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Taxonomy for colorectal cancer screening promotion: Lessons from recent randomized controlled trials

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ABSTRACT

Objective. To derive a taxonomy for colorectal cancer screening that advances Randomized Controlled Trials (RCTs) and screening uptake.

Design. Detailed publication review, multiple interviews with principal investigators (PIs) and collaboration with PIs as co-authors produced a CRCS intervention taxonomy. Semi-structured interview questions with PIs (Drs. Inadomi, Myers, Green, Gupta, Jerant and Ritvo) yielded details about trial conduct. Interview comparisons led to an iterative process informing serial interviews until a consensus was obtained on final taxonomy structure.

Results. These taxonomy headings (**E**ngagement Sponsor, **P**opulation Targeted, **A**lternative Screening Tests, **D**elivery Methods, and **S**upport for Test Performance (**EPADS**)) were used to compare studies. Exemplary insights emphasized: 1) direct test delivery to patients; 2) linguistic-ethnic matching of staff to minority subjects; and 3) authorization of navigators to schedule or refer for colonoscopies and/or distribute stool blood tests during screening promotion.

Conclusion. PIs of key RCTs (2012–2015) derived a CRCS taxonomy useful in detailed examination of CRCS promotion and design of future RCTs.

1. Introduction

To identify methods that effectively increase colorectal cancer screening rates, it is useful to critically review information from published randomized controlled trials (RCTs). Generating precise estimates of *specific* intervention effects, however, is difficult as the reporting of critical trial features is often incomplete (Moher et al., 1998; Hill et al., 2002; Toerien et al., 2009; Moher et al., 2012). To address this challenge, we developed and applied a CRC screening trial taxonomy for more precise comparisons of interventions and outcomes across multiple RCTs.

The taxonomy extends previous efforts to compare international (CRC) screening programs by classifying strategies implemented to increase population-based CRC screening uptake (Benson et al., 2012; Swan et al., 2012). Benson et al., for example, with the International Colorectal Cancer Screening Network, defined CRC screening measures and indicators, while compiling data from 26 organized CRC programs and 9 pilot programs in 24 countries (Benson et al., 2012). Swan, Siddiqui and Myers reviewed 20 CRC screening programs in 18 countries, describing contact approaches, screening modalities and

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participation rates (Swan et al., 2012). We now add to these efforts with more complete definitions and categorizations pertaining to all important CRC screening program features.

In this paper we describe the process by which the taxonomy was developed, define the framework's constituent elements, and illustrate its utility through application to six recently published RCTs (Inadomi et al., 2012; Myers et al., 2013; Green et al., 2013; Gupta et al., 2013; Jerant et al., 2014; Ritvo et al., 2015) whose Principal Investigators collaborated in taxonomy development. Lastly, we apply the taxonomy to additional RCTs to further demonstrate the taxonomy's utility (see supplementary materials).

2. Methods

Detailed reviews of publications, interviews with principal investigators (PIs) and PI - collaboration contributed to the intervention taxonomy. The process was facilitated by consultation between two authors (PR, RM), who collaborated on one RCT (Ritvo et al., 2015) and continued to intensively review RCT research (Myers et al., 2013). Their insights guided interview questions with other PIs (Drs. Inadomi (Inadomi et al., 2012), Green (Green et al., 2013), Gupta (Gupta et al., 2013) and Jerant (Jerant et al., 2014)), who responded to these (following) questions on trial conduct: 1) based on what you were unable to include in the publications of the RCT you led, please provide information helpful in more fully understanding the trial; 2) based on your understanding of trial undertakings and outcomes, indicate the relative importance of the additional data conveyed; 3) given your view of the taxonomy being developed, indicate what components are helpful in communicating to other researchers the information conveyed in response to questions 1 and 2 and other pertinent information. Cross-trial interview comparisons informed an iterative process that informed subsequent interviews, that continued until authors reached consensus on final taxonomy structure and applications. Standard thematic analysis was applied to the verbal output from the multiple interviews (Braun and Clarke, 2006; Guest and MacQueen, 2012). This systematic approach helped to identify patterns and logically organize the qualitative data into broader common, representative themes (Braun and Clarke, 2006; Guest and MacQueen, 2012). The PIs were leaders of innovative, influential RCTs as indicated by methods used, effect sizes reported and the impact factor of the journals that published the trial reports.

3. Results

Application of the EPADS taxonomy to six selected RCTs enabled systematic identifications of comparable and differing trial elements. Further application to five additional RCTs (not used in developing the taxonomy) indicated its usefulness in differentially characterizing studies.

The iterative review and interview process led to identifying the following analytic taxonomy criteria (Table 1): Engagement Sponsor, Population Targeted, Alterative Screening Tests, Delivery Methods, and Support for Performance (EPADS).

Engagement sponsor refers to the parties (e.g. health system or government agency, medical practice/provider, research team) that invite individuals to screening participation. **Population targeted** refers to the collectivity (e.g. general population or defined subpopulation) targeted for screening invitation. The varying CRCS test-types (e.g. stool blood test, endoscopy) are viewed as the **Alternative screening tests** offered to target populations. Differing **Delivery methods** place CRCS tests in the hands of population members (mail, telephone, in-person contact) while varying methods provide **Support for performance** of screening (e.g. mailed or telephone reminders, scheduling assistance, follow-up contacts).

Table 1
Colorectal cancer screening intervention taxonomy.

- **Engagement sponsor**
  Health system, practice, provider, researcher.
- **Population targeted**
  General population, subpopulation in practice or community, health care providers.
- **Alternative screening tests**
  Stool blood test (SBT), colonoscopy (CX), flexible sigmoidoscopy (FS), other.
- **Delivery methods**
  Mail, telephone, in-person, other.
- **Support for performance**
  SBT: Reminder by mail, call (live/automatic), other.
  CX: Reminder and/or instructions by mail, call (live/automatic), other.

3.1. Engagement sponsor

Populations are likely to receive a CRCS invitation from a health organization (e.g. governmentally or privately administered), primary care practices, research team members or other screening-oriented organizations and institutions. The population member's perceptions of screening sponsors affect invitation responses. When participants feel closer and more trusting connections with sponsors, they may respond more positively than participants who perceive distant, impersonal or unreliable sponsor relationships.

All of the analyzed trials employed patient engagement strategies that informed patients of a *combined* sponsorship (Table 2). The trials reported by Inadomi et al. (2012), Myers et al. (2013), Green et al. (2013) and, Ritvo et al. (2015) were sponsored by a health care system that included primary care practice services, collaborating with research teams. In the Inadomi et al. (2012) trial, sponsors were identified to patients as the health organization employing primary care providers (the San Francisco Community Health Network) *and* the research team. In the Ritvo et al. CRC screening trial (Ritvo et al., 2015), participants were invited to join the study by a preferred health care program (Group Health Centre), and affiliated primary care providers in association with the research team. In the Myers et al. study (Myers et al., 2013), the Christiana Care Health System, the patient's primary care practice, and the research team were identified as screening initiative sponsors. In the Green et al. project (Green et al., 2013), patients were invited to join the study by the Group Health Institute research team affiliated with the Group Health Cooperative (GHC), which sponsored integration of the research project into routine (e.g. lab, EHR) GHC primary care practice. In the Jerant et al. (2014) study, participants were informed the CRCS initiative was sponsored by the University of California (Davis), the patient's primary care practice, *and* the research team. Patients in the Gupta et al. study (Gupta et al., 2013) were informed the study was sponsored by their health care system (the John Peter Smith Health Network) (JPS) and the research team, although the screening invitation did not specifically identify the patient's primary care practice as being a co-sponsor.

3.2. Population targeted

The varied populations targeted for screening invitation can be characterized by demographic variables (e.g. socioeconomic strata, age,

Table 2
Engagement sponsor.

Sponsor of screening invitation	Jerant et al.	Inadomi et al.	Ritvo et al.	Myers et al.	Gupta et al.	Green et al.
Health care system	✓	✓	✓	✓	✓	✓
Primary care practice	✓	✓	✓	✓	–	✓
Research team members	✓	✓	✓	✓	✓	✓