In Search of Synergy: Strategies for Combining Interventions at Multiple Levels

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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: accumulation, amplification, facilitation, cascade, and convergence. We illustrate these strategies with examples of multilevel interventions to improve the quality of cancer treatment.

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You think that because you understand "one" that you must therefore understand "two" because one and one make two. But you forget that you must also understand "and."—Sufi teaching story

The social ecological perspective provides a powerful conceptual basis for multilevel intervention. Its fundamental insight is that determinants at multiple levels—including intrapersonal, interpersonal, organizational, community, and policy—interact to influence human behavior and health outcomes. The immediate implication of this insight is that interventions that target determinants at multiple levels and mutually reinforce each other are likely to produce larger and longer lasting effects than interventions that target determinants at only one level. As acceptance of this perspective has grown, so has enthusiasm for multilevel interventions focused on a variety of health conditions, including cardiovascular disease, HIV, obesity, and cancer (1).

Although the social ecological perspective offers a compelling justification for developing multilevel interventions, it provides surprisingly little practical guidance for designing them. Proponents of this perspective have recommended that multilevel interventions combine environmental and behavioral interventions that work together in complementary or synergistic ways (1–7). Yet, discussions of how, when, or why interventions at different levels combine or could combine in mutually reinforcing ways are conspicuously missing. Without such guidance, multilevel intervention designers run the risk of combining interventions that produce scattered, redundant, or contradictory effects.

In this article, we use a causal modeling approach—that is, we construct visual representations of cause–effect relationships—to describe five strategies for combining interventions at different levels to produce complementary or synergistic effects. We illustrate these strategies with examples of multilevel interventions to improve the quality of cancer treatment. We conclude with guidance about how this approach could be used to design multilevel interventions and reflect on the limits of this approach.

The Social Ecological Perspective: Promise and Limits

Rooted in general systems theory, the social ecological perspective is a conceptual framework that focuses on the interrelationships between people and their environments. While there are many variants of the social ecological perspective [see (1)], two principles unite them. The first principle is that human health results from the complex interaction of personal factors and multiple aspects of physical and social environments. In addition to biological, psychological, and behavioral factors, health is influenced by geography, architecture, culture, economics, politics, and social relationships (5). In the social ecological perspective, the multiple factors that influence health are described as "levels of influence" and depicted as nested concentric circles representing contextual layers of increasing scope (eg, intrapersonal, interpersonal, organizational, community, and macro-level policy) (1,2,8–10).

The second principle is that the multiple factors that influence health are interdependent—that is, they mutually influence each other. Interdependence holds three important implications for multilevel interventions. The first implication is that causal influence does not flow in only one direction. Physical and social features of the environment influence people's behavior and therefore their health; at the same time, people can influence their health by modifying physical and social features of their surroundings. The second implication is that determinants at one level of influence can modify the effects of determinants at another level. Stokols [(6), page 286] notes, for example, that "the same environmental conditions . . . may affect people's health differently, depending on their personalities, perceptions of environmental controllability, health practices, and financial resources." The third implication is that changes at one level of influence can bring about changes at another level of influence. For example, changes in macro-level policy (eg, reimbursement) can stimulate changes in health-care organizations (eg, provision of patient navigation), which, in turn, can bring about changes in patient behavior (eg, timely follow-up

on abnormal screening results) and outcomes (eg, diagnostic resolution). Likewise, cancer health disparities can prompt the mobilization of advocacy groups and health-care organizations to seek policy-level changes to improve access or quality.

On the basis of these principles, proponents of the social ecological view contend that multilevel interventions should be more effective than single-level interventions in changing health behavior and outcomes (1-6,11,12). Smoking, for example, is influenced by multiple interdependent factors operating at different levels of influence. Thus, a multilevel intervention that combines smoking cessation counseling (an intrapersonal-level intervention) and workplace smoke-free policies (an organizational-level intervention) should be more effective than either intervention alone. However, both proponents and critics acknowledge that more interventions do not necessarily translate into more effect [eg, (5,13)]. Workplace smoking bans, for example, could harden smokers' attitudes and undercut their intentions to quit, making them less likely, not more, to take advantage of smoking cessation counseling programs. The key to designing effective multilevel interventions is to select and combine interventions that work together in complementary or synergistic ways.

Despite widespread agreement on this point, little discussion has occurred about how, when, or why interventions at different levels of influence produce (or could produce) complementary or synergistic effects. Consequently, multilevel intervention designers can find little practical advice for deciding which interventions to combine, and why. Proponents of the social ecological perspective have offered advice for choosing the level at which to intervene and for choosing among intervention options. For example, intervention efforts should focus on "high-leverage" factors—that is, those personal and environmental factors that research indicates have a disproportionate influence on the specific health issue in question (5,11). Furthermore, interventions should be theoretically grounded, evidence based, economically feasible, and consistent with community values and priorities (5,13). Although these criteria are useful for narrowing intervention options, they do not indicate which interventions are likely to work together in mutually reinforcing ways, and which are not.

Similarly, proponents of the social ecological perspective have offered advice on the sequencing of interventions. For example, Sallis et al. (10) argue that environmental interventions should be put into place before educational interventions to avoid promoting unrealistic health behavior (eg, walking in high-crime areas). Likewise, Spence and Lee (12) note that creating walking trails in a community populated predominantly with older adults might not be effective until the joint pain that many residents experience is overcome. Although such advice is useful for guiding the deployment of interventions (an implementation issue), it has limited value for guiding the selection of interventions in a multilevel intervention (a design issue).

In sum, the social ecological perspective offers a comprehensive framework for understanding the multiple interacting determinants of health. Moreover, it provides a compelling basis for the development, testing, and use of multilevel interventions that systematically target mechanisms of change at multiple levels of influence. However, in its present state of development, this perspective imparts little guidance about how to select interventions at different levels that produce (or could produce) complementary or synergistic effects. Without some framework for thinking about how interventions interact in mutually reinforcing ways, multilevel intervention designers run the risk of combining interventions that produce scattered, redundant, or mutually opposing effects (14). To address this issue, we employ a causal modeling framework to explore five strategies for combining interventions at multiple levels that help describe when synergy and complementarity may be produced. The five strategies are accumulation, amplification, facilitation, cascade, and convergence.

A Causal Modeling Approach to Multilevel Intervention Design

Causal models are abstract, often visual, representations that use cause-and-effect logic to describe the behavior of a system. These models can be used to design interventions to clarify the causal relationships between determinants and outcomes and between determinants and determinants. Given the importance of interdependence in the social ecological perspective, we focus on two types of causal relationships: mediation and moderation. *Mediation* refers to the process or pathway through which a cause is linked to an effect. In intervention research, the issue of mediation concerns how a particular intervention produces a desired outcome. Some suggest, for example, that audit and feedback interventions influence physician behavior by triggering self-directed motivation to reduce discrepancies between desired and actual performance (15). In general, interventions are more effective when the mediating process or pathway is strongly related to the desired outcome (16).

Moderation refers to the individual differences or contextual conditions that influence the strength or direction of the relationship between cause and effect. In intervention research, the issue of moderation concerns how such factors intensify or attenuate the intervention effect. For example, it might be that audit and feedback influence physician behavior more strongly for physicians in training than for physicians in practice. Alternatively, the effect of audit and feedback might be stronger in some contexts (eg, cancer screening) than in others (eg, cancer treatment). In general, interventions are more effective when they exhibit a good fit, or high degree of compatibility, with other personal and environmental factors that define a context (17–19).

Mediation and moderation can combine in various ways [see (20,21)]. Mediated moderation occurs if the moderating effect of some individual difference or contextual condition results from differences in the mediating process or pathway. For example, audit and feedback could have differential effects on physician behavior because it triggers self-directed motivation to improve for physicians in training but not for physicians in practice. Alternatively, audit and feedback could have differential effects because it triggers self-directed motivation for physicians in training (one pathway) and peer-induced motivation for physicians in practice (a different but perhaps less potent pathway). Moderated mediation occurs if the mediating process or pathway is intensified or attenuated by an individual difference or contextual condition. For example, audit and feedback might trigger self-directed motivation to improve among all physicians, but its effects on self-directed motivation (and, hence, on physician behavior) is intensified by the social norms and practices of residency training programs.

In mediated moderation, the causal pathway varies for different groups or in different contexts. In moderated mediation, the causal pathway does not differ, but the magnitude of the transmitted effect varies for different groups or in different contexts. Moderated mediation can occur in many ways, suggesting several strategies for combining interventions at different levels to produce complementary or synergistic effects.

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. In 1990, the National Institutes of Health issued a consensus statement recommending chemoradiation therapy (CRT) as adjuvant treatment for stage II and stage III rectal cancer patients (22). Rectal cancer survival rates overall have improved by 15%-20% since that time. More recent recommendations advocate using CRT neoadjuvantly for these patients. Although CRT is now accepted as the standard of care for stage II and stage III rectal cancer, evidence suggests that at least 20%-25% of stage II and stage III rectal cancer patients still do not receive any CRT (23,24). Moreover, studies have documented significant variation in the receipt of CRT by geographic region, stage (II vs III), surgeon specialty, patient age and sex, and patient race/ethnicity (23–27). Although the causal factors giving rise to variation in patterns of care for rectal cancer treatment are not well understood, extrapolation from studies of practice patterns in breast cancer treatment suggests several possible determinants at various levels of influence, such as provider knowledge or distance to a radiation facility (see Table 1). More research is needed to verify that these hypothesized causal factors affect the receipt or nonreceipt of CRT for locally advanced rectal cancer. For the purposes of illustration, however, we suggest that the determinants shown in Table 1 are plausible. Likewise, for the purposes of illustration, we assume that the interventions discussed below are evidence based, economically feasible, and consistent with community values and

priorities. We make these assumptions to shift attention away from the merits of specific interventions and toward the logic for combining interventions at different levels.

Five Strategies for Combining Interventions at Different Levels

In our description of strategies for combining interventions at different levels, we distinguish three important factors: interventions, targets, and settings. An intervention is a strategy for changing a given state of affairs. An intervention target refers to the level of influence of the determinant (or causal factor) that an intervention attempts to modify (2,9). For example, an organization-level intervention is one that attempts to change an organization-level determinant of behavior (eg, organizational policy, procedures, staffing, or resource allocation). Although the intervention's ultimate goal might be to change physician behavior, its proximal goal of changing an organizational determinant of physician makes it an organizationlevel intervention. An organization-level intervention can occur in a variety of settings, including multiple organizations of the same type (eg, physician practices) or different types (eg, physician practices and hospitals). An intervention setting refers to the social system in which the intervention target (ie, determinant) is reached (2,9). Intervention settings can range in scope from individuals, to dyads, to groups, to organizations, to communities, to societies.

In the social ecological perspective, what defines the level of an intervention is the level of influence of the determinant or causal factor (intervention target) not the social unit to which an intervention is directed or in which an intervention is implemented (intervention setting) (1,2,8–11,28,29). This distinction is subtle but important. Audit and feedback provides a useful illustration. Although scientific knowledge of *how* audit and feedback works is limited, control theory suggests that the presentation of information indicating that a discrepancy exists between actual performance and desired or expected performance motivates a behavioral response to reduce the discrepancy (15,30,31). Thus, from a control

Table 1. Possible determinants of nonreceipt of adjuvant rectal cancer treatment

Level of influence	Possible determinant
Intrapersonal (individual)	Patient knowledge, attitudes, and beliefs Patient personal/situational factors (eg, time barriers, financial barriers, transportation barriers) Provider knowledge, attitudes, beliefs Inadequate cues to action for providers
Interpersonal	Poor physician–patient communication Inadequate social support for patient Professional (social) norms about chemoradiation therapy appropriateness
Organizational	Poor communication/planning of multidisciplinary care Fragmented delivery system/poor coordination Organizational policies or "standard practices" that discourage information sharing and/or accountability
Community	Location or distance to radiation facility Shortage of radiation or medical oncologists in specific geographic areas
Macro policy*	Limited or lack of insurance coverage Inadequate reimbursement rates Inadequate incentives to improve care coordination Limited public or professional accountability

^{*} Policy refers to a level of context (state or national policy environment), not an intervention.

theory perspective, audit and feedback represents an intrapersonal-level intervention. Although often implemented in organizational settings, audit and feedback target intrapersonal determinants of physician behavior: knowledge of a performance discrepancy and motivation to reduce that discrepancy. It is possible that audit and feedback also work (or could work) by targeting determinants at other levels of influence. For example, audit and feedback could produce changes in physician behavior by changing organizational culture or interpersonal relationships. Whether audit and feedback work in these ways is not known. Absent more theory and research, it seems reasonable to regard audit and feedback from a control theory perspective as an intrapersonal-level intervention that targets physician motivation to reduce performance discrepancies.

As noted in the introductory chapter in this monograph, there are multiple ways to define the level of an intervention. The biopsychosocial perspective, for example, defines intervention level in terms of the social units to which an intervention is directed, such as individuals, groups, organizations, and policy environments. We follow the social ecological perspective in defining intervention levels in terms of targets (determinants) rather than settings (social units).

The strategies presented below have been simplified to illustrate their utility in multilevel intervention research. They depict a single mediating pathway rather than showing all of the potential mediating pathways through which specific interventions or combinations of interventions might produce their effects. A public reporting intervention, for example, could affect patient motivation and behavior as well as provider motivation and behavior.

Accumulation Strategy

In the accumulation strategy, interventions at different levels produce a cumulative impact on a common mediating pathway or set of mediating pathways. The effect of each intervention is not conditional on the other interventions. Rather, the interventions exhibit what scholars call pooled interdependence (32), meaning that each intervention makes a discrete contribution to the outcome, and in our example the mediating variable, without being dependent on each other. To illustrate, Figure 1 depicts a multilevel intervention focused on increasing surgeons' motivation to ensure that rectal cancer patients receive appropriate CRT following extirpative resection. In this example, surgical practices' CRT rates for rectal cancer treatment are publicly reported to provide



Figure 1. Accumulation strategy. Boxes indicate intervention and level of influence (in parentheses). The diamond indicates the mediator. The oval indicates the outcome. Asterisk indicates that for expositional purposes, the diagram depicts interventions rather than determinants as causes. Public reporting in this instance refers to the publication of practice-level chemoradiation therapy rates. To keep the presentation simple, a single mediating pathway is presented. Other potential effects are not shown.

the practices an incentive for coordinated multidisciplinary care (an organization-level intervention), opinion leaders are used to alter local norms about CRT appropriateness for older patients (an interpersonal-level intervention), and outreach visits targeted at physicians whose patients are less likely to receive CRT are used to change surgeons' attitudes and beliefs (an intrapersonal-level intervention). This approach would be warranted if theory and/or research indicated that 1) all three interventions produce their effects through a common mediating pathway and 2) this mediating pathway is the principal determinant of the desired outcome. A third consideration has less to do with the design of the multilevel intervention than with the implementation of it. Although deployed at different levels, the interventions must reach or converge upon the same intended audience. Differential exposure to the interventions is likely to produce scattered noncumulative effects. Finally, the dose-response relationship between the mediating pathway and the desired outcome is crucial to understand. If the relationship is subject to threshold or ceiling effects (ie, the relationship is nonlinear), the cumulative strategy could produce large effects, small effects, or no effect at all.

Amplification Strategy

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). In ways analogous to moderated mediation, one intervention amplifies the magnitude of the effect of the other intervention(s) on the mediating process or pathway. Figure 2 presents an example in which audit and feedback (an intrapersonal-level intervention) is added to boost the signal of public reporting of surgical practices' CRT rates for rectal cancer treatment (an organization-level intervention) and opinion leaders for altering local norms (an interpersonal-level intervention). This combination would be warranted if theory and/or research indicated that physicians are more responsive to practice-level public reporting or peers' opinions if they have credible individually tailored information that signals a discrepancy between desired and actual performance. In other words, the effects of the public reporting and opinion leader interventions depend on contextual factors. In this example, the contextual factor is a visible performance gap indicating a need for improvement. Amplification strategies could be used selectively to create tailored multilevel interventions that equalize the contextual conditions for different individuals, groups, or organizations.



Figure 2. Amplification strategy. Boxes indicate intervention and level of influence (in parentheses). The diamond indicates the mediator. The oval indicates the outcome. Asterisk indicated that for expositional purposes, the diagram depicts interventions rather than determinants as causes. Public reporting in this instance refers to the publication of practice-level chemoradiation therapy rates. To keep the presentation simple, a single mediating pathway is presented. Other potential effects are not shown.

For example, it might be the case that, when it comes to improving rates of CRT for rectal cancer patients, urban surgeons are more sensitive than rural surgeons to public reporting and peers' opinions. Targeting audit and feedback toward rural surgeons could equalize the sensitivity of these two groups to these other interventions. Using the amplification strategy in this way is analogous to improving person–environment fit (33).

Facilitation Strategy

As in the case of the amplification strategy, in the facilitation strategy, the effect of one or more interventions is 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. As another form of moderated mediation, one intervention removes the barriers or facilitates the effect of the other interventions. To continue the example, Figure 3 depicts a multilevel intervention in which a clinical reminder (an intrapersonal-level intervention) is added to facilitate the motivating effect produced by public reporting of surgical practices' CRT rates for rectal cancer treatment (an organization-level intervention) and opinion leaders for altering local norms (an interpersonal-level intervention). This approach would be warranted if theory and/or research indicated that public reporting and peers' opinions increase surgeons' motivation to ensure that their rectal cancer patients get appropriate CRT, but, to translate their increased motivation into action, they need a cue or reminder. The facilitation strategy is especially useful when the interdependence of multiple determinants is defined by necessary but not sufficient relationships. In the above example, the increased motivation that public reporting and opinion leaders stimulate might be necessary but not sufficient to improve rates of CRT absent some action cue or reminder. Conversely, the action cue or reminder itself might not be sufficient to produce improvement in CRT rates but might be necessary to address in conjunction with other determinants.

Cascade Strategy

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 (32), meaning that the outputs of an intervention at one level become the inputs of an intervention at another level. To illustrate, Figure 4 depicts a multilevel intervention in which advocacy (a policy-level intervention)



Figure 3. Facilitation strategy. Boxes indicate intervention and level of influence (in parentheses). The diamond indicates the mediator. The oval indicates the outcome. Asterisk indicates that for expositional purposes, the diagram depicts interventions rather than determinants as causes. Public reporting in this instance refers to the publication of practice-level chemoradiation therapy rates. To keep the presentation simple, a single mediating pathway is presented. Other potential effects are not shown.

prompts a change in accreditation standards, which, in turn, stimulates hospital managers' and physicians' motivation to initiate tumor board meetings (an organization-level intervention) to promote multidisciplinary care planning. Tumor board meetings reveal that physicians have varying degrees of knowledge of and comfort with current guidelines for rectal cancer treatment. Thus, tumor board meetings prompt outreach visits (an intrapersonallevel intervention) wherein trained professionals meet face-to-face with physicians to provide information about current guidelines, feedback on current performance, and tailored suggestions for overcoming barriers to practice change. The cascade approach would be warranted if theory and/or research indicated that determinants at different levels of influence interrelate primarily through mediation rather than moderation. By linking multiple mediating processes into an integrated causal pathway, cascading interventions create a "circuit" through which the effects of interventions combine and flow. Although "cascade" implies a flow from higher levels of influence to lower ones, this approach can be applied in reverse. Often interventions at one level run up against technical, resource, authority, or other constraints that can only be addressed at higher levels of influence. Community development and community empowerment models of intervention often work in a bottom-up fashion.

Convergence Strategy

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 (32), meaning the outputs of some interventions become the inputs of other interventions and vice versa. For example, the multilevel intervention depicted in Figure 5 combines public reporting of surgical practices CRT rates for rectal cancer treatment (an organization-level intervention) and opinion leaders for altering local norms (an interpersonal-level intervention) to increase surgeons' motivation to ensure that rectal cancer patients receive appropriate CRT. It adds patient education and counseling (an intrapersonal-level intervention) to increase rectal cancer patients' knowledge and motivation to seek appropriate CRT. The physician-directed and patient-directed interventions mutually reinforce each other to promote a different kind of physician-patient interaction, the result of which is increased appropriate receipt of CRT. The convergence strategy would be warranted if research showed that coordinated behavior change by different interdependent parties is necessary to produce a desired outcome. The Chronic Care Model, for example, posits that highquality chronic disease care depends on supportive evidence-based interactions between an informed activated patient and a prepared proactive practice team (34). Although these examples focus on altering the patterns of interaction among individuals, the convergence strategy can be used to alter the patterns of interaction among groups (eg, provider teams), organizations (eg, hospitals and physician practices), and communities (eg, neighborhoods, cities, and states).

Discussion

Researchers and practitioners wishing to deploy multiple interventions at different levels of influence face two pressing questions:

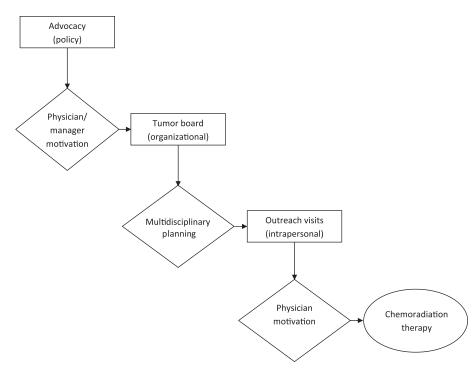


Figure 4. Cascade strategy. Boxes indicate intervention and level of influence (in parentheses). Diamonds indicate mediators. The oval indicates the outcome. For expositional purposes, the diagram depicts interventions rather than determinants as causes. Advocacy in this instance refers to organized efforts to change accreditation standards. To keep the presentation simple, a single mediating pathway from each intervention is presented. Other potential effects are not shown.

Which combinations of interventions are likely to produce complementary or synergistic effects? Why? Funding agencies and policymaking bodies presented with competing proposals for multilevel interventions face these questions as well. The causal modeling approach that we used in this article offers a general framework for thinking through the logic of multilevel intervention design. Moreover, the five strategies that we described provide a starting point for assessing whether, how, and, to some extent, when particular combinations of interventions at different levels of influence could work together in mutually reinforcing ways. For example, having identified "high-leverage" intervention opportunities based on a thorough understanding of the determinants of the problem and having screened intervention options based on theoretical support, empiric evidence, feasibility, and acceptability, researchers and practitioners seeking to develop multilevel interventions could ask 1) which of the remaining intervention options could be combined in complementary or synergistic ways, 2) which of the abovementioned strategies for combining interventions best describes the logical-causal basis for anticipating complementary or synergistic

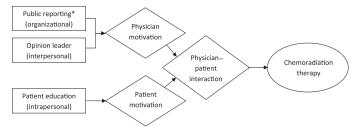


Figure 5. Convergence strategy. Boxes indicate intervention and level of influence (in parentheses). Diamonds indicate mediators. The oval indicates the outcome. Asterisk indicates that for expositional purposes, the diagram depicts interventions rather than determinants as causes. Public reporting in this instance refers to the publication of practice-level chemoradiation therapy rates. To keep the presentation simple, a single mediating pathway is presented. Other potential effects are not shown.

effects, and 3) what theory or evidence supports the logical-causal case for expecting complementarity or synergy from the proposed multilevel intervention? The causal modeling approach described in this article complements intervention planning models, such as Predisposing, Reinforcing and Enabling Constructs in Educational Diagnosis and Evaluation (PRECEDE)-Policy, Regulatory, and Organizational Constructs in Educational and Environmental Development (PROCEED) (35) and Intervention Mapping (36), by focusing attention on the causal-logical basis for selecting and combining interventions at multiple levels. With respect to PRECEDE-PROCEED, for example, the causal modeling approach could be used to think through the design of interventions that target predisposing, enabling, and reinforcing factors at different levels of influence. In a similar vein, funding agencies and policymaking bodies could ask whether those proposing multilevel interventions offer sound causal reasoning that the interventions they plan to combine will produce complementary or synergistic effects.

Our discussion of strategies for combining interventions at different levels is by no means exhaustive. The five strategies that we identify could themselves be combined in various ways, and other strategies might also be possible. The essential point, in our view, is that multilevel interventions should be designed based on sound causal reasoning about the likely interactions among the combined interventions and not simply on the merits of the individual interventions themselves. As the Sufi teaching story mentioned earlier reminds us, we must know the "and" to know how one and one make two.

Theory and research play a critical role in clarifying the logical basis for combining interventions at multiple levels. For theory and research to fulfill this role, however, three advances must occur. First, most theories focus on a single level of influence. Psychological theories focus on intrapersonal determinants. Organizational theories focus on organization-level determinants. Political theories focus on policy-level determinants. What we

need are theories that explain how determinants at multiple levels interact to produce health and other important outcomes. Second, most empiric studies focus on "independent variables," using statistics or experimental design to isolate the hypothesized causal relationship of one variable (determinant) and another (outcome). What we need is more cross-level research that examines the interdependence of variables (determinants) at multiple levels of influence. Interdependence can be explored as cross-level interactions in multilevel models (37,38), an approach suitable for large-N studies, or as "conjunctural causality" in qualitative complexity analysis, an approach suitable for small-N studies (39-41). Cross-level research of either variety could inform theory and intervention design. Third, most interventions designed to change the behavior of health professionals—including outreach visits, audit and feedback, and clinical reminders-depend on causal mechanisms that are poorly understood (42). We need more specificity about the mediating processes through which these interventions produce desired outcomes and under what conditions these

Finally, it is important to recognize that interventions at multiple levels interact not only with each other (as described in this article) but also with other contextual factors in the settings into which they are introduced (eg, sociopolitical processes) (43–45). Rather than viewing multilevel interventions as "packages," Hawe et al. (14) propose that we see them as events that occur in social systems characterized by complexity, nonlinearity, and sensitivity to initial conditions. This perspective implies value in coupling our conceptual approach to multilevel intervention design with systems dynamics models to explore how proposed multilevel interventions are likely to unfold dynamically in specific settings (43).

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