Title

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Journal

Pediatrics, 149(Suppl 5)

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Publication Date

2022-05-01

DOI

10.1542/peds.2021-053509E

Peer reviewed

Building a Life Course Intervention Research Framework

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abstract

OBJECTIVES: To report on first steps toward building a Life Course Intervention Research Framework (LCIRF) to guide researchers studying interventions to improve lifelong health.

METHODS: The Life Course Intervention Research Network, a collaborative national network of >75 researchers, service providers, community representatives and thought leaders, participated in an iterative review process. Building on the revised Medical Research Council Guidance for Developing and Evaluating Complex Interventions, they identified 12 additional key models with features for inclusion in the LCIRF, then incorporated the 12 characteristics identified by the Life Course Intervention Research Network as actionable features of Life Course Interventions to produce the new LCIRF.

RESULTS: The LCIRF sets out a detailed step-wise approach to intervention development: (1) conceptualization and planning, (2) design, (3) implementation, (4) evaluation, and (5) spreading and scaling of interventions. Each step is infused with life course intervention characteristics including a focus on (1) collaborative codesign (2) health optimization, (3) supporting emerging health development capabilities (4) strategic timing, (5) multilevel approaches, and (6) health equity. Key features include a detailed transdisciplinary knowledge synthesis to inform intervention development; formation of strong partnerships with family, community, and youth representatives in intervention codesign; a means of testing the impact of each intervention on biobehavioral processes underlying emerging health trajectories; and close attention to intervention context.

CONCLUSIONS: This first iteration of the LCIRF has been largely expert driven. Next steps will involve widespread partner engagement in framework refinement and further development. Implementation will require changes to the way intervention studies are organized and funded.

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Dr Russ led the development of this manuscript; Ms Hotez and Ms Berghaus supported the development of this manuscript; Ms Hoover, Ms Verbiest, Mr Schor, and Dr Halfon provided guidance and expert consultation to this manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2021-053509E

Accepted for publication Oct 27, 2021

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FUNDING: This project is supported by the Health Resources and Services Administration of the US Department of Health and Human Services under award UA6MC32492, the Life Course Intervention Research Network. The information, content and/or conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by Health Resources and Services Administration, US Department of Health and Human Services, or the US Government.

CONFLICT OF INTEREST DISCLOSURES: The authors have indicated they have no potential conflicts of interest to disclose.

Life course intervention research (LCIR) is an emerging discipline within the growing field of life course health science. It combines the principles of intervention research with those of Life Course Health Development (LCHD) to improve the development of health over the life course. The LCHD model[1–3] posits that health is an emergent set of developmental capacities that manifest and adapt over the lifespan. Health depends on internal genetic, epigenetic, biologic and physiologic systems, external environments and circumstances, and the reciprocal interactions or relationships between them. Health development is a complex, nonlinear process occurring in multiple dimensions (time, place), and at multiple levels (eg, individual, family, society) and phases (eg, preconception, peri-conception, early childhood, adolescence), adapting to circumstances in an effort to promote resilience.[2] It is particularly vulnerable to change during biologically, culturally, and socially conditioned sensitive periods.

As such, there is much more to LCIR than studying interventions early in life or extending the follow-up time horizon of traditional interventions. Instead, each stage of research can reflect the principles of LCHD, opening up new approaches to interventions at individual, family, community, and system levels. LCIR aims to more effectively address contemporary child health challenges, such as BMIs associated with adverse health outcomes,[4,5] neurodevelopmental differences,[6–9] and mental health challenges,[10,11] as well as longstanding health disparities such as the Black-White gap in birth outcomes.[12,13] There is growing understanding that the genesis of these health issues involves accumulated and compounding risks that act across lifetimes and even generations, at individual, family, and community levels.[2,14–16] Realization that specific experiences and exposures during sensitive periods of development can have an outsized impact on future health due to the combination of their nature and timing is driving change in the scope, complexity, and duration of intervention studies, with implications for their design and implementation.

Recognizing that the active pursuit of health equity requires effective life course interventions, the Health Resources and Services Administration Maternal and Child Health Bureau funded the Life Course Intervention Research Network (LCIRN). This transdisciplinary group of researchers, practitioners, community stakeholders, and family representatives has been tasked with developing a life course approach to intervention research. As a first step in creating an actionable research agenda, the network identified characteristics of life course interventions, based on the principles of LCHD, to serve as a guide for researchers developing interventions, reported separately.[17] While these characteristics help inform the development of interventions to improve health across the life course, they are insufficient to guide LCIR studies. A new framework is needed to combine these characteristics with detailed steps for intervention development, design, testing, and for translation of successful interventions into practice. These steps support the goals of optimizing health development and well-being and creating more systemic change. This paper aims to combine knowledge from the fields of intervention research and LCHD in a first iteration of a new Life Course Intervention Research Framework.

METHODS

Life Course Intervention Research Network

The LCIRN is a collaborative network of ~75 active members committed to improving life course trajectories and outcomes for children and families using an LCHD approach (https://lcirn.ucla.edu). The National Coordinating Center (NCC) is based at the University of California, Los Angeles, with 2 research cores (family and community engagement, and race, place, class and gender), and 9 current research nodes tackling adversity and resilience, attention-deficit/hyperactivity disorder (ADHD), early childhood mental health, family health development, measurement of family functioning, school health, success after prematurity, youth justice, and youth-led participatory action research at institutions across the United States.

Discussions around developing a research methodology and framework informed by intervention research and anchored in life course theory began at an LCIRN meeting in 2019 attended by forty members, including steering committee and advisory board representatives. Following the meeting, a core team of 4 researchers at the NCC reviewed existing models and frameworks for intervention research that could be readily adapted or applied to LCIR, with the initial emphasis on identifying a comprehensive framework for intervention research that could be added to or adapted for life course interventions. These interventions are rarely simple. They are frequently multilevel and equity-focused, requiring different intervention approaches in different circumstances and contexts. Thus, a comprehensive intervention framework was needed that is designed to incorporate more complex and innovative

interventions and to facilitate codesign processes with stakeholders and researchers. Following a literature review and iterative discussion within the core team the NCC identified the "Guidance on how to develop complex interventions to improve health and healthcare"[18] based in part on a revised and expanded Medical Research Council Framework,[19,20] and informed by a systematic methods review[21] and stakeholder interviews.[22] This comprehensive guidance breaks down intervention research into >15 discrete areas or tasks, starting with conception of the problem and planning of the study, and moving through design, implementation, testing, evaluation, and spread. This detailed framework appeared readily adaptable to LCIR.

The NCC developed version (A) of the Life Course Intervention Research Framework (LCIRF), combining the 7 original LCHD principles (health development, unfolding, complexity, timing, plasticity, thriving and harmony)[3] with an adapted version of O'Cathain's guidance[18] (Table 1). Although all principles should apply to all stages, for simplicity, Table 1 lists just 2 to 4 LCHD principles for each step. The LCIRN steering committee operationalized and expanded these LCHD principles into 12 characteristics of life course interventions through an iterative collaborative process, including a Modified Delphi review, that has been reported on separately.[17] These 12 characteristics were more comprehensible in plain language and more actionable in real-life interventions. Mindful that the framework needed to be sufficiently robust to guide research, yet also easily useable by youth, family, and community partners, the group streamlined it into 5 stages: conception and planning, design, implementation, evaluation, and translation.

The 15 members of the steering committee also identified 12 additional approaches, models, or frameworks with elements relevant to the LCIRF. The NCC reviewed the models and summarized their main components (Table 2). Steering committee members and NCC Core members suggested elements from the models that they felt were key for inclusion in a comprehensive LCIR framework. They based their recommendations on their experience and on their understanding of emerging directions in the literature and suggested ways in which these elements might be incorporated. Members of the core team also consulted with researchers with expertise in Youth-led Participatory Action Research (YPAR) and Community-Based Participatory Research (CBPR) to better understand potential links with LCIR. Following this process, the NCC core team incorporated key elements from these additional models to create the LCIRF(B) that delineates the steps in the 5 stages (Fig 1 A-C).

LCIRF(B) was further simplified and combined with the 12 characteristics of life course interventions to produce an actionable version, the LCIRF(C) (Table 3). Table 3 considers the entire process of LCIR and is designed to be used together with Fig 1 A-C. For example, researchers in the planning stage can consult both Fig 1A and the first column in Table 3 for detailed steps and ways to apply life course characteristics to research conceptualization and planning.

RESULTS

LCIRF(A) (Table 1) breaks down the process of developing an intervention from initial conceptualization to eventual spreading and scaling through 16 steps, each of which requires attention to detail, documentation, and funding. Researchers are prompted to consider the principles of LCHD at each stage as they design their intervention and study.

Table 2 lists additional intervention research approaches and models that influenced framework development. These include community-based participatory research,[24] youth-led participatory action research,[26] and action research.[24,25] These approaches incorporate active roles for youth, family, and community representatives as partners with transdisciplinary teams of researchers and administrators, adding their expertise both in terms of lived experience of an issue or condition, and deep contextual understanding of the environments in which the interventions will be implemented. The inclusion of these approaches into the LCIRF resonates with the concept of human-centered design; the intervention being designed with the end-user in mind from the beginning. Engaging a diverse set of "users" from the start should facilitate the eventual spreading and scaling of successful interventions, avoiding "boutique" interventions that only work for a limited proportion of the population. These approaches drove the evolving LCIRF toward inclusion of youth, family, and community voices at every stage of intervention development, rejecting models in which pivotal decisions were taken by professional groups working alone with community groups brought in later.

The National Institute of Health Stage Model[27] and Five Phase Model[28] group the steps of intervention research into a series of stages or phases, with each step informing the next until lessons learned from the final stages suggest new problems that need to be

TABLE 1 Life Course Intervention Research Framework (A)

Intervention Steps	Description	Life Course Health Development Principles:Health Development, Unfolding, Complexity, Timing, Plasticity, Thriving, Harmony
Conception	Identify problem or issue in need of intervention.	Consider all areas of health development the problem might impact (Health Development) Consider potential neurodevelopmental, behavioral, and epigenetic pathways involved (Unfolding) Include broad environmental factors in a full examination of the exposome- social, economic, neighborhood, policy, etc (Complexity) Consider panomic factors: genetic, epigenetic, molecular, microbiome, biological (Complexity)
Planning	Convene a group to plan the intervention.	Include biological, genetic, social, and psychological scientists along with clinicians (Unfolding) Include context experts: end-users, families, community members, local service providers, local government representatives (Complexity) Include those knowledgeable in the history of the population - historians or elders (Plasticity)
Development	Assess the causes of the problem in this context.	What factors influence the timing or life stage of the problem in the target population? (Timing) How does the problem disrupt harmony in their life or community? (Harmony)
Evidence review	Review evidence of effectiveness or failure of prior interventions for this problem.	What do the results suggest about the neurodevelopmental, behavioral, and epigenetic processes and pathways involved? Which ones are mutable with interventions? (Unfolding) Did any subgroups thrive with prior interventions and, if so, why? (Thriving)
Incorporate conceptual model	Identify a conceptual model or theory of change, eg, behavior change, efficiency-based.	How will the intervention impact outcomes and what is the process of change? (Health Development) Does the theory of change incorporate evolutionary or development principles? (Plasticity)
Content	Codesign the intervention: content, format, level, and mode of delivery.	Which health pathways will the intervention target and how? (Health Development) How will components of the intervention interact with each other and with factors in the exposome? (Complexity) Are the components focused on achieving thriving and optimal well-being, not just absence of illness? (Thriving)
Evaluation plan	Decide on measures and data collection methods. Consider existing data, new measures, qualitative and quantitative data. Include pathway, process, and outcome measures.	Include measures of whole-person health development (Health Development) Include measures that monitor epigenetics (eg, DNA methylation patterns), neurobiology, eg, cortisol, candidate pathway biomarkers, individual, family, social and community-level measures over time (Unfolding) Consider measuring intergenerational effects of the intervention (Plasticity) Include measures of positive health at individual, family, and community levels (Thriving)

TABLE 1 Continued

Intervention Steps	Description	Life Course Health Development Principles:Health Development, Unfolding, Complexity, Timing, Plasticity, Thriving, Harmony
Cost	Consider real-world issues about cost and delivery of the proposed intervention. Assess feasibility and scalability.	Consider whether the expected impact on health development justifies the cost. (Health Development) Consider how the intervention might affect health development throughout the entire lifespan when calculating cost effectiveness. (Unfolding) Consider how the cost of the intervention might differ based on physical or social environments (Complexity)
Ethics and IRB	Submit and obtain ethics and IRB approval.	Fully explore potential short and long-term health development impacts, especially potential for harm (Health Development) Ensure IRB approval includes all physical and social environments in which intervention will be administered. Consider whether multiple IRB approvals are required (Complexity) Consult local community ethics boards as appropriate. (Plasticity)
Prototype	Make a prototype of the intervention and pilot test on a small sample.	Although the pilot test will be short-term, include measures of impact that point to longer-term health and development trends (Unfolding) Ensure the pilot is delivered at the correct time and life stage even if sample size is small. (Timing)
Pilot study	Study impacts, acceptability, and feasibility.	Design evaluation to assess both positive and unintended negative consequences on any aspect of health development (Health Development) With participants and providers, consider whether this is the optimal timing (Timing) Assess whether participants feel the intervention is helping them to thrive or not and why? (Thriving)
Refine	Refine intervention and consider larger pilot with a different or more diverse sample. Finalize evaluation strategy.	Refine based on preliminary evaluation findings and especially unexpected effects (Health Development) Consider both impact and process in refining the intervention (Unfolding) Determine whether the intervention needs small adjustments to work best in different physical or social environments. Document fully any such adjustments in research reports. (Complexity)
Implement	Deliver intervention to entire study population.	Aim to improve healthy development across all study subjects, not just reduce incidence and prevalence of a disease or condition (Health Development) Document long-term differences in impact of the intervention on each member of the study population, eg, some may avoid disease but not thrive, others thrive. (Thriving)
Evaluate	Evaluate based on plan. Use mixed methods approach.	Measure health trajectories, latent pathways, latent classes. Descriptive and quantitative studies of process and outcome. Subgroup analysis where appropriate. Comparison with control groups when appropriate. (Unfolding)

TABLE 1 Continued

Intervention Steps	Description	Life Course Health Development Principles:Health Development, Unfolding, Complexity, Timing, Plasticity, Thriving, Harmony
		Incorporate time into statistical analyses e.g. time series analysis, time trends, trajectory construction, structural breaks, stationarity, latent path analysis (Timing)
		Place evaluation in historic and cultural context. Eliminate biases in evaluation, eg, avoid viewing through a narrow or inappropriate cultural or racial and ethnic lens. (Plasticity)
Publish	Publish findings in a range of formats (eg, peer-reviewed journals, community-based publications, policy briefs).	Publish findings related to biological, social, physical, and whole health changes over the short and, where possible, long term. Ensure any negative long-term outcomes are still published (Unfolding)
		Ensure community members who contributed are recognized with coauthorship or other acknowledgments. (Complexity)
Translate	Translate effective interventions into widespread practice (spread and scale)	Ensure all effective aspects of the intervention are translated into practice (Unfolding)
		Ensure spread of intervention occurs in a culturally appropriate manner (Plasticity);
		Continue to monitor and ensure spread does not have a deleterious effect on subgroups. (Thriving)

Adapted from O'Cathain.[18,21]

studied, feeding back into new topics for basic research. The adaptive interventions,[29] Just-In-Time Adaptive Interventions,[31] and Sequential Multiple Assignment Randomized Trials (SMART) trial designs[36] provide options to tailor studies to different populations and levels of need, considering individual circumstances, intervention context, and for SMART trials, each individual's initial response to an intervention.[36] They allow more flexibility in intervention delivery, meeting people where they are, and potentially moving to a model where each subject of an intervention could be engaged in an iterative process with researchers navigating through a series of intervention decisions informed both by expert opinion and client preference, yet still conducted with sufficient rigor to yield meaningful data and conclusions.

Roger's Diffusion of Innovation Model[32,33] and the Model for Improvement[34] are of most relevance for late-stage efficacy and effectiveness studies, and for scaling and spreading strategies for successful interventions. These later stages of intervention research blur the boundaries between implementation science and quality improvement models. Although randomized control trails (RCTs) can still be employed at this stage, many implementation science questions are best addressed through quasi-experimental designs including pre and post, interrupted time series, and stepped-wedge designs where all participants receive the intervention, but in a staggered fashion.[37]

Now informed by the additional models, intervention steps were grouped into 5 main stages, each with key steps and activities: (1) conceptualization and planning, (2) design, (3) implementation, (4) evaluation, and (5) translation or spread and scale. Figures 1–3 provide detail on activities and other considerations at each stage. The third and current version, LCIRF(C) (Table 3) applies the 12 characteristics of life course interventions[17] to the 5 stages of LCIR.

DISCUSSION

There is growing consensus that most contemporary public health challenges, especially health inequities, are so-called "wicked" problems[38] not amenable to simple medical or pharmacological solutions.[39] This has led to interest in complex, multilevel, and sustained intervention approaches that are adaptive and responsive to changing circumstances. The LCHD approach[1,2] brings a complex adaptive system perspective[40] to intervention research. Each person's physical, mental, socio-emotional, and spiritual health results from multiple risk and protective factors operating throughout the lifespan,[1,2] and the impact of those factors varies based on the life stage and context. Consequently, interventions designed to address these health issues must impact multiple risks, operate at

TABLE 2 Key Approaches and Models to Guide Development of the Life Course Intervention Research Framework

Approach, Model or Framework	Description
Community-Based Participatory Research[23]	An approach to research that involves collective, reflective, and systematic inquiry. Researchers and stakeholders engage as equal partners in all steps of the research process.
Action Research[24]	A research philosophy and methodology widely used in social sciences and education that seeks transformative change through the simultaneous process of taking action and doing research, linking the 2 with critical reflection.[25]
Youth-led Participatory Action Research[26]	An approach to scientific inquiry and social change grounded in principles of equity. Young people are engaged in identifying problems relevant to them, conducting research to understand the problems, and advocating for change based on research evidence.
National Institute of Health Stage Model[27]	Stage 0: basic science research to identify potential mechanisms or components of an intervention, Stage I: intervention generation and refinement, Stage II: efficacy research in clinical trials; Stage III: efficacy research in community trials, Stage IV: effectiveness trials; Stage V: implementation and dissemination. Lessons learned from Stage V then influence further basic science research (Stage 0). The model is neither prescriptive nor linear. Interventions are not fully developed until they can be implemented for everyone in the population who would benefit.
Five Phase Model[28]	Preclinical Studies generate hypotheses; Feasibility Studies; Early Efficacy; Late Efficacy; Effectiveness Studies.
Adaptive intervention[29]	A sequence of decision rules that specify whether, how, when, and based on which measures to alter the "dosage" (duration, frequency, or amount), type or delivery of the treatment or intervention at decision stages in the course of care. AIs have four elements: decision stages; treatment options; tailoring variables that capture information about the individual; and a decision rule.
SMART (Sequential Multiple Assignment Randomized Trial)[30]	A special factorial study design that uses experimental design principles to answer critical questions around adaptive interventions. In a multistage RCT, participants are randomized at the first stage of treatment and management, then depending on response, may be randomized at a second or third stage based on a decision tree. SMART designs are increasingly being applied to longitudinal study designs.
JITAI (Just in Time Adaptive interventions)[31]	An intervention design aiming to provide the right type and amount of support, at the right time, by adapting to an individual's changing internal and contextual state. Mobile technologies are making this type of intervention more prevalent.
Diffusion of Innovations[32,33]	Diffusion of innovation theory explains how, over time, an idea or product gains momentum and diffuses or spreads through a population or social system. People fall into 5 categories: Innovators, Early Adopters, Early Majority, Late Majority and Laggards. Five factors influence adoption of an innovation: Relative Advantage, Compatibility, Complexity, Trialability and Observability. The theory did not originate in public health, works better for adoption of new behaviors rather than cessation of old ones, and does not consider the role of individual resources or social supports.
Model for Improvement – PDSA Cycles[34]	Testing a change by planning it, trying it, testing the results, and acting on what is learned. It is an action-oriented learning model often used in spreading and scaling interventions and in quality improvement initiatives.
Complex Systems Science[35]	Investigation of how reciprocal relationships between the components of a system result in its collective behaviors

strategic times, and be responsive to lived context.

LCIR and Health Equity

Health equity from the start of life must be a public health priority, as small differences and disadvantages early on tend to compound over time, leading to larger and more intractable problems later.[41] A purposeful focus on equity from the start means designing life course interventions to correct emerging health issues early, while also supporting each child's health development capabilities, building resilience and reserves into their health development trajectories from the start.[42] This approach expands on the health promotion efforts of the past but goes further, treating the development of health as an active process in which protective actions, experiences, and

A

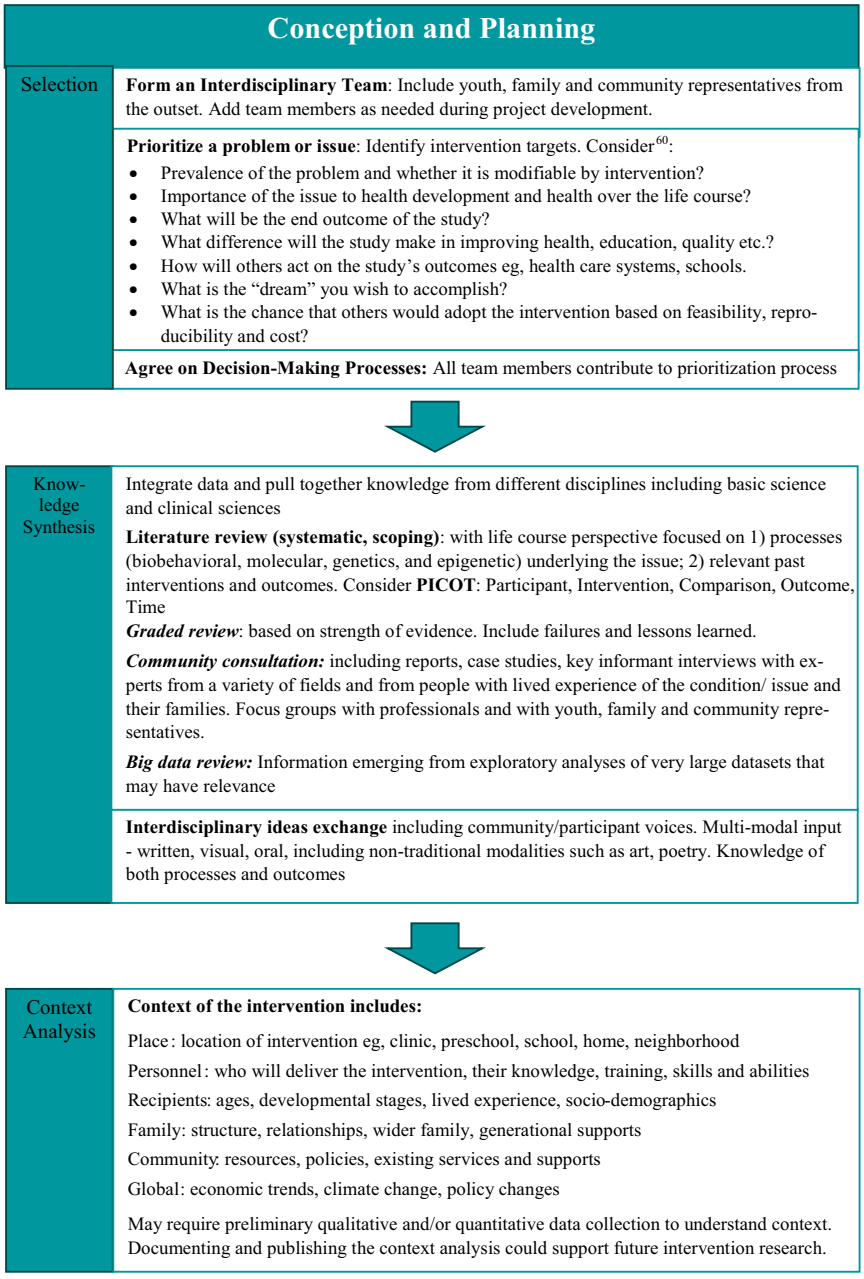
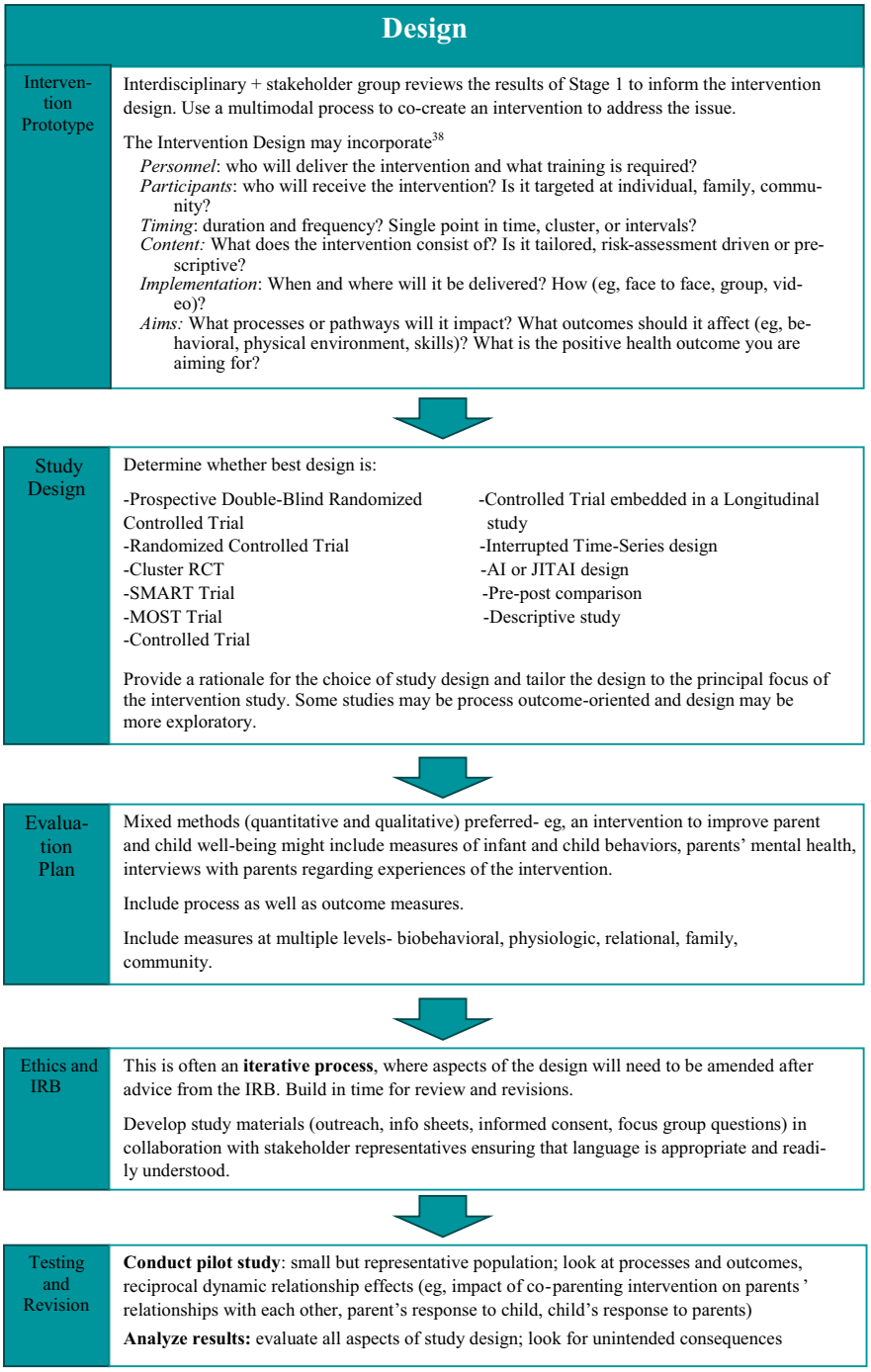


FIGURE 1

A, provides details on activities and other considerations for life course research at stage 1: conception and planning. B, provides details on activities and other considerations for life course research at stage 2: design. C, provides details on activities and other considerations for life course research at stages 3–5: implementation, evaluation, and translation. While much of the stage content represented in this figure applies to all intervention research, not just life course intervention research, the detailed steps are included here for clarity with the specific life course content relevant to each stage being depicted in Table 3.

B



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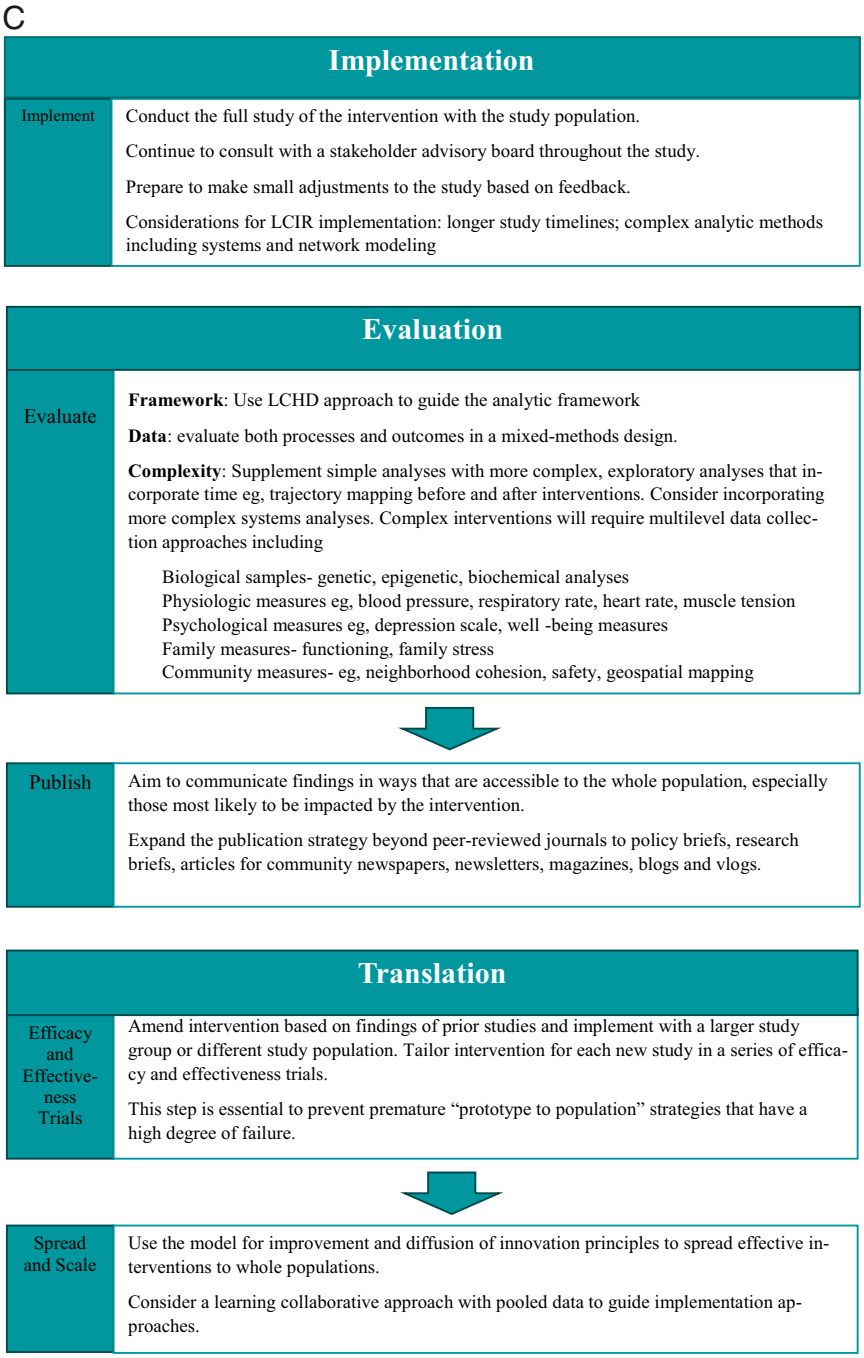

FIGURE 1
Continued.

exposures build on each other across developmental stages.

Life Course Interventions and Social and Structural Determinants of Health

The LCHD model also aims to serve as an organizing framework for addressing social determinants of health. Long understood to have a profound impact on health, factors such as relationships, economic stability, education, health care access, and neighborhood environment[43] have traditionally been regarded as outside the purview of clinicians. While a full discussion of all the possible categorizations of social determinants is beyond the scope of this paper, it is of note that contemporary researchers expand this list to include the "structural determinants of health,"[44] including

TABLE 3 Life Course Intervention Research Framework (C)

LCIR Characteristic	Conceptualization and Planning	Design	Implementation	Evaluation	Translation or Spread and Scale
Optimization focused	Intervention aims to optimize health development, not just prevent or treat problem.	Include optimal health focus in forming study questions and evaluation.	Implementation maintains focus on goal of optimal health as applied to a larger study population.	Include measure of optimal health at individual, family, and community levels.	Incorporate different definitions of optimal health for different populations.
Developmentally focused	Consider developmental stage of the recipient (child, family, or community).	Design is tailored to the developmental age of the recipient.	Tailor delivery strategy, system, and context to recipient's developmental stage(s).	Include measures of developmental processes, pathways, and outcomes	Adjust spread strategy for any differences in developmental age.
Longitudinally focused	Consider antecedents and potential long-term consequences of the intervention.	Design intervention to impact the most important developmental processes for positive health and/or resilience.	Maintain focus on long-term, not just short-term - goals.	Include longer-term trajectory measures, latent class analysis, longitudinal structural equation modeling.	Maintain long-term (life course) focus during spread.
Strategically timed	Based on knowledge synthesis, and context, determine the most impactful timing for intervention.	Consider duration, intensity, and timing of delivery in intervention design.	Implement at most strategic time.	Evaluate acceptability, feasibility, and effectiveness of timing.	Ensure optimal timing or duration of intervention is maintained in spread strategy.
Multilevel or holistic	Consider whether intervention should target 1 or multiple ecosystem levels-individual, family, community.	Incorporate plans for implementation of elements at every targeted level.	Monitor impact of intervention at all levels.	Include individual (eg, biomarkers), family, and community-level qualitative and quantitative measures.	Ensure effective components at all intervention levels are spread and scaled
Vertically, longitudinally and horizontally integrated	Consider potential links between intervention and existing services across sectors, disciplines, and age groups.	Use pilot study to test potential integration of new intervention with existing services.	Link intervention with existing services during implementation wherever possible.	Measure effectiveness and utility of links between intervention and other services and sectors.	Plan for integration with existing services and systems as part of spread strategy.
Addresses emerging health development capabilities	Identify processes and pathways relevant to the target health development capability and review evidence for ways to intervene.	Address emerging health development capabilities in the study aims and research questions.	Measure and monitor emerging capabilities during implementation phase.	Evaluate for both positive and negative impacts on emerging health development capabilities.	Test intervention with different populations and determine whether impacts on emerging health capabilities are maintained.
Strengths-based	Identify individual, family, and community strengths and build on them to develop intervention.	Incorporate individual, family, and community strengths into intervention design.	Use strengths during implementation, monitor ways in which strengths interact with intervention.	Evaluate interactions between individual, family, and community strengths and elements of the intervention.	Work with individual, family, and community strengths in spreading intervention.
Collaboratively codesigned	Transdisciplinary research team and youth, family, and community representatives work together to plan study.	End users partner with professionals in human-centered codesign of intervention.	Continue to consult stakeholder, community, and family advisory board throughout implementation to advise on adjustments and adaptations.	Work with stakeholder representatives and end users to guide, interpret and report on evaluation.	Engage different populations and representatives during spread and scale.

TABLE 3 Continued

LCIR Characteristic	Conceptualization and Planning	Design	Implementation	Evaluation	Translation or Spread and Scale
Family-centered	Consider family views and context in developing intervention.	Engage families in intervention design, consider family units as the intervention recipient if appropriate.	Consider family context and views and beliefs in intervention implementation.	Include family perspective in evaluation by qualitative as well as quantitative methods.	Engage diverse families from different populations during spread and scale.
Antiracist	Consider racism as a potential causative or contributing factor and address it in intervention planning. Incorporate antiracist research principles. Consider theoretical frameworks developed by non-White scholars.	Review intervention design with diverse researchers and stakeholders. Note potential influence of racism in perspectives or actions, and/or opportunities to address them in design.	Monitor implementation for bias and interpersonal and/or institutional racism.	Evaluate perceptions of racism in intervention design, delivery, or impact. Present findings in context and consider practice and policy implications.	Ensure spread proceeds in accordance with antiracist research principles.
Equity-focused	Determine who could benefit most from intervention and develop for them.	Tailor the intervention to those who would benefit the most. Adapt for other groups as needed.	Monitor implementation to determine if intervention is reaching those with most to gain.	Determine whether the intervention reached the target population, especially the most disadvantaged.	Ensure spread maintains focus on reaching the groups with most to gain from the intervention.

This table illustrates the application of the 12 characteristics of life course interventions, identified in prior work, to each of the stages of intervention design and testing. While it is not realistic to expect researchers to apply all characteristics to all stages, this framework is intended as a reference that researchers can consult when developing and designing interventions from a life course perspective. This table represents just the first iteration of this work, designed to stimulate discussion. Revision and refinement will occur as more researchers gain experience with life course intervention methodology and analysis strategies and suggest improvements.

racism, classism, and gender discrimination as powerful drivers of health development pathways and hence, as appropriate targets for LCIR.

Interventions to equitably improve health across the life course can and must address these broader levels of influence if they are to be effective. No single intervention can address all of these levels and factors, but LCIR must, at least at times, include coordination and integration of discrete interventions with wider programmatic efforts to address social and structural determinants of health.

Advances in Intervention Research

Two recent advances in intervention research are highly relevant to LCIR. First, a recognition that intervention development, design, and refinement benefit from stakeholder involvement at every stage, providing both an end-user perspective for a codesign process and a greater understanding of the intervention context.[18] Second, intervention development benefits from being broken down into distinct stages, each with substeps that provide a solid foundation for the next stage. Rushing through or omitting these steps in a "prototype to population" approach too often results in promising interventions failing to spread and scale. Each of these approaches is incorporated into the LCIRF(C). The Framework is divided into 5 stages (Fig 1), each of which merits further discussion below, with the 12 characteristics of life course interventions[17] integrated into each stage.

I. CONCEPTION AND PLANNING

A marked shift in the intervention development literature from an emphasis on professionally driven processes to collaboration between professionals and consumers based on human-centered design principles[45] necessitates forming new partnerships to conduct intervention research. Codesign goes beyond consultation or engagement of community members or intervention users, and instead acknowledges users as "experts of their own experiences" to improve design.[46,47] Collaborative stakeholders bring local knowledge into intervention design in ways that may better address issues of health equity and sustainability of change than traditional top-down approaches.[48] In child health, families of children with special health care needs are experts in that lived experience and valuable partners in intervention codesign.[49]

The Dynamics of Research Teams

All team members work together as equal partners bringing different

perspectives on the prioritization of issues, mechanisms, and pathways underlying these issues and intervention strategies to address them.[50,51] Power and social relationships within teams need to be managed carefully so that all voices are heard, all options explored, and the process is productive.[52] Discovering the best ways to form intervention development teams, manage information exchange, and make decisions represents fertile new ground for research.

The Quality and Scope of Knowledge Synthesis

While graded literature reviews are a valuable resource, an over-reliance on the results of RCTs with statistically significant, yet clinically modest intervention impacts may have, paradoxically, limited progress and obscured subgroup effects.[53] A majority of intervention study subjects are White, non-Hispanic, resulting in uncertainty as to whether results are truly generalizable to Black, Asian and Hispanic populations.[54] Studies that demonstrate intervention impact, yet lack a causal explanation for the mechanism of action have limited value. In contrast, studies that focus on mediating variables that might be amenable to intervention, such as quality of parent-child interactions, are particularly valuable, being better aligned with the LCHD focus on emerging health development processes. Similarly, studies that address key moderators, such as family strengths and cultural values which tend to persist over time, yield valuable information to inform life course interventions.

Supplementing traditional literature reviews with "grey literature," key informant interviews, and focus groups can enhance this knowledge synthesis. A transdisciplinary exchange of ideas can also give a more complete picture of potential targets for intervention and contextual understanding. E-surveys provide a route for input from a wide range of stakeholders within a short time frame.

II. DESIGN

This stage comprises design of the intervention and the study methodology, including the evaluation plan.

Intervention Design

Codesign based on human-centered design principles results in interventions that lend themselves to end-user adaptations, facilitating spreading and scaling through diverse populations. Factors such as the intensity, frequency, and duration of interventions are important, being mindful that interventions with negative RCTs might have had a measured impact if the duration or frequency had been different. Similarly, the genesis and agent of an intervention matter, an intervention delivered in the context of an emotional relationship (eg, mother to child), may differ from 1 delivered by a health care worker. Third, the intervention location (home, clinic, or school) impacts meaning, acceptability, and feasibility. Fourth, timing impacts how well the intervention is aligned with sensitive periods, such as transitions and turning points. A checklist delineating the who, where, what, when, why, and how of the intervention will assist the team to document and report on each aspect and build a prototype.

Study Design

A full consideration of intervention study designs is beyond the scope of this paper. Studies that test a conceptual model need to define the core elements of the model at this stage and the plan for testing it. A growing emphasis in LCIR on better understanding the processes and pathways that underlie emerging health development capabilities and trajectories of health is leading to a shift in study designs from outcome-oriented to process oriented. This has resulted in cautious support for the "intervention as research" approach of simply performing an intervention and closely monitoring its effects on a system[55,56] using pre and post designs or interrupted time series as a legitimate form of knowledge acquisition, even in the absence of an RCT. Understanding how an intervention impacts a biobehavioral process over time can give valuable information, both about the way the process unfolds and ways to intervene to improve or optimize that process.

More flexible, user-responsive study designs, eg, adaptive and SMART designs, tailored to individual needs have much to offer in individual health optimization efforts. Embedding interventions in longitudinal cohort studies has the advantage of a built-in long-term follow-up strategy, but the scope and focus may be constrained by the cohort study design. Studies with shorter periods of follow-up will still be valuable if they can study intervention impacts on emerging health development pathways, but longer-term effects would have to be inferred, risking significant over- or under-estimates.

Evaluation Plan Design

Traditional evaluation approaches reliant largely on outcome measures work well when the outcome is clearly defined, eg, curing an illness, but are more challenging when the process or outcome occurs on a spectrum, or has features that are difficult to measure. Complex interventions with elements that address multiple ecosystem levels and aim for synergistic impacts require more complex evaluation plans,[57] and in LCIR, the study of

processes may prove to be just as, if not more important, than outcomes. A focus on achieving optimal health requires new measures of thriving and flourishing, some of which will be determined by the community's own definitions of these concepts. A suite of measures, including biological, physiologic, epigenetic, psychological, relational, and environmental, are needed. Mixed methods designs are becoming best practice, providing qualitative and quantitative data on both the study context and participant experiences. Stakeholder engagement in evaluation design supports acceptability and usability of evaluation measures, tools, and processes.

Pilot Study

The design phase culminates in a pilot, which is usually a short-term, time-limited intervention closely monitored for intermediate, process-related effects. Evaluations must be short-term but thorough, incorporating mixed methods and actively searching for negative as well as positive intervention impacts. Much can be learned from unsuccessful interventions, especially from unanticipated negative effects. Ideally, this phase results in an intervention that is adaptable or customizable to different populations.

III. IMPLEMENTATION

Traditionally the focus of funding, the implementation phase, refers to conducting the main study following a successful pilot. Much of the essential preparatory conceptual and design work must already be completed. Youth, family, and community representatives should remain engaged throughout, advising on adjustments needed to improve intervention implementation, and a community advisory board may be helpful in monitoring implementation. Additionally, a communications strategy should sustain community engagement and update stakeholders on progress. Flexible, responsive protocol adjustments represent good practice, as opposed to an over-reliance on protocol fidelity at the expense of effective implementation. This requires greater responsiveness of Institutional review boards. in reviewing requests for protocol adjustments, and greater openness of journals to transparent reporting.

IV. EVALUATION

In the evaluation stage, data collected during implementation, based on the evaluation plan, are analyzed and interpreted. Analysis strategies might test the validity of existing conceptual models, allowing for delineation of mediator and moderator effects and of path analysis. Relevant multilevel modeling and time-related analysis strategies may include structural equation modeling, factor analysis, path analysis, growth modeling, and latent class analysis. A full exploration of all the processes contributing to health trajectories over time creates analytic challenges, as many of these processes are nonlinear and incorporate dynamic 2-way interactions. Further research is needed into new methodologies that can address these more complex, "big data" types of analyses. Engaging stakeholders throughout the evaluation process, particularly in data interpretation, may help identify some of the less-apparent impacts (both positive and negative) and will support the next stage, translation.

V. TRANSLATION

Even with repeated demonstrations of effectiveness, a new intervention should be trialed and adjusted for varied populations and settings. Spreading an intervention throughout a population and translating it into everyday practice incorporates both implementation research and quality improvement approaches,[58,59] with RCTs seldom warranted or practical. Under-studied, under-reported and often not regarded as "real research," this stage is very important if the intervention is to succeed. Understanding and reporting barriers to implementation prevents repeated mistakes across multiple intervention targets and modalities. From a life course perspective, failing to adopt or spread an effective intervention can have long-term effects on population health. At the conclusion of this stage, publishing lessons learned informs both basic and intervention development research, and the cycle of intervention development begins again.

Challenges and Opportunities

Considering some of the differences between LCIR and more traditional intervention research highlights the challenges and opportunities of this new approach. First, the complex, multilayered nature of many life course interventions can make them conceptually challenging to design and resource-intensive to implement. They require more complex approaches to evaluation using higher-level statistical techniques and modeling strategies, often requiring specialized training. Determining which components of an intervention are key to its success is a real challenge with major implications for resource allocation. This type of research will require new methodologies and study approaches yet to be developed. A shift from RCTs to other study designs creates real risk of spurious associations, while limited resources for long-term follow-up studies risks over-reliance on inferred potential long-term

impacts of interventions. At the same time, LCIR holds greater potential to change life-long trajectories compared with simpler time-limited approaches to intervention research. LCIR also offers a strategy for reaching health equity in a way that traditional intervention research does not by disrupting pathways and operating through bio-behavioral mechanisms influenced by social and structural determinants of health.

LIMITATIONS AND STRENGTHS

There are significant limitations to this approach to developing the LCIRF. First, we did not exhaustively review the many models and frameworks that have been applied to individual steps in intervention research, to single types of specialist interventions, or to interventions with special populations. Instead, we sought first to identify intervention frameworks or guidelines that were comprehensive in scope, addressing all of the steps in intervention research, of which the O'Cathain guidelines[18] are most readily applicable to the types of complex, multilevel interventions envisaged by life course researchers. Second, this preliminary LCIR Framework has yet to undergo significant review and revisions by a diverse group of interdisciplinary life course researchers as well as stakeholder representatives. At present, it is the result of deliberations by a limited group of life course researchers. Third, it is not yet known if this framework will prove useful to researchers in the field. Strengths of the framework include its comprehensive description of steps for each stage of intervention design and development, the participation of family representatives in its development, and its incorporation of life course characteristics into all stages of the intervention development process.

CONCLUSIONS

The LCIRN has begun the process of building a Life Course Intervention Research Framework to assist researchers to adopt a more structured approach to theory testing, to describe with more rigor their life course intervention development process, and to communicate the study details transparently with coresearchers, community members, funders, and reviewers. The LCIRF is not meant to be exhaustive, but to serve as a starting or reference point for intervention researchers interested in addressing life course issues, and as a roadmap or checklist for professionals and communities, assisting them to collaborate on intervention research. Although still a work in progress, the LCIRF combines the best of intervention design principles with the characteristics of life course interventions to guide this evolving LCIR discipline.

ABBREVIATIONS

LCHD: Life Course Health Development
LCIRF: Life Course Intervention Research Framework
LCIRN: Life Course Intervention Research Network
LCIR: life course intervention research
NCC: National Coordinating Center
RCT: randomized controlled trial
SMART: Sequential Multiple Assignment Randomized Trials

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