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TARGET ARTICLE

Partnering With Patients to Bridge Gaps in Consent for Acute Care Research

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ABSTRACT

Clinical trials for acute conditions such as myocardial infarction and stroke pose challenges related to informed consent due to time limitations, stress, and severe illness. Consent processes should be sensitive to the context in which trials are conducted and to needs of patients and surrogate decision-makers. This manuscript describes a collaborative effort between ethicists, researchers, patients, and surrogates to develop patient-driven, patient-centered approaches to consent for clinical trials in acute myocardial infarction and stroke.

Our group identified important ways in which existing consent processes and forms for clinical trials fail to meet patients' and surrogates' needs in the acute context. We collaborated to create model forms and consent processes that are substantially shorter and, hopefully, better-matched to patients' and surrogates' needs and expectations from the perspective of content, structure, and tone. These changes, however, challenge some common conventions regarding consent.

KEYWORDS

Informed consent; research ethics; acute care; patient-centered care; myocardial infarction; stroke

INTRODUCTION

It seems self-evident that informed consent processes for clinical research should be centered around needs of potential participants. In practice, however, consent processes and the materials used to facilitate them often seem far from participant-centered (Dickert et al. 2018). Consent forms are frequently long and technical, follow rigid templates, and contain language that appears to prioritize institutional protection (Paasche-Orlow et al. 2013; Paasche-Orlow, Taylor, and Brancati 2003). In recognition of these issues, the recently revised Common Rule emphasizes presentation of meaningful content, requires a "key information" section, and enshrines the "reasonable person" standard (U.S. Department of Health and Human Services 2018).

The acute care context brings this absence of participant-centeredness into stark relief. Patients having acute myocardial infarction (MI) are asked to make clinical trial enrollment decisions while being rushed for emergent coronary interventions. This is a high-stress situation, patients are often physically uncomfortable, and decision-making must happen within minutes. In acute stroke trials, there are similar pressures, but decisions are often made by surrogate decision-makers (Dickert et al. 2019). In both cases, handing a patient or surrogate a long, technical consent form that cannot be read (much less understood) in the necessary timeframe seems insensitive to the context and the decision-maker's needs.

One reaction is to claim that consent is impossible, meaningless, and inappropriate in these settings and that such trials should be conducted under an exception from informed consent (EFIC) (Shaw 2014; Tognoni and Geraci 1997). However, MI patients and stroke surrogates are usually not formally incapacitated and not obviously appropriate for EFIC (Dickert et al. 2016). More importantly, available data suggest most people in these situations prefer to be asked for permission upfront rather than waiving consent, even when their decisions may not be well-informed (Dickert, Hendershot, et al. 2017; Dickert et al. 2019; Gammelgaard et al. 2004; Gammelgaard et al. 2004). These views reflect an often under-recognized reality that consent processes serve functions beyond facilitating an informed, autonomous decision (Dickert, Eyal, et al. 2017).

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Acute care studies present challenges for investigators, coordinators, and IRBs. The typical approach has been to utilize standard institutional templates and not to tailor consent forms or materials to these situations. Though some studies have incorporated shorter forms, verbal consent, or assent (Frobert et al. 2013; Gammelgaard et al. 2004; Selker et al. 2012), the development of context-sensitive processes or materials has not been described in detail or published and has not, to our knowledge, involved partnering with patients or surrogates.

An important part of the solution is to ask patients and surrogates what they want out of the consent process in these situations and design materials to meet those needs. This approach seems in keeping with the ethical goals and functions of informed consent and the revised Common Rule. Here, we describe our experience as a group- composed of ethicists, researchers, patients, and surrogates- collaborating to develop patient-driven, patient-centered approaches to research enrollment decisions in trials for acute MI and stroke.

COLLABORATIVE APPROACH

The Patient-Centered Approaches to Research Enrollment Decisions in Acute Cardiovascular Disease (P-CARE) study was designed to: (1) understand patients' and surrogates' experiences of the consent process in acute MI and stroke trials; (2) develop model consent processes for clinical trials in these conditions; and (3) study implementation of a patient-centered consent process within a clinical trial. A core element of P-CARE was a patient advisory panel (PAP) comprised of patients and surrogates who have experienced these conditions and experienced patient-family advisors.

The Patient-Advisory Panel

The patient advisory panel (PAP) for the P-CARE study consisted of 9 members (see Table 1). The patient co-chair previously chaired the Emory Patient and Family Advisor council. Panelists include: patients with a history of MI; patients with a history of stroke; family members who served as a surrogate decision-maker for someone with stroke; and a patient-family advocate with a family member who has heart disease. Panel members were recruited through a previous interview study related to consent for MI research, local stroke research teams, and the Emory Patient and Family Advisor (PFA) Council. One individual, who replaced a member who resigned for health reasons, was recruited from the P-CARE interview study.

Table 1. Patient advisory panel members.

	Overall ($n = 9$) *N* or mean (SD)
Age	59.1 (15.0)
Gender	
Female	6
Male	3
Race	
Black	3
White	6
Role	
Advisor	2
MI patient	3
Stroke patient	3
Stroke surrogate	1

Consultants and Other Advisors

In addition to the PAP, the P-CARE study involved a team of co-investigators, consultants, and advisors with expertise in research ethics, clinical trial conduct, health literacy, and research regulation. The PAP and Emory P-CARE team took primary responsibility for development of P-CARE consent processes, but materials were vetted by these consultants and advisors (see Supplementary Appendix). In addition, the local IRB director, a health literacy expert, and trial investigators were invited to present at PAP meetings.

Sequence of Meetings and Approach to Analysis

The sequence of PAP meetings (Figure 1) and the approach to analysis are described in more detail in the Supplementary Appendix. In preparation for this project, PAP members received education on key concepts related to clinical trial design, regulatory aspects of informed consent, and health literacy. The PAP also participated in construction of the interview guide that was implemented in the first part of the P-CARE study. The panel then reviewed consent materials from a range of clinical trials in acute MI and stroke (representing a range of trial designs) and developed consent processes and materials for each of them through an iterative process. Several PAP-created consent forms were then vetted by a series of experts and stakeholders and further revised. Finally, a consent form and information sheet were developed and implemented within an ongoing trial of early invasive versus surgical management of intracerebral hemorrhage (NCT02880878).

Figure 1. Development process.

REVIEW OF EXISTING CONSENT FORMS AND PROCESSES

In reviewing consent forms that were approved and used in clinical trials for acute MI and stroke and discussing their experiences and data from the P-CARE interview study, the group identified a range of concerns and potential barriers to context-sensitive engagement. Key concerns about consent forms related to structure, content, tone, and style.

Structure of Consent Forms

One problem identified with almost all forms the group reviewed was length. Among a sample of 6 forms, the average length was 9 pages (range 6–11). Given real time constraints associated with decision-making in both stroke and acute MI contexts, the group felt it was unrealistic to expect patients or surrogates to be able to read, process, or use that amount of information meaningfully. PAP members who had been enrolled (or served as surrogate) in clinical trials in acute settings echoed P-CARE interview participants in saying they could not read the entire form at the time they had to make a decision (Scicluna et al. 2019; Dickert et al. 2019). They felt that, in order to respect participants, consent forms ought to be "useable" in the timeframe within which individuals must make a decision.

The order in which information is presented was also seen as problematic. First, what the group considered to be irrelevant information accounted for much of the early portions of consent forms. This included headers with technical titles and information about funding agencies and investigators. Perhaps more importantly, it included generic introductions and descriptions about research participation. PAP members felt that the first page is critical "real estate" and that the opportunity to communicate valuable information was lost by filling early parts of consent forms with information that "I could care less about." Moreover, PAP members felt that presentation of what they considered to be generic information (about being a research subject) early was a sign for participants that the consent form was not designed around their needs in that situation.

Second, the group felt the order of information in forms did not reflect the order in which conversations typically occur or relative priority of information for participants, and that information was "repeated over and over again." Particularly in the acute setting, the group felt the consent form should have a logical sequence and should be designed to be reviewed in real-time during discussion with an investigator. In addition to helping to make the consent form more useful to participants, the group felt that designing consent forms this way could help structure conversations and provide guidance to individuals conducting them.

Content of Forms

In addition to being long, consent forms frequently contained technical descriptions of trials or procedures. This issue was not restricted to any particular section of the form; it included everything from the title and funding agency to information about risks, benefits, and study purpose. Particularly in the context of an emergent clinical situation, the group felt that simplification of language and use of accessible, familiar terms was essential. PAP members felt that both long and technical forms were likely to overload time-crunched and stressed individuals with information that is difficult to understand or unlikely to be related to participation. Moreover, PAP members felt that they, and most participants, lack the requisite "medical knowledge to sort through the mud."

Two specific sections—risk and follow-up activities—were frequently identified as problematic due to too much information. PAP members felt that several types of over-disclosure reduced clarity and potentially inflated perceived risk. First, there were often risks listed that related to clinical care and not study participation. For example, in stroke trials, risks related to imaging that patients already had or would have again for clinical reasons were sometimes described. Similarly, a consent form for a study involving assignment to a specific device for an intravascular procedure described detailed risks regarding the procedure (unrelated to the specific device) when everyone asked to be in the study was having the procedure performed for clinical purposes. Some forms also

Table 2. Examples of changes to consent form language.

Content	Original	P-CARE Form
Randomization	You will be randomized (like the flip of a coin) to the group that receives IABP or the group that does not receive IABP	A computer will randomly assign you to be in one treatment group. *You have an equal (50/50) chance of being in either group*
Follow-up	You will have follow up visits at 24-48 hours, 5–7 days or when you are discharged from the hospital (whichever is sooner), and at 30 days and 90 days after you joined the study (describes each for ½ a page)	Regardless of which group you are in, you will have 4 follow-up checks over the next 3 months. Details of these visits are included in the accompanying study information sheet.
Benefits	Participation in this study may or may not help to improve your condition. It is also possible that your condition may worsen. There is no guarantee that you will personally benefit by participating in this research study.	The main goal of this study is to improve care for patients with heart attacks. Being in this study may not benefit you directly. It is possible that the medicine may work faster when taken crushed rather than whole, but doctors do not know which way is better.

disclosed very remote risks and did not "group" relevant risks together. The latter concern arose, for example, when a trial involved use of a drug that could cause bleeding. From the PAP's perspective, articulation of the bleeding risk, with clarity that this could involve serious bleeding such as bleeding in the brain, was more helpful and less likely to inflate risk than describing multiple potential forms of bleeding.

Though perhaps not as consequential as over-disclosure of risks, the panel found detailed descriptions of follow-up activities to be distracting. The precise schedule of visits and types of assessments incorporated in follow-up, for example, were felt not to be helpful and ran the risk of being overwhelming. In contrast, this information was felt to be very useful from the perspective of a patient who has already agreed to be a participant in a trial.

The PAP felt that there was often a problematic *absence* of information related to reasons for joining a study and trial-related benefits. These gaps were linked. Specifically, PAP members who had made decisions about research participation in acute settings described that a principal reason for deciding to participate was the potential for direct benefit. Similarly, this was a common response among P-CARE interviewees (Dickert et al. 2019). Consent forms, however, often contained generic statements about how individual subjects "may or may not benefit from participating in the study" and that "findings will help doctors to learn … " without articulating the nature of potential direct benefits (Table 2). PAP members were sensitive to concerns about over-statement of benefit and the need for clarity about uncertainty but felt it was important to state specifically how participation might be beneficial. For a study involving an intervention for acute MI, for example, they felt it was important to state the potential for reducing the severity of heart attack or "damage to the heart." In addition to lack of clarity about potential for benefit, PAP members felt that there was often not a statement of the importance of the research question. They felt that it was valuable to patients/surrogates to know why the trial was important to improve care.

The financial considerations and compensation for injury sections were routinely viewed as problematic by PAP members. This was due to a combination of over-disclosure and ambiguity. Often forms stated that institutions and sponsors bear no direct responsibility for injury, that insurance would be billed for care not directly related to the study, that insurance companies vary regarding what they cover, and that the patient may be billed for care not reimbursed by insurance. PAP members felt this typical disclosure was inappropriately vague, amounting to a statement that says little more than "there may be financial consequences." The potential financial impact of research participation was a salient concern for PAP members, but they felt the ambiguity in consent documents provided little information and sowed doubt. As one member stated, "you might get to that part and say forget it."

Tone and Style of Forms

PAP members felt that many consent forms had a "proceed at your own risk" tone that they found off-putting and unhelpful. Just as there was an absence of content regarding reasons for participation and potential benefits of enrollment, the emphasis of forms was often on the ability of patients and surrogates to decline participation. They felt that this tone was different from the more collaborative tone of investigators and coordinators with whom they had interacted in the context of being asked for consent. This is, importantly, a subtle issue. PAP members did not in any way believe that consent forms should obscure risks or be anything but clear about the fact that participation in a clinical trial is optional. However, they

felt the form should emulate the tone of a thoughtful clinician or investigator rather than an exculpatory or legalistic form.

PAP members also did not endorse some of the language commonly used to describe randomization. For example, despite recognizing that it was intended to make an abstract concept more concrete, there was a shared sentiment that the term "flip of a coin" in particular was trivializing in the context of severe, acute illness. Simply stating that interventions are assigned "by a computer" and that there is an equal chance of receiving either treatment (in a two-arm trial) was felt to be clear without being trivializing (Table 2).

Barriers or Facilitators Unrelated to Consent Forms

Although much of the material that PAP members reviewed came from consent forms, the process of consent and communication for acute MI and stroke trials beyond forms was discussed extensively. PAP members shared their own experiences and reviewed data from the earlier interview study.

One of the most important determinants of the consent experience, from PAP members' perspectives, was the demeanor, tone, and style of interaction of the investigator or other study staff at the time of consent. In the acute setting, it is rare for a patient or family member to have had any prior contact with the individual who is asking them to provide consent for trial enrollment. In this context, it is especially important that the investigator communicate trustworthiness, professional expertise, and compassion. These themes reflect the emphasis of many participants interviewed in the key informant interview portion of this study as well (Scicluna et al. 2019).

Another focus was the fact that consent processes are often inappropriately treated as discrete; communication about a study should and often does extend beyond the initial consent process and may involve content beyond what is contained in the consent form. A significant determinant of PAP members' positive experience in clinical trials— which was also revealed in the key informant interview study— was the experience of communication with coordinators and investigators afterwards (Dickert et al. 2019, Scicluna et al. 2019). PAP members felt that post-enrollment communication is a way to help educate and engage individuals in the research process and an opportunity for participants to ask questions and to learn more about the study. It was also viewed as an opportunity to demonstrate respect and gratitude toward participants, to earn trust, and as revealed in discussion with prior enrollees, to remind individuals assigned to control arms that their participation is valuable. The latter insight was stimulated by a particular individual's recounting of feeling "dumped" when his mother was assigned to the control arm in a trial of procedural versus medical therapy.

On a more practical level, PAP members felt that different information is relevant regarding ongoing participation and initial enrollment. Detailed information regarding follow-up assessments and visits, for example, was viewed as relevant to the post-enrollment period. However, few studies have formal processes for communication (either written or verbal) after enrollment has occurred.

CONSTRUCTING PATIENT-DRIVEN CONSENT PROCESSES

Having identified the above gaps and areas for improvement, PAP members and P-CARE team members collaborated to develop processes that represented improvements. The goal was to address all possible areas for improvement while recognizing that any proposed processes or materials needed to be approvable and implementable within existing regulations. We focused on three components of the process: the consent form; a separate information sheet; and post-enrollment communication. As described above, we worked through example studies serially and then compared the materials developed for each study with others in order to ensure consistency of approach where appropriate (example forms available at http://www.eccri.emory.edu/ethics.html).

Changes to the Consent Form

The structure of consent forms was changed in important ways. The most obvious change is that PAP-driven forms (referred to as P-CARE forms) were shorter. On average, we reduced the length from about 9 pages to 3 or 4 pages. This is without substantial modification of language regarding issues such as compensation for injury or privacy protections, which tend to be more "fixed" due to institutional policy and legal determinations. In most cases, what most patients would consider key details of the study were described in 2 or 3 pages.

The PAP and P-CARE team chose to structure forms around key questions to which PAP members thought patients would expect answers and in an

order that represented how investigators might discuss them. As illustrated in the available examples (http://www.eccri.emory.edu/ethics.html), P-CARE forms began immediately with a concrete, several sentence description of the study and an initial series of questions including the following: What is this study about?; How is this different from what would be done normally?; How is it decided what group you will be in?; What will be required of you?; What are the possible benefits of being in the study?; What are the possible risks of being in the study?; and What is the alternative to being in the study? This structure was designed to demarcate content effectively so that the document would be "scannable," an important goal in acute situations characterized by time constraints. This order was also intended to allow the document to be followed in real time. PAP members hoped that this organization would potentially help investigators or coordinators structure a consent conversation and provide useful language in relevant domains.

Other structural elements were designed to make P-CARE forms easy to read. We chose short paragraphs with short, clear sentences and avoided technical terms. The reading level of all of forms was 7.1 on average, using Flesch-Kincaid scoring. Of note, we did use short paragraphs rather than bulleted lists. After trying both approaches, the PAP felt that the paragraph form made the documents easier to read and less "choppy."

In response to the concern about nonspecific, generic language occupying the high-visibility, high-yield part of the consent form, we excluded much of that information and described at the outset the problem for which the patient was being treated, the basic nature of the trial being conducted, and the fact that research participation is voluntary. Where possible, information about the trial sponsor and investigators was moved to the end of the form in order to bring the most valuable information to patients/surrogates forward.

We also made important changes to content. Regarding potential benefits, we included an explicit statement about the major potential benefit associated with the intervention being studied (all reviewed studies were intervention trials with a prospect of direct benefit) but clarified that the chance of benefit was uncertain and that research is designed to build knowledge and help future patients (Table 2). This approach was felt by PAP members to be most honest and helpful. We removed risks that were not related to the study (e.g. general procedural risks to which all patients would be exposed regardless of study group) or that were exceedingly remote. We also removed risks that are not really applicable but are often included *pro forma* (e.g. risks of becoming pregnant during a study when the study is a one-time intervention delivered immediately during a very acute illness). We clustered risks into groups or types as much as possible to avoid "laundry lists" that potentially cloud appreciation of meaningful risk.

We adopted an innovative approach regarding procedural risks in trials where interventions require a separate clinical consent for individuals randomized to the procedural arm. The clinical consent process typically covers risks related to anesthesia, blood transfusion, and other general surgical risks. Many of these trials are unblinded, and the clinical procedural or surgical consent process is only conducted with those randomized to the procedure. For these trials, we described general procedural risks briefly in the research consent form and stated clearly that they would be discussed in the surgical/procedural consent for those randomized to that arm. This approach, which represents a variant of a staged consent process, was chosen to help participants focus on the research participation decision and to avoid overloading individuals randomized to medical therapy. This approach was driven by input from patients and surrogates, especially one surrogate who described the sense of being "dumped" when his mother was randomized to control after he made what he felt was an agonizingly detailed decision about acceptance of the surgical procedure. From his perspective, separating the decision about randomization from a consideration of procedural details would have made the initial trial participation decision more straightforward, would have made the decision-making process more familiar, and would have lessened the emotional toll of being randomized to control.

A final content change related to follow-up procedures or tests. Many forms that we reviewed contained descriptions of each follow-up appointment or assessment. PAP members felt that the consent form was not an effective place for these details to be communicated because they lengthened the form, potentially obscured "bigger picture" understanding, and were most relevant after the acute stage of illness and only to individuals who agree to be in the study. For this reason, follow-up activities or procedures were grouped and described more generally. If a study involved three follow-up phone assessments, for example, it was simply stated in the consent form that "you will be contacted by phone to see how you are

doing three times over the next 2 months" rather than going into detail about types of questions and length of phone calls (Table 2). Greater detail (sometimes with a table or chart) was provided in the information sheet, which was explicitly intended to function as a reference or "user's guide" to the study.

In response to concerns regarding the style and tone of consent forms, P-CARE forms involved several key strategies. PAP members were sensitive to the need to avoid language that insinuated that trial enrollment is a "bad idea" and that made consent forms feel exculpatory. Early emphasis on the nature of the problem being addressed, including why the research question is important, was one way forms addressed this concern, as was the more direct mention of potential benefit (with acknowledgement of uncertainty). P-CARE forms remained very clear that participation is voluntary and that patients will not be disadvantaged if they decline. Finally, as described earlier, PAP language describing assignment "by a computer," "by chance," and involving an "equal chance" of being assigned to either arm was used in place of metaphors such as "flip of a coin."

A persistent source of frustration on the part of PAP members related to sections of forms addressing financial considerations and care in the event of harm or injury. The primary source of frustration was with institutional policies in this respect. PAP members felt that it was largely inappropriate to ask patients and surrogates to enroll in a trial with undefined financial implications and with an ambiguous plan for treatment. The changes made to the consent forms in these domains were thus superficial. The language was simplified, and the forms encouraged individuals to ask study staff if they have specific questions.

Information Sheet

The information sheet was designed to address several key concerns. Most importantly, consent forms are intended to help people decide whether they want to participate in a study. People have different informational needs over the course of the study after enrollment. In many cases, consent forms are used to serve both functions. In the acute setting, where time constraints and other challenges to consent exist, we felt these functions were best separated. The information sheet allowed more substantial explanation of the nature of the study and detail about follow-up activities and procedures. It was designed to help facilitate engagement and education of participants regarding the study more than could be achieved at the time of initial consent and to provide a "user's guide" to being a participant.

Although there was substantial attention to avoidance of conflicting information in the information sheet and consent form, we made no attempt to avoid overlap. The information sheet was designed to contain any information that would be helpful to individuals in the study. In other words, it is not designed as a supplement but rather as a stand-alone document that participants could use and refer to after enrollment.

In most cases, the P-CARE team envisioned that the information sheet would be distributed at the same time as the consent form. However, splitting them allows for tailoring of the information sheet to treatment arm in the case of unblinded studies. For example, in a trial of early surgical versus conservative management of intracerebral hemorrhage, there was a separate information sheet created for individuals assigned to each intervention arm. The surgical group contained information about post-operative considerations, for example, that were irrelevant to individuals in the conservative arm. Similarly, that information sheet included language emphasizing the contribution of individuals assigned to conservative therapy. This was suggested and endorsed by patients to combat the perception that they were no longer a valuable part of the study. Obviously, creation of different materials for different trial arms is only possible in unblinded studies.

Post-Enrollment Communication

A central finding from earlier phases of this project, and from PAP meetings, was the importance of post-enrollment communication. The information sheet was designed to help facilitate education and engagement and was intended to represent a readable and valuable resource. However, PAP members felt strongly that engaging participants in discussions about the trial after enrollment has occurred, giving people an opportunity to ask questions and understand the research process, and demonstrating respect and appreciation for involvement in the study is essential. An integral part of the P-CARE process is thus ensuring that participants have an opportunity to discuss the study with study staff after enrollment.

Vetting Process

Materials developed by the P-CARE team were vetted by multiple stakeholders. This included expert

consultants, local IRB chairs, patient-family advisors, and a focus group of interview participants recruited from the earlier P-CARE interview study. In general, the processes were well-received. Some feedback was explicitly incorporated into the P-CARE process. For example, creation of separate information sheets by treatment assignment was a response to suggestions revealed during the focus group and reinforced by PFAs. IRB chairs felt the consent forms met required elements of informed consent and suggested several minor modifications. However, they acknowledged that IRBs often request more comprehensive consent forms out of concern that regulatory entities may consider less detailed forms to be inadequate.

IMPLICATIONS FOR RESEARCH CONSENT

Available data indicate that most patients and surrogates prefer to be involved in a consent process in the acute setting rather than being enrolled without consent despite questions in the literature about the value of these processes (Tognoni and Geraci 1997; Shaw 2014; Dickert et al. 2015; Dickert, Hendershot, et al. 2017; Dickert et al. 2019). We assembled a group of patients, family members, and content experts to design context-sensitive consent processes for these trials based on what matters to them. This project, and the creation of a patient-driven consent process for acute care research, provides novel and practical information for investigators, research teams, and IRB members considering these trials. We believe there are several key implications.

The most important practical implication is the need to be thoughtful about who is using and reading a consent form and in what context. PAP members felt that it is disingenuous and disrespectful to give a patient or surrogate in a stressful situation a consent form that they could not read in the timeframe within which a decision must be made. The length of consent forms is well-recognized and widely-lamented. It is important to acknowledge that shorter consent forms or other consent interventions have not yielded dramatic changes in domains such as understanding of key content for clinical research, though some improvements have been documented (Kinnersley et al. 2013; Synnot et al. 2014; Nishimura et al. 2013). This literature is, however, under-developed and narrowly focused on participant comprehension (Gillies et al. 2018; Dickert, Eyal, et al. 2017). Moreover, PAP members believed that long, complex forms in the acute context convey a lack of respect for individuals asked to sign them and simply lack "face validity."

The attention of PAP members to the order and priority of information is important and novel. IRBs appropriately focus on the extent to which key regulatory elements are covered. However, there seems to be less attention to the order in which they are presented. The use of rigid templates may magnify this issue. Many templates, for example, are categorized by technical information such as sponsor information, highly-technical study titles, names of investigators. PAP members found many of these distracting and better placed at the end, where possible. More importantly, PAP members had strong reactions against commonly-included boilerplate introductions addressing generic issues about "what is research?" and heavily emphasizing freedom to decline participation before even describing what is being asked and why. As described earlier, PAP members felt that important information about the study itself and what it means to participate should be presented early. They also felt that the consent form should mimic an effective conversation such that it can be used and "followed" in real-time. The latter feature, it is hoped, may even help the form to serve as a sort of training tool for presenting study information. PAP members' attention to the potential expressive harm of putting generic study information upfront in the consent form is also novel. The potential for sending a signal that the form is "not for you" and promoting lack of attention is not often recognized and has not been empirically evaluated; however, it is possible that these elements could have a negative impact on functions of consent such as promoting trust, understanding, or appreciation of how a particular study aligns with an individual's preferences or affects his or her welfare.

Another critical element of the P-CARE consent process is its focus on the decision at hand. PAP members strongly endorsed the idea that research consent in an acute context should focus on what patients/surrogates need to do right then for that decision. We worked to eliminate, where possible, clinical information not germane to research enrollment, and we shifted content that was material to ongoing participation, but not to initial enrollment, to information sheets. Some information that "reasonable persons" might want to know but that is not about initial enrollment may be more meaningfully presented elsewhere. The process of sorting through what information represents a high priority to actual decision-makers is especially critical in the acute care context, but it has taken on increased importance more broadly in the context of the need to present "key, concise information" upfront as required by the

recently revised Common Rule (U.S. Department of Health and Human Services 2018). The questions in the P-CARE example forms may provide helpful guidance regarding what information is useful to include in these new sections. More importantly, the process of partnering with actual decision-makers to identify what matters to *them* may be invaluable to investigators and IRBs.

Yet another key insight revealed in this process is the importance of attending to engagement of patients and surrogates beyond the consent encounter. PAP members and P-CARE interview participants spoke of the value of post-enrollment communication, and the information sheet and post-enrollment encounter that characterize the P-CARE process represent efforts to address this. Attending to these issues is an important part of what it means to respect patients, and meaningful post-enrollment communication has potential to increase engagement and communicate the value of individuals' contributions. It also may help to advance transparency and to promote trust and integrity.

A final substantive issue revealed through this process is the importance of tone. Getting consent right requires listening to patients and surrogates and recognizing the context in which materials will be used. Some tonal dimensions of consent forms are underrecognized but straightforward to address. For example, descriptions of randomization as "flipping a coin" were felt to be trivializing. Other empirical work has demonstrated that this and other analogies may not be effective and may be perceived in other unintentionally problematic ways (Jepson et al. 2018; Krieger et al. 2017). Further work may reveal optimal ways to communicate this information, but attention to tone and unintentional connotations of analogies may be an easy and important way to enhance respect as well as potentially understanding of key considerations necessary to improve the extent to which enrollment decisions are informed and authentic. Addressing these issues also raises no specific regulatory concerns.

Other issues related to tone have greater ethical implications and are more complex. There may be deep concerns about shifts toward more positive framing of research participation, more explicit mention of potential benefits, and more direct articulation of the importance of a particular study. We suspect that much of the more "negative" valence that tends to predominate is rooted in strong, well-intentioned desires to avoid therapeutic misconception or misestimation (Appelbaum et al. 1987; Horng and Grady 2003), a belief that a more negative valence emphasizing the opportunity to decline is "protective," and a concern that an emphasis on the importance of research may push individuals into enrolling in studies. These are challenging issues, and a balanced approach is essential. However, knowing the potential benefits of participation and the potential value of a study are crucial to making informed, authentic enrollment decisions. Working as a team with patients and surrogates has provided insights into ways that many standard views (and the practices that they drive) may ignore the real experiences and informational needs of patients and surrogates. Improvements in these domains may enhance the extent to which consent processes, in both acute care and other contexts, are transparent and help decision-makers to make decisions that are authentic and account for important welfare considerations.

We recognize that there are limitations to this work. Most importantly, it is the work of one team. We represent a diverse group of researchers, patients, and surrogates, but other teams could develop different processes. Sharing of similar work by different groups could help to identify areas of consensus and disagreement and would be very helpful for researchers, ethicists, and IRB members. It is also important to recognize that most current consent conventions are based on little or no empirical evidence and lack any direct foundation in patients' or surrogates' experiences or views. In this respect, we believe the processes developed in this project represent a good start. Related to the fact that this was the work of a single group, the PAP met multiple times over a period of years; members became very familiar and comfortable with each other and with the research team. The PAP environment was highly collaborative and conducive to open discussion and resolution of any disagreements, and PAP members developed a significant understanding of the details of acute care research. These aspects of the P-CARE study do not limit the value of the insights produced, but this intensive process would not be feasible to reproduce in order to design a consent process for a single trial. Developing more scalable approaches to engaging relevant patients and surrogates is an area for further exploration. Finally, despite the fact the P-CARE consent processes were developed based on robust studies of patients' and surrogates' experiences and PAP members' firsthand experiences, the value and impact of these processes require empirical testing. We are engaged in this work currently by implementing these processes within ongoing clinical trials and are committed to

studying the experiences of participants and research teams in using them.

CONCLUSIONS

Working as a team of researchers, patients, and surrogates, we have identified gaps in current consent processes for clinical trials in acute MI and stroke. We have highlighted ways in which traditional consent processes and materials fail to attend to the emergency context and do not appear to meet decision-makers' needs. We have proposed alterations in tone, structure, and content that we hope represent a step toward making these processes more attentive to the needs of the individuals they are truly intended to serve and a more effective demonstration of respect for patients and surrogates in difficult situations.

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