Original Study

# Screen Failure Rates in Contemporary Randomized Clinical Phase II/III Therapeutic Trials in Genitourinary Malignancies

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## Abstract

**Screen failures in clinical trials incur significant costs. We reviewed 50 trials in advanced genitourinary cancers to determine the rate and reasons for screen failures. Forty-eight percent of trials published screen failure data and rates averaged between 20% and 30%. The main reason was patient ineligibility, highlighting the need to better enforce the recording of screen failure information and reconsider trials' eligibility criteria.**

**Background:** Screen failures, defined as individuals who undergo screening but are not enrolled in a clinical trial, incur significant costs without contributing valuable data to the study. Despite these costs, there are few published data about the rate or reasons for screen failures in advanced genitourinary cancer clinical trials. **Materials and Methods:** We reviewed 50 phase II and III trials in advanced genitourinary cancers conducted between 1999 and 2016. **Results:** Of the 50 trials, only 48% (24 of 50) published screen failure rates: 68% (13 of 19) of those in prostate cancer, 33% (6 of 18) in kidney cancer, and 58% (5 of 13) in bladder cancer. Among the phase III trials in prostate cancer, the mean screen failure rate was 26% (range, 12%-45%). The main reason for screen failure was reported as ineligibility. Among the phase III trials in kidney cancer, the mean screen failure rate was 25% (range, 21%-29%), with the most frequent reasons being ineligibility and patient refusal. Among the phase II/III trials in bladder cancer, the mean screen failure rate was 19% (range, 4%-28%), with the main reasons being ineligibility and patient refusal. **Conclusion:** Contemporary trials in genitourinary cancer reported screen failure rates of approximately 20% to 30%. Many trials did not report on the numbers of, and reasons for, screen failures. Greater standardization of definitions, methods, and reporting are needed to better understand and decrease screen failure rates in genitourinary cancer clinical trials.

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## Introduction

There is significant cost associated with conducting clinical trials, with oncology trials incurring the highest average cost at approximately $59,500 per patient,[1] and this cost is rapidly rising. For instance, from 1990 to 2000, the cost of drug development was estimated to increase at an annual rate that was 7.4% higher than inflation, with clinical trials as the largest contributor to the rising costs.[2] Efforts are now under way to analyze and improve trial design and conduct to reduce unnecessary costs and improve efficiency.

One aspect of trial design and conduct that has not been fully examined is the initial screening process, during which time it is determined if a potential study candidate meets eligibility criteria. Screening consists of obtaining consent, performing a history and physical examination, and protocol-specified laboratory tests and imaging studies, which cost effort, time, and resources estimated at approximately $2000 per patient.[3,4] Patients who are deemed ineligible during the screening process are considered "screen failures" and are unable to provide usable data for the clinical trial.

According to the Consolidated Standards of Reporting Trials (CONSORT) 2010 flow diagram for randomized trials, study investigators are encouraged to document screen failure

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information, including the number of subjects assessed for eligibility but not randomized and the reasons for screen failure, to indicate if the trial population is representative of the general population.[5] Collecting screening data might also be useful in identifying narrow inclusion criteria or adjusting patient recruitment methods if screen failure rates are too high.[6]

Despite this suggestion, screening data are not collected in many studies. In an investigation conducted by Elm et al on screening logs in clinical trials, 23% of the screening logs were returned with "no data to report" although the studies had screened patients.[6] In addition to inconsistencies in reporting screen failures, Elm et al reported that there is no standard and specific definition of a "screened patient," with some studies including patients who have not undergone the screening process and other studies including only patients who signed informed consent forms,[6] making it difficult to amalgamate and analyze screen failure data from multiple different trials.

Currently, there are few published data about the rate or reasons for screen failures in contemporary, randomized phase II and III trials in genitourinary cancer. Screen failures can result in significant use of resources and expense, and might ultimately affect the generalizability of trial results. To develop strategies to try and reduce screen failures, the first step and primary aim of this study was to understand how often and specifically why screen failures happen.

## Materials and Methods

We defined screen failures as individuals who underwent screening but were not enrolled in the trial.

We sought completed, randomized trials that assessed hormonal, chemotherapy, immunotherapy, or other targeted therapies for advanced prostate, kidney, or bladder cancer that started between 1999 and 2016, included at least 25 participants in the entire trial, and were published in English as a full article in a peer-reviewed journal. We searched ClinicalTrials.gov using the terms: "prostate cancer," "kidney cancer," "bladder cancer"; and the filters: "phase III trials," "phase II trials," "interventional studies," "start date 1999 onwards," and "closed studies." We searched for study publications in PubMed.

We found 267 phase III trials in prostate cancer, 18 of which were eligible; 114 phase III trials in kidney cancer, 18 of which were eligible; 44 phase III trials in bladder cancer, 9 of which were eligible; and 164 phase II trials in bladder cancer, 5 of which were eligible (Figure 1). Phase II trials were included in bladder cancer because of the small number of eligible phase III trials.

**Figure 1** Methods Flow Chart