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# Disparities in infant mortality from all-infectious, vaccine-preventable, and non-vaccine preventable diseases in relation to parental education

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ABSTRACT

*Background:* The burden of infectious diseases in infants is substantial. Parental education has been considered as a critical factor for predicting infant mortality. However, even though some studies have been done about relationship between infectious disease and parent's education level, no researches have been conducted specifically about vaccine-preventable and non-vaccine-preventable disease mortality by parent's educational level.
*Purpose:* This study aimed to compare infant mortality rates from all-infectious diseases, vaccine-preventable and non-vaccine-preventable diseases by mother's and father's education levels.
*Methods:* We used 2017 US Linked Birth and Infant Death Data from National Center for Health Statistics, which included 3,153,574 live births and 13,870 deaths.

To identify the association between each mother's and father's education level and all-infectious disease, vaccine-preventable disease, and non-vaccine-preventable disease infant mortality, logistic regression analyses were conducted by using educational level 1 as the reference. All-infectious diseases, vaccine-preventable and non-vaccine-preventable diseases were identified by vaccination recommendation of 2017 CDC guideline. Education levels were classified into four groups: level 1, through 12th grade with no diploma; Level 2, high school graduate or GED completed; Level 3, some college credit but no degree or associate degree; and Level 4, bachelor's degree, master's degree, doctorate or professional degree.
*Results:* Higher parents' education level was appreciably associated with lower infant mortality from all-cause, all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases. Moreover, each mother's and father's education level was correlated to infant mortality due to vaccine-preventable diseases on the whole education level, while all-infectious disease and non-vaccine-preventable disease mortality is related with parent's education level only if their education level is fairly high. In other words, the adjusted odds for vaccine-preventable disease mortality were significantly lower than that for all-infectious and non-vaccine-preventable disease mortality at education level 2 and 3 and still smaller at education level 4.
*Conclusion:* These finding implies that each mother's and father's higher education level was associated with lower infant mortality rate from all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases. Furthermore, each level of mother's and father's education was more likely to be related to infant mortality by vaccine-preventable diseases than that of infant mortality by all-infectious diseases, and non-vaccine-preventable diseases.



## 1. Introduction

Infants are highly susceptible to infection because of their immature immune system [1]. Despite the great advances that have taken place in controlling infectious diseases [2,3], the

*Abbreviations:* BMI, body mass index; CI, confidence interval; CDC, Centers for Disease Control and Prevention; GED, general educational development; Hib, haemophilus influenzae type B; ICD, international classification of diseases; NICU, neonatal intensive care unit; OR, odds ratio; PCV, pneumococcal conjugate vaccine; RR, relative risk.

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infection-associated disease burden in infants stemming from length of hospital stay and related costs remains substantial [4].

Vaccination is one of the most effective ways of preventing and controlling infectious diseases in infants and young children [1]. For example, McGovern (2015) found that children with complete vaccination coverage had a lower relative risk (RR) of mortality (RR = 0.73; 95% CI 0.68–0.77) than those with no vaccination [5]. Therefore, if vaccines exist for a given infectious disease, the primary concern becomes assessing the most important factors for successful immunization rates to reduce vaccine-preventable disease mortality among children. It is likewise necessary to investigate how to reduce non-vaccine-preventable disease mortality in children.

Undoubtedly, optimal compliance that produces high coverage and timely vaccination is a critical part of the response to vaccine-preventable diseases [6]. Also, household economic status has significant effects on children's health outcomes due to disparities in the accessibility and availability of medical resources [7]. For example, vaccine compliance is great when parental education level is high, and low levels of maternal education are associated with suboptimal compliance [8–10]. As might be expected, household economic status has a positive relationship to parents' education level [11], which in turn has a positive influence on vaccine compliance. Thus, parental education is an important variable to evaluate the risk of infant mortality from infectious diseases.

Many recent studies have focused on the relationship between only maternal education level, not that of both parents, and children's mortality [12,13] indicating that maternal education is the best predictor of health inequalities in children [14,15]. There are no data that show an association between paternal educational attainment and infant mortality from vaccine-preventable and non-vaccine-preventable diseases. Some studies have highlighted parental education as a contributing factor in immunization compliance, but they have not drawn any separate conclusions on the effects of parental education level on mortality from both vaccine-preventable and non-vaccine-preventable diseases [16]. As mortality is a more serious and ultimate health event than vaccine compliance for children's health outcomes, it is necessary to investigate separate effects on mortality from both vaccine-preventable and non-vaccine-preventable diseases in terms of mother's and father's education levels. This approach may help produce measurements or make more efficient plans to monitor infant mortality from infectious diseases. In this study, we compared rates of infant mortality from all-infectious, vaccine-preventable and non-vaccine-preventable diseases with respect to mother's and father's education levels.

## 2. Methods

### *2.1. Data source and study population*

We used national data from 2017 US Linked Birth and Infant Death Data set from the National Center for Health Statistics at the Centers for Disease Control and Prevention (CDC). These data covered all births occurring in the US and matched death certificates for each infant aged <1 year. In 2017, 99.6% of infant death certificates were successfully linked with a birth certificate. The data set included demographic and health information on all births collected from vital statistics from 2017 in all 50 states, the District of Columbia. This file provided maternal and paternal sociodemographic characteristics, basic and pregnancy-related maternal health condition, previous obstetric history, labor- and delivery-related complications, infant health condition, and birth outcome.

A total of 3,864,754 live births and 22,197 unweighted infant deaths were included [17]. Due to the heterogeneity between single and multiple births, we excluded twin, triplets or other multiple births (n = 132,536). We also excluded 578,644 individuals who had missing information on parental education level, maternal characteristics, or infant characteristics. After this, the final sample births were 3,153,574 infants (Fig. 1).

## 3. Maternal and paternal education level

The original data set categorized parental education level into completed 8th grade or less, 9th through 12th grade with no diploma, high school graduate or GED completed, some college credit but no degree, associate degree (AA, AS), bachelor's degree (BA, AB, BS), master's degree (MA, MS, MEng, MEd, MSW, MBA), doctorate (PhD, EdD), and professional degree (MD, DDS, DVM, LLB, JD). We re-categorized these into level 1 (through 12th grade with no diploma), level 2 (high school graduate or GED completed), level 3 (some college credit but no degree or associate degree), and level 4 (bachelor's degree, master's degree, doctorate or professional degree).

## 4. Infant mortality from all-cause and all-infectious diseases

Infant mortality was defined as death from day of birth to the 365th day. Infant mortality was classified as all-cause mortality, all-infectious disease mortality, vaccine-preventable disease mortality, and non-vaccine-preventable disease mortality. The International Classification of Diseases, Tenth Revision (ICD-10), provided 130 selected causes of infant death that were used to classify diseases into all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases (Table 1). Vaccine-preventable diseases were defined as those infectious diseases that can be prevented or alleviated by vaccines within the childhood immunization schedule of the first 12 months. For all diseases for which the vaccines require multiple doses to have a full effect, if the first dose is to be given within the first 12 months, we refer to them as vaccine-preventable, regardless of whether the second or later dose schedules fall within first year or not.

In the 2017 CDC recommendations for childhood and adolescent immunization schedule, we identified the following vaccines for children younger than or equal to 1 year: hepatitis A and B; rotavirus; diphtheria; tetanus; acellular pertussis; haemophilus influenzae type B (Hib); pneumococcal conjugate vaccine (PCV); inactivated polio; influenza; measles, mumps, and rubella; varicella; and meningococcal diseases [18]. Even though the Bacillus Calmette–Guérin vaccine is recommended for infants in many developing and developed countries, including China, India, Singapore, South Korea, and New Zealand, it is not included in the US CDC guideline [19]. Therefore, we exclude Bacillus Calmette–Guérin vaccine in the vaccine-preventable disease list.

## 5. Covariates

Other variables of interest included maternal and infant demographics, basic and pregnancy-related clinical health conditions, and payment information. The maternal demographic variables were age (≤24, 25–29, 30–34, or ≥ 35 years) and ethnicity (whites, blacks, Hispanics, or others). BMIs were categorized into four groups: underweight (<18.5 kg/m$^2$), normal weight (18.5–24.9 kg/m$^2$), overweight (25.0–29.9 kg/m$^2$), or obese (≥30.0 kg/m$^2$). The categories of prenatal care initiation were 1st trimester, 2nd trimester, 3rd trimester, or no prenatal care. Maternal smoking in pregnancy, pregestational or gestational diabetes, and pregestational or gestational hypertension or eclampsia were assessed as

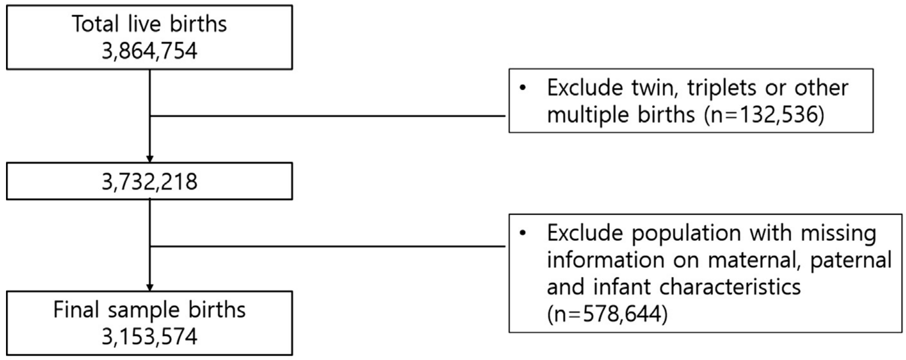


**Fig. 1.** Flow chart of the study population.

**Table 1**
Infectious disease classification* for infant.

| Vaccine-preventable disease | Vaccine-unpreventable disease |
|---|---|
| Certain intestinal infectious diseases (A00-A08) | Certain infectious and parasitic diseases (A00-B99) |
| Diarrhea and gastroenteritis of infectious origin (A09) | Tuberculosis (A16-A19) |
| Tetanus (A33,A35) | Septicemia (A40-A41) |
| Diphtheria (A36) | Congenital syphilis (A50) |
| Whooping cough (A37) | Gonococcal infection (A54) |
| Meningococcal infection (A39) | Viral diseases (A80-B34) |
| Acute poliomyelitis (A80) | Human immunodeficiency virus (HIV) disease (B20-B24) |
| Varicella (chickenpox) (B01) | Other and unspecified viral diseases (A81-B00,B02-B04,B06-B19,B25,B27-B34) |
| Measles (B05) | Candidiasis (B37) |
| Mumps (B26) | Malaria (B50-B54) |
| Meningitis (G00,G03) | Pneumocystosis (B59) |
| Influenza and pneumonia (J10-J18) | All other and unspecified infectious and parasitic diseases (A20-A32,A38,A42-A49, A51-A53,A55-A79,B35-B36,B38-B49,B55-B58,B60-B99) |
| Influenza (J10-J11) | Pericarditis, endocarditis and myocarditis (I30,I33,I40) |
| Pneumonia (J12-J18) | Acute upper respiratory infections (J00-J06) |
| | Acute bronchitis and acute bronchiolitis (J20-J21) |
| | Bronchitis, chronic and unspecified (J40-J42) |
| | Pneumonitis due to solids and liquids (J69) |
| | Newborn affected by chorioamnionitis (P02.7) |
| | Congenital pneumonia (P23) |
| | Infections specific to the perinatal period (P35-P39) |
| | Bacterial sepsis of newborn (P36) |
| | Omphalitis of newborn with or without mild hemorrhage (P38) |
| | All other infections specific to the perinatal period (P35,P37,P39) |

* This classification was based on pathogens targeted by CDC guidelines for the Recommended Childhood and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2017.

yes or no. Health insurance coverage was assessed as payment sources: Medicaid, private insurance, self-pay, or others. Infant characteristics included sex (boy or girl), live birth order (1st, 2nd, 3rd, 4th or higher), and perinatal complications such as Neonatal Intensive Care Unit (NICU) admission record, and antibiotics administration record, assessed as yes or no.

### *5.1. Statistical analysis*

We performed chi-square tests to compare the maternal and infant characteristics according to infant mortality. The all-cause, all-infectious disease, vaccine-preventable disease, and non-vaccine-preventable disease mortality rates for infants were computed as the number of each kind of death before 1 year of age divided by the total number of live births and multiplied by 1,000. To identify the association between parent's education level and each infant mortality, unadjusted and adjusted logistic regression analyses were conducted. Logistic regression models were adjusted for multiple covariates, including the maternal characteristics of age, race, BMI, prenatal care initiation, smoking status, pregestational or gestational diabetes, pregestational or gestational hypertension or eclampsia, and the infant confounding factors of sex, live birth order, NICU admission record, and antibiotics administration record. Using educational level 1 as the reference, odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated for level 2, 3, and 4. All analysis were performed using SAS 9.4 software (SAS Institute, Cary, NC, USA), and the threshold for statistical significance was set at $\alpha$ = 0.05.

## 6. Results

Table 2 presents the maternal and infant characteristics by total delivery, all-cause mortality, all-infectious disease mortality, vaccine-preventable disease mortality, and non-vaccine-preventable disease mortality. Among 3,153,574 infants delivered in 2017, 13,870 infant deaths were found, where 1,237 infants died of infectious diseases. Those infectious disease deaths were composed of 257 vaccine-preventable disease and 980 non-vaccine-preventable disease deaths. Infant deaths were more likely to occur for mother who were younger than 24 years old (5.61), were black (8.09), were obese (5.80), did not initiate prenatal care (19.35), were cigarette smokers (8.55), had pre-gestational, gestational hypertension and eclampsia (5.67), and care paid for Medicaid (5.59) or self-pay (4.62). Infants who had a birth-order number of 4 or higher birth order (5.91), NICU admission record (23.49) or antibiotics administration record (22.17) were more susceptible to death. A similar trend in mother and infant characteristics was observed for all-infectious disease mortality. A comparison of demographic characteristics between vaccine-preventable and non-vaccine-preventable disease mortality showed that the mothers whose infants died from vaccine-preventable diseases were more likely to be obese (0.12), cigarette smokers (0.18), hypertension (0.16), Medicaid (0.12) or self-payer (0.12) and their infants were tended to be fourth or higher in the birth order (0.12).

Table 3 shows the rates of infant mortality (per 1000 live births) from all-cause, all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases relative to the parent's education level. Mothers and fathers at education level 4 showed the lowest rates for all-cause mortality (2.87 and 2.74), all-infectious disease mortality (0.24 and 0.23), vaccine-

**Table 2**
Characteristics of mothers and infants according to total delivery, all-cause mortality, all-infectious disease mortality, vaccine-preventable disease mortality and vaccine-unpreventable disease mortality for infant and their rates per 1000 live births unit: no (%).

| Characteristics | No (%) of infant delivery | No (%) of infant death | | | |
|---|---|---|---|---|---|
| | | All-cause[a)] | All-infectious disease[b)] | Vaccine-preventable disease[c)] | Vaccine-unpreventable disease[d)] |
| | (n = 3,153,574) | (n = 13,870) | n = 1,237 | n = 257 | n = 980 |
| Mother | | | | | |
| Age | | | | | |
| ≤24 | 693,412 | 3,891 (5.61) | 360 (0.52) | 83 (0.12) | 277 (0.40) |
| 25–29 | 928,310 | 3,901 (4.20) | 343 (0.37) | 68 (0.07) | 275 (0.30) |
| 30–34 | 948,683 | 3,533 (3.72) | 302 (0.32) | 64 (0.07) | 238 (0.25) |
| 35≤ | 583,169 | 2,545 (4.36) | 232 (0.40) | 42 (0.07) | 190 (0.33) |
| Race | | | | | |
| whites | 1,761,495 | 6,677 (3.79) | 512 (0.29) | 110 (0.06) | 402 (0.23) |
| blacks | 374,467 | 3,030 (8.09) | 292 (0.78) | 63 (0.17) | 229 (0.61) |
| Hispanics | 269,585 | 975 (3.62) | 112 (0.42) | 18 (0.07) | 94 (0.35) |
| others | 748,027 | 3,188 (4.26) | 321 (0.43) | 66 (0.09) | 255 (0.34) |
| BMI | | | | | |
| underweight | 101,369 | 469 (4.63) | 35 (0.35) | 5 (0.05) | 33 (0.33) |
| normal | 1,388,165 | 5,091 (3.67) | 443 (0.32) | 89 (0.06) | 354 (0.25) |
| overweight | 832,748 | 3,491 (4.19) | 301 (0.36) | 67 (0.08) | 234 (0.28) |
| obesity | 831,292 | 4,819 (5.80) | 458 (0.55) | 96 (0.12) | 362 (0.44) |
| Prenatal care initiation | | | | | |
| 1st trimester | 2,524,424 | 10,266 (4.07) | 948 (0.38) | 189 (0.07) | 759 (0.30) |
| 2nd trimester | 474,964 | 2,462 (5.18) | 210 (0.44) | 50 (0.11) | 160 (0.34) |
| 3rd trimester | 118,844 | 458 (3.85) | 17 (0.14) | 4 (0.03) | 13 (0.11) |
| non | 35,342 | 684 (19.35) | 62 (1.75) | 14 (0.40) | 48 (1.36) |
| Cigarette smoking | | | | | |
| no | 2,982,756 | 12,410 (4.16) | 1,122 (0.38) | 227 (0.08) | 895 (0.30) |
| yes | 170,818 | 1,460 (8.55) | 115 (0.67) | 30 (0.18) | 85 (0.50) |
| Diabetes mellitus[e)] | | | | | |
| no | 2,917,615 | 12,894 (4.42) | 1,144 (0.39) | 236 (0.08) | 908 (0.31) |
| yes | 235,959 | 976 (4.14) | 93 (0.39) | 21 (0.09) | 72 (0.31) |
| Hypertension[f)] | | | | | |
| no | 2,890,640 | 12,379 (4.28) | 1,067 (0.37) | 215 (0.07) | 852 (0.29) |
| yes | 262,934 | 1,491 (5.67) | 170 (0.65) | 42 (0.16) | 128 (0.49) |
| Health insurance coverage | | | | | |
| Medicaid | 1,194,333 | 6,682 (5.59) | 581 (0.49) | 140 (0.12) | 441 (0.37) |
| Private insurance | 1,705,652 | 6,028 (3.53) | 540 (0.32) | 91 (0.05) | 449 (0.26) |
| Self-pay | 130,644 | 603 (4.62) | 61 (0.47) | 16 (0.12) | 45 (0.34) |
| Others | 122,945 | 557 (4.53) | 55 (0.45) | 10 (0.08) | 45 (0.37) |
| Infant | | | | | |
| Sex | | | | | |
| boy | 1,614,726 | 7,723 (4.78) | 693 (0.43) | 155 (0.10) | 538 (0.33) |
| girl | 1,538,848 | 6,147 (3.99) | 545 (0.35) | 102 (0.07) | 442 (0.29) |
| Live birth order | | | | | |
| 1st | 1,194,811 | 5,281 (4.42) | 508 (0.43) | 88 (0.07) | 420 (0.35) |
| 2nd | 1,042,952 | 3,975 (3.81) | 312 (0.30) | 66 (0.06) | 246 (0.24) |
| 3rd | 540,911 | 2,397 (4.43) | 236 (0.44) | 59 (0.11) | 177 (0.33) |
| 4th or higher | 374,900 | 2,217 (5.91) | 181 (0.48) | 44 (0.12) | 137 (0.37) |
| NICU admission | | | | | |
| no | 2,891,623 | 7,718 (2.67) | 530 (0.18) | 107 (0.04) | 423 (0.15) |
| yes | 261,951 | 6,152 (23.49) | 707 (2.7) | 150 (0.57) | 557 (2.13) |
| Antibiotics administration | | | | | |
| no | 3,086,002 | 12,372 (4.01) | 1,013 (0.33) | 213 (0.07) | 800 (0.26) |
| yes | 67,572 | 1,498 (22.17) | 224 (3.31) | 44 (0.65) | 180 (2.66) |

a) All p-values of all-cause mortality versus maternal and infant characteristics were < 0.05.
b) All p-values of all-infectious disease mortality versus maternal and infant characteristics were < 0.05 except diabetes mellitus.
c) All p-values of vaccine-preventable disease mortality versus maternal and infant characteristics were < 0.05 except diabetes mellitus.
d) All p-values of vaccine-unpreventable disease mortality versus maternal and infant characteristics were < 0.05 except diabetes mellitus and sex.
e) Yes, if mother had pregestational or gestational diabetes mellitus.
f) Yes, if mother had pregestational or gestational hypertension or eclampsia.

preventable disease mortality (0.05 and 0.04), and non-vaccine-preventable disease mortality (0.19 and 0.20). Moreover, these rates gradually increased as mother and father's education level fell

Table 4 and Fig. 2 shows the unadjusted and adjusted OR (95% CI) between parent's education level and infant mortality due to all-causes, all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases, by using educational level 1 as the reference. If we do not focus on statistical significance of ORs on this observational study, both lower unadjusted and adjusted ORs of mortality due to all-infectious, vaccine-preventable and non-vaccine-preventable diseases were associated with mother's and father's higher education level [20]. By adjustment, ORs of infectious disease mortality for mother and ORs of non-vaccine-preventable disease mortality for father at education level 3 became statistically non-significant, while ORs of vaccine-preventable disease mortality remained statistically significant at the same education level.

**Table 3**
Infant mortality rates (per 1000 live births) by mother's and father's education level.

| Educational level | Level 4 | Level 3 | Level 2 | Level 1 |
|---|---|---|---|---|
| Mother | | | | |
| All-cause | 2.87 | 4.62 | 5.68 | 6.17 |
| All-infectious disease | 0.24 | 0.44 | 0.51 | 0.56 |
| Vaccine-preventable disease | 0.05 | 0.07 | 0.10 | 0.17 |
| Vaccine-unpreventable disease | 0.19 | 0.36 | 0.41 | 0.38 |
| Father | | | | |
| All-cause | 2.74 | 4.32 | 5.61 | 5.75 |
| All-infectious disease | 0.23 | 0.39 | 0.49 | 0.55 |
| Vaccine-preventable disease | 0.04 | 0.07 | 0.10 | 0.16 |
| Vaccine-unpreventable disease | 0.20 | 0.32 | 0.39 | 0.39 |

Level 1, through 12th grade with no diploma; Level 2, high school graduate or GED completed; Level 3, some college credit but no degree or associate degree; and Level 4, bachelor's degree, master's degree, doctorate or professional degree.

**Table 4**
ORs* (95% CIs) for infant mortalities by mother's and father's education level.

| Infant mortality | Level 4 | | Level 3 | | Level 2 | | Level 1 | |
|---|---|---|---|---|---|---|---|---|
| | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
| Mother | | | | | | | | |
| All-cause | 0.46 (0.44–0.49) | 0.61 (0.57–0.65) | 0.75 (0.71–0.79) | 0.8 (0.76–0.85) | 0.92 (0.87–0.97) | 0.92 (0.87–0.97) | 1 (reference) | |
| All-infectious disease | 0.43 (0.35–0.51) | 0.56 (0.45–0.70) | 0.78 (0.66–0.93) | 0.84 (0.70–1.01) | 0.91 (0.77–1.08) | 0.92 (0.77–1.10) | 1 (reference) | |
| Vaccine-preventable disease | 0.27 (0.19–0.39) | 0.51 (0.32–0.81) | 0.43 (0.30–0.61) | 0.52 (0.36–0.76) | 0.58 (0.41–0.81) | 0.61 (0.43–0.86) | 1 (reference) | |
| Vaccine-unpreventable disease | 0.50 (0.40–0.62) | 0.60 (0.46–0.78) | 0.95 (0.77–1.16) | 0.98 (0.79–1.22) | 1.06 (0.87–1.30) | 1.06 (0.86–1.31) | 1 (reference) | |
| Father | | | | | | | | |
| All-cause | 0.48 (0.45–0.50) | 0.64 (0.60–0.69) | 0.75 (0.71–0.79) | 0.83 (0.79–0.88) | 0.98 (0.93–1.02) | 0.96 (0.92–1.01) | 1 (reference) | |
| All-infectious disease | 0.43 (0.35–0.51) | 0.60 (0.48–0.74) | 0.71 (0.60–0.84) | 0.80 (0.67–0.96) | 0.90 (0.76–1.05) | 0.90 (0.76–1.06) | 1 (reference) | |
| Vaccine-preventable disease | 0.25 (0.17–0.37) | 0.43 (0.27–0.69) | 0.44 (0.31–0.62) | 0.54 (0.37–0.80) | 0.67 (0.49–0.91) | 0.68 (0.49–0.95) | 1 (reference) | |
| Vaccine-unpreventable disease | 0.50 (0.40–0.61) | 0.66 (0.51–0.84) | 0.82 (0.67–0.99) | 0.90 (0.73–1.11) | 0.99 (0.82–1.19) | 0.98 (0.81–1.19) | 1 (reference) | |

*ORs was adjusted for maternal characteristics (i.e., age, race, BMI, prenatal care initiation, smoking status, pregestational or gestational diabetes, pregestational or gestational hypertension or eclampsia) and infant characteristics (i.e., sex, live birth order, gestational age, and SGA).
Level 1, through 12th grade with no diploma; Level 2, high school graduate or GED completed; Level 3, some college credit but no degree or associate degree; and Level 4, bachelor's degree, master's degree, doctorate or professional degree.

ORs for education level 2 were almost close to 1 except that of vaccine-preventable disease mortality, which were far smaller 1 (adjusted model of vaccine-preventable diseases at education level 2: for mother OR = 0.61, 95% CI 0.43–0.86, for father OR = 0.68, 95% CI 0.49–0.95).

While ORs of all-infectious disease, and non-vaccine-preventable disease mortality were smaller at education level 4 than at education level 2 and 3 regardless of statistical significance, ORs of vaccine-preventable disease mortality were much smaller than ORs for all-infectious disease and non-vaccine-preventable disease mortality at education level 2 and 3, and were still smaller at education level 4 (adjusted model of vaccine-preventable diseases; at education level 2: for mother OR = 0.61, 95% CI 0.43–0.86, for father OR = 0.68, 95% CI 0.49–0.95; at education level 3: for mother OR = 0.52, 95% CI 0.36–0.76, for father OR = 0.54, 95% CI 0.37–0.80; at education level 4: for mother OR = 0.51, 95% CI 0.32–0.81, for father OR = 0.43, 95% CI 0.27–0.69).

When comparing ORs for mothers and fathers, the results show that ORs for all-infectious, vaccine-preventable disease, and non-vaccine-preventable disease mortality were similar to each other.

## 7. Discussion

In a large and representative data set for US infants, we found that parents' education level was significantly associated with

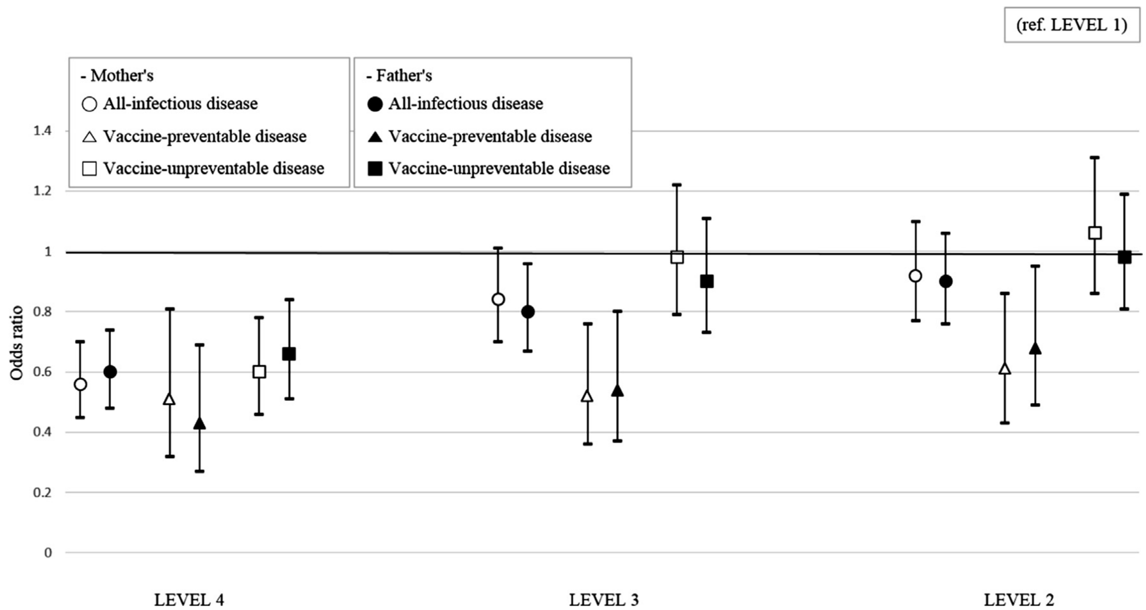


**Fig. 2.** ORs (95% CI) for infant mortality according to mother's and father's education level. Level 1, through 12th grade with no diploma, was designated as a reference group. Level 2, high school graduate or GED completed; Level 3, some college credit but no degree or associate degree; and Level 4, bachelor's degree, master's degree, doctorate or professional degree.

infant mortality from all-cause, all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases. Moreover, each mother's and father's education level was more likely to be related to the infant mortality due to vaccine-preventable diseases than that of infant mortality due to all-infectious diseases, and non-vaccine-preventable diseases. The adjusted odds for vaccine-preventable disease mortality were significantly lower in mothers and fathers with education level 4 than with education level 1 by 49% and 57%. This strong relationship was already shown at the education level 2 & 3, where each OR of vaccine-preventable disease mortality were 0.61 & 0.52, and 0.68 & 0.54 for mothers and fathers, respectively. Even though adjusted odds for all-infectious disease and non-vaccine-preventable disease mortality were fairly lower in mothers and fathers with education level 4 than with education level 1, the association were weaker at education level 3 than at education level 4 and were not clear at education level 2. We also noted statistically significant odds of vaccine-preventable disease mortality in infants whose parent's education was level 2 and 3, whereas this was not a significant factor for all-infectious diseases and non-vaccine-preventable diseases when the parent's educational attainment was level 2.

Much attention has been paid to parent's educational level, especially the mother's education, as a key indicator predicting infant survival [12,13]. Our study found that higher levels of mother' and father's education were associated with reduced overall infant mortality. Of note are the differential effects of parent's education on vaccine-preventable and not non-vaccine-preventable disease related health outcomes. This means that vaccine-preventable disease mortality was influenced by parent's education level to a larger extent, while total infectious disease and non-vaccine-preventable disease mortality were relatively less affected by the parent's education level. We cannot be certain why vaccine-related infant deaths vary depending on parental education level; however, differences in vaccine compliance or economic status may be a clue.

For vaccine-preventable diseases, the factors that increase vaccine compliance in terms of both high immunization coverage and timeliness are especially important. Luman et al. (2005) examined the timeliness of receipt of vaccination for each recommended vaccine among US children aged 19 to 35 months. More than 1 in 3 children were undervaccinated for more than 6 months during their first 24 months of life, and more than half of children received multiple vaccines late. That study examined maternal factors leading to underimmunization and found that mothers who were not college graduates were associated with severely delayed vaccination [8]. This is consistent with our work, in that mother's education level from education level 1 to education level 4 is negatively correlated with the ORs of vaccine-preventable disease mortality, which could be explained by better vaccine compliance. Ultimately, higher levels of parent's education may play a positive role in eliminating barriers to vaccination, such as by decreasing misconceptions regarding vaccine side effects and invalidity and placing a higher priority on children's vaccination in daily life and overcoming religious convictions that produce vaccine refusal [9,21].

For all-infectious disease and non-vaccine-preventable disease mortality, regardless of intermediate factors between vaccine-preventable disease mortality and parent's education level discussed above, the household economic level, which are greatly determined by the education level, can affect children's health through a disparity of accessibility and availability of medical resources, resulting in the unmet medical needs for the children of poor income families [11]. For example, compared to children with private health insurance, children who had no health insurance were six times more likely to get along without medical services and four times as inclined to have their care delayed [7]. This is evident from the fact that those with low incomes, are at the high risk of being uninsured [22]. Therefore, we might guess that unlike vaccine-preventable disease mortality, which is relatively more influenced by vaccine compliance, household income level seems to be a primary determining factor for all-infectious disease and non-vaccine-preventable disease mortality. Moreover, because nowadays nearly half of mothers were sole or primary breadwinners, contributing at least half of family income, we found no big difference between all-infectious and non-vaccine-preventable disease infant mortality according to each mother's and father's education level [23].

To the best of our knowledge, this is the first study to show effect of different magnitudes of mother's and father's education level on infant mortality from all-infectious diseases, vaccine-preventable diseases and non-vaccine-preventable diseases. Several limitations of our study should be addressed. Firstly, our concern was with mortality from vaccine-preventable and non-vaccine-preventable diseases, but no one-to-one relationship was obvious in the data between vaccines and the targeted diseases. Thus, if a disease is mainly caused by certain specific virus or bacteria, which in turn can be prevented or eliminated by vaccines, we classified it as a vaccine-preventable disease. For example, Rota virus is the most common cause of severe gastroenteritis in infants and children such that it is responsible for up to 500,000 diarrheal deaths each year worldwide [24]. Streptococcus pneumonia is the most common cause of bacterial pathogen of community acquired pneumonia for children and PCV is used to protect infants against diseases caused by the bacterium Streptococcus pneumonia (*S. pneumonia*) [25]. For infants and children aged < 5 years, the three most common causes of bacterial meningitis and sepsis were Hib, *S. pneumonia*, and Neisseria meningitides (*N. meningitides*), and Meningococcal vaccine refers to the vaccines used to prevent infection by *N. meningitides* [26]. On the other hand, if an infectious disease is not predominantly attributed to specific pathogen, we determined it as a non-vaccine-preventable disease. This approach should be reviewed using specific pathogen data in future studies. Secondly, vaccination effects take time to be seen. It is known that early protective efficacy, known as a primary immune response peak, appears 2 weeks after getting a vaccine to develop antibodies and memory cells [27]. Because the early protective effect is primarily provided by the induction of antigen-specific antibodies, it is reasonable to suppose that the time required for the vaccination effect may be short in reference to infant death [28]. Thirdly, high education level is not always a promoter of vaccination for children and rather could be a barrier of vaccination [29]. In a US study by Feifei Wei et al., 2009′s paper, however, acknowledged that ambiguous definition of vaccine refusal, defined as true vaccine refusal plus medical contraindication, might cause uncertainty of the result which asserts that caregivers' higher education might lead to vaccine hesitancy for their children [30]. Moreover, the conclusion was derived from 6-year-children and did not have meaningful result for 2-year-children. Thus, further research about the relationship between a parent's high education level and vaccine refusal for their infant should be required. Fourthly, we used the 2017 US infant birth and linked death data, so our results may not be generalizable to other countries or to other time periods. Moreover, the exclusion of missing data from the analysis and some of the imputed values in the data set may lead to distortion in the relationship between education level and mortalities. We excluded 578,644 infants due to missing data, accounting for approximately 15% of original total live births. Finally, we did not consider various factors affecting infant mortality, such as the environment (e.g., air pollution or accessibility to medical facilities), religion (e.g., resistant to invasive medical treatment). Therefore, future studies should consider these additional variables and clarify the causal link between parent's education level and infant mortality.

In conclusion, each higher level of mother's and father's education was associated with lower infant mortality rate from all-infectious diseases, vaccine-preventable diseases, and non-vaccine-preventable diseases. Moreover, each mother's and father's education level was more likely to be related to infant mortality by vaccine-preventable diseases than that of infant mortality by all-infectious diseases, and non-vaccine-preventable diseases. Therefore, we might expect that vaccine-preventable disease mortality may be reduced more efficiently by improvements to the parent's education level. Our results might imply that improvement programs for parent's education level would be very efficacious measures to reduce vaccine-preventable disease mortality. In addition, promoting intervention of intermediate factors linking parent's education and infant infectious disease mortality may be helpful. For instance, reminder system that relate to children's immunization schedule, public education program for vaccines schedules or vaccine benefits and safety, and financial support for medical expenses regarding vaccination and emergent infectious diseases may be promising measures for improving immunization rates.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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**Institution and Ethics approval and informed consent:** IRB review and approval were not needed because the source of this study data is public and analysis of the data will not make the data individually identifiable.

## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2021.08.009.

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