

Correspondence



Outcomes in Young Adulthood for Very-Low-Birth-Weight Infants

To the Editor: Hack et al. (Jan. 17 issue)¹ report that 20-year-olds who had very low birth weight have a lower rate of risk-taking behavior than their normal-birth-weight peers, and the authors describe this finding as “reassuring.” McCormick and Richardson, in their editorial,² suggest that the avoidance of risk-taking behavior indicates a special “resilience” in very-low-birth-weight children and their families.

I disagree. As the parent of a very-low-birth-weight adult, the moderator of an Internet list for parents of preterm children, and the author of a book on prematurity, I am in close contact with many families with very-low-birth-weight children. Our children, even when they do not have major neurosensory handicaps, often have cognitive and behavioral deficits that isolate them from both their peers and their peers’ risk-taking behavior. Our children’s isolation and withdrawal are actually caused by a lack of social and intellectual resilience. As a result, many of us worry that our children will never become fully functioning members of society.

Unfortunately, recent research supports our fears. In a report on a national cohort of prematurely born teens in the Netherlands, Walther et al.³ estimate that, because of social and cognitive problems, 40 percent of very-low-birth-weight children will never live independently. This Dutch cohort was born only a few years later than the group studied by Hack et al. and has a similar rate of neurosensory impairment (10 percent).

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2. McCormick MC, Richardson DK. Premature infants grow up. *N Engl J Med* 2002;346:197-8.
3. Walther FJ, den Ouden AL, Verloove-Vanhorick SP. Looking back in time: outcome of a national cohort of very preterm infants born in the Netherlands in 1983. *Early Hum Dev* 2000;59:175-91.

To the Editor: Hack et al. use either a general equivalency diploma or a standard high-school diploma as a measure of academic achievement. The two are not equivalent.¹ If the authors had used only the latter criterion as a measure of academic success, it is likely that the shortfall in academic achievement among very-low-birth-weight persons would be even more dramatic than that presented. In a nationally representative study,² we found that a low-birth-weight child is 74 percent less likely than his or her normal-birth-weight sibling to complete high school by 19 years of age.

In addition, it is not surprising that the less fortunate very-low-birth-weight adults who have chronic disabilities such as blindness, cerebral palsy, or lung disease would be unlikely to be found on the wrong side of the law. Hack and her colleagues state that the relation persisted when they limited their comparison to healthy very-low-birth-weight adults and normal-birth-weight adults. These results should be presented.

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1. Cameron SV, Heckman JJ. The nonequivalence of high school equivalents. *J Labor Econ* 1993;11:1-47.
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To the Editor: Hack and colleagues state that very-low-birth-weight babies have a significantly lower mean IQ at

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20 years of age than do the members of a control group (87 vs. 92). Although this difference may achieve statistical significance, such a difference is not considered meaningful by those who specialize in assessing cognitive development. Both scores are rated as falling within the average range. IQ scores are not finite measures of a characteristic in a given person; they are merely scores of someone's performance on a given test at a given time and are subject to errors of measurement. In this case, the range of "true" scores results in considerable overlap between the two groups of subjects.

It is known that low-birth-weight babies are at risk for cognitive deficits. What parents of these babies want to know is the nature and extent of this risk. Hack et al. do not emphasize that 120 of the low-birth-weight adults had normal IQs of 85 or higher.

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To the Editor: Hack et al. report higher rates of neurosensory impairment among very-low-birth-weight infants. Since premature infants frequently have retinal problems that may have lifelong consequences, I wonder whether the authors were able to identify visual impairment as one of the serious neurosensory problems.

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The authors reply:

To the Editor: We agree with Harrison that social isolation may have a role in the study subjects' tendency to engage in less risk-taking behavior. However, we do not have information on social relationships.

The estimate of Walther et al. that 40 percent of very-low-birth-weight children will not live independently was based on the responses to questions asked over the telephone of parents of 14-year-old children.¹ We interviewed and tested young adults. Although fewer very-low-birth-weight men than control men were in college, more were working (47 percent vs. 27 percent, $P < 0.01$). Very-low-birth-weight women did not differ significantly from control women in terms of rates of college enrollment or employment. These results indicate that most very-low-birth-weight adults will be able to work and live independently, although men might lag behind in educational attainment.

In response to Conley and Bennett: we performed additional analyses excluding subjects with a general equivalency diploma. The rates of high-school graduation for very-low-birth-weight and normal-birth-weight men were 60 percent and 68 percent, respectively ($P = 0.28$); the rates for women were 77 percent and 84 percent, respectively ($P = 0.07$). When subjects with neurosensory impairment, a subnormal IQ, or both were excluded, the rates of alcohol use for very-low-birth-weight and normal-birth-weight subjects were 69 percent and 84 percent, respectively ($P =$

0.001), and the rates of illicit-drug use were 37 percent and 47 percent, respectively ($P = 0.02$). Fewer men with very low birth weight than with normal birth weight had been in contact with the police for drug-related or alcohol-related offenses (13 percent vs. 29 percent, $P = 0.008$). When we excluded all subjects with chronic conditions (neurosensory, medical, or psychiatric conditions or subnormal IQ), subjects with very low birth weight still had lower rates of alcohol use (68 percent vs. 83 percent, $P = 0.001$) and illicit-drug use (36 percent vs. 49 percent, $P = 0.009$) than normal-birth-weight subjects. Among men, the rates of contact with police for offenses related to drugs or alcohol were 14 percent and 28 percent, respectively ($P = 0.04$).

Tasman asks about visual impairment. Four very-low-birth-weight subjects (1.7 percent) had blindness due to retinopathy of prematurity (bilateral in one subject and unilateral in three).

We agree with Zach that many of the very-low-birth-weight subjects had normal IQs in young adulthood. However, as we noted in the discussion, our results are applicable only to current survivors of neonatal intensive care with birth weights between 1000 g and 1500 g. We have serious concern about children born during the 1990s weighing less than 1000 g, who may not function well as young adults.^{2,3}

In Table 3 of our article, the total number of normal-birth-weight men with postsecondary study should have been 56 rather than 57.

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1. Walther FJ, den Ouden AL, Verloove-Vanhorick SP. Looking back in time: outcome of a national cohort of very preterm infants born in the Netherlands in 1983. *Early Hum Dev* 2000;59:175-91.

2. Hack M, Wilson-Costello D, Friedman H, Taylor GH, Schluchter M, Fanaroff AA. Neurodevelopment and predictors of outcomes of children with birth weights of less than 1000 g: 1992-1995. *Arch Pediatr Adolesc Med* 2000;154:725-31.

3. Vohr BR, Wright LL, Dusick AM, et al. Neurodevelopmental and functional outcomes of extremely low birth weight infants in the National Institute of Child Health and Human Development Neonatal Research Network, 1993-1994. *Pediatrics* 2000;105:1216-26.

The editorialists reply:

To the Editor: Ms. Harrison offers an alternative hypothesis for the relative absence of risk-taking behavior observed in the group of young adults studied by Hack et al. Both our somewhat more optimistic hypothesis of resilience and hers of social isolation are testable in follow-up studies of very-low-birth-weight children now approaching adulthood. Her letter underscores the importance of not simply reporting on the outcomes of these vulnerable children, but also exploring the mechanisms that cause them, as we have argued elsewhere.¹ Well-targeted interventions have been demonstrated to effect changes in preschool cognitive and behavioral outcomes in very-low-birth-weight children.² Understanding the mechanisms behind other adverse out-

comes could lead to the development of strategies for amelioration.

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1. McCormick MC. Conceptualizing child health status: observations from studies of very premature infants. *Perspect Biol Med* 1999;42:372-86.
2. McCormick MC, McCarton C, Tonascia J, Brooks-Gunn J. Early educational intervention for very low birth weight infants: results from the Infant Health and Development Program. *J Pediatr* 1993;123:527-33.

Oral and Topical Corticosteroids in Bullous Pemphigoid

To the Editor: Joly et al. (Jan. 31 issue)¹ report mortality rates among patients with bullous pemphigoid that are substantially higher than those in four previous British and American studies (a one-year mortality rate of 19 percent, a two-year mortality rate of 6 percent, and three-year mortality rates of 28 percent and 30 percent²) but similar to that in another French study (a one-year mortality rate of 41 percent³), suggesting that survival of patients with bullous pemphigoid may vary according to the ethnic background. Thus, the findings reported by Joly et al. cannot be extrapolated to all patients with bullous pemphigoid, and additional randomized trials are necessary for validation.

With regard to the editorial by Stern,⁴ since linear deposition of IgG and C3 are found in the epidermal basement membrane in patients with diseases other than bullous pemphigoid, indirect immunofluorescence studies of salt-split skin, not positive histopathological studies demonstrating such deposition, are considered to be the diagnostic standard.² One study found that 15 percent of patients with linear IgG or C3 deposits in the basement membrane had epidermolysis bullosa acquisita or bullous systemic lupus erythematosus.⁵ Although patients with cicatricial pemphigoid, linear IgA disease, or chronic bullous disease of childhood may uncommonly have autoantibodies against type VII collagen, most would classify these patients as having epidermolysis bullosa acquisita. LAD-1 is part of bullous pemphigoid antigen 2,⁶ not a 97-kD protein distinct from bullous pemphigoid antigen 2. Bullous pemphigoid and herpes gestationis are not immunologically identical, since patients with herpes gestationis have specific HLA associations, avid complement-fixing IgG antibodies, and linear C3 deposits, whereas patients with bullous pemphigoid have no HLA associations, less avid complement-fixing IgG antibodies, and linear deposits of C3 and IgG.

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1. Joly P, Roujeau J-C, Benichou J, et al. A comparison of oral and topical corticosteroids in patients with bullous pemphigoid. *N Engl J Med* 2002; 346:321-7.

2. Korman NJ. Bullous pemphigoid: the latest in diagnosis, prognosis, and therapy. *Arch Dermatol* 1998;134:1137-41.
3. Roujeau J-C, Lok C, Bastuji-Garin S, Mhalla S, Enginger V, Bernard P. High risk of death in elderly patients with extensive bullous pemphigoid. *Arch Dermatol* 1998;134:465-9.
4. Stern RS. Bullous pemphigoid therapy — think globally, act locally. *N Engl J Med* 2002;346:364-7.
5. Vaillant L, Bernard P, Joly P, et al. Evaluation of clinical criteria for diagnosis of bullous pemphigoid. *Arch Dermatol* 1998;134:1075-80.
6. Zone JJ, Taylor TB, Meyer LJ, Petersen MJ. The 97 kDa linear IgA bullous disease antigen is identical to a portion of the extracellular domain of the 180 kDa bullous pemphigoid antigen, BPAG2. *J Invest Dermatol* 1998;110:207-10.

To the Editor: A recent systematic review of treatments for bullous pemphigoid¹ highlights the increased mortality associated with higher doses of oral prednisolone. There is good evidence to support the use of 20 to 40 mg of prednisolone (0.5 mg per kilogram of body weight) in combination with topical therapy and other nontoxic antiinflammatory drugs, such as minocycline and nicotinamide.^{1,2} Given that Joly et al. did not compare prednisone at a dose of 1 mg per kilogram per day with prednisone at a dose of 0.5 mg per kilogram per day for the treatment of extensive bullous pemphigoid, one cannot conclude that the lower dose would not be appropriate. Further evaluation is required to determine the optimal dose and the optimal proportions of corticosteroids to be delivered by the oral and topical routes.

The serious drawback to topical therapy alone in the study by Joly et al. was that some patients required nursing assistance. The authors do not report the number of patients who required such care or the cost of delivery. We do not believe that the main conclusion, that oral corticosteroids are no longer justified for treatment of severe bullous pemphigoid, is correct.

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To the Editor: An overlooked explanation for the finding that clobetasol, a highly potent topical corticosteroid, is as effective as prednisone for the treatment of bullous pemphigoid is that the medication is absorbed through the skin, resulting in blood corticosteroid levels similar to those achieved by systemic therapy.

Topically applied clobetasol is absorbed rapidly; 12.5 mg applied to normal skin results in peak plasma levels one fourth as high as those attained with 10 mg of prednisone (i.e., 6 to 7 ng per milliliter vs. 24.5 ng per milliliter).^{1,2} Blood levels in patients with bullous pemphigoid are probably higher than that, since corticosteroid absorption is increased by a factor of 16 when skin is blistered,³ as it is in this disease. Furthermore, the potency of clobetasol is much