM validation studies published between April 1997 and February 2020 (Figure 1). Table 1 summarizes characteristics of the populations used in these validation studies, and Table 3[72–94] presents detailed information on the complete set of identified validation studies. Of the 81 novel SCA CPMs, 33 (41%) were validated at least once, and only 4 (5%) were validated at least 3 times (Figure 5). The 3 most rigorously validated models were the OHCA score,[23] the cardiac arrest hospital prognosis score,[42] and the good outcome following attempted resuscitation score[33] (Table 4). All but one validation study reported discrimination (n=61, 98%). The median c-statistic was 0.81 (IQR, 0.74–0.85) (Figure 4B). Only 29 of the 62 validations (47%) reported information on calibration. Of the 33 validated models,

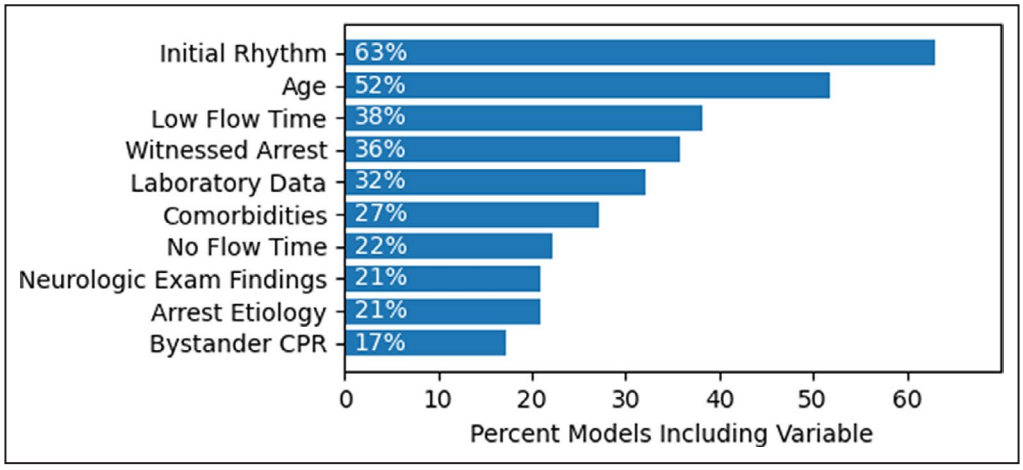

Figure 3. The top 10 most frequently included predictive covariates (or covariate classes) included in novel sudden cardiac arrest clinical predictive models.
CPR indicates cardiopulmonary resuscitation.

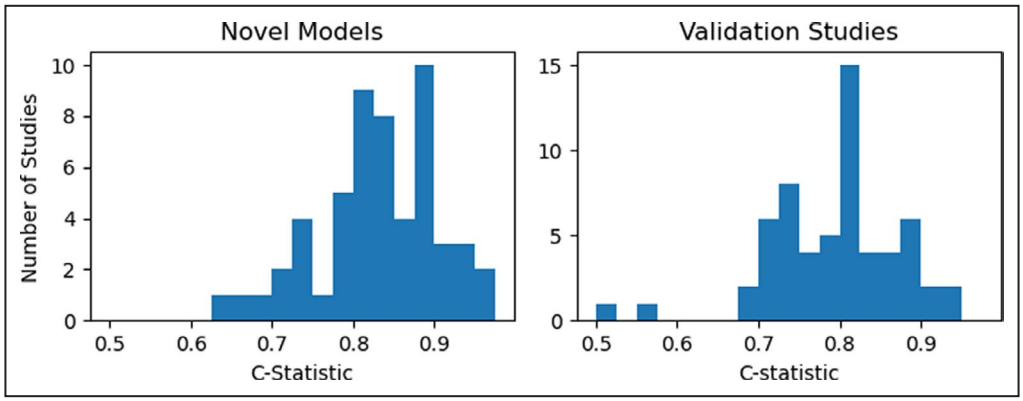

Figure 4. Histograms showing distributions of discrimination for novel sudden cardiac arrest clinical predictive models (A) and validation studies (B).

discrimination was reported in both model generation and validation publications for 26 models. For these models, the median percentage change in discrimination was –1.6% (IQR, –10.6% to 8.2%) (Figure 6).

IHCAs Versus OHCAs

We stratified SCA CPMs by whether the index SCA occurred in out-of-hospital or in-hospital settings. We identified 55 models (68%) of OHCA with a median derivation population of 577 (IQR, 128–835) and median rate of events per variable of 17 (IQR, 8–56). We identified 17 models (21%) of IHCA with median derivation population of 710 (IQR, 219–22 626) and median rate of events per variable of 35 (IQR, 9–515). Discrimination was higher for OHCA models (median c-statistic, 0.85; IQR, 0.82–0.90) than for IHCA models (median c-statistic, 0.78; IQR, 0.75–0.80).

DISCUSSION

In the present study, we have shown that there are a broad variety of models available for predicting clinical outcomes following SCA. We found that the median c-statistic of novel SCA CPMs was 0.84, suggesting that in general these models are good at discriminating between patients who are likely to have a good outcome from those who are likely to have a poor outcome after a SCA (to put this in context, the cardiac failure or dysfunction, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65–74 and sex category [female] score which has been widely used for determining stroke risk in patients with atrial fibrillation had discriminations of 0.61 and 0.67 during derivation and validation, respectively[95,96]).

This strong discrimination was maintained during external validation; in SCA CPMs that were validated at least once, matched comparison of discrimination from model generation and validation studies showed a median percentage change in discrimination of only –1.6%. This is in stark contrast to CPMs in other areas of cardiovascular disease. For example, we have previously examined CPMs related to valvular heart disease. The percentage change in discrimination of valvular heart disease CPMs was on the order of –30%.[97] In another study in which we validated 3 major CPMs of acute heart failure, we found percentage decrements in discrimination of between –19% and –30%.[98] Other groups have found similar effects in carotid revascularation[99] and hospital readmission following acute myocardial infarction.[100]

Predictive Variables in SCA CPMs

One of the unique aspects of SCA CPMs compared with CPMs in other cardiovascular diseases is that predictions are made not just on characteristics of the individual patient, but also on characteristics of the cardiac arrest that a particular patient experiences. We found that the most frequently used predictive variables were event specific (eg, duration of cardiopulmonary resuscitation and initial SCA cardiac rhythm) rather than patient specific (eg, age and sex). The fact that these variables were so frequently selected after multivariate analysis suggests that they are strong predictors of outcome. This reliance on event-specific variables may make SCA CPMs less sensitive to difference in the composition of patient population.

From a clinical perspective, this finding that predictions were largely independent of patient-specific variables is counterintuitive. Several studies have shown that comorbidities, such as diabetes mellitus,[101] liver disease,[102] and malignancy,[103,104] are independent predictors of poor outcome in SCA. One possible explanation for this discrepancy is that there is covariance between these comorbidity variables and other variables that are more strongly associated with SCA outcome. Nonshockable rhythm, for example, is significantly more likely in patients experiencing SCA with underlying diabetes mellitus,

Table 3. List of the Identified Validation Studies With Information Detailing the Validation Population, Associated Outcome Rates, Discrimination, and Calibration Method if Investigated

Validation PMID	Novel Model PMID	Model No.	Population Size	Event Rate, %	C-Statistic	Calibration Reported
9107612[72]	2741977	1	656	5	0.52	No
9541764[73]	9462599	1	62	53	0.92	No
9541764[73]	9462599	2	62	47	0.93	No
12782522[74]	7241728	1	575	4	0.33	Yes
17082207[23]	17082207	1	210	25	0.88	Yes
20655699[26]	2551011	1	591	10	0.82	No
20655699[26]	7241728	1	591	13	0.79	No
20655699[26]	12533358	1	591	21	0.73	No
21482007[27]	21482007	1	212	46	0.87	No
21482007[27]	21482007	2	423	5	0.87	No
21494106[75]	17082207	1	128	23	0.85	Yes
21515626[28]	21515626	1	2218	44	0.73	No
22281225[76]	17082207	1	122	35	0.79	No
23844724[32]	23844724	1	82 330	5	0.81	No
23844724[32]	23844724	2	82 330	2	0.88	No
24107638[34]	24107638	1	14 435	12	0.73	No
24107638[34]	24107638	2	14 435	12	0.71	No
24830872[36]	24830872	1	7791	45	0.72	Yes
24830872[36]	24830872	1	1657	46	0.72	Yes
24830872[36]	24830872	2	7791	18	0.81	Yes
24830872[36]	24830872	2	1657	19	0.80	Yes
24960427[37]	24960427	1	297	58	0.81	No
25636896[77]	21756969	1	393	41	0.82	Yes
25636896[77]	21756969	1	214	41	0.83	Yes
25828128[39]	25828128	1	29	66	0.89	Yes
26393849[78]	2741977	1	26 327	24	0.69	No
26393849[78]	22641228	1	26 327	24	0.79	Yes
26393849[78]	24018585	1	26 327	24	0.71	No
26497161[42]	26497161	1	367	33	0.85	Yes
26497161[42]	26497161	1	1129	25	0.91	Yes
26689743[43]	26689743	1	96	65	0.82	No
27404694[79]	24018585	1	287	16	0.85	No
28049389[80]	24107638	1	287	16	0.77	No
28049389[80]	24107638	2	287	16	0.71	No
28356134[81]	21515626	1	680	50	0.71	Yes
28410590[44]	17082207	1	933	47	0.75	Yes
28410590[44]	26497161	1	933	47	0.75	Yes
28528323[46]	28528323	1	344	21	0.81	Yes
29500154[82]	17082207	1	150	22	0.57	No
29723201[83]	17082207	1	173	31	0.74	No
29723607[84]	24018585	1	717	22	0.82	Yes
29942359[55]	29942359	1	31	NR	0.90	No
30001950[56]	30001950	1	91	46	0.82	No
30138383[85]	22641228	1	796	12	0.79	Yes
30261969[57]	30261969	1	67	NR	NR	No
30391369[86]	17082207	1	349	43	0.81	Yes

(*Continued*)

Table 3. Continued

Validation PMID	Novel Model PMID	Model No.	Population Size	Event Rate, %	C-Statistic	Calibration Reported
30391369[86]	26497161	1	349	43	0.86	Yes
30447262[87]	21515626	1	2041	29	0.76	Yes
30807816[63]	17082207	1	437	NR	0.86	No
30819521[64]	30819521	1	859	2	0.88	Yes
30940473[88]	29481910	1	122	42	0.82	Yes
30981847[89]	25443259	1	274	29	0.82	Yes
31078496[90]	24018585	1	2845	11	0.75	Yes
31078496[90]	24018585	1	16 154	15	0.76	Yes
31153943[66]	31153943	1	151	42	0.93	No
31306716[91]	17082207	1	336	45	0.79	No
31306716[91]	26497161	1	336	45	0.81	No
31512185[92]	24018585	1	403	17	0.68	No
31730900[69]	31730900	1	1806	23	0.88	Yes
31980268[71]	31980268	1	747	26	0.77	No
31987887[93]	26497161	1	176	6	0.81	No
32035177y[94]	21515626	1	63 059	8	0.74	Yes

NR indicates not reported; PMID, PubMed identification number.

liver disease, and malignancy.[105] In SCA CPMs identified in this study, we identified several examples of comorbidity (eg, diabetes mellitus,[30,43] chronic kidney disease,[39,46] and malignancy[44]) dropout in favor of initial rhythm or other strong event-specific variables.

Impacts of Location of Arrest

Models that examined outcomes after OHCA performed better on average than those that examined outcomes after IHCA, with median C-statistics of 0.85 and 0.78, respectively. Although the CPMs for these 2 different populations share many of the same predictive variables, the magnitudes/values of these variables are different. Medical response times to OHCA are slower compared with IHCA[106]; it follows that much longer durations of no-flow and low-flow circulation[51,107] are found in OHCA. Large surveys of both OHCA and IHCA have also shown that initial rhythm is less likely to be shockable in OHCA (13%)[108] compared with IHCA (21%).[109] The impact of arrest location on variable magnitudes is further complicated by the fact that the directionality of these changes may differ depending on the variable. For example, although OHCA tends to be longer and less likely to be shockable than IHCA, victims of IHCA tend to be sicker and have higher burdens of comorbidity at baseline compared with their OHCA counterparts.[110]

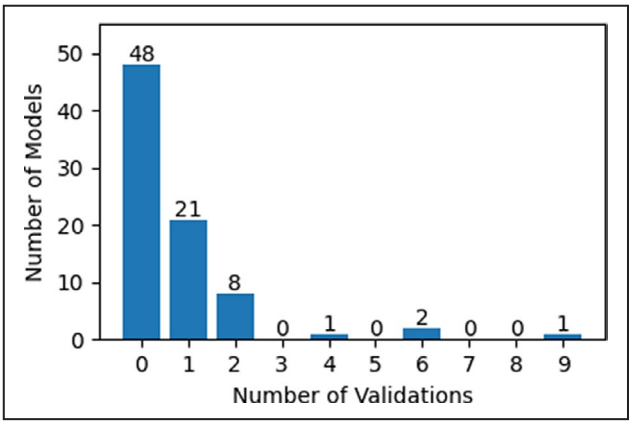

Figure 5. A bar chart showing the number of times each of the novel sudden cardiac arrest clinical predictive models was validated.

Patients experiencing OHCA also have lower rates of survival and neurologic recovery than those experiencing IHCA.[111] Although sensitivity and specificity are often assumed to be independent of the outcome rate in a population, these metrics[112,113] can differ based on the underlying case mix of the population being studied. Discrimination is thus affected by heterogeneity and will tend to be better in more heterogeneous populations.

Finally, OHCA models were derived from smaller populations than IHCA models and had lower numbers of positive outcome per model covariate. This may have predisposed these OHCA models to relative overfitting compared with their IHCA counterparts and may in part explain the better discrimination of OHCA models.

Clinical Implications

The primary clinical use of these CPMs is in assisting physicians and surrogate decision makers with

Table 4. Characteristics of the Top 3 Most Rigorously Validated SCA CPMs

Model Name	Arrest Setting	Outcome Time Frame	C-Statistic	No. of Validation Studies	Median Validation C-Statistic	% Change in Discrimination
OHCA score	OHCA	Intermediate	0.82	9	0.79	–9
CAHP score	OHCA	Intermediate	0.93	6	0.83	–23
GO-FAR score	IHCA	Intermediate	0.78	6	0.755	–9

CAHP indicates cardiac arrest hospital prognosis; CPM, clinical predictive model; GO-FAR, good outcome following attempted resuscitation; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; and SCA, sudden cardiac arrest.

decisions on intensification, continuation, or withdrawal of care. For this purpose, SCA CPMs offer several advantages compared with guidance based on the anecdotal experiences of an individual physician. In studies of end-of-life counseling, miscommunication between physician and surrogate decision makers has been identified as a primary driver of inappropriately optimistic expectations of prognosis.[114] These optimistic expectations have been shown to significantly increase duration of intensive care unit hospitalization and cost without improving patient outcomes.[115] Quantitative assessments of prognosis, such as those offered by SCA CPMs, also leave less room for misinterpretation than qualitative assessments.[116,117]

Inappropriate early withdrawal of life-sustaining treatment attributable to perceived poor prognosis is a major cause of preventable death in victims of SCA (and may in part contribute to the high c-statistics found in these CPMs by making bad outcomes easier to predict). Two cohort studies that matched SCA victims for whom care was withdrawn before 72 hours to those who received continued treatment estimated that 16% to 19% of patients who received withdrawal of care would have otherwise gone on to have good neurologic recovery.[118,119] Subjective impressions of poor prognosis from physicians are thought to be a major contributor to this inappropriate withdrawal of life-sustaining treatment.[120] In this case, SCA CPMs have the advantage of objectivity and may help to reduce the intrusion of physician-held personal biases into discussions on withdrawal of care.[121] Nevertheless, these theoretical advantages should be examined empirically, ideally in clinical trials.

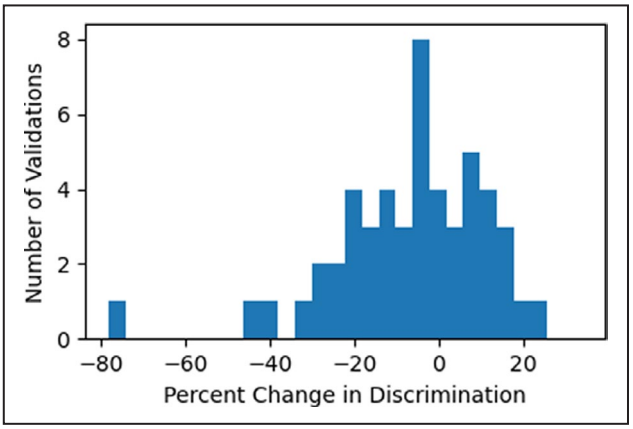

Figure 6. Histogram of the percentage change in discrimination between initial sudden cardiac arrest clinical predictive model derivation and subsequent external validation.
Some models were validated more than once.

Because prophesies of mortality can be self-fulfilling,[122–124] predictions in SCA should be made with care. Identifying when medical care is likely to be futile generally requires a high degree of certainty[125] because the consequences of a false-positive prediction are so dire. Although we identified 3 SCA CPMs (the OHCA score, the cardiac arrest hospital prognosis score, and the good outcome following attempted resuscitation score) that performed well using conventional measures of discrimination, it is unclear whether they can provide the confidence necessary to support futility claims.[126] Any CPM-based prediction should be interpreted in the broader context of an individual patient's overall clinical picture.

Limitations

There are several limitations to this work. Although we applied a systematic approach to the identification of novel SCA CPMs and their validations, our search was limited to the Medline and Scopus databases. It is possible that there are models and/or validation studies present in alternative databases that we failed to include. In addition, our ability to examine variable effects across models was limited by model heterogeneity. The inconsistent reporting of c-statistic SE made formal, weighted statistical comparisons between groups of CPMs impossible.

CONCLUSIONS

There is a wide selection of CPMs designed for prognostication following SCA. These models demonstrated excellent ability to discriminate between patients experiencing SCA with good and poor prognosis. The most commonly used predictive variables were initial cardiac rhythm, patient age, and whether

an SCA was witnessed. Discrimination remained high for those models that underwent external validation; however, few CPMs have been rigorously validated, and calibration is rarely reported. Although these quantitative assessments of prognosis may be helpful for decision making on withdrawal of care in arrest survivors, they should be interpreted in the broader context of an individual patient's overall clinical picture.

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Disclosures

None.

Supplementary Material

Figure S1

REFERENCES

1. American College of Cardiology/American Heart Association Task Force on Clinical Data Standards (ACC/AHA/HRS Writing Committee to Develop Data Standards on Electrophysiology), Buxton AE, Calkins H, Callans DJ, DiMarco JP, Fisher JD, Greene HL, Haines DE, Hayes DL, Heidenreich PA, Miller JM, et al. ACC/AHA/HRS 2006 key data elements and definitions for electrophysiological studies and procedures: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Data Standards (ACC/AHA/HRS Writing Committee to Develop Data Standards on Electrophysiology). *Circulation*. 2006;114:2534–2570.
2. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation*. 2019;139:e56–e528.
3. Daya MR, Schmicker RH, Zive DM, Rea TD, Nichol G, Buick JE, Brooks S, Christenson J, MacPhee R, Craig A, et al. Out-of-hospital cardiac arrest survival improving over time: results from the Resuscitation Outcomes Consortium (ROC). *Resuscitation*. 2015;91:108–115.
4. Ofoma UR, Basnet S, Berger A, Kirchner HL, Girotra S; American Heart Association Get With The Guidelines – Resuscitation Investigators. Trends in survival after in-hospital cardiac arrest during nights and weekends. *J Am Coll Cardiol*. 2018;71:402–411.
5. Wessler BS, Lai YHL, Kramer W, Cangelosi M, Raman G, Lutz JS, Kent DM. Clinical prediction models for cardiovascular disease: Tufts predictive analytics and comparative effectiveness clinical prediction model database. *Circ Cardiovasc Qual Outcomes*. 2015;8:368–375.
6. Moons KG, de Groot JA, Bouwmeester W, Vergouwe Y, Mallett S, Altman DG, Reitsma JB, Collins GS. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. *PLoS Med*. 2014;11:e1001744.
7. Wolff RF, Moons KG, Riley RD, Whiting PF, Westwood M, Collins GS, Reitsma JB, Kleijnen J, Mallett S; PROBAST Group. PROBAST: a tool to assess the risk of bias and applicability of prediction model studies. *Ann Intern Med*. 2019;170:51–58.
8. Moons KG, Wolff RF, Riley RD, Whiting PF, Westwood M, Collins GS, Reitsma JB, Kleijnen J, Mallett S. PROBAST: a tool to assess risk of bias and applicability of prediction model studies: explanation and elaboration. *Ann Intern Med*. 2019;170:W1–W33.
9. Woodhouse SP, Case CC, Siskind V, Eller H. Prediction of hospital discharge in immediate survivors of ventricular fibrillation or asystole. *Resuscitation*. 1992;23:77–82.
10. Martens PR, Mullie A, Buylaert W, Calle P, van Hoeyweghen R; The Belgian Cerebral Resuscitation Study Group. Early prediction of non-survival for patients suffering cardiac arrest–a word of caution. *Intensive Care Med*. 1992;18:11–14.
11. Marwick TH, Case CC, Siskind V, Woodhouse SP. Prediction of survival from resuscitation: a prognostic index derived from multivariate logistic model analysis. *Resuscitation*. 1991;22:129–137.
12. Kentsch M, Stendel M, Berkel H, Mueller-Esch G. Early prediction of prognosis in out-of-hospital cardiac arrest. *Intensive Care Med*. 1990;16:378–383.
13. Delooz HH, Lewi PJ; The Cerebral Resuscitation Study Group. Early prognostic indices after cardiopulmonary resuscitation (CPR). *Resuscitation*. 1989;17(suppl):S149–S155; discussion S199–S206.
14. George AL Jr, Folk BP III, Crecelius PL, Campbell WB. Pre-arrest morbidity and other correlates of survival after in-hospital cardiopulmonary arrest. *Am J Med*. 1989;87:28–34.
15. Eisenberg M, Hallstrom A, Bergner L. The ACLS score: predicting survival from out-of-hospital cardiac arrest. *JAMA*. 1981;246:50–52.
16. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. *Circulation*. 1997;96:3308–3313.
17. Thompson RJ, McCullough PA, Kahn JK, O'Neill WW. Prediction of death and neurologic outcome in the emergency department in out-of-hospital cardiac arrest survivors. *Am J Cardiol*. 1998;81:17–21.
18. Monsieurs KG, De Cauwer H, Wuyts FL, Bossaert LL. A rule for early outcome classification of out-of-hospital cardiac arrest patients presenting with ventricular fibrillation. *Resuscitation*. 1998;36:37–44.
19. Cooper S, Evans C. Resuscitation Predictor Scoring Scale for inhospital cardiac arrests. *Emerg Med J*. 2003;20:6–9.
20. Geppert A, Zorn G, Delle-Karth G, Koreny M, Siostrzonek P, Heinz G, Huber K. Plasma concentrations of von Willebrand factor and intracellular adhesion molecule-1 for prediction of outcome after successful cardiopulmonary resuscitation. *Crit Care Med*. 2003;31:805–811.
21. Danciu SC, Klein L, Hosseini MM, Ibrahim L, Coyle BW, Kehoe RF. A predictive model for survival after in-hospital cardiopulmonary arrest. *Resuscitation*. 2004;62:35–42.
22. Haukoos JS, Lewis RJ, Niemann JT. Prediction rules for estimating neurologic outcome following out-of-hospital cardiac arrest. *Resuscitation*. 2004;63:145–155.
23. Adrie C, Cariou A, Mourvillier B, Laurent I, Dabbane H, Hantala F, Rhaoui A, Thuong M, Monchi M. Predicting survival with good neurological recovery at hospital admission after successful resuscitation of out-of-hospital cardiac arrest: the OHCA score. *Eur Heart J*. 2006;27:2840–2845.
24. Nishiuchi T, Hayashino Y, Fukuhara S, Iwami T, Hayashi Y, Hiraide A, Ikeuchi H, Yukioka H, Matsuoka T. Survival rate and factors associated with 1-month survival of witnessed out-of-hospital cardiac arrest of cardiac origin with ventricular fibrillation and pulseless ventricular tachycardia: the Utstein Osaka project. *Resuscitation*. 2008;78:307–313.
25. Menegazzi JJ, Hsieh M, Niemann JT, Swor RA. Derivation of clinical predictors of failed rescue shock during out-of-hospital ventricular fibrillation. *Prehosp Emerg Care*. 2008;12:347–351.
26. Sladjana A. A prediction survival model for out-of-hospital cardiopulmonary resuscitations. *J Crit Care*. 2011;26:223.e11–223.e18.
27. Hayakawa K, Tasaki O, Hamasaki T, Sakai T, Shiozaki T, Nakagawa Y, Ogura H, Kuwagata Y, Kajino K, Iwami T, et al. Prognostic indicators and outcome prediction model for patients with return of spontaneous circulation from cardiopulmonary arrest: the Utstein Osaka Project. *Resuscitation*. 2011;82:874–880.
28. Gräsner JT, Meybohm P, Lefering R, Wnent J, Bahr J, Messelken M, Jantzen T, Franz R, Scholz J, Schleppers A, et al. ROSC after cardiac arrest–the RACA score to predict outcome after out-of-hospital cardiac arrest. *Eur Heart J*. 2011;32:1649–1656.
29. Rittenberger JC, Tisherman SA, Holm MB, Guyette FX, Callaway CW. An early, novel illness severity score to predict outcome after cardiac arrest. *Resuscitation*. 2011;82:1399–1404.
30. Okada K, Ohde S, Otani N, Sera T, Mochizuki T, Aoki M, Ishimatsu S. Prediction protocol for neurological outcome for survivors of

out-of-hospital cardiac arrest treated with targeted temperature management. *Resuscitation*. 2012;83:734–739.
31. Chan PS, Spertus JA, Krumholz HM, Berg RA, Li Y, Sasson C, Nallamothu BK; Get With The Guidelines-Resuscitation Registry Investigators. A validated prediction tool for initial survivors of in-hospital cardiac arrest. *Arch Intern Med*. 2012;172:947–953.
32. Goto Y, Maeda T, Goto Y. Decision-tree model for predicting outcomes after out-of-hospital cardiac arrest in the emergency department. *Crit Care*. 2013;17:R133.
33. Ebell MH, Jang W, Shen Y, Geocadin RG; Get With The Guidelines-Resuscitation Investigators. Development and validation of the Good Outcome Following Attempted Resuscitation (GO-FAR) score to predict neurologically intact survival after in-hospital cardiopulmonary resuscitation. *JAMA Intern Med*. 2013;173:1872–1878.
34. Ebell MH, Afonso AM, Geocadin RG; American Heart Association's Get With The Guidelines-Resuscitation (formerly National Registry of Cardiopulmonary Resuscitation) Investigators. Prediction of survival to discharge following cardiopulmonary resuscitation using classification and regression trees. *Crit Care Med*. 2013;41:2688–2697.
35. Ishikawa S, Niwano S, Imaki R, Takeuchi I, Irie W, Toyooka T, Soma K, Kurihara K, Izumi T. Usefulness of a simple prognostication score in prediction of the prognoses of patients with out-of-hospital cardiac arrests. *Int Heart J*. 2013;54:362–370.
36. Harrison DA, Patel K, Nixon E, Soar J, Smith GB, Gwinnutt C, Nolan JP, Rowan KM; National Cardiac Arrest Audit. Development and validation of risk models to predict outcomes following in-hospital cardiac arrest attended by a hospital-based resuscitation team. *Resuscitation*. 2014;85:993–1000.
37. Aschauer S, Dorffner G, Sterz F, Erdogmus A, Laggner A. A prediction tool for initial out-of-hospital cardiac arrest survivors. *Resuscitation*. 2014;85:1225–1231.
38. Park SB, Yang JH, Park TK, Cho YH, Sung K, Chung CR, Park CM, Jeon K, Song YB, Hahn JY, et al. Developing a risk prediction model for survival to discharge in cardiac arrest patients who undergo extracorporeal membrane oxygenation. *Int J Cardiol*. 2014;177:1031–1035.
39. Filgueiras-Rama D, Calvo CJ, Salvador-Montañés Ó, Cádenas R, Ruiz-Cantador J, Armada E, Rey JR, Merino JL, Peinado R, Pérez-Castellano N, et al. Spectral analysis-based risk score enables early prediction of mortality and cerebral performance in patients undergoing therapeutic hypothermia for ventricular fibrillation and comatose status. *Int J Cardiol*. 2015;186:250–258.
40. Rauber M, Štajer D, Noč M, Schlegel TT, Starc V. High resolution ECG-aided early prognostic model for comatose survivors of out of hospital cardiac arrest. *J Electrocardiol*. 2015;48:544–550.
41. Albaeni A, Eid SM, Vaidya D, Chandra-Strobos N. Predicting survival with good neurological outcome within 24 hours following out of hospital cardiac arrest: the application and validation of a novel clinical score. *J Neurol Transl Neurosci*. 2014;2:1041.
42. Maupain C, Bougouin W, Lamhaut L, Deye N, Diehl JL, Geri G, Perier MC, Beganton F, Marijon E, Jouven X, et al. The CAHP (Cardiac Arrest Hospital Prognosis) score: a tool for risk stratification after out-of-hospital cardiac arrest. *Eur Heart J*. 2016;37:3222–3228.
43. Voicu S, Baud FJ, Malissin I, Deye N, Bihry N, Vivien B, Brun PY, Sideris G, Henry P, Megarbane B. Can mortality due to circulatory failure in comatose out-of-hospital cardiac arrest patients be predicted on admission? A study in a retrospective derivation cohort validated in a prospective cohort. *J Crit Care*. 2016;32:56–62.
44. Martinell L, Nielsen N, Herlitz J, Karlsson T, Horn J, Wise MP, Undén J, Rylander C. Early predictors of poor outcome after out-of-hospital cardiac arrest. *Crit Care*. 2017;21:96.
45. Nishikimi M, Matsuda N, Matsui K, Takahashi K, Ejima T, Liu K, Ogura T, Higashi M, Umino H, Makishi G, et al. A novel scoring system for predicting the neurologic prognosis prior to the initiation of induced hypothermia in cases of post-cardiac arrest syndrome: the CAST score. *Scand J Trauma Resusc Emerg Med*. 2017;25:49.
46. Kiehl EL, Parker AM, Matar RM, Gottbrecht MF, Johansen MC, Adams MP, Griffiths LA, Dunn SP, Bidwell KL, Menon V, et al. C-GRApH: a validated scoring system for early stratification of neurologic outcome after out-of-hospital cardiac arrest treated with targeted temperature management. *J Am Heart Assoc*. 2017;6:e003821. DOI: 10.1161/JAHA.116.003821.
47. Stammet P, Dankiewicz J, Nielsen N, Fays F, Collignon O, Hassager C, Wanscher M, Undèn J, Wetterslev J, Pellis T, et al. Protein S100 as outcome predictor after out-of-hospital cardiac arrest and targeted temperature management at 33 °C and 36 °C. *Crit Care*. 2017;21:153.
48. Potpara TS, Mihajlovic M, Stankovic S, Jozic T, Jozic I, Asanin MR, Ahmad R, Lip GYH. External validation of the simple NULL-PLEASE clinical score in predicting outcome of out-of-hospital cardiac arrest. *Am J Med*. 2017;130:1464.e13–1464.e21.
49. Lee SW, Han KS, Park JS, Lee JS, Kim SJ. Prognostic indicators of survival and survival prediction model following extracorporeal cardiopulmonary resuscitation in patients with sudden refractory cardiac arrest. *Ann Intensive Care*. 2017;7:87.
50. Bascom KE, Dziodzio J, Vasaiwala S, Mooney M, Patel N, McPherson J, McMullan P, Unger B, Nielsen N, Friberg H, et al. Derivation and validation of the CREST model for very early prediction of circulatory etiology death in patients without ST-segment-elevation myocardial infarction after cardiac arrest. *Circulation*. 2018;137:273–282.
51. Funada A, Goto Y, Tada H, Teramoto R, Shimojima M, Hayashi K, Kawashiri MA, Yamagishi M. Duration of cardiopulmonary resuscitation in patients without prehospital return of spontaneous circulation after out-of-hospital cardiac arrest: results from a severity stratification analysis. *Resuscitation*. 2018;124:69–75.
52. Pasquier M, Hugli O, Paal P, Darocha T, Blancher M, Husby P, Silfvast T, Carron PN, Rousson V. Hypothermia outcome prediction after extracorporeal life support for hypothermic cardiac arrest patients: the HOPE score. *Resuscitation*. 2018;126:58–64.
53. Saczkowski RS, Brown DJA, Abu-Laban RB, Fradet G, Schulze CJ, Kuzak ND. Prediction and risk stratification of survival in accidental hypothermia requiring extracorporeal life support: an individual patient data meta-analysis. *Resuscitation*. 2018;127:51–57.
54. Hsu CH, Haac BE, Drake M, Bernard AC, Aiolfi A, Inaba K, Hinson HE, Agarwal C, Galante J, Tibbits EM, et al. EAST Multicenter Trial on targeted temperature management for hanging-induced cardiac arrest. *J Trauma Acute Care Surg*. 2018;85:37–47.
55. Huang W, Teo GKW, Tan JW, Ahmad NS, Koh HH, Ong MEH. Influence of comorbidities and clinical prediction model on neurological prognostication post out-of-hospital cardiac arrest. *Heart Asia*. 2018;10:e011016.
56. Pérez-Castellanos A, Martínez-Sellés M, Uribarri A, Devesa-Cordero C, Sánchez-Salado JC, Ariza-Solé A, Sousa I, Juárez M, Fernández-Avilés F. Development and external validation of an early prognostic model for survivors of out-of-hospital cardiac arrest. *Rev Esp Cardiol (Engl Ed)*. 2019;72:535–542.
57. Hirt LS, Kandan SR, Rahbi H, Dastidar A, Khawaja MZ, Mozid A, Dorman S, Johnson TW, Spratt JC, Strange JW. Three factors combined predict futility of emergency coronary angiography after out-of-hospital cardiac arrest. *J Am Coll Cardiol*. 2018;72:1753–1755.
58. Shin SM, Kim KS, Suh GJ, Kim K, Kwon WY, Shin J, Jo YH, Lee JH, Lee H, Kim J, et al. Prediction of neurological outcomes following the return of spontaneous circulation in patients with out-of-hospital cardiac arrest: retrospective fast-and-frugal tree analysis. *Resuscitation*. 2018;133:65–70.
59. Gupta A, Ladejobi A, Munir MB, Pasupula DK, Bhonsale A, Kancharla K, Wang NC, Jain S, Saba S. Derivation and validation of a new score to predict long-term survival after sudden cardiac arrest. *Pacing Clin Electrophysiol*. 2018;41:1585–1590.
60. Eertmans W, Tran TMP, Genbrugge C, Peene L, Mesotten D, Dens J, Jans F, De Deyne C. A prediction model for good neurological outcome in successfully resuscitated out-of-hospital cardiac arrest patients. *Scand J Trauma Resusc Emerg Med*. 2018;26:93.
61. Seewald S, Obermaier M, Lefering R, Bohn A, Georgieff M, Muth CM, Gräsner JT, Masterson S, Scholz J, Wnent J. Application of mechanical cardiopulmonary resuscitation devices and their value in out-of-hospital cardiac arrest: a retrospective analysis of the German Resuscitation Registry. *PLoS One*. 2019;14:e0208113.
62. Tat RM, Golea A, Vesa ŞC, Ionescu D. Resistin-can it be a new early marker for prognosis in patients who survive after a cardiac arrest? A pilot study. *PLoS One*. 2019;14:e0210666.
63. Lee HY, Jung YH, Jeung KW, Lee BK, Youn CS, Mamadjonov N, Kim JW, Heo T, Min YI. Ion shift index as a promising prognostic indicator in adult patients resuscitated from cardiac arrest. *Resuscitation*. 2019;137:116–123.
64. Shih HM, Chen YC, Chen CY, Huang FW, Chang SS, Yu SH, Wu SY, Chen WK. Derivation and validation of the SWAP score for very early prediction of neurologic outcome in patients with out-of-hospital cardiac arrest. *Ann Emerg Med*. 2019;73:578–588.

65. May TL, Lary CW, Riker RR, Friberg H, Patel N, Søreide E, McPherson JA, Undén J, Hand R, Sunde K, et al. Variability in functional outcome and treatment practices by treatment center after out-of-hospital cardiac arrest: analysis of International Cardiac Arrest Registry. *Intensive Care Med*. 2019;45:637–646.
66. Nishikimi M, Ogura T, Nishida K, Takahashi K, Nakamura M, Matsui S, Matsuda N, Iwami T. External validation of a risk classification at the emergency department of post-cardiac arrest syndrome patients undergoing targeted temperature management. *Resuscitation*. 2019;140:135–141.
67. Piscator E, Göransson K, Forsberg S, Bottai M, Ebell M, Herlitz J, Djärv T. Prearrest prediction of favourable neurological survival following in-hospital cardiac arrest: the Prediction of outcome for In-Hospital Cardiac Arrest (PIHCA) score. *Resuscitation*. 2019;143:92–99.
68. Balan P, Hsi B, Thangam M, Zhao Y, Monlezun D, Arain S, Charitakis K, Dhoble A, Johnson N, Anderson HV, et al. The cardiac arrest survival score: a predictive algorithm for in-hospital mortality after out-of-hospital cardiac arrest. *Resuscitation*. 2019;144:46–53.
69. Seewald S, Wnent J, Lefering R, Fischer M, Bohn A, Jantzen T, Brenner S, Masterson S, Bein B, Scholz J, et al. CaRdiac Arrest Survival Score (CRASS)—a tool to predict good neurological outcome after out-of-hospital cardiac arrest. *Resuscitation*. 2020;146:66–73.
70. George N, Thai TN, Chan PS, Ebell MH. Predicting the probability of survival with mild or moderate neurological dysfunction after in-hospital cardiopulmonary arrest: the GO-FAR 2 score. *Resuscitation*. 2020;146:162–169.
71. Baldi E, Caputo ML, Savastano S, Burkart R, Klersy C, Benvenuti C, Sgromo V, Palo A, Cianella R, Cacciatore E, et al. An Utstein-based model score to predict survival to hospital admission: the UB-ROSC score. *Int J Cardiol*. 2020;308:84–89.
72. Ebell MH, Kruse JA, Smith M, Novak J, Drader-Wilcox J. Failure of three decision rules to predict the outcome of in-hospital cardiopulmonary resuscitation. *Med Decis Making*. 1997;17:171–177.
73. McCullough PA, Thompson RJ, Tobin KJ, Kahn JK, O'Neill WW. Validation of a decision support tool for the evaluation of cardiac arrest victims. *Clin Cardiol*. 1998;21:195–200.
74. Haukoos JS, Lewis RJ, Stratton SJ, Niemann JT. Is the ACLS score a valid prediction rule for survival after cardiac arrest? *Acad Emerg Med*. 2003;10:621–626.
75. Hunziker S, Bivens MJ, Cocchi MN, Miller J, Salciccioli J, Howell MD, Donnino MW. International validation of the out-of-hospital cardiac arrest score in the United States. *Crit Care Med*. 2011;39:1670–1674.
76. Skrifvars MB, Varghese B, Parr MJ. Survival and outcome prediction using the Apache III and the out-of-hospital cardiac arrest (OHCA) score in patients treated in the intensive care unit (ICU) following out-of-hospital, in-hospital or ICU cardiac arrest. *Resuscitation*. 2012;83:728–733.
77. Coppler PJ, Elmer J, Calderon L, Sabedra A, Doshi AA, Callaway CW, Rittenberger JC, Dezfulian C; Post Cardiac Arrest Service. Validation of the Pittsburgh Cardiac Arrest Category illness severity score. *Resuscitation*. 2015;89:86–92.
78. Fendler TJ, Spertus JA, Kennedy KF, Chen LM, Perman SM, Chan PS; American Heart Association's Get With The Guidelines–Resuscitation Investigators. Alignment of do-not-resuscitate status with patients' likelihood of favorable neurological survival after in-hospital cardiac arrest. *JAMA*. 2015;314:1264–1271.
79. Ohlsson MA, Kennedy LM, Ebell MH, Juhlin T, Melander O. Validation of the good outcome following attempted resuscitation score on in-hospital cardiac arrest in southern Sweden. *Int J Cardiol*. 2016;221:294–297.
80. Guilbault RWR, Ohlsson MA, Afonso AM, Ebell MH. External validation of two classification and regression tree models to predict the outcome of inpatient cardiopulmonary resuscitation. *J Intensive Care Med*. 2017;32:333–338.
81. Kupari P, Skrifvars M, Kuisma M. External validation of the ROSC after cardiac arrest (RACA) score in a physician staffed emergency medical service system. *Scand J Trauma Resusc Emerg Med*. 2017;25:34.
82. Velly L, Perlbarg V, Boulier T, Adam N, Delphine S, Luyt CE, Battisti V, Torkomian G, Arbelot C, Chabanne R, et al. Use of brain diffusion tensor imaging for the prediction of long-term neurological outcomes in patients after cardiac arrest: a multicentre, international, prospective, observational, cohort study. *Lancet Neurol*. 2018;17:317–326.
83. Choi JY, Jang JH, Lim YS, Jang JY, Lee G, Yang HJ, Cho JS, Hyun SY. Performance on the APACHE II, SAPS II, SOFA and the OHCA score of post-cardiac arrest patients treated with therapeutic hypothermia. *PLoS One*. 2018;13:e0196197.
84. Piscator E, Göransson K, Bruchfeld S, Hammar U, El Gharbi S, Ebell M, Herlitz J, Djärv T. Predicting neurologically intact survival after in-hospital cardiac arrest-external validation of the Good Outcome Following Attempted Resuscitation score. *Resuscitation*. 2018;128:63–69.
85. Wang CH, Chang WT, Huang CH, Tsai MS, Yu PH, Wu YW, Chen WJ. Validation of the Cardiac Arrest Survival Postresuscitation In-hospital (CASPRI) score in an East Asian population. *PLoS One*. 2018;13:e0202938.
86. Isenschmid C, Luescher T, Rasiah R, Kalt J, Tondorf T, Gamp M, Becker C, Tisljar K, Sutter R, Schuetz P, et al. Performance of clinical risk scores to predict mortality and neurological outcome in cardiac arrest patients. *Resuscitation*. 2019;136:21–29.
87. Caputo ML, Baldi E, Savastano S, Burkart R, Benvenuti C, Klersy C, Cianella R, Anselmi L, Moccetti T, Mauri R, et al. Validation of the return of spontaneous circulation after cardiac arrest (RACA) score in two different national territories. *Resuscitation*. 2019;134:62–68.
88. Pasquier M, Rousson V, Darocha T, Bouzat P, Kosiński S, Sawamoto K, Champigneulle B, Wiberg S, Wanscher MCJ, Brodmann Maeder M, et al. Hypothermia outcome prediction after extracorporeal life support for hypothermic cardiac arrest patients: an external validation of the HOPE score. *Resuscitation*. 2019;139:321–328.
89. Ryu JA, Chung CR, Cho YH, Sung K, Jeon K, Suh GY, Park TK, Lee JM, Song YB, Hahn JY, et al. Neurologic outcomes in patients who undergo extracorporeal cardiopulmonary resuscitation. *Ann Thorac Surg*. 2019;108:749–755.
90. Thai TN, Ebell MH. Prospective validation of the Good Outcome Following Attempted Resuscitation (GO-FAR) score for in-hospital cardiac arrest prognosis. *Resuscitation*. 2019;140:2–8.
91. Luescher T, Mueller J, Isenschmid C, Kalt J, Rasiah R, Tondorf T, Gamp M, Becker C, Sutter R, Tisljar K, et al. Neuron-specific enolase (NSE) improves clinical risk scores for prediction of neurological outcome and death in cardiac arrest patients: results from a prospective trial. *Resuscitation*. 2019;142:50–60.
92. Rubins JB, Kinzie SD, Rubins DM. Predicting outcomes of in-hospital cardiac arrest: retrospective US validation of the good outcome following attempted resuscitation score. *J Gen Intern Med*. 2019;34:2530–2535.
93. Sauneuf B, Dupeyrat J, Souloy X, Leclerc M, Courteille B, Canoville B, Ramakers M, Goddé F, Beygui F, du Cheyron D, et al. The CAHP (cardiac arrest hospital prognosis) score: a tool for risk stratification after out-of-hospital cardiac arrest in elderly patients. *Resuscitation*. 2020;148:200–206.
94. Liu N, Ong MEH, Ho AFW, Pek PP, Lu TC, Khruekarnchana P, Song KJ, Tanaka H, Naroo GY, Gan HN, et al. Validation of the ROSC after cardiac arrest (RACA) score in Pan-Asian out-of-hospital cardiac arrest patients. *Resuscitation*. 2020;149:53–59.
95. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. *Chest*. 2010;137:263–272.
96. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *Eur Heart J*. 2012;33:1500–1510.
97. Wessler BS, Lundquist CM, Koethe B, Park JG, Brown K, Williamson T, Ajlan M, Natto Z, Lutz JS, Paulus JK, et al. Clinical prediction models for valvular heart disease. *J Am Heart Assoc*. 2019;8:e011972. DOI: 10.1161/JAHA.119.011972.
98. Wessler BS, Ruthazer R, Udelson JE, Gheorghiade M, Zannad F, Maggioni A, Konstam MA, Kent DM. Regional validation and recalibration of clinical predictive models for patients with acute heart failure. *J Am Heart Assoc*. 2017;6:e006121. DOI: 10.1161/JAHA.117.006121.
99. Volkers EJ, Algra A, Kappelle LJ, Jansen O, Howard G, Hendrikse J, Halliday A, Gregson J, Fraedrich G, Eckstein HH, et al. Prediction models for clinical outcome after a carotid revascularization procedure. *Stroke*. 2018;49:1880–1885.
100. Smith LN, Makam AN, Darden D, Mayo H, Das SR, Halm EA, Nguyen OK. Acute myocardial infarction readmission risk prediction models: a systematic review of model performance. *Circ Cardiovasc Qual Outcomes*. 2018;11:e003885. DOI: 10.1161/CIRCOUTCOMES.117.003885

101. Echouffo-Tcheugui JB, Kolte D, Khera S, Bhatt DL, Fonarow GC. Comparison of survival after in-hospital cardiac arrest in patients with versus without diabetes mellitus. *Am J Cardiol*. 2018;121:671–677.
102. Ufere NN, Brahmania M, Sey M, Teriaky A, El-Jawahri A, Walley KR, Celi LA, Chung RT, Rush B. Outcomes of in-hospital cardiopulmonary resuscitation for patients with end-stage liver disease. *Liver Int*. 2019;39:1256–1262.
103. Kang SB, Kim KS, Suh GJ, Kwon WY, You KM, Park MJ, Ko JI, Kim T. Long-term survival of out-of-hospital cardiac arrest patients with malignancy. *Am J Emerg Med*. 2017;35:1457–1461.
104. Bruckel JT, Wong SL, Chan PS, Bradley SM, Nallamothu BK. Patterns of resuscitation care and survival after in-hospital cardiac arrest in patients with advanced cancer. *J Oncol Pract*. 2017;13:e821–e830.
105. Granfeldt A, Wissenberg M, Hansen SM, Lippert FK, Lang-Jensen T, Hendriksen OM, Torp-Pedersen C, Christensen EF, Christiansen CF. Clinical predictors of shockable versus non-shockable rhythms in patients with out-of-hospital cardiac arrest. *Resuscitation*. 2016;108:40–47.
106. Grunau B, Kawano T, Scheuermeyer F, Tallon J, Reynolds J, Besserer F, Barbic D, Brooks S, Christenson J. Early advanced life support attendance is associated with improved survival and neurologic outcomes after non-traumatic out-of-hospital cardiac arrest in a tiered prehospital response system. *Resuscitation*. 2019;135:137–144.
107. Rohlin O, Taeri T, Netzereab S, Ullemark E, Djärv T. Duration of CPR and impact on 30-day survival after ROSC for in-hospital cardiac arrest—a Swedish cohort study. *Resuscitation*. 2018;132:1–5.
108. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, Rea T, Lowe R, Brown T, Dreyer J, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300:1423–1431.
109. Kolte D, Khera S, Aronow WS, Palaniswamy C, Mujib M, Ahn C, Iwai S, Jain D, Sule S, Ahmed A, et al. Regional variation in the incidence and outcomes of in-hospital cardiac arrest in the United States. *Circulation*. 2015;131:1415–1425.
110. Efendijev I, Folger D, Raj R, Reinikainen M, Pekkarinen PT, Litonius E, Skrifvars MB. Outcomes and healthcare-associated costs one year after intensive care-treated cardiac arrest. *Resuscitation*. 2018;131:128–134.
111. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Després JP, Fullerton HJ, Howard VJ, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29–e322.
112. Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. *N Engl J Med*. 1978;299:926–930.
113. Willis BH. Spectrum bias—why clinicians need to be cautious when applying diagnostic test studies. *Fam Pract*. 2008;25:390–396.
114. Nelson JE, Puntillo KA, Pronovost PJ, Walker AS, McAdam JL, Ilaoa D, Penrod J. In their own words: patients and families define high-quality palliative care in the intensive care unit. *Crit Care Med*. 2010;38:808–818.
115. White DB, Carson S, Anderson W, Steingrub J, Bird G, Curtis JR, Matthay M, Peterson M, Buddadhumaruk P, Shields AM, et al. A multicenter study of the causes and consequences of optimistic expectations about prognosis by surrogate decision-makers in ICUs. *Crit Care Med*. 2019;47:1184–1193.
116. Nakao MA, Axelrod S. Numbers are better than words: verbal specifications of frequency have no place in medicine. *Am J Med*. 1983;74:1061–1065.
117. Littenberg B, Nease RF Jr. When numbers get serious. *J Gen Intern Med*. 1994;9:295–296.
118. Elmer J, Torres C, Aufderheide TP, Austin MA, Callaway CW, Golan E, Herren H, Jasti J, Kudenchuk PJ, Scales DC, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. *Resuscitation*. 2016;102:127–135.
119. May TL, Ruthazer R, Riker RR, Friberg H, Patel N, Soreide E, Hand R, Stammet P, Dupont A, Hirsch KG, et al. Early withdrawal of life support after resuscitation from cardiac arrest is common and may result in additional deaths. *Resuscitation*. 2019;139:308–313.
120. Hemphill JC III, White DB. Clinical nihilism in neuroemergencies. *Emerg Med Clin North Am*. 2009;27:27–37.
121. Bogardus ST Jr, Holmboe E, Jekel JF. Perils, pitfalls, and possibilities in talking about medical risk. *JAMA*. 1999;281:1037–1041.
122. Cook D, Rocker G, Marshall J, Sjokvist P, Dodek P, Griffith L, Freitag A, Varon J, Bradley C, Levy M, et al. Withdrawal of mechanical ventilation in anticipation of death in the intensive care unit. *N Engl J Med*. 2003;349:1123–1132.
123. Becker KJ, Baxter AB, Cohen WA, Bybee HM, Tirschwell DL, Newell DW, Winn HR, Longstreth WT Jr. Withdrawal of support in intracerebral hemorrhage may lead to self-fulfilling prophecies. *Neurology*. 2001;56:766–772.
124. Wilkinson D. The self-fulfilling prophecy in intensive care. *Theor Med Bioeth*. 2009;30:401–410.
125. Prendergast TJ. Futility and the common cold: how requests for antibiotics can illuminate care at the end of life. *Chest*. 1995;107:836–844.
126. Gabbay E, Calvo-Broce J, Meyer KB, Trikalinos TA, Cohen J, Kent DM. The empirical basis for determinations of medical futility. *J Gen Intern Med*. 2010;25:1083–1089.

SUPPLEMENTAL MATERIAL

Figure S1. The specific OVID medline search used to collect abstracts for initial screening.

OVID MedLine Search
((predict$ adj1 model$) or (predict$ adj1 instrument$) or (predict$ adj1 score$) or (predict$ adj1 index)).mp.
((prognos$ adj1 model$) or (prognos$ adj1 instrument$) or (prognos$ adj1 score$) or (prognos$ adj1 index)).mp.
((risk adj1 model$) or (risk adj1 instrument$) or (risk adj1 score$) or (risk adj1 index) or (risk assessment model or risk assessment instrument or risk assessment score)).mp.
cardiac arrest/ or exp heart arrest/ or exp sudden death/ or exp cardiopulmonary resuscitation/ or exp cardio-pulmonary resuscitation/ or exp CPR/ or exp ventricular fibrillation/ or exp pulseless ventricular tachycardia/ or exp pulseless electrical activity/ or exp death, sudden/ or exp heart arrest, induced/
(201504$ or 201505$ or 201506$ or 201507$ or 201508$ or 201509$ or 201510$ or 201511$ or 201512$ or 2016$ or 2017$ or 2018$).ed.