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REGULAR ARTICLE

The Impact of Communicating Uncertainty on Public Responses to Precision Medicine Research

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Abstract

Background Precision medicine research depends upon recruiting large and diverse participant cohorts to provide genetic, environmental, and lifestyle data. How prospective participants react to information about this research, including depictions of uncertainty, is not well understood.

Purpose The current study examined public responses to precision medicine research, focusing on reactions toward (a) uncertainty about the scientific impact of sharing data for research, and (b) uncertainty about the privacy, security, or intended uses of participant data.

Methods U.S. adults (N = 674; 51.9% male; 50% non-Hispanic white; M_{age} = 42.23) participated in an online experimental survey. Participants read a manipulated news article about precision medicine research that conveyed either certainty or uncertainty of each type (scientific, data). Participants then rated their attitudes toward the research, trust in the researchers, and willingness to join a cohort. We tested direct and mediated paths between message condition and outcomes and examined individual characteristics as moderators.

Results Overall attitudes were positive and a majority of participants (65%) reported being somewhat or very likely to participate in precision medicine research if invited. Conveying uncertainty of either type had no overall main effect on outcomes. Instead, those who reported perceiving greater uncertainty had lower attitudes, trust, and willingness to join, while those with more tolerance for uncertainty, support for science, and scientific understanding responded favorably to the scientific uncertainty disclosure.

Conclusions Findings suggest responses to precision medicine research uncertainty are nuanced and that successful cohort enrollment may be well-supported by a transparent approach to communicating with prospective participants.

Keywords: Precision medicine · Genomics · Research recruitment · Uncertainty · Communication

Introduction

The goal of precision medicine (PM) is to prevent or treat diseases more precisely by tailoring approaches to a person's genetic, physiological, environment and lifestyle factors [1, 2]. Today, PM remains an emerging concept with considerable research needed to become a clinical reality, and large segments of the public are being recruited into PM research cohorts, such as the National Institutes of Health-led All of Us research program, to support discovery [1]. These research programs collect volunteers' DNA and other health-relevant information, including clinical diagnoses, data from wearables, and self-reported health behaviors.

Because the nature of PM research is highly exploratory and largely correlational, it is expected to involve a great deal of uncertainty in its early stages [3]. For prospective PM research participants, two forms of uncertainty are salient: uncertainty about the scientific benefit of sharing one's personal health data for research (*scientific* uncertainty) and uncertainty about the privacy, security, and intended uses of one's data (*data* uncertainty). Scientific and data related uncertainties in PM

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research have not been widely communicated to the public. Instead, PM is typically described by highlighting anticipated benefits and presenting these in rather certain terms, without mention of caveats and limitations [4, 5]. Highly certain claims have characterized most news coverage of PM research [4] as well as public facing research program recruitment efforts [6]. However, transparency about the research process is considered key to supporting informed decisions about PM research participation from a diverse group of volunteers [2, 7–9]. Calls have been issued for research to identify which communication approaches support informed decision making—while ideally also building public support, engagement, and trust—in this novel biomedical research domain [7–13].

Answering this call, the current study compared the effects of describing scientific and data related aspects of PM research participation as certain or uncertain. The varied depictions were embedded in a news story, which is often the public's first point of contact with information about emerging biomedical research. Potentially, conveying certainty or uncertainty in news stories has an impact on public reactions toward the research, and it is possible that effects vary by uncertainty type. In this study, an online panel of U.S. adults read these varied depictions and then reported attitudes toward participating in PM research, trust in the researchers, and willingness to join a research cohort. We also examined uncertainty perceptions as mediators and individual characteristics as moderators of these communication effects.

How Individuals Process Uncertainty: Theoretical Frameworks

No theoretical framework exists yet to explain how individuals process and respond to scientific or data uncertainty in PM research. However, two adjacent theories may be relevant: Uncertainty Management Theory (UMT) and Uncertainty in Illness Theory (UIT). Each is focused on how people handle illness-related uncertainty and, if applicable to the current context, would suggest that responses are likely to be complex and based on a range of factors. For example, a key postulate of UMT is that uncertainty is not always appraised negatively and people do not necessarily seek to reduce it [14]. Instead, people appraise and act on uncertain information based on their underlying motivations in a given context (e.g., to get accurate information or to maintain hope). UIT similarly posits that people interpret uncertain information subjectively and in accordance with their coping strategy [15]. If these theoretical perspectives apply in the context of PM research, we may expect responses to PM uncertainty to be nuanced, influenced by individual motivations and perceptual filters, and not inherently negative [14, 15].

According to UMT, an uncertain situation often has multiple layers or aspects of uncertainty, and a person may respond differently to each aspect [14]. In PM research, it could be that participants are generally fine with scientific uncertainty, but not comfortable with uncertainty about how their data will be used. Or, conversely, it could be that most people are willing to sacrifice data certainty, but only if scientific benefit is guaranteed. A third possibility is that people are comfortable with one source of uncertainty but not multiple. There may be general trends across the population or responses may vary considerably among individuals.

Uncertainties for the Precision Medicine Research Participant

PM research is characterized by high uncertainty, including forms of scientific uncertainty that limit the utility of research findings [3, 4, 16] and uncertainties related to governance of participant data [17, 18]. Although these uncertainties are often disclosed in participant consent forms, they are rarely mentioned in public communication about the research [4–6]. Arguably, it is this public-facing information that people use to form opinions about PM research and decide whether to participate. It is unclear whether describing aspects of PM research as certain or uncertain will influence public interest and engagement.

It is especially important to consider the perspectives of racially and ethnically diverse participants, who are typically underrepresented in research and may be wary of the biomedical research enterprise [19]. Many PM research programs, including All of Us, seek to recruit racially and ethnically diverse participants [8, 9]. Yet several studies and reviews report heightened concerns about genetic research participation among ethnic/racial minorities, citing concerns about data stewardship and scientific implications [20–23]. It is clear that to preserve transparency and support informed decision making will require a clearer understanding of responses to PM uncertainties from a diverse pool of prospective research participants.

Scientific Uncertainty in Precision Medicine Research

"Scientific uncertainty" is a broad concept that can take many forms [24]. Forms of scientific uncertainty in PM research pertain to whether the research efforts will produce findings that are accurate, meaningful, generalizable, and clinically useful [3, 16]. Although PM is expected to reduce uncertainty in the long term, PM research might increase uncertainty in the short term when studies produce results that are not clearly interpretable or actionable.

In deciding whether to participate in PM research, participants may consider the likely scientific impact of sharing their biosamples and personal or medical information. A message indicating uncertain benefit could dampen people's attitudes and desire to contribute. However, people participate in health research for reasons other than advancing scientific knowledge, such as curiosity and feeling a duty to contribute their time [25]. Extant research has focused primarily on research participants' reactions to potential uncertain scientific benefit to *themselves* (e.g., receiving genomic test results of uncertain significance) [26–28]. However, generating knowledge for individual research participants is not a goal of most PM research. Thus, it is important to understand how prospective PM research participants feel about uncertain scientific benefit to society. Outside the context of genetics, perceiving scientific evidence to be uncertain has not been related to lower engagement with science (e.g., the desire to be a citizen scientist) [29]. In that study, perceived scientific uncertainty was positively correlated with supportive attitudes toward science [29]—perhaps because it was viewed as more realistic and less hyped. This finding suggests that conveying uncertain scientific benefit of PM research might have a neutral or even positive effect on public attitudes and willingness to participate.

Whether conveying scientific uncertainty should lower or heighten trust in the scientists conducting PM research is also unclear [30]. Some scholars argue that transparency can undermine public trust in expert institutions [31], while others claim transparency is essential to preserving trust, especially in the context of genetic research [7]. PM researchers could worry that drawing attention to uncertainties will make the biomedical research enterprise seem less credible, and thereby make potential volunteers less likely to enroll. Yet it is also possible that being informed about uncertainties upfront increases public trust. In the context of cancer research, past work found a positive relationship between fuller disclosures of scientific uncertainty and audience trust in the scientists [32] and journalists [32, 33]. However, in another study, communicating scientific uncertainty lowered trust in public health officials [34]. Whether a disclosure about the uncertain scientific benefit of sharing data for PM research will influence trust merits further investigation.

Data Uncertainty in Precision Medicine Research

The privacy and security of participants' personal data are additional sources of uncertainty for PM research participants. Those who join PM research programs may be asked to share DNA samples, geospatial information, electronic medical records (EMRs), data from wearables, and a swathe of other health-relevant data [35, 36]. Although precautions will be taken in PM research programs to anonymize participant data, as well as to limit data access to known and authorized entities, data protection strategies are still in development. Concerns have been raised about data privacy, including concerns about the possibility of re-identification of data and the potential for discrimination [8, 37, 38]. Data gathered for PM research could face some of the same security vulnerabilities as data used in other health contexts [39]. For example, EMRs have been a repeated target of employee error and misuse [40]. Despite these inevitable uncertainties, privacy and security of participant data are often presented to the public as guaranteed [41, 42].

Future use of data also represents a source of uncertainty for research participants. PM research is exploratory, and most PM research programs are gathering a wide array of participant information for data mining. The data are stored for an undefined duration and used for purposes unknown at the time of participant consent, requiring volunteers to give "broad consent" [21]. Scholars have cautioned, "keeping data private and secure will not assure that these data will not be misused" [7, p. 10]. Participants will not know who accesses their data or for what purposes.

Lay attitudes toward privacy of health data have been explored more generally [43] and opinions about providing broad consent for research have also been examined [44–48]. In these studies, people had mixed feelings toward sharing their data. In a study of attitudes toward sharing genomic data despite data-related uncertainty, participants' privacy and confidentiality concerns did not necessarily preclude them from willingness to share [47]. It is unclear whether uncertainties in PM research will foster reactions similar to other biomedical research contexts, since PM entails collection of a much wider range of personal data from multiple sources (e.g., genetic, environment, and lifestyle data) for indeterminate future use [1, 17, 36].

Communicating data uncertainty could also impact trust in the research institutions. Current approaches to communicating about data governance in PM research have emphasized privacy and security of participant data without noting possible limitations or caveats. One such caveat is that participants' anonymity cannot be guaranteed if, for example, they reveal their participation on social media. Other elements of uncertainty include not knowing who will have access to participants' data and how it will be used. The reality is that once a participant's data are in the database, they cannot be removed if a participant withdraws from participation. One study found that willingness to participate in PM research did not vary significantly between those who were offered transparency about which studies were using their data, and those who were not offered this [49]. However, the study did find people significantly less willing to participate if the data would be used by pharmaceutical company researchers or by government researchers other than the NIH. The impact of disclosing data uncertainty on trust in PM researchers has not yet been examined. Such transparency could lessen trust, or alternatively it could heighten trust as a gesture of transparency, especially if the public is already aware of such limitations.

Individual Characteristics and Perceptions of Uncertainty

Individual perceptions of uncertainty may be complex and based not only on the information that is communicated. For example, science journalists have argued that audiences engage in motivated reasoning when reading science news articles [50]. This notion aligns with tenets of UMT and UIT claiming that uncertainty appraisal is affected by individual motivations and prior experiences [14, 15]. In the context of PM, perceived uncertainty might be shaped by a person's motivation for participating or prior beliefs about the research. This makes it important to examine uncertainty perceptions and whether these mediate effects of uncertainty disclosure.

Just as perceptions of uncertainty may be complex, how people respond to the uncertainty they perceive might also be shaped by various factors. Theory and prior research point to three individual characteristics that appear fruitful to examine in this context. First, people are thought to differ in their dispositional tolerance for uncertainty [51–54]. Though typically studied in relation to uncertainty about a person's own health (e.g., an illness diagnosis), medical ambiguity aversion has also been studied as a predictor of responses to scientific uncertainty about a public health risk [34]. Conceivably, one's comfort with uncertainty, either in general or in health contexts, could shape their response to uncertainties in PM research participation. Second, previously held attitudes toward science can influence how people perceive or respond to communication of uncertainty [55]. Thus, support for scientific research could be a preexisting stance that influences how people react to PM uncertainty. Third, past work indicates that understanding the nature of scientific research may influence responses to uncertainty [34, 56]. For example, a recent study found participants to be more affected by how information was framed when they were less familiar with the scientific topic [57]. Moreover, being familiar with science as an ongoing and fallible process should make individuals more tolerant of scientific uncertainty [29]. Thus, someone with a greater understanding of the concept of a scientific study may be more likely to respond neutrally or even favorably to disclosure of uncertainties inherent to the conduct of research.

Current Study: Hypotheses and Research Questions

This study examined effects of disclosing scientific and data related uncertainties in PM research. Given limited and mixed prior findings, we posed nondirectional research questions. We asked whether responses—namely, (a) attitudes about participating, (b) trust in the researchers, and (c) willingness to participate if invited—would differ when scientific uncertainty (RQ1) or data uncertainty (RQ2), as opposed to certainty, was communicated. We also tested for interaction effects, in case (a) attitudes, (b) trust, or (c) willingness to participate differ by uncertainty type (RQ3) or when both types (vs. just one) are communicated (RQ4).

Guided by uncertainty management frameworks and empirical findings from relevant domains, we also predicted influential roles of uncertainty perceptions and individual characteristics. We expected perceptions of scientific uncertainty (H1) and data uncertainty (H2) to mediate the relationship between uncertainty disclosure and (a) attitudes, (b) trust, and (c) willingness to participate. We also expected the effect of communicating scientific uncertainty on (a) attitudes, (b) trust, and (c) willingness to participate to be moderated directly or indirectly by uncertainty tolerance (H3), support for science (H4), and scientific understanding (H5). We similarly expected the effects of communicating data uncertainty (a–c) to be moderated by uncertainty tolerance (H6), support for science (H7), and scientific understanding (H8). Hypotheses and research questions are depicted in Fig. 1.

Methods

Sampling Procedures

Adults 18 and older living in the United States were recruited through Qualtrics Panel Services during February and March of 2019 to participate in an online experiment. Given the importance of including diverse

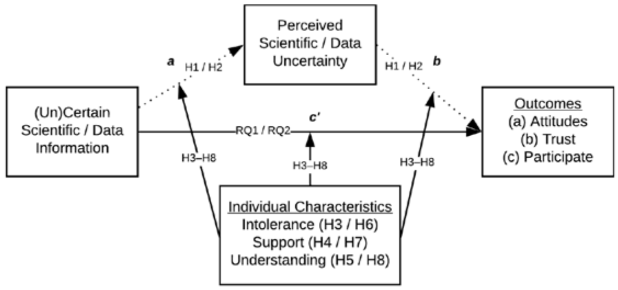

Fig. 1. Conceptual diagram of hypothesized relationships. *Notes*. This diagram mirrors the conceptual diagram for PROCESS Model 59 (Hayes, 2018). The *a* and *b* paths represent the two pathways comprising the indirect effect of disclosure, and the *c'* path represents the direct effect of disclosure after indirect effects are accounted for. Moderation of the overall indirect effect (full moderated mediation) is not depicted, but is reported in text.

participants in PM research, we specified quotas for sex, race, and ethnicity, so that the sample would be comprised of an even split of male and female participants, with at least 20% identifying as Hispanic and at least 40% identifying as nonwhite.

G*Power was used to identify a target sample size for the study. For a two-way ANCOVA with power .95, G*Power identified target sample sizes of 210 ($f = 0.25$), 580 ($f = 0.15$), and 1302 ($f = 0.10$; Cohen, 1992). Past research in this area has observed small-to-medium sized effects; the current study targeted a sample size of 580 to consistently identify effects of this size. The final sample size, after incomplete responses were removed, was 674. That sample provides adequate power (0.80) for effects as small as 0.11.

Study Design

We embedded a modified news article in the survey that described scientific discovery and data privacy/security as certain or uncertain. Participants were randomly assigned to one of the four article conditions in a 2 (scientific: certain, uncertain) × 2 (data: certain, uncertain) between-participants design. Before article exposure, participants reported sociodemographic and other individual difference information. After reading the article, they were asked to reflect on the content and answer questions about their reactions toward aspects of PM research. Measures were the same across conditions. After completion, participants were debriefed about the article manipulation and shown the original news article. Median time to complete the survey was 12 min. The study was approved by the University of Utah IRB.

Survey and Stimulus Development

The questionnaire and experimental stimuli were tested and refined through a process of cognitive interviewing ($N = 5$) and pilot testing with a separate student sample ($N = 180$). The base for the stimulus was a *Chicago Tribune* article about PM research, which we shortened and modified to contain a statement of certainty or uncertainty for each domain. The uncertainty statements were depicted using a "normalizing" frame [34] explaining that uncertainty in each domain can be expected given the complex nature of the research process. Results from pilot testing led us to add "callout boxes," a common feature of news articles, containing repeated, condensed versions of the (un)certainty statements. This served to strengthen the manipulation and ensure that participants who skimmed the article would still get the main takeaways. After establishing efficacy of the instrument, the study proceeded to data collection. Stimuli are presented in Supplementary Material 1.

Quality Checks

After collecting an initial sample of 732 responses, nonmeaningful survey responses were removed from the data, yielding a final sample of 674. Cases were removed if participants did not pass the attention check (a multiple-choice question about the article topic), gave a nonmeaningful (i.e., gibberish or off-topic) answer to open-ended questions, completed the survey in under one-third median time, or spent less than 5 s reading the stimulus article.

Measures

Attitudes toward participating

Participants responded to the question "In your opinion, participating in precision medicine research like what was described in the article would be…" Response options were on a 7-point semantic differential scale with the anchors: *worthless/valuable, bad/good, harmful/beneficial, not helpful/helpful, unproductive/productive, foolish/wise,* and *not useful/useful* ($M = 5.52$, $SD = 1.3$; $\alpha = 0.96$).

Trust in the researchers

Participants completed a 3-item scale using items that represent the "trustworthy" dimension of credibility [58]. They reported the extent to which they thought the organizations leading the research program in the article were *trustworthy*, *honest*, and *ethical* (1 = *strongly disagree*, 5 = *strongly agree*; $M = 3.52$, $SD = 0.83$, $\alpha = 0.90$).

Willingness to participate

A single item asked participants: "If you are invited to participate in a precision medicine research program like the one described in the article, how likely are you to join?" (*not at all likely*, *somewhat likely*, *very likely*, or *not sure*). “Not sure” responses were excluded from main analyses; rationale and an analysis including “not sure” responses are provided in Supplementary Material 4.

Perceived uncertainty

Perceptions of scientific and data uncertainty were measured with items created for this study. Participants were asked to rate how certain they feel, based on the article, about each aspect of the research (i.e., that “Participant data will lead to scientific discoveries that benefit people’s health” and that “Participant data will be kept private and secure over time”; 1 = *not at all certain* to 5 = *extremely certain*). The prompts were worded in terms of certainty, as this was deemed a more natural way for participants to consider the question. The scales were then reversed for analyses, so a higher value represents greater uncertainty.

Intolerance of uncertainty

The 12-item Intolerance of Uncertainty short-form scale [59] was used to assess dispositional orientation toward ambiguous situations and future uncertainty. Items included “It frustrates me not having all the information I need” and “The smallest doubt can stop me from acting” (1 = *not at all characteristic of me*, 5 = *entirely characteristic of me*; $M = 2.71$, $SD = 0.81$; $\alpha = 0.90$).

Support for scientific research

An item from the NSF Science & Engineering Indicators used in prior uncertainty research [32] asked how much participants agree that “Even if it brings no immediate benefits, scientific research that advances the frontiers of knowledge is necessary and should be supported by the Federal Government” (1 = *strongly disagree*, 5 = *strongly agree*; $M = 3.92$, $SD = 1.06$).

Understanding of a scientific study

Another item from the NSF Indicators asked participants to rate their understanding of the concept of a “scientific study” (1 = *little understanding*, 2 = *general sense*, 3 = *clear understanding*; $M = 2.37$, $SD = 0.61$). Responses from a fourth “do not know” category (<1% of sample) were treated as missing in analyses.

Prior awareness of PM

To gauge general awareness of PM research, participants were asked whether they had heard about precision medicine or the All of Us research program. Sixty-six participants, or roughly 10%, answered *yes*; roughly 90% answered *no* or *not sure*.

Analysis

All analyses were conducted using SPSS version 22. Income and ethnicity were imbalanced across conditions and thus controlled for in all analyses, with income treated as a six-level variable and ethnicity treated as binary (see Supplementary Table 2). Separate univariate two-way ANCOVA models were used to estimate the direct effects of communicating uncertainty on each primary outcome (RQ1–RQ2). To answer RQ3 and RQ4, interaction terms were included in univariate ANCOVA models. Simple mediation analyses were conducted using the regression-based path analysis tool PROCESS (model 4) in SPSS, in order to examine perceived uncertainty as a mediator (H1 and H2). Conditional process (moderated mediation) analyses were conducted using PROCESS model 59 to answer H3–H8. Model 59 tests whether direct or indirect effects are conditional upon values of a moderator [60]. Thus, this model was used to examine whether each individual difference variable moderated the direct path from message to outcome, or the path from message to perception, or the path from perception to outcome (see Fig. 1). It is plausible that individual characteristics would influence any of these processing pathways, and there is not prior guidance from theory to inform predictions. Thus, testing all possible conditional direct and indirect effects can help to illuminate where in the process these variables exert influence and help to build theory. The Johnson-Neyman technique was used to probe interactions and identify regions of significance at different values of the moderator [60]. In line with Hayes’s recommendation, the threshold for probing interactions was set at $p < .10$.

Results

Bivariate correlations between study variables are reported in Table 1.

Participant Characteristics

In the final analytic sample ($N = 674$), 43.5% of respondents identified as nonwhite or mixed race and 18.7% identified as Hispanic, while 50% identified as non-Hispanic white. The sample was comprised of 47.9% females (51.9% male and 0.1% nonbinary gender) ages 18–84 ($M_{\text{age}} = 42.23$, $SD = 14.67$), and 61.1% had completed a two-year college degree or more. The sample was diverse across ages and levels of education and income. Full participant characteristics are reported in Supplementary Table 2.

Table 1. Bivariate correlations between study variables

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	ComSciU	—														
2	ComDataU	.01	—													
3	PSU	.16***	.06	—												
4	PDU	.04	.16***	.49***	—											
5	Attitudes	.02	−.03	−.51***	−.45***	—										
6	Trust	.04	−.02	−.39***	−.46***	.53***	—									
7	Participate	−.02	−.02	−.45***	−.47***	.47***	.50***	—								
8	Race	−.05	−.04	−.02	−.02	.01	−.02	.11**	—							
9	Ethnicity	.16***	.00	.03	.00	−.01	.01	−.05	−.15***	—						
10	Income	.12**	−.03	.00	−.06	.06	.09*	.07†	−.06	.13**	—					
11	Education	.07†	.02	.04	−.01	.00	.05	−.04	.00	.12**	.45***	—				
12	Age	.04	−.03	.12**	.09*	.01	−.03	−.11**	−.04	.22***	.08*	.11**	—			
13	IUS	−.04	.08*	−.10*	−.12**	.05	.06	.10*	.00	−.06	−.12**	−.05	−.23***	—		
14	UndStudy	.03	−.03	−.18***	−.11**	.11**	.10*	.08*	.01	.04	.09*	.11**	−.05	−.06	—	
15	Support	−.01	.01	−.18***	−.15***	.28***	.35***	.18***	−.02	.11**	.06	.13**	.06	.04	.18***	—
16	HeardPM	.00	.00	.10*	.13**	−.04	−.16***	−.21***	−.14***	.02	−.12**	−.09*	.11**	−.09*	−.18***	−.05

Notes. $N = 674$. ComSciU and ComDatU = conditions grouped by factor (0 = certain, 1 = uncertain); PSU = perceived scientific uncertainty, PDU = perceived data uncertainty, race (1= white, 2 = nonwhite), ethnicity (1 = Hispanic, 2 = non-Hispanic), IUS = intolerance of uncertainty, UndStudy = understands ‘scientific study’, support = support science, HeardPM = heard of PM (0 = no, 1 = yes). Participate is treated as a 3-level continuous variable ($N = 597$).

$^{\dagger}p < .10$, $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Table 2. Main effects for scientific and data uncertainty disclosure

	Scientific benefit of PM			Data use in PM		
	Scientific certainty ($N = 302$)	Scientific uncertainty ($N = 372$)	$F(df)$, p-value	Data certainty ($N = 329$)	Data uncertainty ($N = 345$)	$F(df)$, p-value
Perceived scientific uncertainty	2.38 (.99)	2.72 (1.01)	$F(1,668) = 17.48$, $p < .001$	2.51 (1.03)	2.62 (1.00)	$F(1,668) = 2.17$, $p = .14$
Perceived data uncertainty	2.85 (1.14)	2.94 (1.17)	$F(1,668) = 1.32$, $p = .25$	2.71 (1.14)	3.08 (1.14)	$F(1,668) = 15.55$, $p < .001$
Attitudes	5.49 (1.43)	5.55 (1.21)	$F(1,668) = .20$, $p = .66$	5.57 (1.33)	5.48 (1.29)	$F(1,668) = .66$, $p = .42$
Researcher trust	3.48 (0.86)	3.55 (0.80)	$F(1,668) = .86$, $p = .35$	3.54 (0.84)	3.51 (0.82)	$F(1,668) = .09$, $p = .76$
Willing to participate[a]	2.03 (0.75)	2.00 (0.75)	$F(1,591) = .25$, $p = .62$	2.03 (0.75)	2.00 (0.76)	$F(1,591) = .10$, $p = .66$

Notes. Results of two-way ANCOVAs grouped by factor, controlling for ethnicity and income. Means (standard deviations) are reported. See Supplementary Tables 3a and 3b for means by condition.

[a] Variable treated as continuous, excluding "not sure" responses (group sizes for scientific factor: certainty $N = 266$, uncertainty $N = 331$; Data factor: certainty $N = 296$, uncertainty $N = 301$). Effects were similar when "not sure" category was included (see Supplementary Material 4).

Main Effects of Communicating Uncertainty (RQ1 and RQ2)

Two-way ANCOVAs, with income and ethnicity as covariates, showed no main effect of communicating scientific uncertainty—compared to certainty—on (a) attitudes toward PM research, (b) researcher trustworthiness, or (c) willingness to participate (RQ1). Similarly, there was no main effect of communicating data uncertainty on (a) attitudes, (b) trust, or (c) willingness to participate (RQ2). Participants' uncertainty perceptions did, however, align with their respective conditions, indicating the article manipulations were perceived as intended. Results are reported by factor in Table 2 and by condition in Supplementary Material 3.

Interaction Effects Between Types of Uncertainty (RQ3 and RQ4)

We examined whether one uncertainty type would have a stronger impact than the other (RQ3) and whether effects would be stronger when both uncertainty types were communicated instead of just one type (RQ4). There was no overall interaction effect for attitudes, $F(1,668) = 0.06$, $p = .81$; trust, $F(1,668) = 1.03$, $p = .31$; or willingness to participate, $F(1,591) = 0.19$, $p = .66$. Pairwise comparisons indicated no difference between groups 2 and 3 (scientific uncertainty only vs. data uncertainty only) on outcomes, and no difference between Group 4 versus 2 (both types vs. scientific only) or between Group 4 versus 3 (both types vs. data only) on outcomes.

Perceived Uncertainty as a Mediator (H1 and H2)

Consistent with the hypothesized pathways, both perceived scientific uncertainty (H1) and perceived data uncertainty (H2) mediated the relationship between message condition and outcomes. Disclosing scientific uncertainty led to higher perceived scientific uncertainty, which led to less favorable (a) attitudes, (b) trust, and (c) willingness to participate. The same pattern emerged for data uncertainty. When accounting for these indirect effects, there were positive direct effects of scientific uncertainty disclosure on attitudes and trust. Coefficients are reported in Table 3.

Individual Differences: Moderated Mediation Analyses (H3–H8)

Three individual characteristics were examined as moderators of the direct or indirect effects of disclosure of scientific uncertainty (H3–H5) and data uncertainty (H6–H8). Results are reported below. Visual depictions of significant paths are presented in Supplementary Material 5. The labels "low," "moderate," and "high" correspond approximately with 1 standard deviation below the mean, values near the mean, and 1 standard deviation above the mean, respectively.

Scientific Uncertainty Disclosure

Intolerance of uncertainty (H3)

The index of moderated mediation was not significant for (a) attitudes, (b) trust, or (c) willingness to join. In other words, the negative indirect effect of disclosure

Table 3. Mediation test by DV for perceived uncertainty

		Indirect effect of X on Y		Model paths			
DV	Mediator	*b* (*SE*)	95% CI	*a* path	*b* path	*c* path	*c'* path
Scientific uncertainty							
Attitudes	Perceived scientific uncertainty	–0.23 (0.05)	–.03325, –0.1215	0.33 (.08)***	–0.68 (0.04)**	0.05 (0.10)	0.27 (0.09)*
Researcher Trust		–0.11 (0.03)	–0.1632, –0.0584	0.33 (.08)***	–0.33 (0.03)**	0.06 (0.07)	0.18 (0.06)*
Willing to Participate[a]		–0.10 (0.03)	–0.1607, –0.0441	0.30 (0.09)**	–0.33 (0.03)**	–0.03 (0.06)	0.07 (0.06)
Data uncertainty							
Attitudes	Perceived data uncertainty	–0.18 (0.05)	–0.0927, –0.2785	0.36 (0.09)***	–0.52 (0.04)***	–0.08 (0.10)	0.10 (0.09)
Researcher Trust		–0.14 (0.04)	–0.0755, –0.1794	0.36 (0.09)***	–0.33 (0.02)***	–0.03 (0.06)	0.09 (0.06)
Willing to Participate[a]		–0.10 (0.03)	–0.0440, –0.1630	0.33 (0.09)**	–0.31 (0.02)***	–0.02 (0.06)	0.08 (0.05)

Notes. The table reports simple mediation tests (PROCESS Model 4 with 5,000 bootstraps) with income and ethnicity included as covariates. The first two columns of data report the indirect effect of communicating uncertainty on outcomes via perceived uncertainty. The last four columns report the coefficients and standard errors for each path in the model (*a* = path from IV to mediator, *b* = path from mediator to DV, *c* = total effect, *c'* = direct effect). All indirect effects can be considered statistically significant as the confidence intervals do not overlap zero.

[a] $N = 597$.

$^{*}p < .01$ $^{**}p < .001$ $^{***}p < .0001$.

via perceived uncertainty held at all levels of intolerance. Answering H3a, intolerance of uncertainty moderated the direct pathway: disclosing uncertainty had a positive effect on attitudes for those with low to moderate intolerance ($M \leq 3.20$ on a 5-point scale; 74% of sample). Answering H3b, disclosing uncertainty also had a positive direct effect on trust for those with low to moderate intolerance ($M \leq 3.20$). However, intolerance of uncertainty also moderated the *b* path such that the negative relationship between perceived uncertainty and trust attenuated as uncertainty intolerance *increased* (from an effect of –0.45 at low intolerance to –0.15 at high intolerance). Answering H3c, intolerance did not moderate the direct or *b* paths for willingness to participate. Intolerance of uncertainty did not moderate the *a* path from message to perceived scientific uncertainty.

Support for science (H4)

The index of moderated mediation was significant for (a) attitudes, (b) trust, and (c) willingness to join. For all three outcomes, the negative indirect effect of disclosure via perceived uncertainty was only significant for those with support at or above the sample mean (4 or above on a 5-point scale; 70.5% of sample); for those low in support for science, the indirect effect was small and not significant. Answering H4a, support for science moderated the *b* path such that the negative relationship between perceived uncertainty and attitudes attenuated as support increased (from an effect of –0.82 at low support to –0.57 at high support). Additionally, with support and perceived uncertainty accounted for, a direct positive effect of communicating uncertainty on attitudes was now significant at all levels of support. Answering H4b, disclosing uncertainty had a direct positive effect on trust for those with support at the sample mean or higher (4 or above). Support did not moderate the *b* path from perceived uncertainty to trust. Answering H4c, support did not moderate the direct or *b* paths for willingness to join. Support did not moderate the *a* path from message to perceived uncertainty.

Understanding of a scientific study (H5)

The index of moderated mediation was not significant for (a) attitudes or (b) trust, but was significant for (c) willingness to join. For those reporting high understanding of the concept of a scientific study, the negative indirect effect of disclosure on willingness via perceived uncertainty was small and nonsignificant. Answering H5a, understanding moderated the direct pathway: disclosing uncertainty had a positive effect on attitudes for those at the mean level of understanding or higher ($M \geq 1.89$; 93% of sample). Answering H5b, disclosing uncertainty also had a positive effect on trust for those at mid to high understanding ($M \geq 2.19$; 44% of the sample). At the same time, understanding moderated the *b* path such that the negative relationship between perceived uncertainty and trust strengthened as understanding increased (from an effect of –0.19 at low understanding to –0.38 at high understanding). Answering H5c, disclosing uncertainty had a direct positive effect on willingness only for those with low understanding (6% of the sample). Understanding did not moderate the *a* path from message to perceived uncertainty.

Data Uncertainty Disclosure

Intolerance of uncertainty (H6)

The index of moderated mediation was not significant for (a) attitudes, (b) trust, or (c) willingness to join, meaning the negative indirect effects of disclosure via perceived uncertainty held at all levels of intolerance. Answering H6a, intolerance of uncertainty moderated the direct pathway such that disclosing data uncertainty had a positive effect on attitudes for those with *high* intolerance ($M \geq 3.39$ on a 5-point scale, or 20.77% of the sample)—opposite from its effect for disclosure of scientific uncertainty. Further, intolerance moderated the *b* path such that the negative relationship between perceived uncertainty and attitudes attenuated as intolerance increased (from an effect of –0.68 at low intolerance to –0.31 at high intolerance). Answering H6b, there was again a conditional direct effect: at higher levels of intolerance ($M \geq 3.02$; 32.49% of the sample), disclosing data uncertainty had a positive effect on trust. Further, the negative relationship between perceived uncertainty and trust attenuated as intolerance increased (from an effect of –0.45 at low intolerance to –0.17 at high intolerance). Answering H6c, there was no conditional effect of intolerance of uncertainty on the direct or *b* paths for willingness to participate. Lastly, intolerance did not moderate the *a* path from message to perceived data uncertainty.

Support for science (H7)

The index of moderated mediation was not significant for (a) attitudes, (b) trust, or (c) willingness to join, meaning the negative indirect effects of disclosure via perceived uncertainty held at all levels of support. Answering H7a–c, support for science did not moderate the direct or *b* paths. Support for science also did not moderate the *a* path from message to perceived data uncertainty.

Understanding of a scientific study (H8)

The index of moderated mediation was not significant for (a) attitudes or (b) trust, or (c) willingness to join, meaning the negative indirect effects via perceived uncertainty held at all levels of understanding. Answering H8a–c, understanding did not moderate the direct or *b* paths. Understanding of a scientific study also did not moderate the *a* path from message to perceived data uncertainty.

Follow-up Analyses: Perceived Ethicality

Given that ethical implications are central to discussions of both PM research [7–9] and transparent science communication [61], we conducted post hoc analyses to examine the effect of disclosure for the single ethicality item from the broader trust scale. Three notable findings emerged. First, message factor influenced perceived ethicality of the researchers, with the scientific uncertainty messages generating more perceived ethicality ($M = 3.62$, $SD = 0.88$) than the scientific certainty messages ($M = 3.48$, $SD = 0.94$; $t(672) = 1.96$, $p = 0.048$)—an effect that did not emerge for the full trustworthiness scale. Second, ethicality ratings were higher for disclosure of scientific uncertainty ($M = 3.68$, $SD = 0.85$) than data uncertainty ($M = 3.47$, $SD = 0.91$), $t(331) = 2.15$, $p = 0.03$. Given these results, we tested perceived ethicality as a mediator in parallel to perceived scientific uncertainty. While the negative indirect path via perceived uncertainty remained, perceived ethicality positively mediated the relationship between scientific uncertainty disclosure and attitudes (effect = 0.06, boot $SE = 0.03$, boot 95% CI: 0.01, 0.12) and willingness to participate (effect = 0.06, boot $SE = 0.03$, boot 95% CI: 0.01, 0.12; see path coefficients in Supplementary Material 6).

Discussion

Embedded in a news article experiment, this study examined public responses to the communication of two types of PM research uncertainty: uncertain scientific impact and uncertain future use and governance of participant data. Overall, attitudes toward participating in PM research were favorable ($M = 5.5$ on a 7-point scale), consistent with other surveys [49]. A majority of respondents reported being somewhat (39%) or very (26%) likely to participate in PM research if invited, and trust in the research organizations was generally high ($M = 3.5$ out of 5). Communicating scientific or data uncertainty did not uniformly affect attitudes, trust, or willingness to participate. Further, neither type of uncertainty appeared to loom larger for participants, and communicating both types together also did not significantly impact outcomes.

Indirect and Conditional Effects of Uncertainty Disclosure

A second goal of this study was to examine the influence of uncertainty perceptions and individual characteristics on reactions to uncertainty disclosure. Perceived uncertainty negatively mediated the relationship between disclosure and all outcomes for both scientific and data uncertainty. But uncertainty perceptions appeared only somewhat driven by disclosure: correlations between perceiving uncertainty and receiving an uncertain (vs. certain) message were small ($r = 0.16$) for each uncertainty type. This suggests other factors, in addition to message content, likely influenced uncertainty perceptions.

Three individual difference variables were examined as moderators of the direct or indirect effects of uncertainty disclosure. As described before and shown in Supplementary Material 5, none of these characteristics moderated the path from message to perceived uncertainty. However, they did moderate the direct and b paths in nuanced ways. For those higher in support for science, the scientific uncertainty disclosure had a direct positive effect on trust in the scientists. For those reporting that they understand the concept of a scientific study, the disclosure had a direct positive effect on both trust and attitudes toward participating. These two characteristics did not moderate processing pathways for data uncertainty. One possible reason for these moderation patterns is that scientific uncertainty disclosure is well-received by those with greater interest in or familiarity with science. Interestingly, higher self-rated understanding also associated with a stronger negative indirect effect on trust via perceived uncertainty. This suggests possible competing motivational pathways: for some people, a better understanding of science might lead them to expect uncertainty and appreciate its disclosure, while for others, it might lead to more interest in the success of the research and thus greater disappointment about possible lack of benefit. Results of the parallel mediation analyses shown in Supplementary Material 6 lend further support to the possibility of these competing pathways, as disclosure produced positive effects via greater perceived ethicality but negative effects via perceived uncertain benefit. Future research should try to identify factors that influence which motivational path an individual follows.

Support for science showed an alternate pattern, however: higher support *attenuated* the negative indirect effect of disclosure on attitudes via perceived uncertainty. Given that participants were asked to rate the value of scientific research "even if it brings no immediate benefits," it makes sense that perceiving uncertainty would not dampen attitudes for those higher in support.

Dispositional uncertainty tolerance also played a complex role in participants' evaluations, operating in different ways for scientific and data uncertainty. Disclosing scientific uncertainty had a direct positive impact on attitudes and trust for those *more* tolerant of uncertainty (as one would expect), while disclosing data uncertainty had a direct positive impact on attitudes and trust for those *less* tolerant of uncertainty. For both scientific and data uncertainty, negative indirect effects of uncertainty disclosure *attenuated* as intolerance increased. Why would intolerance of uncertainty associate with more favorable reactions to its disclosure in some cases? Potentially, people who dislike uncertainty are more apt to tune it out—a possibility that seems supported by the inverse correlations between intolerance of uncertainty and perceived uncertainty of both types (see Table 1). Instead of being more sensitive to uncertainty depictions, discomfort with uncertainty might cause some people to feel less prepared to process it and thus to selectively ignore it. At the same time, uncertainty tolerance did not moderate the path from condition to perceptions, so it may be that those less tolerant tend to perceive less uncertainty regardless of what is communicated. The relationship between uncertainty tolerance and uncertainty perceptions merits further exploration.

Strengths, Limitations, and Future Directions

This study is the first to examine whether uncertainty—specifically, communication about scientific and data uncertainty—is likely to influence public responses to PM research. Prior surveys did not portray either aspect of uncertainty when soliciting public attitudes about PM research [49], making this important to investigate. Another strength of this study is that it used a real news article as the base for the experimental manipulation, rendering it similar to what audiences would naturally encounter. A third strength of this research is the diversity of the sample in terms of race and ethnicity, age, education, and income levels. Understanding the perspectives of individuals from diverse groups, especially racial/ethnic minority groups, is critical because their inclusion in PM research is essential to fair outcomes [7, 8].

Some limitations should also be noted. First, we used an internet panel and assessed self-reported willingness to participate rather than actual participation. Thus, our findings are most applicable to public communication, such as news, op-eds, and media-based recruitment campaigns, where individuals may first hear about PM research opportunities but not yet be deciding whether to participate. While use of promissory language is common in those formats, it is uncommon in formal research recruitment materials and consent forms; yet future studies could build on our findings to examine how best to convey uncertainty in those contexts, as well.

Second, participants who received statements of certainty may have come away from this study with an unrealistic sense of the scientific and data related implications of PM research. Our content was based on language observed in real news articles and op-eds about this type of research, making it similar to what someone might encounter in daily life. To avoid misinforming participants, we debriefed them about the article manipulations at the end of the study. We hasten to note that individuals would glean a more realistic picture of the prospective benefits and risks of participation during the consent process if they ultimately decide to participate in PM research.

The difference between the two types of uncertainty should also be emphasized: while scientific uncertainty refers to uncertain *benefit to society* in this context, data uncertainty refers to uncertain *risk to the participant*. Although disclosing data related uncertainty did not have an overall impact on hypothetical willingness to volunteer among our sample, this factor might loom larger for individuals actually deciding whether to participate in PM research. Relatedly, being invited to participate in an actual setting might motivate people to scrutinize the information more closely than the participants did in our study. Thus, follow-up studies should examine the impact of uncertainty disclosure on additional outcomes, such as information-seeking and actual decision to participate.

The current study presented each aspect of uncertainty as an inherent part of the PM research process, and this "normalized uncertainty" frame [34, 62] may have contributed to participants' general receptiveness toward PM despite uncertainty disclosures, especially for scientific uncertainty and among those tolerant of uncertainty or more invested in science. Thus, future research might compare effects of uncertainty disclosure *with* and *without* a normalizing frame. Future experiments could also examine whether some uncertainty-framing approaches are optimal for engaging audiences based on specific characteristics such as intolerance for uncertainty, as well as other variables not studied here. Lastly, future studies could include a control message unrelated to PM to test for simple information effects.

Future studies should also examine factors that influence willingness to participate, which was largely unexplained by message condition and individual difference moderators in our study. It also remains unclear which factors, beyond message condition, might have shaped uncertainty perceptions. Several audience characteristics correlated with each of these variables, as shown in Table 1, and these deserve further attention in future studies. For example, higher age correlated with lower willingness to participate and higher perceived uncertainty. Attention to both age differences and cohort effects will be important in future research in this context.

Those with more support for science and understanding of a scientific study—variables that might be related to higher scientific literacy or interest—reported greater willingness to participate and less perceived uncertainty. Potentially, motivated reasoning could again explain the results, with the perceived (un)certainty measures capturing optimism or pessimism about the research. Individuals who are more enthusiastic about research in general might feel more confident of positive outcomes. Although the items asked participants to appraise the level of certainty *based on the article*, it is highly plausible that respondents drew upon their attitudes toward biomedical research more broadly. Most participants (90%) said they had not previously heard of PM. Nonetheless, people often draw on relevant past beliefs, attitudes, and experiences when evaluating information about new scientific initiatives [55] and when evaluating uncertainty [15]. This aligns with key theoretical postulates of UIT, which claims that people appraise uncertainty as an opportunity or a danger based on relevant prior knowledge or experiences [15], and UMT, which posits that people manage uncertainty depending on their motivations (e.g., to maintain hope) [14].

Lastly, while there was no main effect of disclosure on trust, a *post hoc* analysis of the ethical item separated from the trust scale showed that participants who received the scientific uncertainty (vs. certainty) articles rated the research institutions as more ethical. Ethicality may represent something unique and distinct from trustworthiness in this context. Although we consider this finding tentative, a potential relationship between communicating scientific (un)certainty and perceived ethicality merits further testing—ideally with an expanded, multi-item ethicality measure—given the important link between ethicality and transparency in PM research [7–9].

Conclusion

Given the ethical implications of novel PM research, which is characterized by numerous uncertainties, it is critical to understand which communication approaches will support an informed public—including prospective research volunteers [7, 8, 11]. In the current study, disclosure of scientific and data related uncertainties did not have a main effect on attitudes toward participating, trust in the researchers, or willingness to join a PM cohort, and scientific uncertainty disclosure led to higher perceived researcher ethicality. Beyond this, responses appeared largely shaped by individual characteristics and perceptual filters. A next step is to uncover *why* certain groups are less comfortable with uncertainty in order to develop messages that address their concerns. Additionally, for those low in scientific understanding or tolerance for uncertainty, enhancing the "normalized uncertainty" frame [34, 62]—for example, by providing further information to help audiences understand that some uncertainty is inevitable in the process of scientific discovery—could support the aims of both transparency and effective recruitment of a diverse group of volunteers. The potential utility of normalized uncertainty frames for promoting public engagement in PM—both in public communication and in formal recruitment and consent processes—warrants further study.

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