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Original article

Relative importance of benefits and risks associated with antithrombotic therapies for acute coronary syndrome: patient and physician perspectives

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Abstract

Background:
In acute coronary syndrome (ACS), antithrombotic therapies prevent thrombotic events, but also increase bleeding risk. Knowledge is limited about how patients and physicians balance these benefits and risks.

Objective:
To quantify US patient and physician preferences for outcomes associated with antithrombotic therapies in ACS.

Methods:
Two independent web-based surveys were conducted using best–worst scaling in board-certified cardiologists and adult patients hospitalized within the last 5 years due to heart attack and who used aspirin or prescription antithrombotic therapies. Participants selected best and worst of three possible outcomes across a series of questions. Outcomes included death, various levels of stroke, myocardial infarction (MI), and bleeding. Data were analyzed using a maximum difference model employing random-parameters logit. Relative importance of each outcome was estimated relative to death.

Findings:
Patients ($n = 206$) and physicians ($n = 273$) who met face validity requirements, viewed death and nonfatal major disabling stroke as nearly equivalent and most important outcomes to avoid. Relative to death and disabling stroke, physicians considered nondisabling stroke, all nonfatal bleeding, and mild MI all as least important to avoid, while patients considered all bleeds, except major bleeding requiring transfusion, as least important to avoid. Physicians considered severe MI equivalent to 0.92 (0.02 SE) deaths. Patients (~0.35 [0.04] deaths) and physicians (~0.64 [0.05] deaths) had different views for nonfatal moderate stroke. Patients viewed nonfatal major bleeding requiring transfusion ~0.13 (0.02) deaths, and nonfatal heart attack ~0.09 (0.02) deaths.

Conclusion:
US patients and physicians agree on the relative importance of avoiding death, disabling stroke and bleeding without transfusions. Differing perspectives on bleeding requiring transfusions, MI, and moderately disabling stroke suggest that patients and physicians may have different benefit–risk preferences. Transparent discussion between physicians and patients in ACS treatment shared decision-making seems warranted, although limitations of survey methodology and cultural differences compared with US participants should be considered.

Introduction

Acute coronary syndrome (ACS) is the most severe manifestation of coronary heart disease that results primarily from atherosclerotic plaque rupture and thrombus formation[1]. ACS includes three conditions: unstable angina, non-ST-elevation myocardial infarction (MI) and ST-elevation MI. Patients with ACS have a progressive risk of severe clinical consequences including MI, ischemic stroke or death[2]. Despite available treatments, ACS is a cause of high morbidity and mortality. According to the Heart Disease and Stroke Statistics 2013 update of the American Heart Association, an estimated 1,411,000 US hospital discharges in 2010 were due to ACS[2,3].

The cornerstone of pharmacotherapy for ACS is antithrombotic therapy, including both antiplatelet therapy and anticoagulant therapy[4,5]. While there are a variety of regimens, dual therapy, using aspirin plus clopidogrel, remains the mainstay of therapy in preventing thrombotic and major cardiovascular events[6,7]. However, despite advancement in antithrombotic therapy, the rate of cardiovascular events after an index event remains high in ACS patients, e.g., cumulative mortality rates from hospital admission to 180 days were approximately 11% for patients with ST depression, 12% for patients with ST elevation, and approximately 5% for the 'neither' group as shown in the Global Registry of Acute Coronary Events (GRACE study)[8]. Furthermore, based on a report from the American Heart Association (2013 Update), 386,324 Americans died of coronary heart disease in 2009 suggesting that, approximately every 34 seconds, one American has a coronary event and, approximately every 1 minute, an American will die of one[2].

Given this unmet medical need, a triple therapy regimen, i.e., dual antiplatelet plus anticoagulant therapy, has been tested[9–11]. However, the challenge of weighing the incremental efficacy benefit of adding another therapy with the risk of bleeding raises the question of tradeoffs between benefits and risks. While treatment decisions are often complex for any particular antithrombotic therapy, there is limited empirical information on the inherent tradeoffs and value judgments from the patients' and physicians' perspectives, particularly at the level of detail needed for ACS. The current study aimed to quantify the US patients' and physicians' preferences for health outcomes associated with antithrombotic therapies in ACS at this level of detail.

Methods

Survey design and implementation

Survey design

The study included two surveys administered independently to physicians or patients. The selection and definitions of ACS treatment outcomes included in the surveys were developed in consultation with clinical experts. Separate outcome labels and definitions were included in the physician and patient surveys (Table 1). The physician survey used clinical terms that are commonly used in clinical studies to define each outcome, whereas the patient survey used patient-oriented language to define each outcome. The relevance of the outcomes, along with the labels and definitions used to describe the outcomes, were tested in semi-structured, face-to-face, pretest interviews with physicians and patients. The pretest interviews revealed that clinicians clearly distinguished between mild and severe MIs based on their clinical characteristics and severity, while patients did not. Therefore, the physician survey included both mild and moderate MI (both nonfatal), but the patient survey included only 'nonfatal heart attack' among the outcomes (Table 1). With the exception of MI, the set of outcomes was the same in both the patient and physician surveys.

Table 1. Outcomes associated with acute coronary syndrome treatment included in the physician and patient surveys[a].

Physician Survey	Patient Survey
Death	Death
Disabling stroke	Nonfatal major disabling stroke
Moderately disabling stroke	Nonfatal moderate stroke
Nondisabling stroke	Nonfatal minor stroke
Nonfatal myocardial infarction (mild)	Nonfatal heart attack
Nonfatal myocardial infarction (severe)	
Severe recurrent cardiac ischemia	Nonfatal severe recurrent heart-related chest pain
Major bleeding requiring transfusion	Nonfatal major bleeding – transfusion
Major bleeding not requiring transfusion	Nonfatal major bleeding – no transfusion
Non-major, clinically relevant bleeding	Nonfatal moderate bleeding

[a]All outcomes other than death were clearly defined as being nonfatal. The word 'nonfatal' was added to all outcome labels in the patient survey and the myocardial infarction outcomes in the physician survey to reinforce this and lessen potential confusion.

Each outcome was described with four elements: event, treatment, short-term consequences, and long-term consequences. Physicians and patients were asked to study the definitions of these outcomes; and their comprehension of these definitions was tested before presenting them with the choice questions. In order to ensure patients understood the ACS outcomes in the survey, they were tested for understanding of the various endpoints such as stroke, heart attack, and bleeding. If they misunderstood the definition of an event or failed the comprehension question, they received training on these endpoints again. The patient survey also elicited information about each patient's self-reported health history and ACS treatment

experience. The physician survey elicited information about the physicians' clinical experience treating ACS.

Pretesting

Pretest interviews were conducted with both physicians and patients to confirm that the included outcomes were of concern to respondents; to assess their ability to understand and accept the outcomes as relevant to the treatment decision; and to assess their willingness and ability to rank the outcomes associated with ACS treatment. Pretesting was also conducted to evaluate qualitatively the methods used to define and describe the ACS treatment outcomes included in the surveys. In addition, physicians were asked to compare the outcome definitions in the patient survey to those in the physician survey to ensure that the definitions in both surveys conveyed the same clinical information.

The face-to-face pretest interviews were conducted in December 2011, in Philadelphia, Pennsylvania. Ten board-certified cardiologists were included in the pretesting of the physician survey. The pretesting interviews for patients included 10 patients who were ≥18 years old, had a history of hospitalization due to heart attack within the last 5 years, and had either current or previous use of aspirin or prescription antithrombotic therapies.

The interviews were conducted by team members who were experts in interviewing techniques. During each interview, physicians and patients were encouraged to think aloud and describe their thoughts. In addition, the interviewer used direct questions or probes to understand the response process. Observations from the pretest were used to refine the survey (e.g., changing wording). Pretest findings confirmed that the selected ACS treatment outcomes were of concern to patients and physicians and that all respondents were able to rank the relative importance of the outcomes.

Final survey instrument: best–worst scaling approach

The physicians and patients were presented with multiple best–worst scaling questions[12]. Each question included three outcomes, which varied across questions, and physicians and patients were asked to select the best and worst outcomes in each question. Physicians were instructed to select the outcomes that were most important and least important for a patient to avoid (Figure 1). Patients were instructed to select the outcomes that were most and least bothersome (Figure 2). The screenshots of physician and patient surveys have been provided (Supplementary information).

The final set of questions in each survey was determined using an experimental design. Ten outcomes in the physician survey yielded 120 unique combinations of three outcomes. Nine outcomes in the patient survey yielded 84 unique combinations of three outcomes. The design

Outcome MOST IMPORTANT TO AVOID *(Please Check ONE)*		Outcome LEAST IMPORTANT TO AVOID *(Please Check ONE)*
○	Death	○
○	Disabling stroke	○
○	No-major, clinically relevant bleeding	○

Figure 1. Example of physician best–worst scaling question.

Outcome MOST IMPORTANT TO AVOID *(Please Check ONE)*		Outcome LEAST IMPORTANT TO AVOID *(Please Check ONE)*
○	Death	○
○	Non-fatal major disabling stroke	○
○	Non-fatal heart attack	○

Figure 2. Example of patient best–worst scaling question.

was split into blocks; 120 outcome sets in the physician survey were split into eight blocks of 15 questions and 84 outcome sets in the patient survey were split into six blocks of 14 questions. Each respondent was randomly assigned to one block when answering the survey.

Survey sample and implementation

Recruitment

Knowledge Networks, a survey research company, administered the final online survey to patients from their consumer panel and to physicians from their Physicians Consulting Network. The planned sample sizes were 200 physicians and 200 patients. Although these samples sizes were generally considered to be sufficient for stable preference results, they were not powered or intended as *a priori* for statistical hypothesis testing.

Ethics

The study was approved by the Institutional Review Board (IRB) of the Office of Research Protection and Ethics at RTI International. Patients provided informed consent to participate in the survey. The physician study was exempted from IRB review, but the physicians who participated in the study provided informed consent.

Statistical analysis

Patterns in the responses to the best–worst scaling questions were analyzed using a maximum difference (MaxDiff) model. The MaxDiff model is based on random utility theory and the assumption that the best–worst pair chosen in any given set of outcomes represents the greatest utility difference among all possible best–worst pairs in the set. Relative importance weights were

estimated using random-parameters logit (RPL). RPL avoids potential estimation bias from unobserved preference heterogeneity among respondents by estimating a distribution of importance weights across the sample and accounts for within-sample correlation when respondents answer multiple questions[13,14].

The estimated coefficients from the RPL model can be interpreted as relative importance weights. Each estimated coefficient represents the relative importance of avoiding each outcome relative to death, which was the omitted category in the model and treated as a reference outcome. Larger coefficients indicate that the outcome was more important to avoid (worse). Conversely, smaller coefficients indicate that the outcome was better or less important to avoid. To calculate importance scores from the importance weights, we used a probability-based rescaling procedure[15]. The reference outcome (death) had an importance score of 1 and the importance score for any other outcome was the importance of that outcome relative to the reference outcome. The importance score for each outcome was interpreted as the impact of that outcome on utility relative to the utility of death. If the importance score for an outcome was <1, then the outcome was preferred to death. If the importance score for an outcome was >1, then the outcome was worse than death. The importance score represented the number of deaths required to yield a utility change equivalent to one occurrence of each outcome.

Face validity test

Answers to the choice questions were evaluated for face validity in a posthoc analysis. Respondents failed the face validity test if they chose an outcome other than disabling stroke or moderately disabling stroke as worse than death in any single question. The results presented in this paper are for patients and physicians who passed this face validity test and were thus assumed to have had a good understanding of the clinical outcomes, paid close attention to the survey, and took the exercise seriously.

Results

Physician characteristics and pattern of treating ACS

Out of 1390 cardiologists in the US invited to participate in the survey in February 2012, a total of 283 (20.4%) responded to the invitation and 281 (99.3%) of these respondents completed the survey. The majority of physicians were men (88.6%) with a specialty in general cardiology (76.9%) and had been in practice for >15 years (65.8%). Approximately half (53%) of the physicians treated more than 20 patients per month (Table 2). Most physicians said they prescribed dual antiplatelet therapy for their patients both during and after hospitalization, but did not regularly prescribe anticoagulants. The majority (73%) of physicians adjusted the dose of dual antiplatelet therapies if the patient showed risk factors for bleeding.

Table 2. Physician characteristics and pattern of acute coronary syndrome treatment.

Characteristics	Respondents ($n = 281$)
Sex, *n* (%)	
Men	249 (88.6)
Women	32 (11.4)
Years in practice since completion of medical training, *n* (%)	
0–5	6 (2.1)
6–10	34 (12.1)
11–15	56 (19.9)
>15	185 (65.8)
Major area of specialization, *n* (%)	
General cardiology	216 (76.9)
Electrophysiology	2 (0.7)
Echocardiography/imaging	11 (3.9)
Heart failure/transplantation	4 (1.4)
Interventional	47 (16.7)
Other	1 (0.4)
Monthly treatment of patients with acute coronary syndrome, *n* (%)	
<10	26 (9.3)
10–20	106 (37.7)
>20	149 (53.0)
Prescribe dual antiplatelet therapy (i.e., aspirin + clopidogrel, aspirin + ticagrelor, aspirin + prasugrel) to acute coronary syndrome patients during hospitalization, *n* (%)	
0–25%	3 (1.1)
26–50%	12 (4.3)
51–75%	49 (17.4)
76–100%	217 (77.2)
Prescribe dual antiplatelet therapy (i.e., aspirin + clopidogrel, aspirin + ticagrelor, aspirin + prasugrel) to acute coronary syndrome patients after discharge from the hospitalization, *n* (%)	
0–25%	10 (3.6)
26–50%	15 (5.3)
51–75%	52 (18.5)
76–100%	204 (72.6)
Prescribe anticoagulants (i.e., warfarin or enoxaparin) in addition to dual antiplatelet therapy after discharge from the hospitalization, *n* (%)	
0–25%	219 (77.9)
26–50%	39 (13.9)
51–75%	9 (3.2)
76–100%	14 (5.0)
Adjusted the dose of anticoagulants if the patient showed risk factor for bleeding, *n* (%)	205 (73.0)
Physicians who adjusted the dose of anticoagulants for the patients who showed risk factor for bleeding have adjusted the dose of anticoagulants, *n* (%)	$n = 205$
All patients with these risk factors	63 (30.7)
More than half of patients with these risk factors	96 (46.8)
Less than half of patients with these risk factors	43 (21.0)
None of the patients with these risk factors	3 (1.5)

Patient characteristics and pattern of ACS treatment

Of the 825 patients in the US invited to participate in the survey in January and February 2012, 623 patients (75.5%) responded to the invitation and 305 (49.0%) of these respondents were eligible to participate, consented, and completed the survey. The median age of patient participants was 65 years (range: 38–89 years). The majority of them were men (67.2%), and white, non-Hispanic (83.6%). A total of 110 patients (36.1%) had experienced ≥2 heart attacks and the mean (SD) number of years since the last heart attack was 4.1 (3.9) years (Table 3). Patients had used either aspirin only (19.9%) or both aspirin and antithrombotic therapies (71.2%) after heart attacks or after their discharge from hospital due to the most recent heart attack. A large proportion of patients (93.0%) reported never missing or skipping a dose of aspirin or antithrombotic therapies or missing them no more than once a month. Patients had undergone some type of cardiac procedure or therapies including coronary angiogram (76.7%), angioplasty (68.2%), heart surgery (29.5%) procedures or physical therapy or cardiac rehabilitation (46.6%).

The majority of the patients understood the ACS outcomes included in the survey, although their comprehension appeared to vary across different outcomes examined; e.g., 95.4% of the patients answered the stroke endpoints question correctly, while 72.1% of the patients answered the heart attack endpoints question correctly, and 63.9%

Table 3. Patient characteristics, history of acute coronary syndrome and its treatment.

Parameters	Respondents ($n = 305$)
Age (years), mean (SD)	65.1 (10.3)
Age category (years), *n* (%)	
18–44	3 (1.0)
45–65	160 (52.5)
>65	142 (46.6)
Sex, *n* (%)	
Men	205 (67.2)
Women	100 (32.8)
Ethnicity, *n* (%)	
White, non-Hispanic	255 (83.6)
Black, non-Hispanic	13 (4.3)
Other, non-Hispanic	9 (3.0)
Hispanic	15 (4.9)
2+ races, non-Hispanic	13 (4.3)
Mean (SD) number of years since the last hospitalization due to heart attack	4.1 (3.9)
Heart attacks during the lifetime, *n* (%)	
1	186 (61.0)
2	56 (18.4)
≥3	54 (17.7)
Didn't know	9 (3.0)
Medicines prescribed by doctors after heart attacks, *n* (%)	
Neither aspirin nor antithrombotic therapies	5 (1.6)
Aspirin only	120 (39.3)
Antithrombotic therapies only	10 (3.3)
Both aspirin and antithrombotic therapies	170 (55.7)
Medicines prescribed after release from hospital after most recent heart attack, *n* (%)	
Neither aspirin nor antithrombotic therapies	3 (1.0)
Aspirin only	60 (19.9)
Antithrombotic therapies only	20 (6.6)
Both aspirin and antithrombotic therapies	215 (71.2)
Missing or didn't know	7 (2.3)
Patients skipped or missed the dose of aspirin or antithrombotic therapies, *n* (%)	$n = 300$
Almost every day	3 (1.0)
About 3–4 times per week	2 (0.7)
About 1–2 times per week	16 (5.4)
About once a month	86 (28.9)
Never	191 (64.1)
Unanswered	2 (0.7)
Patient underwent the following procedures or therapies any time, *n* (%)	
Coronary angiogram	234 (76.7)
Angioplasty	208 (68.2)
Heart surgery	90 (29.5)
Physical therapy or cardiac rehabilitation	142 (46.6)
Occupational therapy	26 (8.5)
None of the above	7 (2.3)
Patients with other disease ailments, *n* (%)	
Diabetes	103 (33.9)
Hypertension	231 (76.0)
Heart failure	109 (35.9)
High cholesterol	255 (83.9)
Missing	1
Patient's history of stroke, *n* (%)	
Minor stroke	
Yes	45 (14.9)
No	231 (76.2)
Didn't know or missing	29 (9.5)
Moderate stroke that resulted in some disability	
Yes	14 (4.6)
No	284 (94.0)
Didn't know or missing	7 (2.3)
Major stroke that resulted in significant disability	
Yes	4 (1.3)
No	296 (98.3)
Didn't know or missing	5 (1.6)
Severe, recurrent, heart-related chest pain	
Yes	103 (33.8)
No	177 (58.0)
Didn't know	25 (8.2)
Patient's history of bleeding, *n* (%)	
Moderate bleeding	
Yes	79 (25.9)
No	214 (70.2)
Didn't know	12 (3.9)
Internal bleeding – no blood transfusion	
Yes	21 (6.9)
No	272 (89.8)
Didn't know	10 (3.3)
Internal bleeding – blood transfusion	
Yes	21 (6.9)
No	280 (91.8)
Didn't know	4 (1.3)

(continued)

Table 3. Continued.

SD, standard deviation.

patients answered the bleeding endpoints question correctly before the survey was presented to them (Table 4). As patients were provided a review of the definitions of those outcomes whose questions they answered incorrectly, these results underestimate the degree of patient understanding of the outcomes. Comprehension was not retested after this additional training.

Face validity test

Eight physicians (2.8%) and 99 patients (32.5%) failed the face validity test. Therefore, the final sample sizes used in the analyses were 273 physicians and 206 patients.

Table 4. Patient understanding of the acute coronary syndrome outcome descriptions included in survey after initial review of their definitions.

Category	Respondents ($n = 305$)
Which of the following types of stroke will not result in any permanent disability? *n* (%)	
Nonfatal minor stroke (Correct)	291 (95.4%)
Nonfatal moderate stroke (Incorrect)	12 (3.9%)
Nonfatal major disabling stroke (Incorrect)	2 (0.7%)
Which of these two outcomes is most likely to result in permanent damage to your heart? *n* (%)	
Nonfatal heart attack (Correct)	220 (72.1%)
Nonfatal severe recurrent heart-related chest pain (Incorrect)	85 (27.9%)
Which of the following types of bleeding will result in permanent disability? *n* (%)	
Nonfatal moderate bleeding (Incorrect)	13 (4.3%)
Nonfatal major bleeding – no transfusion (Incorrect)	22 (7.2%)
Nonfatal major bleeding – transfusion (Incorrect)	75 (24.6%)
None of the above (Correct)	195 (63.9%)

Outcome importance scores

For physicians, disabling stroke was equivalent to death, and all forms of bleeding (nonfatal, non-stroke bleeding), mild MI, nondisabling stroke and severe recurrent ischemia were essentially viewed as least important. On average, severe MI was equivalent to 0.92 (standard error, SE: 0.02) deaths, moderately disabling stroke was equivalent to 0.64 (0.05) deaths, and the remaining ACS outcomes were each equivalent to ≤0.03 deaths (Figure 3).

For patients, nonfatal major disabling stroke was equivalent to death, while nonfatal minor stroke, nonfatal major bleeding not requiring transfusion, nonfatal severe recurrent chest pain and nonfatal moderate bleeding were all essentially tied as the least important. On average, nonfatal moderate stroke was equivalent to 0.35 (0.04) deaths (in other words, patients found one death equivalent to approximately 2.85 nonfatal moderate strokes [=1 stroke/0.35 deaths]), nonfatal major bleeding requiring transfusion was equivalent to 0.13 (0.02) deaths, nonfatal heart attack was equivalent to 0.09 (0.02) deaths, and the remaining ACS outcomes were each equivalent to ≤0.03 deaths (Figure 4).

Discussion

To quantify the preferences of US patients and physicians for outcomes associated with antithrombotic therapies in ACS, two independent web-based surveys were administered to patients and physicians. The results of this study showed that patients and physicians have similar views on the relative importance of avoiding death, disabling stroke, and bleeding that does not require transfusion. However, differences between patients and physicians

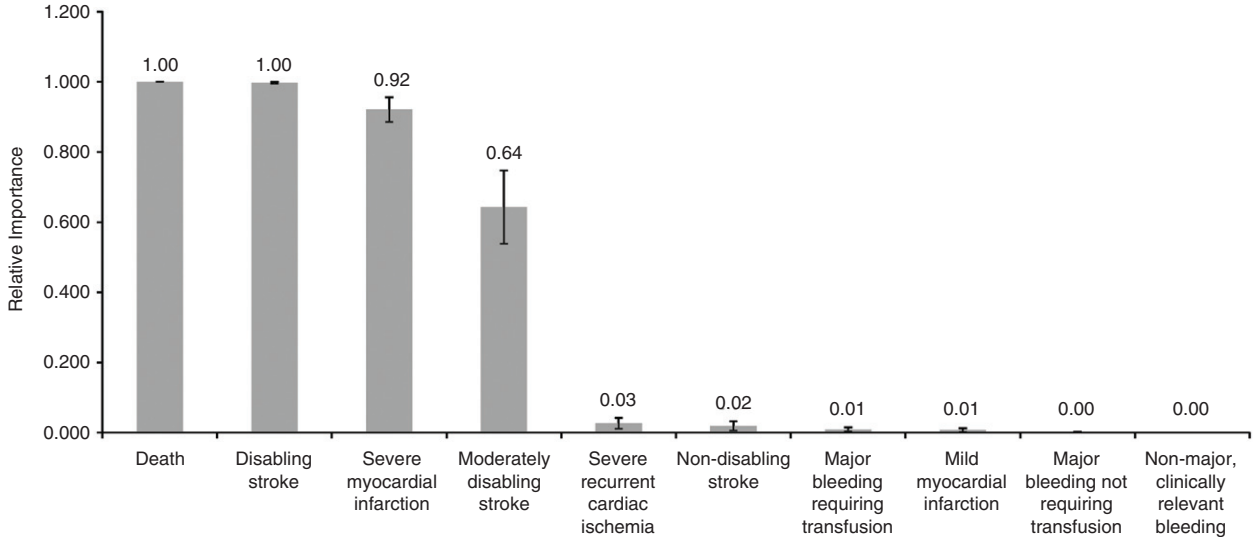

Figure 3. Relative importance of treatment outcomes to physicians who passed the face validity test ($n = 273$).

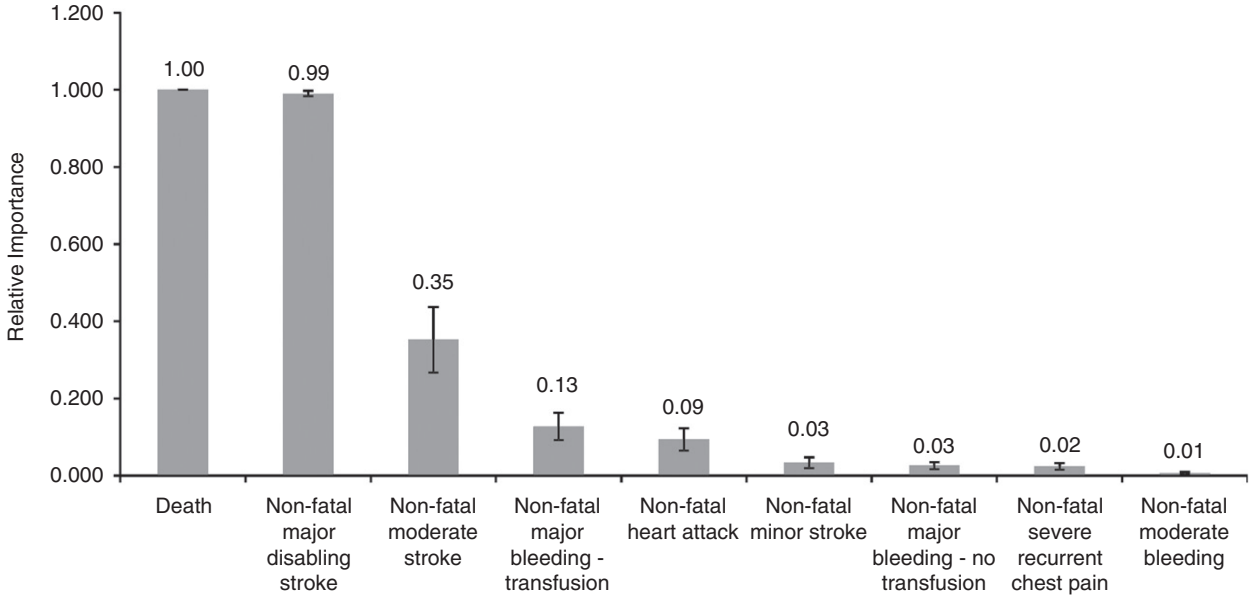

Figure 4. Relative importance of treatment outcomes to patients who passed the face validity test ($n = 206$).

were observed for the relative importance of bleeding requiring transfusions, MI, and moderately disabling stroke. These differences in perspectives on the relative importance of ACS treatment outcomes suggest that patients and physicians may have different benefit–risk preferences when evaluating ACS treatment alternatives.

Patients' importance scores for major disabling stroke, moderate and minor stroke in this study were in line with health-state utility values for thrombolytic treatment for stroke (0.93 [mild stroke], 0.77 [moderately severe stroke], 0.10 [severe stroke])[16]. Patients' preferences for outcomes of ACS treatment are systematically different from physicians' preferences. These differences can be informative, especially from a regulatory and treatment decision perspective. Several studies for other therapies have reported differences in the treatment opinions of patients and physicians. For the thrombolytic treatment for stroke, most patients wanted to receive detailed information on the benefits and risks of thrombolysis, and preferred to be involved in shared physician–patient decision-making for better treatment outcomes[16]. Discordant views of the patients and physicians were observed based on utility functions of safety and therapy in a gastroenterology study, wherein the patient rejected the therapy favored by the physician (more concerned about safety), and physicians rejected the therapy favored by patients (more concerned about therapeutic effect)[17]. A consistent finding in all such studies is the difference between patients' and physicians' preferences, although the proportion of patients preferring shared decision-making may vary[18,19].

Antithrombotic therapy guidelines such as the Institute for Clinical Symptoms Improvement and related guidelines[20] propose that patients should be encouraged and empowered to play an active role in the self-management of their treatment. However, it is not entirely clear how the proposal is implemented in clinical practice. Recently, Food and Drug administration (FDA) in its Prescription Drug User Fee Act V Plan[21] highlighted a new initiative called 'Patient-Focused Drug Development' which might help in making better treatment decisions taking into consideration the patient's viewpoint. FDA has recognized that patients have a unique and valuable perspective on benefits and risks related to any treatment. Hence, a more systematic and comprehensive approach of obtaining patient preferences may facilitate drug development and FDA's review process and decision-making[21]. Therefore, the current study makes a valuable contribution in the context of this new development.

Several aspects related to the study are of note, which may be helpful to the interpretation of the results. With the intent to obtain a valid estimate of preferences, the questions in the experimental design were split into blocks, thereby limiting the number of questions posed to respondents. This was expected to reduce measurement error due to respondent fatigue, as observed in other studies[22–24]. Moreover, for the data of patients who may have provided inconsistent or invalid responses to the questions, face validity was applied and the respondents who failed the test of face validity were excluded from the analysis. This was under the assumption that if those participants lacked a basic understanding of or capability of comparing health outcomes, then their responses to survey questions may not reflect true preferences. In this study, the proportion of patients who passed the face validity test and provided valid responses was consistent with a study using the same best–worst scaling technique for dermatology

consultation (50%)[25]. However, analysis with the full set of patients showed results similar to those for the face-validity sample.

The importance of this study should also be weighed against some of its limitations. Although best–worst scaling methodology represents a simple and intuitive design structure to survey the outcomes of interest, the results are specific to the context in which the questions were asked. Specifically, the importance of any individual outcome included in the study is estimated relative to the full set of outcomes included in the study. If the full set of outcomes included in the study were different, it is possible that the relative importance of any individual outcome could be different. In this study, however, the set of outcomes was determined in consultation with clinical experts to represent the outcomes relevant in evaluating ACS treatment outcomes. Additionally, because the results of these surveys were based on respondents drawn from online panels of US patients and physicians engaged for the purpose of completing surveys, the generalizability of the study findings may be limited to the US. Differences in cultural health perspectives and healthcare systems may alter the views of patients and healthcare providers, as demonstrated, for example, by the systematic differences in the stated trade-off preferences for chronic hepatitis B treatment outcomes among physicians in Germany, France, Italy, Spain, and Turkey[19].

In spite of an array of currently available therapies, ACS patients continue to face a high risk of a subsequent cardiovascular event. Because of this challenge, in clinical practice, there will always be an interesting dilemma about the trade-off between benefits (preventing ischemic events) and risks (causing bleeding) associated with antithrombotic therapies. While the views from healthcare providers are important, patients' preferences must also be considered, fundamentally because they are the consumers of healthcare products and because they could ultimately suffer from these clinical events. Our study further underscores the importance of this concept and supports the notion that, in some aspects, patients may have different views about their disease than their physicians. Therefore, in an individualized medicine healthcare environment, clear communications between physicians and patients are warranted in the treatment decision making to meet each patient's needs.

Conclusion

The results of this study indicated that US physicians and patients viewed death and disabling stroke as the most important outcomes to avoid, and nonfatal moderate bleeding or non-major clinically relevant bleeding as least important when considering antithrombotic therapy in ACS. The notable differences in the relative importance of nondisabling stroke, major bleeding requiring a transfusion and MI between patients and physicians provide evidence that patients and physicians may have different benefit–risk preferences for these events and emphasize the need for a transparent discussion and shared decision-making between physicians and patients regarding benefits and risks in making ACS treatment decisions.

Transparency

Declaration of funding

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Author contributions: C.P. and A.B.H. served as subject matter experts and contributed to the development and conduct of the study, as well as the analyses and study report. Z.Y. and B.L. contributed to the development and design of the study. P.B. and J.A.B. contributed to the conceptual discussion of the study. All authors contributed to the interpretation of the study results, writing/reviewing/editing, and final approval of the manuscript. All authors met ICMJE criteria and all those who fulfilled those criteria are listed as authors. All authors had access to the study data and made the final decision about where to publish these data and approved submission to this journal.

Declaration of financial/other relationships

Z.Y., B.L., and P.B. have disclosed that they are employees of Janssen Research & Development LLC and own stocks in Johnson & Johnson, the parent company of Janssen. J.A.B. has disclosed that he is an employee of, and stockholder in, Johnson & Johnson. B.L. has disclosed that he is a stockholder in Johnson & Johnson, Baxter International Inc., Pharmaceutical Holders Trust, and Zimmer Holdings Inc. C.P. and A.B.H. have disclosed that they are employees of RTI Health Solutions, USA, an independent scientific research organization. The study that is the subject of this manuscript was conducted by RTI Health Solutions and funded by Janssen.

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