Effectiveness of Health Care Services for Pregnant Women and Infants

Andrew D. Racine
Theodore J. Joyce
Michael Grossman

Andrew D. Racine, M.D., Ph.D., is assistant professor of pediatrics at Columbia University College of Physicians and Surgeons and a faculty research fellow at the National Bureau of Economic Research.

Theodore J. Joyce, Ph.D., is associate professor of economics and of finance at City University of New York, Baruch College, and a research associate at the National Bureau of Economic Research.

Michael Grossman, Ph.D., is distinguished professor of economics at the City University of New York Graduate School and a research associate at the National Bureau of Economic Research.

Abstract

The authors of this paper focus on the health care services received by pregnant women and infants, and consider the ways in which these services affect child health outcomes. They examine the impact of prenatal, obstetrical, and neonatal care on two measures of infant health: the rate of low birth weight births and the rate of infant mortality. There is strong evidence that these two outcomes respond favorably to the application of appropriate health services, particularly prenatal care and neonatal intensive care. The delivery of prenatal care in the United States needs improvement: slightly more than 76% of women received early care in 1989, and discrepancies in prompt receipt of care among different ethnic and economic groups are large and persistent. Improved distribution of prenatal care services could have a significant impact on the rate of low birth weight births and infant deaths. In addition, expanded regionalization of prenatal, obstetric, and neonatal care in a coordinated approach to the entire continuum of gestation, labor, delivery, and early development holds out the promise of continued improvement in infant health. Health care initiatives need to focus more on the needs of poor families and of mothers and infants with special problems, especially high-risk pregnancies resulting from maternal substance abuse and pregnancies complicated by HIV infection. The authors describe advances in obstetrical technology and neonatology, and conclude that efforts to identify programs and activities which offer the greatest potential for improving newborn survival with the least investment should have high priority.

Children are developing organisms. They continually grow and differentiate from one physical and psychological state to the next. An understanding of childhood health status, therefore, begins with an understanding of the conditions out of which children emerge. Intrauterine and neonatal environments are crucial determinants of a child's well-being. A mother's health throughout pregnancy, the process of labor and delivery, and a child's experiences during the first critical hours and days of life will influence health status for months and years

afterward. Moreover, poor birth outcomes have been associated with impeded cognitive development, reductions in years of formal schooling completed, and lower levels of lifetime earnings and other measures of economic well-being.[1]

Recognition of these principles has led policy analysts to give increasing attention to prenatal and neonatal health care services. In this paper we focus on health care services received by pregnant women and infants, and consider the ways in which these services affect child health outcomes. For our purposes, these services include prenatal medical care received by women during the course of their pregnancies, obstetrical care received at the time of delivery, and medical care received by newborn infants during the first 28 days of life (the neonatal period). We consider trends in these services over time, differentials in the receipt of these services among various groups in the population, and the impact utilization of these services has on child health outcomes.

Two population outcome measures to which we devote particular attention are rates of low birth weight (LBW) and infant mortality. A low birth weight baby is one born weighing less than 2,500 grams (about 5½ pounds). The LBW rate is the number of such births per 1,000 live births in the population in a given year. The infant mortality rate is measured by the annual number of deaths among children in the first year of life per 1,000 live births. Because LBW babies have a higher risk of death than normal weight babies, these two rates are closely related. Though birth weight and infant mortality each have a genetic component, birth weight depends very much upon the length and quality of the fetal experience during pregnancy while infant mortality depends also upon the type of care, medical and otherwise, that a child receives after birth. Therefore, these two measures may tell us much about the effectiveness of prenatal and neonatal care.

We begin with a discussion of prenatal care and its relationship to low birth weight and then proceed to a consideration of obstetrical and neonatal care and how they affect infant mortality. We shall also mention some promising new technologies being applied in the field of neonatology.

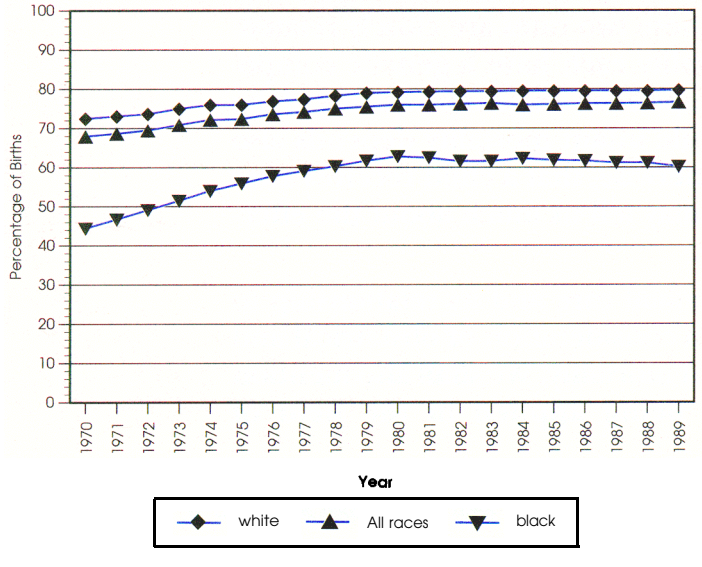
Prenatal Care

Much of what influences the health of a newborn baby is beyond the control of policymakers. Factors such as maternal weight and height at the beginning of pregnancy, heritable genetic conditions, a mother's previous obstetric history, ethnicity, and marital status are conditions that are, to a large extent, fixed with

respect to most policy options. Other factors, however, are amenable to change. A woman's nutritional condition during pregnancy, and her exposure to substances known to be harmful to developing fetuses, her blood pressure, blood sugar levels, and her exposure to sexually transmitted diseases are some of the environmental factors that can influence the health of her newborn baby. These and other conditions, especially if identified early in pregnancy, can be treated so as to improve neonatal outcome. In general, the earlier in the course of fetal development that interventions are initiated, the more favorable the result. For this reason attention to maternal health during the course of pregnancy is central to improving newborn health.

Prenatal care has been shown to be a crucial avenue by which interventions in maternal and thus newborn health status can be delivered. What services are included under this rubric, how receipt of these services has changed over time, and what the evidence is for their effectiveness are considered below.

Figure 1. Percentage of Births with Early* Prenatal Care, 1970 – 1989



*First prenatal care visit within 3 months of conception (first trimester).

Source; National Center for Health Statistics, U.S. Department of Health and Human Services. Advance Report of Final Natality Statistics, 1989. Monthly Vital Statistics Report, vol. 40, no. 8, supplement, Hyattsville, MD: Public Health Service, 1991.

The Content of Prenatal Care

Access, utilization, and the efficacy of prenatal care have dominated the infant health policy and research agenda for the past 20 years. Until recently, the actual content of prenatal care received relatively little attention. One reason for this omission may have been the repeatedly observed association between the initiation of early prenatal care and healthy infant outcomes. Whatever the content of prenatal care, it seemed to work. The policy implications appeared straightforward: expand prenatal care utilization, and infant health will improve.

Unfortunately, though increasing utilization seems to be a necessary condition for improvements in infant health, it may not be sufficient. As we shall see, for example, when we consider low birth weight rates in more detail, white/black differences in rates of low birth weight and infant mortality have persisted over time despite significant relative gains in the percentage of black women receiving early prenatal care (see figure 1). And although researchers and policymakers can cite a wealth of studies that appear to demonstrate the effectiveness of prenatal care, specific explanations of how the intervention operates remain conspicuously absent from most discussions.

The standard guidelines for prenatal care as recommended by the American College of Obstetricians and Gynecologists (ACOG) call for care to begin as early as possible in the first trimester of pregnancy.[2] Additional visits are recommended every 4 weeks until the 28th week, followed by visits every 2 to 3 weeks until the 36th week. Beyond the 36th week, visits should occur weekly until delivery for a total of 13 to 15 visits over the course of a normal pregnancy. By contrast, the Public Health Service Expert Panel on the Content of Prenatal Care recommends only 7 visits for healthy women who have had previous, uncomplicated deliveries and 9 visits for first-time mothers.[3]

Both the ACOG and the Panel emphasize that prenatal care should have three basic components: early and continuous risk assessment, health promotion, and when necessary, medical and/or psychological intervention. Although the Panel recommends fewer visits for a healthy woman than does the ACOG, the Panel's most novel contribution is its emphasis on enriching the content of care and on ex-

panding the time frame for prenatal care.[3] Panel members urge, for example, that a preconception visit occur as one of the 7 or 9 recommended visits. Such a consultation permits the identification of medical or behavioral problems before conception and offers the mother and clinician the greatest range of options, from delaying the pregnancy to providing immunizations that would be contraindicated once the woman becomes pregnant. Prenatal care, according to Panel members, should also be viewed as a means of promoting the health and well-being of the entire family. Thus, they highlight attention to parenting skills and family counseling as ways to enhance the care and nurturing of the fetus beyond delivery.

The Panel's report focuses on the identification and management of high-risk pregnancies. This includes the possible use of specialized tests such as amniocentesis and ultrasound imaging to screen the genetic and structural development of the fetus; the use of routine blood pressure and blood sugar monitoring, and other blood tests to detect exposure to certain viruses and to verify the mother's blood type; and the occasional use of more specialized tests to evaluate fetal well-being.

Yet the advantages of the more highly specialized of these strategies may be limited. As an example, consider amniocentesis, a procedure in which fluid is removed from the sac containing the fetus to detect the presence of genetic abnormalities. Because congenital abnormalities are a leading cause of neonatal mortality and about 25% of birth defects are primarily of gene tic origin,[4] early recognition of these conditions in time to permit termination of unwanted pregnancies could have a considerable impact on neonatal mortality.

But who should be screened using this procedure? At one time it was thought that amniocentesis should target women over 35 years of age who are at increased risk for having babies with Down's syndrome, one of the more common identifiable chromosomal disorders, which affect about 5,000 newborns a year. Yet, the majority of Down's syndrome births are to younger women,[5] so a policy of targeting women over 35 years of age for testing cannot by itself substantially reduce the incidence of the syndrome. Furthermore, it is now appreciated that approximately 5% of chromosomal defects which result in Down's syndrome originate with the father,[6] making identification of appropriate candidates for screening even more difficult. Therefore, without knowing whom to target, even effective screening procedures such as amniocentesis may have limited impact on overall outcomes.

The recent expansion of Medicaid eligibility for pregnant women may improve the utilization of prenatal care, but that may not be sufficient to improve birth outcomes substantially.

The content of prenatal care recommended by the Panel, including home visits, case management, substance abuse treatment programs, and three categories of psychological risk assessment, is comprehensive and ambitious. Despite the lack of cost-effectiveness evaluations of many of its recommendations, the Panel has outlined a broad agenda that focuses much more sharply on the policy-relevant questions that need to be addressed. The recent expansion of Medicaid eligibility for pregnant women may improve the utilization of prenatal care, but that may not be sufficient to improve birth outcomes substantially.[7] (See also the Hill article in this journal issue.) By focusing on the content of prenatal care, the Panel has developed a more general framework for understanding why nonspecific interventions may yield disappointing results.

Trends and Differentials in Prenatal Care

As we have seen, standard medical protocol calls for the initiation of prenatal care within the first 3 months of pregnancy. For a time the United States appeared to be making significant progress in the numbers of women receiving early care. Trends in the percentage of live births for which care began in the first trimester by race for the years 1970 through 1989 are shown in figure 1. For white women, the percent receiving early care rose by 9.7% between 1970 and 1980 and then remained the same. For black women, it increased dramatically by 40.5% in the decade of the 1970s and then declined by 2.1% in the decade of the 1980s. The percentage of live births in which there was either no prenatal care or in which prenatal care began in the third trimester conversely

decreased in the 1970s and then either leveled off or increased (not shown).

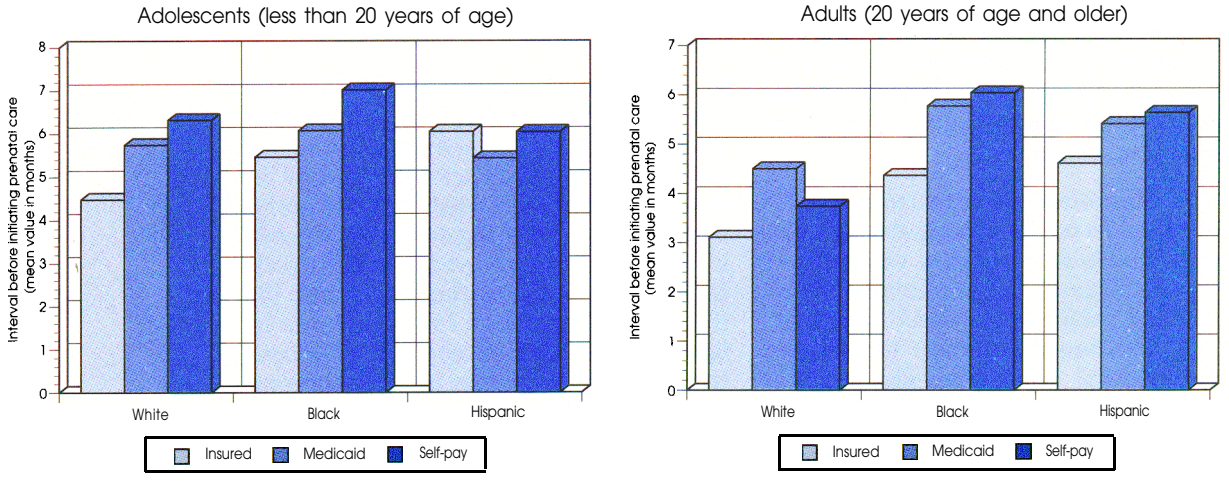
Figure 1 documents the discrepancy in the prompt initiation of prenatal care between blacks and whites. The rapid increase in the number of black women who received early care in the 1970s reduced but did not eliminate this discrepancy. In 1988, 79.4% of white women and 61.1% of black women began care in the first trimester.[8] In the same year, the percentage of black women who received third trimester or no care was more than double the percentage of white women who received third trimester or no care (10.9% versus 5.0%).[8] Teenagers and unmarried women are also at substantially increased risk of obtaining late or no prenatal care.[9] Overall, just over 75% of pregnant women received prenatal care in 1989, far below the Public Health Service 1990 goal of early prenatal care for 90% of all pregnant women regardless of race or ethnicity.[10]

Women whose births are financed by Medicaid have been found to delay longer before initiating prenatal care than women whose births are financed by private health insurance.

In 1988 the Institute of Medicine conducted a detailed review of the literature dealing with a variety of determinants of the inadequate receipt of prenatal care.[11] In addition to age, race, and marital status, the Institute identified poverty, lack of education, lack of health insurance, high birth order, and residence in inner cities and isolated rural areas as key determinants of this outcome (see the Klerman article in this journal issue). The importance of almost all of these factors persisted in analyses that assessed the independent effect of a given factor with other factors held constant.[12] The implication is that an effective strategy to address the problem of inadequate prenatal care may need to operate on several fronts simultaneously.

Lowering financial barriers to the receipt of prenatal care has been a popular tactic of public policymakers because it appears feasible given the traditional tools at their disposal (see the Hill article in this journal issue), but conventional approaches to these problems have their limitations. Medicaid, for example, is often chosen as a convenient vehicle to alleviate financial barriers for poor pregnant women. Yet women whose births are

Figure 2. Interval Between Date of Last Menstrual Period and First Prenatal Visit by Insurance Status, New York City, 1984



Source: Joyce, T.J., and Grossman, M. Pregnancy Wantedness and the Early Initiation of Prenatal Care. *Demography* (February 1990) 27,1:1-17.

financed by Medicaid have been found to delay longer before initiating prenatal care than women whose births are financed by private health insurance.[11,13-15] Figure 2 depicts the magnitudes of these differentials among New York City women of various age, race, and ethnic groups in 1984. Black adults on Medicaid can be seen to delay the initiation of prenatal care approximately 1 month longer than black adults with private health insurance. Similar differentials are observed for white Medicaid versus white private insurance patients regardless of age. Somewhat smaller differentials are also found between the Medicaid and self-pay categories for adolescents and Hispanic adults. These differences are all statistically significant in a multivariate analysis which controlled for a number of confounding factors in addition to age, ethnicity, and insurance status.[14]

Why do pregnant women with Medicaid receive less prenatal care than women with private health insurance? The Institute of Medicine lists factors such as the time-consuming nature of the Medicaid enrollment process, the failure of some physicians to accept Medicaid patients, long travel times and clinic waits, and lack of information and unfavorable attitudes concerning prenatal care. These factors underscore the potential value of outreach programs and programs that aim to deliver, as opposed to finance, prenatal care for the poor.[11]

Beyond the financial barriers to prenatal care, certain demographic factors have begun to receive increasing attention. Marital status has been of particular relevance in this regard because changes in this factor have been dramatic over the decade of the 1980s. The number of births to unmarried mothers rose 64% over this period. And while the birth rate (that is the number of births per 1,000 women in a given category) for married women actually declined 6% between 1980 and 1989, the birth rate for unmarried women increased 42%. As a result of these trends, more than 1 baby in 4 was born to an unmarried mother by 1989.[16] The increase in the birth rate for unmarried women has alarming implications for infant health because unmarried mothers are more than three times as likely as married mothers to obtain late or no prenatal care and because the association of marital status and receipt of prenatal care remains largely unelucidated. It will be important to determine whether unmarried women receive less prenatal care because of financial barriers, educational differentials, general lack of social support, or other factors which may be difficult to measure. Each of these explanations implies different policy approaches.

Efficacy of Prenatal Care

The consensus of an extensive literature on the efficacy of prenatal care is that care works. In particular, women who initiate care earlier in their pregnancies give birth to healthier infants, are less likely to give birth to an infant weighing less than 2,500 grams, and are less likely to give birth to an infant who dies in the neonatal period. Following a detailed review of the literature, the Office of Technology Assessment concluded: "The weight of the evidence on the effectiveness of prenatal care . . . supports the contention that birth outcomes can be improved with earlier or more comprehensive prenatal care. . . . The evidence appears to support the value of both early and frequent prenatal care and the provision of enhanced services to adolescents and high-risk women."[17] Several years earlier, the Institute of Medicine reached a similar conclusion: "The overwhelming weight of the evidence is that prenatal care reduces low birth weight. This finding is strong enough to support a broad, national commitment to ensuring that all pregnant women, especially those at medical or socioeconomic risk, receive high-quality care."[18]

The evidence appears to support the value of both early and frequent prenatal care and the provision of enhanced services to adolescents and high-risk women.

While this consensus is impressive, certain considerations suggest that caution is required in interpreting and applying it. Despite the agreement, for example, of most researchers and policy analysts that prenatal care improves newborn health, there is no consensus on the quantitative relationship between the intensity of care delivered and the improvement in birth outcomes. Yet this may be the critical issue in deciding how to allocate scarce re-

sources among different programs designed to achieve better newborn health outcomes.

No agreement exists on the relative magnitude of the effect of prenatal care because studies on this subject do not use data from prospective, randomized controlled trials. This raises the possibility that the results which emerge are biased and either over- or underestimate the true effect of prenatal care on newborn health outcomes.[19]

For example, the true effect of prenatal care is underestimated in studies where women who anticipate a problematic birth outcome based on conditions unknown to the researcher seek out more care while women with positive expectations seek out less. The opposite occurs when the early care group is dominated by women who eat more nutritiously, suffer less stress, smoke less, and receive more emotional support from their families. Omission of these hard-to-measure factors overstates the impact of care.

The importance of correctly measuring the efficacy of prenatal care is illustrated by consideration of the Public Health Service goal of care within the first trimester of pregnancy for 90% of all pregnant women. To achieve this goal, the number of white women receiving early care must rise by approximately 12%, and the number of black women receiving such care must rise by almost 50%. Achieving this goal may be a costly undertaking, and even if care is efficacious, birth outcomes may not improve substantially if there are marked differences in the content of care or in other characteristics between new and current recipients. Moreover, it is not clear that limited resources would be better spent increasing the proportion of women who receive early care rather than increasing the number of women who get intermediate care (second trimester care) by reducing the number who get late or no care. Recent research by Joyce suggests that most of the gains to prenatal care in New York City accrued from moving women from the inadequate care to the intermediate care category and that the gains from moving women from the intermediate care category to the early/adequate care category are much smaller.[20] The Joyce study does not address the issues of how care works or of whether resources are better spent on increasing the rates of earlier initiation of care or on enhancing the content of care for women at particular risk for an unfavorable birth outcome. These are all important questions for those with limited resources looking to implement programs to improve birth outcomes.

In considering what we know about the receipt of prenatal care services and its effect on infant health outcomes, we are left in a situation in which we have good theoretical reasons to believe that prenatal care is important to produce healthy newborns; we have evidence, imperfect though it is, that groups who receive more prenatal care have better neonatal outcomes than groups who receive less, though how much better those outcomes are remains a subject of dispute; and we can see that over time, for different groups, as the receipt of prenatal care increases, so does the percentage of good outcomes.

Yet our knowledge is far from complete, chiefly because we do not know how prenatal care works or, for that matter, how well. And though these questions become relevant only once the issue of whether prenatal care works has been definitively addressed, they are still of great importance in and of themselves. If, for example, prenatal care serves principally to identify high-risk women early and intervenes to minimize the effect of preexisting risk factors in these women, then from the standpoint of policy alternatives, populations in which known risk factors are particularly prevalent should be preferentially recruited into prenatal care. This might involve extensive outreach and case management efforts including reducing financial barriers, relocating facilities into underserved areas, and providing child care for women using these services.

If, on the other hand, improved neonatal outcomes derive from the elimination of risk factors either before or very early on in the pregnancy, then one could argue that strategies such as reducing exposure to tobacco, to illicit substances, or to other environmental stresses should receive priority. Settings other than prenatal service centers may more efficiently produce these policy objectives. Future research on these critical questions will be of enormous utility to policymakers.

Obstetric and Neonatal Care

If birth weight is a valid indicator of the intrauterine experience and thus, indirectly, of the effectiveness of prenatal care services, infant mortality (death within the first year of life) is an indicator of the quality and impact of obstetric and neonatal care services. Because, in countries like the United States, most children who die in the first year of life do so in the first month, those factors that influence the birth process and the immediate postnatal condition of the baby may be expected to have a discernible impact on the infant mortality rate. To appreciate what the receipt of obstetric and neonatal care means for the health status of children, we begin with a look at infant mortality.

Infant Mortality

Much progress has been made in reducing the U.S. infant mortality rate during the twentieth century. It fell from 100 deaths per 1,000 live births in 1915 to 9.1 deaths per 1,000 live births in 1990.[21] Improvements in medical care and advances in medical technology played an important role in this process, particularly the introduction of sulfonamide and other anti-microbial drugs in the period from 1935 to 1950[22] and advances in neonatology since the late 1960s.[23,24] Until recently, the only interruption in the downward trend in infant mortality occurred in the late 1950s and early 1960s.[25]

There are two components of infant mortality: neonatal mortality and postneonatal mortality. The former refers to deaths of infants before the first 28 days of life, while the latter refers to deaths of infants between the ages of 28 and 365 days. Neonatal deaths are usually caused by congenital abnormalities, conditions associated with prematurity, and complications of delivery; while postneonatal mortality results primarily from sudden infant death syndrome (SIDS), infectious diseases, and accidents. In the early 1900s, approximately 70% of all infant deaths occurred in the postneonatal period. By 1989, only 36% of infant deaths occurred in the postneonatal period. Unlike earlier in this century, recent trends in the infant mortality rate have been dominated by declines in the neonatal mortality rate. Today, the mortality rate (that is, the chance of dying) for a baby's first month of life is more than twice as high as the mortality rate during the remainder of the first year.

Neonatal mortality, in turn, is highly negatively correlated with birth weight so that the birth weight distribution of a population is a major determinant of its neonatal mortality rate. Those populations with higher proportions of low (less than 2,500 grams) and very low (less than 1,500 grams) birth weight babies have higher rates of neonatal mortality. Once the distribution of birth weights in a population is taken into account, the mortality rates specific to each birth weight category are determinants of overall neonatal mortality. By multiplying the proportion of births in each birth weight group by the birth weight specific mortality rate for that group, one arrives at the overall neonatal mortality rate for a population.

Despite the rapid decline in infant mortality, substantial differences in this outcome and in its most proximate determinant—low birth weight—have persisted between different groups over time.[26,27] The most notable of these is the excess mortality of black babies who presently experience an infant mortality rate twice that of their white counterparts. In addition, the black low birth weight rate has typically been more than twice as large as the white rate. Among the Hispanic population, Puerto Rican women give birth to LBW infants at approximately three-fourths the rate of blacks, while the low birth weight rates of other Hispanics are similar to those of white non-Hispanics.[28]

Black babies presently experience an infant mortality rate twice that of their white counterparts.

In addition, the U.S. infant mortality rate remains higher than those of a number of other developed countries even when the rate is limited to whites.[17] Finally, Marks and others report that in 1980 "differences between the States of the U.S. in infant . . . mortality are greater than those between the U.S. and the countries of Scandinavia [with the lowest infant mortality]."[29]

These facts have led some observers to conclude that U.S. infant mortality policy has reached a crossroad.[30] Two decades of dramatic declines in infant mortality have failed to improve the survival prospects of black infants relative to white infants or of white infants born in the United States relative to those born in other developed countries. Moreover, during the decade of the 1980s, tentative evidence emerged that the period of rapid decline may have ended. The fall in mortality slowed to an average year-to-year reduction of 2.5%,[31] and the incidence of low birth weight stopped declining. In 1984 the fraction of LBW births reached an all-time low for both races: 5.59% for whites and 12.36% for blacks. The corresponding figures in 1989 were 5.7% for whites and 13.5% for blacks.[16,32]

The U.S. infant mortality rate remains higher than those of a number of other developed counties even when the rate is limited to whites.

The infant mortality rate in 1990 was 6% less than the rate in 1989.[33] The introduction of treatment with artificial surfactant, which helps prevent deaths of premature infants from respiratory distress syndrome, and the expansions in Medicaid coverage for prenatal care may have contributed to this decline.[31] Obviously it is too early to determine whether this change represents a reversal of the deceleration in the downward trend during the 1980s. It is clear, however, that three important 1990 infant health goals of the Public Health Service as set forth in *The 1990 Health Objectives for the Nation: A Midcourse Review* have not been met.[10] These are an infant mortality rate no higher than 12 per 1,000 live births for any minority group (the black rate was 17.6 per 1,000 live births in 1988), a low birth weight rate of 5% of all infants, and a low birth weight rate of 9% for any minority group.

Trends in Obstetric Services

Where a child is born, how that child is delivered, and who attends the delivery may all be important determinants of neonatal outcome under certain circumstances. The volume of obstetrical procedures in the hospital where birth occurs, for example, has been shown to be related to survivorship in low birth weight babies though not in term, normal birth weight babies.[34] Recent trends indicate that increasing numbers of infants in the United States are being born in the hospital. For white infants the percentage of babies born in a hospital rose from 96.6% in 1975 to 98.7% in 1989, while for nonwhite infants the comparable percentages were 94.6% in 1975 and 99% in 1989.[35]

In addition to in-hospital deliveries, cesarean section rates have also been on the rise since the middle of the 1960s. In 1965 the chances of being born via cesarean section were about 1 in 20. By 1989 the likelihood had increased to 1 in 4. Most authors attribute this rise to the increase in electronic fetal monitoring, changes in the legal atmosphere surrounding obstetrical care, and the policy of discouraging spontaneous vaginal deliveries in women who have undergone previous cesarean sections.[36] The increase in these procedures has not been shown to have any positive contribution to neonatal outcome.[37]

Trends in Neonatal intensive Care

As we noted earlier, the most important component of infant mortality in the United States today is the death rate of babies less than 28 days old. This rate, in turn, depends upon the distribution of birth weights in a population and the specific death rate associated with each birth weight category.

In the first part of this paper we discussed some of the factors that influence the birth weight distribution of a population, particularly the provision of adequate prenatal care for pregnant women. We now turn our attention to developments that have influenced birth weight specific mortality rates. The most important of these has been the expansion in the availability of neonatal intensive care services.

Over the past 2 decades in the United States, the single most significant trend in the delivery of neonatal health services has been the emergence of regionalization as a guiding principle in the provision of care for high-risk mothers and newborn babies.[38] Many hospitals began to introduce intensive care units for newborns during the decade of the 1960s, but it was not until the early 1970s that a comprehensive set of guidelines was developed to organize the distribution of these services within given geographic areas by incremental levels of intensity.

The 1977 National Foundation–March of Dimes recommendations,[39] subsequently refined by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists,[40] include three levels of infant care: (1) Level I nurseries to provide routine newborn care; (2) Level II nurseries, manned by board certified pediatricians, to provide care to seriously ill infants with life-threatening conditions for finite periods and to maintain ongoing liaisons with (3) Level III nurseries which serve as regional referral centers offering the most sophisticated neonatal care including specialized respiratory support systems, pediatric surgery services, and infant transport teams capable of delivering seriously ill neonates to and from the hospital.

In practice there has been some blurring of the distinction between Level II and Level III nurseries as the competition for patients has intensified in recent years.[41] Nevertheless, specific standards have arisen for adequate staffing, physical design, ancillary services, and transport facilities appropriate to the most advanced levels of neonatal care.[40,42]

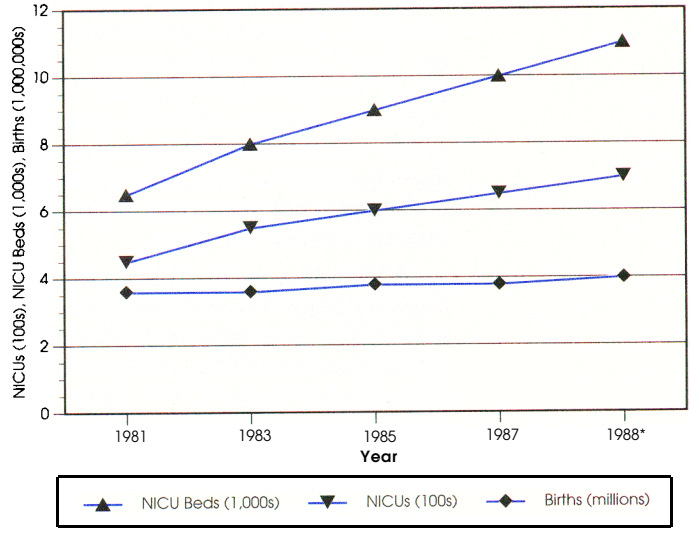
During the decade of the 1980s, the number of Neonatal Intensive Care Units (NICUs)—combined Level II and Level III units—in U.S. hospitals has risen dramatically (see figure 3). While the total number of hospitals, as surveyed by the American Hospital Association in their annual survey, rose 14.33% from 1979 to 1988, the number of NICUs climbed 44.33% from 485 to 700 and the number of NICU beds increased 66.97% from 6,591 to 11,005 during this period.[43]

Although no national data bases exist which provide information on the utilization rates of these NICUs, the Office of Technology Assessment (1987) estimated that there were between 150,000 and 200,000 admissions to NICUs annually in the mid-1980s.[44] In recent years, anecdotal evidence suggests that a greater and greater proportion of NICU admissions have gone to infants weighing less than 1,500 grams while the proportion of admissions of moderately low birth weight infants has declined.[44] One study from Cleveland reported increases in the numbers of extremely low birth weight admissions (babies born weighing less than 751 grams) from the early to the late 1980s of 30%.[45] Whether these trends result from recent tendencies to focus more aggressive resuscitative efforts on smaller and smaller neonates remains to be fully elucidated. Whatever the origin of this trend to lower birth weight NICU admissions, this development inevitably forces policymakers to confront the question of how much improvement in health outcomes can reasonably be anticipated from such high tech attention to smaller and smaller babies.

Efficacy of Neonatal Intensive Care

In view of the rapid growth in the number of NICUs during the past 15 years, the substantial expense attendant upon caring for newborns in such environments, and

Figure 3. Trends in Number of NICUs, NICU Beds, and Births



*Note 2-year time span except from 1987 to 1988.

Source: American Hospital Association, Hospital Statistics. Chicago: American Hospital Association, 1980, 1989.

the trend to lower birth weight NICU admissions, it was inevitable that questions would arise as to whether the expenditure of such prodigious resources was worthwhile. (See the Lewit and Monheit article in this journal issue.) Clinicians, epidemiologists, and economists have all addressed this issue, with each group approaching it from the vantage point of its own particular discipline.

As practitioners, neonatologists have been anxious to demonstrate that the specific content of care provided by NICUs makes a difference in the outcome of patients treated there.

As practitioners, neonatologists have been anxious to demonstrate that the specific content of care provided by NICUs makes a difference in the outcome of patients treated there. To make this case, investigators have applied two different methods. One approach compares the experiences of successive cohorts of infants treated at the same institution during two time periods to show how the development of new technologies has improved birth weight specific survival rates for all but the very smallest babies.[45,46] Increasing willingness to refer high-risk pregnancies to centers with neonatal intensive care units, the antenatal use of steroids to hasten fetal lung development, improvements in techniques to assist breathing artificially, and the ability to provide adequate intravenous nutrition to extremely immature infants have all been implicated in the trend toward increased birth weight specific survival over time.

A second type of study makes use of cross-sectional comparisons among several NICUs to demonstrate that different applications of similar technologies may also affect outcomes.[47,49] After controlling for the potentially confounding influences of race, birth weight, and gender, these investigations were still able to demonstrate significant intercenter differences in various outcome measures. The results of these studies imply that appropriate application of assisted mechanical ventilation in NICUs can significantly reduce morbidity and mortality among immature newborns.

Epidemiologists have looked at the impact of neonatal intensive care on the mortality rates of entire populations and have come to the conclusion that new neonatal technologies, properly distributed, provide significant improvements in this measure of health status. For example, an early Canadian study covering the period 1967 to 1974 documented a 43% decrease in the neonatal mortality rate for the province of Quebec coincident with several important institutional developments including (1) an increase in the proportion of sick and premature newborns cared for in referral centers; (2) the establishment of perinatal intensive care units in two university hospitals; and (3) the regionalization of the high-risk obstetric service associated with McGill University, where fully 14% of the province's births occurred.[50] The authors of this study were able to show that the improvement resulted from decreases in mortality rates within birth weight categories, not from any dramatic shift in the birth weight distribution itself, and that the diffusion of specialized care both to high-risk mothers and their newborn infants played a significant role in the observed decline in Quebec's neonatal mortality rates. Subsequently, Lee and his colleagues arrived at similar conclusions using data from the United States for the period between 1950 and 1975.[51]

When considering the effectiveness of neonatal intensive care, economists have used their particular skills to accomplish two functions: (1) to estimate the magnitude of improvement in outcome associated with neonatal intensive care and (2) to construct cost-benefit or cost-effectiveness analyses of these services.

As an example of the first type of contribution, Harris reported that an increase in the annual volume of deliveries in the hospital of birth lowered the probability of neonatal death (including late fetal death) among black babies in Massachusetts in 1975–1976.[52] A 10% increase in the annual volume of deliveries was found to lower the death rate by approximately 5%.[53] A similar approach using data for white infants born in Michigan in 1984 found that birth in a hospital with a neonatal intensive care unit lowered the probability of a late fetal or neonatal death by approximately 30%.

This type of analysis has been generalized to examine the impact of the use of

neonatal intensive care services on neonatal mortality using data that cover almost the entire U.S. population. These studies show that a 10% increase in neonatal intensive care use was found to lower the mortality rate of white low birth weight infants by 2%. For black infants, a 10% increase in use lowered the death rate by 3%. These findings indicate how much improvement in mortality can be expected from increases in the availability of neonatal intensive care to low birth weight babies.[54]

Cost-effectiveness of Neonatal Intensive Care

Faced with limited resources and the need to make decisions about the implementation of costly but effective programs to improve infant health, policymakers have increasingly relied on the tools of cost-benefit and cost-effectiveness analysis to help determine whether the observed improvements in health are worth the costs expended to achieve them. Yet these techniques are not easy to apply.[55] First, because traditional accounting practices within hospitals use revenue from one source to offset shortfalls elsewhere (a practice known as cost shifting), dollar costs of neonatal intensive care are often difficult to determine accurately. Furthermore, costs of the long-term care required by some severely disabled NICU survivors are also difficult to estimate. On the benefits side, the probabilities of various outcomes are not easily determined and vary substantially among institutions. Moreover, to perform a full cost-benefit analysis, it is necessary to assign a monetary value to survival with and without different degrees of disability. This often proves an intractable problem. As a result of these difficulties, the conclusions drawn from cost-benefit studies must be regarded with caution.

Despite these and other obstacles, however, attempts have been made to compare the costs and benefits of neonatal intensive care in monetary terms. Budetti and his colleagues concluded that, while NICU care for babies weighing less than 1,500 grams was marginally cost-effective given the data available to them at the time of their analysis, such care for infants weighing less than 1,000 grams was not.[55] Because of the potentially large expenditures required to care for severely disabled NICU survivors, as the numbers of such survivors increased in lower birth weight groups, Budetti and his colleagues found that the costs of providing this type of care began to substantially outweigh the benefits. Other investigators have reached similar conclusions.[56]

To perform a full cost-benefit analysis, it is necessary to assign a monetary value to survival with and without different degrees of disability.

In a very careful analysis conducted in Hamilton-Wentworth County in Ontario, Boyle and others used cost-benefit, cost-effectiveness, and cost-utility analysis to evaluate NICU care.[57] In the last of these approaches, an attempt is made to adjust life-years gained by a factor which takes into account the quality of life for individuals who survive with disabilities. As in previous studies, the findings were birth weight dependent. For infants in the 1,000- to 1,499-gram range, the cost of neonatal intensive care was found to be $59,500 (1978 Canadian dollars) per survivor, $2,900 per life-year gained, or $3,200 per quality-adjusted life-year gained. The corresponding figures for infants in the 500- to 999-gram category were $102,500, $9,300, and $22,400. The authors concluded that "by every economic measure neonatal intensive care for infants weighing 1,000 grams to 1,499 grams is superior to neonatal intensive care for infants weighing 500 grams to 999 grams." Neonatal intensive care for the lower birth weight group appeared to generate a net economic loss in all scenarios analyzed. Yet, when the analysis focused on clinical outcomes, it yielded a different conclusion. Here it was found that neonatal intensive care for infants weighing 750 grams to 999 grams at birth resulted in the largest survival gain for any subgroup. The apparent inconsistency introduced by evaluating neonatal intensive care from these alternative perspectives highlights the difficulties attendant to decision making regarding high-cost, high technology medical services.

As authors of these and other studies are quick to point out, cost-benefit analyses can help identify those programs that not only provide a health benefit to participants but also pay for themselves in an economic sense. Programs that are considered cost-beneficial produce not only a

survivor for the cost outlay, but also the future economic productivity of that survivor. Because this situation is akin to a man's going into a store to buy a loaf of bread and coming out with not only the bread but also more money than when he went in, it is a very restrictive criterion by which to judge a medical intervention. More pertinent questions to pose, especially if costs outweigh the benefits in dollars generated by a program, are (1) whether society deems the net costs worth undertaking in view of the health benefits produced by the program under consideration and/or (2) whether alternative, less costly strategies exist to achieve similar health outcomes.

Knowing that the economic costs of caring for very low birth weight infants (those weighing less than 1,000 grams) outweigh the economic benefits forces policymakers to decide either that these expenditures are worthwhile despite the costs or that alternative strategies for saving infants' lives need to be entertained.

A recent study by Joyce, Corman, and Grossman speaks directly to this dilemma.[58] They found that expansion of prenatal care is a more cost-effective method of saving additional infant lives than expansion of neonatal intensive care. For whites, the cost of saving an additional life by expanding the number of women who receive prenatal care in the first trimester is $31 per additional life saved in 1984 dollars. The cost of saving an additional life by expanding the number of low birth weight babies who receive neonatal intensive care is $2,834 per additional life saved. The comparable figures for black women and infants are $39 in the case of prenatal care and $2,150 in the case of neonatal intensive care.[59] These cost-effectiveness ratios although suggestive are far from definitive because they do not consider improvements in neonatal intensive care technology. As with many policy alternatives, changes in technology, particularly in rapidly developing fields of inquiry, may be expected to shift the advantage of one or another approach to a given problem over time.

New Neonatal Technologies

Faced with the desire to improve the health of newborns and rapidly rising costs for the care of sick infants, the policymakers' dilemma is that not all technological innovations with potential clinical application may be cost saving. Two examples of recent improvements in NICU respiratory care, artificial surfactant and extracorporeal membrane oxygenation (ECMO), illustrate this point.

During the first week of life, many premature infants are faced with the problem of breathing effectively with immature lungs. When clinically significant, this problem is called respiratory distress syndrome (RDS). RDS results from the failure of the premature infants' lungs to produce surfactant, a substance that allows the small air sacs in the lungs of premature infants to remain inflated during all phases of respiration. Providing premature newborns with exogenous surfactant ameliorates RDS. Since the efficacy of exogenous surfactant was demonstrated in 1980, it has been synthesized commercially and is now instilled in the windpipes of newly born premature infants in an attempt either to prevent or to treat RDS and thereby decrease the accompanying morbidity and mortality.

The early experience with artificial surfactant has been favorable.[60-68] At a wholesale cost of approximately $900 per treatment for a neonate, it is relatively inexpensive and can be administered at virtually any Level II or Level III nursery without special equipment or monitoring. A recent analysis from England suggested that the use of surfactant was cost-effective in very low birth weight infants,[69] and there has been speculation that the dissemination of the use of this material was responsible for the decline in infant mortality witnessed in 1991.[70]

The second technology mentioned, ECMO, is a technique for bypassing the newborns' lungs altogether by placing the

child on a machine similar to one used during open heart surgery. Not indicated for routine use in premature babies with RDS, ECMO is reserved for desperately ill, full-term babies whose condition is unresponsive to the conventional treatment of respiratory assistance. Very few newborns are candidates for ECMO so the potential effect of ECMO on neonatal mortality is limited. Nonetheless there appear to be more centers in the United States with the capability to perform ECMO than are warranted by the number of infants who would benefit from the therapy.[71] Accordingly, there is concern that the therapy may be used inappropriately and that costs associated with this technique may be difficult to contain. As Southgate, who studied the use of ECMO in Georgia concluded, "Short-sighted proliferation of ECMO units will almost certainly result in an increased consumption of shrinking health care dollars, as well as the unnecessary duplication of services. . . ."[72]

Careful analysis of both the cost and the clinical efficacy of new technologies would be helpful in guiding the allocation of resources so as to optimize both infant survival and the ultimate health of survivors.

Conclusion

We have considered the impact of prenatal, obstetrical, and neonatal care on the most important and easily measured outcomes of infant health, namely the rate of low birth weight births and the rate of infant mortality. Though not all the studies published to date have been well controlled, abundant evidence has accumulated demonstrating that these two outcome measures do respond to the application of appropriate health services.

Despite the recent slowing in the rate of decline of infant mortality and the leveling off in the decline of the low birth weight rate, there are continued reasons for optimism. The discrepancies that persist between white and nonwhite low birth weight rates imply that an improved distribution of prenatal care services could have a significant impact on the rate of low birth weight births. The development of new agents to aid in the treatment of respiratory distress syndrome raises hope that more widespread application of such treatments will significantly improve neonatal survival as well. Finally, expanded regionalization of prenatal, obstetric, and neonatal care in a coordinated approach to the entire continuum of gestation, labor, delivery, and early development holds out the promise of greater progress on both fronts. Though there is reason to be optimistic, recent experience has highlighted the needs of mothers and infants with emerging special problems. These include the increase in high-risk pregnancies caused by maternal substance abuse (see the Spring 1991 issue of *The Future of Children,* which deals with this problem) and pregnancies complicated by HIV infection which, although few in number, present the problems of severe chronic illness in both the mother and the infant (see the article by Perrin and Guyer in this [Winter 1992] journal issue for a more complete discussion of HIV infection in children). Perhaps the greatest challenge, however, because of the sheer number of individuals affected, is to improve birth outcomes in the face of increasing rates of poverty and an increase in the number of births to poor families.[18]

The advance of obstetrical technology into more advanced genetic and fetal screening,[73] fetal therapies to ameliorate potentially serious infant conditions before birth,[74,75] and other technologies such as home uterine monitoring to detect possible premature labor[76] as well as continued advances in neonatology may present both problems and benefits. Though there is clearly progress to be made, the politics of competing claims on limited resources dictates that those programs and activities which can deliver the greatest potential improvement in newborn survival for the least investment are likely to prove the most attractive to decision makers. The effort to identify such programs and activities deserves a prominent place on the research agenda in the immediate future.

We are indebted to Victor R. Fuchs and Eugene M. Lewit for helpful comments on an earlier draft. We wish to thank Patricia DeVries for research assistance.

1. Edwards, L.N., and Grossman, M. The relationship between children's health and intellectual development. In *Health: What is it worth?*, S.J. Mushkin, and D.W. Dunlop, eds. Elmsford, NY: Pergamon Press, 1979, pp. 273-314.

2. American College of Obstetricians and Gynecologists. *Standards for obstetric-gynecologic services.* 7th ed. Washington, DC: ACOG, 1989.

3. U.S. Department of Health and Human Services. *Caring for our future: The content of prenatal care.* Washington, DC: U.S. DHHS, 1989.

4. Wilson, J.G. *Environment and birth defects.* New York: Academic Press, 1973.

5. Based on estimated rates of Down's syndrome among women of different ages (20 to 49 years) as reported by Hirschhorn, K. Prenatal disturbances. In *Nelson textbook of pediatrics,* 14th ed. R.E. Behrman, R.M. Kliegman, W.E. Nelson, and V.C. Vaughan, eds. Philadelphia: W.B. Saunders Company, 1992, p. 284. And 1989 distribution of live births by age of mother as reported in National Center for Health Statistics, U.S. Department of Health and Human Services. *Advance report of final natality statistics, 1989.* Monthly Vital Statistics Report, vol. 40, no. 8, supplement. Hyattsville, MD: Public Health Service, 1991.

6. Antonarakis, S.E., Lewis, J.G., Adelsberger, P.A., et al. Parental origin of the extra chromosome in Trisomy 21 revisited: DNA polymorphism analysis suggests that in 95% of cases the origin is maternal. *American Journal of Human Genetics* (1990) 47:A 97.

7. Schlesinger, M., and Kronebusch, K. The failure of prenatal care policy for the poor. *Health Affairs* (Winter 1990) 9,4:91-111.

8. National Center for Health Statistics, U.S. Department of Health and Human Services. *Advance report of final natality statistics, 1988.* Monthly Vital Statistics Report, vol. 39, no. 4, supplement. Hyattsville, MD: Public Health Service, 1990.

9. Singh, S., Torres, A., and Forrest, J.D. The need for prenatal care in the U.S.: Evidence from the 1980 National Natality Survey. *Family Planning Perspectives* (May-June 1985) 17,3:118-124.

10. Public Health Service, U.S. Department of Health and Human Services. *The 1990 health objectives for the nation: A midcourse review.* Washington, DC: Office of Disease Prevention and Health Promotion, 1986.

11. Institute of Medicine. *Prenatal care: Reaching mothers, reaching infants.* S.S. Brown, ed. Washington, DC: National Academy Press, 1988.

12. The one exception was race. But this conclusion must be interpreted with caution because almost all of the studies reviewed were conducted on a race-specific basis or specified a fairly complex set of interactions among race, ethnicity, and poverty.

13. Grossman, M., and Joyce, T.J. Unobservables, pregnancy resolutions, and birth weight production functions in New York City. *Journal of Political Economy* (October 1990) 98,5:983-1007.

14. Joyce, T.J., and Grossman, M. Pregnancy wantedness and the early initiation of prenatal care. *Demography* (February 1990) 27,1:1-17.

15. Howell, E.M., et al. A comparison of Medicaid and non-Medicaid obstetrical care in California. *Health Care Financing Review* (Summer 1991) 12,4:1-15.

16. National Center for Health Statistics, U.S. Department of Health and Human Services. *Advance report of final natality statistics, 1989.* Monthly Vital Statistics Report, vol. 40, no. 8, supplement. Hyattsville, MD: Public Health Service, 1991.

17. Office of Technology Assessment, U.S. Congress. *Healthy children: Investing in the future.* Washington, DC: U.S. Government Printing Office (OTA-H-345), 1988.

18. Institute of Medicine. *Preventing low birthweight.* Washington, DC: National Academy Press, 1985, p. 146.

19. To estimate the magnitude of the true effect of prenatal care on infant health, one must control for the impact of other determinants of newborn health outcomes which are themselves correlated with prenatal care. Otherwise one ends up attributing to prenatal care influences originating from some other source. The most effective way to isolate the prenatal care effect would be to perform a clinical trial in which a set of pregnant women would be divided at random into two groups: one that receives prenatal care in the first trimester and one that does not. Such an approach would ensure that the two groups of women would be as similar as possible in all respects other than their receipt of prenatal care. Thereafter, any observed differences in birth weight or infant survival between the two groups of women would be most likely due to differences in the receipt of early prenatal care.

20. Joyce, T.J. Self selection, prenatal care, and birthweight among blacks, whites, and Hispanics in New York City. National Bureau of Economic Research Working Paper No. 3549, revised April 1991.

21. The rate of decline was 3.1% per year annually compounded. Fuchs, Victor R. *How we live: An economic perspective on Americans from birth to death.* Cambridge, MA: Harvard University Press, 1983. National Center for Health Statistics, U.S. Department of Health and Human Services. *Annual summary of births, marriages, divorces, and deaths, United States, 1990.* Monthly Vital Statistics Report, vol. 39, no. 13. Hyattsville, MD: Public Health Service, 1991.
22. Fuchs, V.R. *Who shall live? Health, economics, and social choice.* New York: Basic Books, 1974.
23. McCormick, M.C. The contribution of low birth weight to infant mortality and childhood morbidity. *New England Journal of Medicine* (January 10, 1985) 312,2:82-90.
24. Paneth, N. Technology at birth. *American Journal of Public Health* (July 1990) 80,7:791-92.
25. Between 1955 and 1964, the rate of decline eased to less than 1% per year but then accelerated to 4.1% per year between 1964 and 1984. Corman, H., Joyce, T.J., and Grossman, M. Birth outcome production functions in the U.S. *Journal of Human Resources* (Summer 1987) 22,3:339-60.
26. Wegman, M.E. Annual summary of vital statistics—1990. *Pediatrics* (December 1991)88,6:1081-92.
27. Given the importance of neonatal mortality in total infant mortality, differences in the latter rate among groups in the population at a moment in time mirror differences in the former.
28. U.S. Department of Health and Human Services. *Report of the Secretary's Task Force on Black and Minority Health.* Volume VI: Infant mortality and low birthweight. Washington, DC: U.S. Department of Health and Human Services, 1986.
29. Marks, J.S., et al. Variations in state-specific infant mortality risks. *Public Health Reports* (March-April 1987) 102,2:146-50.
30. National Commission to Prevent Infant Mortality. *Troubling trends persist: Shortchanging America's next generation.* Washington, DC: National Commission to Prevent Infant Mortality, 1992.
31. Hilts, P.J. U.S. reports drop in infant deaths. *New York Times,* April 7, 1991, pp. 1, 8.
32. National Center for Health Statistics, U.S. Department of Health and Human Services. *Health U.S. 1990.* DHHS Pub. No. (PHS) 90-1232. Hyattsville, MD: Public Health Service, 1991.
33. National Center for Health Statistics, U.S. Department of Health and Human Services. *Annual summary of births, marriages, divorces, and deaths, United States, 1990.* Monthly Vital Statistics Report, vol. 39, no. 13. Hyattsville, MD: Public Health Service, 1991.
34. Mayfield, J.A., et al. The relation of obstetrical volume and nursery level to perinatal mortality. *American Journal of Public Health* (July 1990) 80,7:819-23.
35. The percent of nonwhite babies born in hospital exceed the percentage for white babies because fewer nonwhite infants underwent scheduled deliveries at home or in freestanding birthing centers. Birthing centers have recently been shown to be a safe, low-cost alternative to hospital delivery for suitably screened low-risk mothers. Rooks, J.P., Weatherby, N.L., Ernst, E.K.M., et al. Outcomes of care in birth centers: The national birth center study. *New England Journal of Medicine* (December 28, 1989) 321,26:1804-11.
36. Goyert, C.L., Bottoms, S.F., Treadwell, M.C., and Nehra, P.C. The physician factor in cesarean birth rates. *New England Journal of Medicine* (1989) 320:706-709.
37. Haynes de Regt, R., Minkoff, H.L., Feldman, J., and Schwartz, R.H. Relation of private or clinic care to the cesarean birth rate. *New England Journal of Medicine* (1986) 315:619-24.
38. Rudolph, C.S., and Borker, S.R. *Regionalization: Issues in intensive care for high risk newborns and their families.* New York: Praeger, 1987.
39. National Committee on Perinatal Health. *Toward improving the outcome of pregnancy: Recommendations for the regional development of maternal and perinatal health services.* White Plains, NY: The National Foundation-March of Dimes, 1977.
40. American Academy of Pediatrics/American College of Obstetricians and Gynecologists. *Guidelines for perinatal care, 2d ed.* Washington, DC, 1988.
41. Gagnon, D., Allison-Cooke, S., and Schwartz, R.M. Perinatal care: The threat of deregionalization. *Pediatric Annals* (July 1988) 17,7:447-52.
42. Ross Planning Associates. *1982 guide to centers providing perinatal and neonatal special care.* Columbus, OH: Ross Laboratories, 1982.

43. American Hospital Association. *Hospital statistics.* Chicago: American Hospital Association, 1980, 1989.

44. Office of Technology Assessment, U.S. Congress. *Neonatal intensive care for low birthweight infants: Costs and effectiveness.* Washington, DC: U.S. Government Printing Office (OTA-HCS-38), 1987.

45. Hack, M., and Fanaroff, A.A. Outcomes of extremely-low-birth-weight infants between 1982 and 1988. *New England Journal of Medicine* (December 14, 1989) 321:1642-47.

46. Cohen, R.S., Stevenson, D.K., Malachowski, N., et al. Favorable results of neonatal intensive care for very low-birth-weight infants. *Pediatrics* (May 1982) 69,5:621-25.

47. Avery, M.E., Tooley, W.H., Keller, J.B., et al. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. *Pediatrics* (January 1987) 79,1:2630.

48. Horbar, J.D., McAuliffe, T.L., Adler, S.M., et al. Variability in 28-day outcomes for very low birth weight infants: An analysis of 11 neonatal intensive care units. *Pediatrics* (October 1988) 82,4:554-59.

49. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Network. *Pediatrics* (May 1991) 87,5:587-97.

50. Usher, R. Changing mortality rates with perinatal intensive care and regionalization. *Seminars in Perinatology* (July 1977) 1,3:309-19.

51. Lee and others concluded that the major factor responsible for declining birth weight specific mortality over that period was improvement in perinatal medical care because the birth weight specific mortality rates did not change appreciably in the first 10 years of that period and from 1967-1975, a time when the birth weight distribution actually worsened somewhat and other important factors were unchanged, neonatal mortality declined 35%. Lee, K., et al. Neonatal mortality: An analysis of the recent improvement in the U.S. *American Journal of Public Health* (January 1980) 70,1:15-21.

52. Harris, J.E. Prenatal medical care and infant mortality. In *Economic Aspects of Health.* V.R. Fuchs, ed. Chicago: University of Chicago Press, 1982, pp. 15-52.

53. Harris controlled for gestational age, birth weight, prenatal care, mother's age, mother's education, marital status, and parity in arriving at the estimated effect.

54. Joyce, T.J., Corman, H., and Grossman, M. A cost-effectiveness analysis of strategies to reduce infant mortality. *Medical Care* (April 1988) 26,4:348-60.

55. Budetti, P., Barrand, N., McManus, P., et al. The costs and effectiveness of neonatal intensive care. Case study 10. In Background paper 2: Case studies of medical technologies. *The implications of cost-effectiveness analysis of medical technology.* Washington, DC: Office of Technology Assessment, August 1981.

56. Walker, D.B., Feldman, A., Vohr, B., and Oh, W. Cost-benefit analysis of neonatal intensive care for infants weighing less than 1,000 grams at birth. *Pediatrics* (July 1984) 74,1:20-25.

57. Boyle, M.H., Torrance, G.W., Sinclair, J.C., and Horwood, S.P. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. *New England Journal of Medicine* (June 2, 1983) 308,22:1330-37.

58. See note no. 54, Joyce, et al., pp. 354-59.

59. These figures are averages of the high and low estimates presented by Joyce, Corman, and Grossman (see note no. 54).

60. Hallman, M., Merritt, T.A., Jarvenpaa, A.L., et al. Exogenous human surfactant for treatment of severe respiratory distress syndrome: A randomized prospective clinical trial. *Journal of Pediatrics* (1985) 106:963-69.

61. Kwong, M.S., Egan, E.A., Notter, R.H., and Shapiro, D.L. Double-blind clinical trial of calf lung surfactant extract for the prevention of hyaline membrane disease in extremely premature infants. *Pediatrics* (1985) 76:585-92.

62. Enhorning, G., Shennan, A., Possmayer, R., et al. Prevention of neonatal respiratory distress syndrome by tracheal instillation of surfactant: A randomized clinical trial. *Pediatrics* (August 1985) 76,2:145-53.

63. Merritt, T.A., Hallman, M., Bloom, B.T., et al. Prophylactic treatment of very premature infants with human surfactant. *New England Journal of Medicine* (1986) 315:785-90.

64. Gitlin, J.D., Soll, R.F., Parad, R.B., et al. Randomized controlled trial of exogenous surfactant for the treatment of hyaline membrane disease. *Pediatrics* (January 1987) 79,1:31-37.

65. Fujiwara, T., Konishi, M., Chida, S., et al. Surfactant replacement therapy with a single postventilatory dose of a reconstituted bovine surfactant in preterm neonates with respiratory distress syndrome: Final analysis of a multicenter, double-blind, randomized trial and comparison with similar trials. *Pediatrics* (November 1990) 86,5:753-64.

66. Hennes, H.M., Lee, M.B., Rimm, A.A., and Shapiro, D.L. Surfactant replacement therapy in respiratory distress syndrome. *American Journal of Diseases of Children* (January 1991) 145:102-104.

67. Phibbs, R.H., Ballard, R.A., Clements, J.A., et al. Initial clinical trial of EXOSURF, a protein-free synthetic surfactant, for the prophylaxis and early treatment of hyaline membrane disease. *Pediatrics* (July 1991) 88,1:1-18.

68. Liechty, E.A., Donovan, E., Purohit, D., et al. Reduction of neonatal mortality after multiple doses of bovine surfactant in low birth weight neonates with respiratory distress syndrome. *Pediatrics* (July 1991) 88,1:19-28.

69. Mugford, M., Piercy, J., and Chalmers, I. Cost implications of different approaches to prevention of respiratory distress syndrome. *Archives of Diseases of Childhood* (1991) 66:757-64.

70. F-D-C Reports, Inc. Lung surfactants responsible for 8% drop in U.S. infant mortality: Smoking linked to low birth weight. *The Blue Sheet,* April 29, 1992, pp. 4-5.

71. Cole, C.H., Jilson, E., and Kessler, D. ECMO: Regional evaluation of need and applicability of selection criteria. *American Journal of Diseases of Children* (December 1988) 142:1320-24.

72. Southgate, W. M., Howell, C.G., and Kanto, W.P. Need for and impact on neonatal mortality of extracorporeal membrane oxygenation in infants greater than 2,500-gram birth weight. *Pediatrics* (July 1990) 86,1:71-74.

73. Dickerman, L.H., and Park, V.M. Cytogenic and molecular aspects of genetic disease and prenatal diagnosis. In *Neonatal-Perinatal Medicine,* Fanaroff, A.A., and Martin, R.J., Mosby Year Book: St. Louis, MO, 1992.

74. Harrison, M.R., Adzick, N.S., Longaker, M.T., et al. Successful repair in utero of a fetal diaphragmatic hernia after removal of herniated viscera from the left thorax. *New England Journal of Medicine* (May 31, 1990) 33,22:1582-84.

75. Harrison, M.R., Filly, R.A., Parer, J.R.T., et al. Management of the fetus with a urinary track malformation. *Journal of the American Medical Association* (1981) 246:635-39.

76. Mou, S.M., Sunderji, S.G., Gall, S., et al. Multicenter randomized clinical trial of home uterine activity monitoring for detection of preterm labor. *American Journal of Obstetrics and Gynecology* (1992) 165:858-66.