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Prognostication after cardiac arrest: Results of an international, multi-professional survey

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Abstract

Aim: We explored preferences for prognostic test performance characteristics and error tolerance in decisions regarding withdrawal or continuation of life-sustaining therapy (LST) after cardiac arrest in a diverse cohort of medical providers.

Methodology: We distributed a survey through professional societies and research networks. We asked demographic characteristics, preferences for prognostic test performance characteristics and views on acceptable false positive rates for decisions about LST after cardiac arrest.

Results: Overall, 640 respondents participated in our survey. Most respondents were attending physicians (74%) with >10 years of experience (59%) and practiced at academic centers (77%). Common specialties were neurology (22%), neuro- or general critical care (24%) and palliative care (31%). The majority (56%) felt an acceptable FPR for withdrawal of LST from patients who

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might otherwise have recovered was ≤0.1%. Acceptable FPRs for continuing LST in patients with unrecognized irrecoverable injury was higher, with 59% choosing a threshold ≤1%.

Compared to providers with > 10 years of experience, those with <5 years thought lower FPRs were acceptable (P<0.001 for both). Palliative care providers accepted significantly higher FPRs for withdrawal of LST (P<0.0001), and critical care providers accepted significantly higher FPRs for provision of long-term LST (P=0.02). With regard to test performance characteristics, providers favored accuracy over timeliness, and prefer tests be optimized to predict unfavorable rather than favorable outcomes.

Conclusion: Medical providers are comfortable with low acceptable FPR for withdrawal (≤0.1%) and continuation (≤1%) of LST after cardiac arrest. These FPRs may be lower than can be achieved with current prognostic modalities.

Introduction

Cardiac arrest is common and deadly. Most patients who survive to hospitalization after return of spontaneous circulation (ROSC) are initially comatose.[3] Although some awaken after days to weeks and may enjoy favourable recovery, as many as 4 in 10 die after withdrawal of life-sustaining therapy (WLST) because treating teams and/or surrogates anticipate a poor neurological prognosis.[4–6] In the days after ROSC, it is challenging to differentiate patients who might awaken from coma and recover from those who cannot. Inappropriate pessimism may increase mortality by leading to WLST in patients who might otherwise recover.[4] Unfortunately, delaying neurological prognostication to avoid inappropriate WLST necessitates that patients with unrecognized irrecoverable injury receive ongoing critical care while providers gather sufficient prognostic data to feel confident in their prognosis. Such care is expensive and may be emotionally burdensome to providers and families.

Development of novel methods for timely and accurate neurological prognostication after cardiac arrest is an area of active research. However, there is little literature describing providers’ preferences with regards to prognostic test performance characteristics. Moreover, providers’ tolerance and professional norms for accepting uncertainty or error in prognostic test results (e.g. false positive rates) have not been well characterized. New prognostic modalities should be developed with performance characteristics that meet providers’ needs, but these must be better understood. We queried medical providers’ to elicit their values and preferences with regard to prognostic test performance and tolerance for error or uncertainty. Our aim was to gather data from a diverse cohort of respondents in terms of profession, specialty and geography. Our primary hypothesis was that most providers would feel a false positive rate of 1% for WLST based on perceived poor neurological prognosis, or one death of a patient who otherwise would have recovered per 100 cases, is acceptable.

Methods

The University of Pittsburgh Institutional Review Board approved all aspects of the study. We developed and distributed a brief survey with 16 questions (Table 1). Questions 1 to 8 focused on respondent demographics and current practice, particularly in domains that we hypothesized might affect personal preferences and risk tolerance with regard to prognostication. Questions 9 to 11 assessed providers' tolerance for error (false positive rate) when altering patient care based on a prognostic assessment and whether providers prefer tests to predict favorable or unfavorable outcome. Remaining questions assumed that longer periods of observation would yield additional information that improved prognostic accuracy and so explored preferences for the balance between timeliness and accuracy in several question formats.

Before widely distributing the survey, we carried out a small-scale informal pilot of the draft version. We selected 10 content experts globally to review the draft specifically to check wording, ensure that potential answers were clear, and estimate the total time necessary for completion. We also asked these testers for recommendations of networks through which the survey could be distributed. We made minor changes to the survey after this testing, then proceeded with distribution. We composed the original survey in English. Prior to distribution, we asked international colleagues whether English fluency in their country of residence was sufficient that most respondents would be expected to easily complete the English version. When this was the case, we distributed the survey in English. Based on this feedback, we translated the survey into Hebrew, Japanese and Korean, and distributed both the English and translated version to professional networks in Israel, Japan and Korea.

All responses were anonymous. We collected results between September 2017 and May 2018. We distributed our survey electronically through multiple professional societies including Neurocritical Care Society, American Academy of Hospice and Palliative Medicine, Japanese Society of Education for Physicians and Trainees in Intensive Care (JSEPTIC), Emergency Medicine Alliance, and the American Academy of Neurology. We also distributed the survey through international research consortia with expertise in neurological prognostication and post-arrest care including the Targeted Temperature Management (TTM) investigators, the Korean Hypothermia Research Network (KOHRN), the North American Post-Arrest Research Consortium (NPARC) and the Targeted Therapeutic Mild Hypercapnea after Resuscitated Cardiac Arrest (TAME) investigators.

Statistical Analysis

We used descriptive statistics to summarize population characteristics and responses. We used Chi2 tests to compare distributions of categorical variables and tests of proportions to compare binary variables. To explore differences in beliefs about acceptable FPRs (Questions 9 and 10) we used generalized linear models to predict log-transformed FPRs as a continuous response variable across levels of predictor factor variables. We used Stata v14 (StataCorp, College Station, Texas, USA) for statistical analyses and the ggplot2 package in R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) for data visualization and to create figures.

Data Availability

Anonymized data will be shared by request from any qualified investigator for purposes of replicating procedures and results.

Results

We had 640 respondents to our survey. Median time for survey completion was 8.1 [interquartile range (IQR) 5.8 – 12.0] minutes and the overall completion rate was 98.8%. Most respondents practice in North America (69%), followed by Asia (19%) and Europe (7%) (Table 2, Figure 1). The majority of respondents (74%) were attending physicians with greater than 10 years of clinical practice (59%), and most (75%) worked at academic medical centers. Providers are from a variety of medical specialities including palliative care (31%), neurocritical care or general critical care (24%), and general neurology (22%). The most common prognostic modalities used by respondents in clinical practice were physical examination (93%), electroencephalography (77%), brain computerized tomography (76%) and magnetic resonance imaging (73%). Fewer providers reported using somatosensory evoked potentials (38%) or serum biomarkers (13% neuron specific enolase, 2% S100b).

Providers varied in their reported acceptable FPR for recommending WLST for a patient who might otherwise have recovered (Table 1, Question 9). The majority of providers (56%) who thought this FPR to be important believed an FPR of 0.1% or less is acceptable, and 24% believed an FPR of 0.01% or less is acceptable (Figure 2a). Belief about acceptable FPR in this scenario differed across medical specialties ($P < 0.001$), a difference that was driven by greater acceptance of error among palliative care specialists. Among palliative care providers, 57% believed an FPR of 1% or more is acceptable (B coefficient 0.88, 95% confidence interval (CI) 0.39 to 1.37, compared to neurologists, $P < 0.001$). There were no differences in beliefs between intensivists, emergency physicians, internal medicine physicians or neurologists. Compared to providers with greater than 10 year of clinical experience, those with less than 5 years experience believed a lower FPR was acceptable with 63% versus 47% believing a rate of 0.1% or less is acceptable (B coefficient −0.68, 95%CI −1.18 to −0.19), $P = 0.007$). There were no differences in belief about this FPR across geographic region, gender, or religion.

Providers also varied in their reported acceptable FPR for recommending long-term support for patients who are ultimately determined to have no potential for recovery (Table 1, Question 10). The majority of providers (59%) who thought this error rate to be important believed an FPR of 1% or less is acceptable, and 33% believed an FPR of 0.1% or less is acceptable (Figure 2b). Compared to WLST where 9% felt the error rate to be unimportant, 19% felt that errors in recommending long-term support are unimportant ($P < 0.001$). Intensive care providers were comfortable with higher FPRs recommending long-term support (B coefficient 0.87, 95%CI 0.23 to 1.51 compared to neurologists, $P = 0.007$) with no differences in belief across other specialties. Compared to providers with >10 years clinical experience, those with <5 years experience believed lower FPRs were acceptable (B coefficient −0.73, 95%CI −1.33 to 0.14, $P = 0.02$). Again, there were no differences in belief about this FPR across geographic region, gender, or religion.

Overall, 74% of providers prefer prognostic tests that accurately predict unfavourable outcome rather than favourable outcome (Table 1, Question 13), and overall favour accuracy of prognostic information to rapidity of available information (Table 1, Question 11) (Figure 3). Phrased differently (Table 1, Question 12), providers reported the most useful test overall was one that was very accurate (but not perfectly so), based on data available within the first 14 days of admission, and predictive of favourable outcome (Figure 4), a different response than when the outcome predicted was considered separately from the timeliness and accuracy of available data.

Finally, we posed a series of gambler-style questions to explore providers' willingness to delay WLST for additional information that would reduce imprecision in their prognostic assessment (Table 1, Questions 14–16). Providers were more willing to delay prognostication by 24 hours than by 3–5 days, and were more willing to delay earlier in a patient's hospital course (day 3) than later in the hospital course (day 14) (Figure 5). Consistent with providers' beliefs about acceptable false positive rates, a minority indicated they would delay prognostication for additional information that resulted in uncertainty that still exceeded 0 to 1%. By contrast, the majority would wait an additional 24 hours for incremental gains in confidence at or below 0 to 1%, even when starting with considerable confidence (0 to 0.1%). These responses did not significantly differ across geographic regions.

Discussion

Medical providers are often called upon to synthesize clinical information and diagnostic test results to estimate a patient's prognosis and make treatment recommendations. We sought to understand providers' values and preferences regarding prognostic test performance and their beliefs about acceptable error rates when making recommendations about life-sustaining therapy when treating comatose survivors of cardiac arrest. A major finding of our study is that majority of providers believe a FPR ≤0.1% is acceptable when recommending WLST for perceived poor neurological prognosis. Consistent with this threshold, most providers indicated willingness to delay WLST for days in the hypothetical scenario where additional information would reduce uncertainty in the true FPR below 0.1%. These beliefs are striking when viewed in the context of the published performance characteristics of criteria commonly used to inform decisions about WLST. Among these, even tests believed to invariably predict poor outcome (i.e. FPR = 0%) have considerable statistically uncertainty characterized by 95% confidence intervals around their 0% FPR estimate that uniformly exceed 1%.[7, 8] Our results indicated that the majority of providers view this degree of uncertainty as unacceptable.

To our knowledge, professional norms regarding errors in recommendations about life-sustaining therapy have not been characterized previously, but have been explored in other clinical scenarios. Among patients evaluated for acute decompensated heart failure, emergency physicians consider rates of death or serious complications <1% to define the population at "low risk" of adverse outcome.[9] In patients undergoing diagnostic workup for acute myocardial infarction, surveys of providers suggest failure to diagnose ≤0.5% to as much as 2% of cases is acceptable.[10, 11] Among patients presenting with acute onset headache and negative brain imaging, tolerance for missed diagnosis of subarachnoid hemorrhage was nearly 3% among emergency physicians and over 1% among neurologists.[12] We note that in these potentially life-threatening conditions, tolerance for error was 5 to 30-fold higher than what we identified for WLST after cardiac arrest. It is likely possible to achieve FPRs at or below some of these more liberal thresholds using current prognostic modalities.[7, 8]

There are several possible interpretations of our findings. First, many providers may have unrealistic expectations for prognostic test performance, or are unaware of the statistical uncertainty in commonly used prognostic tools, and so currently use tests with FPRs they view as ethically unacceptable. To address this, development of better prognostic modalities is urgently needed. Alternatively, it may be that combining multiple prognostic modalities and serial assessments over time reduce the likelihood of in appropriate WLST in clinical practice in a manner only superficially explored in the literature. If providers demand FPRs <1%, future investigations must work to quantify the incremental improvement in prognostic certainty when multiple potentially correlated prognostic measures are combined in specific clinical situations. It may also be that clinical providers are susceptible to confirmation bias and perform multiple diagnostics until attaining a result that aligns with their pre-test assessment despite the fact that this may be falsely reassuring.

In our study, providers with >10 years of clinical experience felt significantly higher FPRs were acceptable compared to providers with <5 years experience, consistent with studies showing increased tolerance of uncertainty with experience among general practitioners.[13] This may reflect that experience leads to more realistic expectations. Alternatively, since medical errors contribute to burnout among providers, it may be that those providers who strive for FPRs that are impossible using current diagnostic modalities are less likely to continue in long-term clinical practice.[14–16] We also found that palliative care providers were significantly more tolerant of error when making the decision for WLST. The clinical experience of palliative care providers may result in greater comfort with death and dying, or may offer a unique perspective of the potential for long-term suffering among those surviving with severe brain injury. No major geographic differences were observed when comparing acceptable FPRs. These results are striking because international cultural norms and laws are highly variable and WLST is illegal in some places, yet convention in other countries.

Beyond quantifying error tolerance, we explored the characteristics of prognostic tests that are important to providers. When asked without consideration of the timeliness of available information, the large majority of providers indicated that they prefer prognostic tests to predict unfavourable outcome. Most providers also indicate that they prefer accuracy over the rapidity with which prognostic test results become available. Indeed, most respondents were willing to wait up to 14 days for a very accurate prognostic tool that predicts good outcome. This willingness to defer neurological prognostication is in sharp contrast to practice patterns in hospitals across the United States and Canada, where data suggest the most common day for patients to die after WLST for perceived poor neurological prognosis is the day of admission.[4] This discrepancy may reflect that the burden of medical decision-making is typically shared between families and providers. Because our survey targeted only providers, we are unable to determine the extent to which decisions about timing of WLST are driven by families' willingness to delay prognostication.

Our study has several important some limitations. Although we distributed the survey internationally, majority of our respondents practice in North America. This may limit the generalizability of our findings to other settings, although we found no significant heterogeneity across geographic regions in any responses. More than 90% of respondents were physicians, preventing meaningful conclusions to be drawn about differences across professions. Similarly, most respondents practiced at academic medical centers, were physicians and had >10 years of clinical experience, limiting our ability to generalize our findings to other settings and providers. As a voluntary survey, bias among individuals who chose to respond is an additional threat to generalizability. Using our methods for dissemination (for example, email distribution across professional society networks), we are unable to quantify response rate. Finally, to avoid overcomplicating our survey or reducing generalizability of our findings, in most questions we did not provide extensive clinical histories. In clinical practice, providers and families consider multiple factors such as patients' values and prior quality of life that may affect views of an acceptable FPR on a case-by-case basis.

Conclusion

In conclusion, we quantified providers' beliefs about acceptable error rates when deciding to withdraw or continue life-sustaining therapy after cardiac arrest. We further characterized providers' preferences for other performance characteristics of prognostic modalities. It is our hope that our findings will help inform researchers who develop or test novel prognostic tools to ensure such tools meet providers' needs and have sufficient precision to be clinically useful.

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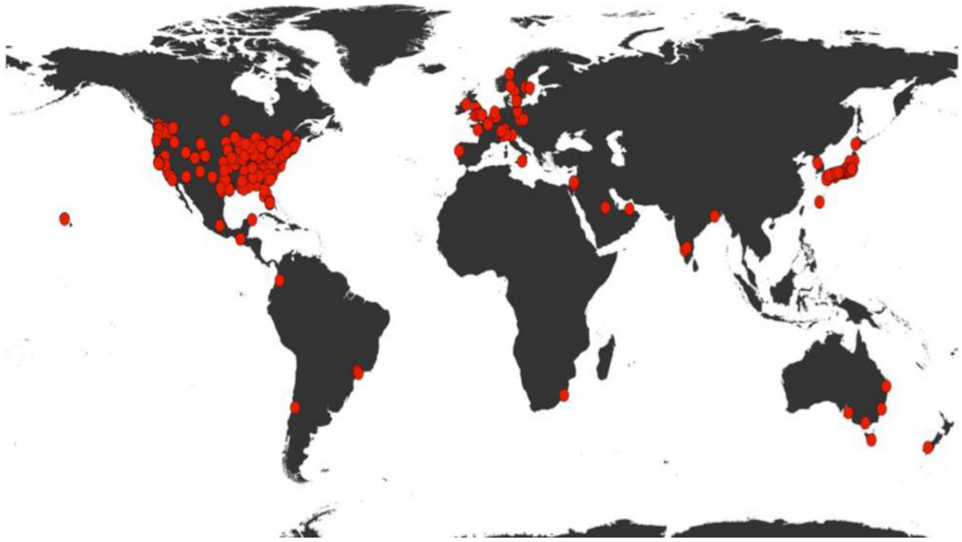

Figure 1:
Global distribution of survey respondents.

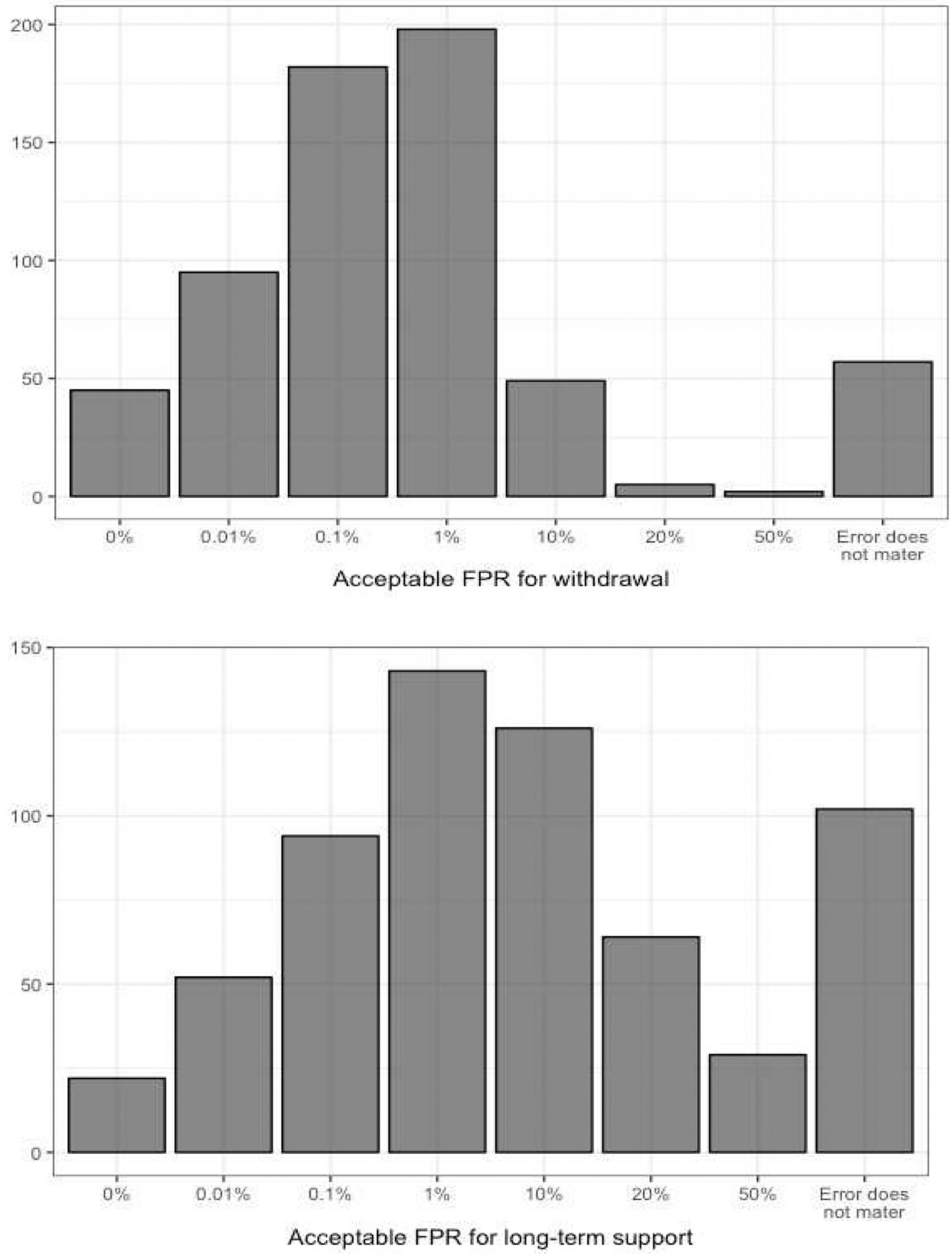

Figure 2:

Distribution of responses when providers were asked what they believed an acceptable false positive rate for WLST from patients who would otherwise have recovered (2a) or provision of long-term support to patients with no potential to recover (2b).

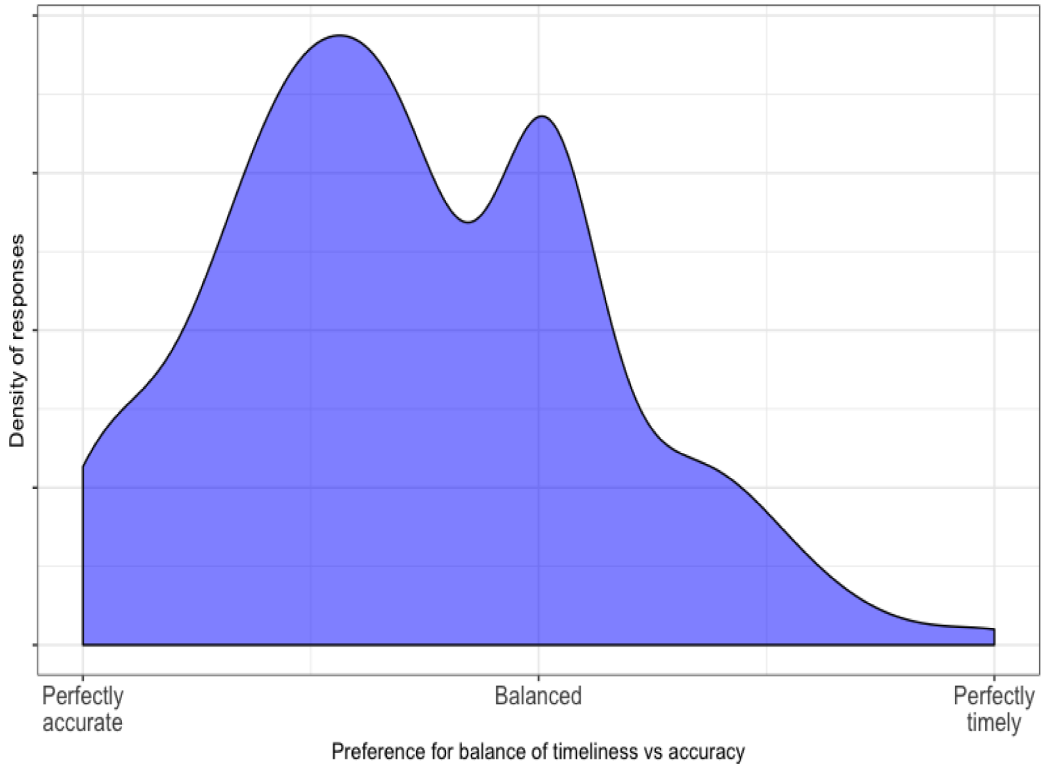

Figure 3:
Providers were asked to use a slide bar to indicate their preferred balance of timeliness versus accuracy of available prognostic information.

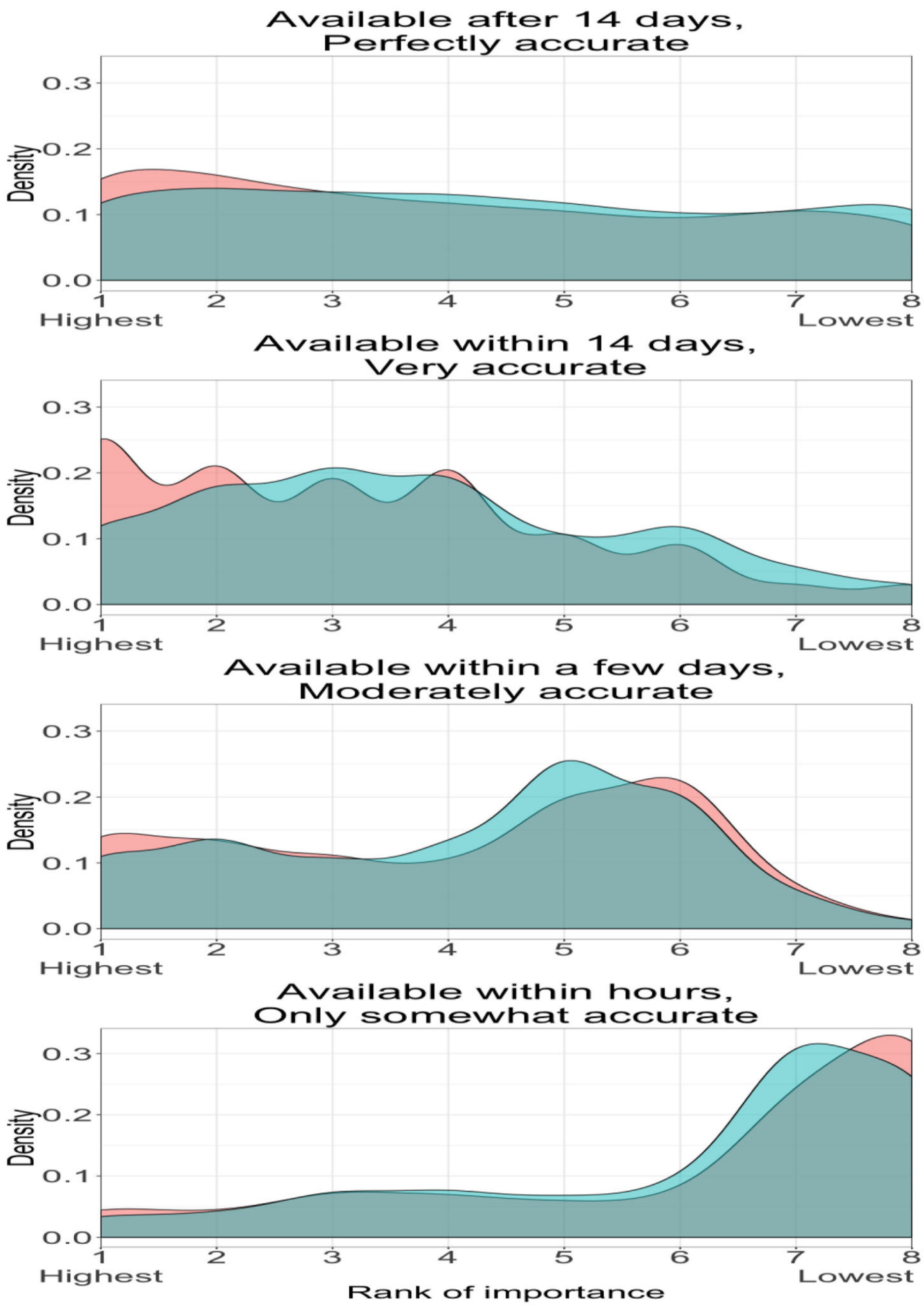

Figure 4:
Providers were asked to rank in in order of preference fixed permutations of accuracy and timeliness, and given the option for each of a test that predicted favourable outcome (red) or unfavourable outcome (green).

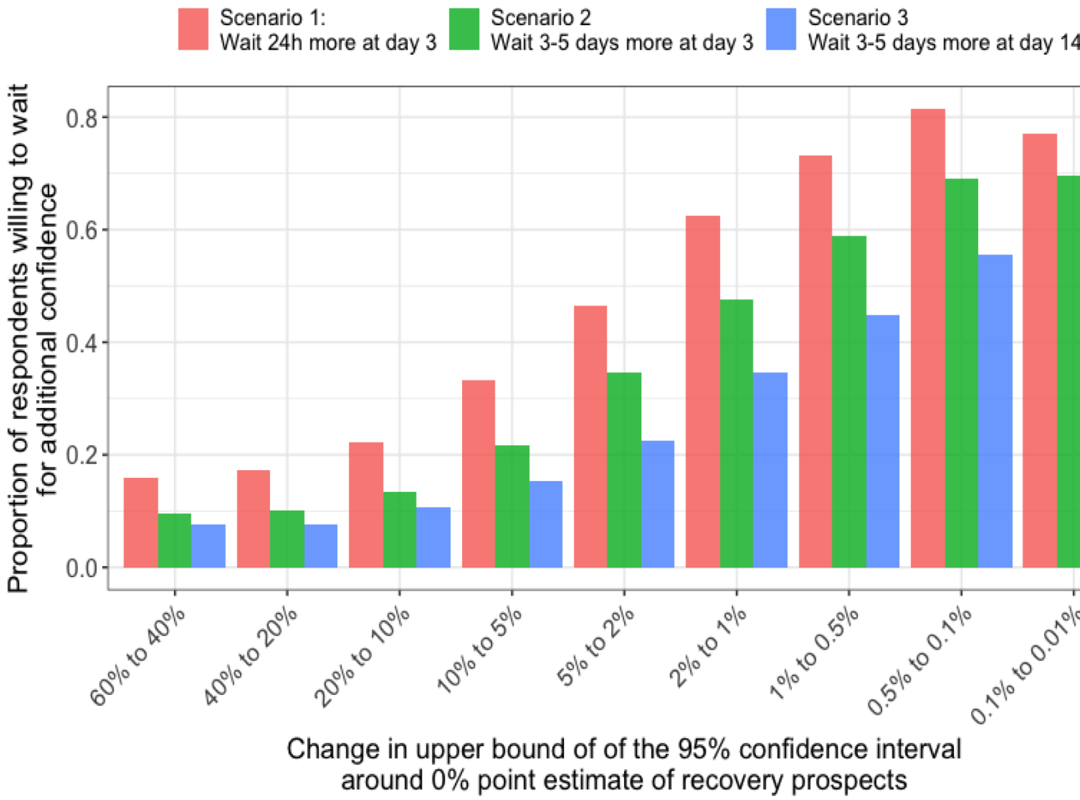

Figure 5:

Providers were offered three clinical scenarios, listed in Table 1. Each scenario described a case starting with some uncertainty around a 0% point estimate of potential for good outcome. Providers were asked if they would wait for additional information that would decrease uncertainty by a specified amount. The x-axis reflects the stepwise hypothetical change in uncertainty presented to respondents, as reflected by the narrowing of the upper bound of a 95% confidence interval (CI) around the 0% point estimate. The y-axis reflects the proportion of respondents indicating they would be willing to wait for this additional certainty.

Table 1 –

Summary of survey questions and response options.

Question synopsis	Answer format
1. What is your current primary job title?	Radio button (e.g. attending physician; nurse)
2. How many years have you been involved in clinical patient care?	Radio button (e.g. <5 years; >10 years)
3. What is the main clinical setting in which you work?	Radio button (e.g. teaching hospital; clinic)
4. What medical specialty do you practice for most of your clinical work?	Free text
5. What is your gender?	Radio button (e.g. male)
6. Where in the world do you practice?	Radio button (e.g. Europe; Australia)
7. With which belief system do you most associate?	Radio button (e.g. Muslim; not religious)
8. Which prognostic tests do you currently use in your practice?	Multiple check box (e.g. CT scan; NSE serum biomarker)
9. You perform a test that predicts a patient will not awaken from coma and advise withdrawal of life-sustaining therapy. If the objective is to never make an error, life-sustaining therapy can never be withdrawn because no test is perfect. What is an acceptable error rate (i.e. the patient could have awakened with good recovery had life-sustaining therapy been continued)?	Radio button (e.g. 1 error in 100 cases (1% false positive rate); 1 error in 10 cases (10% false positive rate))
10. Same scenario as Question 9, but the test predicts good outcome and you advise long-term support. What is an acceptable error rate (i.e. long-term care is a continued in a patient with no potential to recover)?	Radio button (e.g. 1 error in 100 cases (1% false positive rate); 1 error in 10 cases (10% false positive rate))
11. One way to improve accuracy in a prognostic decision is to delay until more data are available. However, this has financial, ethical and emotional costs. For the most useful prognostic test, what is the balance between accuracy and length of time until data are available?	Slide bar, ranging from highly accurate to very timely
12. Please rank the prognostic tool that would be most useful to you. Sub-questions offered all 8 combinations of accuracy and speed (perfectly accurate but unavailable for at least 14 days; very accurate and available within 14 days; moderately accurate and available within a few days; poorly accuracy but available within hours) and outcome predicted (favorable or unfavorable)	8-item rank
13.1 prefer my prognostic test to be optimized to predict:	Radio button (good outcome; bad outcome)
14–16. You are asked to advise the family of a 65y/o previously functional patient with several pre-existing medical comorbidities whether there is a chance of good outcome. They would withdraw life-sustaining therapy if the patient "has no chance" of experiencing this outcome.	
14. At day 3,1 would wait 24h longer for additional data that would let me refine confidence in my prediction of the likelihood of good outcome from:	Yes/no (e.g. 0–60% good outcome to 0–40% good outcome;
15. At day 3,1 would wait 5 to 7 days longer for additional data that would let me refine confidence in my prediction of the likelihood of good outcome from:	
16. At day 14, I would wait 5 to 7 days longer for additional data that would let me refine confidence in my prediction of the likelihood of good outcome from:	0–2% good outcome to 0–1% good outcome)

Table 2:

Demographic characteristics of survey respondents

Demographic characteristic	Number of respondent (n = 640)
Female gender	385 (60)
Years of clinical practice	
< 5 years	103 (16)
5 to 10 years	152 (24)
> 10 years	376 (59)
Primary clinical setting	
Teaching hospital	477 (74)
Other hospital	83 (13)
Clinic	40 (6)
Hospice	22 (3)
No clinical work	11 (2)
Primary job title	
Attending physician	475 (74)
Fellow	62 (10)
Resident	42 (7)
Advanced practice provider	38 (6)
Nurse	10 (2)
Researcher	8 (1)
Region of practice	
North America	442 (69)
Asia	119 (19)
Europe	47 (7)
Australia	10 (2)
Other	14 (2)
Medical specialty	
Neurology	142 (22)
Palliative care	199 (31)
Critical care or neurocritical care	151 (24)
Emergency medicine	*65* (10)
Internal medicine	35 (5)
Other	41 (6)
Religious beliefs	
Not religious	239 (37)
Protestant	111 (17)
Catholic	89 (14)
Jewish	47 (7)

Demographic characteristic	Number of respondent (n = 640)
Buddhist	40 (6)
Hindu	28 (4)
Other	55 (9)
Prefer not to answer	26 (4)

Data are presented as raw numbers with corresponding percentages.