Overcoming Barriers *to Patient Enrollment in Therapeutic Clinical Trials for Cancer*

Recommendations

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Introduction

The objective of cancer research is to generate new knowledge that can be used to improve survival and quality of life for patients with cancer. Clinical trials are the key step in advancing potential new treatments for patients with cancer from the research setting to the cancer care clinic, and patient participation in trials is crucial to their success. Most patients express a willingness to participate in clinical research, yet only a small fraction ultimately end up enrolling in a cancer clinical trial. In fact, analyses show that around 20% of cancer clinical trials fail due to insufficient patient enrollment.

The disconnect between patient interest and actual participation in cancer clinical trials is due to numerous barriers that discourage or prevent patients from enrolling. These barriers are discussed in greater detail in the accompanying document "Barriers to Patient Enrollment in Therapeutic Clinical Trials for Cancer: A Landscape Report." In the report, the barriers are divided into provider and institutional barriers, patient barriers, and trial-design barriers.

While the barriers facing patients are numerous, the magnitude of each category of barriers varies significantly. For instance, studies indicate that more than 55% of patients seeking cancer care will not have a clinical trial available for their condition at the location where they are seeking treatment, and another 17% will not meet eligibility requirements. As a result, the population of patients who could possibly enroll in a local trial is just over a quarter of all patients. In other words, the barrier for nearly 75% of patients is the fact that their local institution does not have a clinical trial for which they are eligible.

Successfully overcoming barriers to patient enrollment requires not only understanding the barriers, but developing specific steps to address these barriers. The following consensus recommendations have been developed and endorsed by the array of stakeholders listed at the end of this document. These recommendations address a broad spectrum of barriers that are further detailed in the companion report. The recommendations are grouped by category, and require both programmatic activities and policy changes to be realized.

Note: ***All recommendations are directed at cancer therapeutic trials and cancer patients.***

Provider and Institutional Barriers

Context: Providers and institutions have a significant impact on cancer clinical trial enrollment through decisions regarding which and how many trials to open at a site, the quantity and type of research personnel employed, whether and how they identify and attempt to enroll patients in open trials, as well as investment in other research infrastructure. Together, these factors account for the largest influence on whether patients are able to enroll in a clinical trial.

1) Build and maintain a pool of diverse, research-trained staff which includes dedicated research positions as well as providers with multiple roles, with special attention to developing workforce reflective of underrepresented populations.

2) Maintain or increase funding from all trial sponsors, including NCI, for dedicated site research staff who can open trials and recruit patients, so that trial conduct is scalable and sustainable.

3) Provide dual-role staff—clinical staff providing patient care along with fulfilling research roles—with appropriate incentives to promote their participation in clinical research activities.
   a) Institutions should create protected time, a range of incentives, additional resources, and recognition for dual-role staff to conduct clinical research.
   b) Fully utilize nonmonetary incentives like quality or accreditation metrics to drive clinical research activity.

4) Sites should manage trial portfolios so that they match patient characteristics in the community that is served by a practice's catchment area.

5) Stakeholders should collaborate to develop free or affordable technology, tools and processes targeted toward non-research sites/providers that make matching patients to trial opportunities and referral of patients interested in trial participation easier.

6) In order to achieve robust accrual, sites should employ protocols or technology to make prescreening incoming patients for trial eligibility more scalable and systematic.
   a) Ensure that matching tools are easily available to providers in their workflow
   b) Standardize eligibility criteria so that it is machine-searchable
   c) Standardize clinical trial protocols into formats easily incorporated into EMRs

7) Create and implement ways to streamline the process and reduce effort needed to open clinical trials
   a) Expand use of standardized contracting for clinical trial conduct (e.g. Accelerated Clinical Trial Agreement, TransCelerate, Society for Clinical Research Sites, etc.)
   b) Continue to develop operational and contracting models for research enabled sites to participate in clinical trials just-in-time, where clinical trials are opened where applicable patients are identified.
   c) Expand and encourage use of Central IRBs for multi-site trials.
   d) Smaller practice sites should consider participation in research networks as a way to gain access to shared research infrastructure and clinical trials.

Patient Barriers

Context: On average, only a quarter of patients have local trials available for which they are eligible to enroll. Not all eligible patients are asked to enroll, but typically over half of those asked consent. The four most-cited reasons for declining participation are: fear of side effects, loss of control, logistics involved in participation, and cost concerns.

Recommendations:

8) Present cancer patients with specifically identified trial options as part of the physician-patient treatment decision discussion using evidence based methods.

9) Promote general awareness among cancer patients and their families of clinical trial participation as a viable treatment option early during the course of patient care.

10) Non-site specific trial matching and navigation services should be available for patients not provided trial options by their provider or institution. These services should clearly communicate roles and objectives.

11) Research stakeholders should develop evidence-based methods, materials and resources for:
    a) Just-in-time clinical trial education
    b) Patient-facing decision support

    These methods, materials, and resources should be collected, evaluated and made available to the community. Research programs should provide these resources and services to patients, families and caregivers.

12) Improve informed consent documents and processes to ensure education and comprehension by patients of the research in which they are contemplating participation.

13) Provide cost transparency by providing full coverage analyses on all trials to clearly articulate responsibility for all anticipated trial costs.
    a) Trial sponsors should collaborate with institutions to clearly define sponsor obligations with respect to covering supplies and services related to trials.
    b) Sites should provide patients considering enrolling in trials with information that enables the patients to consider how their direct and indirect costs would differ if they enrolled in the trial or received care outside the trial.

14) Ensure coverage of routine patient care costs incurred in cancer clinical trials by all payers.
    a) Further the implementation of existing federal requirements for private insurers to cover cancer clinical trial routine patient care costs in order to provide timely enrollment and avoid administrative burdens to enrolling patients on clinical trials.
    b) Bolster state requirements to cover routine patient care costs in cancer trials.
    c) Require state and federal insurance authorities to enforce routine patient care requirements.
    d) Ensure Medicaid coverage in all states and territories of routine patient care costs in cancer clinical trials.

15) Shield patients from out-of-pocket ancillary costs of trial participation such as travel, parking, and housing.
    a) Clarify policies to ensure reimbursement of ancillary costs is not seen as undue influence and ensure awareness of allowable reimbursements.
    b) Fully utilize existing support resources (e.g. ACS Hope Lodge, Road to Recovery, Lazarex Foundation, non-emergency medical transport), and develop new resources that shield or offset ancillary costs associated with trial participation.

16) Design trials to be more patient-centric by using patient input during the design and implementation phases.

17) Trial sponsors and research programs should explore the use of technology or other tools to reduce patient time and travel burdens associated with clinical trial participation.

Recommendations

Trial-Design Barriers

Context: Trial-design features like inclusion/exclusion criteria significantly affect the number of patients eligible to participate in a clinical trial.

18) Modernize eligibility/inclusion/exclusion criteria to achieve the most relevant parameters that will ensure scientific integrity without unnecessarily excluding patients.
    a) Ensure eligibility criteria do not preferentially exclude a racial or demographic group, e.g. upper age limits, or excluding comorbidities more highly associated with demographic or socioeconomic subgroup unless specific rationale for exclusion exists.

19) Encourage broad-panel biomarker testing programs to help promote simultaneous pre-screening for multiple targeted therapy trials.

20) Develop and share resources that can be used for detailed assessment of accrual feasibility during the design phase of trials. These include patient and trial databases and modeling software.

Disparities

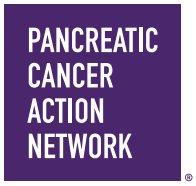
Context: The demographics of participants in registrational trials for cancer drugs do not match the demographics of the U.S. cancer population, due in large part to many of these trials occurring outside of the U.S. Participants in NCI trials skew significantly younger than the U.S. cancer population and both minorities and the poor are also underrepresented in such trials.

21) Ensure that research sites selected for multi-site trials have diverse patient populations that reflect the broader population with cancer.

22) Provide clinical trial navigation services for patients from medically underserved groups to connect with publicly available support resources and culturally sensitive education materials.

23) Seek engagement and partnerships with community leaders and community-based organizations–especially those serving racial and ethnic minority groups as well as medically underserved communities–to effectively disseminate information about the importance of clinical research participation as a social justice issue.

These recommendations have been endorsed by the following organizations:



An accompanying report is available at: https://www.acscan.org/policy-resources/clinical-trial-barriers