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Individuals with diabetes preferred that future trials use patient-important outcomes and provide pragmatic inferences

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Abstract

Objective: We sought to examine patients' preferences regarding the design of diabetes trials. Specifically, do patients prefer trials to focus on patient-important outcomes (vs. surrogate outcomes) and provide practical/pragmatic answers (vs. mechanistic/explanatory answers)?

Study Design and Setting: We mailed a questionnaire to a stratified random sample of 4,796 patients with diabetes receiving care from 371 primary care clinicians in the US Midwest. Medical record review provided data on hemoglobin A1c (HbA1c). Descriptive statistics, logistic regression, and multiple regression techniques were used for analysis.

Results: We received completed surveys from 2,036 patients (response rate of 42.5%). On average, respondents were 65 years old, had 11 years of diabetes, and had excellent glycemic control (HbA1c = 7%). Most patients (>75%) chose patient-important outcomes rather than HbA1c as their first choice for a trial primary outcome and preferred a practical trial design. Patients with poor glycemic control (HbA1c > 8.0%) were more likely to prefer HbA1c as a primary end point (odds ratio: 1.5; 95% confidence interval: 1.1, 2.1).

Conclusion: Individuals with diabetes report a strong preference for practical trials measuring the effect of treatments on patient-important outcomes. To our knowledge, this is the first report of patients endorsing key elements of the comparative effectiveness agenda.

Keywords: Trial design; Values and preferences; Pragmatic; Explanatory; Survey; Surrogate; Patient-important outcomes

1. Introduction

The Patient Protection and Affordable Care Act of 2010, the health care reform law, incorporates a strong agenda supporting the conduct of comparative effectiveness research. The law mandates the constitution and funding of an independent nonprofit organization, the Patient-Centered Outcomes Research Institute, to promote the conduct and dissemination of this research. This form of research has to be most informative to decision makers, a hallmark of practical trials [1]. Furthermore, research should directly address the effects of health care on outcomes that matter to patients (patient-important outcomes, such as death, stroke, myocardial infarction, pain, quality of life, and patient satisfaction). To our knowledge, however, the preferences of patients regarding this research remain unknown.

Mechanistic trials, also known as explanatory trials, refer to experiments that address a biological relationship and provide ''proof of concept'' evidence that helps researchers make decisions about further research. As a result, these trials often take the participants, use interventions, and measure the physiological or disease-specific objective outcomes that allow researchers to draw mechanistic inferences. On the other hand, practical trials refer to

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What is new?

- Researchers all-too-rarely consult patients about their values and preferences in terms of the research agenda.
- This is the first report that shows patients' opinion about diabetes trial design and outcomes.
- Most patients prefer trials that measure patient-important outcomes and provide pragmatic/practical inferences.

experiments that provide evidence about the effectiveness of interventions that helps either clinician–patient dyads or policymakers make informed decisions. Their structure will reflect this goal (e.g., for clinician–patient dyads, practical trials may need to enroll only highly compliant patients, whereas for public health decision making, ''all comers'' may be optimal). Common to all practical trials is the measure of patient-important outcomes [1].

Judging by the proportion of public funding that goes to mechanistic research and by the extensive press coverage of early-stage investigations, it may appear as if the public is mostly interested in discovery of new treatments and their effect on mechanisms of health and disease. We have recently measured the extent to which clinical trials in diabetes emphasize surrogate end points. Only 20% of published diabetes trials designated their primary end points as outcomes that are important to patients, that is, outcomes that affect the way patients feel, function, or survive [2]. A review of trial registries that address ongoing yet-to-be published trials showed that only one in five future trials will measure patient-important outcomes as primary end points and less than one in two will assess them at all [3]. Thus, we should not expect a change in this trend in future trials.

In diabetes, hemoglobin A1c (HbA1c) is considered by many patients, clinicians, and quality improvement specialists to be a measure of diabetes metabolic control that signals improvement in patient outcomes. Contrary to this expectation, recent trials in patients with type 2 diabetes have found that interventions that effectively lower this marker fail to improve patient-important outcomes [4,5]. Thus, to be confident that our interventions positively influence outcomes important to patients, trials must directly measure those outcomes.

We conducted a cross-sectional survey of patients with diabetes to ascertain their preferences on how clinical trials should be conducted in terms of study design and end points. Knowing the needs of the primary user and beneficiary of research, the patient, should guide subsequent trial design and thus ensure the evidence from comparative effectiveness research will optimally address the needs of the patient.

2. Methods

2.1. Study setting and patient sample

This study was conducted at 32 practices in the Mayo Health System (MHS). The MHS is a network of clinics and hospitals serving 70 communities in Iowa, Minnesota, and Wisconsin. The MHS includes more than 800 physicians and serves more than a million patients annually. This study was part of a larger project examining the delivery of diabetes care across these practices. The study design was a cross-sectional patient survey administered to a stratified random sample of 4,796 patients of 371 primary care clinicians. The sample frame was an existing MHS diabetes registry. Patients younger than 18 years were excluded from the sample. The survey packet included a cover letter signed by the principal investigator and a local physician champion, the survey booklet, and a postage-paid self-addressed return envelope. The survey was administered by mail during the fall/winter of 2009. After 4 weeks of the initial mailing, nonresponders to the first survey were resent the survey packet. Data about glycemic control (HbA1c level) were obtained from electronic medical records. The Institutional Review Boards at the Mayo Clinic in Rochester, Minnesota, and Franciscan Skemp Healthcare in La Crosse, Wisconsin, approved this study.

2.2. Survey contents

The survey included 25 questions regarding patients' demographic characteristics, assessment of quality of life, duration of diabetes, satisfaction with care, assessment of care delivery for diabetes using the Patient Assessment of Care for Chronic Conditions [6], and description of current diabetes treatment. Two of the questions in this survey aimed at eliciting patients' preferences about future diabetes research (Box). These questions were developed iteratively using a focus group of eight patients with diabetes with extensive experience in interacting with researchers [7]. The focus group provided feedback regarding the language and format of the questions.

2.3. Statistical analysis

We used descriptive statistics for the two questions on trials outcomes and design to examine patient preferences for diabetes-related outcomes. We used logistic regression and multiple regression techniques to examine the factors associated with patients' choices of the outcome as HbA1c (dependent) variable. We included the following variables in our regression models: age, gender, education, diabetes control, duration of diabetes, and number of prescription medications a patient uses. The rationale for choosing these variables was based on our hypothesis that those who are younger or more educated may be more interested in explanatory/mechanistic designs, those with poorly controlled disease may be more interested in the surrogate