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Understanding and Influencing Multilevel Factors Across the Cancer Care Continuum (Taplin et al.)

Multilevel contextual influences upon health have been recognized for many years, though the definitions of those levels vary. This paper provides the definitions of levels, interventions, and other key terms as well as the motivation for expanding the foundation for interventions that address multilevel influences upon health. We define levels to mean the units of human aggregation relevant to health; individuals, families, healthcare delivery teams, and healthcare organizations. We define interventions to mean a specified strategy or set of strategies designed to change the knowledge, perceptions, skills, and/or behavior of individuals, groups, or organizations with the goal of improving patients' health outcomes. There has been a growing interest in the analysis of multilevel influences upon health, but multilevel interventions to affect health are rare. Multilevel interventions are advocated because there is a growing recognition that improvements in technical aspects of care are adopted slowly. We contend that slow adoption is affected by failure to address multilevel contextual issues that affect care delivery. Adoption of a technical improvement in care requires systematic changes in the context of care that are more demanding than having knowledge of the evidence for that improvement. The supplement expands the foundation of our understanding of multilevel influences by demonstrating multilevel thinking in the care process, the state of the art in multilevel interventions in health, time and design considerations in the development of multilevel interventions, measurement of multilevel effects, and application of multilevel influences in practice. The latter includes multilevel considerations for adopting a change in healthcare delivery, as well as the multilevel influences of healthcare reform from the perspective of its designers and the populations it is designed to serve.

Multilevel Factors Impacting Quality: Examples From the Cancer Care Continuum (Zapka et al.)

Background: The cancer care continuum represents several types of care, each of which includes multiple technical and communication steps and interfaces among patients, providers, and organizations. These interactions ultimately affect quality of care and patient outcomes. The complex environmental context of these interactions, as well as community and policy levels, must be considered as we move forward to improve care.
Methods: We use two case scenarios to (1) illustrate the variability, diversity, and interaction of factors from multiple levels that affect the quality of care across the cancer continuum and (2) discuss implications for research and provide hypothetical examples of multilevel interventions. Each scenario includes a targeted review of the literature to illustrate contextual influences upon care, raises questions about their potential effects on outcomes, and sets the stage for theory-informed targeted-intervention strategies.
Findings: The case scenario of cancer screening highlights access issues in older women. The case scenario about cancer survivorship after initial treatment illustrates the multiple factors and challenges faced by patients, their families, and organizations in addressing the complex and variable needs as patients traverse the care continuum. Examples illustrate how multiple strategies could have a positive impact on processes that improve safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity of care, and ultimately affect morbidity and mortality. Table 1 illustrates how multiple determinants at multiple levels can be associated with outcomes of care.
Conclusions: In research and practice, attention must focus on planning and testing strategies that work synergistically at several levels, recognizing that these present challenges in study design, measurement, and data analysis. Despite these challenges, it is an exciting time to push forward with building an evidence base about the potential of multilevel interventions to improve patient and population outcomes.

The targeted review of the literature provides numerous examples of studies that demonstrate how factors from multiple levels are associated with outcomes of care. These are summarized in Table 1. The situations on each of the two case scenarios presented in the manuscript could be considered a single-level issue; e.g., an unscreened woman should take action to get screened, or a patient post-treatment should initiate contact with her oncologist to seek care.

We encourage conference participants to consider their own clinical care and what problems they've experienced as a patient (or as a provider) that could be conceived as a scenario amenable to multilevel intervention strategies. Additionally, we ask participants to consider the following:

- The process of identifying the potential multilevel determinants of care quality for a specified health outcome
  - Do we have models to guide the prioritization of strategies at various levels to produce outcomes that need improvement?
  - What problems within each type of care should be research priorities?

Table 1: Potential Factors by Level Associated with Outcome Measures (*case-specific issues in italics*)

Outcome of Interest	Level of Influence and Examples of Factors Affecting Outcome of Interest						
	Individual Patient	Family/Social Supports	Provider/Team	Organization/Practice Setting	Local Community	State Health Policy	National Health Policy
Case 1: Screening in the Elderly							
Increasing cancer screening rates; reduced Ca morbidity and mortality	▪ *Health and functional status* ▪ *Risk perceptions* ▪ Cultural factors ▪ Knowledge about cancer & screening options ▪ Co-morbidity ▪ *Patterns of health care utilization.* ▪ *Access, (e.g. insurance,* transportation)	▪ *Proximity of family members* ▪ *Interaction with family* ▪ Family attitudes about patient's health status and behaviors ▪ Family and friend prior experiences with screening and cancer ▪ Screening behavior of people in social network	▪ Number of clinic encounters in last year ▪ Clinician knowledge and communication about recommended screenings ▪ Physician incentives ▪ Performance reporting ▪ Time ▪ Team resources	▪ Standard practice concerning patient contact ▪ *Outreach practices (e.g., reminders) by organization/practice* ▪ Opportunities for in-reach during routine visits ▪ Systematic links between providers (e.g., primary and specialty ▪ Medical record system type and quality ▪ Patient education resources ▪ Patient navigation to improve adherence	▪ Community screening promotion efforts (mass media, church, lay advisors) ▪ Specialist capacity	▪ *Insurance coverage, policies, and reimbursement* ▪ Special programs, e.g., CDC-DPH collaborations	▪ Medicare benefits ▪ *National insurance mandates & policies*
Case 2: Cancer Treatment and Transition to Survivorship							
Improve Coordinated / shared follow-up care; reduced morbidity and mortality and improved quality of life	▪ *Life stage* ▪ *Health and functional status* ▪ Treatment toxicity ▪ *Post-tx symptoms* ▪ *Fear of recurrence* ▪ *Lack of control and uncertainty* ▪ Potential for late effects ▪ Lack of info on surveillance needs ▪ *Work and family roles and responsibilities* ▪ Cultural factors	▪ Family understanding, communication and coping ▪ *Problems with sexuality and intimacy* ▪ Employer expectations	▪ *Coordination between oncology treatment team and PCP* ▪ *Follow-up plan* ▪ Opportunities for health promotion and prevention ▪ Patient-provider and provider-provider communication ▪ Knowledge of clinical guidelines ▪ Time	▪ Extent of integrated care delivery ▪ Access to quality EHR ▪ Incentives for care coordination ▪ Availability of reminder systems ▪ Standards for reporting, and surveillance plans	▪ Resources for cancer survivors	▪ Insurance coverage, policies and reimbursement	▪ National policy ▪ Medicare coverage ▪ Professional Society Standards

State-of-the-Art and Future Directions in Multilevel Interventions Across the Cancer Control Continuum
(Stange et al.)

Purpose: To describe the current state of multilevel cancer control intervention research and identify opportunities to advance cancer control through multilevel research.
Methods: We conducted multiple iterations of literature searches to identify the range of scientific articles relevant to multilevel interventions. From this literature, we developed a matrix of article types, characterized how multilevel research currently is conceptualized and implemented, and identified illustrative intervention examples. We identified current controversies and missed opportunities and developed recommendations for future research.
Results: We found a large number of potentially relevant studies, including many outside the field of cancer control. More multilevel articles relate to prevention and screening than other stages of the cancer control continuum. A number of theory articles identify potential opportunities for improved interventions by working across multiple levels. While many studies reference ecological, systems, and complexity models, few studies apply theory systematically to inform interventions. The most informative empirical studies link conceptual models with interventions that target three or more levels, evaluate process measures at several levels, and assess outcomes over more than one level. Opportunities to advance cancer control through multilevel interventions relate to design (dynamic, adaptive, emergent designs that evolve over time and include greater attention to contextual factors and the interfaces between levels), analysis (the use of multimethod approaches that integrate quantitative modeling across multiple levels where relevant data can be generated, qualitative methods that evaluate levels with small numbers and identify the specific inter-level processes that are important for the outcomes of interest, and complex systems and dynamic simulation modeling to provide additional insights in levels where data are sparse), and translation (evaluating and interactively disseminating interventions that are participatory, locally adapted, evolutionary, and focus on how multiple levels interact in context, rather than in isolation).
Conclusions: Multilevel interventions can advance cancer control by using theory and mixed quantitative and qualitative methods. Particular opportunities exist for interventions that create synergy across multiple levels, continually pay attention to context, and adapt over time. Transdisciplinary participatory research approaches can help to realize these opportunities to generate new knowledge to reduce the burden of cancer.

In Search of Synergy: Strategies for Combining Interventions at Multiple Levels (Weiner et al.)

The social ecological perspective provides a compelling justification for multilevel intervention. Yet it offers little guidance for selecting interventions that work together in complementary or synergistic ways. Using a causal modeling framework, we describe five strategies for increasing potential complementarity or synergy among interventions that operate at different levels of influence. Given the importance of interdependence in the social ecological perspective, we focus on two types of causal relationships: mediation and moderation. To illustrate the potential strategies for increasing synergy and complementarity using a moderation/mediation framework, we focus on interventions to improve the quality of treatment of locally advanced rectal cancer. Briefly, in the accumulation strategy, interventions at different levels produce a cumulative impact on a common mediating pathway or set of mediating pathways. The interventions exhibit what scholars call pooled interdependence, meaning that each intervention makes a discrete contribution to the outcome without being dependent on each other. In the amplification strategy, the effect of one or more interventions is conditional on another intervention. One intervention increases the target audience's sensitivity or receptivity to the other intervention(s). That is, one intervention amplifies the magnitude of the effect of the other intervention(s) on the mediating process or pathway. In the facilitation strategy, the effect of one or more interventions is also conditional on another intervention. However, instead of boosting the signal, the conditional intervention clears the mediating pathway for the other intervention(s) to produce the desired outcome. In other words, one intervention removes the barriers or facilitates the effect of the other interventions. In the cascade strategy, an intervention at one level affects the desired outcome in and through one or more interventions at other levels of influence. The interventions demonstrate what scholars refer to as sequential interdependence, meaning that the outputs of an intervention at one level become the inputs of an intervention at another level. Finally, in the convergence strategy, interventions at different levels mutually reinforce each other by altering patterns of interaction among two or more target audiences. The interventions exhibit what scholars call reciprocal interdependence, meaning the outputs of some interventions become the inputs of other interventions and vice versa.

A key issue for discussion is whether theory and research have advanced to the point that they could guide the design of multilevel interventions. Do we have theories that explain how determinants at multiple levels interact to produce health and other important outcomes? Do we have enough cross-level research that examines the interdependence of variables (determinants) at multiple levels of influence? Finally, do we have sufficient grasp of the causal mechanisms that through which commonly used interventions produce their effects?

Time Issues in Multi-level Interventions for Cancer Treatment and Prevention (Alexander et al.)

The concept of time introduces important complexities in estimating intervention effects, program and evaluation design, and measurement and analysis of individual change in multi-level interventions (MLIs). In this paper we discuss: (1) conceptualizing disease life course and treatment theory in MLIs, (2) approaches to incorporating time in research and program design for MLIs in cancer treatment and prevention, (3) analysis of time varying multi-level data in the context of cancer treatment and prevention, and (4) resource considerations and tradeoffs of incorporating time as a dimension of multi-level interventions and analysis. Despite growing recognition that time is a critical element for assessing both individual-level outcomes and higher level changes in organizational, community, and policy contexts, most MLI program designs and evaluations have not addressed these issues. Although analytic techniques for analyzing time-related phenomena are becoming more available and powerful, corresponding progress has not been made in the development of theory to guide the application of these techniques in program design, growth curve modeling, or program implementation. As theoretical development in these areas improves, such inefficiencies will likely be reduced. However, in the near term, we can expect to incur significant costs as empirical work and theoretical development proceed in parallel.

Multilevel Interventions: Study Design and Analysis Issues (Cleary et al.)

Multilevel interventions, such as those implemented at the individual, physician, clinic, health care organization, and/or community level, increasingly are proposed and used in the belief that they will lead to more substantial and sustained changes in critical behaviors related to cancer prevention, detection, and treatment than would interventions at only a single level. This article reviews approaches to the design and analysis of multilevel interventions.

There are well developed and accessible statistical techniques for analyzing multilevel interventions and a well-developed literature on research designs that are applicable to multilevel interventions. However, there are several serious challenges to implementing and evaluating such interventions. For example, without knowing about the way in which the primary outcome and predictor variables vary within and between different units at different levels, it is difficult to determine the sample sizes needed. Furthermore, the units at which interventions will be directed, especially higher level units (e.g., organizations and communities), are often difficult to randomize and/or develop control units for.

Probably as a result of these challenges, empirical evaluations of multilevel interventions in different fields provide surprisingly little information about the impact of intervention components on different levels and rarely evaluate the independent influence of intervention components on the main outcomes of interest. We also found little information in the literature on the cost-effectiveness of different components of multilevel interventions. We suggest that without more convincing evidence of the incremental benefit and probably cost effectiveness of different components, such interventions will not be implemented widely.

Thus, we think it is incumbent upon those arguing for the more complicated multilevel intervention approach to do research that explicates the specific contributions that interventions at different levels make to the desired outcomes and what the cost of those components are. That will require creative designs and sophisticated analyses that account for the complex structure of such data. If we address those challenges, however, we are likely to gain greater insights into the kinds of interventions that can be implemented effectively and efficiently to improve health and health care.

Computer Simulation Models and Multilevel Cancer Control Interventions (Morrissey et al.)

This paper presents an overview of computer simulation modeling as a tool for multilevel cancer care research. In this context, simulation models are computer-based representations using mathematics, rules, and logic to portray cancer and the dynamic multifaceted influences of cancer processes over the lifetime of the organism or system. Simulations have been conducted at various "beneath the skin" or biological scales as well as at various "above the skin" or social-ecological levels of cancer care delivery. Most of these models, however, only deal with 1 or 2 vs. 3 or more levels.

We highlight the multiple functions of simulation modeling. It is a technique for explicitly describing the detailed workings of a system, identifying what is known and unknown about component parts and processes, and developing and evaluating alternate "what-if" scenarios about their interactions. Simulation is also a heuristic tool to generate hypotheses, models, and theories about the mechanisms underlying system behavior. Computer simulations can be used to conduct numerical or "virtual" experiments when real-world experiments are impractical for pragmatic, theoretical, or ethical reasons. They can also be used to identify the most powerful "leverage points," or places in a system where changes are likely to improve outcomes most substantially and to estimate the value of obtaining better information.

The various types of computer simulations are distinguished by several pairs of attributes: stochastic or deterministic, steady-state or dynamic, continuous or discrete, local or distributed. We illustrate these applications in four cancer intervention areas: tobacco control, colorectal cancer screening, cervical cancer screening, and breast cancer with regard to racial disparities in access to care. We suggest ways these models can be expanded in future research to consider interactions involving three or more socio-ecological and/or biological levels.

Looking forward, additional research is needed to address a number of methodological, structural, and communication barriers that stand in the way of creating useful multilevel computer simulation models of cancer interventions and population health. Methodological challenges include information gaps associated with missing or fragmented data; limited understanding about how to integrate and validate complex multilevel models; the need for more efficient computational algorithms and distributed computer networks. All of these create a substantial learning curve for the modeler. Structural challenges include the requirement for multi-disciplinary teams, the shortage of cancer-specific training programs, and the lack of grant review and funding infrastructure specific to modeling disciplines. Communication challenges speak to the lack of a common language to integrate diverse modeling traditions and the need for a CISNET-like "learning community" for multilevel modeling in cancer.

The biggest communication challenge, however, is with external target groups. If we build complex multilevel models of cancer control, will anyone believe them? How can we get these audiences to trust and use them in personal, clinical, and policy decisionmaking?

Multilevel Interventions: Measurement and Measures
(Charns et al.)

The purpose of this paper is to explore the issues/opportunities related to measurement when planning, developing, and implementing multilevel interventions across the cancer care continuum. Specifically, the paper will present the results of a review of the literature on interventions in cancer care. Original articles on this topic are categorized in terms of the phase(s) of the cancer care continuum that are the focus of each study, whether the intervention(s) in the study are single-level or multilevel, and whether measure(s) are single-level or multilevel. Implications for designing interventions and research are discussed, as is the limited information available on measurement in abstracts of articles on cancer care.

Healthcare Reform and Multilevel Interventions and Research: Big Changes Go Hand-in-Hand with Big Science
(Devers et al.)

On March 23, 2010, President Obama signed into law the Patient Protection and Affordable Care Act (ACA) that calls for sweeping changes to the nation's healthcare system in an effort to increase access and improve quality and efficiency. The purpose of this paper is describe and discuss the implications of ACA and other major pieces of legislation passed in 2009,[1] for cancer care and related research. We first identify and describe several major areas and provisions in these landmark pieces of legislation and their implications for the cancer care continuum and research. These major areas and provisions include insurance coverage for cancer care and clinical trials, new provider payment (e.g., shared savings, bundled payments) and delivery models (e.g., patient-centered medical homes, accountable care organizations), electronic medical record (EMR) and health information exchange (HIE), and research (e.g., comparatively effectiveness research). We then describe the implications of the implementation of these provisions for the kinds of health services research required in the cancer arena. Continuing with these major areas and provisions, and select NCI programs such as the Community Cancer Center Program (NCCCP), we illustrate and discuss how the implementation of these reforms occurs at multiple levels of the health system (i.e., national, state, local markets comprising specific health plans, providers, community organizations, and care teams working within and between these organizations, and unique patient populations). They may also target different points in the cancer care continuum (e.g., outreach, screening and prevention, treatment, trials, survivorship) and transitions between them (e.g., community, outpatient, and inpatient). Last, general concepts must be translated into specific and often-complex, multilevel interventions that often vary based on states' and local markets' prior history, interpretation, and current capacities and constraints. Now, more than ever, the environment requires the field to develop and utilize strong multilevel theory, methods, data, and strategies (e.g., partnerships, inter- and transdisciplinary teams) to monitor the implementation and impact of this historic legislation on the structures, processes, and outcomes of cancer care in the U.S. The paper concludes with recommendations for how best to develop this multilevel infrastructure to ensure that the Big Changes underway are accompanied by a new, health services research Big Science approach that helps the field produce the best evidence about what works or does not work in cancer care research and why.

[1] For example, The Health Information Technology for Economic and Clinical Health (HITECH) provision of the American Recovery and Reinvestment Act (ARRA) and the Children's Health Insurance Program Reauthorization Act (CHIPRA).

Implementation and Spread of Multilevel Interventions into Practice: Implications for the Cancer Care Continuity
(Yano et al.)

Abstract : The promise of widespread implementation of efficacious interventions across the cancer continuum into routine practice and policy has yet to be realized. Greater recognition of the importance of multilevel influences in advancing (or hindering) the impact of single-level interventions has motivated the design and testing of multilevel interventions designed to address them. However, implementing research evidence from multilevel interventions into sustainable routine practice and policy presents substantive challenges. As a result, relatively few multilevel interventions (MLIs) have as yet been conducted along the cancer care continuum, and fewer still have been implemented, spread or sustained in practice. The purpose of this paper is therefore to illustrate and examine the concepts underlying the implementation and spread of multilevel interventions into routine practice and policy using a series of cancer and non-cancer exemplars spanning different levels and different stages of the care continuum. Describing their approaches and methods, we critically appraise these exemplars, drawing thematic lessons across them and making recommendations for enhancing implementation and spread of multilevel interventions into practice.

Key Question: During the presentation, I will emphasize defining implementation at multiple levels (i.e., "what does implementation mean?" and "what does implementation mean at each level?"). The goal will be to get the audience to consider the design and evaluation of implementation strategies for the kinds of multilevel interventions to which they have been introduced by previous speakers and/or in their own research.

Most scientific evidence about what works for improving health and health care stems from single-site and single-level interventions, taking decades to move from clinical trial results to care at the bedside or in clinic offices. Inconsistent application of such evidence renders the promise of evidence-based practice—implementation of efficacious interventions into routine clinical care—stubbornly elusive. However, the "voltage drop" in outcomes described across many efforts to implement evidence into real world settings should not be surprising when the highly controlled and homogenized nature of the original efficacy studies are taken into account. Fostering the adoption, implementation, spread and sustainability of new evidence requires explicit attention to the multiple levels of contextual influence surrounding any particular single-level intervention (e.g., communities/families surrounding patients; organizations and policies affecting providers/teams). Context may be defined as situational factors (e.g., social or normative environments, institutional structures, workplace conditions, community attributes, industry- or economy-wide characteristics) that have the potential to influence the availability and quality of resources and capabilities of enacting intervention changes at each level. Taking an efficacious intervention to scale in other settings and circumstances therefore requires the design and evaluation of strategies that explicitly consider the many contextual factors relevant to the evidence being implemented. The resulting "implementation intervention" is itself multilevel, mapping to the original MLI, considering stakeholders in the new processes underlying each level of the MLI, and the balance between

core elements of the evidence and adapting their form to local contexts in ways that foster their adoption and implementation.

Using cancer and non-cancer exemplars, we describe lessons learned about implementation and spread of MLIs into practice and policy. These lessons include attention to the combinations and phases of MLI implementation (e.g., number of levels, depth of work at each level, inter-dependencies across levels, social marketing of implementation activity, value of rapid cycle improvement methods, top-down vs. bottom-up implementation); the importance of partnerships within and across levels (e.g., team building, role specification, accountability, resources); implementation barriers and facilitators (e.g., organizational supports, turf and silos); the roles of policy context, fiscal climate and performance incentives (e.g., aligning implementation objectives); determinants of spread (e.g., timing, applicability, champions, quality monitoring programs); use of theory; and measurement/design of MLI implementation studies.

Linking Multilevel Approaches to Issues in Health Policy (Warnecke et al.)

Policy generally is set at the state or national levels; yet its effectiveness is often determined by its administration in local contexts. Thus, multilevel analyses can assess the possible impact of policy on an issue like disparity in breast cancer mortality. Programs such as the National Breast and Cervical Cancer Early Detection Program , the National Preventive Services Task Force, Medicaid, Medicare, and the Community Health Centers Program reflect policy to address the disparity. However, administration and implementation by states in areas where disparities exist often has a significant impact on their effectiveness. Thus, implementation context is a second level. The outcome, stage at diagnosis as an approximation for mortality, is the third level. We use a multilevel model developed by the eight Centers for Population Health and Health Disparities, funded by NIH to demonstrate the value of multilevel research from the local perspective as we examine three pathways through which local impact affects policy designed to address disparities in breast cancer mortality. Context in this paper is defined by area of residence. The three policy issues are: access to mammography for early detection of breast cancer, the quality of the mammography in the available sites, and finally the effects of environmental stress in women's living conditions upon the aggressiveness of their disease when it occurs. Finally, we examine how community intervention has made policy, based on a multilevel analysis of factors related to quality of mammography screening, that may result in improved quality and access.

Multilevel Approaches and Challenges of Implementing Genomic Medicine (Khoury et al.)

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 (GM) into current cancer practice. We explore how multilevel research can contribute to implementation and dissemination of GM. We first review the rapidly developing scientific discoveries in GM 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 GM into policy and practice and consider challenges for successful implementation. We synthesize existing information in a framework of multilevel intervention methodology and make recommendations for future research on the integration of GM into the cancer care continuum.