POLICY

Losing the War Against Obesity: The Need for a Developmental Perspective

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Developed countries are struggling to control epidemics of obesity and related chronic diseases; thus, we can expect only limited success from applying the current approaches to the developing world, which is experiencing an alarming increase in such disorders. This failure results in part from the fact that our focus on adult life-styles, although important, ignores data that suggest that biological and cultural factors operating early in life affect adult health status. To stem the rising obesity burden in developing countries, scientists and policy-makers must address obesity-promoting factors from early development to adulthood.

The high prevalence of obesity and its related social and economic costs in wealthy industrialized countries are well recognized; however, the number of obese individuals is also rising rapidly in low- and middle-income countries, which lack the infrastructure to support a large obese population suffering from related, often chronic, diseases (for example, cardiovascular disease, diabetes, certain cancers, liver and kidney damage, and reproductive deficits) (*1*). The United Nations (UN) General Assembly will meet in September to address the growing threat from obesity and its related morbidities, with particular emphasis on the developing world. To this end, it is crucial that we apply lessons from the failure of wealthy countries to curb obesity and not extend ineffective strategies to the developing world (*2*). In this Commentary, we explore the reasons behind this failure in the context of important cultural and biological insights (Fig. 1).

PERCEPTIONS OF BODY WEIGHT AND DISEASE

The complex cultural, sociological, spiritual, and emotional forces that surround food and eating can differ across divergent societies, along with body image and concepts of the ideal physique. For societies that view obesity as a sign of health, wealth, and prestige, the promotion of weight loss as an aspiration will be difficult to achieve. Furthermore, the relation between adiposity and disease risk is not simple or consistent. Not all obese people develop the associated diseases described above, a fact that weakens the argument for focusing on obesity reduction in the minds of many lay people. Populations and individuals display differences in fat deposition. Visceral or ectopic fat—which accumulates in the abdomen; in organs such as the liver, skeletal muscle, heart, and pancreas; and possibly in the arteries—is associated with a higher risk of developing obesity-associated disorders than is accumulation of subcutaneous (under the skin) fat (*3*). These physiological phenomena are reflected in population differences, such as the higher prevalence of diabetes among South Asians as compared with Europeans in the UK at any waist-to-hip ratio (*4*). However, the probabilistic relationship between obesity and disease risk is not easily translated to the individual level; thus, the concept of personal risk is often poorly understood. This reality dampens the impact of public health measures, and the situation is made worse by the time lag between induction of risk and adverse outcome because obesity and its related diseases can emerge slowly over several years. People naturally have a lower level of commitment to efforts that have an immediate cost but delayed benefits, and this differential may well be influenced by their social circumstances (*5*).

The widespread use of high body mass index (BMI) as the primary measure of obesity, although useful in population studies, may be misleading at the individual level (*6*). For example, elite athletes are not obese but can have high BMIs because of their muscularity. More easily understood measures, such as waist circumference (which is used as an index of visceral fat) and percentage body fat (total fat weight divided by total body weight), are now readily measurable with low-cost devices and may be more effective at assessing obesity than is BMI.

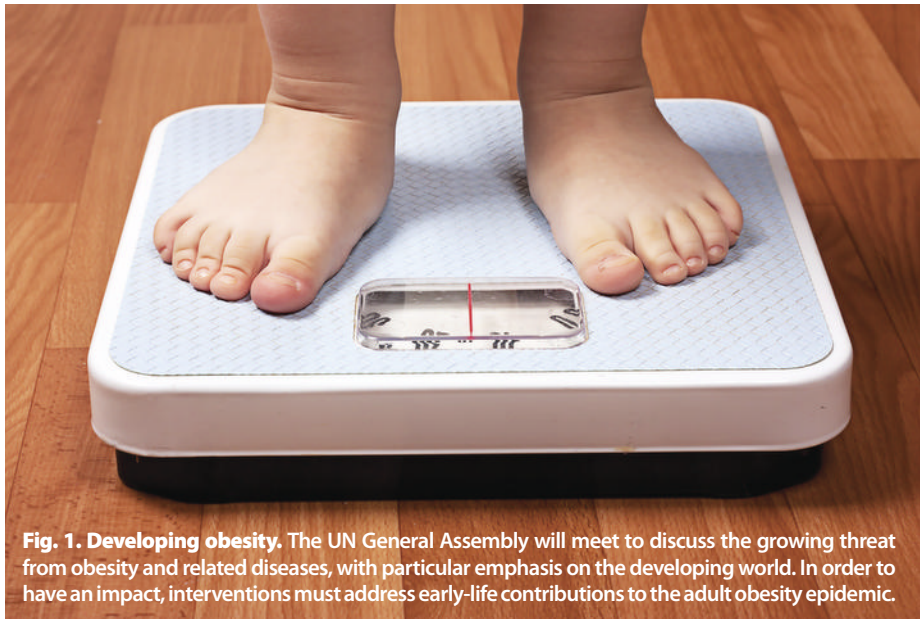

Fig. 1. Developing obesity. The UN General Assembly will meet to discuss the growing threat from obesity and related diseases, with particular emphasis on the developing world. In order to have an impact, interventions must address early-life contributions to the adult obesity epidemic.

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WHY ARE WE FAILING?

Several powerful conditions converge to drive the obesity epidemic. First, weight loss is made difficult by neuroendocrine signals

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programmed to return body weight to a previously established set point (*7*). Second, many people now live sedentary lifestyles with readily available sources of energy-dense food—the basis for so-called obesogenic conditions. It has been suggested that humans evolved with a bias toward a positive energy balance because fat stores provide protection against transient undernutrition (*8*). But in places where food is plentiful and many occupations require only a limited amount of physical activity, as is the case in many developed countries, individuals can exceed their evolved capacity to maintain energy balance—a phenomenon that has been termed "evolutionary mismatch" (*8*). Any effective strategy for dealing with obesity and the prevention of related diseases must consequently address a universal truth: As societies undergo economic transition toward affluence—which comes with global influences and greater access to refined foods—their citizens will increasingly live in an environment that favors this mismatch. Furthermore, in such an environment individuals with a lower socioeconomic status are at greater risk for obesity than are people of means, in part because poorer-quality refined foods are cheaper than fresh foods, and because their economic situations make it more difficult to access medical care and invest in costly life-style changes that have delayed benefits (*5*).

Although it has been argued that the energy expended in daily living has fallen substantially in almost all societies since the industrial revolution, actual measurements of energy expenditure in several populations do not consistently support an across-the-board reduction of energy in recent history (*9*). These findings call into question the relative contribution of reduced energy expenditure to the accumulation of body fat (*10*). Furthermore, although exercise undeniably pays considerable health dividends, humans have evolved to use energy for physical activity efficiently; thus, weight management strategies that depend heavily on increasing energy expenditure through physical activity are unlikely to be successful interventions at the population level.

Despite these concerns, the basic interventional recipe to prevent obesity and associated diseases has remained largely unchanged: reduce smoking, reduce salt intake, promote changes in food consumption, increase physical activity, and treat disease aggressively once it has developed (*2*). There is also a move to extrapolate from the success in reducing tobacco use through structural, legislative, and economic measures to the fight for control of diet and physical activity. However, such interventions are likely to be politically unpalatable because they represent a greater intervention of the state into fundamental aspects of a person's autonomy—what they eat and how they look. Although smoking is discretionary, eating is not. Moreover, the tobacco industry can be targeted in a way the food industry cannot because a successful food industry is essential to global food security, which is a high priority for many developing countries. Unacceptable practices in the food industry must be curtailed, such as the marketing of poor-quality food to children and promoting high fat– and high sugar–containing foods of dubious nutritional value (for example, most sweetened carbonated beverages). However, partnerships between the academic and public health sectors and the food industry will be needed to develop healthy nutrition and promote disease prevention practices.

The basis of most of the current disease prevention programs is the assumption that, like lung cancer in smokers, obesity and its related diseases result directly from our life-style choices—what and how much we eat, and how effectively and regularly we exercise. This bias underlies the move toward extensive, although highly variable, requirements for the labeling of packaged foods. But a more damaging repercussion of this emphasis on individual responsibility is that some state and federal governments have withdrawn from active intervention because of concerns about adverse reactions to perceptions of interference in an individual's choice of life-style (*11*). Yet, the perception of the state's role in battling the obesity epidemic would be very different if the biological basis of obesity was understood by policy-makers.

BIOLOGICAL DETERMINANTS

Both genetic and developmental factors contribute to the substantial variation between individuals regarding the risk of obesity and related diseases in an obesogenic environment. Twin studies have suggested a strong genetic component to obesity (*12*), but such studies do not easily distinguish between genetic effects and intrauterine epigenetic effects; epigenetic changes alter patterns of gene expression—not by modifying a gene's DNA sequence but through DNA methylation and enzymatic modifications of histone proteins that package genomic DNA. Studies of weight loss and weight gain under controlled conditions in monozygotic twins (*13*) in fact reveal considerable variation between members of a pair, suggesting that nongenetic factors are also operating even when the genetic background is the same. Although single-gene mutations have been shown to underlie some cases of severe familial morbid obesity, including genetic aberrations that affect appetite control (*14*), for moderate obesity and obesity-associated diseases, the size of the attributable risk derived from genome-wide association studies has been disappointingly modest (*15*): Genetic variation may account for only ~10 to 15% of relative risk (*16*).

There is compelling evidence of a sizeable contribution of early-life influences on the risk of becoming an obese adolescent or adult and of developing obesity-associated diseases in adulthood (*17*). Indeed, the rapidly rising incidence of childhood obesity is testimony to the contributions of early-life processes (Fig. 1). Developmental factors can affect adult disease risk via several pathways, all of which depend on developmental plasticity (*18*)—the processes by which embryo, fetus, and infant physiology responds to the environment and contributes to the adult phenotype. These effects are now believed to be mediated by epigenetic changes. Early-life exposures such as maternal under- or overnutrition and neonatal over feeding have been shown experimentally to affect satiety, food preference, muscle mass, and insulin resistance in the offspring. These changes, accompanied by modulations in body composition and cardiovascular and metabolic function, are associated with alterations in the offspring's epigenetic state (*19*–*21*). Maternal stress, toxin exposure, and altered maternal-infant interactions have also been linked to changes in the offspring's epigenetic state (*22*–*24*). Although there is compelling epidemiological and experimental evidence that being born with a low birth weight (even though well within the population's normal range) or premature increases the risk of both visceral obesity and associated diseases (*17*, *25*), it is now clear that these developmental processes operate to some degree in all pregnancies. Furthermore, developmental factors can influence the risk of developing obesity and its associated diseases independent of birth weight, and in individuals with birth weights well within the normal range (*17*). For example, a recent study showed that the

epigenetic state of the *retinoid X receptor-α* gene regulatory region (also called the promoter) measured at birth can explain more than 25% of the variance in fat mass at age 9 years in unselected normal UK children (*26*). The epigenetic state of the relevant gene was in turn strongly associated with the mother's carbohydrate intake during early pregnancy.

In the offspring of rats that are fed an unbalanced diet in pregnancy, epigenetic modifications have been demonstrated to be reversible (*19*, *27*), suggesting the exciting possibility that epigenetic measurements may be used to measure risk and to monitor the efficacy of interventions. This, in turn, focuses attention on the nutrition and health of mothers and young children as effective points of intervention. A robust illustration of the importance of considering subtle variations in otherwise normal development is demonstrated by studies of first-born children, who tend to be slightly lighter at birth than their younger siblings. This is probably a consequence of lesser dilation of the uterine vessels in first, relative to subsequent, pregnancies. In evolutionary terms, the first pregnancy was likely to have occurred before completed growth of the maternal pelvis, which does not reach maximal dimensions until four years after menarche. Thus, greater fetal size constraints in the first pregnancy would have led to a less risky delivery and would confer a fitness advantage (*28*). It was shown recently that first-born children have significantly greater truncal obesity as adults relative to second- or later-born siblings (*29*). Will the marked demographic changes in family size in the West, or in China, confer a greater risk of developing obesity now that their populations have a larger proportion of first-born children?

In many populations, the incidence of maternal obesity is rising (*30*), and this is a risk factor for the development of obesity in childhood (*31*). Again, epigenetic processes probably play a role. Experiments in rats show epigenetic changes in the livers of offspring of dams fed a high-fat diet (*32*). Children of mothers with gestational diabetes mellitus (GDM)—diabetes that appears during pregnancy and then resolves after pregnancy—have a greater propensity to develop type 2 diabetes as adults. In some populations, such as in Singapore, the incidence of GDM has climbed to more than 20% of pregnancies, presumably because of the rapid nutritional and economic transition and change in maternal diets. A recent analysis of Canadian indigenous people suggests that up to 30% of those affected by type 2 diabetes were children of GDM pregnancies (*33*). Rigorous treatment of GDM is thus an important priority for reducing the transmission of type 2 diabetes and related diseases to the next generation.

The early transition of infants from breast feeding to bottled formula increases the risk of developing childhood obesity by about 20% (*34*). However, it has not yet been determined whether this risk increase results from overnutrition, changes in learned feeding behavior, or alterations in the development of the gut microbiome, which may affect later metabolic control (*35*).

The longer-term effects of the infant environment merit much more investigation. For example, taste and food preference appear to be set early in life and can be influenced by maternal food intake in utero and during lactation (*36*, *37*). Executive functions, including self-control, are established in childhood and influence how eating and exercise behaviors are established (*38*)—a first-born child may be indulged in ways that subsequent siblings are not. Once again, it may be possible to reverse the adverse effects of the early environment; for example, nutritional education in preschool- and school-aged children (*39*, *40*) has long-term beneficial effects.

A PATH AHEAD

These recent scientific insights into the importance of human development in setting the predisposition to obesity and associated diseases later in life now necessitate translation into risk-reduction interventions. This is not to say that current initiatives should be reduced. Strategies to reduce tobacco use must be continued, along with those aimed at promoting health and exercise. Society must care for those adults who are already ill and assist those who are far along the pathway to disease. However, these activities are clearly insufficient to halt the rise in obesity and related diseases. Focusing on adults alone will have limited effects, especially in developing and recently developed societies, and a longer-term perspective is needed. The origins of both obesity and its associated diseases are multidimensional, but it is clear that one's sensitivity to the adverse effects of an obesogenic environment is dependent on both genetic factors and—of particular importance in terms of prevention—developmental exposures. Therefore, optimizing the nutritional environment of the embryo, fetus, and neonate may be an important component of a low-cost preventative intervention. Indeed, pregnancy, childhood, and parenthood are times in the life course when individuals are likely to be in contact with health care and welfare agencies and can be motivated to adopt healthy behaviors.

A broad range of technical expertise is needed if progress is to be made after the meeting of the UN General Assembly in September. A variety of agencies, such as the World Health Organization, UN Development Programme, UN Women's Programme, the UN Children's Fund (UNICEF), and the Food and Agriculture Organization of the UN, as well as multinational nongovernmental organizations and philanthropic organizations, will need to be fully involved in devising and promoting a plan to curb the obesity epidemic. We argue that a life-course approach is required, albeit one that is sensitive to the cultural, social, and developmental environments of different populations, in particular those at high risk for obesity and its associated diseases (*41*).

Locally appropriate strategies need to be developed and applied, some of which can be built on those being used to address women's and infants' health through the Millennium Development Goals; these include a focus on maternal health and nutrition before and during pregnancy, individualized health care during pregnancy, promotion of breast feeding, attention to the selection of appropriate weaning foods, and the promotion of exercise and healthy eating in preschool- and school-aged children (including the provision of nutritional education) (*41*, *42*). If the UN summit were to adopt such a translational agenda, we may see enhanced progress in efforts to reduce the burden of obesity-associated diseases, especially in countries that are undergoing socioeconomic transitions. However, if the outcome of the summit is merely to reiterate the catechism of weight loss, exercise, and smoking cessation in adults, we fear that an important opportunity will have been lost.

REFERENCES AND NOTES

1. M. M. Finucane, G. A. Stevens, M. J. Cowan, G. Danaei, J. K. Lin, C. J. Paciorek, G. M. Singh, H. R. Gutierrez, Y. Lu, A. N. Bahalim, F. Farzadfar, L. M. Riley, M. Ezzati, Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index), National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. *Lancet* **377**, 557–567 (2011).
2. R. Beaglehole, R. Bonita, R. Horton, C. Adams, G. Alleyne, P. Asaria, V. Baugh, H. Bekedam, N. Billo, S. Casswell, M. Cecchini, R. Colagiuri, S. Colagiuri, T. Collins, S.

Ebrahim, M. Engelgau, G. Galea, T. Gaziano, R. Geneau, A. Haines, J. Hospedales, P. Jha, A. Keeling, S. Leeder, P. Lincoln, M. McKee, J. Mackay, R. Magnusson, R. Moodie, M. Mwatsama, S. Nishtar, B. Norrving, D. Patterson, P. Piot, J. Ralston, M. Rani, K. S. Reddy, F. Sassi, N. Sheron, D. Stuckler, I. Suh, J. Torode, C. Varghese, J. Watt, Lancet NCD Action Group and the NCD Alliance, Priority actions for the non-communicable disease crisis. *Lancet* **377**, 1438–1447 (2011).

3. O. Hamdy, S. Porramatikul, E. Al-Ozairi, Metabolic obesity: The paradox between visceral and subcutaneous fat. *Curr. Diabetes Rev.* **2**, 367–373 (2006).
4. P. M. McKeigue, B. Shah, M. G. Marmot, Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* **337**, 382–386 (1991).
5. D. Nettle, Dying young and living fast: Variation in life history across English neighbourhoods. *Behav. Ecol.* **21**, 387–395 (2010).
6. A. M. Nevill, A. D. Stewart, T. Olds, R. Holder, Relationship between adiposity and body size reveals limitations of BMI. *Am. J. Phys. Anthropol.* **129**, 151–156 (2006).
7. E. Jéquier, L. Tappy, Regulation of body weight in humans. *Physiol. Rev.* **79**, 451–480 (1999).
8. P. Gluckman, M. Hanson, *Mismatch: Why Our World No Longer Fits Our Bodies* (Oxford Univ. Press, Oxford, 2006).
9. L. R. Dugas, R. Harders, S. Merrill, K. Ebersole, D. A. Shoham, E. C. Rush, F. K. Assah, T. Forrester, R. A. Durazo-Arvizu, A. Luke, Energy expenditure in adults living in developing compared with industrialized countries: A meta-analysis of doubly labeled water studies. *Am. J. Clin. Nutr.* **93**, 427–441 (2011).
10. K. E. Ebersole, L. R. Dugas, R. A. Durazo-Arvizut, A. A. Adeyemo, B. O. Tayo, O. O. Omotade, W. R. Brieger, D. A. Schoeller, R. S. Cooper, A. H. Luke, Energy expenditure and adiposity in Nigerian and African-American women. *Obesity (Silver Spring)* **16**, 2148–2154 (2008).
11. K. Jochelson, Nanny or steward? The role of government in public health. *Public Health* **120**, 1149–1155 (2006).
12. A. J. Stunkard, T. T. Foch, Z. Hrubec, A twin study of human obesity. *JAMA* **256**, 51–54 (1986).
13. C. Bouchard, Gene-environment interactions in the etiology of obesity: Defining the fundamentals. *Obesity (Silver Spring)* **16**, (Suppl 3), S5–S10 (2008).
14. T. Rankinen, A. Zuberi, Y. C. Chagnon, S. J. Weisnagel, G. Argyropoulos, B. Walts, L. Pérusse, C. Bouchard, The human obesity gene map: The 2005 update. *Obesity (Silver Spring)* **14**, 529–644 (2006).
15. T. A. Manolio, F. S. Collins, N. J. Cox, D. B. Goldstein, L. A. Hindorff, D. J. Hunter, M. I. McCarthy, E. M. Ramos, L. R. Cardon, A. Chakravarti, J. H. Cho, A. E. Guttmacher, A. Kong, L. Kruglyak, E. Mardis, C. N. Rotimi, M. Slatkin, D. Valle, A. S. Whittemore, M. Boehnke, A. G. Clark, E. E. Eichler, G. Gibson, J. L. Haines, T. F. C. Mackay, S. A. McCarroll, P. M. Visscher, Finding the missing heritability of complex diseases. *Nature* **461**, 747–753 (2009).
16. E. Ahlqvist, T. S. Ahluwalia, L. Groop, Genetics of type 2 diabetes. *Clin. Chem.* **57**, 241–254 (2011).
17. K. Godfrey, in *Developmental Origins of Health and Disease*, P. D. Gluckman and M. A. Hanson, Eds. (Cambridge Univ. Press, Cambridge, 2006), pp. 6–32.
18. P. D. Gluckman, M. A. Hanson, F. M. Low, The role of developmental plasticity and epigenetics in human health. *Birth Defects Res. C Embryo Today* **93**, 12–18 (2011).
19. P. D. Gluckman, K. A. Lillycrop, M. H. Vickers, A. B. Pleasants, E. S. Phillips, A. S. Beedle, G. C. Burdge, M. A. Hanson, Metabolic plasticity during mammalian development is directionally dependent on early nutritional status. *Proc. Natl. Acad. Sci. U.S.A.* **104**, 12796–12800 (2007).
20. R. S. Strakovsky, X. Zhang, D. Zhou, Y.-X. Pan, Gestational high fat diet programs hepatic phosphoenolpyruvate carboxykinase gene expression and histone modification in neonatal offspring rats. *J. Physiol.* **589**, 2707–2717 (2011).
21. A. Plagemann, T. Harder, M. Brunn, A. Harder, K. Roepke, M. Wittrock-Staar, T. Ziska, K. Schellong, E. Rodekamp, K. Melchior, J. W. Dudenhausen, Hypothalamic proopiomelanocortin promoter methylation becomes altered by early overfeeding: An epigenetic model of obesity and the metabolic syndrome. *J. Physiol.* **587**, 4963–4976 (2009).
22. T. F. Oberlander, J. Weinberg, M. Papsdorf, R. Grunau, S. Misri, A. M. Devlin, Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (*NR3C1*) and infant cortisol stress responses. *Epigenetics* **3**, 97–106 (2008).
23. M. K. Skinner, M. Manikkam, C. Guerrero-Bosagna, Epigenetic transgenerational actions of environmental factors in disease etiology. *Trends Endocrinol. Metab.* **21**, 214–222 (2010).
24. F. A. Champagne, Epigenetic mechanisms and the transgenerational effects of maternal care. *Front. Neuroendocrinol.* **29**, 386–397 (2008).
25. P. L. Hofman, F. Regan, M. Harris, E. Robinson, W. Jackson, W. S. Cutfield, The metabolic consequences of prematurity. *Growth Horm. IGF Res.* **14** (suppl. A), S136–S139 (2004).
26. K. M. Godfrey, A. Sheppard, P. D. Gluckman, K. A. Lillycrop, G. C. Burdge, C. McLean, J. Rodford, J. L. Slater-Jefferies, E. Garratt, S. R. Crozier, B. S. Emerald, C. R. Gale, H. M. Inskip, C. Cooper, M. A. Hanson, Epigenetic gene promoter methylation at birth is associated with child's later adiposity. *Diabetes* **60**, 1528–1534 (2011).
27. M. H. Vickers, P. D. Gluckman, A. H. Coveny, P. L. Hofman, W. S. Cutfield, A. Gertler, B. H. Breier, M. Harris, Neonatal leptin treatment reverses developmental programming. *Endocrinology* **146**, 4211–4216 (2005).
28. P. D. Gluckman, M. A. Hanson, Maternal constraint of fetal growth and its consequences. *Semin. Fetal Neonatal Med.* **9**, 419–425 (2004).
29. R. M. Reynolds, C. Osmond, D. I. W. Phillips, K. M. Godfrey, Maternal BMI, parity, and pregnancy weight gain: Influences on offspring adiposity in young adulthood. *J. Clin. Endocrinol. Metab.* **95**, 5365–5369 (2010).
30. Y. Yogev, P. M. Catalano, Pregnancy and obesity. *Obstet. Gynecol. Clin. North Am.* **36**, 285–300, viii (2009).
31. P. M. Catalano, K. Farrell, A. Thomas, L. Huston-Presley, P. Mencin, S. H. de Mouzon, S. B. Amini, Perinatal risk factors for childhood obesity and metabolic dysregulation. *Am. J. Clin. Nutr.* **90**, 1303–1313 (2009).
32. K. J. Dudley, D. M. Sloboda, K. L. Connor, J. Beltrand, M. H. Vickers, Offspring of mothers fed a high fat diet display hepatic cell cycle inhibition and associated changes in gene expression and DNA methylation. *PLoS ONE* **6**, e21662 (2011).
33. N. D. Osgood, R. F. Dyck, W. K. Grassmann, The inter- and intragenerational impact of gestational diabetes on the epidemic of type 2 diabetes. *Am. J. Public Health* **101**, 173–179 (2011).
34. S. Arenz, R. Rückerl, B. Koletzko, R. von Kries, Breast-feeding and childhood obesity—A systematic review. *Int. J. Obes. Relat. Metab. Disord.* **28**, 1247–1256 (2004).
35. P. J. Turnbaugh, M. Hamady, T. Yatsunenko, B. L. Cantarel, A. Duncan, R. E. Ley, M. L. Sogin, W. J. Jones, B. A. Roe, J. P. Affourtit, M. Egholm, B. Henrissat, A. C. Heath, R. Knight, J. I. Gordon, A core gut microbiome in obese and lean twins. *Nature* **457**, 480–484 (2009).
36. G. K. Beauchamp, J. A. Mennella, Early flavor learning and its impact on later feeding behavior. *J. Pediatr. Gastroenterol. Nutr.* **48**, (Suppl 1), S25–S30 (2009).
37. J. Todrank, G. Heth, D. Restrepo, Effects of in utero odorant exposure on neuroanatomical development of the olfactory bulb and odour preferences. *Proc. Biol. Sci.* **278**, 1949–1955 (2011).10.1098/rspb.2010.2314
38. T. A. Wills, C. R. Isasi, D. Mendoza, M. G. Ainette, Self-control constructs related to measures of dietary intake and physical activity in adolescents. *J. Adolesc. Health* **41**, 551–558 (2007).
39. J. C. Lumeng, N. Kaciroti, D. E. Frisvold, Changes in body mass index z score over the course of the academic year among children attending Head Start. *Acad. Pediatr* **10**, 179–186 (2010).
40. J. J. Heckman, S. H. Moon, R. Pinto, P. A. Savelyev, A. Yavitz, The rate of return to the High/Scope Perry Preschool Program. *J. Public Econ.* **94**, 114–128 (2010).
41. P. D. Gluckman, M. A. Hanson, P. Bateson, A. S. Beedle, C. M. Law, Z. A. Bhutta, K. V. Anokhin, P. Bougnères, G. R. Chandak, P. Dasgupta, G. D. Smith, P. T. Ellison, T. E. Forrester, S. F. Gilbert, E. Jablonka, H. Kaplan, A. M. Prentice, S. J. Simpson, R. Uauy, M. J. West-Eberhard, Towards a new developmental synthesis: Adaptive developmental plasticity and human disease. *Lancet* **373**, 1654–1657 (2009).
42. *Promoting Optimal Fetal Development: Report of a Technical Consultation* (World Health Organization, Geneva, Switzerland, 2006).
43. **Disclaimer:** P.D.G. is also Chief Science Advisor to the Prime Minister of New Zealand. This paper is written in his academic role, and the opinions expressed in this paper are personal and do not reflect those of the New Zealand Government. **Funding:** P.D.G. is funded by the National Research Centre for Growth and Development; M.H. is funded by the British Heart Foundation. **Competing interests:** The authors have spoken at academic meetings supported by nutrition companies and received travel expenses and honoraria to attend those meetings.

10.1126/scitranslmed.3002554

Citation: P. D. Gluckman, M. Hanson, P. Zimmet, T. Forrester, Losing the war against obesity: The need for a developmental perspective. *Sci. Transl. Med.* **3**, 93cm19 (2011).

Science Translational Medicine

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Sci Transl Med **3**, 93cm1993cm19.
DOI: 10.1126/scitranslmed.3002554