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Follow-up to abnormal cancer screening tests: Considering the multilevel context of care

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Abstract

The call for multilevel interventions to improve the quality of follow-up to abnormal cancer screening has been out for a decade but published work emphasizes individual approaches, and conceptualizations differ regarding the definition of levels. To investigate the scope and methods being undertaken in this focused area of follow-up to abnormal tests (breast, colon, cervical), we reviewed recent literature and grants (2007-2012) funded by the National Cancer Institute. A structured search yielded 16 grants with varying definitions of “follow-up” (e.g. completion of recommended tests, time to diagnosis); most included minority racial/ethnic group participants. Ten grants concentrated on measurement/intervention development, and 13 piloted or tested interventions (categories not mutually exclusive). All studies considered patient level factors and effects. While some directed interventions at provider levels, few measured group characteristics and effects of interventions on the providers or levels other than the patient. Multilevel interventions are being proposed, but clarity regarding endpoints, definition of levels, and measures is needed. The differences in the conceptualization of levels and factors that affect practice need empirical exploration and we need to measure their salient characteristics to advance our understanding of how context affects cancer care delivery in a changing practice and policy environment.

Introduction

Periodic screening is a well-established strategy for reducing the incidence of cervical and colorectal cancer through the treatment of cancer precursors, and minimizing cancer morbidity and mortality of cervical, breast and colon cancer (1-4). While screening rates have generally increased since the 1980s for the three cancers, and cancer morbidity is declining (5-7), challenges remain (5-8). Rates of advanced-disease-at-diagnosis and failure

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in follow-up of abnormal screening tests persist, particularly in racial minorities and other underserved groups (5-14).

Although there are no national estimates of the proportion of individuals without follow-up after receiving abnormal screening tests, several reviews of studies in specific populations suggest the rates are high, but vary substantially (15-19). A review by Yabroff and colleagues summarized the prevalence of follow-up after abnormal breast, cervical, and colorectal cancer screening tests (15) and found that the majority of studies showed a failure in follow-up in 25% or more cases; some reported failures in more than 50% of cases. Recent estimates demonstrate a persistent problem such that 17% of abnormal mammographic, 12% of abnormal Pap, and 41% of abnormal fecal occult blood screening tests remain unexamined in specific populations (12, 20, 21). The mammographic study compared follow-up in facilities serving populations with relatively less education and more racial minorities and demonstrated follow-up was lower by 4-5% compared to more educated, Caucasian populations.

Considering the importance and challenge of completing follow up to abnormal screening tests, we updated our background literature review and performed an audit of funded NCI proposals to deepen our understanding of relevant work and form the basis for this commentary (22, 23).

Background

To guide intervention strategy development and evaluation, several conceptualizations of levels exist. For example, Mandelblatt and colleagues build on the work by Anderson and Aday to identify patients, primary care providers, and cancer care providers as three relevant groups linked by communication and affected by the individual or medical care environment in which they operate (24). While the research does not explicitly include the idea of “levels” in its conceptualization, the lead author refers to the patient and provider levels in her conclusion. Bastani et al explicitly call out levels in their conceptualization of factors affecting follow-up and labels them patient, provider, practice, and policy (25). In our conceptualization of the context of care, we build on the ecological model of Engel and suggest that there is successive nesting of patients within families, within provider teams in organizations, nested within communities that are affected by state and national level factors including professional and public policies (26).

Furthermore, we recognize that screening is a process, not a discrete event (27-30), and this provides an opportunity to consider improvements in multiple points along the care process (22, 23, 31). We can achieve higher rates of mortality reduction by assuring that the complete process of additional testing and evaluation subsequent to an abnormal screening test always occurs, particularly among populations with few resources. The question is how to achieve these improvements (22, 32).

Bastani and others have called for considering multilevel interventions (25). The above examples of conceptualizations can all be called multilevel and all assume these levels and their interaction affect the likelihood of follow-up testing after an abnormal screening, albeit in potentially very different ways (23). For example, the age and demographic

characteristics of individual patients, how provider teams are organized, whether organizations have direct mail reminders to individuals due for follow-up testing and whether professional policies require direct patient notification of abnormal results are all factors from different levels of our ecological model of care that may affect follow-up (23). Furthermore, what the follow-up evaluation involves, how the reporting is done (i.e. standard electronic medical records), and who does the reporting may differ with physician community standards, the reimbursement offered through insurance, and the presence or absence of programs like Medicaid for low income groups. All these factors affect whether follow-up to abnormal screening occurs, occurs correctly (15) or incompletely or expeditiously (33), and therefore when and whether they reach treatment or are told they do not have cancer.

To address this problem, published intervention research has focused on educational, navigational, and reminder intervention strategies with individual providers or patients, it has been limited in its focus on the effects of such strategies on provider teams or organizations, or the simultaneous effects of organization, provider teams and individuals on follow-up to abnormal screening (22, 25, 34, 35) despite longstanding calls for such work (25, 36, 37). Published research does not completely reflect the increased awareness in the research community regarding the multilevel context of care so we also audited funded research to characterize the research progress on multilevel interventions to improve the follow-up of abnormal screening (38).

Identification and Auditing of NCI Funded Research related to Follow-Up of Abnormal Screening Tests

To assess the state of emerging multilevel research, we conducted a structured review of grant applications funded for at least one year by the National Cancer Institute (NCI) from 2007-2012. We explored the characteristics of intervention and observational studies. We were particularly interested in whether multilevel interventions were tested, how people defined levels and whether definitions of “follow-up” were clearly specified and measured.

We used NCI’s Division of Cancer Control and Population Sciences (DCCPS) Portfolio Management Application (PMA) to identify awarded grants in their first year between October 2007 and April 2012, based on their NIH extramural research funding activity code (i.e., R01, R03, R13, R15, R21, P01, U01) (39). Training grants were excluded. We conducted separate keyword searches of the full text of grant applications to identify projects concerned with follow-up to abnormal cancer screening. Search terms included: a) cancer screening follow-up, and b) follow-up mammogram; or mammography; or digital mammography; or mammogram; or MRI; or magnetic resonance imaging; or Pap and HPV; or human papilloma virus; or Pap; or fecal occult blood test; or colonoscopy; or sigmoidoscopy.

PMA searches yielded 272 funded grants. The grant identification and selection process followed PRISMA guidelines (40) to review abstracts and eliminate duplicates (n=57), and studies that focused on biological sciences or studies that used the term “follow-up” as a reference to the data collection process of doing baseline and follow-up assessments (n=136)

as opposed to our interest in the health care process of follow-up evaluation after an abnormal cancer screening tests. The full text of these grant applications were reviewed with 51 rated as ineligible. Sixteen funded proposals were rated eligible for detailed auditing.

A detailed standardized audit form was designed (Supplementary Material). While this was not a systematic review of findings of research studies, we were aware of the standards for systematic reviews, particularly the standard concerning the itemized steps of developing a protocol (41). The audit form included major design domains for research (later noted in Tables 1 and 2) and each had standardized definition and categories. A pilot coding of 4 proposals by all 4 auditors refined the coding criteria and audit form structure. After this process, the 16 grants were fully independently coded by two auditors. Following four auditors' independent reviews of their assigned grants, data were entered into an Excel spreadsheet. Any differences in the codes between the two assigned authors were noted and resolved by all 4 auditors.

Characteristics of Funded Studies

As reported in Table 1, of the 16 studies, 7 focused on cervical cancer, 4 on breast and 3 on colon cancers, and 2 studies considered multiple cancers. The majority of grants with a larger scope (i.e. R01 as compared with R21) focused on cervical cancer tests. The operational definition of "follow-up" was variable, referring to the various steps within the process of care (42). Operational definitions with highest frequency were receipt of recommended additional tests and time to initiation of diagnostic test follow-up. Studies evaluating the appropriateness of follow-up were the minority (n=2), while the remainder investigated various steps in the follow-up process (e.g. referral to appropriate subspecialty).

Table 2 summarizes the research methods proposed in the studies. Given that the variable funding mechanisms reflect differing project aims and scopes of work, the research methods were also variable. Considering the research continuum (43, 44), the majority proposed intervention research with 11 testing an intervention strategy. Studies also proposed descriptive epidemiological research questions regarding behavioral and organizational factors affecting follow-up, measurement/instrument development and/or tested intervention strategies. With respect to design, the broad categories of study design (45), controlled trials, quasi-experimental designs and non-experimental designs were represented. Qualitative, quantitative and mixed methods of data sources were proposed. Few studies incorporated economic research questions and analyses. A wide variety of models (e.g. the chronic care model) and theories (e.g. social cognitive theory, theory of reasoned action) guided the proposed research. The vast majority of studies focused on impact or outcome measures at the individual patient level proposing a variety of data sources and statistical methods.

The ages of the populations to be studied reflected the guidelines for a specific screening test. However, there were variations across studies (e.g. ages >18, or 18-64 years for cervical screening). Only one study of colorectal cancer screening included people over 75 years. Consistent with national goals regarding health disparities (46), a majority of studies planned to include participants from racial and ethnic populations, as highlighted in Table 2.

Interestingly, given the relationship between insurance status and screening behavior (47, 48), many studies (n=10) were unclear whether they planned to investigate the mediating influence of insurance on follow-up of abnormal tests. A variety of settings were proposed, including practice networks, hospital out-patient clinics, community health centers, the Veterans Administration Hospitals, and managed care organizations.

Among the 11 grants that focused on testing the efficacy or effectiveness of interventions, several targeted a practice or practice system level and included strategies such as adding a case manager component to a practice intervention or conducting the trial in a practice-based primary care research network. A small number proposed targeting the community, such as engaging religious congregations to promote the training and use of lay health advisors. Table 3 provides examples of the intervention studies, highlighting the proposed intervention target level, characteristics, strategies and research methods. The small number and heterogeneity of the studies prevented a simple classification so we have provided examples using broad ecological model levels of individual, practice and community.

Observations

While only a modest number of funded grant applications between 2007 and 2012 addressed issues related to the process of follow-up of abnormal screening tests, the interest in maximizing performance of the steps and interfaces of care to improve outcomes across the continuum of cancer care was evident and growing within the research community (49-53). The studies proposed by the funded grants, however, reflect a traditional focus on the outcomes at the individual level. While multilevel interventions and measures were proposed, they frequently were operationalized as “process measures” (e.g. clinician referrals to patient navigator) and did not include assessments of the effect of the intervention on providers or provider team functioning. This bi-directional effect is a key concept of multilevel research. Furthermore, few examined characteristics of provider teams or organizations as mediators between the intervention and patient outcome.

We and others argue it is time to conceptualize a new approach to intervention strategy development and measurement (23, 54, 55). This approach would view the problem of follow-up to abnormal screening as a multilevel issue (14, 56) and consider bidirectional interactions. The challenge is to identify potentially modifiable factors among individuals, family members, providers and/or organizations that can be targeted in interventions that will improve the likelihood of follow-up for the patient (23, 36).

Potential reasons for the limited studies in the research pipeline include several scientific and practical challenges, though we did not evaluate studies that were rejected. Some possible reasons for rejections include the complexity of such interventions (55). Another is that they are expensive and large because cluster randomized trials are an appropriate consideration (57). Other potentially appropriate quasi-experimental designs should therefore also be considered (57, 58). Finally, multilevel interventions may be disruptive of teams and organizations being pressed to meet the business demands of medicine.

Since we could not evaluate these explanations, we acknowledge the limitations of the structured portfolio audit. We do not have the number (denominator) of all grants that were

submitted but not funded, which does not permit comparisons on content and methods of those unfunded proposals. It is also limited in that it is a review of NCI funded projects so it does not include the work in other public and private agencies. As always, criteria being audited required interpretation and judgment, some grants may involve multiple research methods, which might be categorized in several ways. We did, however, search not only the abstracts, but the full proposals of the potentially appropriate proposals and also conducted a reliability review for every audit.

Recommendations for Future Research in the Emerging Context of Care

Several priority topics and methodological recommendations evolve from this review. An important research task is to clearly define “follow-up” to abnormal screening tests, to allow the comparison of outcomes across studies and refine and test intervention foci and strategies. These definitions could consider multiple measures within the process, e.g. time to follow-up test appointment, or completion of all tests as was done in recently reported navigation studies (59). Potential mediating endpoints could be identified and examined discretely such as: 1) scheduling the appointment, 2) initiating the diagnostic work-up, 3) completing any diagnostic work-up, 4) completing the recommended diagnostic work-up, 5) reporting results to the referring physician, 6) reporting results to the patient, and 7) initiating therapy among those with cancer. The reasons for failures at each of these points could be different and therefore amenable to different intervention strategies.

Explication of the steps and interfaces where breakdowns are most likely to occur, the levels most amenable to intervention and the most productive interactions among levels will contribute to improving future work to increase follow-up completion. An excellent example is articulated by Sarfaty et al (60). Seven steps were identified in colorectal cancer screening via stool blood test (SBT), including follow-up for positive SBTs. The investigators’ work further identified that how the steps occurred varied widely across 15 primary care practices, suggesting need to allow tailoring when testing interventions for practice performance improvement. Additionally, different levels and the measures of effect at these levels need explicit operational definition, development of reliable and valid measures, and inclusion in future research and analyses (53, 61).

The majority of the funded studies in the last five years proposed familiar intervention strategies. Examples are reminders by various modes such as letters or calls to patients or electronic reminders to clinicians (30), or navigators or case managers to “fix” a challenging process for patients on an individual basis (62, 63). Emerging studies show promise that navigation can improve follow-up of mammography and colorectal cancer tests for the underserved but they have not explored the effect of the navigator on the provider team or organization. Furthermore the effects are not universal, and may occur after 90 days and not change cancer stage (64, 65). For example, providing case management did not promote timely follow-up to abnormal mammography even when the diagnostic care was free (66).

Future research needs to evaluate the effects of such strategies on the provider team functions and organizational systems and structure (57). Multilevel effects may be bi-directional so analyses plans should consider mediators, and endpoints at levels other than

the person with the abnormal screen. For example, when patients could be referred to a navigator, how many clinicians actually made appropriate referrals? If navigators are added to a practice, how do they interact with providers, and what is their role with patients? Are they incorporated into explicit communication flow? If clinicians are made aware of community resources to offer, how many patients report they actually discussed and were encouraged to use the resources (67)? End points at the provider level might include acceptance of the navigator, metrics of team functioning, and enthusiasm for the intervention (68). Related considerations include whether multilevel interventions deliver better outcomes than single level interventions, and whether understanding the multilevel effects will speed adoption (69, 70).

Increasing emphasis has been placed on the need to consider potential adoption and diffusion of efficacious interventions during the early phases of research (71). Despite this emphasis, based on this review of recently funded research, more observational studies (organizational or health systems epidemiology) that clarify the team and organizational and influences that may affect or be affected by follow-up care delivery after an abnormal screening test are needed. The PROSPR initiative is a good example of such work (72).

Given that late-stage diagnoses persist among minority groups, inclusion of them as research participants remains a priority. Additionally, concern is emerging about screening appropriateness in the older old age groups, and studies to date rarely include people over 75 years (73, 74).

Another research need involves cost effectiveness or, at minimum, basic cost analysis. While studies have assessed the cost effectiveness of screening in reducing mortality, few studies address the cost effectiveness of implementing intervention strategies to improve the screening process (75). Studies are needed to examine which category or combination of multilevel strategies is most effective. A recent analysis found that navigation increased the likelihood of follow-up occurring but did not shorten the time-to completion among those who received it, and cost \$275/completion. Such information will inform realistic planning for subsequent intervention research as well as ultimate diffusion and implementation (58).

The U.S. health system is changing rapidly, bolstered by new legislation such as the Affordable Care Act and the variation in adoption of the Medicaid portion of this act (76). Provisions of the Act that encourage Accountable Care Organizations and Patient Centered Medical Homes prompt further recognition of the need to change practices to promote value and quality care delivery. While historical reimbursement and professional norms did not encourage integrated care across providers and steps in care, Accountable Care Organizations and Patient Centered Medical Homes offer opportunities- to test follow-up interventions because they incent consideration of system designs that affect the processes of care including organizational relationships necessary to achieve the diagnostic evaluation and use of interdisciplinary teams (77, 78). The focus on patient-centered care requires competencies at patient, provider and organizational levels (79). Another important piece of legislation, the Health Information Technology for Economic and Clinical Health Act (HITECH) (80), turned attention and motivation toward achieving meaningful use of electronic health records including their use in tracking follow-up testing after abnormal

screening (81-83) and increased communication between providers caring for a common patient (84). Increased attention has focused on the impact of interventions based on electronic medical records (EMRs), for example on reduced time to resolution of abnormal screening tests (85). Simultaneously, however, there are studies which emphasize caution in assuming the validity of EMR measures' data elements given differences in systems and "information overload" for clinicians. These studies stressed the need to account for user behaviors and organizational characteristics (86, 87).

Conclusions

There is a longstanding call to consider the multilevel context of care when considering interventions to improve care quality (25, 37). The changing incentives of Accountable Care Organizations and Patient Center Medical Homes are creating opportunities to undertake such research, the problem of follow-up to abnormal screening tests offers a discrete problem that needs attention. Multilevel interventions are being proposed but clarity regarding endpoints, definition of levels, and measures is needed. While several frameworks describe the multilevel context of care they differ with respect to what levels mean. The differences need to be explored empirically and we need to understand the salient characteristics of levels. Therefore, to advance our understanding the effects of context on care delivery, we need more explicit definitions of levels, their measures as covariates, and how they are affected by interventions. Furthermore the complexity of the research encourages us to address multilevel problems in discrete areas. Follow-up to abnormal screening is one such area and we argue here it that it is an underexplored area in which to evaluate the benefits of a multilevel perspective.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

General study characteristics by screening test type (n=16)*

		Breast	Colon	Cervical	Multiple	TOTAL
Cancer site		4	3	7	2	16
Mechanism	R01	1	1	5	1	8
	R21	2	2	1	0	5
	U01	1	0	0	1	2
	R03	0	0	1	0	1
Care type	Detection	3	3	6	1	13
	Diagnosis	4	3	6	2	15
	Treatment	0	0	3	0	3
Follow-up criterion	Time to diagnostic test follow-up	2	0	2	1	5
	Completion of recommended additional tests	0	1	3	1	5
	Results reported to MD/practice	0	1	0	1	2
	Test result reported to patient	0	0	1	1	2
	Diagnosis	0	0	1	2	3
	Time to diagnosis	0	0	0	1	1
	Appropriateness of follow-up	1	1	0	0	2

* For some characteristics, the total number may be more than 16 studies, because of multiple responses.

Table 2

Selected research domains and methods (n=16 studies)*

RESEARCH CONTINUUM	n
Prevalence in selected population	7
Behavioral-organizational epidemiology	10
Measurement/instrument development	10
Theory testing/development	6
Intervention design/mapping	6
Piloting of intervention	2
Testing of intervention	11
Dissemination-diffusion planning	3
Economic Analyses: (cost of intervention-3, cost of evaluation-1, cost-effectiveness-2)	3
DESIGN	
Experimental	
RCT – Individual level	5
RCT – Group level	3
Quasi-experimental	
Time Series	1
Prospective cohort	3
Non-experimental	
Secondary data analyses	1
Convenience sample descriptive	3
MODELS	
Chronic Care Model	3
Ecological Model	2
Precede-Proceed	2
Other – each cited once (e.g. Preventive health model, Community Based Approaches Model, Health Belief Model, RE-AIM, Access to cancer care model)	9
THEORIES	
Social Cognitive/Learning Model	3
Theory of Reasoned Action/Theory of Planned Behavior	3
Diffusion Theory	2
Other - each cited once (e.g. Grounded theory, locus of control, Cognitive-Social Health Information-Processing Model)	8
DATA SOURCES	
Qualitative strategies (focus groups and key informant interviews): Patients (n=10), clinicians (n=5) and others (n=4).	12
Surveys: Patients (n=11), clinicians (n=2)	11
Medical records and summary reports	10
LEVELS OF MEASURES	

RESEARCH CONTINUUM	n
Individual patient	16
Lay individual/advisors	2
Health care provider	4
Group (Family)	2
Organizations	2
Community	6
STATISTICAL METHODS	
Qualitative	10
Descriptive	12
Hierarchical	3
Time series	2
Regression	12
POPULATION FOCUS AGE	
Screening eligible, but variable groups, e.g. 5-79, 16+, depending on screening test	16
POPULATION INCLUSION - PATIENT RACE/ETHNICITY	
Hispanic	10
Asian	6
African American	11
Caucasian	14
American Indian	3
Alaska Native	2
Hawaiian	1
Pacific Asian Islander	2

* Total may be >16 studies due to multiple responses

Table 3

Nature of intervention (n=11 intervention studies)

Intervention Strategies Targeted to the Individual Level	
Comments	Example
Intervention strategies included in-person education (n=4), telephone calls (n=4), mailings (n=5). * The majority of interventions (n=7) were delivered or managed by one person, a nurse or study staff member. Some involved multiple staff, such as a practice manager working with primary care physicians. A few used multiple strategies by nurses, navigators, a lay navigator, social worker and physician.	One study investigated the performance of follow-up (colposcopy and subsequent medical recommendations) of abnormal Pap and HPV tests using a 3-group study design randomized at the patient level; 1) Standard care (SC) plus barriers assessment and counseling delivered via telephone, 2) SC plus tailored barriers information via home mail, and 3) SC plus letter notifying patient of abnormal test, the need to undergo colposcopy, an appointment date and telephone appointment confirmation assessment via letter. Numerous patient mediating and moderating measures were included. Patients were 18+ years of age who were tested at a hospital-based women's care center. Intervention was delivered by study staff. The study planned a cost analysis of intervention options.
Interventions Strategies Targeted at the Practice or Practice Systems Level	
Strategies in several studies included information technology innovation. Several considered staff re-design (e.g. a cancer prevention specialist/training for interdisciplinary teams, adding a case manager or lay health worker) and staff training (e.g., navigator training women volunteers)	Acknowledging that barriers to screening include patient and provider variables, one study designed practice level changes to be implemented within a primary care practice network. The network used an electronic medical record and established specialist referrals. The intervention was a colorectal cancer screening module using a prospective cohort design. Strategies were designed to supplement the existing medical records; the services of a cancer prevention specialist was added to provide education and facilitate ordering and follow-up (in-person, mailings and phone calls to home).
Intervention Strategies Aimed at the Community Level or Community Organizations	
No study tried to change community level factors, but a few involved organizations at the community level. Some studies, however, collected measures at the community level for use in the study design.	One study investigated the impact of faith-based lay health advisors on the use of and follow-up to abnormal Pap tests. It used a group randomized (50 religious congregations) experimental design. Formative work included community inventories (e.g. transportation, communication, health resources) to provide information to use in the training of lay advisors who would then talk with women about overcoming barriers.

*Frequencies may be greater than 16 because some studies studied more than one strategy.