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Original article

Population impact of preterm birth and low birth weight on developmental disabilities in US children

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ABSTRACT

Purpose: Although previous studies demonstrate associations between adverse perinatal outcomes and developmental disabilities (DDs), study of population impacts is limited.
Methods: We computed relative risks adjusted (aRRs) for sociodemographic factors and component and summary population attributable fractions (PAFs) for associations between very low birth weight (VLBW, all preterm births), moderately low birth weight (MLBW) + Preterm, MLBW at term, and normal birth weight (NBW) + Preterm and seven DDs (cerebral palsy [CP], autism spectrum disorder [ASD], intellectual disability [ID], behavioral-conduct disorders, attention-deficit-hyperactivity disorder [ADHD], learning disability [LD], and other developmental delay) among children aged 3–17 years in the 2011–2012 National Survey of Children's Health.
Results: VLBW-Preterm, MLBW-Preterm and NBW-Preterm were strongly to moderately associated with CP (aRRs: 43.5, 10.1, and 2.2, respectively; all significant) and also associated with ID, ASD, LD, and other developmental delay (aRR ranges: VLBW-Preterm 2.8–5.3; MLBW-Preterm 1.9–2.8; and NBW-Preterm 1.6–2.3). Summary PAFs for preterm birth and/or LBW were 55% for CP, 10%–20% for ASD, ID, LD, and other developmental delay, and less than 5% for ADHD and behavioral-conduct disorders. Findings were similar whether we assessed DDs as independent outcomes or within mutually exclusive categories accounting for DD co-occurrence.
Conclusions: Preterm birth has a sizable impact on child neurodevelopment. However, relative associations and population impacts vary widely by DD type.

Introduction

Developmental disabilities (DDs) are chronic conditions associated with significant impairments in physical, cognitive, behavioral, and/or speech/language functioning. The prevalence of DDs in US children is estimated at 15% overall [1] and ranges from less than 1% (e.g., cerebral palsy [CP]) [2] to 9% (e.g., attention-deficit-hyperactivity disorder [ADHD]) [3]. In addition to functional limitations, children with DDs have increased prevalence of many health conditions including asthma, eczema, gastrointestinal disorders, and obesity [4,5]. Although the causes of a few DDs are well defined (e.g., intellectual disability [ID] linked to select genetic conditions or fetal alcohol syndrome), for most DDs, etiology is complex and multifactorial [6–10].

Although numerous studies document associations between preterm birth (PTB) and low birth weight (LBW) and DDs such as CP [8,11,12], ID [12–17], autism spectrum disorder (ASD) [12,13,18], ADHD [12,19,20], learning disability (LD) [12,21], and general developmental delay [12,22,23], there is limited assessment of population impacts. Studies of population attributable fractions (PAFs) in US populations include an assessment of the Georgia Pregnancy Risk Assessment Monitoring System which estimated 42% of CP cases and 13% of ID cases were attributable to LBW [24], an assessment of North Dakota registry data which estimated 8% of ASD cases were attributable to low gestation and 8% were attributable to LBW [25], and an assessment of the Autism and Developmental Disabilities Monitoring Network which estimated 12% of ASD cases were attributable to PTB, LBW, and Cesarean delivery [26]. Studies from other countries of the impacts of various

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pregnancy complications and/or outcomes on ASD [27], ADHD [20], and developmental delays [28] reported moderate PAFs for the various perinatal factors studied. These past studies had notable limitations. Most did not assess the known overlap between the perinatal factors studied, all only assessed one or two DDs, and none assessed potential effects from co-occurring DDs. A high proportion of children with DDs meet diagnostic criteria for multiple DDs [29,30]. Boulet et al. [29] reported that 43%–96% of US children with specific DD diagnoses had more than one DD diagnosis.

Using data from the 2011–2012 National Survey of Children's Health (NSCH), we assessed associations and population impacts of PTB and LBW on subsequent DDs including CP, ID, ASD, ADHD, LD, behavioral or conduct problems or disorder (BCD), and other developmental delay. In addition to assessing a broad array of DDs side by side, we designed analyses to account for DD co-occurrence and examined a finer gradation of PTB and LBW risk than prior studies. To our knowledge, this is the largest and most comprehensive assessment of PAFs for DDs in a US population and the first-to-consider DD co-occurrence.

Materials and methods

Study population

The NSCH is a periodic random-digit-dial health survey of US noninstitutionalized children. Households are the primary sampling unit; from contacted households with children, one child is randomly selected. The survey is administered to a parent or guardian knowledgeable about the selected child's health. The overall response rate for the 2011–2012 NSCH was 23% [31]. Nonresponse was more common for cell-phone numbers than landlines. Among contacted households with children, the interview completion rate was 54% and 41% for landline and cell-phone calls, respectively. An empiric assessment indicated that sampling weight nonresponse adjustment greatly reduced the maximum estimated bias for key survey indicators [31].

Sample selection

From the 95,677 completed 2011–2012 NSCH interviews, we initially selected 81,590 children 3–17 years of age. We excluded younger children because most DDs are not diagnosed before the age of 3 years. We additionally excluded children missing data on DDs, birth weight, PTB, sex, and race-ethnicity, and children with implausible birth weight-PTB data. Our final sample size was 74,565.

Ascertainment and categorization of DDs

We assessed CP, ASD, ID, BCD, ADHD, LD, and other developmental delay. Each DD was ascertained using two questions: "Has a doctor or other health care provider ever told you that [CHILD] had [CONDITION], even if [he/she] does not have the condition now?" and "Does [CHILD] currently have [CONDITION]?" Verbiage for the initial LD question was expanded slightly to include school officials in addition to health care providers. We classified children as having a given DD if the parent/guardian responded affirmatively to both questions.

To account for DD co-occurrence, we created mutually exclusive DD outcomes. For children for whom more than one DD was reported, the following order of precedence was used to determine the mutually exclusive outcome assignment: CP-ASD-ID-BCD-ADHD-LD-other developmental delay. With this ordering, DDs that typically have the most pervasive functional impacts and most well-established associations with LBW and PTB are given preference [11–16,29]. ASD was given preference over ID because a previous analysis demonstrated that associations between PTB/LBW and ASD with ID were more comparable to associations for ASD only than ID only [13]. This ordering also allowed us to assess the "other developmental delay" category without the contributing effects of other specific diagnoses.

Parents who reported their child had a DD were asked to rate the severity level (mild, moderate, or severe). No instructions were provided about how to assign the rating. We categorized each DD as mild or moderate-severe. We combined moderate and severe ratings because of sample size constraints and empirical assessments which indicated comparability in the results for these two categories.

Perinatal risk factors

Respondents were asked: "What was [CHILD]'s birth weight?" and "Was [CHILD] born prematurely, that is, more than 3 weeks before [his/her] due date?" Response options for the birth weight question allowed for reporting in pounds, ounces, or grams. All data were converted to grams for analysis. We classified children as very LBW (VLBW)-Preterm ($<$1500 g, PTB = yes); moderately LBW (MLBW)-Preterm (1500–2499 g, PTB = yes); MLBW-Term (1500–2499 g, PTB = no); normal birth weight (NBW)-Preterm ($\geq$2500 g, PTB = yes); or NBW-Term ($\geq$2500 g, PTB = no). NBW-Term served as the referent category. All VLBW births included in this analysis were preterm. We excluded 121 children (0.15%) classified as both VLBW and term as implausible because birth weights less than 1500 g are less than the third percentile of the expected birth weight distribution at 37 or more weeks' gestation [32].

Potential confounders

Potential confounders were child age, sex, race-ethnicity, maternal education, and maternal age at child's birth. Because for both maternal age and education, there were moderate numbers of missing values, we created separate "missing" categories rather than exclude these children.

Statistical analyses

In initial analyses, we compared distributions of potential confounders across the mutually exclusive DD groups and tested for general statistical differences using χ^2 tests.

For core analyses, we assessed each DD two ways: as independent outcomes without consideration of co-occurring DDs and within the mutually exclusive categories that accounted for DD co-occurrence. For each DD outcome, we computed proportionate distributions of birth weight and gestational age and constructed logistic regression models to calculate adjusted relative risks (aRRs) and 95 percent confidence intervals (CIs) for associations with birth weight-gestational age factors. Using those data, we computed adjusted component PAFs which estimate population impact of each birth weight-gestational age factor on each DD outcome and summary PAFs which estimate the combined population impact of being born either LBW or PTB. CIs around PAF estimates were calculated using the Bonferroni inequality method [33].

In supplemental analyses, we estimated PAFs for mild versus moderate or severe DDs. Given the large US racial disparity in PTB [34], we also separately assessed non-Hispanic white (NHW) and non-Hispanic black (NHB) children. We did not examine other racial-ethnic subgroups because of sample size constraints. Subgroup analyses were based on DD outcomes without consideration of co-occurring DDs.