Collecting Comprehensive and Representative Input

HYPOTHETICAL SCENARIO: A PATIENT EXPERIENCE SURVEY WITH A LOWER-THAN-EXPECTED RESPONSE RATE

Disclaimer: This hypothetical scenario provides practical supplemental information to illustrate some important concepts presented in FDA's draft guidance on *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input*, which the Agency displayed for public comment on June 12, 2018. This hypothetical scenario should not be construed as formal advice from FDA. FDA encourages stakeholders who are considering collecting and submitting patient experience data to have early interactions with FDA. As the science of patient input matures, or in response to comments received on FDA's guidance, the scenario may be updated. The scenario focuses on a specific methodological issue and does not address all aspects of good research design, conduct, analysis, reporting, data protection, and patient privacy, including all potential legal obligations.

SITUATION

A patient group has conducted a survey to supplement an externally-led Patient-Focused Drug Development meeting on a common symptomatic condition. The purpose of this survey was to capture a more representative sample of patients' perspectives on their most bothersome symptoms, associated impacts, and current approaches to managing their condition. The patient group hopes that the results of this survey can broadly inform medical product development and FDA's benefit-risk assessments for this disease area. The patient group plans to submit a study report to FDA for posting on FDA's External Resources or Information Related to Patients' Experience webpage.

To administer the survey, the patient group teamed up with a clinical researcher who is affiliated with a large healthcare system serving more than a million people. The healthcare system maintains a database that includes demographic and clinical information on its patient members. The clinical researcher has an institutional review board (IRB)-approved protocol to conduct the study and identify potential study participants using the healthcare system's database. Approximately 10,000 patients were identified as satisfying the definition of this survey's target patient population. Email invitations were sent to all 10,000 individuals through a secured web portal. The survey was open for one week. At the end of the week, 150 people had completed the survey. The response rate was much lower than anticipated or desired. The patient group has a limited budget and wonders how best to proceed with the study.

A POTENTIAL CONCERN FOR MEDICAL PRODUCT DEVELOPMENT

Low response rate

In this hypothetical situation (and without any other information), the primary concern of a low response rate is non-response bias. Simply put, individuals who responded to the survey may differ from those who did not, by such characteristics as age, disease phenotype/genotype, symptom severity, socioeconomic factors, and life situations. For example, it may be that the survey respondents tended to be people with more severe forms of disease or people who have more free time to complete surveys. To the extent that patient perspectives vary according to various characteristics, and to the extent that these characteristics differ substantially between responders and non-responders, the survey results may be subject to non-response bias. Non-response bias limits the ability to generalize the perspectives of the responders to the non-responders or to the patient population overall.

HOW COULD RESEARCHERS ENHANCE THE RESEARCH EFFORT?

There are a number of ways that the patient group and clinical researcher team could proceed, depending on their goals and resource constraints. A few options are outlined below. The suggestions below do not represent an exhaustive list of options. It is important to keep in mind that some advanced planning in design of the survey and its sampling approach may have mitigated the risk of low response and the potential impact of non-response bias.

End the study and analyze the results

If resources are severely constrained, it is possible to end the s and analyze the results of the 150 individuals who responded. However, the patient group should clearly recognize the limitations of this study and not overinterpret the results based on these 150 individuals.

The patient group may also need to reconsider how the survey results may be useful for medical product development. The research may be useful for identifying potential areas of unmet need or suggesting symptoms that could be further explored as clinical trial endpoints. However, additional research studies would be necessary to directly inform development of clinical outcomes assessments for clinical trials.

In their study report, the team should summarize relevant demographics and other information about the population that did respond and about the entire survey population. They should discuss potential ways in which the 150 people who responded may be similar or different from the people who did not respond. In addition, it would be useful to include a summary of other available research that may provide insight on the target patient population's experiences and perspectives. For example, in their discussion of the findings on the survey respondents' most bothersome symptoms, the patient group may note in their report other symptoms that have been identified in the literature as being highly bothersome to some patients.

Re-administer the survey

If some additional resources are available, the team could re-administer the survey, taking efforts to follow up with non-responders. A week may not have been

sufficient time for invited patients to respond. The researchers and patient groups should also make efforts to follow up with potential participants, at least through email, and perhaps through text, phone, or mail. This will likely incur an additional cost and may require patient privacy considerations. Ideally, any efforts to increase participation would happen before any analysis of the survey results to minimize potential biases in the survey analyses or reporting of findings.

Although they may help improve precision, higher participation rates may not completely address concerns about non-response bias and generalizability of the survey results. Confidence in the generalizability of survey results depends on a number of factors in addition to response rate, such as the underlying target population, the endpoints one is trying to learn about, and the study objectives. To increase confidence, the study report should include the components outlined above, including information about patients who responded versus those who did not respond and a summary of other available research.

Conduct the study again, modifying the sampling approach and survey design

Ideally, if resources allow, the patient group would consider conducting the study again, modifying the sampling approach and survey design based on learnings from the original survey research, drawing a sample from same healthcare system population. A carefully developed sampling scheme may be able to achieve the research objectives more efficiently than the original approach taken (for example, by sampling a subset of individuals rather than inviting all 10,000 individuals). Doing so will allow for setting recruitment targets and oversampling patients with certain characteristics. Assessing the characteristics of the non-responders from the original study may provide insights that can inform development of the sampling approach for the revised study.

A new study could also build in a robust follow-up plan that includes well-designed email reminders, and possibly more direct follow up through phone or text. Having a smaller sample can allow for more manageable and cost-effective follow-up methods.

The study may also require some modifications to its design. Keep in mind that a well-designed study (including such things as the survey instrument, the invitation email, and participation incentives) is important to maximizing the survey response and survey completion rates. For example, it may be that the original survey was burdensome or difficult to complete. Assessing the dropout rate (the number of people who started the survey but did not finish) may provide an indication of the survey burden. In this case, it may be useful to simplify the survey instrument and focus the survey on questions that most closely align with the research objectives. It is always useful to conduct adequate pre-testing of your questionnaire in advance of administering the survey.

FOR MORE INFORMATION:

www.fda.gov/FDAgov/Drugs/DevelopmentApprovalProcess/ucm610279