A Framework to Address Challenges in Communicating the Developmental Origins of Health and Disease

Liana Winett  
_OHSU/PSU School of Public Health_

Lawrence Wallack  
_OHSU/PSU School of Public Health_

Dawn M. Richardson  
_Portland State University, dawn.richardson@pdx.edu_

Janne Boone-Heinonen  
_Oregon Health & Science University_

Lynne C. Messer  
_Portland State University, lymesser@pdx.edu_

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Dr. Liana Winett, DrPH, MPH, MCHES,
School of Community Health and OHSU/PSU School of Public Health, Portland State University, PO Box 751, Portland, OR 97201

Dr. Lawrence Wallack, DrPH, MPH, MS,
School of Community Health and OHSU/PSU School of Public Health, Portland State University, PO Box 751, Portland, OR 97201

Dr. Dawn Richardson, DrPH, MPH,
School of Community Health and OHSU/PSU School of Public Health, Portland State University, PO Box 751, Portland, OR 97201

Dr. Janne Boone-Heinonen, PhD, MPH, and
Public Health and Preventive Medicine and OHSU/PSU School of Public Health, Oregon Health and Science University, 3181 Sam Jackson Park Road, Portland, OR 97239

Dr. Lynne Messer, PhD, MPH
School of Community Health and OHSU/PSU School of Public Health, Portland State University, PO Box 751, Portland, OR 97201

Abstract

Findings from the field of Developmental Origins of Health and Disease (DOHaD) suggest that some of the most pressing public health problems facing communities today may begin much earlier than previously understood. In particular, this body of work provides evidence that social, physical, chemical, environmental, and behavioral influences in early life play a significant role in establishing vulnerabilities for chronic disease later in life. Further, because this work points to the importance of adverse environmental exposures that cluster in population groups, it suggests that existing opportunities to intervene at a population level may need to refocus their efforts “upstream” to sufficiently combat the fundamental causes of disease. To translate these findings into improved public health, however, the distance between scientific discovery and population application will need to be bridged by conversations across a breadth of disciplines and social roles. And importantly, those involved will likely begin without a shared vocabulary or conceptual starting point. The purpose of this paper is to support and inform the translation of DOHaD findings from the bench to population-level health promotion and disease prevention, by:

1)
Discussing the unique communication challenges inherent to translation of DOHaD for broad audiences, 2) Introducing the First-hit/Second-hit Framework with an epidemiologic planning matrix as a model for conceptualizing and structuring communication around DOHaD, and 3) Discussing the ways in which patterns of communicating DOHaD findings can expand the range of solutions considered, and encourage discussion of population-level solutions in relation to one another, rather than in isolation.

Keywords
Developmental Origins of Health and Disease (DOHaD); Epigenetics; Message Framing; Mother-blame; Community-blame; First-hit/Second-hit Framework

Introduction
There is burgeoning scientific evidence that social, physical, chemical, environmental, and behavioral influences in early life play a significant role in establishing vulnerabilities for chronic disease later in life [1–6]. Much of this work has been collected in the field now referred to as the Developmental Origins of Health and Disease (DOHaD) [2–4]. The mechanisms for disease vulnerability this field reveals have been linked to obesity, heart disease, diabetes, and some cancers, in addition to cognitive development, educational performance, and mental health issues [7–14]. These changes result, in part, from adverse exposures to the reproductive environment and developing organ systems during – and even prior to – gestation, as well as during the very early days of childhood [15–19]. A key mechanism by which these influences exert themselves is epigenetics. This has been described as “the biochemical process through which some genes are expressed and others remain silent, and it reinforces and explains the powerful impact that the environment has on human development. Epigenetic effects occur not only through diet, chemical exposure, and high levels of environmental stress, but also through chronic poverty and racism” [In 20, also 21–22]. As such, the research that comprises the field of DOHaD indicates that much chronic disease results less from genetic predisposition than from genetic responses to environmental stressors; this is to say that the “epigenetic process of gene regulation is where nature and nurture come together” [23].

It may be, then, that some of the most pressing public health problems facing communities today begin much earlier than previously understood, and that existing opportunities to intervene at a population level need to refocus “upstream” to sufficiently combat the fundamental causes of disease. To translate DOHaD into improved public health, however, the distance between scientific discovery and population application will need to be bridged by conversations across a breadth of disciplines and social roles. And, it is important to recognize that this breadth means that those involved will likely begin without a shared vocabulary or conceptual starting point.

This is a definitional moment for those scientists, public health professionals, policy makers, community members, and others working to move DOHaD findings from the bench to population-level health promotion and disease prevention. The purpose of this paper is to support the extension of the science into applied arenas by:
1. Providing an introduction to communication framing, in general, and challenges in communicating DOHaD, in particular.

2. Introducing the First-hit/Second-hit framework with a planning matrix as a model for conceptualizing and structuring communication around DOHaD, and as a beginning step toward addressing some of the inherent framing challenges.

3. Discussing the ways in which patterns of communicating DOHaD can expand the range of solutions considered; moreover, how – by cutting across traditional professional and academic boundaries – the framework may encourage discussion of solutions in relation to one another, rather than in isolation.

We conclude by offering recommendations for the application of the communication planning tool to the translation of DOHaD findings for broad audience engagement.

**The DOHaD Communication Task**

Those seeking to bridge DOHaD research and practice encounter a communication task fraught with difficulty [24]. First, having emerged over the past three decades, this is a relatively new body of science that is undergoing constant clarification and is marked by great complexity. For many, it represents a very different way of conceptualizing the onset of disease risk. Second, the specific vocabulary that animates this science (e.g., “programming,” “wiring,” “embedding,” “imprinting,” “poor control”) and the range of language used to describe the “quality” of a person’s physical constitution can prove problematic when used in non-scientific arenas [24].

Perhaps the most vexing of the communication problems marking this field, and those on which we focus in this paper, relate to the unintended consequences of reporting causal associations. Because DOHaD suggests that disease vulnerability can be rooted in any combination of factors ranging from the individual-level to those established in social, political, economic, and physical environments, there is the risk that in discussing one key aspect in isolation from the total picture we may present a distorted view of the complete range of opportunities to effect change. And as we will discuss, in so doing we also run the risk of inadvertently holding at fault those who are at greatest risk.

**The Importance of Communication Frames**

When researchers and others communicate about the nature and urgency of DOHaD, they do so through what sociologists and cognitive scientists call “frames” [25–29]. Frames are the ideological structures, grounded in cultural values, that people use to process and understand the external cues they perceive [30]. Frames tell us which features are within a problem’s parameters, and which are outside of it [29, 31]. Because they characterize a problem as being of a particular type (and thus not another), frames also tell us literally and by abstraction what the problem is, why it matters, what can be done about it, and who is responsible [31]. Importantly, cognitive science demonstrates that the frames we use to interpret problems lead us to particular understanding of the range of solutions available, and may also functionally limit our ability to consider possibilities outside of that range [28].
Frames can be invoked by any cue (e.g., words, metaphor, imagery, core arguments, appeals to values) that leads us to filing an issue into a particular mental category [32]. The importance lies in the articulated meaning that accompanies those cues. For example, if we frame a problem as a “public health issue,” we are suggesting that it is important because of its population health impact; that it is amenable to the tools, techniques, and actions of public health professionals; and that there likely will be an emphasis on primary prevention through broad population-level action. If we were to frame that same problem as a “criminal justice issue,” by contrast, we would suggest its importance and urgency are rooted in concern for law and order; that it is amenable to the tools, techniques, and actions of law enforcement professionals; and that there likely will be an emphasis on deterrence and punishment. And, if we were to say that same problem was a “behavioral issue,” we would be suggesting that it is important because of the effects on the person involved (or the effects that person has on others), that the persons responsible are those exhibiting the behavior, and that the likely tools available are those that sculpt individual habits and practices [e.g., 33]. Thus, by acting as the cognitive structures and filters with which we organize and process the information we receive, frames also help us consider the range of possible action going forward.

Two DOHaD Framing Challenges

**The Risk of Mother-blame**—As we and others have noted, there is a tendency in communicating DOHaD to frame it disproportionately around the biology, behaviors, and life circumstances of the most proximal link in the gestational chain: the mother [24, 34–36]. Common experimental designs evident within the field of DOHaD may contribute to this frame, as they typically compare health outcomes across proximal exposures -- the mother’s constitution, her pregnancy experience, and her actions during or prior to it. When associations are found, the public spotlight tends to focus on these same maternal factors unless and until subsequent research and/or more expansive framing situates initial findings in their broader contexts. Communicating across that divide is part of the challenge.

We have identified three additional potential contributors to the tendency toward mother-blame in DOHaD communications [24]. First, cognitive linguistics explains that people’s minds create unavoidable associations, or “cognitive maps,” between concepts nested within categories. [37–39]. Because “pregnancy” is a category including “fetus + mother,” this cognitive map may foster a predisposition toward conceptualizing gestational problems from the narrow perspective of the maternal environment. Second, much of the language that commonly characterizes discussion of the science (e.g., “her pregnancy,” “the intrauterine environment she provides,” “the mother’s prolonged stress,” “if the baby had been poorly nourished prior to birth”) pinpoints epigenetic phenomena within, or more directly, as being of the mother [24, 34, 36]. Third, there is a dominant personal responsibility frame anchoring much of Western narrative, and thus also shaping our mental processing of problems and solutions [40–43]. This readily accessed cognitive map can predispose us to understand that health risks established during gestation are primarily the product of the mother’s choices and behaviors, or at very least a function of her constitution. While we acknowledge that other frames exist that do not hold mothers primarily culpable for the
health of their offspring, cognitive science tells us that extra cognitive work is required for such less dominant frames to rise above the dominant maps and guide our thinking. [39].

The importance of mothers in the lives of their infants and children is without question. Yet to circumscribe the extent of the problem and solutions to their bodies and behaviors excludes the critical influences and constraints of the broader societies in which women are pregnant and children develop and grow. A robust translation and integration of DOHaD findings into applied health promotion/disease prevention work requires highlighting the less readily accessed cognitive maps that connect individuals to the environments in which they exist.

The Risk of Community-blame—At the same time communicators of the science underlying DOHaD run the risk of an inadvertent and generalized blaming of mothers, there is a second potential risk to be aware of that is similarly problematic but perhaps less obvious -- and, indeed, may emerge in reaction to the first. This is that in seeking to avoid the threat of mother-blame our response may be to instead focus our attention on the contexts in which women reside, including their neighborhoods and communities. Such refocusing is important, and reflects the public health orientation to population-level understanding and intervention. Yet, if we settle on the community as the point of concern without linking it to the larger societal forces within which its circumstances come to be and are sustained, we can also simultaneously diminish the very communities needing the most support. Thus, communicators of DOHaD must also be alert to the risk for community-blame that can directly result from efforts to overcome mother-blame.

Community-blame can lead to a kind of categorical stigmatization [44–48]. Such “degrading marks” on communities evolve through characterizations casting them as undesirable places without resources, capacity, or inherent value [44, 49]. These portrayals are further perpetuated through media coverage and academic discourse, which variously describe disadvantaged communities as “poverty-stricken,” “crime-ridden,” “vulnerable,” and “needy” [50]. Characterizations such as these can create a double jeopardy for groups already dealing with significant health challenges, as they can send the unintended message that the very communities most in need of social and economic investment are instead hopeless and beyond repair.

Further, focusing on decontextualized community factors may limit our effectiveness in addressing DOHaD-related problems. First, we may miss important root causes of disparate health outcomes -- the “causes of the causes,” or the powerful social forces that result in differential risks borne across social groups [in 51, also 52–53]. Second, by missing the macro dimensions of the problem, we may fail to engage the range of stakeholders required for robust discussion of solutions [54]. Finally, messages that are perceived to tarnish communities may (understandably) invite resistance from members of the very communities we seek to help [54–55].

Community level influences are important in the ecology of DOHaD phenomena and are a critical part of the conversation about solutions. And yet -- as is the case with mother-blame
we risk holding community members accountable for the circumstances in which they find themselves, which they neither independently created nor are well-positioned to change.

**Orienting DOHaD Communication**

We have argued that to avoid misplaced blame, DOHaD phenomena must be articulated within the context of the systems that give rise to them. Here, we present a systems model that we believe may provide a first step toward structuring more comprehensive and inclusive communications. It is important to note that developing frames, and ultimately messages, involves far more than the core perspective around which they are crafted [56]. But, articulating that core perspective is the first step [56–57].

The model we propose draws from two complementary public health frameworks. The first is the First-hit/Second-hit framework, previously articulated in the “Two-hit hypothesis” of cancer [58–59], etiology of schizophrenia, [60–61] automobile injury prevention [62], and recently in explaining processes underlying DOHaD [63–64]. The second is a planning tool originally developed to support a comprehensive public health approach to injury prevention, which we adapt to demonstrate the interrelationships among first-hit/second-hit variables [65]. We explain, below, how each informs the DOHaD communication work ahead. Importantly, we believe that these tools allow us to tell the story of the systems and systems breakdowns that give rise to DOHaD risk, and in so doing, help to avoid mother- and community-blame pitfalls.

**First Hit/Second Hit Framework**

The First- and Second-hits framework provides a means to explain how lifelong health can be adversely affected by a series of “hits,” or insults, experienced at critical developmental intervals and across the lifespan. These insults can have enduring effects both on an individual’s predisposition to disease, as well as on the disease predispositions of subsequent generations [63–64].

“First hits” in DOHaD are adverse exposures experienced by the mother that induce disease vulnerabilities prior to birth. Examples of first hits studied include insufficient nutrient flow during gestation, high calorie malnutrition, environmental toxicants, and stress hormones [7, 22, 23, 66–70]. For example, inadequate nutritional flow has been associated with enduring disease-predisposing alterations in the heart, kidneys, and liver of the developing fetus [71–72]. These adverse effects persist across the lifespan and translate to increased risk for diabetes, hypertension, and heart disease. Gestational exposures to environmental toxicants or stress hormones also have been associated with similar adverse effects on fetal development and subsequent disease risk [73–78]. Importantly, each of these first hit exposures may be initiated, perpetuated, magnified, or limited by the broader physical and social contexts in which people exist.

“Second hits,” then, are additional exposures encountered by offspring after birth and throughout their lives. Second hits take many forms, but the most extensively researched include nutrition, social stress, and environmental toxicants [73–78]. Second hits can activate or exacerbate the initial biological vulnerabilities developed as a result of first hits.
That is, for those who were primed during gestation for potential onset of disease, second hits may further heighten vulnerabilities to poor health and adult illness.

Importantly, the occurrence of first- and second-hits are not random, but rather cluster along the same social, racial, and economic stratifications that divide communities [79–86]. Therefore, those most likely to experience first hits are also at the highest risk of exposure to second hits. And, because of intergenerational transfer of risk in DOHaD, the “second hits” of the current reproductive age generation can become the “first hits” of the next. For example, due to the effects of racial and/or socioeconomic segregation, children born to pregnant women living in neighborhoods with significant social disadvantage are likely to remain in the same or similar neighborhoods as they age. This sets the stage for not only initial and subsequent vulnerabilities in this first generation of offspring, but as they reach reproductive age, also provides conditions in which the enduring environmental stressors can be mediated through them to establish vulnerabilities in the next generation. It is through this cycle that persistent health disparities can be perpetuated and magnified within communities: this cycle lies at the intersection of biological vulnerability (first hits), modifiability of risk (second hits), and social vulnerability (resources/ability to modify risk).

The First- and Second-hits Framework, by detailing the staged, multi-level, and mutual influences in DOHaD, offers important structure to communicating the science. In particular, it: 1) explicates the critical interconnections among a broad scope of chronological influences that communicators need to be prepared to articulate, and 2) provides a model with which to illustrate the importance of lifelong social, environmental, and physical contexts in the likelihood of disease.

**First-hit/Second-hit Planning Matrix**

We draw from the Haddon Matrix, an innovative approach developed for injury prevention that applies epidemiological principles to the understanding of non-infectious health outcomes [65, 87–88]. It has subsequently been expanded to a variety of public health issues [e.g., 89–92]. In particular, the matrix aligns the epidemiologic triad of host, agent, and environment with opportunities for prevention in the pre-event, event, and post-event phases of a health phenomenon. To reflect the increasing focus on place-based interventions in public health -- and because a particular communication challenge in speaking to this body of science is adequately incorporating the breadth of context -- we have adapted this tool to further specify the multiple nested physical and social environments in which effects occur. Table 1 illustrates the use of the tool, using examples of the types of DOHaD influences that may populate it.

We believe the matrix is particularly well suited to illustrating and speaking to the causal factors identified through the First- and Second-hits framework because it specifies the chronological and systemic nature of influences. In addition, the matrix provides visual structure to the idea of staged “hits,” and it places the people affected along the continuum of influences so that we can also describe what influences them. Further, by drawing connections to the larger contexts in which risk develops, it allows communicators to speak to any one factor under study without excluding other critical influences. The matrix
provides a structure for planning deeper communication among broad constituencies, by emphasizing interconnections among factors in the cells.

Using the First-hit /Second-hit Framework as Conceptual and Communication Model

In using this matrix (Table 1), scientists, public health professionals, policy makers, and community members, together, can place each causal factor or solution being discussed in relation to the full range of strategies required to meaningfully move the needle on health promotion and disease prevention. For example, maternal nutrition programs can be discussed in relation to food access, affordability, and safety. Prenatal stress management programs can be situated in the context of the need for economic stability, universal living wage, and broad based social opportunity. And, the need for quality, affordable prenatal and pediatric health care can also be described alongside the equally important needs for safe and secure housing that is free of toxic substances. The matrix, when populated with a full range of contributing factors for the aspects of DOHaD being addressed, helps bridge the breadth of causal variables revealed by exploratory science and community prevention, positions these factors in time relative to when people develop vulnerabilities, and specifies the impact of place on the range of solutions available.

This tool also helps us more expansively portray the people involved in DOHaD phenomena, and thus is a first step toward appropriately sharing responsibility. For example, whereas much research frames the mother as the environment as the fetus, the matrix also allows us to demonstrate that society is the environment of the mother. We also can show that she is one of several “hosts” in these processes, simultaneously exposed to and affected by multiple intersecting environments and acting as a conduit through which environments exert influence. Similarly, through the specification of place and intervention options, we can speak of communities in the contexts of the larger social forces in which they operate.

Specifically, the matrix serves as a conceptual, strategic, and communication planning tool for scientists and others wishing to broaden conversations about the etiology of and potential remedies for DOHaD. First, as a conceptual tool the matrix incorporates multiple sources of cause and effect (from the individual to societal), a range of contributing factors (from the behavioral to political and economic), and sequential phases in the causal chain (initial and subsequent vulnerabilities). As such, the framework can provide communicators and audiences a robust portrayal of the range of factors that contribute to DOHaD effects.

Second, the matrix can serve as a strategic planning tool that provides communicators and audiences a means to map the connections among individual efforts toward a more comprehensive approach. And, by providing a broad portfolio of approaches and points of intervention, it allows audiences to determine in which areas activities are most robust and in which they may be lacking. Thus, it positions communicators and their audiences to evaluate any one approach in relation to others, and creates meaningful connection to other possible solutions.

Third, as a communication planning tool the matrix provides a model with which to describe and illustrate the essential and oftentimes reciprocal interconnections between the social determinants of health and their biological impacts. Moreover, it helps people frame
the message around the levels of social effect, seating not only mothers (and others) in their
larger contexts, but also placing communities relative to the larger societies that shape them.
Finally, because the model helps reach across disciplinary silos and traditional boundaries to
emphasize the interconnections among contributions, it invites voices into the conversation
that had not previously been included.

Conclusion

Every Institute of Medicine report begins with a quote from Goethe: “Knowing is not
enough; we must apply. Willing is not enough; we must do.” These early efforts to translate
findings from the field of DOHaD for broad audiences will establish widely shared frames
about what this science means and how it can be translated into community benefit.
Importantly, these initial frames will also suggest who or what bears responsibility in both
the genesis of problems observed and in their resolution.

How we communicate about an issue is rooted in how we understand that issue. The First-
hit/Second-hit matrix provides a useful starting point for expanding our thinking about
DOHaD and suggesting new ways to talk about it. In particular, we believe that the First-hit/
Second-hit framework can help move beyond the traditional variable-by-variable portrayals
of the problem to instead bridge the divide between science and community application. By
introducing new and broader means of characterizing and speaking to the problem, we can
change the questions people ask, and thus also the range of solutions to be considered.
Moreover, providing the broader picture will help people speak concretely about potential
starting points of intervention, and can help do so through a systems perspective.

This is the beginning of a conversation about how this framework can be adapted to meet
DOHaD’s specific communication needs. It is important to note that the matrix is a living
instrument, requiring ongoing reevaluation and clarification as circumstances surrounding a
health problem and its potential strategies evolve. Maintaining the matrix’s currency will
necessitate the continued investment and involvement of a breadth of professional, scientific,
and lay constituencies, all who have a recognized stake in this issue [88].

Subsequent steps to developing this approach include empirically determining:

- Which variables should populate each cell in the table for any given problem
  illuminated by DOHaD, in order to reinforce the continuum of causes, problems,
  and consequences, and to support the most inclusive public dialogue?

- What specific language, phrasing, verbal “imagery,” and mental models -- all
  components of issue framing -- are most supportive of audience engagement with
  these issues and in what ways? Similarly, which may in fact be obstructive?

- How do we balance the short-term need to provide explanations of key findings
  with the long-term need for conversations about population-level change?

Communicating the field of DOHaD and engaging others in the conversation about how to
move forward based on this knowledge will undoubtedly require sensitivity and
thoughtfulness. Framing research can provide us with new insights into how policy makers,
public health professionals, and community organizations hear, interpret, and respond to DOHaD findings. Our society has long struggled with a gap between what science tells us and how we structure our programs and policies in response. The potentially paradigm-shifting potential of DOHaD and epigenetic mechanisms provides us with an opportunity to develop a communication approach that is as sophisticated as the science that is changing our understanding of the world.

Acknowledgments

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References

Papers of particular interest, published recently, have been highlighted as:

• Of importance
  •• Of outstanding importance


the first and second hits framework can be applied to mitigating fetal priming effects within the domain of public health. [PubMed: 26522092]


Table 1
First-hit/Second-hit Planning Matrix for Communicating Developmental Origins of Health and Disease (DOHaD) With Broad Audiences*

<table>
<thead>
<tr>
<th>Host</th>
<th>Agent</th>
<th>Environment (Place) – Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td>Nutritional, Physical, and Social Stress</td>
<td>Pre-gestation (1st Hit)</td>
</tr>
</tbody>
</table>
| Developing girl through woman of reproductive age | Nutrient flow, toxic exposures, and control levels affecting reproductive environment of future mother | • Safe, toxicant-free, secure housing  
• Economic security  
• Healthy food preparation facilities and skills  
• Family support for healthy eating and physical activity  
• Adherence to immunization schedules |
| | **Home** | School | Workplace | Community | Society |
| | • Safe, toxicant-free school facilities | • Healthy food vending and service policies  
• Health, nutrition, and physical education |
| | • Safe, toxicant-free school facilities | • Adherence to immunization schedules  
• Anti-hunger and anti-poverty programs  
• Skilled early childhood educators  
• Healthy food service programs in child care  
• Safe recreational facilities for young children |
| | • Safe, toxicant-free school facilities | • Safe, toxicant-free workplaces  
• Living wage  
• Health insurance |
| | • Safe, toxicant-free school facilities | • Adherence to immunization schedules  
• Anti-hunger and anti-poverty programs  
• Skilled early childhood educators  
• Healthy food service programs in child care  
• Safe recreational facilities for young children |
| | • Safe, toxicant-free school facilities | • Safe, toxicant-free workplaces  
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• Skilled early childhood educators  
• Healthy food service programs in child care  
• Safe recreational facilities for young children |
| | • Safe, toxicant-free school facilities | • Safe, toxicant-free workplaces  
• Living wage  
• Health insurance |
| Intrauterine /First 1000 days post-conception (1st Hit) | Pregnant woman and other family members: Developing fetus  
Male or female child to age 2 | Nutrient flow, toxic exposures, and control levels affecting development of offspring’s organ systems |
| | **Home** | School | Workplace | Community | Society |
| | • Safe, toxicant-free, secure housing  
• Economic security  
• Healthy food preparation facilities and skills  
• Breastfeeding support in household  
• Social support  
• Adherence to immunization schedules |
| | • Safe, toxicant-free, secure housing  
• Economic security  
• Healthy food preparation facilities and skills  
• Breastfeeding support in household  
• Social support  
• Adherence to immunization schedules |
| | • Safe, toxicant-free, secure housing  
• Economic security  
• Healthy food preparation facilities and skills  
• Breastfeeding support in household  
• Social support  
• Adherence to immunization schedules |
| | • Safe, toxicant-free, secure housing  
• Economic security  
• Healthy food preparation facilities and skills  
• Breastfeeding support in household  
• Social support  
• Adherence to immunization schedules |
| Later childhood through adulthood (2nd Hit) | Developing male or female who has already experienced 1st hit exposures  
Nurturant flow, toxic exposures, and control levels compounding and activating initial |
| | **Home** | School | Workplace | Community | Society |
| | • Safe, toxicant-free, secure housing  
• Economic security |
| | • Safe, toxicant-free, secure housing  
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| | • Safe, toxicant-free, secure housing  
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<td></td>
<td></td>
<td>School: • Health, nutrition, and physical education programs • Safe, accessible recreational facilities • Healthy food vending and service policies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Workplace: • Paid sick time • Healthy, affordable cafeteria &amp; food storage options • Workplace health promotion and injury prevention programs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Community: • Grocery store zoning • Community health centers • Family recreational facilities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Society:</td>
</tr>
</tbody>
</table>

One of the strengths of the matrix is that it highlights interacting causal factors in the different phases of the health problem. For this reason, single factors may appear in more than one cell. Social factors transcend all DOHaD phases, and are combined into a single column. Factors provided are examples and are not exhaustive.

Matrix Adapted From: