Multilevel Research and the Challenges of Implementing Genomic Medicine

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Advances in genomics and related fields promise a new era of personalized medicine in the cancer care continuum. Nevertheless, there are fundamental challenges in integrating genomic medicine into cancer practice. We explore how multilevel research can contribute to implementation of genomic medicine. We first review the rapidly developing scientific discoveries in this field and the paucity of current applications that are ready for implementation in clinical and public health programs. We then define a multidisciplinary translational research agenda for successful integration of genomic medicine into policy and practice and consider challenges for successful implementation. We illustrate the agenda using the example of Lynch syndrome testing in newly diagnosed cases of colorectal cancer and cascade testing in relatives. We synthesize existing information in a framework for future multilevel research for integrating genomic medicine into the cancer care continuum.

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The Promise and Challenge of Implementing Genomic Medicine

Typical indications for cancer genetic testing include predispositional/susceptibility testing to predict risk; diagnostic testing to confirm a hereditary cancer syndrome; prognostic testing to predict natural history, such as severity or risk of recurrence; and pharmacogenomic testing to predict drug response, which might influence drug dosage or selection. Genetic tests are available to assess inherited and acquired genetic variation. Nevertheless, little intervention research has compared cancer health outcomes based on genomic medicine applications with current approaches. In addition, the potential for misuse of these applications has not been systematically examined. Genomic medicine is now a subject of considerable interest for comparative effectiveness research (13). In addition, even when the utility of a genomic application has been documented, very little research has evaluated implementation; assessed quality of testing and decision making; defined educational needs of providers, patients, and the public; evaluated its cost-effectiveness; or measured impact on population health outcomes. Such research could influence the organization and delivery of genomic medicine, as well as related health professional curricula, clinical guidelines, and public policy.

Khoury et al. (14) described four phases of translational research from basic discovery to clinical and population research that can reduce the burden of cancer (T1–T4). Understanding barriers and facilitators across these phases is crucial in maximizing the net positive population health benefits without exacerbating existing disparities. Currently, a vibrant research enterprise is underway in genomic discovery and T1 (which bridges discovery to candidate health applications, or “bench to beside”) but little genomics research conducted and published in T2 (which assesses...
candidate genomic applications in practice), T3 (implementing and integrating genomics into clinical practice), and T4 (evaluating population health impact of genomic medicine). Schully et al. (15) found that less than 2% of cancer genomics research funded by the National Cancer Institute and less than 0.5% of published cancer genomics research is T2 and beyond. Even though many genomic tests are available in practice, most tests assessed by evidence reviews have insufficient information on clinical utility and cost-effectiveness (16). Furthermore, in our targeted review, we found no real examples of multilevel research in genomic medicine as defined by Taplin et al. (11) in this supplement. However, the case study of Lynch syndrome presented below may give an early indication of the utility of multilevel approaches in genomic medicine.

**Multilevel Influences in Genomic Medicine**

To illustrate how genomics can overlay and complicate the cancer care continuum, we revisit, using a genomic lens, the two case scenarios discussed by Zapka et al. in this monograph (17). Scenario 1 is the case study of Ms Smith, a 66-year-old retired African American. The case demonstrated multiple factors that influence cancer screening (Table 1, (17)), including race, gender, health care–seeking behaviors, and community and health-care organizations. One important variable that could be added to this scenario is family history, an important risk factor for many cancers. The presence of certain patterns of family history, especially early onset cancers among multiple relatives, on either maternal or paternal side of the family, may indicate hereditary forms of cancer (eg, colorectal, breast, and ovarian cancer), thus affecting the initiation and frequency of cancer screening patterns not only for Ms Smith but also for other family members (27). Unfortunately, many people do not know about genetic transmission of cancer susceptibility and their family history of cancer (28). Additionally, family history is not systematically collected during medical encounters and is not consistently documented to identify at risk individuals. To meet this woman’s needs in a world of genomic medicine, there will be an increasing need for provider training, preparation of the organization for the testing process, a provider referral resource for people testing positive (along with follow-up), and ways of addressing the needs of the relatives who will also be affected by the information.

The second scenario discussed by Zapka et al. (17) is that of Zoe, the 42-year-old woman diagnosed with breast cancer. The case illustrated the transition from therapy to survivorship and the multiple levels of influences that affect it (Table 1). What if Zoe’s tumor was discovered to have a HER2 mutation, a known prognostic marker which would affect treatment regimen (as HER2 status determines whether or not trastuzumab should be used) and survival prospects (29)? In addition, there are a number of emerging genomic markers, such as breast cancer gene expression profiles (3), or pharmacogenomic traits (2) that can affect a patient’s decision regarding the use of chemotherapy. The presence of this “new” type of, albeit incomplete but

<table>
<thead>
<tr>
<th>Level</th>
<th>Examples of factors</th>
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<tbody>
<tr>
<td><strong>Patient with CRC</strong></td>
<td>Understanding the importance of diagnosing Lynch syndrome and cascade screening in their relatives; addressing the need for informed consent; understanding dynamics with other relatives; assessing whether screening of CRC patients for Lynch syndrome will improve their own outcomes; assessing how communication of information with relatives will be managed</td>
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<td><strong>Relatives of CRC patients</strong></td>
<td>Health and functional status, health perception, cultural factors; knowledge about cancer screening, comorbidity; patterns of health-care use; access to health-care services and insurance which could be different from those of the affected patient with CRC; geographic proximity to patients; family attitudes about screening; psychosocial impact of communication about Lynch syndrome risk through affected relatives with CRC</td>
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<td><strong>Provider team</strong></td>
<td>Knowledge and communication about Lynch syndrome screening recommendations in newly diagnosed cases of CRC; incentives for diagnosing and reporting Lynch syndrome, timing, knowledge of genetics and genetic counseling referral patterns; for patients who are positive for Lynch syndrome; coordination between various specialties (pathology, gastroenterology, oncology, genetics); reimbursement of initiating contact with relatives of patients with CRC</td>
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<td><strong>Laboratory process</strong></td>
<td>Comparing performance of different methods and approaches for screening for Lynch syndrome (eg, microsatellite instability and IHC, as well as use of DNA sequencing technology for specific screening results, ie, IHC staining for MLH1 protein); do we need local/centralized laboratories to undertake screening</td>
</tr>
<tr>
<td><strong>Health-care organization</strong></td>
<td>Policies for screening cases, integration of information, guidelines into EHRs; presence of decision support tools; standard practices on contacts of patients and relatives; interface and communication between different parts of the organization (eg, pathology, oncology, primary care, genetics)</td>
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<td><strong>Community/state</strong></td>
<td>Insurance coverage and reimbursement; existence of state guidelines for recording Lynch syndrome in medical records and in cancer registries data; state efforts to promote adoption of guidelines; certification of qualified laboratory personnel</td>
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<td><strong>National health policy</strong></td>
<td>Medicare and Medicaid benefits for testing for Lynch; national policies and oversight and regulation of genomic tests and performance of laboratories; dealing with patent issues around genomic tests; professional societies standards and involvement of multiple groups (eg, oncology, pathology, genetics, gastroenterology); possible recommendations of advisory committees for universal screening similar to newborn screening; question of necessity of a centralized laboratory testing process for implementation</td>
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* Information for this table is derived from references (17–26). CRC = colorectal cancer; EHR = electronic health record; IHC = immunohistochemistry; MLH1 = mutL homolog 1.
rapidly changing information, can only complicate Zoe's cancer care and transition to survivorship.

To illustrate multiple levels in genomic medicine, we review the laboratory testing process in genomic medicine and relate it to traditional levels including individual, familial/social, health-care organizations, community, and the regulatory and policy environment.

The Laboratory Testing Process
Genetic testing has three phases (30,31). The preanalytic phase includes determining whether a particular test is indicated, selecting and ordering the test, obtaining informed consent, and collecting appropriate specimens. Many genetic tests are offered based on family history and other characteristics, such as age, sex, and ancestry. The provider and patient discuss potential benefits, risks, and limitations of the test, and implications for relatives. The analytic phase includes specimen processing and generating results. Most genetic tests are developed by a laboratory (ie, not marketed as kits) and overseen for use by the Food and Drug Administration (31). Oversight of laboratories is provided by the Clinical Laboratory Improvement Amendments (CLIA) of 1988 (31). The postanalytic phase includes interpreting and communicating results and patient management. The traditional delivery pathway for genetic testing services involves clinical geneticists, who provide consultation to patients and their families (32,33).

With the ever increasing number of genomic applications, primary care providers will become increasingly responsible for its delivery (34–36). Unfortunately, the health-care workforce is not prepared to integrate genomics into practice (37). Errors are likely to occur during pre- and postanalytic phases (38–41). These include a lack of recognition of patients with indications for testing, errors in selecting the appropriate test and method, insufficient collection of personal and family information, and inadequate informed consent. In the postanalytic phase, misinterpretation of test results can lead to inappropriate management, adverse patient outcomes, increased costs, and increased health disparities (42). Strategies to reduce errors are available at multiple levels; some target providers through educational initiatives and clinical decision support in electronic health records (EHRs); others target organizations by creating a standardized and understandable genetic laboratory report or integrating genetic counselors/nurse geneticists in practice settings; others target patients and providers through community-level interventions such as using Internet resources to increase access to information; and finally, at the state or national policy level, by initiatives designed to increase the genetics professional workforce.

Patient–Provider Interactions
Each phase of the genetic testing process requires a multilevel perspective. Targeting provider and health-care team behavior is central to the delivery of genomic medicine. Provider behavior is influenced at many levels, including the community and policy environment, organizational structure and processes, provider characteristics, and patient–provider encounter characteristics (43–46). Provider characteristics, such as knowledge of genomics, medical specialty, years since medical school graduation, and geographic practice area, may play a role in receptivity to genomic medicine. Interventions targeting relevant patient–provider encounter characteristics that may influence adoption and implementation of genomic testing include patient knowledge and information needs, risk perception processes, patient concerns regarding genetic discrimination, cultural similarities between the patient and provider, and time available for delivery of genetic testing services. It is increasingly recognized that adopting and delivering genomic applications is not a one-time decision and implementation event that may be replicated by simple imitation but needs to be considered a dynamic ongoing series of encounters and decisions in an organizational and strategic planning context.

Patient–provider health communication and patient-centered health technologies can enhance productive encounters between activated patients (47) and proactive provider teams (48,49). Patient activation—the extent to which patients are engaged in their care and treatment/prevention planning (50)—may be especially important in genomic medicine. Key psychosocial factors include self-efficacy, coping and problem-solving style, and self-management skills, preferences, and risk and illness perceptions to enhance informed decision-making (51). Other issues include patients’ expectations of providers, experience of and trust in health-care systems, understanding of complex medical issues, such as health risks, treatment benefits and potential harms, and levels of health literacy (52) and health numeracy (53).

Family and Social Support
Family and social support systems also are important intervention targets in cancer care generally, and genomic medicine in particular. Spouses and family members provide support, even sacrificing their careers or living situations for loved ones, but also can also be affected by stress and conflict (54). Cancer-related treatment decisions and associated personal and financial stress can surface long-standing family interaction patterns and dysfunctions. Consideration of the genetics of cancer and treatment has direct implications for family members. To adequately care for an individual with a genetic alteration in cancer, the provider must anticipate that patient’s family will have questions and concerns (55). How those concerns influence the patient’s adherence to care may need consideration to maximize the impact of therapy.

Health-Care Organizations
Health-care organizations represent an important intervention level in the translation of evidence-based recommendations, including genomic medicine, into clinical care (56,57). They need to comply with national, state, and local policies while creating an environment that supports patient care (58). In the United States, health care is delivered through multiple generally nonintegrated systems (59). The result is highly variable service delivery and inadequately measured outcomes. In 2003, Schuster et al. (60) noted that patients with chronic illness receive only 60% of recommended treatments, whereas 20% of the interventions rendered are contraindicated (60). This finding has been confirmed in the oncological setting (61,62), as well as in breast cancer genetics practice (63). A 2003 report indicated that nearly 50% of the care in the United States is delivered in practices with one or two physicians and 82% in practices of nine or fewer physicians (64). Data specific to oncology practice are not available, but in a 2007 American Society for Clinical Oncology (ASCO) workforce survey, 9% of oncologists...
report practicing solo, 8% are in a partnership, and 46% are in either a single specialty (32%) or multispecialty (14%) group practice (65). Urban–rural care and survival disparities also could support these findings, given that multidisciplinary care is less likely to be available in these areas (66,67). The problem is likely to worsen as the sheer volume and complexity of genomic information increases. Although it is tempting to target the care provider as the “problem” and direct remediation strategies at the provider to “correct” the problem, interventions directed toward individuals (providers and patients), groups (medical practices), and more complex organizational levels are more likely to succeed (68).

EHR systems have been proposed as a solution to the problems outlined above (69). Fully functional EHRs will be a valuable tool in care because of their ability to collect, aggregate, and synthesize information that can subsequently be distilled and presented to providers and patients in real time. This may be of particular relevance to genomic medicine where disparate data on disease status in relatives, and an increasing amount of laboratory-based information must be aggregated. However, EHRs alone are not sufficient to improve patient care and safety (70–72). Availability of EHRs is also an issue; as of 2008, only 4% of practitioners have access to a fully functional EHR system and 13% to a basic EHR system (73). The situation is slightly more encouraging for oncologists, as a survey done by the ASCO EHR workgroup indicates that EHR adoption may be approaching 25%, although the functionality of the EHRs was not defined (74). This is an issue even for hospital-based practitioners, as only 1.5% of hospitals surveyed have comprehensive systems and an additional 7.6% have a basic system (75).

Acknowledging the potential impact of policy, we focus on the role of health-care organizations in the translation of genomic medicine as a critical level of research to improve patient care. Although genomic medicine may increase the volume and complexity of the information needed by providers, the fundamental challenges for genomic medicine are similar to those encountered in any clinical improvement effort for developing the appropriate structure and processes for care. A key element to improve practice is the development and application of clinical guidelines, and ASCO has produced 25 to date (76,77). Guidelines, like EHRs, are necessary but not sufficient to improve care. If an organization recommends the use of a genetic test, then it must ensure the availability and adequacy of the all steps of the testing process. Examples of barriers were identified in medical oncology by Hains et al. (78). Factors involved in guideline development and implementation processes are discussed elsewhere (79,80).

Most health-care organizations do not have the capability to translate guidelines into clinical practice. In a survey of organizations redesigning their health-care delivery, Wang et al. (81) identified four success factors: 1) direct involvement of leadership; 2) strategic alignment of improvement efforts with organizational priorities; 3) systematic establishment of performance appraisal systems for continuous improvement; and 4) proactive development of champions, teams, and staff. In surgical oncology, the Ontario health system improved compliance with guidelines by using a community of practices model (82). Central to the effort was knowledge management that assessed not only scientific evidence but implementation factors (eg, feasibility, adaptability, and transparency to evaluation). The authors concluded that customization of guidelines to match the care delivery setting was essential to success. The process to implement a tumor-based screening program to identify patients with Lynch syndrome (Table 1) in a large health-care system was recently described (18).

Community
Although community research on methods to increase implementation of genomic medicine is limited (83), several interventions have been found effective in increasing the delivery of various cancer-related clinical services, such as tobacco cessation therapies, immunization (eg, to prevent cervical cancer), and cancer screening. These interventions include numerous approaches that influence behavior at many levels, such as health system policy changes to increase access to service, thereby reducing costs or structural barriers; health plan or health provider use of systems or registries to identify patients in need of the service and to provide reminders to providers and patients; public education; and individually tailored education and shared decision making using one-on-one counseling (84–87). Ongoing monitoring of individual or organizational performance by the community or through a state health department or in the future, an accountable care organization, provides measures and comparisons that may be difficult to attain. Providing feedback based on such measures has been effective in increasing delivery of recommended cancer services by providers, for national organizations in increasing delivery of services by health plans, and for governmental organizations in increasing the delivery of effective tobacco control policy interventions by state and local governments (88–90). Public health intervention strategies found to be effective in increasing use of cancer clinical services may also be effective in enhancing implementation of genomic medicine. For example, state health departments might identify all health plans/health insurers in their states and evaluate coverage for each recommended genetics service, including counseling, testing, and related care. They could promote insurance policy changes to improve access by providing feedback to the health plans on coverage provided by other plans. Similar interventions could be undertaken to evaluate and promote policy changes with health-care provider groups and state associations of health professionals. State and local health departments could use existing communications channels to provide effective educational materials to the public and providers on recommended genomic services.

State policy may be a useful context for designing intervention research or comparing “natural experiments” in genomic medicine implementation. State-level surveillance systems such as the Behavioral Risk Factor Surveillance System (91) could be used to monitor variation in the reported use of widely services across states, such as consultation for BRCA1 gene testing. State cancer registries (92) could be used to track variation in use of KRAS gene testing for decision making in cancer therapy. States might experiment with available online decision support tools in formats compatible with EHRs to assess differential effectiveness while permitting customization in different settings (93).

Policy and Oversight
Rapid growth in genetic testing poses policy and oversight challenges. Several policy levels potentially influence the uptake of genomic
medicine in cancer, including the national health policy environment (national health reform, reimbursement policies), the state health policy environment (insurance and licensure regulations), and the local community environment (eg, local health-care markets and professional norms). Three sets of issues are considered: 1) regulatory issues concerning direct-to-consumer marketing of genetic testing and reimbursement and/or insurance coverage of genomic medicine, 2) public health policy, specifically the development of licensure and training standards for genomic medicine-related professionals and technical personnel, and 3) market structure affecting developers of genomic medicine.

Most direct-to-consumer genetic tests have unknown clinical validity and utility (94). Although most personal genetic tests are marketed online, recently, a pharmacy chain announced briefly the intent (95) to sell these products in stores nationwide. These tests include genetic susceptibility for many illnesses. In 2008, a multidisciplinary National Institutes of Health–CDC workshop identified knowledge gaps in personal genomics and recommended multilevel clinical and population research to fill these gaps (94). Many have cautioned against widespread use of personal genetic tests, especially given the insufficient evidence on the predictive value of newly discovered genetic risk factors (94–96). The extent to which medical professionals are able to provide counseling is not well understood, and some evidence suggests that referrals for genetic counseling do not necessarily increase in areas where consumer interest in genetic testing has increased (97,98).

Policy oversight greatly affects the diffusion and availability of genomic medicine, which involves insurance coverage policies through state-mandated benefit policies, Medicare/Medicaid coverage policies, and third-party insurance plans. State insurance law tends to focus on legal issues related to discrimination and privacy. Mandates for specific tests are rare, although coverage of genetic counseling services can lower access barriers. As with most treatment innovations, coverage is tied to efficacy and medical necessity. Private insurers perform technology assessment, and each insurer makes its own decision regarding coverage using internal resources, technology assessment resources, online coverage bulletins from other payers and Medicare coverage decisions.

Khoury et al. (99), among others, have discussed the development of “coverage with evidence development,” a model used by the Centers for Medicare & Medicaid Services (CMS) to allow Medicare coverage of experimental treatments under controlled research protocols. This model currently allows coverage of a limited number of technologies with assured clinical data accrual for those patients. However, CMS has resisted issuing national coverage determination policies, in part, for fear of the cost implications. This leaves coverage determination to local policies by fiscal intermediaries under contract to CMS, with the potential for wide variation. CMS also has developed a “new technology add-on payment program,” to allow additional payments for the use of breakthrough technologies on an inpatient basis. Early evaluation of the program suggests that it may help remove some genomic medicine payment barriers in hospitals; however, the growing use of these technologies in ambulatory settings may mitigate the benefits of this program (100).

A final factor concerns the market structure influencing the development of genomic medicine. In his extensive reviews (101–106), Burns explores the impact of merger and acquisition activity on the financial performance of pharmaceutical firms and future innovation. Classical industrial organization arguments for mergers and acquisitions stress the need to achieve economies of scale and to speed entry into new markets. However, Burns data show that recent waves of merger and acquisition events have concentrated on mega-mergers among the largest pharmaceutical firms. This has led to a highly concentrated pharmaceutical market but few positive effects on innovation. Biopharmaceutical pipelines continue to be constricted due to unclear guidelines and inadequate laboratory capacity. Mega-mergers seem closely related to increased environmental pressures, including proliferation of health maintenance organization pharmacy benefit managers and regulatory constraints. More recently, Pricewaterhouse Cooper has shown that the “flurry of deal activity” in the in vitro diagnostics included both mergers and acquisitions and strategic alliances (106).

**Putting It Together: Toward a Multilevel Research Agenda in Genomic Medicine**

Multiple levels inform policy and practice in genomic medicine. Taken together, all levels of the “onion” have a potential role in informing what works and what does not work in implementing genomic medicine. As discussed in the chapter by Stange et al. in this monograph (107), it is not so much the number of levels of the onion, or sheer number of multilevel activities conducted, but the interplay and alignment of activities across levels appears to be critical (107). Several types of research can inform this area, including surveillance, observational, interventional, implementation, and dissemination research. A key question remains concerning where to start, as Weiner et al. (108) describe in this supplement. Next steps depend upon the intervention and research question and conceptual mapping of question-to-research-design. Such mapping helps to reveal the combination and possibly the sequencing of multilevel factors and interventions. The current genomic medicine literature is sparse on this topic. The following example uses the Weiner et al. (108) Convergence and Facilitation Intervention Strategy as an example of how such multilevel research designs could be conceived in cancer genomic medicine (see Figure 1).

Lynch syndrome is a common cause of inherited colorectal cancer (CRC), accounting for approximately 3% of all CRC cases in the United States. In 2009, the Evaluation of Genomic Applications in Practice and Prevention (EGAPP), an independent multidisciplinary working group, recommended screening for Lynch syndrome in all newly diagnosed CRC cases to reduce morbidity and mortality in family members (19). Risk of CRC morbidity and mortality can be dramatically lowered by using colonoscopy at an earlier age and greater frequency than recommended in the general population. By identifying Lynch syndrome mutations in CRC cases, family-specific analyses can be performed to identify at-risk relatives. To explore multilevel challenges for implementing the working group’s recommendation, the CDC convened a multidisciplinary panel. Participants identified challenges and research strategies. These include lack of patient, family, and provider knowledge of Lynch syndrome and testing issues; informed consent issues on probands; use of genetic services; psychosocial impact; responsibility of cascading...
Figure 1. Potential convergence and facilitation of intervention strategies: Lynch syndrome testing. Box indicates intervention and level of influence (in parentheses). Diamond indicates the mediator. Oval indicates the outcome. Convergence intervention strategies are those interventions at multiple levels that mutually reinforce each other by altering patterns of interaction among two or more target audiences. A facilitation strategy is one that enables another strategy to reach an objective.

from probands to relatives, patient, provider, and relatives’ compliance; testing limitations; public health and policy infrastructure needs; as well as cost effectiveness for implementation in the “real” world (20). In spite of the EGAPP working group recommendations for screening and the recently published favorable cost-effectiveness analysis for screening (21), there is still lack of consensus on who should be screened for Lynch syndrome (22). There is incomplete knowledge of this syndrome among healthcare providers (23). The CDC participants discussed how research at multiple levels can be brought together to implement Lynch syndrome recommendation. A distinguishing feature of this scenario is the need to include multilevel intervention among family members, who can come from different geographic locations and communities as well as health delivery systems, in addition to the biological and cultural set of interactions that are unique to families. Family dynamics are important in encouraging patients with Lynch syndrome to inform their relatives of their increased risk and have been rarely evaluated [see recent study from Japan, (24)]. In addition, knowledge about how family members at risk perceive their situation is quite limited (25). At the health system level, the lack of consensus and provider awareness has also been associated with divergent referral and testing practices (26). Furthermore, the ability of available information systems to track patients and families to assure appropriate referral, counseling, and testing is limited. Finally, payment and coverage barriers must be overcome at the federal and state level, to align incentives with clinical care.

Table 1 shows a summary of multilevel factors involved and what questions need to be answered individually and in combination. Several health-care plans have recently implemented pilot projects for Lynch syndrome screening including Intermountain Healthcare in Utah (18). In that context, a combination of literature reviews, simulation modeling, and stakeholder consultations have identified the most efficient protocol for implementation. The evaluation of a multilevel approach to Lynch syndrome and genomic medicine in general will benefit from the theoretical framework established by Taplin et al. (11) and illustrated throughout this monograph [e.g. (17)].

In conclusion, we need a multilevel research agenda that allows us to accelerate the implementation and evaluation of genomic applications. Tunis et al. (109) and the CONSORT group on pragmatic trials (110) have characterized this pathway by thinking about research applications that affect further research, clinical policy, care delivery, and health-care outcomes. Drawing from their formulation, we should conduct simultaneously, not sequentially, multidisciplinary research that enhances the knowledge base and the quality of future implementation research that can influence practice and policy. Our progress through this translational pathway has barely begun for genomic medicine. The literature is scant, and our knowledge is more anecdotal than systematic about how genomic discoveries are used. The challenges of acquiring a deeper understanding of how these factors influence policy and practice point to a new frontier for genomics in cancer control research.

References


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