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Pragmatic study designs for older adults with cancer: Report from the U13 conference

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ABSTRACT

Cancer is a disease occurring disproportionately in older adults. However, the evidence base regarding how best to care for these patients remains limited due to their underrepresentation in cancer clinical trials. Pragmatic clinical trials represent a promising approach for enhancing the evidence base in geriatric oncology by allowing investigators to enroll older, frailer patients onto cancer clinical trials. These trials are more accessible, less resource intensive, and place minimal additional burden on participating patients. Additionally, these trials can be designed to measure endpoints directly relevant to older adults, such as quality of life, functional independence and treatment tolerability which are often not addressed in standard clinical trials. Therefore, pragmatic clinical trials allow researchers to include patients for whom the treatment will ultimately be applied and to utilize meaningful endpoints. Examples of pragmatic studies include both large, simple trials and cluster randomized trials. These study designs allow investigators to conduct clinical trials within the context of everyday practice. Further, researchers can devise these studies to place minimal burden on the patient, the treating clinicians and the participating institutions. In order to be successful, pragmatic trials must efficiently utilize the electronic medical record for data capture while also maximizing patient recruitment, enrollment and retention. Additionally, by strategically utilizing pragmatic clinical trials to test therapies

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and interventions that have previously shown efficacy in younger, fitter patients, these trials represent a potential mechanism to improve the evidence base in geriatric oncology and enhance care for older adults with cancer.

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1. Introduction

The burden of cancer disproportionally impacts older adults and, as our population ages, cancer incidence is expected to continue to rise.[1,2] Projections suggest that by 2030 the number of new cancer diagnoses will increase by 67% in adults age 65 years and older.[1] Additionally, studies suggest that older patients with cancer experience poorer survival rates compared to younger patients. Further, older cancer patients are more likely to be undertreated and experience premature discontinuation of treatment for their stage of cancer.[3–6] Unfortunately, the evidence base for how to optimally treat older adults with cancer is still underdeveloped and older adults, especially less fit older adults, are underrepresented in cancer clinical trials.[7–9] Therefore, a critical need exists to develop research that addresses the evidence gaps regarding older patients with cancer.

The Cancer and Aging Research Group (CARG), in collaboration with the National Institute on Aging (NIA) and the National Cancer Institute (NCI), has been holding a linked conference series funded by a U13 grant (Co-PI: Hurria, Mohile, Dale) to examine the level of evidence and areas of highest research priority in geriatric oncology. The initial conference, held in 2010, found that clinical trial infrastructure often fails to meet the needs of older cancer patients and rarely incorporates geriatric-specific data into the existing framework.[10–12] The second conference, held in 2012, provided recommendations for improving geriatric oncology research and sought to focus on how best to design and implement clinical trials for older adults with cancer.[13] From May 13 to 14, 2015, CARG/NIA/NCI held the third conference in this series. The goal of this conference was to focus on the design and implementation of intervention studies to improve or maintain the quality of survivorship in older adults with cancer. This article summarizes the section focused on methodology, with an emphasis on pragmatic clinical trials.

1.1. What is a "Pragmatic" Trial?

Clinical trials designed for older and less fit adults with cancer need to be more accessible, less resource intensive, and place minimal additional burden on the participating patient.[13] For these reasons, pragmatic clinical trials may be well-suited for improving the evidence base in geriatric oncology. These trials are typically performed in the context of standard care, recruit patients from a variety of practice settings, and use broader, more inclusive eligibility criteria.[14] In 1967, Schwartz and Lellouch introduced the idea of a pragmatic trial to describe studies which help compare different options for care and determine which treatment to use in "real-world" settings.[15] Although traditional pragmatic trials and randomized, controlled trials (RCTs) both rely on randomization to balance baseline differences between treatment and control groups, these trial designs differ in some key ways. Pragmatic trials stand in contrast to randomized, controlled, explanatory trials, which answer a scientific question or test a hypothesis about the efficacy of an intervention. While the more widely-used explanatory trials help determine the efficacy of the intervention under ideal conditions, pragmatic trials help determine the effectiveness of an intervention in day-to-day practice (see Table 1).[16]

1.2. Pragmatic Trials Represent a Promising Study Design in Geriatric Oncology Research

In geriatric oncology, pragmatic clinical trials can help serve the much-needed purpose of increasing our knowledge of how to best to treat older adults with cancer. Data suggests that older adults are no more averse to participating in clinical trials than younger patients.[17,18] However, clinicians often do not offer clinical trials as an option to many older cancer patients, usually due to concerns related to treatment