ARTICLE

Impact of Specific Medical Interventions in Early Childhood on Increasing the Prevalence of Later Intellectual Disability

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Importance: For the past 100 years, medicine in industrialized nations has become increasingly focused on specific medical interventions designed to improve the health of individual patients. Substantial evidence suggests that broader improvements in public health, nutrition, and economic well-being are more salient than medical or surgical interventions for the remarkable decrease in infant and child deaths since 1900. Less is known about the impact of specific medical interventions on morbidity such as intellectual disability (ID).

Objective: To explore the impact of medical interventions in early childhood on increasing the prevalence of later ID, as reported in the literature from 1950 through 2000.

Design: We reviewed the medical literature and other data from 1950 through 2000 to construct estimates of the condition-specific prevalence of ID over time. We further explored the existing literature to document historically relevant influences on condition-specific prevalence, including the introduction of effective interventions, the timing of these introductions, and the likelihood of their widespread use.

Setting: Twentieth century United States and Western Europe.

Participants: Populations of children who received a life-saving intervention within the first 5 years of life and were evaluated for ID after 5 years of age.

Main Outcome Measures: Case-specific prevalence of ID from 1950 through 2000.

Results: Low birth weight is associated with approximately 10% to 15% of the total prevalence of ID. No other new medical therapies introduced during this period were associated with a clinically significant increase in ID prevalence.

Conclusions and Relevance: Previous research has shown that specific medical interventions, such as newborn screening for congenital thyroid deficiency and phenylketonuria, have decreased the prevalence of ID approximately 16% in the United States since 1950. These results suggest that other medical interventions, particularly the advent of intensive care technologies, have also increased the prevalence of ID.

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For the past 100 years, medicine in the United States and other industrial nations has become increasingly focused on specific medical interventions designed to improve the health of individual patients.[1,2] However, McKeown[3] and others[4] have demonstrated that effective interventions such as antibiotics and immunizations became widely available only after 1940 and, as such, cannot account for the earlier dramatic reduction in premature mortality among populations in England and the United States, which began in the late 19th century. Instead, widespread improvements in nutrition and public health are probably responsible for much of the population health gains during the past century, including reduced infant mortality and increased life expectancy.[5-9] More recently, public health leaders have called for a renewed focus on the social determinants of health as the key to improving the health of populations.[10,11]

In a recent analysis, Brosco et al[12] examined the historical epidemiology of intellectual disability (ID). As deaths among infants and children have become increasingly rare during the past half century, mortality rates have become a less sensitive measure of population health. Because it is related to numerous genetic and environmental factors, ID may be a more useful indicator of population health in the United States. To understand this indica-

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tor, we chose the period since 1950 because that decade marked the beginning of a critical period for the development and dissemination of new policies in the United States designed to reduce the burden of what was then called "mental retardation." Inspired by family advocacy groups and spearheaded by the Kennedy administration, state and federal government agencies invested in research and public health programs designed to provide specific medical intervention, including universal newborn screening programs for conditions such as phenylketonuria and hypothyroidism. Antibiotic treatment reduced cases of congenital syphilis, vaccines nearly eliminated the birth of infants with congenital rubella syndrome, and various treatments of Rh incompatibility decreased the incidence of ID caused by hyperbilirubinemia. Together, these medical interventions prevented approximately 16.1% of the number of cases of ID that would have occurred without specific medical intervention.

In the next phase of this research, we explored a corollary research question: Did any medical interventions *add* to the number of persons with ID during the past half century? Throughout this period, spectacular advances in surgical techniques and in critical care medicine, especially among neonates, have saved the lives of many infants and children who otherwise would have died. Some of these children have gone on to meet criteria for ID, raising the possibility that medical science may also have unintentionally increased the number of children with ID.

METHODS

Our study consisted of 2 main steps: (1) identification of candidate conditions and (2) estimation of a condition's contribution to the prevalence of ID since 1950.

STEP 1: IDENTIFICATION OF CANDIDATE CONDITIONS

We used data from the most recent epidemiological research on the etiology of ID to identify medical conditions commonly associated with ID. We then determined which of these conditions met all 3 of the following criteria: (1) the condition contributes significantly to the current prevalence of ID (ie, at least 1 peer-reviewed epidemiological study between 1950 and 2000 suggested that the condition is associated with at least 1% of cases of ID in the general population); (2) medical treatment or technology for the condition was introduced between 1950 and 2000; and (3) the medical treatment or technology was demonstrated in at least 1 peer-reviewed study between 1950 and 2000 to significantly reduce condition-specific mortality. We considered premature birth as one such condition, defining it as low birth weight (LBW), or a birth weight less than 2500 g. (In 1950, nearly all states began to include birth weight data on the certificates of live birth; data on other measures of prematurity, such as gestational age, were not consistently available during the study period.[13])

STEP 2: CONTRIBUTION OF CONDITION TO PREVALENCE OF ID

To estimate the change since 1950 for conditions identified in step 1, we used data gathered from existing epidemiological resources to create a 5-decade analysis of the prevalence of ID in children. Methods are described in a previous publication.[12] In brief, we defined ID as a score 2 SDs below the mean on a validated test of cognitive ability. We then used a common set of variables to construct estimates of the condition-specific prevalence of ID since 1950, including incidence and natural history of the condition, the efficacy of the intervention, and the population-wide availability of the intervention. We intended to use these data to estimate the population-attributable risk of each condition to the lifetime prevalence of ID.

To adjust for the effect of changes in treatment-associated mortality on incidence of ID, we conducted a comprehensive literature search for any peer-reviewed studies or review articles on each selected condition that included death as an outcome. To ascertain the association between the condition and ID, we conducted a comprehensive literature search for any studies on each selected condition that included a standardized measure of cognitive ability as an outcome. Because ID is difficult to assess in early childhood, we excluded studies of children who were not evaluated after their sixth birthday. To avoid undue selection bias, we also excluded studies with an attrition rate greater than 30%, studies that excluded low-performing students, and studies that reported results based on cohorts included in other publications.

RESULTS

STEP 1: IDENTIFICATION OF CANDIDATE CONDITIONS

The results of step 1 are listed in **Table 1**. In 3 large population-based studies, children born with LBW (<2500 g) contributed the largest percentage of all patients with ID (10%-15%).[14-16] The neonatal intensive care unit (NICU), an intervention listed in Table 1, includes a broad set of perinatal critical care practices for neonates that have emerged since 1950, with both developments specific to neonatal care, such as intrapartum steroids, positive pressure ventilation, surfactant, and hyperalimentation, and more general medical advances, such as antibiotics, transport systems, and red blood cell transfusions.[17,18] Hypoxic or ischemic birth and perinatal accidents accounted for approximately 5% of cases of ID, and such perinatal events are treated by many of the same interventions as the LBW group. Given changes in terminology for perinatal events, however, as well as emerging ideas about the etiology of ID in such cases, it is not possible to estimate the change in the prevalence of ID caused by perinatal events since 1950. One other candidate condition, meningitis, contributed significantly to the current prevalence of ID (2.1%). As reported elsewhere,[12] however, improved meningitis treatment contributed to a significant and remarkable *decrease* in ID between 1950 and 2000.

STEP 2: CONTRIBUTION OF CONDITION TO PREVALENCE OF ID

The incidence of LBW first peaked in the mid-1960s (8.3%) and then reached a nadir in the early 1980s (6.7%) before beginning to increase in the past 3 decades.[13] A total of 8.18% of live-born neonates in the United States were of LBW in 2008.[19] Mortality rates for LBW infants have declined re-

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Table 1. Condition-Specific Prevalence of ID With Published Source

Condition	Description	Potential Intervention	Total Cases of ID, %	Source
Low birth weight	<2500 g	NICU	15.8	Yeargin-Allsopp et al[14]
			15.4	Croen et al[15]
			10.7	Strømme and Hagberg[16]
Hypoxic or ischemic birth or perinatal event	Intrauterine, intrapartum	OB, NICU	5.2	Yeargin-Allsopp et al[14]
	Perinatal event	OB, NICU	4.5	Strømme and Hagberg[16]
	Neonatal anoxia	NICU	0.1	Yeargin-Allsopp et al[14]
Meningitis	All causes of meningitis (perinatal and postnatal)	Antibiotics, antivirals, antifungals; NICU or PICU	2.1	Yeargin-Allsopp et al[14]
Brain malformations	Hydrocephaly	Surgical repair; NICU or PICU	0.6	Yeargin-Allsopp et al[14]
	Spina bifida	Surgical repair; NICU or PICU	0.3	Yeargin-Allsopp et al[14]
Congenital infections	Congenital infections, unspecified	Antibiotics, antivirals, antifungals; NICU	0.4	Croen et al[15]
	Cytomegalovirus	Antivirals; NICU	0.6	Yeargin-Allsopp et al[14]
	Rubella	NICU	0.6	Strømme and Hagberg[16]
	Rubella	NICU	0.1	Yeargin-Allsopp et al[14]
	Syphilis	Antibiotics, NICU	0.1	Yeargin-Allsopp et al[14]
Infection or parasitic disease	Unspecified	PICU	0.3	Croen et al[15]
	Viral encephalitis	Anitvirals, PICU	0.1	Yeargin-Allsopp et al[14]
Malignancy	Brain tumor	Chemotherapy, radiation, or surgery; PICU	0.3	Yeargin-Allsopp et al[14]
Traumatic brain injury	Head trauma	NICU or PICU	0.8	Yeargin-Allsopp et al[14]
	Postneonatal anoxia	PICU	0.4	Yeargin-Allsopp et al[14]
	Cerebrovascular accident	Thrombolytics, NICU, PICU	0.3	Yeargin-Allsopp et al[14]

Abbreviations: ID, intellectual disability; NICU, neonatal intensive care unit; OB, obstetrical interventions (eg, fetal monitoring and early cesarean section); PICU, pediatric intensive care unit.

markably in the United States, from more than 90% to less than 20% among those with the lowest birth weights.[20-24] Regarding ID as an outcome of LBW, 29 of the 82 published studies reviewed met inclusion and exclusion criteria. The results are shown in **Table 2**. Since 1950, the prevalence of ID in LBW individuals has ranged between 2% and 27%, and ID is correlated with birth weight.

Given the variability in LBW outcomes since 1950, valid estimates of population-attributable risk for the relative contribution of NICUs to the lifetime prevalence of ID could not be performed. Although ID outcome studies in LBW infants appear to be comparable, variability in inclusion criteria (eg, birth weight) and tests used (including consideration of the Flynn effect[25]) make it inappropriate to apply outcomes from single studies to whole populations across several decades.

DISCUSSION

We were unable to estimate with any precision the independent contribution of specific medical interventions to the prevalence of ID. Nonetheless, our study revealed that, among the medical technologies introduced between 1950 and 2000, NICU treatment of LBW infants is the most significant contributor to the increased prevalence of ID. In the first third of the 20th century, the predominant causes of ID were infections and metabolic conditions,[12] and infant mortality was greater than 100 deaths per 1000 live births.[26] By 1960, overall infant mortality dropped to 23.3 per 1000, yet remained high for LBW infants, ranging from 899.1 for birth weights of 500 to 999 g to 61.0 for 2000 to 2499 g.[20] Since 1960, infant mortality rates have declined for all groups, most dramatically for the smallest infants, while the number of LBW infants has increased. These trends led, by the year 2000, to an association with LBW in approximately 10% to 15% of children with ID.

Several limitations reduce our ability to assess the relative contribution of NICU technology to the incidence of ID. There have been no large population-based studies of the etiology of ID in the past decade, so it is possible that very recent advances in NICU care, such as improved ventilation technique and attention to the neonate's developmental environment, may have lowered the contribution of LBW infants to the overall prevalence of ID. On the other hand, aggressive treatment of infants born at still earlier gestations may have increased the prevalence of ID. The data from our study also do not allow us to distinguish between LBW and prematurity or to accurately attribute the contributions of infants with the lowest birth weights. Finally, our study cannot exclude the possibility that some other factor has led to an increase in ID among LBW infants and that the interventions used in the NICU have actually prevented what would have otherwise been a greater increase in the prevalence of ID.

The traditional goals of medicine have been to reduce mortality and to reduce suffering, whereas the goal of public health is to improve the aggregate health of the population. As deaths among children have decreased dramatically during the past century, developmental and behavior outcomes have become more sensitive indicators of child health. Our use of ID in this study as a measure of population health is not meant to diminish the value of the life of a person with a developmental disability, nor do we impugn the dedicated professionals whose remarkable work in NICUs has saved thousands of lives; in contrast, we seek to explore the limits of the biomedical model.

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Table 2. Prevalence of ID in LBW Infants

Year of Birth	Source (Publication Date)[a]	Mean Testing Age, y	Population Birth Weight, g	No. of Children in Study With IQ Data	Children With ID, %
1948-1956	Drillien et al (1961)	School age	≤1360	49	22
1955-1960	Drillien et al (1967)	School age	<1360	48	19
1974-1985	Whitfield et al (1997)	8	<800	115	16 for boys, 12 for girls
1975-1980	Hirata et al (1983)	7	501-750	18	17
1977-1979	Hack et al (2004)	20	<1500	242	8 for boys, 6 for girls
1979-1980	Doyle et al (2001)	14	500-999	79	20
1977-1981	Saigal et al (1991)	8	501-1000	113	8-12
1977-1982	Saigal et al (2003)	8	500-999	155	25
1979-1980	Doyle et al (2005)	8	500-999	87	18
1978-1980	Ross et al (1991)	7-8	≤1500	88	8
1980	Teplin et al (1991)	6	<1001	28	14
1981-1986	Grunau et al (2004)	17	≤800	72	19
1982-1986	Taylor et al (2000)	11	750-1499	55	15
			<750	60	37
1982-1986	Hack et al (1994)	7	<750	68	21
		7	750-1499	65	8
1983	Saigal et al (2003)	10	500-1000	118	26
1980-1987	Resnick et al (1998)	School age	500-749	201	14
			750-999	527	10
			1000-1499	1514	7
			1500-2499	3252	5
1984-1987	Saigal et al (2003)	10	500-1000	83	15
1985-1986	Saigal et al (2003)	9	500-1000	80	27
1985-1986	Stjernqvist et al (1998)	10	500-1480	61	15
1985-1987	Doyle et al (2005)	8	500-999	206	16
1985-1987	D'Angio et al (1998)	7	<1500	127	19
1985-1990	Bowen et al (2002)	8	<1000	82	10
1986-1988	Elgen et al (1991)	11	<2000	130	2
1988-1991	Gabrielson et al (2002)	10	450-1450	43	14
1989-1992	Vohr et al (2003)	8	600-1250	328	8 without IVH, 21-40 with IVH
1987-1989	Chaudhari et al (2003)	12	<2000	180	13
1989-1991	Short et al (2003)	8	<1500	98	20 with BPD,
				75	11 without BPD
1991-1992	Doyle et al (2005)	9	500-999	224	16.5
1992-1995	Drotar et al (2006)	8	<1000	219	15
1995	Marlow et al (2005)	6	<25 wk gestation	241	21

Abbreviations: BPD, bronchopulmonary dysplasia; ID, intellectual disability; IVH, intraventricular hemorrhage; LBW, low birth weight.
[a] References available on request.

This study has several policy implications. Reducing the incidence of LBW, particularly premature birth, has been a focus of US public health efforts for decades, involving the concerted efforts of public health professionals, epidemiologists, maternal and child health practitioners, preventive care specialists, policymakers, advocates, and researchers across many fields. Similarly, research will continue on how to improve long-term developmental outcomes through NICU practice as well as early developmental intervention after hospital discharge. This study highlights the need to continue pursuing these established policy objectives.

This study and related work also reveal the need to reexamine our nation's century-long focus on specific medical interventions, as opposed to social or public health interventions, as the key to improving child and maternal health. For example, there is evidence in the United States and internationally that broad social interventions, such as environmental lead abatement[27,28] and improved nutrition,[29-31] have done more to decrease the prevalence of ID than specific medical interventions. Differences in preconception risk factors, including substance abuse, continue to exacerbate health disparities.[32] During the past decade, several authors[33,34] have called for a "public health approach" to studying ID, concluding that socioeconomic status markers, such as maternal education, must be addressed to confront the continuing high rates of ID in the United States. Both the general association between poverty and ill health,[35] as well as the specific association between ID and maternal factors,[36] have been known for more than a century. The challenge of the 21st century will be to address the factors that improve developmental outcomes for all children.

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REFERENCES

1. Rothman DJ. *Beginnings Count: The Technological Imperative in American Health Care.* New York, NY: Oxford University Press; 1997.
2. Rosenberg CE. Inward vision & outward glance: the shaping of the American hospital, 1880-1914. *Bull Hist Med.* 1979;53(3):346-391.
3. McKeown T. *The Modern Rise of Population.* London, England: Edward Arnold; 1976.
4. McKinlay JB, McKinlay SM, Beaglehole R. A review of the evidence concerning the impact of medical measures on recent mortality and morbidity in the United States. *Int J Health Serv.* 1989;19(2):181-208.
5. Szreter S. The importance of social intervention in Britain's mortality decline c. 1850–1914: a reinterpretation of the role of public health. *Soc Hist Med.* 1988; 1:1-37.
6. Link BG, Phelan JC. McKeown and the idea that social conditions are fundamental causes of disease. *Am J Public Health.* 2002;92(5):730-732.
7. Colgrove J. The McKeown thesis: a historical controversy and its enduring influence. *Am J Public Health.* 2002;92(5):725-729.
8. Szreter S. Rethinking McKeown: the relationship between public health and social change. *Am J Public Health.* 2002;92(5):722-725.
9. Meckel R. *Save the Babies: American Public Health Reform and the Prevention of Infant Mortality.* Baltimore, MD: Johns Hopkins University Press; 1990.
10. Marmot M. Social determinants of health inequalities. *Lancet.* 2005;365(9464): 1099-1104.
11. Marmot MG, Bell R. Action on health disparities in the United States: commission on social determinants of health. *JAMA.* 2009;301(11):1169-1171.
12. Brosco JP, Mattingly M, Sanders LM. Impact of specific medical interventions on reducing the prevalence of mental retardation. *Arch Pediatr Adolesc Med.* 2006; 160(3):302-309.
13. Brosco JP, Sanders LM, Guez G, Lantos JD. Historical trends in low birth weight. *Arch Pediatr Adolesc Med.* 2010;164(1):99-100.
14. Yeargin-Allsopp M, Murphy CC, Cordero JF, Decouflé P, Hollowell JG. Reported biomedical causes and associated medical conditions for mental retardation among 10-year-old children, metropolitan Atlanta, 1985 to 1987. *Dev Med Child Neurol.* 1997;39(3):142-149.
15. Croen LA, Grether JK, Selvin S. The epidemiology of mental retardation of unknown cause. *Pediatrics.* 2001;107(6):E86.
16. Strømme P, Hagberg G. Aetiology in severe and mild mental retardation: a population-based study of Norwegian children. *Dev Med Child Neurol.* 2000;42(2): 76-86.
17. Baker JP. Classics in pediatrics. The smallest preterm infants: reasons for optimism and new dilemmas. *Arch Pediatr Adolesc Med.* 2011;165(8):689-691.
18. Philip AG. The evolution of neonatology. *Pediatr Res.* 2005;58(4):799-815.
19. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Osterman MJ. Births: final data for 2008. *Natl Vital Stat Rep.* 2010;59(1):1-3-71.
20. Buehler JW, Kleinman JC, Hogue CJ, Strauss LT, Smith JC. Birth weight-specific infant mortality, United States, 1960 and 1980. *Public Health Rep.* 1987; 102(2):151-161.
21. Centers for Disease Control and Prevention (CDC). Infant mortality and low birth weight among black and white infants—United States, 1980-2000. *MMWR Morb Mortal Wkly Rep.* 2002;51(27):589-592.
22. Horbar JD, Badger GJ, Carpenter JH, et al; Members of the Vermont Oxford Network. Trends in mortality and morbidity for very low birth weight infants, 1991-1999. *Pediatrics.* 2002;110(1, pt 1):143-151.
23. Horbar JD, Carpenter JH, Badger GJ, et al; Members of the Vermont Oxford Network. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. *Pediatrics.* 2012;129(6):1019-1026.
24. Baker JP. *The Machine in the Nursery: Incubator Technology and the Origins of Newborn Intensive Care.* Baltimore, MD: Johns Hopkins University Press; 1996.
25. Flynn JR. IQ gains over time:ttoward finding the causes. In: Neisser U, ed. *The Rising Curve.* Washington, DC: American Psychological Association; 1998: 25-66.
26. Brosco JP. The early history of the infant mortality rate in America: "a reflection upon the past and a prophecy of the future." *Pediatrics.* 1999;103(2):478-485.
27. Nevin R. Trends in preschool lead exposure, mental retardation, and scholastic achievement: association or causation? *Environ Res.* 2009;109(3):301-310.
28. Warren C. *Brush With Death: A Social History of Lead Poisoning.* Baltimore, MD: Johns Hopkins University Press; 2000.
29. Lynn R. In support of the nutrition theory. In: Neisser U, ed. *The Rising Curve.* Washington, DC: American Psychological Association; 1998:207-218.
30. Martorell R. Nutrition and the worldwide rise in IQ scores. In: Neisser U, ed. *The Rising Curve.* Washington, DC: American Psychological Association; 1998:183-206.
31. Sigman M, Whaley SE. The role of nutrition in the development of intelligence. In: Neisser U, ed. *The Rising Curve.* Washington, DC: American Psychological Association; 1998:155-182.
32. Denny CH, Floyd RL, Green PP, Hayes DK. Racial and ethnic disparities in preconception risk factors and preconception care. *J Womens Health (Larchmt).* 2012;21(7):720-729.
33. Leonard H, Wen X. The epidemiology of mental retardation: challenges and opportunities in the new millennium. *Ment Retard Dev Disabil Res Rev.* 2002; 8(3):117-134.
34. Chapman DA, Scott KG, Stanton-Chapman TL. Public health approach to the study of mental retardation. *Am J Ment Retard.* 2008;113(2):102-116.
35. Coleman W. *Death Is a Social Disease: Public Health and Political Economy in Early Industrial France.* Madison: University of Wisconsin Press; 1982.
36. Zenderland L. *Measuring Minds: Henry Herbert Goddard and the Origins of American Intelligence Testing.* Cambridge, England: Cambridge University Press; 1998.

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