Matern Child Health J (2016) 20:935–940
DOI 10.1007/s10995-016-1970-8

COMMENTARY

Developmental Origins, Epigenetics, and Equity: Moving Upstream

Lawrence Wallack[1,2] · **Kent Thornburg**[2,3]

Published online: 30 March 2016

Abstract The Developmental Origins of Health and Disease and the related science of epigenetics redefines the meaning of what constitutes upstream approaches to significant social and public health problems. An increasingly frequent concept being expressed is "When it comes to your health, your zip code may be more important than your genetic code". Epigenetics explains how the environment—our zip code—literally gets under our skin, creates biological changes that increase our vulnerability for disease, and even children's prospects for social success, over their life course and into future generations. This science requires us to rethink where disease comes from and the best way to promote health. It identifies the most fundamental social equity issue in our society: that initial social and biological disadvantage, established even prior to birth, and linked to the social experience of prior generations, is made worse by adverse environments throughout the life course. But at the same time, it provides hope because it tells us that a concerted focus on using public policy to improve our social, physical, and economic environments can ultimately change our biology and the trajectory of health and social success into future generations.

Keywords Developmental origins · Upstream · Epigenetics · Zipcode · Barker Hypothesis · Health equity

Significance

What is already known? Vulnerability for chronic and other diseases, physical and mental, is "programmed" into human biology much earlier than we thought–preconception through the first 1000 days to about age two. Nutrition is critical, and we now know that impacts of intergenerational disease-generating "toxic" stress caused by interlocking systems of oppression that lead to institutional racism, financial deprivation, and lack of opportunity and limited access to resources resulting in disadvantaged position in society must also be addressed.

What this study adds? This paper provides a framework for starting to translate the science into public health program and policy.

The field of public health is rooted in a powerful upstream–downstream metaphor. The story is that public health workers are so busy downstream trying to pull increasing numbers of drowning people out of the river that they do not have time to go upstream and see what is causing so many people to fall in [1]. Downstream activities will help some but will never be sufficient to significantly reduce the problem as more and more people will continue to fall in

This commentary is based on a talk by Lawrence Wallack that was part of a City Club of Portland forum with Rachael Banks on Epigenetics and Equity: The health and social impacts of racism and inequality. I want to express my appreciation to the following people who provided valuable editing suggestions: Monica Cuneo, Lori Dorfman, Cat McGinnis, Linda Nettekoven, Justine Pope, Jon Purnell, and Liana Winett.

✉ Lawrence Wallack
Wallack@pdx.edu

Kent Thornburg
thornbur@ohsu.edu

[1] Center for Public Health Studies, Portland State University, Portland, OR, USA

[2] Bob and Charlee Moore Institute for Nutrition & Wellness, Oregon Health & Science University, Portland, OR, USA

[3] Center for Developmental Health, Knight Cardiovascular Institute, Portland, OR, USA

upstream. The mission of public health is prevention and this means working upstream "to fulfill society's interest in assuring conditions in which people can be healthy [2]." Newly emerging research on the developmental origins of health disease (DOHaD) and the related epigenetic process highlights the urgency of going upstream and challenges us to rethink the very nature of what we mean by upstream thinking. The idea of "assuring conditions" is a radical concept that requires an equity lens that can incorporate a fairness or social justice approach to public health [3–5]. The purpose of this commentary is to stimulate thinking about how DOHaD, epigenetics, and equity might be integrated as a basis for a renewed commitment to move upstream to better confront root causes of vexing public health and social problems.

Here are some general definitions to begin to move the discussion.

Developmental origins of health and disease is a body of research that has shown that the risk of chronic diseases such as type 2 diabetes, stroke, heart disease and even some cancers is determined by environmental conditions before pregnancy through the first 1000 days following conception up to about age two [6–16]. Risk for compromised cognitive function and significant mental health issues is also established in that time period [17–21].

Second, epigenetics is the process by which our genes respond to environmental cues [22–27]. These responses can influence how our genes are programmed to regulate biological functions. 'Epi' refers to being above the usual regulation of the genes. The genetic code does not change in response to the environment, but the biological switches that turn those genes on and off do. These altered regulatory commands can be passed from parent to child so that altered gene expression patterns that affect one's health all the way into adulthood can be passed generation to generation.

Third, health equity seeks to reduce group differences in health outcomes that are unjust, predictable, and preventable [28, 29]. Developmental origins is the ultimate social and health equity lens because it helps us understand how life history, sociology and biology combine to create lifelong prospects for health and social success at the earliest stages [30, 31].

The public health field is grounded in an ethical framework of social justice [3]—the idea that social inequality follows from the adverse impact of privilege, power, and exclusion that are powerfully linked to health inequity. The collective policy decisions we make as a community determine the distribution of risks and benefits, obstacles and opportunities, disease and health among our members. And, the public policies we debate and implement today will determine the public health problems we face tomorrow.

Robert Wood Johnson Foundation senior vice president James Marks, commenting on the publication of the Foundation's *Commission to Build a Healthier America* concluded "When it comes to your health, your zip code may be more important than your genetic code [32]." Epigenetics helps explain how the environment, our zip code, literally gets under our skin, creates biological changes that increase our vulnerability for disease, and even our children's prospects for social success over their life course and into future generations. This science requires us to rethink where disease comes from and the best way to promote health. It identifies the most fundamental social equity issue in our society: that initial social and biological disadvantage, established prior to birth, and even linked to the social experience of previous generations, is made worse by adverse environments throughout the life course [17]. But at the same time, it provides hope because it tells us that a concerted focus on improving our environments can ultimately change our biology and the trajectory of disease into future generations.

The idea of developmental origins was generated in the late 1980s by David Barker, an English physician and epidemiologist, who published the hypothesis that the risk for heart disease and other chronic diseases originated in the earliest developmental stages and not later in life [6–8, 33]. Barker's data, and subsequent additional data from around the world, found that chronic diseases such as diabetes, hypertension, stroke, and heart disease were programmed into our systems as a result of social stress and nutritional deficiency during the critical developmental period of pre pregnancy up to about age two. Poor nutrition, associated with disadvantaged living conditions, slowed fetal growth and forced developmental tradeoffs that harmed longer-term health. Low birth weight alone predicted a substantial increased risk of chronic diseases like type two diabetes and heart disease later in life.

The Barker Hypothesis inspired substantial new scientific investigation on the origins of disease. As a result of this and related research we now understand [9, 11, 14, 34, 35]:

- The First Thousand Days from conception to about age two is the most critical and sensitive time for development. During this period of time, more than any other, the body is highly sensitive to the levels of nutrition and stress. The risk for chronic diseases is programmed into the function of key organs, settings in metabolism and hormonal feedback are altered, and an increased vulnerability to adverse environments later in life is embedded into a person for life;
- Our genes are not a deterministic blueprint for our health but a collection of infinite possibilities that are switched on-or-off depending on the conditions our mothers experienced prior to and during pregnancy, and on the nutrition and social environment we have as

infants. This research suggests that people mostly get chronic diseases *not* because of the genes they inherit but because of how those genes act in response to environmental stresses. This epigenetic process of gene regulation is where nature and nurture come together.

- The pregnant woman is the environment of the developing fetus, but importantly *the community is the environment of the mother*. The two main factors in the community environment that impact healthy development are availability of appropriate nutrition and the level of social stress experienced prior to and during pregnancy. These are a developmental recipe for vulnerability at birth, poor school performance and social skills early in life, and poor health over the life course.

One way to think about this is as a "double hit [36–39]." The *first hit* is the biological embedding and vulnerability that is created from the experience of previous generations through the first 1000 days post conception and may create an increased sensitivity to adverse family and community environments encountered later in life. Then, the *second hit* comes from hostile environments marked by racial and other discrimination, inequality, and social disadvantage that creates constant wear and tear on human systems and increases the likelihood that the original vulnerability will transform into later disease [40]. Because some of these changes can be transmitted across generations, the "second hit" of one generation can become the "first hit" of the next.

So how does this process work? As we all know, each of us comes from an egg that developed through embryonic and fetal stages before we were born. The developing egg, embryo, and fetus read signals from the mother about the environment it will be entering [41]—is there a scarcity or abundance of nutrients; is the environment safe or threatening [35, 42]? These signals are translated into changes in genetic function that provides instructions to the cells on how to grow and function—these are epigenetic changes. These epigenetic changes in the womb are made in response to the environment and may be passed on for up to two generations and may in some cases be reversible [17, 43].

When the developing fetus gets a signal that the biological environment has limited nutrients, for example, this represents a forecast and it begins to program its systems accordingly. This requires making tradeoffs in terms of which organs get the energy for optimal growth and development. This means that some organs such as the kidney may be built "on the cheap" with limited capacity for life. Other metabolic and biological systems are likewise programmed with a strategy for making the most of a nutrient poor environment. These systems are then set for the life of the person; damage done early is carried forth throughout the lifespan [8–11, 17, 19, 21–25, 35].

The fetus also gets a second forecast regarding how safe or threatening the environment is. If a pregnant woman lives in a highly stressful environment that might be marked by poverty, racial discrimination, lack of opportunity, personal insecurity and other aspects of social disadvantage—a level of toxic stress—then high levels of cortisol are passed to the developing fetus [17–19]. Cortisol is the body's primary stress hormone that normally alters our immune system to ensure that biological resources are available to fight whatever threat is before us.

However, high continuous levels of cortisol in the fetus create two problems. The first is that when chronic stress is present the stress response systems in the brain are permanently wired to remain on a "short fuse and high alert status [17, p. 2257]." This takes a heavy toll on the immune system. The second problem is that the higher levels of cortisol in the fetus inhibit growth of fetal organs and create the biological changes that cause increased risk for chronic diseases. Thus, poor nutrition and toxic social stress are equal culprits that must be addressed simultaneously.

Further, higher levels of cortisol in the womb are associated with cognitive problems including poor self-regulation and impulse control, memory problems, lower language skills, and limited reasoning, planning and judgment. Of course, these are the very skills that children need to be successful in school and beyond.

The pre natal exposure to high stress and low nutrition represent the first hit. This initial vulnerability or risk is amplified by continuing difficult social and economic conditions and poor environments [19, 40, 44–46]—the less desirable zip codes. This is the second hit. Multiply these effects by large populations living in conditions that create and sustain high levels of stress, limited access to nutritious food, poor housing, and limited educational and employment opportunity and you can see how chronic disease clusters and social problems emerge.

Frederick Douglas the great African American abolitionist said, "It is easier to build strong children than repair broken men." We all want to do this. We have a moment before us where our best science, our most compassionate values, and our desire to act with conviction to make a difference can all converge. This is a place where the science of the laboratory and the wisdom of the community point to places where we can make an important difference—"Thus, the current revolution in biology offers compelling investment opportunities in the prenatal and early childhood period for policy makers whose responsibilities lie in the realms of population health… [47, p. 17305]." We may not be able to change genes, but we can change the environments that influence how our genes are expressed. We can change the racism, discrimination,

inequality and continued disadvantage that get under our individual and collective skin [28, 30, 31, 46].

Here are some steps we can take:

First, we need to better recognize the monumental significance of the social, economic, and nutritional environments of pregnant women and those about to enter childbearing age. Using an equity lens to assess policy and resource allocation we can commit to build more just and supportive environments that can increase the chance for both good health and social success.

Second, new knowledge on related areas of developmental origins of health and disease, adverse childhood experiences [48], life course [49] and early childhood education is rapidly increasing [50]. The basic science on the possible epigenetic mechanisms underlying the early stage of the life course is enormously promising. To realize the opportunities, build on this research, and translate this knowledge into public health benefit we need to develop an overall conceptual model and organizing framework to guide the integration of multidisciplinary research, policy development and community practice. An interesting starting point would be further elaboration of the first hit-second hit concept [36–40].

Third, we need to better build on existing effort and successes of the good work happening now in our communities on maternal and child health issues, as well as on broader social determinants such as housing, racial justice, food systems and economic development. We need to connect these efforts, build and expand that work, and further accelerate progress in our communities.

Fourth, we need to link and leverage efforts in some key areas. For example, places around the country are making substantial investments in early childhood education to address the very problems that the science of developmental origins identifies. Early childhood education programs need to link with pre pregnancy and pregnancy programs. They need to focus on prevention because there will never be enough funding to provide the kind of early childhood education services that increasing numbers of children will need. We need to take a new look at early childhood education with a science of developmental origins lens.

Fifth, there are policies that we can support to improve the pre natal and post natal situation for families. One example is paid parental leave. Currently the US has few examples of the impact of this policy but the ones that do exist, in combination with the vast experience of OECD countries, tell us that parental leave impacts current and future generations and has strong equity effects [51–54]. This category of policy is a fundamental "upstream" strategy that can be a catalyst for increased understanding of, and attention to, the urgency of family support and the potential benefits.

These are starting points and building blocks. But at the same time we will require bigger ideas and greater efforts to make necessary progress. Expanded and enhanced social services are necessary but not sufficient. It will take real social change focused on the underlying, interconnected social conditions that are at the root of health inequity. This magnitude of change will require the kind of political will that can only be found within the energy of a powerful social movement that shifts the very way we think about these issues and we need to think in terms of what a social movement might look like [55–57].

There is a wonderful quote from Thomas Pynchon's book Gravity's Rainbow, "If they can get you asking the wrong questions, the answers don't matter." Here are some "right questions" that we need to be asking and that help create an upstream vision:

- If any particular geographic area or region were to become the healthiest place in the world to be pregnant and have a child, what would it look like?
- How would it be different than it is now, what would need to change?
- What kinds of policies would be required to move toward that vision?
- How can we create a social movement built on this collective vision to force the necessary political will to demand change?
- How can existing partnerships be expanded?
- How can we develop new partnerships with new allies to move ahead?
- What political barriers must we overcome?

Can we "get there from here?" We have to. We need to find points of leverage that can move us from the level of change on which we are now engaged to a much more expansive level. Crisis is a good motivator for change, and obesity and diabetes may be the prompt we need. What will our health care and social systems do in in the year 2050 when roughly one in three adults in the U.S. is projected to have diabetes [58]? What will economic opportunity look like with increasing income inequality and large pockets of educational failure that lock populations out of social mobility? We can use the science of developmental origins and focus on social policy and prevention to make a difference.

There is a Chinese symbol that represents the Carp Dragon and is the story of a carp fish that swims upstream until it reaches a waterfall that blocks its journey. Despite great struggle the carp cannot get over this waterfall. At the point of maximum exertion and almost fatal fatigue the carp transforms into a dragon and flies over the waterfall.

What will it take for us to transcend our waterfall? We are aware enough to appreciate the urgency of our current health crisis including the adverse social circumstances that increasing numbers of people face, we are smart enough to

figure this out, but we need to be wise enough to understand that we can't succeed simply by doing more of what we have been doing. We need to work on this as if our collective future depends on it, because it does.

The emerging science of DOHaD provides an opportunity for policy makers with various interests in health, education, and social well-being to focus on the common roots of problems that minimize human potential. These roots, we now know, occur very early in the developmental stages and need to be understood as the interaction of the biological and social. To take advantage of this opportunity policy makers will need to overcome traditional siloed thinking, rethink narrow problem definition, and embrace more visionary, and perhaps risky, comprehensive approaches to prevention. These approaches will need to be considered across the entire life course but must be rooted in that critical period of the first 1000 days when the epigenetic impact of adverse environments is greatest, particularly on the most disadvantaged populations. The ever-present scarcity of resources to apply to problems will always necessitate the placing of bets seeking to maximize the greatest impact. We can increase our odds of success by using science to reduce uncertainty in policy development and hopefully overcome the usual politics.

References

1. McKinlay, J. (1986). A case for refocusing upstream: The political economy of illness. In P. Conrad & R. Kern (Eds.), *The Sociology of Health and Illness* (pp. 484–500). New York: St. Martin's Press.
2. Committee for the Study of the Future of Public Health. (1988). *The future of public health*. Washington, DC: National Academy Press.
3. Beauchamp, D. (1976). Public health as social justice. *Inquiry, XIII*, 3–14.
4. Mann, J. (1997). Medicine and public health, ethics and human rights. *The Hastings Center Report, 27*, 6–13.
5. Marmot, M. (2005). Social determinants of health inequities. *The Lancet, 365*, 1099–1104.
6. Godfrey, K., & Barker, D. (2001). Fetal programming and adult health. *Public Health Nutrition, 4*, 611–624.
7. Barker, D. (2004). The developmental origins of adult disease. *Journal of the American College of Nutrition, 23*, 588S–595S.
8. Barker, D. (2012). Developmental origins of chronic disease. *Public Health Nutrition, 126*, 185–189.
9. Barker, D. J., & Thornburg, K. L. (2013). The obstetric origins of health for a lifetime. *Clinical Obstetrics and Gynecology, 56*, 511–519.
10. Hanson, M. (2014). Understanding the origins of diabetes. *JAMA, 311*, 575–576.
11. Gluckman, P. D., Hanson, M. A., Cooper, C., & Thornburg, K. L. (2008). Effect of in utero and early-life conditions on adult health and disease. *The New England Journal of Medicine, 359*, 61–73.
12. Roseboom, T., van der Meulen, J., Ravelli, A., Osmond, C., Barker, D., & Bleker, O. (2001). Effects of prenatal exposure to the Dutch famine on adult disease in later life: An overview. *Molecular and Cellular Endocrinology, 185*, 93–98.
13. Schulz, L. C. (2010). The Dutch Hunger Winter and the developmental origins of health and disease. *Proceedings of the National Academy of Sciences of the United States of America, 107*, 16757–16758.
14. Barouki, R., Gluckman, P. D., Grandjean, P., Hanson, M., & Heindel, J. J. (2012). Developmental origins of non-communicable disease: Implications for research and public health. *Environmental Health: A Global Access Science Source, 11*, 42.
15. Barnes, S. K., & Ozanne, S. E. (2011). Pathways linking the early environment to long-term health and lifespan. *Progress in Biophysics and Molecular Biology, 106*, 323–336.
16. Bhatia, J., Bhutta, Z. A., & Kalhan, S. C. (2013). *Maternal and child nutrition: The first 1,000 days. Nestle Nutrition Institute workshop series*. Basel: Karger Publishing.
17. Shonkoff, J. P., Boyce, W. T., & McEwen, B. S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *JAMA, 301*, 2252–2259.
18. Monk, C., Georgieff, M. K., & Osterholm, E. A. (2013). Research review: Maternal prenatal distress and poor nutrition—Mutually influencing risk factors affecting infant neurocognitive development. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 54*, 115–130.
19. Hertzman, C., & Boyce, T. (2010). How experience gets under the skin to create gradients in developmental health. *Annual Review of Public Health, 2010*(31), 329–347.
20. Figlio, D., & Guryan, J. (2014). The effects of poor neonatal health on children's cognitive development. *American Economic Review, 104*, 3921–3955.
21. Van den Bergh, B. R., Mulder, E. J., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: Links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews, 29*, 237–258.
22. Thayer, Z. M., & Kuzawa, C. W. (2011). Biological memories of past environments: Epigenetic pathways to health disparities. *Epigenetics: Official Journal of the DNA Methylation Society, 6*, 798–803.
23. Waterland, R. A., & Michels, K. B. (2007). Epigenetic epidemiology of the developmental origins hypothesis. *Annual Review of Nutrition, 27*, 363–388.
24. Wadhwa, P. D., Buss, C., Entringer, S., & Swanson, J. M. (2009). Developmental origins of health and disease: Brief history of the approach and current focus on epigenetic mechanisms. *Seminars in Reproductive Medicine, 27*, 358–368.
25. Hunter, R. G. (2012). Epigenetic effects of stress and corticosteroids in the brain. *Frontiers in Cellular Neuroscience, 6*, 18.
26. Rothstein, M. A., Cai, Y., & Marchant, G. E. (2009). The ghost in our genes: Legal and ethical implications of epigenetics. *Health Matrix, 19*, 1–62.
27. Zeisel, S. H. (2009). Epigenetic mechanisms for nutrition determinants of later health outcomes. *American Journal of Clinical Nutrition, 89*, 1488S–1493S.
28. Braveman, P. A., Cubbin, C., Egerter, S., Williams, D. R., & Pamuk, E. (2010). Socioeconomic disparities in health in the United States: What the patterns tell us. *American Journal of Public Health, 100*(Suppl 1), S186–S196.
29. Stapleton, G., Schroder-Back, P., & Townend, D. (2013). Equity in public health: An epigenetic perspective. *Public Health Genomics, 16*, 135–144.
30. Braveman, P., & Barclay, C. (2009). Health disparities beginning in childhood: A life-course perspective. *Pediatrics, 124*(Suppl 3), S163–S175.

31. Combs-Orme, T. (2013). Epigenetics and the social work imperative. *Social Work, 58*, 23–30.
32. Marks, J. (2011). *Why your zip code may be more important to your health than your genetic code*. Huffington Post.
33. Barker, D. J. (2007). The origins of the developmental origins theory. *Journal of Internal Medicine, 261*, 412–417.
34. de Boo, H. A., & Harding, J. E. (2006). The developmental origins of adult disease (Barker) hypothesis. *The Australian & New Zealand Journal of Obstetrics & Gynaecology, 46*, 4–14.
35. Kuzawa, C., & Quinn, E. (2009). Developmental origins of adult function and health: Evolutionary hypotheses. *Annual Review of Anthropology, 38*, 131–147.
36. Boone-Heinonen, J., Messer, L. C., Fortmann, S. P., Wallack, L., & Thornburg, K. L. (2015). From fatalism to mitigation: A conceptual framework for mitigating fetal programming of chronic disease by maternal obesity. *Preventive Medicine, 81*, 451–459.
37. Messer, L. (2015). Developmental programming: Priming disease susceptibility for subsequent generations. *Current Epidemiology Reports, 2*(1), 37–51.
38. Cervantes-Rodriguez, M., Martinez-Gomez, M., Cuevas, E., Nicolas, L., Castelan, F., Nathanielsz, P. W., et al. (2014). Sugared water consumption by adult offspring of mothers fed a protein-restricted diet during pregnancy results in increased offspring adiposity: The second hit effect. *The British Journal of Nutrition, 111*, 616–624.
39. Bagby, S. P. (2007). Maternal nutrition, low nephron number, and hypertension in later life: Pathways of nutritional programming. *The Journal of Nutrition, 137*, 1066–1072.
40. McEwen, B. S. (2012). Brain on stress: How the social environment gets under the skin. *Proceedings of the National Academy of Sciences of the United States of America, 109*(Suppl 2), 17180–17185.
41. Eckert, J. J., Porter, R., Watkins, A. J., Burt, E., Brooks, S., Leese, H. J., et al. (2012). Metabolic induction and early responses of mouse blastocyst developmental programming following maternal low protein diet affecting life-long health. *PLoS ONE, 7*, e52791.
42. Gluckman, P. (2006). *Mismatch: Why our world no longer fits our bodies*. Oxford: University Press.
43. Szyf, M., & Meaney, M. J. (2008). Epigenetics, behaviour, and health. *Allergy, Asthma, and Clinical Immunology: Official Journal of the Canadian Society of Allergy and Clinical Immunology, 4*, 37–49.
44. Furumoto-Dawson, A., Gehlert, S., Sohmer, D., Olopade, O., & Sacks, T. (2007). Early-life conditions and mechanisms of population health vulnerabilities. *Health Affairs (Project Hope), 26*, 1238–1248.
45. Olden, K., Lin, Y. S., Gruber, D., & Sonawane, B. (2014). Epigenome: Biosensor of cumulative exposure to chemical and nonchemical stressors related to environmental justice. *American Journal of Public Health, 104*, 1816–1821.
46. Kuzawa, C. W., & Sweet, E. (2009). Epigenetics and the embodiment of race: Developmental origins of US racial disparities in cardiovascular health. *American Journal of Human Biology: The Official Journal of the Human Biology Council, 21*, 2–15.
47. Shonkoff, J. P. (2012). Leveraging the biology of adversity to address the roots of disparities in health and development. *Proceedings of the National Academy of Sciences of the United States of America, 109*(Suppl 2), 17302–17307.
48. Bethell, C. D., Newacheck, P., Hawes, E., & Halfon, N. (2014). Adverse childhood experiences: Assessing the impact on health and school engagement and the mitigating role of resilience. *Health Affairs (Project Hope), 33*, 2106–2115.
49. Lu, M. C., & Halfon, N. (2003). Racial and ethnic disparities in birth outcomes: A life-course perspective. *Maternal and Child Health Journal, 7*, 13–30.
50. Heckman, J. J. (2007). The economics, technology, and neuroscience of human capability formation. *Proceedings of the National Academy of Sciences of the United States of America, 104*, 13250–13255.
51. Aitken, Z., Garrett, C. C., Hewitt, B., Keogh, L., Hocking, J. S., & Kavanagh, A. M. (1982). The maternal health outcomes of paid maternity leave: A systematic review. *Social Science and Medicine, 2015*(130), 32–41.
52. Carneiro, P. (2015). A flying start? Maternity leave benefits and long-run outcomes of children. *Journal of Political Economy,*. doi:10.1086/679627.
53. Rossin-Slater, M., Ruhm, C. J., & Waldfogel, J. (2013). The effects of California's paid family leave program on mothers' leave-taking and subsequent labor market outcomes. *Journal of Policy Analysis and Management: The Journal of the Association for Public Policy Analysis and Management, 32*, 224–245.
54. Tanaka, S. (2005). Parental leave and child health across OECD countries. *The Economic Journal, 115*, F7–F28.
55. Halfon, N., Wise, P. H., & Forrest, C. B. (2014). The changing nature of children's health development: New challenges require major policy solutions. *Health Affairs (Project Hope), 33*, 2116–2124.
56. Webb, B. (2012). *Moving upstream: Policy strategies to address social, economic, and environmental conditions that shape health inequities*. Washington, DC: Health Policy Institute, Joint Center for Political and Economic Studies.
57. Masters, B., & Osborn, T. (2010). Social movements and philanthropy: How foundations can support movement building. *The Foundation Review, 2*, 12–27.
58. Boyle, J. P., Thompson, T. J., Gregg, E. W., Barker, L. E., & Williamson, D. F. (2010). Projection of the year 2050 burden of diabetes in the US adult population: Dynamic modeling of incidence, mortality, and prediabetes prevalence. *Population Health Metrics, 8*, 29.