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Multiple trials within the cmRCT design; an example within a colorectal cancer cohort

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INTRODUCTION

The cmRCT-design aims to facilitate multiple trials in an efficient cohort structure. This new design poses some methodological and ethical considerations. Here we present an example of multiple sequential trials within a cmRCT colorectal cancer cohort (PLCRC) and the challenges that were encountered.

PLCRC

PLCRC is a Dutch multicenter colorectal cancer cohort in which colorectal cancer patients of all stages are included. Within PLCRC, baseline and follow-up data, patient reported outcome measures and biomaterials are collected. PLCRC was set up to facilitate multiple trials in a real-world setting according to the cmRCT-design.

TRIALS WITHIN PLCRC

Currently, two trials are undertaken within PLCRC, i.e. the RECTAL BOOST study and the SPONGE trial. The RECTAL BOOST evaluates the efficacy of boost radiation in addition to standard chemoradiation in patients with locally advanced rectal cancer. The SPONGE trial assesses the effect of a retractor sponge in laparoscopic colorectal surgery on hospital stay and postoperative complication. Both trials include rectal cancer patients from the same study population. Patients may therefore participate in both trials.

ETHICAL ISSUES

As consequence of the staged-informed consent, participants who have not given consent for future random selection are considered ineligible for any trial within the cohort. Currently, no dynamic informed consent structure within PLCRC exists. Also, aggregated disclosure of trial results may induce disappointment of not being selected for any of the interventions. Besides, broad consent for future, yet unknown studies, may not always be appropriate since some of these studies are known at baseline.

METHODOLOGIAL ISSUES

Patients having received the boost intervention potentially have a higher risk on acute toxicity, which could result in perioperative complications and thereby prolonged hospital stay in participants of the SPONGE trial. Interacting interventions may affect the generalizability and require stratified random selection. Investigation of interactions requires substantial – and possibly unrealistic - sample sizes. Furthermore, refusal of the intervention may be related to a previous intervention, which could lead to (selection) bias and possibly impair generalizability.