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Disparities in the Context of Opportunities for Cancer Prevention in Early Life

Greta M. Massetti, PhD, **Cheryll C. Thomas, MSPH**, and **Kathleen R. Ragan, MSPH, CHES**
Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

Persistent health disparities are a major contributor to disproportionate burden of cancer for some populations. Health disparities in cancer incidence and mortality may reflect differences in exposures to risk factors early in life. Understanding the distribution of exposures to early life risk and protective factors for cancer across different populations can shed light on opportunities to promote health equity at earlier developmental stages. Disparities may differentially influence risk for cancer during early life and create opportunities to promote health equity. Potential risk and protective factors for cancer in early life reveal patterns of disparities in their exposure. These disparities in exposures can manifest in downstream disparities in risk for cancer. These risk and protective factors include adverse childhood experiences; maternal alcohol consumption in pregnancy; childhood obesity; high or low birth weight; benzene exposure; use of assisted reproductive technologies; pesticide and insecticide exposure; isolated cryptorchidism; early pubertal timing; exposure to radiation; exposure to tobacco in utero and in early life; allergies, asthma, and atopy; and early exposure to infection. Disparities on the basis of racial and ethnic minority status, economic disadvantage, disability status, sex, geography, and nation of origin can occur in these risk and protective factors. Vulnerable populations experience disproportionally greater exposure to risk factors in early life. Addressing disparities in risk factors in early life can advance opportunities for prevention, promote health equity, and possibly reduce risk for subsequent development of cancer.

Differences in cancer incidence and death rates may be explained by disparities in exposures to risk factors that, in turn, manifest in differential health outcomes, for example, by sex, age, education, income, social class, disability, geographic location, and immigration status.[1] Disparities can also occur in risk factors for cancer. In this article, we examine the ways various populations experience differential exposure to risk for cancer during early life. By identifying disparities within certain risk factors that occur in utero or in childhood, we may

Address correspondence to Greta M. Massetti, PhD, Division of Cancer Prevention and Control, 4770 Buford Hwy NE, MS K76, Atlanta, GA 30341. gmassetti@cdc.gov.

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be able to identify opportunities for cancer prevention during early life. In this article, we highlight factors that were selected on the basis of several criteria. The factors we examined (1) occurred in early life (in the prenatal period through age 10); (2) were identified by a group of subject matter experts consulting with the Centers for Disease Control and Prevention (CDC)[2]; and (3) had at least 1 meta-analysis that demonstrated an empirical association with cancer occurrence. Based on these criteria, we selected the following factors: adverse childhood experiences[3]; maternal alcohol consumption in pregnancy[4]; assisted reproductive technology (ART)[5, 6]; childhood obesity[7, 8]; high or low birth weight[9–11]; exposure to radiation,[12, 13] benzene,[14, 15] pesticides, or insecticides[16–19]; isolated cryptorchidism[10, 20]; early onset of puberty[21–23]; exposure to parental tobacco smoke in utero[24, 25] and in childhood[26]; allergies, asthma, and atopy[27–29]; and early exposure to infection and early day care.[30] Table 1 summarizes information on the timing of potential exposure to each of these factors, the associated cancers, and the cited meta-analyses revealing associations between the factors and the cancer outcome. In some cases, the exposure to the risk or protective factor occurs in utero through maternal exposure, whereas for other factors the exposure occurs in childhood. We summarized the demographic (racial and ethnic minority; sex; disability status; age; Table 2) and contextual (economic disadvantage; geographic differences; nation of origin status; Table 3) disparities in the occurrence of these risk and protective factors. We conclude by exploring opportunities to advance health equity by lessening disparities in exposure to risk factors and promoting cancer prevention in early life, thereby potentially reducing cancer health disparities.

DISPARITIES IN EARLY LIFE RISK FACTORS FOR CANCER

Adverse Childhood Experiences

Adverse childhood experiences result in significant levels of harmful stress among children, and include child maltreatment, loss of a parent, exposure to interparental violence, parental drug or alcohol abuse, parental depression, and parental imprisonment.[95] Most of the work has focused on child maltreatment, which has multiple negative effects on health (including cancer), both immediate and long-term (Table 1). The CDC defines child maltreatment as any act of commission or omission by a parent or other caregiver that results in harm, potential for harm, or threat of harm to a child, including neglect and physical and sexual abuse.[96] Substantial evidence exists that maltreatment causes “toxic stress” that can disrupt the development of the nervous and immune systems and increase risk for health problems throughout development and into adulthood.[31, 95, 97] Findings indicate that such toxic stress has detrimental effects on developing chemical, hormonal, and physiologic systems that help individuals adapt to stressful events.[3,95,97–99]

Studies have identified populations that bear a disproportionate burden of child maltreatment. Younger children are at increased risk for physical abuse, and abusive head trauma is a major cause of injury in young children.[38] Children with certain disabilities are also more likely to experience physical abuse and neglect,[31] particularly those whose disabilities increase caregiver burden.[36, 37] In the United States, girls are at higher risk of sexual abuse victimization, but other types of abuse occur similarly for boys and girls.[35] The occurrence of abuse is associated with economic disadvantage. Physically abusive parents are more likely to be poor and unemployed and to have less education than parents who are not abusive.[31] Single mothers in the United States are more likely to report using harsh physical abuse than 2-parent families.[32] Communities with high unemployment rates and poverty experience higher rates of abuse.[33] Geographic differences within the United States have not been studied to yield conclusive assessments because of state-by-state variation in definition of and data collection procedures for child abuse. Although some studies have revealed that racial and ethnic minorities and first-and second-generation immigrants are at increased risk for child maltreatment, other studies revealed that the relationship weakened or disappeared after adjusting for other sociodemographic characteristics, suggesting that socioeconomic status (SES) or related sociodemographic factors account for the relationship between race, ethnicity, and immigration status and child maltreatment risk.[34] Although boys have a greater risk for physical abuse internationally, conclusive research on sex disparities in the United States is lacking.

Maternal Alcohol Consumption During Pregnancy

The CDC recommends abstaining from alcohol consumption if a woman is pregnant or might be pregnant (including women who are trying to become pregnant), but a substantial proportion of women in the United States continue to drink during pregnancy.[39, 40] Some studies have revealed that non-Hispanic white women are more likely to drink any alcohol or binge drink during their pregnancy compared with women of other racial/ethnic groups in the United States, whereas others have not revealed racial differences.[39, 40] Several studies have revealed that pregnant women who are employed, unmarried, college graduates, or have incomes of at least $50 000 are more likely to consume alcohol.[39, 40] National trends revealed that pregnant women 35 years and older are 2 to 3 times more likely to drink any alcohol during pregnancy compared with those 24 years and younger.[39, 40] However, results from a study of 3 rural states revealed that women who were between 21 and 25 years old, unemployed, unmarried, and had either low ($0–$20 000) or high income ($50 000+) were more likely to drink while pregnant.[41] Alcohol consumption among pregnant women varied by state.[40, 74] Compared with women born in Mexico, Mexican-American women born in the United States are more likely to drink alcohol during pregnancy.[75]

ART

Use of ART has increased steadily in the United States, contributing to 1.5% of births nationally.[100] ART in the United States reveals demographic and contextual patterns of use that imply differences in exposure risk. Nationally, women under age 35 have the highest prevalence of ART utilization, whereas women over age 44 have the lowest.[42] However, in some states, more embryo transfer procedures are performed among women aged 35 to 40 years than among younger age groups.[77] These patterns suggest geographic variation in ART use. ART procedures are expensive and are often excluded from insurance policies; as such, women who receive ART tend to have higher education, work full time, and have higher incomes.[76] We were unable to find data on differences in ART use for women with disabilities, or disparities in nation of origin.

Childhood Obesity

Obesity in childhood may increase the risk for multiple cancers in adulthood.[7, 8] Significant disparities in childhood obesity rates are present on the basis of age, sex, race and ethnicity, economic disadvantage, geography, and nation of origin. Obesity prevalence increases with age and the prevalence is higher among Hispanics and non-Hispanic blacks and lowest among non-Hispanic Asians compared with non-Hispanic whites.[43] Childhood obesity varied by the adult head of household's education level with higher prevalence among those who did not complete high school compared with those who completed college.[43] Non-Hispanic white children whose head of household completed college have the lowest prevalence of obesity.[43] Although patterns vary across development, boys have higher rates of obesity than girls overall.[44] For geographic disparities, there are differences in prevalence of obesity by state,[78] and first-generation immigrant children have lower rates of childhood obesity than native-born US children have.[79] Rates of obesity for children with disabilities are 38% higher than for children without disabilities[45]; children with mobility limitations and intellectual disabilities are at greatest risk.[46, 47]

Birth Weight

Rates of low birth weight are higher among non-Hispanic black infants than non-Hispanic white and Hispanic infants,[48] whereas rates of high birth weight are highest among American Indian and Alaska Native infants compared with white, Hispanic, Asian or Pacific Islander, and black infants.[49] Male infants are more likely to be high birth weight.[50] Women younger than 25 and older than 45 are more likely to have low birth weight infants, across all races and ethnicities,[48] and older women have higher rates of high birth weight.[51] There are also socioeconomic disparities in risk for low birth weight. Women who are single or have lower educational attainment are more likely to have low birth weight infants,[80] whereas married women are more likely to have high birth weight infants.[81] Some states, such as Alabama, Louisiana, and Mississippi, have higher rates of low birth weight births than the national average.[48] Compared with women born in Mexico, US-born Mexican-American women are at a higher risk of delivering low birth weight infants.[75]

Benzene

Environmental benzene exposure from tobacco smoke, fuel evaporation at gasoline filling stations, and industrial sources is absorbed by inhalation or direct skin contact, binds strongly to brain and fatty tissues, and can cross the placenta.[101] Among boys and girls aged 6 to 11, higher levels were found in non-Hispanic white children compared with non-Hispanic Asian children, with no differences by sex.[52] Among adults, higher benzene exposures were found among Mexican Americans compared with non-Hispanic whites and non-Hispanic blacks, those with less than a high school education compared with those with a high school diploma or greater, and those with a lower family income compared with those with higher incomes.[52] These differences in exposure among adults could indicate similar patterns of exposure for children. Variations in benzene exposure by census tracts have been found through spatial correlation analyses.[82]

Pesticides (Including Herbicides and Insecticides)

Pesticide exposure may occur indirectly from parental exposure or directly through their own contact indoors or outdoors.[17] With pesticide use higher in agricultural and rural and inner city areas than in urban or suburban areas, disparities exist in exposure to pesticides by race/ethnicity and urban/rural status. Children in rural and inner-city areas have higher rates of exposure to pesticides.[84] Bio-monitoring studies have revealed higher pesticide levels among Mexican Americans and non-Hispanic blacks compared with high income, non-Hispanic whites, as a result of geographic distribution of residence.[53] Children of farmers may have more exposure to pesticides than children whose parents are not farmers.[85, 86] Additional disparities by sex, SES, and nativity (foreign-born versus US-born) status exist for parents, which in turn indicate disparities in exposure for their children. On average, farmworkers are foreign-born men and have not completed high school.[83]

Isolated Cryptorchidism

Cryptorchidism (undescended testicles) affects ~3% to 6% of term and 30% of preterm male newborns and is the most common congenital abnormality of the male genitourinary tract in the United States. Although some predisposing factors for cryptorchidism have been identified (such as prematurity and low birth weight), research on potential underlying disparities is limited. Preliminary research in a study with a small sample size suggested lower prevalence among African Americans than whites.[54] Risk factors and associated characteristics appear to differ for white and black mothers with sons diagnosed with cryptorchidism.[54] Because white men have higher testicular cancer rates than men of other races/ethnicities, more research is needed to explore whether the possible association between cryptorchidism and testicular cancer differs by race or ethnicity. Women who are younger and those who have had no previous births are more likely to have a child with cryptorchidism.[55] Limited information is available on economic disadvantage and cryptorchidism; 1 study in Denmark revealed an association,[87] but these findings have not been replicated in the United States.

Early Pubertal Onset

Meta-analyses and systematic reviews have documented a possible link between early pubertal onset and cancer risk.[21–23] Young age at menarche is associated with increased risk for breast cancer in girls, as is peak height velocity, or the maximum rate of growth in stature during a growth spurt.[21] There are a number of racial and ethnic differences in pubertal onset for both boys and girls. Compared with white or Hispanic boys, black boys have the lowest average age of pubertal onset.[23] Black girls initiate puberty 1 year earlier than white girls, on average.[56–61] The American Academy of Pediatrics has revealed that all pubertal milestones were achieved earlier in black children compared with whites, controlling for height and weight.[57] Similar differences between black and white children were found in data from the third NHANES,[62] with Mexican American children similar to white children.[56] Lower parental SES is associated with earlier pubertal onset for both boys and girls.[88] Racial and socioeconomic disparities in earlier onset of puberty among girls may be influenced by higher rates of obesity, exposure to endocrine-disrupting chemicals, and stress among black and Hispanic girls and those who are poor.[89] Children with neurodevelopmental disabilities are more likely to experience early puberty.[63]

Radiation

Exposure to ionizing and nonionizing radiation occurs through natural and manmade sources.[102, 103] Because radiation is all around us,[102] disparities related to radiation exposure are more challenging to identify. Exposure to nonionizing radiation comes through high-voltage power lines, transformers, and domestic electrical appliances, with variations in duration and distance from the source with exposure measurements for studies varying over time.[12] Because ionizing radiation is used for medical tests such as radiographs, computed tomography scans, and positron emission tomography scans, exposure is dependent on having these tests. For children who do obtain these tests, lower doses while maintaining clinical benefit may lower risk for cancers.[104] A proxy measure for overexposure to UV radiation is sunburn, and disparities have been observed by race/ethnicity (higher percentages among non-Hispanic whites compared with other races/ethnicities), sex (girls compared with boys), and SES (higher SES compared with lower SES).[64, 65] Because UV exposure also varies by region, geographic disparities are present.[90]

Parental Tobacco Use During the Prenatal Period

Smoking harms nearly every part of the body, including male and female reproductive organs.[105] Paternal smoking is not generally measured, but a study on expectant fathers revealed that smoking did not change significantly from pregnancy to postpartum. For their partners, smoking was significantly lower during pregnancy than postpartum.[106] Disparities in maternal tobacco use by race/ethnicity, SES, urban and rural status, disability, geography, and nativity status exist. Higher percentages of smoking before and during pregnancy were found among American Indian/Alaska Native women compared with other races and ethnicities, women with <12 years of education compared with women with higher education levels, and among women with Medicaid compared with women with other insurance coverage.[66] Pregnant women who live in rural areas, who have disabilities, and who were born in the United States are more likely to smoke compared with women who live in urban areas,[91] who do not have disabilities,[68] and who were born outside the United States.[93] Variations by state were observed in PRAMS, the Pregnancy Risk Assessment Monitoring System.[66]

Environmental Tobacco Exposure During Childhood

Safe levels of environmental tobacco smoke (or secondhand smoke) do not exist and harmful health effects have been observed in children and adults.[107, 108] Variability in secondhand smoke exposure is found by state on the basis of indoor air laws.[92] Additional disparities are found by race and ethnicity, sex, SES, and nativity status. Serum cotinine levels that indicate tobacco smoke exposure among nonsmokers were higher among African American children ages 3 to 11 years than other race and ethnicity groups and higher among those living in lower poverty areas than those living in other poverty areas.[67] Secondhand smoke exposure is higher among English-speaking households compared with Spanish-speaking households.[94]

Allergies, Asthma, and Atopy

Children who are non-Hispanic black have higher rates of asthma than non-Hispanic whites, whereas the relationship is reversed for respiratory allergies. Hispanic children have the lowest rates of both asthma and respiratory allergies. Boys have higher rates of asthma and respiratory allergies than girls, and children older than age 5 have higher rates of both asthma and respiratory allergies than children age 4 and younger. Poor children have higher rates of asthma than the near-poor or nonpoor, and rates of respiratory allergies are lowest among poor children.[69–71] The protective effects of allergies and asthma may be reflected in the epidemiology of the cancers with which they are associated.[109]

Early Exposure to Viral Infection

Research has focused on day care attendance as a proxy measure for actual exposure to viruses. Day care participation has revealed some demographic differences in the families who use day care in early life. A 2005 study of children in northern and central California noted that day care attendance lowered risk of acute lymphocytic leukemia (ALL) in white children,[72] but not in Hispanic children, suggesting potential environmental or biological factors that influence the association between day care attendance and risk of ALL. The proportion of children in day care increases as they get older.[73] Among children ages birth through 4 years whose mother is employed, black children are the most likely to be in day care, whereas Hispanic children are the least likely. Poor children are less likely than children in families with higher incomes to participate in day care in center-based settings. The patterns in higher use of day care among white children and boys mirror the incidence of ALL, in that rates of ALL are higher among white children and boys.[73]

DISCUSSION

In our review and summary of disparities within early life risk factors for cancer, we identified 5 overarching themes that emerge in the literature. The first theme involved the substantial attention that has been paid to documenting disparities on the basis of racial or ethnic minority status, as well as disparities by SES or poverty. Relatively less research is available on sex- and age-related disparities and those due to geographic differences. We found consistent research to suggest that racial and ethnic minority status and low SES/ poverty are associated with greater exposure to early life risk factors for cancer, including adverse childhood experiences, childhood obesity, birth weight, benzene exposure, pesticide exposure, early pubertal timing, and exposure to tobacco in utero and in early childhood. Public health efforts are needed to promote health equity and access to quality health care and social services for populations that experience disproportionate levels of exposure to risk factors. We also note that racial and ethnic minority status and SES may co-occur, yet much of the research has not disentangled the impacts by risk factors. In addition, they have received the greatest levels of research scrutiny, so there is more depth in the literature on these factors.

The second theme involved several prenatal and perinatal risk factors, including alcohol and tobacco consumption in pregnancy, ART use, isolated cryptorchidism, benzene exposure during pregnancy, and birth weight. This clustering emphasizes the critical importance of the prenatal period in promoting health in utero and throughout the life span. Public health efforts focused on improving maternal and infant health factors could contribute to cancer prevention in early life and over the life span.

The third theme relates to the gaps in research that were identified, both within risk factors and across risk factors. There are a number of understudied factors that may contribute to disparities in risk factors for cancer in early life. We found 2 areas that merit attention to identify vulnerable populations: disability-associated disparities and nativity status-related disparities. Approximately 1 in 5 adults in the United States has a disability.[110] We identified research on disability-related disparities in child abuse, childhood obesity, and pubertal timing. Improvements in the health and wellness of people with disabilities can be made by examining their health status and the extent to which they experience disparities in cancer risk factors early in life. The foreign-born population in the United States was ~12.9% (~40 million persons) in 2010, and has grown over the past 40 years.[111] Approximately 25% of children in the United States have at least 1 foreign-born parent. Despite the growing proportion of children who are either foreign-born or have foreign-born parents, disparities in early life risk factors for cancer among this population have not received much attention. We found studies that addressed disparities in nation of origin among Hispanic or Mexican American populations for maternal alcohol consumption during pregnancy, childhood obesity, birth weight, and pesticide exposure. Among these risk factors, first-generation immigrants have lower rates of childhood obesity than native-born children, and pregnant women who were not born in the United States are less likely to smoke, drink alcohol, and have low birth weight infants. Therefore, there appear to be some protective effects among Mexican American first-generation immigrants in early life risk factors for cancer. However, children of immigrants have higher exposure to pesticides, likely as a result of their parents' occupational exposures or geographic residence. Data on disparities within risk factors related to disability and nation of origin could shed additional light on important opportunities to promote health equity among these populations.

The fourth theme involves distinguishing between modifiable and nonmodifiable risk factors. By understanding how risk factors are disproportionally distributed by demographic and contextual characteristics, we can begin to shed light on the mechanisms that underlie the associations between certain risk factors and cancer. Ultimately, it can also lead us to identifying opportunities to reduce or eliminate disparities by placing emphasis on modifiable risk factors and indicate a path toward advancing health equity through reduction of disproportionate exposure to those factors among the most vulnerable populations.

The fifth theme involves the co-occurrence of risk factors for cancer in early life. Although risk and protective factors are often studied independently with adjustments made for other co-occurring risk factors, we must keep in mind that many of the underlying disparities within those risk factors are also interrelated, and the relationships among them are difficult to disentangle. For example, although the causal nature of the association between childhood obesity and pubertal onset is unclear, girls who are obese tend to have earlier pubertal onset.[111] Most of the data on this association come from cross-sectional studies, which do not address the question of whether differences in body mass predate the onset of puberty or whether pubertal changes drive disparate fat patterns across race and ethnicity. In addition, pregnant women who drink alcohol are also more likely to use tobacco. In the largest population-based multisite case-control study in the United States, women who smoked during pregnancy were twice as likely to drink alcohol and 3 times as likely to binge drink when compared with nonsmokers, regardless of race/ethnicity.[40] Disparities in alcohol and tobacco use among pregnant women may be interrelated, and certain populations could have additive or multiplicative risk on the basis of the co-occurrence of these risk factors. Additional research is needed to identify how disparities in exposure to co-occurring risk factors are manifested. For example, disparities in quality of and access to health care are likely to contribute to the association between several risk factors. For example, there are higher rates of childhood obesity, low birth weight, and exposure to tobacco smoke among low-income children, who are less likely to have access to health care to address obesity, prevent low birth weight, and provide counseling for tobacco cessation.

Additional Considerations

There are a number of limitations and considerations in our discussions. First, we mainly focused our review on US-based studies, to constrain the context of the studies in the literature. The findings may not generalize to populations outside of the United States. Second, many of the risk factors are interrelated or co-occur, as we have discussed, and tend to cluster among high-risk populations, and it is difficult to disentangle their relationship with cancer outcomes. Therefore, the disparities in risk factor occurrence are not meant to be interpreted independently. Third, there are some challenges in separating prenatal risk factors and disparities within them as they could relate to maternal health or maternal behaviors or to infant-related health. Fourth, the findings presented here are based on a narrative review. The review intends to highlight areas where opportunities to gain an understanding of how cancer disparities may occur as a function of disparities early in life. It is not intended to provide a thorough, systematic review of all risk factors for cancer or all possible disparities in those factors. Finally, we highlight disparities in early life risk factors for cancer; we did not examine the disparities in cancer outcomes themselves. The discussion is meant to inform our understanding of the potential for disparities in cancer by understanding the potential for indirect relationships across factors that define vulnerable populations, risk factors, and cancer outcomes.

Implications for Public Health Programs and Policies

We have discussed factors in early life that reveal possible associations with increased risk for cancer, with a focus on identifying how disparities within these factors may indicate differential exposure early in life. Risk factors in early life are disproportionally experienced by vulnerable populations, manifesting as demographic and contextual disparities. Public health efforts to address these disparities in the occurrence and exposure of risk factors in early life in vulnerable populations present opportunities to invest in ways to promote health equity and may result in reduction of disparities in cancer over the course of the life span.

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ABBREVIATIONS

ALL	acute lymphocytic leukemia
ART	assisted reproductive technology
CDC	Centers for Disease Control and Prevention
SES	socioeconomic status

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TABLE 1

Early Life Factors Identified by a Group of Subject Matter Experts That Have at Least 1 Meta-analysis Demonstrating a Consistent Empirical Association With Cancer Occurrence

Factor	Timing of Exposure	Associated Cancers	Meta-analyses Reporting Association With Cancer Outcome	OR, RR
Adverse childhood experiences (child maltreatment)	Childhood	Adult cancers	Norman et al 2012[3]	Lung cancer OR = 3.18 All cancers OR = 2.10
Maternal alcohol consumption in pregnancy	Prenatal	Leukemia	Latino-Martel et al 2010[4]	AML OR = 1.56 overall; 2.68 diagnosed ages 0–4
ART	Prenatal	Pediatric cancers (all cancers, hematologic cancers, leukemias, neuroblastomas, retinoblastomas, and others)	Hargreave et al 2013[5]; Williams et al 2011[6]	All cancers RR = 1.33; hematologic cancers RR = 1.59 CNS RR = 1.88 Leukemias RR = 1.65 Neuroblastomas RR = 4.04 Retinoblastomas RR = 1.62
Childhood obesity	Childhood	Adult cancers (esophageal adenocarcinoma, breast cancer, others)	Biro and Wien 2010[7]; Park et al 2012[8]	Esophageal adenocarcinoma RR = 1.52 for men, 1.59 for women Thyroid cancer RR = 1.33 for men Colon cancer RR = 1.24 for men Renal cancer RR = 1.24 for men, 1.34 for women Gallbladder cancer RR = 1.59 for women Breast cancer RR = 1.51 for women
BW	Prenatal	Pediatric (leukemia) and adult testicular cancers	Caughey and Michels 2009[9]; Cook et al 2010[10]; Risnes et al 2011[11]	High BW and ALL OR = 1.23 High BW and AML OR = 1.40 Low BW and AML OR = 1.50 High BW and testicular cancer OR = 1.05 Low BW and testicular cancer OR = 1.34
Benzene	Prenatal and childhood	Acute lymphoblastic leukemia	Pyatt and Hays 2010[15]; Zhou et al 2014[14]	Leukemia OR = 2.20 Acute nonlymphocyctic leukemia OR = 7.0
Pesticides and insecticides	Prenatal and childhood	Pediatric and adult cancers (leukemia, lymphoma, and brain cancer)	Turner et al 2010[16]; Van Maele-Fabry et al 2010[17]; Vinson et al 2011[18]; Wigle et al 2009[19]	Leukemia OR = 1.54 Brain cancer OR = 1.17 Lymphoma OR = 1.84
Isolated cryptorchidism	Prenatal	Testicular cancer	Cook et al 2010[10]; Lip et al 2013[20]	Testicular cancer OR = 4.30 (Cook et al[10]) Testicular cancer RR = 2.90 (Lip et al[20])
Pubertal timing	Childhood	Breast cancer in women; protective effect of later puberty on testicular cancer among men	Biro and Deardorff 2012[21]; Lerro et al 2010[22]; Maule et al 2012[23]	Breast cancer RR = 1.40 Testicular cancer OR = 0.81
Radiation	Childhood	Pediatric (leukemia) and adult (thyroid and breast) cancers	Calvente et al 2010[12]	Nonionizing radiation and leukemia OR = 2.28

Factor	Timing of Exposure	Associated Cancers	Meta-analyses Reporting Association With Cancer Outcome	OR, RR
			(nonionizing radiation); Jansen-van der Weide et al 2010[13] (ionizing radiation)	ALL OR = 4.70 Breast cancer OR = 2.0
Parental smoking during pregnancy	Prenatal	Pediatric (leukemia, non-Hodgkin lymphoma) and adult (lung cancer) cancers	Antonopoulos et al 2011[24]; Liu et al 2011[25]	NHL OR = 1.22 ALL OR = 1.11
Environmental tobacco smoke exposure	Childhood	Adult cancers (lung cancer)	Zhou et al 2012[26]	OR = 1.24
Allergies, asthma, and atopy (protective effect)	Early childhood	Leukemia, gliomas, pancreatic cancer	Dahl et al 2009[27]; Dikalioti et al 2012[28]; Linabery et al 2010[29]	Leukemia OR = 1.24
Day care attendance (protective effect of early exposure to viral infection)	Early childhood	Acute lymphoblastic leukemia	Urayama et al 2010[30]	ALL OR = 0.79

AML, acute myeloid leukemia; BW, birth weight; CNS, central nervous system; NHL, non-Hodgkin's lymphoma; OR, odds ratio; RR, relative risk.

TABLE 2

Demographic Disparities in Early Life Factors Associated With Risk for Pediatric and Adult Cancers

Factor	Race and/or Ethnicity	Sex or Gender	Disability	Age
Adverse childhood experiences (child maltreatment)	Racial and ethnic minorities at greater risk, but confounded with SES[31–34]	Girls at greater risk for sexual abuse; gender differences for other types are unclear[35]	Children with certain disabilities at increased risk for maltreatment[31, 36, 37]	Younger children at increased risk of abuse[38]
Maternal alcohol consumption in pregnancy	Inconsistent findings[39, 40]	NA	Not determined	Mixed findings for age of pregnant women[39–41]
ART	Greater ART use in non-Hispanic white than minority women[42]	NA	Not determined	Higher use of ART in younger women[42]
Childhood obesity	Non-Hispanic blacks and Hispanic children have higher rates of obesity[43]	Boys have higher rates of obesity[44]	Children with disabilities have higher rates of obesity[45–47]	Older children have higher rates[43]
Birth weight	Non-Hispanic blacks have higher rates of low birth weight[48, 49]	Male infants are more likely to be high birth weight[50]	Not determined	Young or older mothers are more likely to have low birth weight infants[48, 51]
Benzene	Higher rates among Mexican American adults than non-Hispanic whites and non-Hispanic blacks[52]	No differences	Not determined	Not determined
Pesticides and insecticides	Higher pesticide levels among Mexican Americans and non-Hispanic blacks than non-Hispanic whites[53]	Not determined	Not determined	Not determined
Isolated cryptorchidism	Higher rates among whites compared with African Americans[54]	NA; this factor is only present in boys	Not determined	Higher rates in younger mothers[55]
Pubertal timing	African American boys have lower age of onset than whites and Hispanics[23, 56–62]	Girls have lower age of pubertal onset[61]	Children with neurodevelopmental disabilities have earlier pubertal onset[63]	NA
Radiation	Higher rates of overexposure to UV radiation among non-Hispanic whites[64, 65]	Greater exposure among girls[64, 65]	Not determined	Not determined
Parental smoking and environmental tobacco smoke	Greater exposure among African American children[66, 67]	No differences	Women who have disabilities are more likely to smoke while pregnant[68]	Not determined
Allergies, asthma, and atopy (protective effect)	Non-Hispanic black children have the highest rates of asthma, non-Hispanic white children have the highest rates of respiratory allergies, and Hispanic children have the lowest rates of both[69–71]	Boys have higher rates of respiratory allergies and asthma[69–71]	Not determined	Children older than 5 have higher rates of respiratory allergies and asthma[69–71]
Day care attendance (protective effect of early exposure to viral infection)	Highest rates of attendance among black children[72, 73]	NA	Not determined	Older children are more likely to attend child care[73]

NA, not available.

TABLE 3

Contextual Disparities in Early Life Factors Associated With Risk for Pediatric and Adult Cancers

Factor	Economic Disadvantage	Geographic Differences	Nation of Origin
Adverse childhood experiences (child maltreatment)	Children of single mothers and those living in poor families or poor communities are at increased risk for abuse[32, 33]	Not determined	Not determined
Maternal alcohol consumption in pregnancy	Pregnant women who are employed, have higher incomes, and are college graduates have higher rates of alcohol use[39, 40]	State-by-state differences in alcohol use in pregnancy[40, 74]	Greater use among US-born Mexican American women than those born in Mexico[75]
ART	Higher rates of ART use among employed women and those with higher education and income[76]	Some variation across states in use of ART[77]	Not determined
Childhood obesity	Children of parents with lower income and/or less education have higher rates of obesity[43]	State-by-state variation in obesity rates[78]	First-generation immigrants have lower rates of obesity than native-born children[79]
Birth weight	Women with lower educational attainment and single women have higher rates of low birth weight infants[80, 81]	State-by-state variation in risk for low birth weight[48]	Mexican American women born in the United States are at higher risk for low birth weight infants than women born in Mexico[75]
Benzene	Higher levels among individuals with lower income and less education[52]	Variation in exposure on the basis of residence and parental occupation[82]	Not determined
Pesticides and insecticides	Higher pesticide levels among low-income children[83]	Higher pesticide use in rural and inner city areas[84]	Children of foreign-born agricultural workers have higher pesticide levels[53, 85, 86]
Isolated cryptorchidism	Possibly higher rates among low SES[87]	Not determined	Not determined
Pubertal timing	Earlier onset for children of parents with lower SES[88, 89]	Not determined	Not determined
Radiation	Higher rates of overexposure to UV radiation among higher SES children[65, 90]	Variation in exposure to UV on the basis of geographic regions[90]	Not determined
Parental smoking and environmental tobacco smoke	Greater exposure among children with low SES[66, 67]	Women in rural areas are more likely to smoke while pregnant[66, 91, 92]	Women born in the United States are more likely to smoke while pregnant[93, 94]
Allergies, asthma, and atopy (protective effect)	Poor children have higher rates of asthma and lower rates of respiratory allergies[69–71]	Not determined	Not determined
Day care attendance (protective effect of early exposure to viral infection)	Poor children are less likely to be in center-based child care.[73]	Not determined	Not determined