Characterizing digital participation in healthcare regulatory processes by a terminal rare disorder community

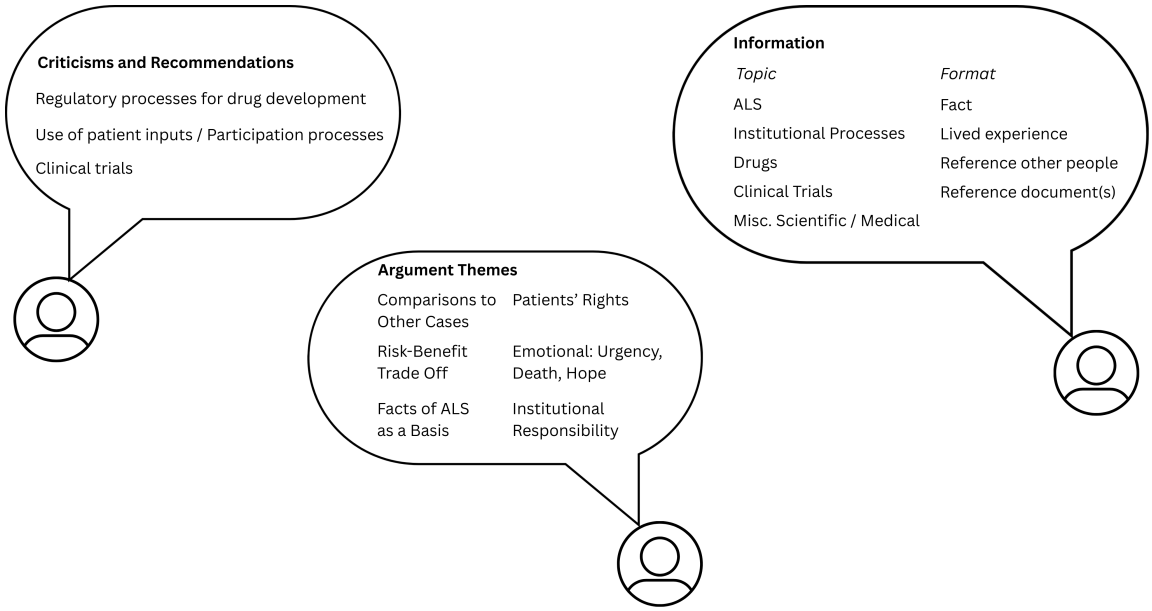

Fig. 1. Our paper characterizes the structure and content of public comments on `regulations.gov` in response to an FDA guidance document for the development of drugs for treating Amyotrophic Lateral Sclerosis (ALS). People's comments include criticisms and recommendations about aspects of drug regulation, specific clinical trial design choices, and how patient inputs are used. Comments sometimes provide information from lived experience or facts and make claims about ALS to support their critiques. We also identify six argument themes that show up across comments.

Public participation in health policy can benefit all: people can potentially improve decisions by contributing insights from lived experience, and policymakers can make better patient-centered decisions. However, digital avenues for health policy participation remain limited. Our work contributes a mixed methods study of a patient community's participation in a health regulatory process via an institutionally-approved digital platform. We inductively coded 162 public comments on an FDA guidance document for the development of drugs for Amyotrophic Lateral Sclerosis (ALS), a terminal rare disorder with no cure and limited treatments. Comments critique guiding principles for ALS drug regulation, recommend specific research and regulatory actions, and occasionally reflect on the participation process. We identify criticisms and recommendations across three topics: drug regulatory processes, clinical trials, and the use of patient inputs. We further identify six argument themes. Our findings highlight opportunities for public participation across different stages of multistakeholder health regulatory processes.

CCS Concepts: • **Human-centered computing → Empirical studies in collaborative and social computing**; **Empirical studies in collaborative and social computing**.

Additional Key Words and Phrases: Participation, Health Policy, Science Policy, Rare Disorder,

Author's Contact Information:

1 Introduction

Public participation in health policy has the potential to improve quality of care for patients, increase transparency about regulations and funding, and hold healthcare systems accountable [47, 52]. Yet digital avenues designed for participating in health policy remain limited. In cases of harm, uncertain medical knowledge, or incomplete institutional understanding of policy outcomes, people often create their own spaces for sharing lived experiences, ideas, and criticisms. Public inputs have affected clinical research regulation, improved the delivery of healthcare, and created new medical knowledge. For example, the AIDS advocacy movement transformed drug approval processes [20], women shared stories of pain on social media that altered clinical procedure guidelines [1, 69], and long COVID advocacy on X gained clinical recognition and shifted research agendas [60]. These attempts at participation have been community-led, taking the form of long-standing offline social movements and social media advocacy. Health and science institutions have led formal public engagement such as public health education initiatives [51] or crowdsourcing public health data via digital platforms (*e.g.* contact tracing) [62], but institutions only occasionally invite the public to participate in health policy *decision* processes.

Health institutions make decisions with data for a number of reasons which might not always align with the objectives of people who are affected by those decisions. A more democratic and practically relevant healthcare system would build on both the *removed expertise* of institutions that deal with matters of fact, and the *situated knowledge* and impassioned reasoning of the public who deal with matters of concern to them [19]. Digital platforms can be powerful tools for supporting such participation. However, in human-computer interaction, digital participation has focused on local communities participating in municipal decision-making such as city planning, transportation, and local resource sharing [21, 34, 42]. Digital participation in health policy processes has rarely been studied. When done, this scholarship has three gaps: it does not focus on direct communication between patient communities and institutional authorities, it is not about participation in regulatory decisions, and it does not study institutionally-approved platforms.

One institutionally provided platform for participating in health policy processes is `regulations.gov`, a site where U.S. regulatory agencies post *dockets* (groups of regulatory documents) for the public to view and comment on. The Food and Drug Administration (FDA) posts dockets to the site which contain rules, patents, industry guidance, and records of communication with citizens and companies. We perform a qualitative analysis of public comments on a FDA docket which contains guidance for the development and regulation of drugs for Amyotrophic Lateral Sclerosis (ALS). ALS is a rare fatal neurodegenerative disorder with no cure and limited treatment options. The ALS community is a great case study for public participation in health-science policy: they are a motivated community that wholeheartedly participates in clinical research processes. Additionally, institutions that regulate ALS drug development (like the FDA) create pathways for the community to provide their inputs.

Our work characterizes participation at the intersection of science, health, and policy. We contribute a study of how a patient community communicates with institutional experts about regulatory decisions on an institutionally-approved platform. Our work provides an empirical contribution, using qualitative analysis of public comments on an ALS drug development guidance document to answer the following research questions:

RQ: How does a patient community participate in policy making processes that affect their lives?

RQ: What kinds of criticisms and recommendations do people make for policy?

The research team inductively coded public comments for structure and content. We identify the criticisms and recommendations that people make along with the information, claims, and arguments they use. People provide criticisms and recommendations on several dimensions of drug development regulatory processes, clinical trials, and

patient participation. Some comments are nonspecific, some engage with guiding principles for research and regulations, and some provide valuable critiques and specific recommendations. We identify several types of information and claims that people use in comments to support their criticisms and recommendations. People employ moral, emotional, and logical reasoning in their comments, often combining multiple types of arguments. Our findings suggest opportunities for digital participation in health policy beyond advocacy or voting: people have inputs across multiple aspects of regulatory processes, research processes, and the design of public participation systems.

2 Related Work

The epistemological and moral benefits of public participation in health are increasingly recognized [47, 52, 58]. Yet studying and implementing digital ways for greater participation in health policy and research can be difficult because of their broad scale and technical knowledge base. People advocate for their perspectives to be considered in institutional health processes, but few human-computer interaction efforts have codified the ideas, concerns, and recommendations that patients have, and how they communicate these directly to regulators on digital platforms.

2.1 Institutional and individual ways of knowing

Health policies can have big impacts on people's lives, such as determining quality of life, access to care, and even survival for people with health disorders and also those without [11]. Social distancing mandates helped prevent the spread of COVID [41]; International Review Board (IRB) processes protect research participants from harm [3]; and clinical hygiene protocols prevent the spread of infection in hospitals [63].

Though the effects fall largely on the public and patients, it is institutions that interpret scientific results; establish clinical and research practices; and overall, develop health policies. Are institutional ways of knowing most suitable for making decisions that most directly affect people with a health disorder? A comprehensive body of work demonstrates important gaps between institutional and individual ways of knowing [19, 24, 28, 31, 67]. Public participation in institutional health decision making processes can bridge these knowledge gaps.

Policy makers attempt to identify problems and make decisions that are beneficial to all stakeholders with the information they have. However, institutional experts don't always have complete information on the specific needs, challenges, and experiences of people [53]. For example, primary caregivers of children with a rare disorder have more visibility into the daily progression of their child's disorder and the specifics of daily care coordination processes than clinical experts [31]. When policy makers are *outsiders* to communities and contexts, inputs from affected people and other stakeholders can prevent unintended consequences and identify opportunities for improvements [53].

Institutional experts and affected people also demonstrate different ways of interpreting data. For example, interview studies of psychiatric patients were analyzed by people who have used mental health services (Service User Researchers) in terms of experiences and feelings while researchers without experience with mental health services analyzed them with more attention to processes and procedures [24]. Similarly, in studies about patient perceptions on electroconvulsive therapy (ECT) procedures, findings were interpreted by clinicians to conclude that patients trusted their doctors, while similar numeric findings were interpreted in patient-led studies to conclude that there were issues with informed consent [58]. This may also apply to health policy: for example, a group of physicians experiencing long COVID symptoms created a manifesto with ideas for research, clinical services, patient involvement and access to services for people with long COVID [4].

People and institutions can have different ways of weighing value tradeoffs in decision processes. What is most important to institutions is not always most important to people (and vice versa). For example, drug developers conduct

clinical trials to determine a drug's safety and effectiveness for a broad population, while patients enroll in clinical trials to gain access to the potential benefits of investigational drugs for their lives [68]. Many health policy issues are *wicked problems* which require the integration of scientific knowledge with ethical, political, and societal considerations that under a democratic ideal would include the values of the public [12]. The disability community has long championed this concept that people should be able to contribute to decisions that affect them under the call "nothing about us without us" [6, 61]. In order to incorporate public and patient ways of knowing into institutional processes, it would be useful to know what people and patients are saying about institutional processes already. Human-computer interaction scholars have documented the ways that some online communities combat institutional health knowledge and processes (*e.g.* public health conspiracies) [38, 43], yet others contribute productively [59]. How might institutional and individual ways of knowing complement each other, rather than combat each other?

2.2 Unique challenges for public participation in health policy

Health policy participation is beset with multiple challenges when compared to other domains where the public participates in decision making. We elucidate some of these challenges by comparing to another setting where human-computer interaction scholars have studied participation: local participatory governance. Successful efforts have brought together institutional and other ways of knowing [10, 17, 33, 34]. However, health policy participation differs from local civic participation in terms of scale, the feasibility of in-person avenues, and the nature of information discussed.

Municipal participation definitionally happens on the city-scale, where people provide inputs on local decisions; *e.g.* San Diego residents evaluated ideas for the redesign of a street [45]. Participation in health policy processes, however, exists along a broader spectrum from individuals to nationwide policy [47]. Individual patients may participate in shared decision-making with their clinician, *e.g.* a patient and their doctor can collaboratively decide which diabetes medication to use [49]. A local community may participate in their city's healthcare processes; *e.g.* a civic group in Jackson, Michigan met with members of their community to determine unmet healthcare needs and developed an electronic community health record [37]. People might also participate in national health policy; *e.g.* the public can comment on regulations from federal agencies such as the Food and Drug Administration (FDA) and the Center for Disease Control (CDC) [23].

While city communities share physical location and experiences, patient communities share experiences often without a shared location [30, 50, 65]. Studies of local participatory civics note that digital participation can complement in-person meetings, and that in-person participation allows for real-time collaborative analysis of public inputs [45, 46]. Yet in-person avenues can be difficult or inequitably accessible for people participating in large-scale health policy. In fact, patient communities, like rare disorder communities, are often distributed across great distances. Digital platforms can be important tools for supporting dispersed patient communities as they raise awareness and communicate with each other and institutional experts [44]. Similarly, digital platforms are a critical avenue for participating in nationwide health policy that affects many geographically scattered lives.

Institutional deliberations often center data in their decisions [9]. In municipal participation, data is used as a source of authority (data visualizations serving as credible representations of truth), as evidence (using bike traffic data to justify the need for new bike facilities), and as rhetoric (data can have persuasive qualities) [42]. When people participate in local governance, data types include city transportation maps, crowdsourced traffic data, and information from google earth [42]. This takes considerably less technical savvy to interpret than many forms of scientific and medical data (results from clinical trials, MRI scans, EKG readings, statistical significance, etc).

When the public discusses health or scientific data with experts, there can be information asymmetry with differing levels of health and data literacy [55]. Motivated patient communities might educate themselves on technical topics: *e.g.* some AIDS activists taught themselves "virology, immunology, molecular biology, and biostatistics" in order to participate in conversations about clinical research [20]. Even without the credentials to thoroughly analyze technical data or discuss scientific concepts, members of the public can still debate value trade offs in decisions about health and medicine based on their lived experience.

2.3 Lack of institutional platforms for participation

When people "participate" in clinical science as research subjects, they may contribute their bodies [56] or their personal data [25]. When people attempt to further participate in *decisions* about clinical research practices or health *policies*, they may have more subjective inputs: experiences of the effects of policies on their lives, arguments about value tradeoffs, critiques of current policies, and recommendations for better processes.

A growing body of work has identified valuable contributions that the public has made across the health research and policy life cycle. People's experiences, ideas, and personal health data have led to the discovery of new phenomena or research agendas. For example, people with long COVID shared experiences and ideas on social media that served as the initial site of discovery of long COVID and led to research on the long-term effects of COVID. [7, 59, 60]. People critique clinical research practices and regulatory processes that use the results of research. For example, AIDS activists argued for changes in clinical trial and drug approval processes [20]. People also use their experiences to evaluate health policy and guidelines which regulate how physicians deliver clinical care. Women who experienced intrauterine device (IUD) insertion procedures shared criticisms of inadequate pain treatment during the procedure and recommended better communication of pain expectations and treatment options [64, 69]. After sharing these testimonies on social media, guidelines from the U.S. Center for Disease Control and Prevention (CDC) and American College of Gynecologists (ACOG) for treating IUD insertion pain were updated accordingly [1, 8].

Though each of these cases resulted in changes to medical research and healthcare processes, they were not supported by institutional platforms or processes for accepting public input. The social media platforms used by people with long COVID and women who shared personal experiences were not designed for communication between the public and health institutions. Studies of online patient communities are often about sensemaking, community building, or informing personal care practices, not about participating in institutional processes [48, 65, 71]. Institutional ways of knowing and people's ways of knowing are mostly understood or studied in silos; transfer of knowledge is often accidental.

3 Context: The ALS Community's Participation in Institutional Regulatory Processes

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder that causes progressive motor impairments such as muscle weakness, and paralysis. There is no cure for ALS and treatment options are limited, so the ALS community is highly motivated to advocate for access to experimental treatments and for advancing clinical research in drug development.

3.1 Drug development and approval process

Drug development and regulation follows a three stage process after preclinical research, shown in Figure 2. 1) Drug developers (*i.e.* sponsors) submit an Investigational New Drug (IND) application for the the Food and Drug Administration (FDA) to review. Such applications include clinical trial design, eligibility criteria (who can participate in

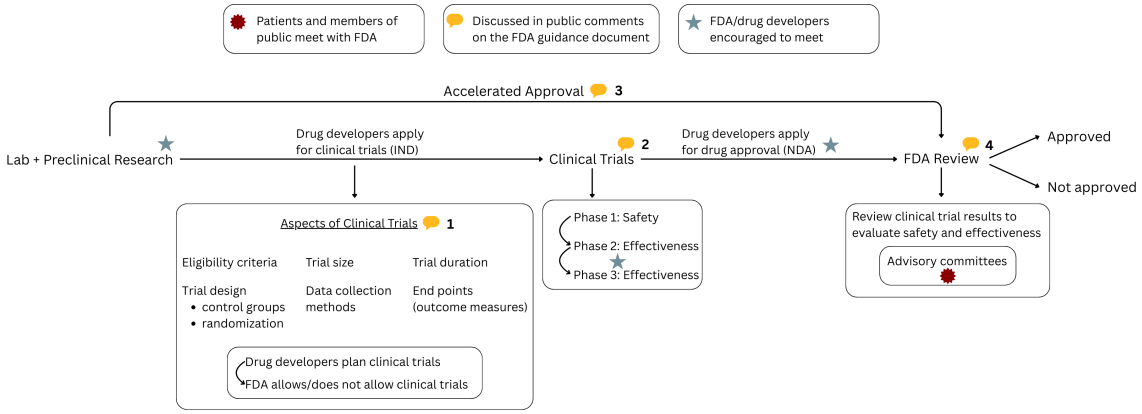

Fig. 2. A section of the drug development and approval process after preclinical research: 1) (Regulatory step) Drug development companies (*i.e.* sponsors) submit an Investigational New Drug (IND) application with detailed plans for clinical trials which the FDA reviews; 2) Clinical trials are conducted by sponsors; 3) (Regulatory step) Sponsors submit a New Drug Application (NDA) to the FDA containing the safety and effectiveness results of clinical trials and plans for marketing the drug which the FDA reviews and uses to make a decision on drug approval

the trial), trial duration, what endpoints are used (the outcome measures for assessing effectiveness), and other specifics of trial protocol. The FDA then decides whether the planned trial is approved to start. 2) Clinical research: testing on humans in clinical trials to determine safety and effectiveness. 3) Drug developers submit a New Drug Application (NDA), containing results from their clinical trials. The FDA reviews the data in the NDA to decide on approval of the drug [14]. Since the approval of trials and drugs is regulated by the FDA, a large part of the ALS community's advocacy is directed toward influencing FDA regulations and decision processes.

3.2 How the ALS community participates

One way the ALS community participates in FDA regulatory processes is on `Regulations.gov`. `Regulations.gov` is a website where over 220 US federal agencies post their regulations for the public to view and comment on. Created as part of an eRulemaking initiative to enable public access to regulatory materials and increase public participation in rulemaking, `regulations.gov` presents a different approach than the previous in-person process for commenting on regulations. Policy documents are provided as *dockets*, which are groups of related regulatory documents and proceedings. The Food and Drug Administration (FDA) posts dockets containing rules, meeting transcripts, drug patents, guidance for industry, records of communication between citizens, companies and the FDA (about drug approvals, food and drug marketing permits, the use medical devices, and penalties for companies that have violated FDA rules), and notices (of meetings, policy changes, or new drug or food products).

People then submit comments on entire dockets or specific documents within dockets. This study analyzes comments on the docket *"Considerations Regarding Food And Drug Administration Review and Regulation of Drugs for the Treatment of Amyotrophic Lateral Sclerosis"*. This docket includes proceedings from a public hearing on the review and regulation of drugs for ALS in 2013, and a draft and final version of an industry guidance document issued by the FDA. The guidance document, *"Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment; Guidance for Industry"* outlines guidelines for clinical trial designs and procedures, treatment effectiveness assessment, and other safety and drug

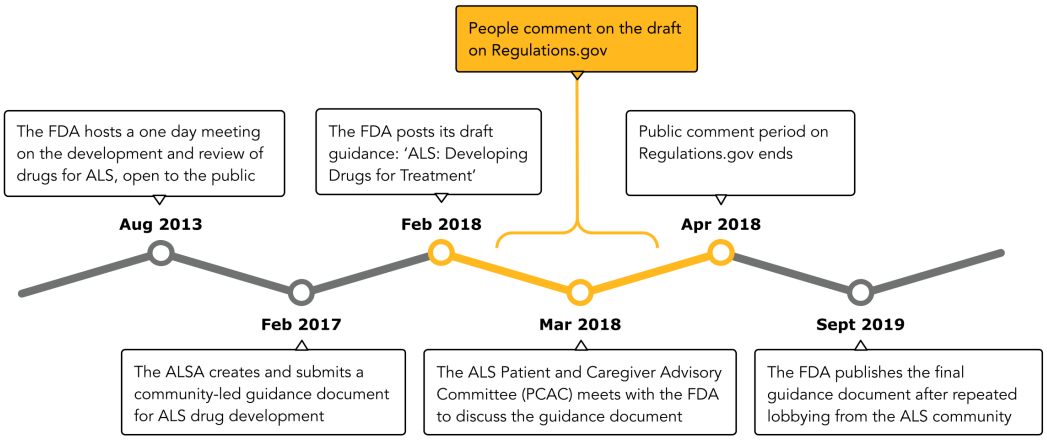

Fig. 3. Timeline of the development of the FDA's guidance for industry, *Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment*

approval considerations. Most comments on the docket are in response to the draft version of this guidance document, posted by the FDA in 2018. Figure 3 shows the timeline of the development of this guidance document.

The ALS community's engagement with the FDA guidance document is a highly relevant case study for understanding how patients participate in health policy processes. Several communities have advocated for health policy change through social media, but the ALS-FDA case study demonstrates both a motivated community and institutionally created pathways for consulting that community. People in the ALS community have inputs for clinical trial processes because enrolling in clinical trials is the main way for ALS patients to gain access to experimental treatments. Members of the ALS community and the ALS Association (ALSA), a nonprofit advocacy organization, advocated heavily for the creation of this drug development guidance, for patient inputs to be reflected in the guidance, and for the FDA to release the revised version promptly after receiving community feedback. The guidance document was updated to include some patient recommendations in its final version posted in 2019.

4 Methods

A mixed methods study answered two research questions: How does a patient community participate in policy-making processes on an institutionally-approved platform? What kinds of criticisms, claims, and recommendations do they make and what information and arguments do they use? The research team developed a codebook through iterative qualitative coding and discussions. A set of 162 comments was coded with the final codebook (4.4) for topics of criticisms and recommendations, topics and formats of information provided, themes of arguments, and the presence of claims about ALS. We calculated the frequency of each code in the 162 coded comments.

4.1 Data Collection

The research team downloaded public comments in response to the FDA policy docket (described in 3.3 and shown in Figure 4) regarding ALS drug development and regulation from the `regulations.gov` website [1]. Comments can be

[1] https://www.regulations.gov/docket/FDA-2013-N-0035/comments

viewed online and bulk downloaded into a csv. Researchers filled out a form with the docket ID (FDA-2013-N-0035), document type (Public Submission), and dates to pull comments from (02/18/2018-04/17/2018), then received an email with the .csv of comment data within minutes.

Comments range in length from 3 words to 701 words. The downloaded public comment data contains the comment text, in addition to metadata shown in Figure 5 which includes: tracking number, document ID, docket ID, posted date, title, comment on document ID, received date, state/province, country, submitter representative, and category.

4.2 Data Selection and Exploration

Between 2013 and 2021, 1,487 public comments were submitted to the docket, and 978 of those were posted publicly after the FDA's processing. The draft guidance document for the development of drugs for ALS was posted on February 18, 2018, and the comment period ended two months later on April 17, 2018. Over two thirds (612/978) of public comments on the docket were submitted in those two months. The research team downloaded these 612 public comments. The data selection pipeline is shown in Figure 6. To explore the data, two members of the research team split the data in half and read through comments. The exploration phase yielded two outcomes for the research team: 1) an initial sense

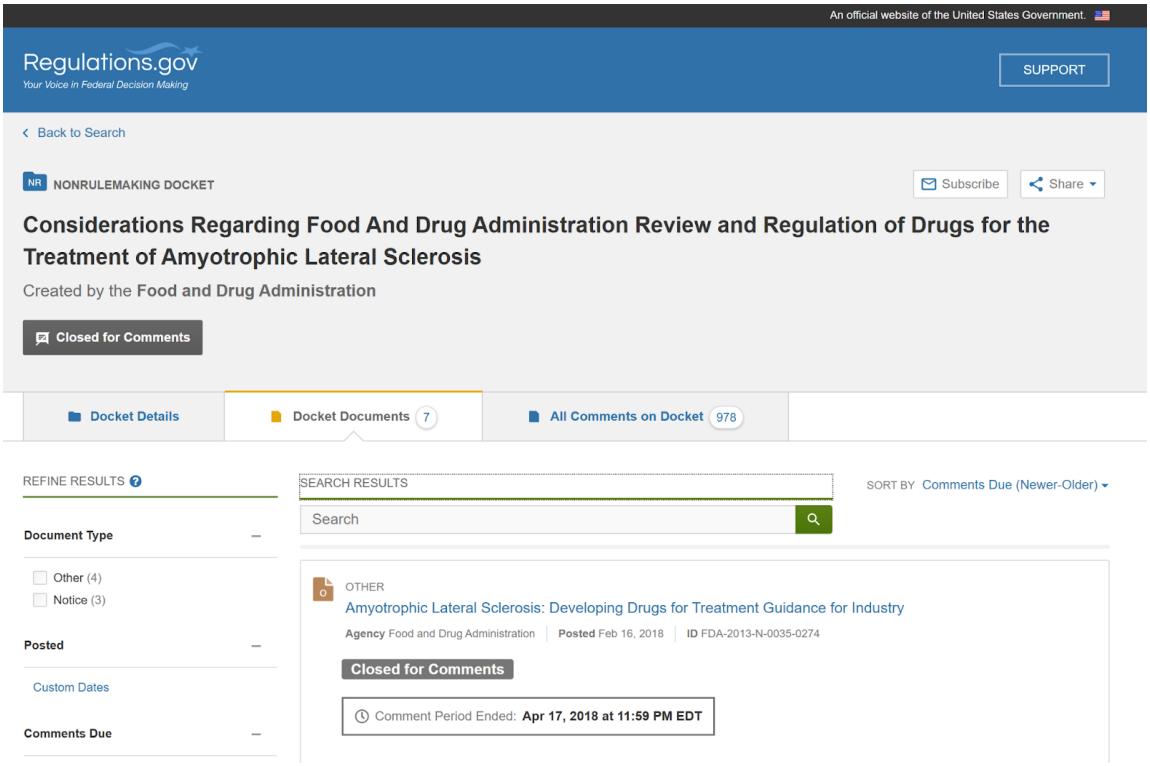

Fig. 4. The docket "Considerations Regarding Food And Drug Administration Review and Regulation of Drugs for the Treatment of Amyotrophic Lateral Sclerosis" on `regulations.gov`. The docket contains records of a public hearing on the review and regulation of drugs for ALS from 2013, a draft guidance for the development of drugs for ALS posted in 2018, and a final guidance document posted in 2019. Anyone can submit a comment on the docket (as an individual, an organization, or anonymously) and these are posted publicly to the docket after being processed by the FDA.[0]

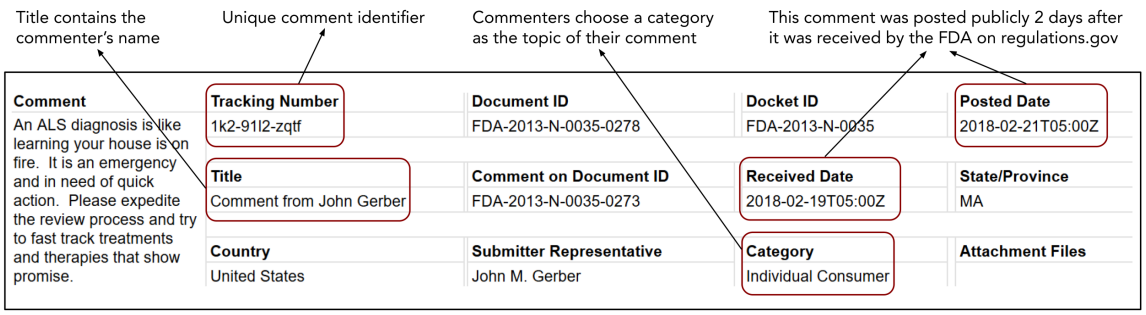

Fig. 5. One entry for a public comment and its metadata, including the comment text, the dates the comment was received by the FDA and then posted, the name of the commenter (or Anonymous), their location (optional), several ID's, and attached files (optional).

of the common, important, and unique aspects of structure and content, 2) familiarization with ALS and FDA context via reading scholarly articles and FDA web pages. Additionally, comments less than 100 words in length were removed because they have similar themes and content as larger comments, but with less depth and specificity. This left 269 comments posted in the two month commenting period for the guidance document, which are 100 words or longer, to be used for developing the codebook.

4.3 Data Coding

The objective of our research is to characterize a patient community's inputs on a digital platform for participating in policy-making processes that affect their lives. The research team conducted an inductive thematic analysis of comments to characterize their structure and content: the criticisms, recommendations, and claims made; and information and arguments used to support criticisms and recommendations. The data coding process consisted of iterative coding, discussions, updates to codes, and a final round of coding with the established codebook.

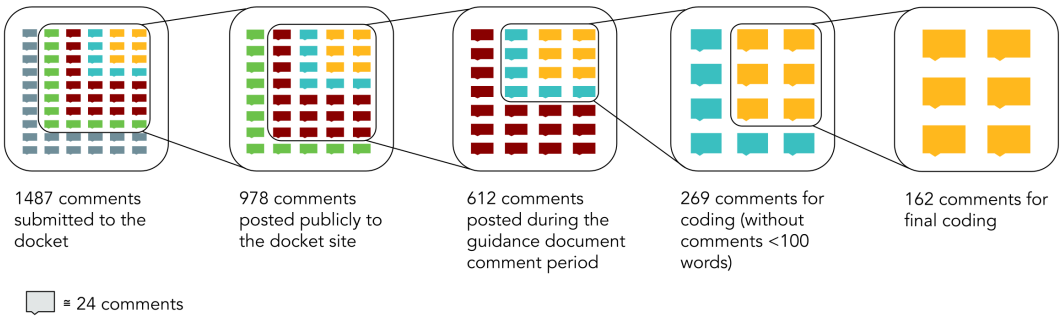

Fig. 6. Illustration of data collection and selection pipeline. 1,487 comments were submitted to the docket, and 978 of these were posted publicly after a review process. The research team downloaded the 612 comments posted during the two month comment period for the draft guidance for ALS drug development, selected the 269 comments longer than 99 words, and randomly sampled 162 of these comments for final coding, leading to our analysis of 26% of total comments on the guidance document and 60% of comments longer than 99 words. (Figure inspired by [43])

4.3.1 Iterative Coding. For the first round of coding, the 269 comments (all over 99 words in length) were sorted into 25 bins by comment length (sorted in ascending order by word count) with eleven comments in each bin. The final bin had five comments. One comment was randomly selected from each bin to generate a subset of 25 comments. This ensured the subset of comments had an even distribution across comment length (over 99 words). Two researchers independently coded these 25 comments to come up with two sets of initial codes, then discussed and combined the codes to form the first version of the codebook.

These researchers iteratively coded randomly selected subsets of 5, 10, 12, or 25 comments (the same subsets for both coders) independently, then discussed with each other, then with the senior author on the manuscript. The codebook was updated at each step. In early iterations, the research team identified several structural categories (such as claims, needs, evidence, arguments, suggestions/requests) and content themes (such as criticizing the FDA, characterizing ALS as a disorder, or describing the experience of living with ALS).

In later iterations, the codebook was updated to decrease ambiguity and overlap between structural categories; and better capture the complex ways that content themes showed up across different structural categories. For example, these sentences were initially categorized as *needs* statements: *"ALS patients need immediate access to promising treatments that have passed safety studies"*, *"We need more innovative trials and quicker approval rates"*, while this sentence was categorized as a *call to action*: *"It is time for the FDA to allow innovative clinical trial designs that ensure the terminally ill ALS population can gain immediate access to promising treatments that have passed safety studies"*. All of these are statements about what should be done, so we combined these two categories into one *recommendations* category. The structural categories evolved throughout iterations to become Criticisms, Recommendations, Claims about the Disorder, and Information.

4.3.2 Iterative Discussions. After each iteration of independently coding the same subset of comments, two researchers discussed their coding results, important aspects of comments, and points of confusion in coding. If the two researchers disagreed on how to code a comment, they discussed their reasoning, developed shared reasoning and codes, and updated codebook definitions for better clarity. Then the third researcher was consulted to discuss points of confusion in coding that could not be resolved. When needed, the third researcher used the current codebook to code selected comments, and suggested updates to the coding categories and reasoning.

4.3.3 Final Coding. Once the codebook was finalized, the research team selected a subset of comments for final coding. The final codebook is described in section 4.4 and Tables 1 and 2. Our team aimed to balance the effort of coding a large number of comments with in-depth analysis of a smaller subset. Comments were sorted by length, binned into groups of ten, and six comments from each bin were randomly selected. This resulted in the 162 comments that were coded by the research team in the final phase. Two researchers coded all 162 comments independently, then resolved differences in coding to create the final set of codes for each comment.

Intercoder reliability (IRR) was assessed using Krippendorff's alpha (α), a metric that accounts for chance agreement, and interpreted according to standard thresholds [39]. For each theme category (Criticisms, Call to Action, ALS Claims, Information, and Argument Type), the annotations from two coders were first expanded into a binary matrix: each row represents one comment, each column represents the presence or absence of each sub-code. Krippendorff's alpha was then computed using this matrix. To estimate the 95% confidence intervals (CI) for each α, a bootstrap procedure with 1,000 resamples was applied. Standard thresholds for interpreting reliability was followed [40], where $\alpha \geq .80$ indicates strong reliability, $.67 \leq \alpha < .80$ indicates acceptable reliability, and $\alpha < .67$ suggests low or problematic

agreement. Overall reliability across all theme categories was also computed by collapsing the data into a single matrix and calculating α with its bootstrap CI.

Overall reliability across all categories was in the acceptable range (α = .681, 95% CI [.652, .709]). Reliability across categories varied: "Recommendations" demonstrated acceptable agreement (α = .691, 95% CI [.648, .730]), "Information" demonstrated acceptable agreement (α = .669, 95% CI [.625, .710]), "Argument Type" showed similar acceptable aggreement (α = .670, 95% CI [.619, .718]), "Criticisms" showed low agreement (α = .654, 95% CI [.601, .702]), and "ALS Claims" showed low agreement (α = .571, 95% CI [.487, .661]).

4.4 Final Codebook

Phrases in comments are first categorized as a Criticism, Recommendation, piece of Information, or Claim about ALS. Criticism, Recommendation, and Information phrases are then coded based on their content with the codes listed in Tables 1 and 2. Each comment is coded as a whole for its argument themes.

Criticisms assert that something is wrong, bad, could be better, or bring up specific issues. A criticism could be specific (Ex: "The use of placebos is a cruel device in the trials of drugs that have already been proven safe in earlier stage FDA trials.") or vague (Ex: "Outdated one size fits all approach to medicine is failing the ALS community"). Criticisms may be implicit, in the form of an antagonistic rhetorical question (Ex: "shouldn't the FDA have moved more swiftly if they were to affect real change in this patient population?") or explicit (Ex: "The FDA guidance document for ALS is totally inadequate").

Recommendations either suggest a way to think about or do something, call for something to be done, or state that some action needs to be taken. They can be an idea, a demand, or a plea. A recommendation might state that an option exists (*e.g. "Historical data from other trials and databases can serve as accurate controls in these trials"*). They may call for an action (*e.g. "Encourage the use of historical data, mobile trial sites and remote data collection"*), a service (*e.g. "ANY drug that shows promise in slowing or reversing ALS's progression should be available to any ALS victim that wants it"*), changes in processes (*e.g. "Use current living ALS population when determining number of participants for clinical trials"*), documents (*e.g. "The draft guidance should start from the point of critiquing the current methodology of ALS trials"*), or policies (*e.g. "Please allow S.204 Right to Try Act of 2017 be put to a Floor Vote in the US House of Representatives and have it passed as soon as possible"*).

As in the above examples, Recommendations can be specific. Recommendations can also be broad, calling for nonspecific actions (*e.g. "Change this document"*) or engaging with guiding principles and ideas rather than concrete policies (*e.g. "We want the FDA to encourage researchers and industry to 'think outside the box' and to become more creative"*).

Claims about ALS / ALS Patients make a subjective statement about ALS (*e.g. "This is an insidious, life-robbing disease"*), about ALS patients or caregivers (*"They know that their fate is sealed, but are willing to try anything"*), what it's like to live with ALS (*e.g. "loosing your ability to walk, talk, give your loved one a kiss or a hug"*), or what kind of approach ALS requires (*e.g. "ALS is a unique disease that requires a unique approach"*).

Information is facts about something or someone. Information often serves to *support* a claim, suggestion, call to action, or criticism. Information can be on any topic and comes in formats such as standalone facts (*e.g. "50% of the people diagnosed pass within 15 months"*), personal experience (*e.g. "My mother was diagnosed with ALS in October 2017. According to ALS experts, her symptoms have been described as 'slow' in progression"*), or references to what other documents or people have said (*e.g. "Please view video following link provided. - Dr. Janet Woodcock at Advocacy 2017. She talks about the collaborated ALSA draft guidance document"*).

Drug Development Regulatory Processes	
Time	Duration of the drug development and approval process or the speed of access to drugs for ALS
Access to Drugs	Patient access to both approved and investigational drugs
Process Cost	The cost of the drug development and approval process
Drug Cost/Insurance	Implications for insurance and costs to patients after the drug development and approval process
Tech	The use of technology in drug development and approval processes
Risk	The risk-benefit trade-off in drug development and approval process procedures
Approach	The general institutional approach in drug development and approval processes ("outdated", "one size fits all", "status quo", "align with the disease", “FDA’s mission”)
Votes/Nonspecific	Votes of support/opposition or unspecific directives to change, not approve, or approve the guidance document or other processes
Clinical Trials	
Time	The time to enroll in trials, the time to complete a trial, or mentions of urgency for trials
Placebos	The use of placebos, single arm trials, randomized controlled trials
Historical Data	The use of historical controls or data enrichment (including historical data from previous trials to supplement the control group data in the analysis of results)
Size/Participant Eligibility	Trial size or trial participant eligibility criteria
Decentralized Trials	Mobile trial sites (clinical trials conducted via labs on wheels), Sattelite trial sites (local clinics as trial sites) or remote data collection (data collected from home for trials via devices)
Endpoints	Existing endpoints and alternative endpoints (outcome measures used to determine the effectiveness of an investigational drug in clinical trials)
Modernization/Tech	The lack of or encouraging the use of technology and modern techniques in clinical trials
Patient and Public Participation	
Guidance Document	The inclusion of patient inputs in the guidance document or the processes for public participation in the creation of the guidance document
Drug Approval Processes	The inclusion of patient inputs in the drug approval decision process
Clinical Trial Design	The use of patient inputs in clinical trial designs and protocol
General	How patient and community perspectives are dealt with in general
Advocacy Organizations	ALS advocacy organizations

Table 1. All codes deal with criticisms and recommendations. Criticism and recommendation codes are grouped into three broad topics: Drug Development Regulatory Processes, Clinical Trials, and Patient Participation / Input

5 Results

99% of coded comments contained criticisms and recommendations. 96% of comments contained some form of information, and 86% of comments made claims about ALS. The emotional urgency argument was the most common and showed up in 95% of comments. Figure 7 shows the breakdown of how many comments included each criticism and recommendation.

Information		Argument Themes	
Topics	Institutional Processes ALS Drugs/Treatments Clinical Trials Miscellaneous Medical/Scientific	**Moral**	Patients' Rights Responsibility of Institutions
		Emotional	Urgency, Death, Hope
Formats	Fact Personal Experience Quoting a Person Quoting a Document	**Logical**	Facts of ALS as a Basis Compare to Other Cases Risk-Benefit Trade-off

Table 2. Codes for Information and Argument themes. Information is coded by topic and format. There are six specific argument themes, grouped broadly as using moral, emotional, or logical reasoning.

5.1 Summary

Patient access to drugs, treatments, and trials were common concerns. Criticisms and recommendations address several components of the drug development and regulatory processes which effect patient access: the FDA's drug approval process, the guidance document, drug development industry sponsors, and clinical trial designs. Some criticisms and recommendations are general: they criticize an idea (*e.g.* risk-aversion) or recommend a principle that the institutional approach should follow (*e.g.* make regulatory and research processes specific to the nature of the disorder). Other criticisms and recommendations are specific to clinical trial design decisions, sections of the relevant guidance document, and concrete regulatory decisions. Criticisms and recommendations are often supported by a characterization of ALS. This characterization is built up with facts about ALS and claims that ALS is unique, urgent, and devastating.

5.2 Criticism and Recommendations

Criticisms and recommendations address the same topics across comments: drug development regulatory processes, clinical trials, and patient participation in decision making. For this reason we coded criticisms and recommendations with the same set of codes, shown in Table 1.

5.2.1 Regulatory Processes. 96% of comments include criticisms and recommendations that address the institutional regulatory processes for the development of drugs. This includes the drug approval processes that the FDA regulates, the document that the FDA released as guidance for drug developers, and the FDA themselves. People's criticisms and recommendations in this theme fall into seven dimensions of institutional drug regulatory processes: time, patient access to drugs, drug prices, cost of institutional processes, technology, risk assessment, and general approach. People also sometimes include extremely nonspecific criticisms and recommendations of the FDA and their processes or "vote" statements in opposition to the guidance document.

Time Mentions of urgency and bureaucratic slowness are common. 70% of comments include time-related criticisms or recommendations. Criticisms include the slowness of the drug development pipeline and the drug approval process.

Reflexively, recommendations include speeding the development and approval processes and considering drugs for the Accelerated Approval program.

> *"Waiting on medications to get through clinical trials and approval takes too long for a disease that has a two to five year survival rate"* -Annette Kenner

> *"Accelerated Approval SHOULD be granted after a successful phase 2 trial!"* -Barb Murphy

Comments also criticize the lack of urgency or call for more urgency in the approval process, the guidance document (both its content and the process for creating the document), and from the FDA in general. 63 coded comments (39%) include the words "urgency", "urgent", or "urgently".

> *"The proposed guidance document doesn't adequately address the urgent needs of patients who have a terminal illness"* -multiple comments(16% of coded comments)

> *"Create an urgent timeline and lifecycle of an ALS Guidance Document. STOP putting it on back burner."* -MaryEllen Woodman

> *"Treat ALS with a sense of urgency"* -multiple comments (2.5% of coded comments)

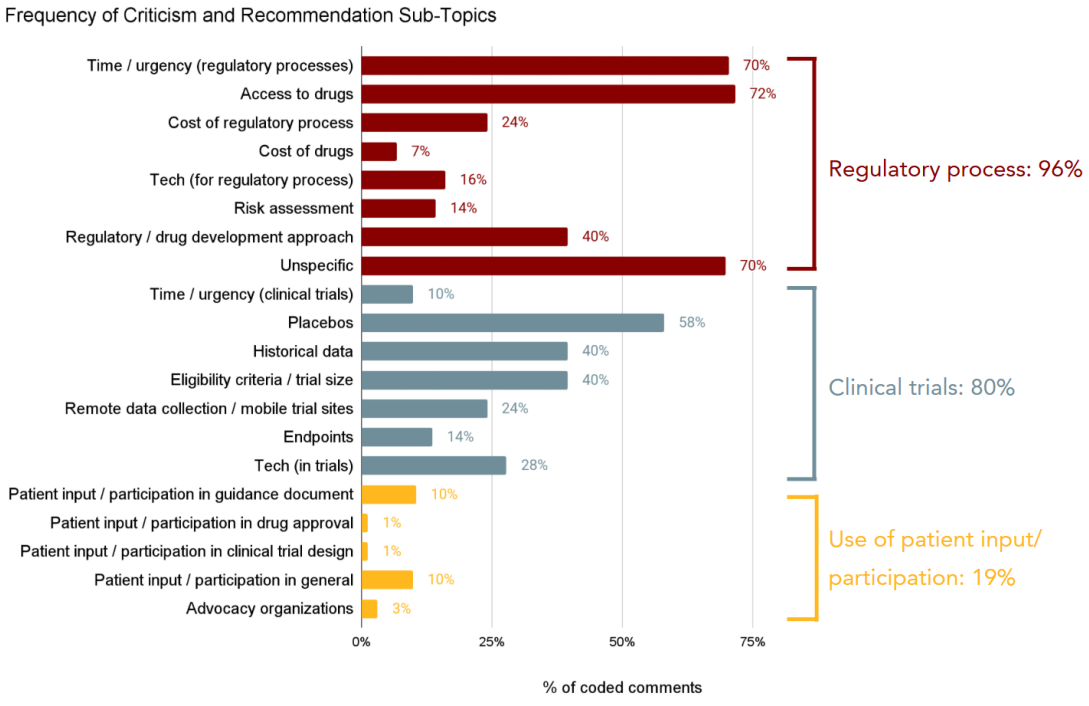

Fig. 7. The portion of comments that each criticism and recommendation code appears in. Most comments contain criticisms and recommendations about regulatory processes (96%), many contain criticisms and recommendations about clinical trials (80%), and less comments contain criticisms and recommendations about participation processes and the use of patient inputs (19%). Criticisms and recommendations about access to drugs (72%), placebos (58%), and urgency/slowness in regulatory processes (70%) are common. Unspecific criticisms and recommendations towards regulatory processes, institutions, and documents are also common (70%).

Access to Drugs One of the most pervasive subthemes in criticisms and recommendations is patient access to drugs (approved drugs and investigational drugs). 72% of comments include criticisms and recommendations about access to drugs or treatments.

General criticisms claim that treatments are not accessible, and that the FDA is blocking access to them. Some comments also mention the lack of viable drugs.

> *"Can you imagine seeing improvement, but can't continue to access the drug or therapy because of regulations? This is wrong and must be changed. I know not all drugs or therapies will have the same results, but if it is showing promise why make a person stop accessing it?"* -Anonymous

> *"Stem cell therapies and promising treatments exist but are not accessible. Why?"* -Anonymous

General recommendations emphasize that ALS patients need and deserve to be given access to experimental drugs.

> *"It is vital for these patients to have access to this [sic] possibly life saving drugs as quickly as possible"* -Mary Law

Some recommendations in this subtheme are a degree more specific. Fourteen comments (9%) call for the "Right to Try". 32% of comments call for people with ALS (pALS) to have access to any investigational drugs that have passed safety studies.

> *"Many states have "the right to die." We want the RIGHT TO TRY."* -Andrea Creath

> *"When a new drug passes your Phase 1 safety and tolerability studies, why can't ALS patients be allowed to start taking this possibly lifesaving drug?"* -David Crowe

Comments also address specific aspects of clinical trials that affect patient access to experimental drugs. These are described in the *Clinical Trials* section under the subthemes: placebos, trial size / eligibility criteria, mobile trial sites / remote data collection.

Cost 24% of coded comments criticize the cost of the approval process.

> *"15 year, billion dollar approval process"* -multiple comments (24% of coded comments)

> *"Don't waste time & money on expensive Phase 3 trials"* -MaryEllen Woodman

A few comments recommend monetary incentives for drug development companies to address the issue that drugs for a rare disorder cannot be widely marketed and thus are not as profitable to develop.

> *"They will not focus on saving lives today because the stock price won't go up until they have approval. There needs to be incentives to get Phase 3 clinical trial level treatments to terminal patients in a way that will not hinder the manufacturer's ultimate objective, which is profit"* -Joey Smith

Cost of Drugs/ Insurance 7% of comments criticize the cost of drugs for ALS and/or call for insurance to cover the cost.

> *"why does Radicava cost $12,000 in Japan where I got it prior to the US approved and $150k now in the US."* -Melissa Barette

> *"If a treatment allows for an increase in quality of life and or life span it must be made available immediately and at a cost Medicare and Part D plans will cover in part or entirely."* -Pete Klinkhammer

One comment specifically describes how clinical trial protocols affect the insurance protocols for approved drugs after they are out of the trial stage.

> *"Given the huge price tag of approved medicines, insurance companies may try to deny a patient coverage if their condition does not match the inclusion criteria for the particular clinical trial that led to the approval of a drug."* -William Lydgate

Technology 16% of comments include criticisms or recommendations for the use of technology in FDA regulatory processes or the encouragement of new technology in the guidance document. These are general criticisms and recommendations which don't typically describe a specific technology. Some comments do mention specific technologies to use in clinical trials which are described in the *Clinical Trials* theme.

> *"the lack of technology in our regulatory system is rapidly failing as the FDA can't keep pace"* -Anonymous

> *"This guidance does not reflect the advances in technology, science, or data collection we have made this last century."* -J Blackford

Risk Assessment 14% of coded comments address how risks and benefits are evaluated for experimental drugs. They criticize the FDA for being too cautious, risk-averse, or in the strong words of 28 different commenters, *"protecting ALS patients to death"*. People recommend allowing pALS to choose the amount of risk they are willing to accept, and call for the risk-benefit tradeoff analysis of drugs for ALS to be fundamentally changed: give less weight to risk and more weight to potential benefits.

> *"We are troubled that an overemphasis on avoiding type I errors (approving a treatment that is in fact dangerous or inefficacious) has created an unbalanced mindset insofar as it has inadvertently neglected the risk of type II errors (slowing or halting the study of truly effective treatments). We believe that ALS-specific guidance must recognize the cost of each type of error: caution can be just as deadly as recklessness."* -Clare Durrett

> *"At this time no one is escaping from this terminal disease, so stop protecting them. The FDA has allowed others groups to participate in "risky" treatments like AIDS or Ebola patients and look how it has turned out for them."* -Ed Martin

Approach 40% of coded comments include criticisms and recommendations for the general institutional approach to drug development and regulation along three related themes: outdated, status quo, or unspecific to the disorder. People criticize the drug approval processes and the contents of the guidance document as outdated or maintaining the status quo.

> *"Why is document being haled as a GOLD standard, I see nothing more than status quo. It screams 20th century medical practices, old and outdated."* - Anonymous

They also criticize drug development processes and the guidance document for being one-size-fits-all rather than adapting to specific aspects of ALS such as its fatality, rapid progression, heterogeneity, accessibility concerns, and limited existing viable treatments.

> *"There is no average patient in ALS and everybody's biology is different. The outdated one size fit [sic] all approach doesn't work and when you are terminal you don't have time to wait."* -Anonymous

Votes or Nonspecific Comments 70% of coded comments include highly nonspecific criticisms or recommendations for the FDA and the guidance document. Some of these are in the form of a pseudo-vote against the guidance document. These call for the guidance document to be revised, substantially changed, or not approved.

There are also nonspecific criticisms and recommendations about the drug development and approval processes directed at the FDA. They state the FDA is cruel or fails to meet their agency's mission statement. They demand the FDA to *"do something"*, *"change the process"*, *"have a heart"*, or get rid of *"red tape"*.

> *"How about the FDA put their red tape away for a while and let some of the greatest minds in science try to save my husband's life?"* -Andrea Creath

5.2.2 Clinical Trials. 80% of comments included criticisms and recommendations specific to clinical trial protocols and designs. Some call broadly for innovation in trial design, the use of technology in trials, or easier access to trials. Many have specific critiques and suggestions for how ALS clinical trials should be done. People provide inputs into several aspects of clinical trials, corresponding to eight subthemes: time, placebos, historical controls / data enrichment, trial designs, trial size / eligibility criteria, mobile trial sites / remote data collection, endpoints, and technology.

Time 10% of comments call for clinical trial designs that match the urgency of ALS in terms of their timeline, and criticize lengthy trial processes.

> *"This disease demands urgency and clinical trial designs deserve the same."* -Beth Mara

> *"If the FDA requires 10,000 patients to be in a trial, for instance, we will literally have to wait years for the trial to be enrolled, much less finished and analyzed."* -Karl Schoettle

> *"He wants to try the new drug Radicava, but it's still in committee in the Houston ALS clinics. He was added to the protocol, and is all approved...but they haven't quite figured out who should pay for it. So months later, he still hasn't had his first dose."* -Andrea Creath

Placebo Placebos are one of the most prevalent subjects of criticism. 58% of comments include either criticisms of the use of placebos, calls to stop the use of placebos entirely, or recommendations to minimize the use of placebos. Commenters claim that it is unethical for a terminal patient to receive a placebo as it removes the possibility of benefit from the experimental drug for that person. Some comments cite comparable drug development guidance documents for other fatal illnesses which mention ethical concerns with placebos and suggest the feasibility of single-arm trials (trials with no placebo control group).

> *"STOP the use of placebos."* -MaryEllen Woodman

> *"I also participated in a year long phase two study and found out 18 months later I was given placebo for an entire year. What if it turns out to be an effective treatment? It's medically irresponsible and immoral to think I was denied access even though my participation was at great personal cost."* -Shelly Hoover

Historical Controls / Data Enrichment Historical controls use existing data from similar previous clinical trials to either entirely replace or supplement the control arm of a new trial [66]. Comments often recommend the use of historical controls instead of placebo control groups so that more patients who enroll in trials receive the actual experimental treatment. Most of these comments simply mention historical controls or using historical data, but a few describe what historical controls are and how they can create statistically significant results to support their recommendation. Recommendations also include the use of historical data to "enrich" or supplement the placebo data collected in new trials, rather than replacing placebo control groups entirely. 40% of comments include either criticisms that historical data is not used or encouraged, or recommendations to use historical data in trials.

> *"Use historical controls from the PROACT data base."* -MaryEllen Woodman

> *"Failing to incorporate outside data means that we are basing our benchmarks on a handful of new patients and are ignoring everything else that we have learned from the past. A straightforward and readily used solution is to enrich the small amount of placebo arm data with external controls based on the placebo arms from similar trials in order to provide a more accurate baseline"* -Eileen Berardi

Trial size / Eligibility criteria 40% of comments include criticisms and recommendations about participant eligibility criteria for clinical trials and the size of participant pools for clinical trials. People criticize eligibility criteria that restrict who can participate in trials, sometimes describing their personal experience being excluded due to age or disease stage. Some comments also recommend smaller trial sizes.

> *"Require that the sum total of studies include trials and studies into the full array of persons living with ALS. It is important to gain a greater understanding as to why persons live beyond the current 2-5 year life is expectancy without the assistance of resperitory [sic] devices."* -Pete Klinkhammer

> *"SMALLER TRIAL SIZES should be encouraged because of the rarity of the disease and its rapid progression."* -Karl Schoettle

Endpoints 14% of comments discuss clinical trial *endpoints*, the measurable outcomes used to assess the effectiveness of a treatment. What the FDA refers to as a *survival endpoint*, commenters more often refer to as *death as an endpoint* highlighting the fatality of ALS. Many comments call for "no death as primary endpoint", and suggest the use of other metrics that measure disease progression such as ALSFRS-R (ALS Functional Rating Scale), FVC (Forced Vital Capacity), and SVC (Slow Vital Capacity).

> *"While ALSFRS-R, FVC, and SVC are not ideal endpoints, they are much more sensitive than survival. Survival analysis explicitly requires researchers to sit idly while sufficient numbers of patients in a placebo arm die before you can make a determination of efficacy."* -Eileen Berardi

Tech 28% of comments broadly call for the use of technology or innovation in trials or criticize the lack of technology/ innovation in trials. Some of these comments specify the technology they would like to see (*e.g.* devices for remote data collection). Comments call for trials to be modernized and for the use of innovative trial designs.

> *"We need to impress upon everyone in the drug development world that the time is now to apply 21 st -century technology"* -Clare Durrett

> *"ALS is non-homogenous. As a result, it urgently requires newer, innovative trial designs to make possible the discovery of viable therapies."* -Jane Williamson

Decentralized Trials 24% of coded comments recommend mobile trials and/or remote data collection, so that pALS can participate in clinical trials from home or without needing to travel as far. Several comments explain the accessibility concerns of travelling for pALS. Justifications for this recommendation mention the benefits for both pALS and clinical research: participation in clinical trials would be easier for pALS, and more people would participate and stay enrolled in trials.

> *"Whenever feasible, sponsors should be encouraged to utilize telemedicine or remote monitoring equipment to minimize the burden of unnecessary clinic visits. This will increase recruitment and retention."* -Katey Kennedy

> *"Support multi-center trial locations & promote the use of video conferencing in conjunction with rural, local neurologist offices to participate in clinical trials."* -William Lydgate

5.2.3 Patient Input / Participation Processes. 19% of coded comments include criticisms and recommendations that address the use of patient inputs and public participation processes. The sentiment around this topic is that people feel they are being ignored by institutional regulators, despite their efforts to participate and existing avenues to participate. Comments state that regulators do not understand the perspective of someone living with the effects of ALS, and that they seem to not care. They criticize both the guidance document and clinical research protocols for not reflecting the patient community's needs. Therefore, they request that more input from people whose lives have been affected by ALS be taken into consideration.

> *"I hope that you will take to heart all of the comments being provided to you and make a decision that is patient Centric versus bureaucratic in nature which tends to be your Hallmark. I wish I could say more to convince you however I don't believe that any appeal will phase any of you involved in this decision process. You are so far removed from the patient that you will never understand."* -Juan Reyes

> *"For the FDA/HHS build into their guidance procedure the inclusion of an representative from the ALS Association, (National) AS WELL AS a person living with ALS, and their caretaker as needed. The person living with ALS is an expert."* -Pete Klinkhammer

Several comments reference past attempts at participating in the development of the guidance document. These include discussions with institutional leaders and a patient created guidance document formed with the ALS Association (ALSA). They criticize how few of these patient recommendations were included in the document despite having been recognized by institutional leaders.

> *"Furthermore, this input from the patient community was received in guidance document meetings coordinated by ALSA - but removed from the published document. The patient community has had numerous discussions with Dr. Janet Woodcock in which we received assurances that innovative trial designs are being embraced, and yet - this guidance actually DISCOURAGES THEM."* -Linda Clark

Though not as common, a few comments (3%) criticize ALS advocacy organizations as not representing all patients' views or not doing enough.

> *"ALSA does not speak for the patients suffering today."* -Mary Law

> *"It would be fantastic if we had an advocacy group taking the lead here but alas."* -Jovanna Ochoa

5.3 Information and ALS Claims

Some comments offer criticisms and recommendations with little explanation or supporting evidence. However, 96% of comments include at least one form of information to support their criticisms and recommendations. 86% of comments make claims about ALS to support their statements.

5.3.1 Information. We categorize information in comments into four formats, and five topic areas. Out of all coded comments, 75% include information in the form of a fact, 58% include personal experience, 6% include information from another person and 5% include information from another document. Topic wise, 85% of comments have information about ALS, 34% about institutional processes, 18% about drugs, 25% about clinical trials, and 19% about other scientific or medical topics. Personal testimonies demonstrate first hand information on what it is like to live with ALS. Personal experiences may also demonstrate information about clinical trial processes and other institutional processes from the perspective of patients going through them. The percentage of comments which contained each possible pairing of topic and format is shown in Figure 8.

> *"There is only one active Phase 3 trial in ALS. Its very promising . The Phase 2 Data was hopeful. Yet; you FDA required them to do a placebo controlled trial. If I go into the trial, I have a 50 percent chance of getting a placebo and I have to have my bone marrow taken . I have to go off Radicava. The trial is almost a year long."* -Melissa Barette

> *"She began her battle with high expectations of some relief or potential cure being presented to her while it could still make a difference. That never happened. We began eager and anxious to participate in clinical trials or radical drug studies. Anything that could make a difference to improve her quality of life. Instead she died from a slow, painful progression with little hope being offered."* -Anonymous

People often share facts about ALS: this topic-format pairing shows up in 48% of coded comments.

> *"ALS is a FATAL disease that is not brought on by personal choices"* - Joey Smith

> *"a disease that has a two to five year survival rate"* -Annette Kenner

> *"a disease like ALS that, as described above, is remarkably heterogeneous, rare enough that large participant pools are hard to recruit, and whose progression and symptomatic profile produce all kinds of statistical noise"* -Clare Durrett

Some comments reference what researchers or institutional regulators have said to bolster their arguments. Quoting or paraphrasing another person is rare (6% of coded comments).

> *"Due to the heterogeneity in progressions, researchers are often uncertain of how representative their placebo arms truly are. After inconclusive trials, researchers often cite the fact that their results could be influenced [sic] an unexpectedly slow progressing placebo arm."* -Eileen Berardi

> *"Commissioner Gottlieb stated in the guidance's press release that a key challenge in this area is that, 'Symptoms and progression of neurological diseases can also vary significantly across patients, and even within patients, and across organ systems.'"* -Katey Kennedy

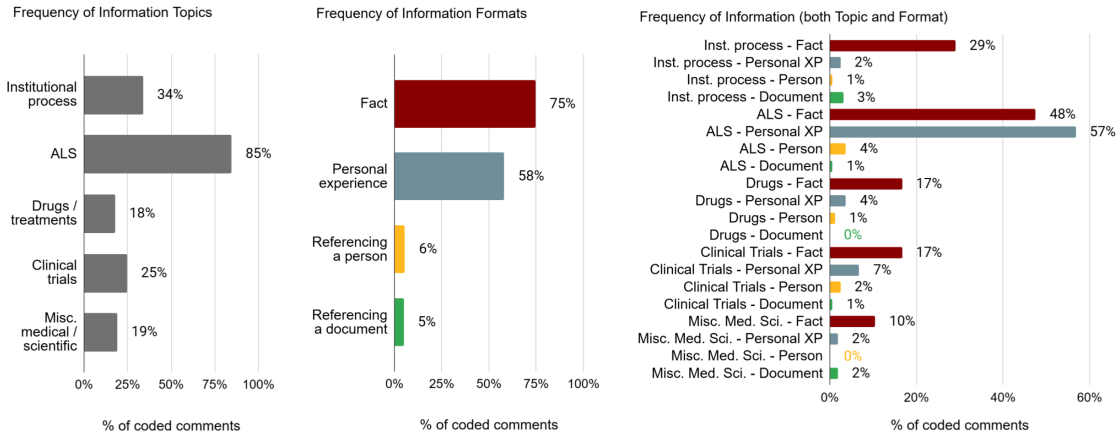

Fig. 8. Comments contained information about institutional processes, ALS, drugs/treatments, clinical trials, and miscellaneous medical or scientific topics. Comments contained information largely in the form of facts or personal experience. Quoting or paraphrasing a person or document were rarely seen. Table 2 lists all information topic and format codes.

5.3.2 ALS Claims. People make claims about ALS as a disorder, what it's like to live with ALS, and about what ALS patients want. These are typically used to support a criticism or recommendation for ALS drug development and regulation. These claims may also contribute to the comment's narrative as a whole, often adding to the emotional argument theme (5.4.3) or risk-benefit trade off argument theme (5.4.6).

People use a variety of emotionally affective terms to characterize ALS including: *"horrible", "devastating", "monster of a disease", "cruel", "ruthless", "miserable", "brutal"*

Claims that ALS is a unique disorder accompany criticisms of "status-quo" regulatory approaches and recommendations for "innovative trial designs".

People make claims about the urgency that ALS patients experience. These claims often support criticisms about the slowness of regulatory processes or calls for greater urgency from regulators and drug developers.

> *"when you are terminal you don't have time to wait"* -Anonymous
>
> *"urgent needs of patients who have a terminal illness"* -several comments (19%)
>
> *"two, three or four years is literally a lifetime for patients with this disease"* - Anonymous

Some claims emphasize that burdens of the disorder fall not only on the patient but on their caregivers and families.

> *"their families suffer along with them"* -Faye Lack
>
> *"we already ask too much of these families"* -two comments (1.2% of coded comments)

Some claim that people with ALS are willing to take on a higher level of risk in order to potentially benefit from experimental treatments. These claims often accompany criticisms and recommendations about how regulators assess risk.

> *"these sufferers have nothing to lose"* -Anonymous
>
> *"Most that suffer from this disease are willing to try anything to not only save their lives but those that follow them"* -Anonymous

5.4 Argument Themes

We identified six types of arguments that commenters make. One comment may contain multiple types of argument themes, combining moral, emotional and logical reasoning. The six argument themes we identify are: Patients' Rights ; FDA's Responsibility; Emotional: Urgency, Death, Hope; Facts of ALS as a Basis; Comparisons to Other Cases; Risk-Benefit Trade Off. Figure 9 displays how often each argument theme is used.

5.4.1 Moral: Patients' Rights. (27% of coded comments) People frequently state that pALS deserve access to potential treatments. People assert that pALS have a right to have a say in their treatment, to assume risk they are willing to assume for themselves ("Right to Try"), and to have their preferences reflected in regulations.

> *"Removing or excluding a patient from a clinical trial, and denying a terminal patient the Right To Try a treatment they need and/or responding to, is akin to telling that patient, 'go home and get your affairs in order. There is nothing more we can do for you.'"* -Mark Berardi
>
> *"They should have the right of immediate access to experimental treatments that have passed safety studies. "* -Anonymous

"We have a right to die with dignity available. Please allow those who suffer that basic right to die with dignity, while providing just 1 ounce of hope with a new drug." -Anonymous

5.4.2 Moral: FDA's Responsibility. (22% of coded comments) People make moral arguments attempting to hold the FDA and the medical research industry accountable to their responsibilities. Five coded comments(3%) mention the FDA mission statement; four of those five comments quote it directly.

> *"As a government agency here for the good of your people you must make changes for ALS"* - multiple comments (1.85% of coded comments)

> *"The FDA's mission statement is "FDA is responsible for advancing the public health by helping speed innovations that make medical products more effective, safer and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health." This guidance document fails to meet this mission statement."* -Michele Kirby

5.4.3 Emotional: Urgency, Death, Hope. (95% of coded comments) Many comments include affective phrases or tone. People describe their difficult experiences living with ALS, caregiving for someone with ALS, or knowing a loved one with ALS. Death is mentioned in 44% of coded comments. Information about the fatal nature of ALS, its rapid progression, and the lack of treatment is also used to bolster the emotional narrative.

> *" I have to look at my mom everyday and say that there is no cure and there is nothing we can do. Imagine if that was your family member.. watching them struggle worse and worse until they can't use any of their body parts and eventually dies."* -Anonymous

> *"My father Mark Harrison has ALS he is currently involved with a trial that is double blind Placebo why would you do this he has ALS its his right to try he is dying everyday is a battle . Im watching my 51 year old dad die. The thought of him not being here to watch me graduate high school mentally affects him and*

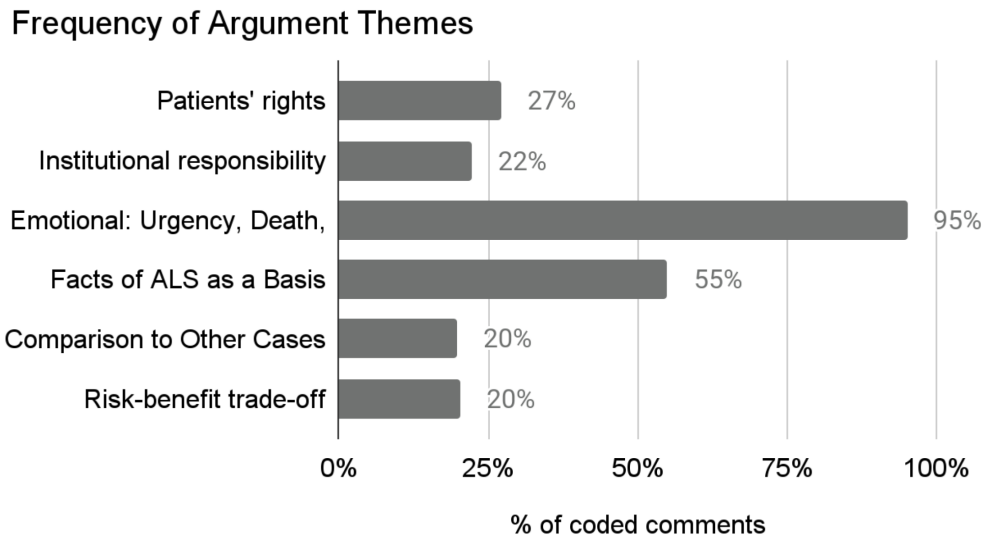

Fig. 9. The most prevalent argument theme was emotional arguments about the urgency, devastating, and fatal nature of ALS.

> *me. He didnt ask for this illness he should be able to receive the really [sic] stem cells to fight this in his trial he is going through all the pain the time the expense that he makes to travel and expense des [sic] for hotels and food not to mention the toll it takes on my mother lifting him and packing all the things he needs to get to these appts. No placebos when it come [sic] to ALS he is fighting for his life wouldnt you want that chance. Sincerely Grant Harrison 16yrs old fighting to see my dad live to watch me grow up"* -Grant Harrison

5.4.4 Logical: Facts of ALS as a Basis. (55% of coded comments) People also build up logical arguments in their comments. Information about ALS and what it's like to live with ALS are used as the premises to argue for specific recommendations or make criticisms. For example, some commenters explain that ALS makes travel very difficult, using this as a reason for implementing mobile trial sites to make participation in clinical trials easier.

> *" It is not easy for patients to physically travel to trial sites. ALS is a debilitating disease. Whenever feasible, sponsors should be encouraged to utilize telemedicine or remote monitoring equipment to minimize the burden of unnecessary clinic visits." -*
>
> *" ALS manifests itself differently in different people with the disease. Progression rates vary as does the nature of progression. Even individuals progress at different rates at different times. To me, however, this is an argument AGAINST placebo control and in favor of substituting a statistical model of progression based on a larger group of participants in previously conducted trials."* -John Koten

5.4.5 Logical: Comparisons to Other Cases. (20% of coded comments) People compare ALS and the processes for developing and approving drugs for ALS to other conditions. They argue that the institutional approach to ALS should be more like the approach for Cancer or AIDS, and should not be the same status quo that is applied to the common cold or acne.

> *"If we compare and contrast the ALS Guidance to the BCG-Unresponsive Nonmuscle Invasive Bladder Cancer Guidance, we wonder why ALS does not raise the same concerns that the cancer document raised about placebo – 'Single-arm trials are appropriate in clinical settings where a randomized, controlled trial is either unethical or not feasible.' Why would this not also apply to ALS? Why is there not consistency at the FDA between cancer and ALS Guidances? Do ethics not cross FDA divisions?"* -two comments (1.2% of coded comments)
>
> *"It's a death sentence disease needing URGENCY - it is not strep throat."* - MaryEllen Woodman (2.5% of coded comments compare to strep throat)

5.4.6 Logical: Risk-Benefit Trade Off. (20% of coded comments) Many people who comment demonstrate a nuanced understanding of the risk-benefit trade-off for the approval of drugs and other clinical decisions. They make arguments about how the risks and benefits are experienced by people living with ALS, who only have a few years left to live and can access limited treatment options.

> *"These patients are willing to accept all the risk why not set protocols that will allow them to legally access drugs earlier in the process."* - Mary Law
>
> *"ALS patients are not afraid of dying, they are afraid that they will die without having the opportunity to try anything and everything to stop the progress of this horrible beast or maybe even stop and reverse."* -Anonymous

6 Discussion

In this section, we discuss implications for the design of techniques that support public participation in health policy decisions. We reflect on challenges in making public comments useful for institutions and contextualize the complex, multi-stakeholder nature of health research, policy, and regulatory processes. By identifying points in such processes where digital participation might be beneficial, we posit a call for more attention to the institutional decision making dimension of health within the human-computer interaction community.

6.1 Challenges for public participation in health policy and research

> *"this comment interface is horrible. Are all comments being tracked?"* -Anonymous

Multiple coded comments critiqued the commenting system itself (this phenomena was also identified in some comments which weren't included in final coding). They said the interface was difficult to use, expressed skepticism that all comments are kept track of or read, openly doubted that comments will affect the guidance document, and speculated that many people commenting have not read the guidance document. Such comments highlight two themes: a possible lack of trust in institutions leading to use of the platform in unique ways, and the possibility that some public inputs are actually unproductive. Such lack of trust echoes prior work which identifies *entrenched distrust* in the relationship between government and the governed [15]. Creating more avenues for participation at the institutional level of health might help mitigate this distrust. For example, a public consultation phone survey for a health financing reform process in Hong Kong caused citizens to report greater satisfaction with the healthcare system and in turn higher levels of trust in their government [27]. Yet the mere existence of avenues for participation does not necessarily beget trust [26].

6.1.1 Many comments opt for volume while skipping on arguments and evidence. During the coding process, the research team identified a substantial amount of repeated content across public comments. Short phrases, lists of demands, and even entire paragraphs appeared repeated in multiple comments. This paragraph (or sections of it) appears in 23% of coded comments.

> *"The proposed guidance document doesn't adequately address the urgent needs of patients who have a terminal illness—especially an illness without effective treatment. It is cruel to withhold access to treatments that have been proven safe and show promise, but are stuck in a 15-year, billion-dollar approval process. It is time for the FDA to stop protecting ALS patients to death. ALS patients need immediate access to promising treatments that have passed safety studies. ALS clinical trials should NOT require placebos and should use historical controls instead."*

This exact text can be traced to a blog post by a prominent figure in the ALS community who described the public commenting process and suggested content to include in the comments. The repetition of this paragraph reveals that community members are collaborating outside of the official public comment platform to strategize about how best to participate. It also suggests that many commenters may not be engaging directly with the guidance document itself but instead adopting ready-made language that reflects their general stance. Repeatedly posted identical content hints at a view that a higher volume of comments will yield changes, although there is no evidence of this.

From a regulatory standpoint, repeated content (whether copied verbatim or paraphrased) can add to the administrative burden of processing and analysis without eliciting new insights [46]. Public commenting guidelines on `regulations.gov` explicitly state that repetitive content (*i.e.* form letters) or an abundance of comments with the same

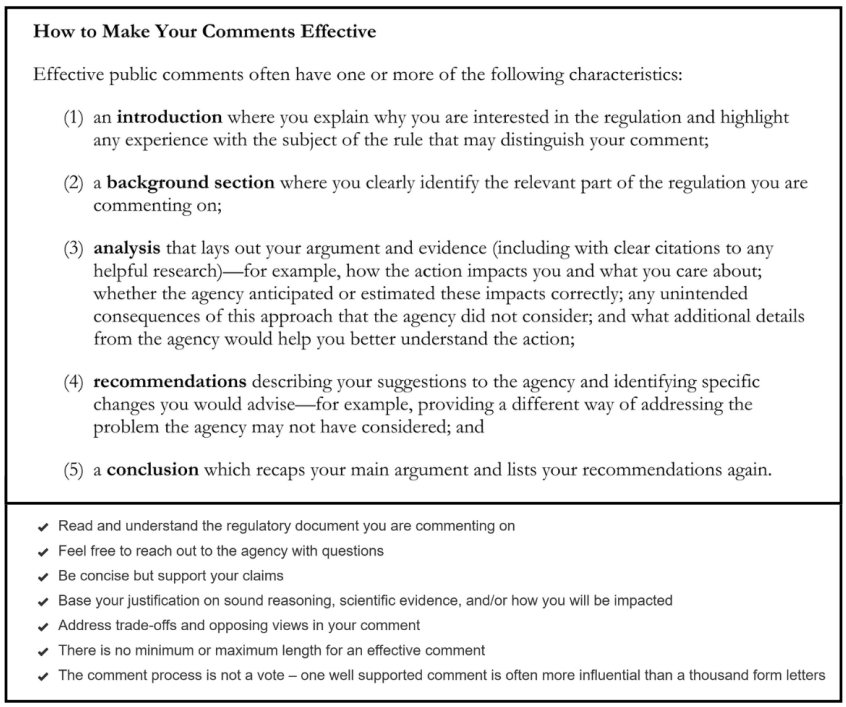

Fig. 10. Snapshots of the Commenter's Checklist on `regulations.gov` which provides suggestions for how to write an effective comment on federal regulations. It includes a ten page document plus a one-page summary with fifteen bullet points. The checklist outlines a five-part structure: introduction, background, analysis, recommendations, and conclusion.

request is not helpful. This *Commenter's Checklist* is linked above the comment text box (snapshots shown in Figure 10). The checklist suggests that an effective comment should include specific information about how proposed regulations affect them, support claims with evidence and analysis, and offer constructive recommendations rather than simply expressing support or opposition.

Many comments appear to not follow the guidelines for an effective comment. For example, 65% of comments make unspecific criticisms or recommendations. Most commenters do follow the initial recommendation to introduce themselves and explain their connection to ALS. However, few comments go on to include substantive analysis or specific recommendations. Instead, they focus on criticizing the guidance document and demanding change, often without clear reasoning or evidence. This pattern suggests that many commenters may not fully engage with the FDA's guidance document or the commenter's checklist. Others may resist following instructions issued by the very authority they are critiquing. In some cases, limited familiarity with regulatory processes or technical content may make it difficult for commenters to engage with the guidance as the FDA intends, leading them to focus more on personal convictions and urgency rather than formal structures of argument.

6.1.2 Lack of transparency hurts people and system designers. People express skepticism that their inputs will be taken into account. Several comments claim that considerations from the ALS Association (ALSA)'s community-created guidance document have been ignored by the FDA. This sense of distrust may be exacerbated by a lack of concrete

feedback on the impact of people's comments. `Regulations.gov` does describe how people can make their comments most effective in the *Commenter's Checklist*. However, there is no mechanistic description of how comments are processed, no explicitly stated links from public input to institutional decisions, and minimal feedback to the public.

Without a feedback loop or assessment of the impact of public participation, participation might feel performative rather than legitimately collaborative [5]. Institutions may use the results of participatory processes as evidence that the public has been consulted, but often do not implement proposed solutions or use public inputs to inform their decisions [35]. People may feel that they are being placated rather than seriously included, leading to comments like this one on the FDA docket: *"you are paid to not just listen ... but HEAR (not codify, pacify nor CA - cover asses)...and DO right"*. Yet institutions face a myriad of financial, legal, administrative, and political challenges that make synthesizing and acting on public inputs difficult [57]. Transparency about these challenges and details of institutional processes may mediate expectations and assist participants in contributing productively [15].

6.2 Commenting strategies that provide complementary knowledge to institutional processes

Many aspects of wellbeing and clinical care are individual: the diet one follows or the care plan one patient receives. There are social dimensions of health as well: the diet of an individual may be affected by the eating customs of their family, and one person's care may be managed by a group of caregivers or supported with social information networks [29, 54, 70]. There are also institutional aspects of health: the nutritional value of a person's diet is affected by how food products are regulated and marketed, and healthcare delivery to individual patients is controlled at a high level by policies and guidelines set by institutional regulators. Our work studies a concrete instance of how institutional processes affect people's health. Many comments demonstrated rich engagement with such policies. We list some examples here.

People make their comments effective by procviding specific criticisms and recommendations that address both the goals of people and the goals of institutions. Some comments critique specific drug development processes mentioned in the guidance document, and provide supporting information and analysis. People suggest changes where they claim the benefits are two-fold: better for ALS patients and better for institutions (the FDA and drug developers). For example, 24% of comments suggest collecting data remotely in clinical trials or using mobile trials sites. When people expand on this recommendation they claim that it will both ease patient accessibility challenges and increase trial enrollment and retention (concerns for clinical trial sponsors). 40% of comments claim that participant eligibility criteria in clinical trials is too restrictive - patients can be excluded from enrolling in a trial because of their age or disease stage. They call for widened eligibility criteria for two reasons: greater patient access to clinical trials (perhaps describing a personal experience of exclusion from a trial); and better science: they claim ALS drug research would be more applicable to the entire population with the disorder if people from a wider range of ages and disease stages are included.

People share lived experience to highlight patient goals, access needs, and assessment of risk. Many comments include personal experiences which describe how the disorder, clinical trials, and regulatory decisions impact their lives. By describing what it's like to live with ALS, they reveal patient challenges and needs. Patient and family experiences of clinical trials convey both the hope they can provide and the issues that arise from certain clinical trial procedures.

Some comments go out of scope but highlight a need for opportunities to participate in different steps of the institutional process. The guidance document that people comment on contains the FDA's nonbinding recommendations for the "clinical development program and clinical trial designs" for drugs to treat ALS. Yet people's comments also discuss aspects of the drug development and approval process which are not covered in the guidance document or are outside the domain of the FDA. For example, comments call for a federal bill to be passed, for insurance to cover

the cost of drugs, or for the approval of specific drugs. These kinds of comments showcase a misplaced effort in the `regulations.gov` comment section for the specified FDA guidance document. However, these comments also demonstrate an important point: people have ideas that can be applicable to various stages of complex institutional processes.

6.3 Opportunities for public participation across multiple stages of multistakeholder health regulatory processes

General public feedback on an entire process may be difficult for institutions to synthesize and use. Structuring participation processes such that the public can provide specific critiques at concrete steps in institutional processes has been a useful strategy in other contexts (*e.g.* a platform for people to evaluate urban designs through micro-activities [45]). Health policy making involves several stages: agenda setting, policy formulation, and policy implementation [17]. Similar stages are seen in health research processes: research agenda setting, study design, and interpretation of results [18]. Each of these stages present an opportunity for public and patient participation.

In the case of drug development and approval, there are several decision points where people might provide inputs. Drug developers decide on clinical trial protocol, such as who is eligible to participate, what the study design is, and how data is collected. Many of the comments we studied included criticisms and recommendations for trial protocol (80% of coded comments). The FDA encourages drug developers to consult patients in their *Patient-Focused Drug Development Guidance Series* [22]. Digital platforms might support direct communication between patients and drug developers at this stage of the process. After trials are completed, there is a data review and approval process conducted by the FDA. Members of the ALS community have shared data and considerations for this decision making process on social media [32], and in Advisory Committees hosted by the FDA [2, 13].

Challenges with trust, summarization, and synthesizing large amounts of text data have been identified in public participation efforts [16, 36, 46]. Future work might further characterize the needs, practices and challenges for health policy makers and patient communities.

There are motivated people and patient communities that want a say in health policy decisions: disability activists, rare disorder communities, and many others use social platforms, offline avenues, and collaborate with nonprofit organizations to attempt to make their ideas heard [6, 32, 44, 61]. Yet these community-led efforts often remain outside the walls of institutions. Digital platforms can open a window for public and patient contributions to be systematically included in regulatory processes.

7 Conclusion

Public participation in health policy can benefit institutions and patient communities, yet there is limited knowledge on what sort of insights patients and the public bring into policy processes. We characterize the ALS community's comments on an institutional guidance document for drug development processes using a mixed methods analysis. Comments include criticisms of general principles in drug regulatory processes, like acceptability of risk, timeliness, flexibility, and specialization of processes to unique disorders. People also contribute ideas for innovative and patient-centered clinical trial processes. Comments include moral arguments about the rights of patients, the role of regulatory institutions, the ethicality of placebos in clinical trials for terminal, uncured disorders; along with logical argument structures that compare the case of ALS to regulatory processes for other conditions or use information about ALS to justify certain criticisms and recommendations. Several of the considerations found in comments may be beneficial for institutions as they attempt to make regulatory and research processes more patient-centered. However, our study also found

that many commenters had unspecific demands and criticisms, repeated the same text verbatim, or made comments on topics outside the scope of the document they commented on. This work demonstrates that online community participation in health regulatory processes can have many challenges, but it also provides useful ideas and feedback to institutional processes.

References

[1] [n. d.]. https://www.acog.org/clinical/clinical-guidance/clinical-consensus/articles/2025/05/pain-management-for-in-office-uterine-and-cervical-procedures

[2] [n. d.]. https://www.als.org/stories-news/fda-committee-unanimously-recommends-accelerated-approval-tofersen

[3] Lura Abbott and Christine Grady. 2011. A systematic review of the empirical literature evaluating IRBs: what we know and what we still need to learn. *J. Empir. Res. Hum. Res. Ethics* 6, 1 (March 2011), 3–19.

[4] Nisreen A Alwan, Emily Attree, Jennifer Mary Blair, Debby Bogaert, Mary-Ann Bowen, John Boyle, Madeleine Bradman, Tracy Ann Briggs, Sarah Burns, Daniel Campion, Katherine Cushing, Brendan Delaney, Chris Dixon, Grace E Dolman, Caitriona Dynan, Ian M Frayling, Nell Freeman-Romilly, Iulia Hammond, Jenny Judge, Linn Järte, Amali Lokugamage, Nathalie MacDermott, Mairi MacKinnon, Visita Majithia, Tanya Northridge, Laura Powell, Clare Rayner, Ginevra Read, Ekta Sahu, Claudia Shand, Amy Small, Cara Strachan, Jake Suett, Becky Sykes, Sharon Taylor, Kevin Thomas, Margarita Thomson, Alexis Wiltshire, and Victoria Woods. 2020. From doctors as patients: a manifesto for tackling persisting symptoms of covid-19. *BMJ* 370 (2020). doi:10.1136/bmj.m3565 arXiv:https://www.bmj.com/content/370/bmj.m3565.full.pdf

[5] Sherry R. Arnstein. 1969. A Ladder Of Citizen Participation. *Journal of the American Institute of Planners* 35, 4 (1969), 216–224. doi:10.1080/01944366908977225 arXiv:https://doi.org/10.1080/01944366908977225

[6] Brooke E. Auxier, Cody L. Buntain, Paul Jaeger, Jennifer Golbeck, and Hernisa Kacorri. 2019. HandsOffMyADA: A Twitter Response to the ADA Education and Reform Act. In *Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems* (Glasgow, Scotland Uk) *(CHI '19)*. Association for Computing Machinery, New York, NY, USA, 1–12. doi:10.1145/3290605.3300757

[7] Kristin Kay Barker, Owen Whooley, Erin F Madden, Emily E Ahrend, and R Neil Greene. 2024. The long tail of COVID and the tale of long COVID: Diagnostic construction and the management of ignorance. *Sociol. Health Illn.* 46, S1 (March 2024), 189–207.

[8] Lisa L. Bayer, Samir Ahuja, Rebecca H. Allen, Melanie A. Gold, Jeffrey P. Levine, Lynn L. Ngo, and Sheila Mody. 2025. Best practices for reducing pain associated with intrauterine device placement. *American Journal of Obstetrics and Gynecology* 232, 5 (2025), 409–421. doi:10.1016/j.ajog.2025.01.039

[9] Kirsten Boehner and Carl DiSalvo. 2016. Data, Design and Civics: An Exploratory Study of Civic Tech. In *Proceedings of the 2016 CHI Conference on Human Factors in Computing Systems* (San Jose, California, USA) *(CHI '16)*. Association for Computing Machinery, New York, NY, USA, 2970–2981. doi:10.1145/2858036.2858326

[10] Morten Bohøj, Nikolaj G. Borchorst, Susanne Bødker, Matthias Korn, and Pär-Ola Zander. 2011. Public deliberation in municipal planning: supporting action and reflection with mobile technology. In *Proceedings of the 5th International Conference on Communities and Technologies* (Brisbane, Australia) *(CT '11)*. Association for Computing Machinery, New York, NY, USA, 88–97. doi:10.1145/2103354.2103367

[11] Deepshikha Chhetri and Fernando Zacarias. 2021. Advocacy for evidence-based policy-making in public health: Experiences and the way forward. *J. Health Manag.* 23, 1 (March 2021), 85–94.

[12] Elizabeth Good Christopherson, Dietram A. Scheufele, and Brooke Smith. 2018. The Civic Science Imperative. *Stanford Social Innovation Review* 16, 2 (2018), 46–52. https://ssir.org/articles/entry/the_civic_science_imperative

[13] Office of the Commissioner. [n. d.]. Advisory committees. https://www.fda.gov/advisory-committees

[14] Office of the Commissioner. [n. d.]. The drug development process. https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process

[15] Eric Corbett and Christopher A Le Dantec. 2018. Exploring Trust in Digital Civics. In *Proceedings of the 2018 Designing Interactive Systems Conference* (Hong Kong China). ACM, New York, NY, USA, 9–20.

[16] Eric Corbett and Christopher A Le Dantec. 2018. The problem of community engagement. In *Proceedings of the 2018 CHI Conference on Human Factors in Computing Systems* (Montreal QC Canada). ACM, New York, NY, USA, 1–13.

[17] Chris Degeling, Lucie Rychetnik, Jackie Street, Rae Thomas, and Stacy M. Carter. 2017. Influencing health policy through public deliberation: Lessons learned from two decades of Citizens'/community juries. *Social Science Medicine* 179 (2017), 166–171. doi:10.1016/j.socscimed.2017.03.003

[18] Amol B Deore, Jayprabha R Dhumane, Rushikesh Wagh, and Rushikesh Sonawane. 2019. The stages of drug discovery and development process. *Asian Journal of Pharmaceutical Research and Development* 7, 6 (2019), 62–67.

[19] Carl DiSalvo, Jonathan Lukens, Thomas Lodato, Tom Jenkins, and Tanyoung Kim. 2014. Making public things: how HCI design can express matters of concern. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems* (Toronto, Ontario, Canada) *(CHI '14)*. Association for Computing Machinery, New York, NY, USA, 2397–2406. doi:10.1145/2556288.2557359

[20] Steven Epstein. 1995. The Construction of Lay Expertise: AIDS Activism and the Forging of Credibility in the Reform of Clinical Trials. *Science, Technology, & Human Values* 20, 4 (1995), 408–437. http://www.jstor.org/stable/689868

[21] Sheena Erete and Jennifer O. Burrell. 2017. Empowered Participation: How Citizens Use Technology in Local Governance. In *Proceedings of the 2017 CHI Conference on Human Factors in Computing Systems* (Denver, Colorado, USA) *(CHI '17)*. Association for Computing Machinery, New York, NY,

USA, 2307–2319. doi:10.1145/3025453.3025996

[22] Center for Drug Evaluation and Research. [n. d.]. Patient-focused drug development guidance series. https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

[23] Assistant Secretary for Public Affairs (ASPA). 2025. HHS agencies offices. https://www.hhs.gov/about/agencies/hhs-agencies-and-offices/index.html

[24] Steven Gillard, Rohan Borschmann, Kati Turner, Norman Goodrich-Purnell, Kathleen Lovell, and Mary Chambers. 2010. 'What difference does it make?' Finding evidence of the impact of mental health service user researchers on research into the experiences of detained psychiatric patients. *Health Expectations* 13, 2 (2010), 185–194. doi:10.1111/j.1369-7625.2010.00596.x arXiv:https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1369-7625.2010.00596.x

[25] Bastian Greshake Tzovaras, Misha Angrist, Kevin Arvai, Mairi Dulaney, Vero Estrada-Galiñanes, Beau Gunderson, Tim Head, Dana Lewis, Oded Nov, Orit Shaer, Athina Tzovara, Jason Bobe, and Mad Price Ball. 2019. Open Humans: A platform for participant-centered research and personal data exploration. *GigaScience* 8, 6 (06 2019), giz076. doi:10.1093/gigascience/giz076 arXiv:https://academic.oup.com/gigascience/article-pdf/8/6/giz076/28864591/giz076.pdf

[26] Mike Harding, Bran Knowles, Nigel Davies, and Mark Rouncefield. 2015. HCI, Civic Engagement & Trust. In *Proceedings of the 33rd Annual ACM Conference on Human Factors in Computing Systems* (Seoul, Republic of Korea) *(CHI '15)*. Association for Computing Machinery, New York, NY, USA, 2833–2842. doi:10.1145/2702123.2702255

[27] Alex Jingwei He and Liang Ma. 2021. Citizen Participation, Perceived Public Service Performance, and Trust in Government: Evidence from Health Policy Reforms in Hong Kong. *Public Performance & Management Review* 44, 3 (2021), 471–493. doi:10.1080/15309576.2020.1780138 arXiv:https://doi.org/10.1080/15309576.2020.1780138

[28] Dorothy Howard and Lilly Irani. 2019. Ways of knowing when research subjects care. In *Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems* (Glasgow Scotland Uk). ACM, New York, NY, USA, 1–16.

[29] Long-Jing Hsu and Chia-Fang Chung. 2024. Dancing with the Roles: Towards Designing Technology that Supports the Multifaceted Roles of Caregivers for Older Adults. In *Proceedings of the 2024 CHI Conference on Human Factors in Computing Systems* (Honolulu, HI, USA) *(CHI '24)*. Association for Computing Machinery, New York, NY, USA, Article 1010, 12 pages. doi:10.1145/3613904.3642728

[30] Jina Huh, Rupa Patel, and Wanda Pratt. 2012. Tackling dilemmas in supporting 'the whole person' in online patient communities. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems* (Austin, Texas, USA) *(CHI '12)*. Association for Computing Machinery, New York, NY, USA, 923–926. doi:10.1145/2207676.2208535

[31] Maia Jacobs, Galina Gheihman, Krzysztof Z. Gajos, and Anoopum S. Gupta. 2019. "I think we know more than our doctors": How Primary Caregivers Manage Care Teams with Limited Disease-related Expertise. *Proc. ACM Hum.-Comput. Interact.* 3, CSCW, Article 159 (Nov. 2019), 22 pages. doi:10.1145/3359261

[32] Nastaran Jadidi and Vineet Pandey. 2025. Rhetoric and Linguistic Strategies in an Online Advocacy Movement. In *Proceedings of the ACM Collective Intelligence Conference (CI '25)*. Association for Computing Machinery, New York, NY, USA, 1–12. doi:10.1145/3715928.3737477

[33] Mahmood Jasim, Enamul Hoque, Ali Sarvghad, and Narges Mahyar. 2021. CommunityPulse: Facilitating Community Input Analysis by Surfacing Hidden Insights, Reflections, and Priorities. In *Proceedings of the 2021 ACM Designing Interactive Systems Conference* (Virtual Event, USA) *(DIS '21)*. Association for Computing Machinery, New York, NY, USA, 846–863. doi:10.1145/3461778.3462132

[34] Ian G. Johnson, Dalya Al-Shahrabi, and John Vines. 2020. From Creating Spaces for Civic Discourse to Creating Resources for Action. In *Proceedings of the 2020 CHI Conference on Human Factors in Computing Systems* (Honolulu, HI, USA) *(CHI '20)*. Association for Computing Machinery, New York, NY, USA, 1–14. doi:10.1145/3313831.3376464

[35] Ian G. Johnson, Alistair MacDonald, Jo Briggs, Jennifer Manuel, Karen Salt, Emma Flynn, and John Vines. 2017. Community Conversational: Supporting and Capturing Deliberative Talk in Local Consultation Processes. In *Proceedings of the 2017 CHI Conference on Human Factors in Computing Systems* (Denver, Colorado, USA) *(CHI '17)*. Association for Computing Machinery, New York, NY, USA, 2320–2333. doi:10.1145/3025453.3025559

[36] Ian G. Johnson, Alistair MacDonald, Jo Briggs, Jennifer Manuel, Karen Salt, Emma Flynn, and John Vines. 2017. Community Conversational: Supporting and Capturing Deliberative Talk in Local Consultation Processes. In *Proceedings of the 2017 CHI Conference on Human Factors in Computing Systems* (Denver, Colorado, USA) *(CHI '17)*. Association for Computing Machinery, New York, NY, USA, 2320–2333. doi:10.1145/3025453.3025559

[37] Elizabeth Kaziunas, Michael S. Klinkman, and Mark S. Ackerman. 2019. Precarious Interventions: Designing for Ecologies of Care. *Proc. ACM Hum.-Comput. Interact.* 3, CSCW, Article 113 (Nov. 2019), 27 pages. doi:10.1145/3359215

[38] Yubo Kou, Xinning Gui, Yunan Chen, and Kathleen Pine. 2017. Conspiracy Talk on Social Media: Collective Sensemaking during a Public Health Crisis. *Proc. ACM Hum.-Comput. Interact.* 1, CSCW, Article 61 (Dec. 2017), 21 pages. doi:10.1145/3134696

[39] Klaus Krippendorff. [n. d.]. Computing Krippendorff's alpha-reliability. https://repository.upenn.edu/entities/publication/034a6030-c584-4d14-9d3d-7b7e8d16df20

[40] Klaus Krippendorff. 2022. *Content analysis an introduction to its methodology.* SAGE Publications.

[41] Bhuma Krishnamachari, Alexander Morris, Diane Zastrow, Andrew Dsida, Brian Harper, and Anthony J. Santella. 2020. Effects of Government Mandated Social Distancing Measures on Cumulative Incidence of COVID-19 in the United States and its Most Populated Cities. *medRxiv* (2020). doi:10.1101/2020.05.22.20110460 arXiv:https://www.medrxiv.org/content/early/2020/05/24/2020.05.22.20110460.full.pdf

[42] Christopher A. Le Dantec, Mariam Asad, Aditi Misra, and Kari E. Watkins. 2015. Planning with Crowdsourced Data: Rhetoric and Representation in Transportation Planning. In *Proceedings of the 18th ACM Conference on Computer Supported Cooperative Work & Social Computing* (Vancouver, BC, Canada) *(CSCW '15)*. Association for Computing Machinery, New York, NY, USA, 1717–1727. doi:10.1145/2675133.2675212

[43] Maxim Lisnic, Cole Polychronis, Alexander Lex, and Marina Kogan. 2023. Misleading Beyond Visual Tricks: How People Actually Lie with Charts. In *Proceedings of the 2023 CHI Conference on Human Factors in Computing Systems* (Hamburg, Germany) *(CHI '23)*. Association for Computing Machinery, New York, NY, USA, Article 817, 21 pages. doi:10.1145/3544548.3580910

[44] Haley MacLeod, Kim Oakes, Danika Geisler, Kay Connelly, and Katie Siek. 2015. Rare World: Towards Technology for Rare Diseases. In *Proceedings of the 33rd Annual ACM Conference on Human Factors in Computing Systems* (Seoul, Republic of Korea) *(CHI '15)*. Association for Computing Machinery, New York, NY, USA, 1145–1154. doi:10.1145/2702123.2702494

[45] Narges Mahyar, Michael R. James, Michelle M. Ng, Reginald A. Wu, and Steven P. Dow. 2018. CommunityCrit: Inviting the Public to Improve and Evaluate Urban Design Ideas through Micro-Activities. In *Proceedings of the 2018 CHI Conference on Human Factors in Computing Systems* (Montreal QC, Canada) *(CHI '18)*. Association for Computing Machinery, New York, NY, USA, 1–14. doi:10.1145/3173574.3173769

[46] Narges Mahyar, Diana V. Nguyen, Maggie Chan, Jiayi Zheng, and Steven P. Dow. 2019. The Civic Data Deluge: Understanding the Challenges of Analyzing Large-Scale Community Input. In *Proceedings of the 2019 on Designing Interactive Systems Conference* (San Diego, CA, USA) *(DIS '19)*. Association for Computing Machinery, New York, NY, USA, 1171–1181. doi:10.1145/3322276.3322354

[47] S. Malfait, A. Van Hecke, G. De Bodt, N. Palsterman, and K. Eeckloo. 2018. Patient and public involvement in hospital policy-making: Identifying key elements for effective participation. *Health Policy* 122, 4 (2018), 380–388. doi:10.1016/j.healthpol.2018.02.007

[48] Ashlee Milton, Leah Ajmani, Michael Ann DeVito, and Stevie Chancellor. 2023. "I See Me Here": Mental Health Content, Community, and Algorithmic Curation on TikTok. In *Proceedings of the 2023 CHI Conference on Human Factors in Computing Systems* (Hamburg, Germany) *(CHI '23)*. Association for Computing Machinery, New York, NY, USA, Article 480, 17 pages. doi:10.1145/3544548.3581489

[49] Victor M Montori, Merel M Ruissen, Ian G Hargraves, Juan P Brito, and Marleen Kunneman. 2023. Shared decision-making as a method of care. *BMJ Evid. Based Med.* 28, 4 (Aug. 2023), 213–217.

[50] Lisa Neal, Kate Oakley, Gitte Lindgaard, David Kaufman, Jan Marco Leimeister, and Ted Selker. 2007. Online health communities. In *CHI '07 Extended Abstracts on Human Factors in Computing Systems* (San Jose, CA, USA) *(CHI EA '07)*. Association for Computing Machinery, New York, NY, USA, 2129–2132. doi:10.1145/1240866.1240965

[51] Don Nutbeam. 2000. Health literacy as a public health goal: a challenge for contemporary health education and communication strategies into the 21st century. *Health Promotion International* 15, 3 (09 2000), 259–267. doi:10.1093/heapro/15.3.259 arXiv:https://academic.oup.com/heapro/article-pdf/15/3/259/9809115/150259.pdf

[52] Josephine Ocloo and Rachel Matthews. 2016. From tokenism to empowerment: progressing patient and public involvement in healthcare improvement. *BMJ Quality & Safety* 25, 8 (2016), 626–632. doi:10.1136/bmjqs-2015-004839 arXiv:https://qualitysafety.bmj.com/content/25/8/626.full.pdf

[53] Kathryn Oliver, Theo Lorenc, Jane Tinkler, and Chris Bonell. 2019. Understanding the unintended consequences of public health policies: the views of policymakers and evaluators. *BMC Public Health* 19, 1 (Aug. 2019), 1057.

[54] Aswati Panicker, Kavya Basu, and Chia-Fang Chung. 2025. Mediated human-food interaction for remote presence in adult family relationships: A social practice theory approach. *Comput. Support. Coop. Work* (April 2025).

[55] Sun Young Park, Yunan Chen, and Shriti Raj. 2017. Beyond Health Literacy: Supporting Patient-Provider Communication during an Emergency Visit. In *Proceedings of the 2017 ACM Conference on Computer Supported Cooperative Work and Social Computing* (Portland, Oregon, USA) *(CSCW '17)*. Association for Computing Machinery, New York, NY, USA, 2179–2192. doi:10.1145/2998181.2998357

[56] David B Resnik and Elizabeth Ness. 2012. Participants' responsibilities in clinical research. *Journal of Medical Ethics* 38, 12 (2012), 746–750. doi:10.1136/medethics-2011-100319 arXiv:https://jme.bmj.com/content/38/12/746.full.pdf

[57] Brandon Reynante, Steven P. Dow, and Narges Mahyar. 2021. A Framework for Open Civic Design: Integrating Public Participation, Crowdsourcing, and Design Thinking. *Digit. Gov.: Res. Pract.* 2, 4, Article 31 (Dec. 2021), 22 pages. doi:10.1145/3487607

[58] Diana Rose. 2014. Patient and public involvement in health research: ethical imperative and/or radical challenge? *J. Health Psychol.* 19, 1 (Jan. 2014), 149–158.

[59] Phillip H. Roth and Mariacarla Gadebusch-Bondio. 2022. The contested meaning of "long COVID" – Patients, doctors, and the politics of subjective evidence. *Social Science & Medicine* 292 (2022), 114619. doi:10.1016/j.socscimed.2021.114619

[60] David Russell, Naomi Spence, Jo-Ana Chase, Tatum Schwartz, Christa Tumminello, and Erin Bouldin. 2022. Support amid uncertainty: Long COVID illness experiences and the role of online communities. *SSM - Qualitative Research in Health* 2 (10 2022), 100177. doi:10.1016/j.ssmqr.2022.100177

[61] Tanushree Sarkar, Anjali J. Forber-Pratt, Rachel Hanebutt, and Mae Cohen. 2021. "Good morning, Twitter! What are you doing today to support the voice of people with #disability?": disability and digital organizing. *Journal of Community Practice* 29, 3 (2021), 299–318. doi:10.1080/10705422.2021.1982802 arXiv:https://doi.org/10.1080/10705422.2021.1982802

[62] Muhammad Shahroz, Farooq Ahmad, Muhammad Shahzad Younis, Nadeem Ahmad, Maged N. Kamel Boulos, Ricardo Vinuesa, and Junaid Qadir. 2021. COVID-19 digital contact tracing applications and techniques: A review post initial deployments. *Transportation Engineering* 5 (2021), 100072. doi:10.1016/j.treng.2021.100072

[63] Xiaoyan Song, David C. Stockwell, Tara Floyd, Billie L. Short, and Nalini Singh. 2013. Improving hand hygiene compliance in health care workers: Strategies and impact on patient outcomes. *American Journal of Infection Control* 41, 10 (2013), e101–e105. doi:10.1016/j.ajic.2013.01.031

[64] Neda Taghinejadi, Helene-Mari van der Westhuizen, Francis Ifeanyi Ayomoh, Wasim Ahmed, Trisha Greenhalgh, and Anne-Marie Boylan. 2024. Pain experiences during intrauterine device procedures: a thematic analysis of tweets. *BMJ Sexual & Reproductive Health* 50, 4 (2024), 271–277. doi:10.1136/bmjsrh-2023-202011 arXiv:https://srh.bmj.com/content/50/4/271.full.pdf

[65] Catherine V. Talbot, Siobhan T. O'Dwyer, Linda Clare, Janet Heaton, and Joel Anderson. 2020. How people with dementia use twitter: A qualitative analysis. *Computers in Human Behavior* 102 (2020), 112–119. doi:10.1016/j.chb.2019.08.005

[66] Kert Viele, Scott Berry, Beat Neuenschwander, Billy Amzal, Fang Chen, Nathan Enas, Brian Hobbs, Joseph G Ibrahim, Nelson Kinnersley, Stacy Lindborg, Sandrine Micallef, Satrajit Roychoudhury, and Laura Thompson. 2014. Use of historical control data for assessing treatment effects in clinical trials. *Pharm. Stat.* 13, 1 (Jan. 2014), 41–54.

[67] Eric von Hippel. 2005. Democratizing innovation: The evolving phenomenon of user innovation. *J. Betriebswirtschaft* 55, 1 (March 2005), 63–78.

[68] David Wendler, Benjamin Krohmal, Ezekiel J Emanuel, Christine Grady, and ESPRIT Group. 2008. Why patients continue to participate in clinical research. *Arch. Intern. Med.* 168, 12 (June 2008), 1294–1299.

[69] Jenny Wu, Esmé Trahair, Megan Happ, and Jonas Swartz. 2023. TikTok, #IUD, and user experience with intrauterine devices reported on social media. *Obstet. Gynecol.* 141, 1 (Jan. 2023), 215–217.

[70] Diyi Yang, Zheng Yao, Joseph Seering, and Robert Kraut. 2019. The Channel Matters: Self-disclosure, Reciprocity and Social Support in Online Cancer Support Groups. In *Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems* (Glasgow, Scotland Uk) *(CHI '19)*. Association for Computing Machinery, New York, NY, USA, 1–15. doi:10.1145/3290605.3300261

[71] Xiaomu Zhou, Si Sun, and Jiang Yang. 2014. Sweet Home: understanding diabetes management via a chinese online community. In *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems* (Toronto, Ontario, Canada) *(CHI '14)*. Association for Computing Machinery, New York, NY, USA, 3997–4006. doi:10.1145/2556288.2557344