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Population Health and the Influence of Medical and Scientific Advances

*J. Michael McGinnis**

Ours is an extraordinary time in the evolution of human health, with unprecedented insights on the nature of the determinants of health, how important they are, how they work, how they interact, and how they might be influenced. It is important therefore to place consideration of the role of genetics into the broader context, to assess how the tools emerging from the genomics revolution may shape the dynamics within and among the various domains of influence on the health of populations.

Some of that context is provided by data about various aspects of the health care delivery system. In 2005, approximately two trillion dollars will be spent for health care in the United States.¹ That amounts to about \$7,000 for each of the nation's inhabitants, and represents sixteen percent of the Gross Domestic Product.² Although this level of investment puts us far ahead of other nations, our returns on investment, in health terms, are limited. In 2004, we ranked twenty-third among nations in life expectancy, far behind countries like Japan, Sweden, and Iceland.³

There are some explanations for this discrepancy. Our technologic superiority in medicine has its downsides in higher rates of medical errors, accounting for as many as 98,000 deaths a year.⁴ But more importantly, we are a nation of great social heterogeneity, different cultures, various ethnicities, and geographically dispersed. We have some groups with chronically

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1. *National Health Expenditures and Selected Economic Indicators, Levels and Average Annual Percent Change: Selected Calendar Years 1990–2013*, Centers for Medicare & Medicaid Services, Office of Actuary, (2003), available at <http://www.cms.hhs.gov/statistics/nhe/projections-2003/t1.asp> (last visited Sept. 14, 2004).

2. *Id.*

3. *Health, United States, 2004 With Chartbook on Trends in the Health of Americans*, Nat'l Center for Health Stat. (2004), available at <http://www.cdc.gov/nchs/data/hus/hus04.pdf> (last visited June 30, 2005).

4. Lucian L. Leape & Donald M. Berwick, *Five Years After To Err Is Human: What Have We Learned?*, 293 *J. Am. Med. Ass'n* 2384 (2005).

lower income streams, newly arrived groups with more acute needs, and a recently widening gap among the various income tiers. Except for our older people, our social support system is a patchwork of policies at the local, state, and federal levels. We have wide discrepancies in access to care and substantial instabilities in the continuity of care. People receive care, but it is expensive, and it is a scramble. Moreover, we are in the midst of a full-blown obesity epidemic in this country. Two-thirds of the population is overweight; the number of overweight adults and children has doubled in the last twenty years.⁵ Finally, we have high rates of low birth weight—which are in part derivative of higher rates of prenatal substance abuse.⁶ And nothing shortens the horizon of life expectancy like an infant death.

How then, in the midst of the challenges, do we identify our primary opportunities for improving the health of Americans? A reasonable starting point is to look at those factors that determine the health of populations, about which we now have a clearer understanding. It was not very long ago that we had a rather fatalistic approach to life—acceptance of accidents, chronic diseases, and other challenges as merely the inevitable consequences of life and the aging process.

We now know that the health of populations is determined by the dynamics in five domains of influence: our genetic predispositions, our social circumstances, our environmental exposures, our behavior patterns, and the medical care we receive.⁷ The topic of genetic predispositions is well covered elsewhere in this volume. Suffice it to say that the human genome numbers three billion base pairs, with around 20,000 to 25,000 genes under current estimates.⁸ These genes exert their influence on health in

5. Allison A. Hedley et al., *Prevalence of Overweight and Obesity Among US children, Adolescents, and Adults, 1999–2002*, 291 J. Am. Med. Ass'n 2847 (2004).

6. *Healthy People 2000 Final Review*, Nat'l Center for Health Stat. (2000), available at <http://www.cdc.gov/nchs/data/hp2000/hp2k01-acc.pdf> (last visited June 30, 2005).

7. J. Michael McGinnis et al., *The Case for More Active Policy Attention to Health Promotion*, 21 Health Affairs 78, 83 (2002).

8. *International Human Genome Sequencing Consortium Describes Finished Human Genome Sequence Researchers Trim Count of Human Genes to 20,000–25,000*, Human Genome Project Information (2004), available at

various fundamental ways. Each of us has embedded in our genetic platform the assembly line blueprint for construction of the proteins which give form to our sizes, our shapes, our personalities, even to the biologic limit of our life expectancies—somewhere between eighty-five and 110 years, if fibroblast tissue cultures are to be believed.⁹ Eons of adaptation has given an approximate form to these instructions, which are essentially similar across individuals, and sets us on a course that we call normal—that is, one which is not markedly disadvantaged from the environments in which we find ourselves.

Under certain circumstances, inborn variance of the code confers some discernable measure of disadvantage. This can be the result of even a single abnormal gene inherited from a parent, as with recessive conditions like cystic fibrosis or dominant conditions like Huntington's disease, or it can be the result of an entire chromosomal region being affected, as in Down's syndrome.

Changes also can occur in the codes of certain cells as a result of epigenetic influences, including interactions with other genes and gene products or various exposures throughout the life cycle. In some carcinogenesis or neural tube defects, for example, environmental triggers can alter the genetic coding signals, resulting in abnormal growth by certain cells or tissues. Knowledge in each of these areas is still primitive, despite the explosion of activity at centers such as the Pennington Biomedical Research Center, but that knowledge is growing rapidly with the completion of the sequencing of the human genome far ahead of schedule. Progress on identifying the locations of disease-linked genes is accelerating, and the number in 2004 had already reached some 1,400.

Still, sequencing the genome leaves open the question of the nature of its influence, which is, in part, our charge here: to understand how the genome plays in complex interaction with these other domains of influence. Although only about two percent of mortality in the U.S. can be attributed to purely genetic

http://www.ornl.gov/sci/techresources/Human_Genome/project/20to25K.shtml
(last visited Oct. 27, 2004).

9. L. Hayflick, P.S. Moorehead, *The Serial Cultivation of Human Diploid Cell Strains*, 25 *Experimental Cell Research* 585 (1961).

diseases,¹⁰ a sizeable proportion of disorders of late onset—like diabetes, cardiovascular disease, and cancer—have an important genetic component. The significance of that component is still uncertain for most conditions. The BRCA1 gene accounts for only about five to ten percent of breast cancers in the United States.¹¹ Only about ten percent of colon cancers may be explained by these yet unidentified genes,¹² and only about one case in twenty of those with elevated serum cholesterol levels may be explained by familial hyperlipidemia.¹³ Studies of monozygotic twins focusing on the occurrence of schizophrenia, and other similar twin studies looking at mental alertness in older people, have found that about half of each could be explained by genetic factors.¹⁴ Some say two-thirds of the risk of obesity may be genetic but, like most predispositions, that risk is expressed only with exposure to lifestyle factors which are controllable. At this point, the best we can say is that the burden of purely genetic diseases is limited, and the vast majority of the genetic contribution is played out in those complex interactions with the other domains of influence.

At birth, our first encounter is with the domain of our social circumstances, about which a great deal more has been learned in recent years. From cradle to grave, our interpersonal linkages matter. Studies consistently have shown that infant nurturing enhances socialization and survival.¹⁵ Adults, including older people, who are socially isolated, have a two to fourfold higher death rate than others.¹⁶ We have learned that prenatal home visits

10. Richard C. Strohman, *Ancient Genomes, Wise Bodies, Unhealthy People: Limits of a Genetic Paradigm in Biology and Medicine*, Wellness: Lecture Series (University of California, Berkeley 1992); P.A. Baird, *The Role of Genetics in Population Health*, in *Why Are Some People Healthy and Others Not?* 133–59 (R.G. Evans et al. eds., Aldine de Gruyter 1994).

11. Betty A. Mincey, *Genetics and the Management of Women at High Risk for Breast Cancer*, 8 *The Oncologist* 466 (2003).

12. Hansjakob Muller, *Hereditary Colorectal Cancer: From Bedside to Bench and Back*, 11 *Annals of Oncology* 7 (Supp. 4) (2000).

13. P. Pajukanta et al., *Linkage of Familial Combined Hyperlipidaemia to Chromosome 1q21-q23*, 18 *Nature Genetics* 369 (1998).

14. K.S. Kendler, *Overview: A Current Perspective on Twin Studies of Schizophrenia*, 140 *Am. J. of Psychiatry* 1413 (1983); J.W. Rowe & R.L. Kahn, *Successful Aging* (Pantheon Books 1st ed. 1998).

15. McGinnis, *supra* note 7, at 81.

16. L.F. Berkman & T. Glass, *Social Integration, Social Networks, Social Support, and Health*, in *Social Epidemiology* 137–73 (L.F. Berkman & I. Kawachi eds., Oxford University Press 2000).

to at-risk mothers can reduce the likelihood of both risky health behaviors and criminal activities some fifteen years hence.¹⁷ For the population as a whole, the most consistent predictor of the likelihood of death in any given year is level of education, with those ages forty-five to sixty-four in the highest levels of education having death rates that are two to five times lower than those in the lowest level.¹⁸ Poverty has been said to account for six percent of U.S. mortality.¹⁹

The observation also has been made that each one percent rise in income inequality, that is, the differential between rich and poor, is associated with approximately a four percent increase in deaths among those on the low end.²⁰ It is difficult to sort out the pecuniary elements of deprivation from the biological, behavioral, and psychological consequences of place. For example, a study of British government workers, virtually none of whom were in poverty, found a threefold difference in death rates between the highest and the lowest positions.²¹ Interesting work on the physiologic mediators of the stress reaction suggests that there may be commonalities in the pathways involved in the way stress gets under the skin, affecting immune competence and metabolic function, to increase the susceptibilities of some of us to various acute and chronic illnesses. A term, allostatic load, has been coined to represent the aggregate impact of various stressors on the body over time. This raises some very interesting possibilities. If we can't eliminate poverty or income disparities, can we identify those who are inherently more susceptible to the adverse health consequences of their conditions and tailor our support interventions accordingly?

17. David Olds, et al., *Long Term Effects of Nurse Home Visitation on Children's Criminal and Antisocial Behavior: 15-Year Follow-up of a Randomized Controlled Trial*, 280 J. Am. Med. Ass'n 1238 (1998).

18. *Health, United States, 1998 with Socioeconomic Status and Health Chartbook*, Nat'l Center for Health Stat. (1998), available at <http://www.cdc.gov/nchs/data/hus/hus98.pdf> (last visited Sept. 6, 2005).

19. Gregory Pappas et al., *The Increasing Disparity in Mortality Between Socioeconomic Groups in the United States, 1960 and 1986*, 329 New Eng. J. of Med. 103 (1993).

20. Michael Wolfson et al., *Relation Between Income Inequality and Mortality: Empirical Demonstration*, 319 Brit. Med. J. 953 (1999).

21. M.G. Marmot et al., *Health Inequalities Among British Civil Servants: The Whitehall II Study*, 337 Lancet 1387 (1991).

To some extent, as part of our social circumstances, we find our conditions also affected in important ways by our physical environments. The places we seek to shape as nurturing and sheltering—home, work, and community environments—sometimes present us with hazards in the form of toxic agents, microbial agents, and structural hazards. Toxic agents from occupational hazards and environmental pollutants—chemical contaminants of food and water supplies, components of commercial products—have been associated in particular with cancers and other diseases of various organ systems. Pollutants that impact respiration such as particulates, sulfur dioxide, and carbon monoxide have been associated with transient increases in daily mortality rates. Occupational exposures alone account for an estimated one to three percent of cardiovascular, chronic respiratory, renal, and neurologic disease deaths, including all of the pneumoconioses.²² Radon and asbestos have each been estimated to contribute in the range of 10,000 cancer deaths per year.²³ The sum of the lower boundaries of various estimates of the mortality burden of toxic agent exposures places their contributions in the range of 60,000 per year.²⁴

Infectious disease threats can also be related to our environmental conditions. Apart from behavior associated with diseases such as HIV and hepatitis B, significant contributions to death in the United States are made by infectious agents in part sheltered and cultured by environmental conditions. More commonly than we see in the news reports, there are incidents of Legionnaires disease, E. coli, and cryptosporidiosis in spite of the fact that immunizations and infection control measures may already prevent as much as 135 million infections and more than 60,000 deaths annually in the United States.²⁵ In all, an estimated 90,000 infectious disease deaths occur in this country each year,

22. P.J. Landrigan & S. Markowitz, *Current Magnitude of Occupational Disease in the United States: Estimates from New York State*, 572 *Annals of the New York Acad. of Sci.* 27 (1989).

23. L.S. Farer & C.W. Schieffelbein, *Respiratory Diseases*, 3 *Am. J. Prev. Med.* 115 (Supp. 1987).

24. J.M. McGinnis & W.H. Foege, *Actual Causes of Death in the United States*, 270 *J. Am. Med. Ass'n* 2207 (1993).

25. J.V. Bennet et al., *Infectious and Parasitic Diseases*, 55 *Am. J. Prev. Med.* 102 (3rd Supp. 1987).

beyond those attributable to sexual behavior or the use of tobacco, alcohol, or illicit drugs.²⁶ And, again, susceptibilities to toxic and infectious agents in our environments vary in theoretically discoverable ways.

The daily choices that we make with respect not only to safety but to diet, physical activity and sex, the substance abuse and addictions to which we fall prey, and our coping strategies in confronting stress, are all important determinants of health. What we choose to eat and how we structure activity into, or out of, our lives has a great bearing on our health prospects. Dietary factors have been associated with coronary heart disease, stroke, diabetes, and cancers of the colon, breast, and prostate. Physical inactivity has been associated with the increased risk for heart disease, colon cancer, diabetes, and osteoporosis. In the face of imprecise information on individual dietary habits and physical activity patterns and, given the basic laws of thermodynamics, obesity is a common intermediary for each. It is difficult, if not impossible, to parse out the share specific to diet or physical activity but, combined, the range of the estimates for their contribution spans from 300,000 to more than 500,000 deaths in America.²⁷

Unprotected sexual intercourse is accountable each year not only for two and one-half million unintended pregnancies and fifteen million new cases of sexually transmitted diseases, but also for deaths from HIV, hepatitis B, cervical cancer, and excess infant mortality.²⁸ Together, about 40,000 deaths in 1995 were related to sexual behavior.²⁹

Substance abuse and addiction inflict a tremendous toll on the health of Americans, although these factors are possibly losing top ranking to the rapid rise in obesity. At more than 400,000 deaths, tobacco has, for a generation, been the leading single

26. McGinnis & Foege, *supra* note 24.

27. *The Surgeon General's Report on Nutrition and Health*, U.S. Dep't. of Health and Hum. Services, Pub. no. 88-50210 (1988).

28. *Health, US, 1992*, Nat'l Center for Health Stat. (1993), available at <http://www.cdc.gov/nchs/data/hus/hus92acc.pdf> (last visited Sept. 6, 2005); *Sexually Transmitted Diseases in America: How Many Cases and at What Cost?*, Prepared for the Kaiser Family Foundation by: Am. Social Health Ass'n. (1998), available at http://www.kff.org/womenshealth/1447-std_rep.cfm#executive (last visited June 30, 2005).

29. *Sexually Transmitted Disease Surveillance, 1990*, Division of STD/HIV Prevention, U.S. Dep't of Health and Hum. Services (1991).

contributor to deaths of Americans.³⁰ Substance abuse as a whole represents the most prominent contributor to the constellation of preventable illness, health costs, and related social problems facing families and communities in the country today. Substance abuse accounted, in 1995, for some 43 million illnesses or injuries and more than half a million deaths.³¹

Another element which might be grouped for the purposes of today's discussion into the arena of behavior is that of our coping strategies—certainly a relevant factor when we have reported in the country approximately 17,000 homicides, 31,000 suicides, three million episodes of child abuse, and a developing and dangerous pattern of what is called "road rage."³² The matter and ways in which we select to cope, or not to cope, registers in a compelling fashion on the health ledgers.

In all, various behavioral choices that we make account for about a million deaths among Americans, all of them, by definition, early deaths, along with the compelling burden of associated illness. Together, behavioral issues represent the greatest domain of influence on the health of the population.³³

Finally, with the myriad of influences on the health of populations, what has medical care got to do with it all? If we consider the question in purely historical terms, the answer would be "not much." John Bunker points out that, over the course of the twentieth century, only about five of the thirty years of increased life expectancy could be attributable to better medical care.³⁴ So, when considering the notion of whether, given past contributions and available technology, much can be expected from better access to higher quality care, we might come down to a discouraging

30. *Annual Smoking-Attributable Mortality, Years of Potential Life Lost, and Economic Costs—United States, 1995–1999*, 51 *Morbidity and Mortality Wkly. Rep.* 300 (2002).

31. J.M. McGinnis & W.H. Foege, *Mortality and Morbidity Attributable to Use of Addictive Substances in the United States, Health and Economic Burdens*, 3 *Proc. of the Ass'n of Am. Physicians* 109 (1999).

32. *Deaths: Preliminary Data for 2003*, *Nat'l Vital Stat. Rep.* vol. 53 no. 15 (2005), available at http://www.cdc.gov/nchs/data/nvst/nvsr53/nvsr53_15.pdf; R.C. Alexander, *Current and Emerging Concepts in Child Abuse*, 21 *Comprehensive Therapy* 726 (1995).

33. McGinnis, *supra* note 7, at 82.

34. J.P. Bunker et al., *The Role of Medical Care in Determining Health: Creating an Inventory of Benefits*, in B.C. Amick III, et al., *Society and Health* 305–341 (Oxford University Press 1995).

conclusion. In fact, in terms of the practical possibilities of the moment, the potential of medical care is most poignantly revealed where it misses the mark, where problems of access or poor quality of care have done harm. The Institute of Medicine, for example, suggests that medical errors alone may account for 44,000 to 98,000 deaths annually.³⁵ On the other hand, the relative contribution of medical care to life expectancy rose during the latter part of the century, and will likely continue to pick up the pace as technology is better able to address the health care needs of an aging population. Bunker estimates that, since 1950, medicine has accounted for half of the seven-year increase in life expectancy.³⁶ And with the potential contributions to enhance quality of life for an aging population, the advent of interventions such as joint replacements, coronary by-pass procedures, and better pharmaceuticals, not to mention the more fundamental advances that we might expect from gene therapy or other products of the genome work, the prospects are strong for solid contributions from medicine in the future.

So, what do the numbers tell us? Some interesting things. If we are doing an inventory of how various factors are currently playing out to shape our health profiles, or at least our vital statistics, we find that the actual causes of death among Americans are not deaths that the coroner tells us are the result of pathophysiologic diagnoses such as heart disease, cancer, and stroke. Rather they are led by tobacco, inactivity and dietary patterns, and alcohol, as noted in Figure 1. These ten items represent a sizeable portion of the deaths that occurred in the year 2000, with behavioral facts accounting for about forty percent of all deaths.

35. Institute of Medicine, *To Err is Human: Building a Safer Health System* (Linda T. Kohn et al. eds., National Academies Press 2000).

36. Bunker, *supra* note 34.

Adjusted Extrapolation

Cause	1990 No.* (est.)	2000 No.* (est.)
Tobacco	375,000	375,000
Diet/activity patterns	300,000	350,000
Alcohol	90,000	80,000
Microbial agents	90,000	80,000
Medical errors	N/A	70,000
Toxic agents	60,000	60,000
Firearms	35,000	30,000
Motor vehicles	25,000	25,000
Sexual behavior	30,000	20,000
Illicit use of drugs	20,000	15,000
Total	1,175,000	1,290,000
All Causes	2,150,000	2,400,000

So what can we conclude if we step up one level above these individual causes and look at how this translates across the domains of influence of health determinants? If we take a snapshot of this point in time and add up the best available estimates to characterize the share of premature deaths caused by problems in each of the domains of influence, here is how it looks: Poor behavioral choices account for about forty percent of early deaths; medical errors and inadequate access to care, about ten percent; environmental factors, such as avoidable toxic and infectious agents in water, air, or food, about five percent; social circumstances, those largely related to disparities, about fifteen percent.³⁷ The balance, the unexplained contribution, presumably comes from inborn predisposition or susceptibility, as we are talking here about early deaths. Of course, no question, this is a rather crude characterization. One such purpose of making this characterization is to give us some perspective on how our current investments stack up against our current opportunities. We spend ninety-five percent of our health dollar to correct ten percent of the deficiencies, leaving only about five percent to address the issues

37. McGinnis & Foege, *supra* note 24.

such as behavior and other influences that have a much larger influence on the health of a population.³⁸

More important is the nature of the influences in play where the domains intersect. Ultimately, the health fate of each of us and the collective fate of our population are determined by the factors acting not mostly in isolation within each of the domains of influence, but where those domains interconnect. Whether a gene is expressed can be determined by environmental exposures or behavioral patterns. The nature and consequences of behavioral choices are affected by our social circumstances. Our genetic predispositions affect the health care we need. Our social circumstances affect the health care we receive. The growing knowledge and evidence based in these areas provide important opportunities for targeted action and analysis that will develop tools to prompt and facilitate change, build the capacities of networks and organizations best positioned to use those tools, and strengthen the levers of policy that directly affect the dynamics shaping these influences.

What are the implications for medical care and population health in the genomic revolution that we are seeing? Well, clearly, the implications for both the effectiveness and the costs of medical care are substantial. On the effectiveness side, we can anticipate that the population-wide impact of therapeutic advances we have seen in the last half century will be accelerated as more fundamental interventions—what Lewis Thomas would term “high technologies,” encompassing those represented by genomics—come into play. And this does not necessarily mean expensive. It is our current dependence on halfway technologies that drives costs—those technologies that we apply to keep diabetes at bay, to treat certain types of cancer, to treat strokes that require extensive rehabilitation, and so forth. It is only when we get to the application of technologies that essentially eliminate the problem that we see our costs begin to drop again. In this sense, the

38. *National Health Expenditure Amounts and Average Annual Percent Change by Type of Expenditure: Selected Calendar Years 1990–2013*, Centers for Medicare and Medicaid Services (2003), available at <http://www.cms.hhs.gov/statistics/nhe/projections-2003/t2.asp> (last visited June 30, 2005); *Effectiveness in Disease and Injury Prevention: Estimated National Spending on Prevention—United States, 1988*, 41 *Morbidity and Mortality Wkly Rep.* 529 (1992).

application of genomic technologies to medical care has the potential not only to make a great deal of difference in our lives, but to begin to reduce the costs of medical care.

It is clear, then, that we ought to expect contributions from genomics that are very important to each of the domains of influence on population health. We can anticipate enhanced capacity to identify and correct our genetic predispositions that place some of us at greater risk for certain leading killers. We can use these tools to identify the most vulnerable population groups among us and, perhaps, even the most vulnerable individuals in certain social circumstances. We will be better able to understand the ways in which environmental threats work and how they interact with other influences. We can use our knowledge of how individuals vary, the impact of their behavioral choices, and how that variation affects their health profiles to target interventions more effectively. And we should be able, ultimately, to use genomic interventions to reverse some of the disease processes. These all bode well for the impact of genomics on population health.