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FASTER RESULTS, BETTER OUTCOMES:

How person-centered trial design improves clinical research

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Introduction

Across the healthcare industry, new and updated initiatives demonstrate the growing commitment to person centricity in clinical research. Some key initiatives include:

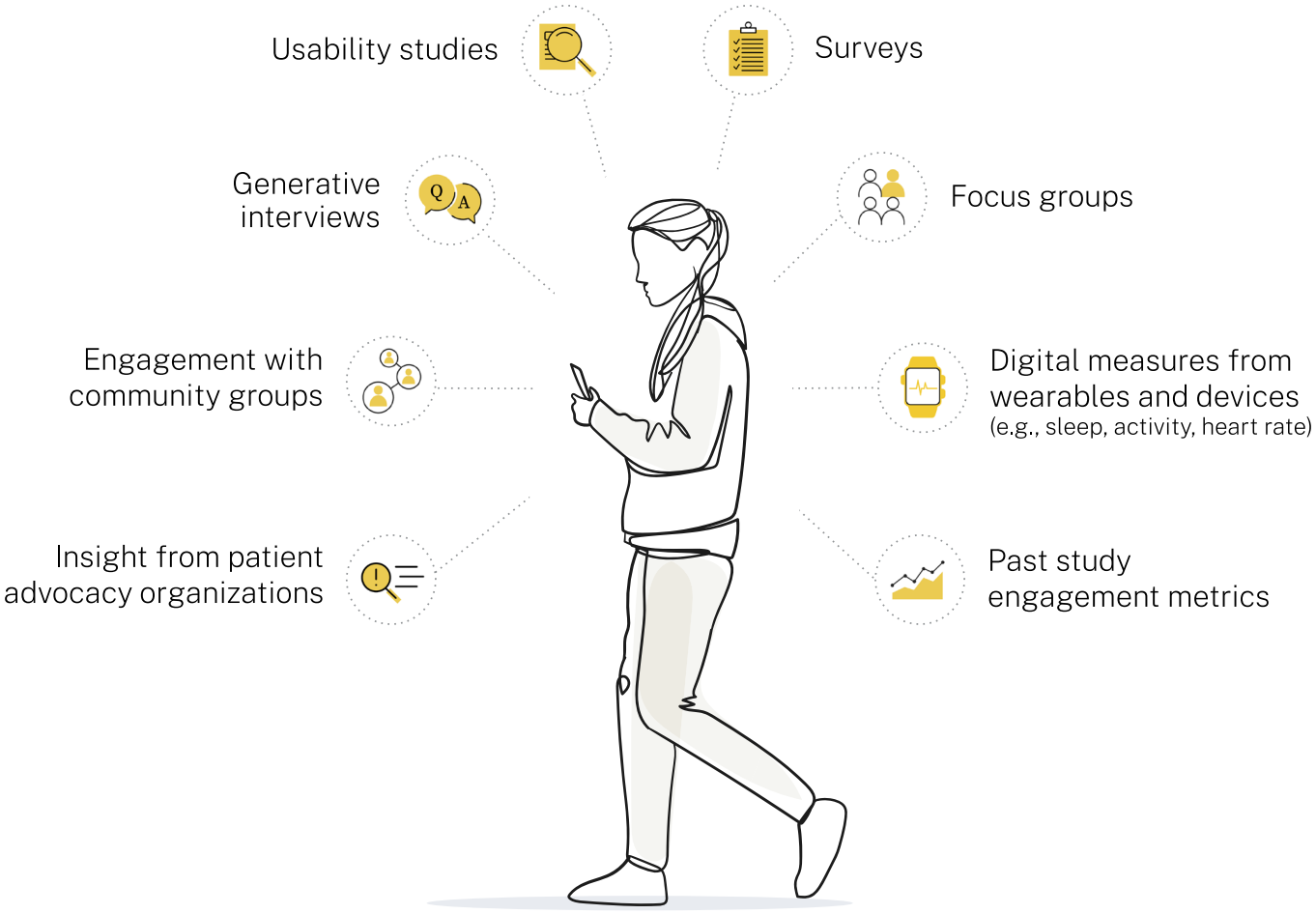
- The Food and Drug Administration's **Patient-Focused Drug Development Program (PFDD)** for a "systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation."

- The **Medical Device Innovation Consortium (MDIC)**, a public-private partnership that spearheads **projects to identify ways to use patient preference information (PPI) for clinical trial design.**

- The National Health Council, which continues to research and **establish patient-centered core impact sets (PC-CIS)**, patient-prioritized lists of the impacts a disease and its treatment have on a person and their family and caregivers.

A key aspect of ensuring delivery of value to individuals is capturing the participant voice for trial design, the importance of which is recognized by the managing organizations of these initiatives. This helps bridge the gap between the outcomes important to clinicians and researchers and those that truly matter to individuals.

Sample methods to capture the participant voice and input



Common gaps in traditional research designs include:

- Missing large segments of the population, such as women, people of color, individuals with a lower socioeconomic status, and people in rural areas
- Failing to reach a representative sample of the specific population being studied
- Inadequately capturing the everyday experiences that affect individuals' health outcomes
- Medical products and interventions that are not successful commercially because they do not provide the benefits important to people or address people's unmet needs

Involving patients and caregivers in study design leads to trials with greater operational, regulatory, and commercial success, due to:

- **Endpoints that matter to participants and caregivers:** These carry more weight with regulators and payers. The FDA has noted that patient acceptance of benefits despite probable risks can support a favorable benefit-risk profile.
- **Less burdensome study design:** Designing trials with study activities that are convenient for participants reduces burden. This can speed up recruitment and enrollment, boost engagement, and improve compliance and completion rates.
- **Greater trust in the outcomes of the study:** Including individual feedback during study design fosters trust in the research and the end product, enhancing market adoption once available.
- **Financial and time savings:** Early participant input prior to phase 2 trials can yield significant returns, including a **500-fold return on the investment** to capture the patient voice. This includes a potential 2.5-year reduction in the time to launch. This estimate is based on avoidance of one protocol amendment and better enrollment, adherence, and retention.

Successfully implementing person-centric approaches requires **overcoming perceived barriers** and a change in mindset regarding clinical trial planning. The following sections describe ways to **design studies that work for, not against, people** and **recruit people where they are, both geographically and mentally** for greater person centricity in your clinical trials.

SECTION 1

Design studies that work for, not against, people

Clinical trial designs informed by participant input recognize and accommodate the real-life needs and experiences of individuals, which can be reflected in the:

- Inclusion/exclusion criteria
- Endpoint selection
- Assessment modality, frequency, timing, and location
- Design of intervention materials

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Senior Director of Product and Portfolio Strategy, Evidation

"Designing studies that deliver value to participants requires us to reorient how we think about research. Reducing burden, motivating participation, and achieving meaningful endpoints are not new concepts, but addressing them requires us to truly involve individuals as partners in research, engaging with them early and in new and different ways. Evidation enables this longitudinal relationship with a platform that meets people where they're at and allows for re-engagement over time."

Inclusion and exclusion criteria for timely, representative enrollment

Using participant input to identify the inclusion and exclusion criteria that more closely reflect the characteristics of the intended population can provide the following benefits:

- **Faster recruitment and enrollment:** Less restrictive eligibility criteria expand the population from which to recruit.
- **More accurate benefit-risk profile:** Adequate representation of the individuals who will use the therapy after approval aids in understanding of the safety risks and real-life benefits across the entire patient population.
- **More efficient endpoint analysis:** Identifying individuals who see value in the intervention can lead to a more precise assessment of its effectiveness for those who will use it in practice. By studying people who see value in the intervention, we can more accurately assess its effectiveness for its intended users.
- **Segmented analyses:** A larger population enables examination of outcomes across different participant subgroups.

Characterizing the intended study population through diverse characteristics and preferences is key to establishing realistic, representative, and efficient inclusion and exclusion criteria.

EXAMPLE 1

Broader inclusion criteria can help achieve a more representative population.

A review of Alzheimer's disease studies found that excluding people with common comorbid conditions often **disqualifies certain racial/ethnic or socioeconomic groups** who are more likely to have these conditions. By widening the inclusion and exclusion criteria to encompass these conditions, we can recruit a broader population and obtain results that better represent those affected by the disease or condition.

EXAMPLE 2

Study efficiency benefits from identifying the sub-population who will actually use the treatment.

Feedback from individuals living with blindness and their families highlighted that a new gene therapy for blindness was not likely to be used by people who had been born blind and lived their whole lives as productive people while fully blind. However, the therapy was likely to be attractive to someone who had lost their sight during their life and wanted it back or to parents of young, blind children. This type of information could refine not only the inclusion and exclusion criteria but also the marketing strategy once the therapy went to market.

Example questions to ask individuals, caregivers, and patient groups:

- Does the proposed research address an unmet need?
- Have there been other studies in which you've been interested in participating but couldn't because of the study requirements? What were those requirements?
- Do any of the inclusion/exclusion criteria present a barrier for someone to participate?
- Would you be interested in using the intervention if it became available?
- What changes, if any, would you recommend for the intervention to be more acceptable or relevant to your life?
- Are there specific considerations that we should address regarding geographic location, cultural aspects, age, gender, race, language, or socioeconomic status when we identify participants for our study?

Prioritizing person-centric outcomes in clinical trials

Including study outcomes that matter to individuals and caregivers is crucial, as these often differ from what sponsors or clinicians prioritize. This approach can lead to:

- **Improved retention:** Participants are more likely to stay in trials that focus on outcomes meaningful to them.
- **Relevant outcomes:** Study results will be more valuable to those who will use the intervention, enhancing its real-world impact.
- **Better reimbursement potential:** When interventions meet participant needs, they are more likely to be reimbursed.
- **Increased adoption:** Both physicians and patients are more likely to embrace an intervention that addresses person-centric outcomes once it's available in the market.

Combining what individuals want with the specific research goals can achieve the study's aims while addressing unmet needs, resulting in better health outcomes and greater satisfaction with treatments.

Surveying individuals informs study outcomes that balance researcher and participant priorities.

EXAMPLE 1

For a study of **a sickle cell disease (SCD) treatment**, the sponsor surveyed people with SCD and their families to help prioritize and expand a list of 22 candidate study endpoints, modes of administration, and adverse events.

- People with SCD identified two important concerns that had been omitted: daily chronic pain and worries about fertility due to treatment.
- Of the original list, people with SCD highlighted that lessening the risk of damage to organs and shortening the length of pain crises were top priorities. Caregivers, on the other hand, thought it was most important to decrease the severity of pain during pain crises and reduce their frequency. Both groups agreed that the lowest priority was lowering the risk of headaches, cognitive issues, and gastrointestinal problems.

EXAMPLE 2

To identify meaningful endpoints for future studies of Parkinson's disease (PD) therapies, a group of government, commercial, and non-profit organizations conducted discussion groups and a survey with people with PD. Although rarely included in PD studies, pain was rated as important by those with the disease.

EXAMPLE 3

Academic researchers generated a list of treatment goals from focus groups and a literature review. **People with schizophrenia and psychiatrists** ranked these goals by their perceived importance. Psychiatrists tended to focus on "textbook" outcomes, while individuals were more concerned with function and living a normal life.

People with schizophrenia want improvements in the following:

- Satisfaction
- Independence
- Physical health
- Activities of daily living
- Work capacity

Psychiatrists overvalue the following:

- Decreased mistrust/hostility
- Improved capacity for emotion
- Improved communication
- Decreased psychotic symptoms
- Improved self-confidence

Example questions to ask individuals, caregivers, and patient groups:

- What symptoms of your disease or condition do you experience as most bothersome?
- What symptoms of your disease would you most like to see change or improve?
- What results would an ideal treatment have?
- What do you wish your treatments did that they don't currently do now?
- Are the outcomes that we've identified important for you?
- What symptoms do you wish your treatment would address?
- How would you rate the severity of your symptoms (e.g., mild, moderate, severe)?
- How would you rank common symptoms in terms of priority for you?
- What side effects from your current treatment are the most troublesome?

Low-burden assessments for better adherence

Minimize the barriers to participation by designing the modality, frequency, timing, and location of assessments to fit within participants' lives.

Willingness to participate in clinical trials increases with decreased clinical trial burden, especially for individuals with greater disease burden.

In a survey delivered on the Evidation platform, we asked about willingness to become involved in clinical trials (n=7,091).

51.8% are unlikely to complete an eligibility screener if they have to travel to an on-site location.

91.6% are likely to complete an online eligibility screener.

50.5% and **40.1%** are unlikely to participate in studies requiring night and/or weekend visits or in-person visits, respectively.

91.1% are likely to participate if the trial is fully virtual. This was consistent across all age groups (from 18 to >60 years).

53% of individuals with a neurological, sleep, or mental health condition reported they were "very likely" to participate in a virtual clinical trial, representing the largest proportion of all individuals with a comorbid condition

Making it easier to meet the study requirements makes it more likely that individuals will agree to participate and be able to complete all the required assessments.

There are a number of factors to consider when making assessment-related decisions and whether the appropriate level of effort is required.

- Imaging or clinician-rated assessments of function often require an in-person visit, but other assessments could be conducted remotely, via telehealth, home health vendors, home-based lab vendors, wearables/sensors/devices, or electronic patient-reported outcomes (PROs).
- Consider whether there is some flexibility around the timing of assessments to allow for competing priorities in participants' lives. Is a day or two either side of the target interval acceptable?

In addition, accurately characterizing the population helps understand how assessments could be designed. Some considerations include:

- **Employment status:** Will taking off of work be a barrier?
- **Family situation (young children or caregiver of an older parent):** Do participants have other priorities that could make it challenging to attend in-person visits?
- **Socioeconomic status:** Would compensation for completing assessments be a motivator?
- **Residential area (rural vs urban):** Do participants have easy access to a site?
- **Level of disability or mobility concerns:** Would in-person visits be a burden?

Example questions to ask individuals, caregivers, and patient groups:

- Would compensation for travel expenses or taking time off work encourage participation?
- Do you require someone to drive you to site visits?
- Do you have young children at home? Would childcare be helpful?
- Would you be willing to complete some (or all) assessments online?
- Do you have a device that connects to the internet? Do you have internet access at home?
- How comfortable are you with using [the device] that will be provided during the study?
- Are there certain days or times of the day when it's easier to complete assessments or attend clinic visits?
- Do you have concerns about how participating will impact your current care?
- Are you willing to receive the intervention in the currently planned form (e.g., inhaled, injected, infused orally)?
- Is the length of planned visits acceptable?
- Is the frequency of planned visits acceptable?
- Is the overall length of the study achievable for you?

Intuitive study materials and tailored support for enhanced engagement

Information or a study assessment that is challenging for participants to understand or use risks poor study engagement and retention. Often, research materials are written using jargon or terminology that is difficult for the general public to understand, especially considering that **36% of U.S. adults have basic or below-basic health literacy.**

Starting with the informed consent form, person-focused content is presented in lay language and short, digestible sections that ensure participants understand:

- What is being asked of them
- What they can expect in return
- How their information is being used

Communicating in ways that participants understand shows respect, ensures they understand what is expected, and increases engagement with study materials.

When designing study materials, consider the following:

- Has digital information been designed specifically for that use, or has the analog version just been converted to a digital format?
- Are there ways that the information could be broken up to aid understanding?
- Could the information be presented in multiple ways (e.g., text, video, images) to meet different learning styles?
- Should the information be translated? Has the translated version of an assessment been validated?
- Are alerts, notifications, or other forms of reminders too frequent or burdensome?
- Does the reading level align with the participants' reading level?
- Are they easy and acceptable to use?

EXAMPLE 1

Participant-friendly materials were created based on Evidation Member feedback.

Population
PHASE 1: 1,595 Evidation Members
PHASE 2: 4 men and 4 women (4 different ethnicities)

Background
A virtual study of an intervention to influence uptake of protective behaviors related to respiratory viral infections (COVID-19, RSV, influenza) was planned for the general public. The materials and intervention needed to be acceptable and easily understood by the proposed study sample.

Approach
Mixed methods formative research project conducted in two phases

PHASE 1
22-question survey regarding behaviors, beliefs, and attitudes about respiratory viral infections (RVI)

Results

- The type, frequency, and delivery of educational materials and alerts were identified.
- We uncovered motivators and barriers for protective behaviors that could be targeted during the intervention:
  - Motivator: concern for others (social responsibility)
  - Motivator: response efficacy
  - Barrier: beliefs about RVI (e.g., you're not contagious when your symptoms are mild)
- The participants needed a greater understanding of the purpose as well as greater motivation to complete a survey about their illness experience 10 days after reporting symptoms.

Actions

Updated the design to:

- Provide evidence of how protective behaviors can be beneficial
- Provide information that challenges beliefs related to the spread, detection, and treatment of RVI
- Share content that appeals to individuals' sense of social responsibility
- Explain why they should complete the surveys about their illness experience
- Add twice-monthly local flu rate insights

PHASE 2

- 2 waves of 1:1 qualitative interviews
- Exposure to wireframes of the digital intervention (prompts for desired health behaviors, education, quizzes, etc)
- Iterative design of the intervention and study materials

Results

- The study and materials were understood, found to be interesting, and considered acceptable by a representative sample of the intended study population.
- The participants wanted acknowledgement of symptom-free weeks and more information about what to do when they're sick.

Actions

Updated the design to:

- Provide education about what to do when sick
- Display personalized cards for reporting fever, high-risk conditions, or a subsequent illness
- Deliver weekly summary insight reports

Overall key findings

- Activities need to be short and simple to account for the individual being sick.
- Members wanted proactive alerts about the spread of RVIs in their area so they could be prepared.
- They also wanted guidance on what to do and when they should do it once they started feeling sick.

Example questions to ask individuals, caregivers, and patient groups:

- How do you normally like to view instructions (e.g., text, video, images)?
- Would you like to receive reminders and notifications to complete tasks?
- What is your primary language?
- How much education did you complete?
- Are the instructions understandable? If not, how could it be written differently?
- Is the way the information presented usable and acceptable?
- Are you familiar with the equipment or devices that you would be asked to use?
- If you need support, how would you prefer to communicate? Via phone call, text, online chat?

SECTION 2

Recruit people where they are, both geographically and mentally

Recruitment methods that place people at the center benefit from:

- Faster recruitment
- Greater number of positive screens for timely enrollment
- An inclusive, representative study population

Recruitment methods that do not consider participant input can miss segments of the population.

Traditional recruitment methods	Gaps in recruitment
Identifying individuals through medical records in large medical centers	Do not reach individuals who do not or cannot visit an urban clinical setting An inability to ensure representation based on social determinants of health (SDOH) and other characteristics that have an impact on health: • Socioeconomic status • Educational level • Level of social support
Physician referrals	Do not reach individuals without regular access to healthcare or physicians aware of or participating in research
Social media advertising	Do not reach individuals who do not engage with social media platforms

Participant feedback during the study planning phase plays an important role in choosing recruitment methods that meet people where they are, both physically and in terms of their readiness to participate in clinical trials. In addition, involving individuals and organizations they trust improves communication and helps overcome negative perceptions about research.

CASE STUDY

Despite beliefs that research is important and beneficial, a considerable percentage of people feel participation is either burdensome or unsafe.

Evidation recently conducted a survey with members to evaluate their attitudes, behaviors, and knowledge about engagement in clinical trials (n=7,091).

76.9% agreed that participation in clinical trials is important.

71% felt that they benefit from health science research.

YET

50.9% felt participating in clinical trials was more trouble than it's worth.

24% felt participation in a clinical trial seems risky.

A flexible, multi-pronged approach can boost recruitment. Consider the following:

- Engage with patient or community groups to recruit within their membership
- Address the barriers that have been discussed in the previous sections to make it easier for people to learn about and determine eligibility for research:
  - Use online eligibility screeners instead of site visits, when possible
  - Educate physicians in the recruitment areas about the research
  - Locate sites in a range of geographic areas, including rural locations
- Provide education about the disease/condition of interest and the benefits of the research
- Survey the population about their preferred recruitment channels
- Offer the ability to speak directly with someone (e.g., help line, someone at the site) regarding questions or concerns about the research

EXAMPLE 1

Providing valuable health information engages people for future recruitment opportunities.

Population

~25,000 men and women aged 60+ years on the Evidation platform

Challenge

A pharma company was struggling to enroll on time and on budget for an investigational RSV vaccine trial, especially for specific sites and locations.

Approach

A pre-recruitment educational campaign, followed by recruitment.

The pre-recruitment educational campaign included:

- Educational articles
- Quizzes on what they learned
- Follow-up infographics of the quiz results

The follow-up recruitment campaign a few weeks later targeted individuals who engaged with the educational materials. Recruitment was refined based on:

- The trial's specific inclusion/exclusion criteria
- Site-based zip codes to target the under-recruiting areas

Results

5x more randomizations with individuals involved in the campaign

50x higher conversion rate for trial enrollment of individuals in the campaign

EXAMPLE 2

Working collaboratively with patient groups during study design also benefits study recruitment.

In the study of a SCD treatment described earlier, the patient group that participated in the endpoint review also partnered with the sponsor for recruitment through its network of US-based community organizations that provide support to people with SCD. Because of the organizations' strategic outreach, a representative population was reached, including those often under-represented in SCD research.

Example questions to ask individuals, caregivers, and patient groups:

- Where do you receive information about health/research? For example:
  - Social media platforms
  - Community centers
  - Churches
  - Online marketplaces, such as Craigslist
  - Online platforms like Evidation
  - Primary care physician/specialist/nurses
  - TV/radio
- What would motivate you to participate in research (e.g., receive high-quality health care at a lower cost or free, to help others, learn more about your health)?
- Who do you trust to recommend a study to you?
- Would you like to be compensated for your time?

Research benefits from viewing patients as people

Core to person-centric trial design is viewing patients and trial participants as people with individual priorities and preferences as well as lives that don't always fit the constraints of highly controlled research. Integrating individual input early in development **benefits the entire trial lifecycle**, from study design to commercialization. However, barriers to including the participant voice often stem from a lack of awareness of how to start. Seeking advice from the FDA or industry consortia, approaching patient advocacy groups, or partnering with companies that have a history of engaging with large populations can streamline the adoption of person-centricity.

To learn how Evidation can help you refine your trial design to better meet people where they are, get in touch with us **here.**