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Adverse Childhood Experiences and the Presence of Cancer Risk Factors in Adulthood: A Scoping Review of the Literature From 2005 to 2015

Katie A. Ports, Ph.D.[a] **[Behavioral Scientist]**, **Dawn M. Holman, MPH**[b] **[Behavioral Scientist]**, **Angie S. Guinn, MPH**[a,*] **[Fellow]**, **Sanjana Pampati, MPH**[c], **Karen E. Dyer, Ph.D.**[d,1] **[Scientist]**, **Melissa T. Merrick, Ph.D.**[a] **[Behavioral Scientist]**, **Natasha Buchanan Lunsford, Ph.D.**[b] **[Behavioral Scientist]**, and **Marilyn Metzler, MPH**[a] **[Public Health Analyst]**

[a]Division of Violence Prevention, National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA, USA

[b]Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA

[c]Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, MI, USA

[d]Virginia Commonwealth University, School of Medicine, Department of Health Behavior and Policy, Richmond, VA, USA

Abstract

Exposure to Adverse Childhood Experiences (ACEs) is associated with a host of harmful outcomes, including increased risk for cancer. A scoping review was conducted to gain a better understanding of how ACEs have been studied in association with risk factors for cancer. This review includes 155 quantitative, peer-reviewed articles published between 2005 and 2015 that examined associations between ACEs and modifiable cancer risk factors, including alcohol, environmental carcinogens, chronic inflammation, sex hormones, immunosuppression, infectious agents, obesity, radiation, ultraviolet (UV) radiation, and tobacco, among U.S. adults. This review highlights the growing body of research connecting ACEs to cancer risk factors, particularly alcohol, obesity, and tobacco. Fewer studies investigated the links between ACEs and chronic inflammation or infectious agents. No included publications investigated associations between ACEs and environmental carcinogens, hormones, immunosuppression, radiation, or ultraviolet

[*]Corresponding author at: Division of Violence Prevention, Centers for Disease Control and Prevention, 4770 Buford Highway, NE, Mailstop F63, Atlanta, GA 30341, USA.

[1]Present address: VA HSR&D Center for the Study of Healthcare Innovation, Implementation and Policy, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA.

Credit Authorship Contribution Statement

Katie A. Ports: Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Writing – Original Draft, Draft Writing – Review & Editing, Visualization. **Dawn M. Holman:** Conceptualization, Methodology, Validation, Formal Analysis, Investigation, Writing – Original Draft, Draft Writing – Review & Editing. **Angie S. Guinn:** Validation, Formal Analysis, Investigation, Writing – Original Draft, Draft Writing – Review & Editing, Visualization. **Sanjana Pampati:** Writing – Original Draft, Draft Writing – Review & Editing, Visualization. **Karen E. Dyer:** Conceptualization, Methodology, Validation, Investigation, Writing – Original Draft. **Melissa T. Merrick:** Conceptualization, Methodology, Validation, Investigation, Writing – Original Draft. **Natasha Buchanan Lunsford:** Conceptualization, Methodology, Validation, Investigation, Writing – Original Draft. **Marilyn Metzler:** Validation, Investigation, Writing – Original Draft.

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radiation. Mitigating the impact of ACEs may provide innovative ways to effect comprehensive, upstream cancer prevention.

Keywords

Adverse Childhood Experiences; Cancer risk; Scoping review; Cancer prevention; Child abuse and neglect prevention

Introduction

Research on Adverse Childhood Experiences (ACEs) has found that exposure to early adversity, especially in the absence of protective factors (e.g., supportive family environments and social networks), can result in a host of harmful outcomes immediately and throughout the life course (Brown et al., 2009; Centers for Disease Control and Prevention, 2014; Dube et al., 2001; Felitti et al., 1998; Fortson, Klevens, Merrick, Gilbert, & Alexander, 2016; Garner et al., 2012; Gilbert et al., 2015; Metzler, Merrick, Klevens, Ports, & Ford, 2017; Shonkoff, 2016; Shonkoff et al., 2012). While definitions vary, ACEs generally include child maltreatment (i.e., child abuse and neglect) and household challenges (i.e., witnessing intimate partner violence, parental separation or divorce, mental illness in the household, substance abuse in the household, or parental incarceration) that happen during the first 18 years of life (Felitti et al., 1998). Research demonstrates that ACEs are prevalent (Felitti et al., 1998; Gilbert et al., 2015), and exposure to ACEs has been linked to underdeveloped executive functioning and altered physiological stress responses (Shonkoff, 2016), mental health problems (Dube et al., 2001; Felitti et al., 1998), chronic health conditions (Felitti et al., 1998; Gilbert et al., 2015), health risk behaviors (Felitti et al., 1998), decreased life opportunities (e.g., education and income) (Metzler et al., 2017), and decreased life expectancy (Brown et al., 2009). These linkages highlight the critical association between childhood experiences and ill health and subsequently the importance of preventing ACEs. To ensure that all children reach their maximal health and life potential, professional technical reports (Fortson et al., 2016; Shonkoff et al., 2012) and policy statements (Garner et al., 2012)have emphasized the importance of implementing strategies that prevent exposure to toxic stress in childhood, as well as mitigating the negative effects of ACEs on development and health across the lifespan. Similarly, the Centers for Disease Control and Prevention (CDC) developed a framework for prevention, *Essentials for Childhood*, to ensure that all children have access to safe, stable, nurturing relationships and environments for optimal health and wellbeing (Centers for Disease Control and Prevention, 2014).

In this paper, the association between ACEs and risk factors or determinant for cancer was of primary concern. Cancer is a leading cause of death worldwide; in 2013, the latest year for which data are available, there were over 1.5 million new cases and nearly 600,000 cancer deaths in the United States (US) (U.S. Cancer Statistics Working Group, 2016). Exposure to ACEs has been linked to cancer in adulthood (Holman et al., 2016). Specifically, a cumulative ACE score is associated with increased risk of reporting exposure to any type of cancer (Bellis et al., 2015; Brown, Thacker, & Cohen, 2013; Felitti et al.,

1998; Kelly-Irving et al., 2013; Morton, Schafer, & Ferraro, 2012), as well as increased risk for lung cancer (Brown et al., 2010). Individual ACE exposure, such as physical and psychological abuse have been associated with risk of any type of cancer (Fuller-Thomson & Brennenstuhl, 2009; Hyland, Alkhalaf, & Whalley, 2013; Morton et al., 2012); sexual abuse has been associated with cervical cancer (Coker, Hopenhayn, DeSimone, Bush, & Crofford, 2009). However, less is known about the mechanisms behind these associations, and whether associations between ACEs and risk factors for cancer explain some of the associations between ACEs and cancer incidence found in previous reviews (Holman et al., 2016). While risk factors for cancer are well known, there has been no attempt to summarize the literature connecting childhood experiences to risk factors for cancer. Causal factors for cancer are complex and likely include multiple factors, including harmful exposures, certain behaviors, and less controllable factors like age and genetics (National Cancer Institute, 2015); some of which may be influenced by ACEs. Summarizing the literature that explores associations between childhood experiences and cancer risk factors may lead to more upstream approaches to cancer prevention that include strategies for pediatric nurses, researchers and other health practitioners that address and prevent exposure to ACEs.

The purpose of this paper was to conduct a scoping study to assess the status of published evidence connecting exposure to ACEs and the presence of cancer risk factors among adults. Scoping reviews allow researchers to synthesize existing literature in terms of volume, nature, and characteristics, particularly when the topic has not been extensively reviewed or is complex or heterogeneous in nature (Arksey & O'Malley, 2005; Mays, Roberts, & Popay, 2001). Given the multi-factorial nature of cancer development over the lifespan and the myriad studies investigating ACEs and adult health, a scoping review has the potential to synthesize a broad body of research connecting childhood experiences and cancer risk, highlight gaps in the research, and offer insight on novel cancer prevention and intervention strategies.

Methodology

This review was conducted in accordance with Arksey and colleagues' methodological framework for scoping reviews (Arksey & O'Malley, 2005), which has been highlighted by the EQUATOR (Enhancing the Quality and Transparency of health research). It included the following phases: (1) identifying the research question(s), (2) identifying relevant studies, (3) study selection, (4) charting the data, and (5) collating/summarizing and reporting the results. The process began with the establishment of a research team consisting of experts in both cancer and childhood adversity prevention and control. The team provided critical insight to all aspects of the review. The review was guided by the questions, “What ACEs are utilized in the peer-reviewed literature pertaining to cancer risk factors?” and “What are the associations between ACEs and cancer risk factors in adulthood?” Below we outline search strategies used to identify studies, the study selection process, including inclusion criteria for selection of studies, and data extraction process for charting and summarizing the results.

Search Strategies Used to Identify Studies

For the purposes of this review, ACEs were defined as exposure to one or more of the following adverse events before the age of 18 years:

- abuse victimization (physical, sexual, and/or psychological)
- neglect (emotional and/or physical)
- household challenges (parental death or serious illness, parental separation or divorce, parental incarceration, substance abuse in the household, domestic violence, mental illness in the household, and/or family poverty), and
- other types of early adversity or trauma as defined in identified articles.

Search terms were selected to capture the traditional ACEs (i.e., abuse, neglect and household challenges) (Table 1); however, within the literature, ACEs has been broadly defined, and researchers have used ACEs to refer to myriad experiences (Fig. 1).

We used the National Cancer Institute's (NCI) list of known cancer risk factors to determine the cancer risk factors that would be included in this review (National Cancer Institute, 2015). Of the factors listed, alcohol, cancer-causing substances in the environment, chronic inflammation, sex hormones, immunosuppression, infectious agents, obesity, radiation, tobacco, and ultraviolet radiation were included. Physical activity was included as a subset of the obesity search terms; however, given that the association between ACEs and obesity and cancer are likely more complex than a simple calorie in versus calorie out relationship, associations between ACEs and physical activity are reported separately. Age was excluded, because age itself is not modifiable.

A string of “NOT” terms was added to exclude irrelevant topics that could inadvertently be captured by the search term “ACE” (e.g., autocapillary electrophoresis). All authors reviewed the final search string for completeness (Table 1). PubMed searches were conducted separately for each cancer risk factor. As such, some articles were considered across multiple risk factors.

Study Selection Process

Studies included in the review were required to be published in peer-reviewed journals and report the statistical association between experiences considered to meet the definition of ACEs and adult cancer incidence. Only studies with samples from the US and published from 2005 to 2015 were included in this review. Studies published online and ahead of print in 2015 were included. Inclusion criteria also included measurement of ACEs before age 18 years, and measurement of cancer risk factors in adulthood (i.e., 18 years or older). Case reports and studies that were not original research, did not involve human subjects, were not written in English were excluded. Grey literature was not included in this review as both ACEs and risk for cancer are well-established fields with myriad peer-reviewed journals.

The initial PubMed search returned 2276 unique articles across the cancer risk factors. Of these, 1945 did not meet study criteria based on a title and abstract review. The full text of

the remaining 331 articles was then reviewed for relevancy; 155 articles were determined eligible for inclusion with 14 articles included across one or more cancer risk factor (N = 22). Fig. 2 provides a flowchart of the study selection process with reasons for study exclusion. See Fig. 3 for a high-level overview of study findings by risk factor and demographics.

Data Extraction for Charting and Summarizing

Reviewers independently abstracted the following data from articles that were included for full review: PubMed ID, title, first author, year of publication, sample size, study population, study design, year(s) of data collection, measure(s) of early adversity, measure(s) of cancer risk factor, statistical analyses used, and reported associations between ACEs and cancer outcomes based on adjusted analyses (i.e., risk, odds, and hazard ratios). Approximately 25% of the abstracted data were checked by a second reviewer to assess reliability. The few discrepancies were resolved through meetings and dialogue when necessary. Reviewers outlined the key information from each study in a table format (Appendix 1) and developed a descriptive summary of the observed patterns (outlined below).

Search Results

In total, 33 different ACEs were measured across the studies. A word cloud (Fig. 1) was constructed to visualize the types of adversities included in the studies. The size of the word reflects the frequency of that measure across studies: physical abuse, emotional abuse, and sexual abuse were the most common ACEs measured. Five studies used data from the original CDC-Kaiser Permanente ACE study (Brown et al., 2010; Dong et al., 2005; Dube et al., 2009; Edwards, Anda, Gu, Dube, & Felitti, 2007; Strine et al., 2012), and 18 used ACE data from the Behavioral Risk Factor Surveillance System (BRFSS), which includes an optional ACE module adapted from the original ACE questionnaire (Campbell, Walker, & Egede, 2016; Chapman et al., 2013; Dube, Cook, & Edwards, 2010; Font & Maguire-Jack, 2016; Ford et al., 2011; Fuller-Thomson, Filippelli, & Lue-Crisostomo, 2013; Gjelsvik, Dumont, & Nunn, 2013; McCauley, Blosnich, & Dichter, 2015; Vander Weg, 2011; Walsh & Cawthon, 2014; Yeoman, Safranek, Buss, Cadwell, & Mannino, 2013). All other studies either used an adapted ACE questionnaire or selected unique, but often overlapping, childhood adversities. The adversity type may have been measured as an individual item, included as part of a summary score, or both. Summary scores, regardless of the ACEs included, will heretofore be referred to as adversity scores. Study findings are summarized below by cancer risk factor.

Alcohol

Alcohol use can increase risk for cancers of the pharynx, larynx, oral cavity, esophagus, liver, colorectal, and female breast cancers (IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, 2012c). ACEs have long been associated with alcohol dependence (Dube et al., 2006; Dube, Anda, Felitti, Edwards, & Croft, 2002; Felitti et al., 1998). In total, 59 articles met inclusion criteria. Alcohol use was characterized using multiple measures, most frequently alcohol dependence (N = 19), binge drinking (N = 11), alcohol abuse (N = 8), general alcohol use (N = 8), frequency of alcohol consumption (N =

8), alcohol-related consequences/problems ($N = 8$), quantity of alcohol consumed ($N = 7$), and other drinking behaviors ($N = 12$). The term "problematic alcohol-related behaviors" will be used in subsequent text to encompass these various measures. Twenty-nine different measures of childhood adversity were used, with the majority of studies including a measure of childhood sexual abuse (CSA; $N = 49$), physical abuse (PA; $N = 42$), and emotional abuse ($N = 30$). One study used data from the original ACE study (Strine et al., 2012), and three studies used data from the BRFSS ACE module (Campbell et al., 2016; Font & Maguire-Jack, 2016; Gjelsvik et al., 2013). Associations between early adversity and problematic alcohol-related behaviors varied by study.

In general, summed adversity scores were positively associated with problematic alcohol-related behaviors (Campbell et al., 2016; Carlson, Harden, Kretsch, Corbin, & Fromme, 2015; Fetzner, McMillan, Sareen, & Asmundson, 2011; Font & Maguire-Jack, 2016; Keyes et al., 2012; Kim et al., 2014; Park, Sher, Todorov, & Heath, 2011; Pilowsky, Keyes, & Hasin, 2009; Shin, Hassamal, & Groves, 2015; Young-Wolff, Kendler, Ericson, & Prescott, 2011). These associations existed among Hispanic (Allem, Soto, Baezconde-Garbanati, & Unger, 2015), and African American and European American (Sartor, Wang, Xu, Kranzler, & Gelernter, 2014) samples, as well as samples of adults with substance abuse histories (Banducci, Hoffman, Lejuez, & Koenen, 2014; Wu, Schairer, Dellor, & Grella, 2010) and alcohol dependence (Elliott et al., 2014; Elliott et al., 2016). In addition, experiencing childhood trauma was associated with earlier onset of alcohol use, earlier age of heaviest drinking, and a shorter delay from onset of alcohol use to heavy alcohol use (Waldrop, Ana, Saladin, McRae, & Brady, 2007). Similarly, among those who reported exposure to child maltreatment (CM), increased risk of transitioning from less severe to more hazardous alcohol use was more likely (La Flair et al., 2013).

Individual ACE types were positively associated with problematic alcohol-related behaviors in adulthood. In general, exposure to childhood physical abuse (CPA) (Anderson, Rabi, Lukas, & Teicher, 2010; Fenton et al., 2013; Fetzner et al., 2011; Font & Maguire-Jack, 2016; Shin, Lee, Jeon, & Wills, 2015), CSA (Corstorphine, Waller, Lawson, & Ganis, 2007; Fenton et al., 2013; Fetzner et al., 2011; Keyes et al., 2012; McMillan, Hanson, Bedrick, & Lapham, 2005; Shin, Lee, et al., 2015), emotional abuse (Campbell et al., 2016; Fenton et al., 2013; Fetzner et al., 2011; Font & Maguire-Jack, 2016), mental illness in the household (Font & Maguire-Jack, 2016), neglect (Fenton et al., 2013; Fetzner et al., 2011), household member incarceration (Gjelsvik et al., 2013), substance abuse in the household (Font & Maguire-Jack, 2016), and parental divorce (Pilowsky et al., 2009) were each associated with one or more problematic alcohol-related behaviors. Exposure to CPA (Schwandt, Heilig, Hommer, George, & Ramchandani, 2013), emotional abuse (Schwandt et al., 2013), emotional neglect (Schwandt et al., 2013), physical neglect (Schwandt et al., 2013), and CSA (Elliott et al., 2014; Schwandt et al., 2013) was associated with problematic alcohol-related behaviors in alcohol-dependent samples. Similarly, among individuals with PTSD, those who were alcohol dependent were more likely to have experienced all abuse categories, as well as neglect, parental divorce, and having absent parents or parents with behavioral and substance abuse problems (Blanco et al., 2013). Among persons seeking treatment for alcoholism, CPA, emotional abuse, and physical neglect exposure were

associated with alcohol dependence severity, but CSA and emotional neglect were not (Schwandt et al., 2013).

Among male-only and female-only samples, neglect (Goldstein, Flett, & Wekerle, 2010; Snyder & Merritt, 2016; Strine et al., 2012), CSA (Drabble, Trocki, Hughes, Korcha, & Lown, 2013; Grayson & Nolen-Hoeksema, 2005; Lown, Nayak, Korcha, & Greenfield, 2011; McCarty, DePadilla, Elifson, & Sterk, 2012; Najdowski & Ullman, 2009; Sartor et al., 2012; Skinner, Kristman-Valente, & Herrenkohl, 2016; Strine et al., 2012; Trent, Stander, Thomsen, & Merrill, 2007; Walsh, Latzman, & Latzman, 2014; Young, Hansen, Gibson, & Ryan, 2006), CPA (Drabble et al., 2013; Jenkins et al., 2011; Lown et al., 2011; McCarty et al., 2012; Strine et al., 2012; Trent et al., 2007; Walsh et al., 2014; Young et al., 2006), emotional abuse (Strine et al., 2012; Young et al., 2006), substance abuse in the household (Strine et al., 2012), mental illness in the household (Strine et al., 2012; Young et al., 2006), and adversity scores (Eames et al., 2014; Hughes, McCabe, Wilsnack, West, & Boyd, 2010; Jenkins et al., 2011; Sartor et al., 2014; Strine et al., 2012) were associated with problematic alcohol-related behaviors.

Among men, incarcerated household member (Strine et al., 2012), parental rejection (Schellekens et al., 2013), household member with problem drinking (Young et al., 2006), and negative life events scores (Schellekens et al., 2013) were also associated with problematic alcohol-related behaviors. In one study, out-of-home placement (e.g., foster care) was associated with adult alcohol dependence among urban, gay/bisexual male American Indians and Alaskan Natives (AI/AN) (Yuan, Duran, Walters, Pearson, & Evans-Campbell, 2014). However, in the same study being adopted decreased the risk of later binge drinking in a sample of urban, lesbian/bisexual female AI/AN (Yuan et al., 2014). Women who experienced CM developed alcohol dependence earlier than women who did not (Oberleitner, Smith, Weinberger, Mazure, & McKee, 2015), and among lesbian women, neglect (Hughes, McCabe, et al., 2010), CSA (Gilmore et al., 2014; Hughes, Johnson, Wilsnack, & Szalacha, 2007), and CPA (Hughes et al., 2007) were associated with alcohol-related problems. In another study, the highest levels of hazardou s drinking were reported by bisexual women with CSA histories compared to heterosexual and lesbian women with CSA histories (Hughes, Szalacha, et al., 2010).

The majority of studies found significant positive associations between ACEs and problematic adult drinking behavior ($N = 35$), but several studies reported mixed effects ($N = 13$), and eleven studies did not find significant associations (Agorastos et al., 2014; Carlson, Oshri, & Kwon, 2015; Horan & Widom, 2015; Hostinar, Lachman, Mroczek, Seeman, & Miller, 2015; Klanecky, McChargue, & Bruggeman, 2012; Klanecky, Woolman, & Becker, 2015; Nikulina, Widom, & Brzustowicz, 2012; Salem et al., 2013; Tyler, Schmitz, & Adams, 2015; Ulibarri, Ulloa, & Salazar, 2015; Ullman & Sigurvinsdottir, 2015). For example, summary adversity scores were not associated with problematic alcohol-related behaviors in multiple study populations, including the MIDUS II Study (Hostinar et al., 2015), male Marines (Agorastos et al., 2014), some samples of college students (Carlson, Oshri, et al., 2015; Goldstein et al., 2010; Klanecky et al., 2012; Klanecky et al., 2015), urban lesbian, gay or bisexual (LGB) AI/AN (Yuan et al., 2014), and recently paroled men (Salem et al., 2013). Individuals with histories of substantiated CM compared to non-abused

controls were not more likely to abuse alcohol (Horan & Widom, 2015; Nikulina et al., 2012). In several studies, CSA was not associated with alcohol-related behaviors among samples of college students (Klanecky et al., 2012; Tyler et al., 2015), men (Skinner et al., 2016), women with sexual assault histories (Ullman & Sigurvinsdottir, 2015), low-income Latina women (Ulibarri et al., 2015), and women identified as early-onset alcohol users (Jenkins et al., 2011).

Cancer-Causing Substances in the Environment

Environmental carcinogenic substances are associated with cancer incidence including arsenic, asbestos, secondhand tobacco smoke, and soot (IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, 2012a, 2012b, 2012d, 2012e). Environmental hazards are often contributors to observed health inequities, especially in low-income populations (Adamkiewicz et al., 2014; Evans & Kantrowitz, 2002; Rosenbaum, Hartley, & Holder, 2011). Given that socioeconomic status is associated with risk of ACE exposure (Sedlak et al., 2010), it is possible that individuals at risk of ACEs are also at greater risk of environmental carcinogens. However, none of the identified articles ($N = 40$) met inclusion criteria.

Chronic Inflammation

Inflammation, a known cancer risk factor, may be one mechanism connecting early trauma to adult health outcomes. Inflammation is a physiological response that promotes a healthy defense against toxins, infections and injuries; however, prolonged or chronic inflammation can cause damage to the body and over time can lead to cancer (Coussens & Werb, 2002). It is hypothesized that those exposed to childhood adversity have increased inflammation levels because stress activates the sympathetic nervous system, triggering inflammation (Danese & McEwen, 2012). In the current review, 22 articles met the inclusion criteria. The studies measured various markers of inflammation, including C-reactive protein (CRP; $N = 18$), interleukin-6 (IL-6; $N = 13$), tumor necrosis factor-alpha (TNF-α; $N = 6$), interleukin-1 beta (IL-1β; $N = 3$), and other markers ($N = 8$). Twenty-three different types of ACEs were measured across the 22 studies.

An ACE score of two or more was associated with a host of inflammation-related autoimmune diseases, including rheumatoid arthritis (Dube et al., 2009). In addition, several indicators of early adversity were associated with inflammation summary scores (Friedman, Karlamangla, Gruenewald, Koretz, & Seeman, 2015; Hostinar et al., 2015), but associations varied widely based on the selected measure of early adversity and the inflammation marker of interest. For example, summary childhood adversity scores significantly predicted increased levels of IL-6 in adulthood (Carpenter et al., 2010; Cho, Bower, Kiefe, Seeman, & Irwin, 2012; Gouin, Glaser, Malarkey, Beversdorf, & Kiecolt-Glaser, 2012; Hartwell et al., 2013; Kiecolt-Glaser et al., 2011; Rooks, Veledar, Goldberg, Bremner, & Vaccarino, 2012; Slopen et al., 2010; Tietjen, Khubchandani, Herial, & Shah, 2012). Among breast cancer survivors, childhood abuse, chaotic home environment, and total adversity scores were associated with elevated IL-6 levels (Crosswell, Bower, & Ganz, 2014). ACE score (Tietjen et al., 2012), emotional abuse (Rooks et al., 2012), court-substantiated neglect (Nikulina & Widom, 2014), prenatal adversity (Slopen et al., 2015), and childhood abuse and/or neglect

experienced by women (Matthews, Chang, Thurston, & Bromberger, 2014) were also associated with elevated IL-6 levels. However, family poverty (Appleton et al., 2012; Nikulina & Widom, 2014), parental education or occupation (Appleton et al., 2012), neighborhood poverty (Nikulina & Widom, 2014), child abuse or neglect (Bertone-Johnson, Whitcomb, Missmer, Karlson, & Rich-Edwards, 2012; Gouin et al., 2012; Schrepf, Markon, & Lutgendorf, 2014), and total adversity scores (Cho et al., 2012; Crosswell et al., 2014; Hartwell et al., 2013; Joung et al., 2014; Schrepf et al., 2014; Slopen et al., 2015; Slopen, Non, Williams, Roberts, & Albert, 2014) were not associated with CRP levels. One study found that compared to children who did not experience bullying, being a victim of bullying predicted higher increases in CRP levels over time (Copeland et al., 2014). Associations between early adversity and TNF-α level also varied. For example, childhood abuse (Gouin et al., 2012; Kiecolt-Glaser et al., 2011) and other types of early adversity (Kiecolt-Glaser et al., 2011) were not associated with TNF-α level. Among breast cancer survivors, adversity was not associated with TNF-α level, but a chaotic home environment was (Crosswell et al., 2014). In contrast, total adversity scores were associated with TNF-α levels (Hartwell et al., 2013; Tietjen et al., 2012), and significant associations between abuse scores and TNF-α levels in an African American sample were found (Smith et al., 2011).

Sex Hormones

Despite playing a key role in the physiological processes of both women and men, estrogens, a group of structurally related, hormonally active molecules that control sex and growth characteristics (NTP (National Toxicology Program), 2016), are also a known risk factor for certain types of cancer, including breast (Henderson, Ross, & Bernstein, 1988; Yager & Davidson, 2006) and endometrial (Henderson et al., 1988). Endogenous estrogen is produced naturally and has been associated with an increased risk of certain cancers among women (Eliassen & Hankinson, 2008; Hsieh, Trichopoulos, Katsouyanni, & Yuasa, 1990; Kelsey, Gammon, & John, 1993; Layde et al., 1989). Additionally, exogenous estrogen, which is not produced naturally but administered as part of estrogen therapy, has also been associated with an increased risk of certain cancers (Colton et al., 1993; Grady, Gebretsadik, Kerlikowske, Ernster, & Petitti, 1995; Herbst, Ulfelder, & Poskanzer, 1971; Schairer et al., 2000; Smith, Prentice, Thompson, & Herrmann, 1975). ACEs have been associated with changes in physiological processes (Shonkoff, 2016), and could impact the production of sex hormones. However, none of the identified articles ($N = 255$) met inclusion criteria.

Immunosuppression

Many medical conditions such as organ transplantations, autoimmune diseases, and inflammatory disorders require long-term immunosuppression therapy. Although immunosuppression improves survival and reduces the risk of organ rejection, patients receiving immunosuppressive drugs face an increased risk for various cancers (Engels et al., 2011). Suppression of an individual's immune system weakens their ability to detect and destroy cancer cells and cancer-causing viral infections. For example, people living with HIV/AIDS have an increased risk of cancer due to immune deficiency, and cancer is a prevalent cause of morbidity within this population (Grulich, van Leeuwen, Falster, & Vajdic, 2007). ACEs have been associated with HIV risk (Felitti et al., 1998) as well as changes in physiological processes (Shonkoff, 2016), and could potentially be associated

with later need of immunosuppression. Search terms revealed 23 potential articles; however, none met our inclusion criteria.

Infectious Agents

Certain bacterial, viral, and parasitic infections are risk factors for specific cancer types (Parkin, 2006). These include hepatitis B virus, hepatitis C virus, *H. pylori*, the human papillomavirus (HPV), and human immunodeficiency virus type 1 (HIV-1) (Mueller, 2003). ACE scores have also been associated with acquiring an HIV infection (Hillis, Anda, Felitti, & Marchbanks, 2001; Lu, Mueser, Rosenberg, & Jankowski, 2008), and a graded relationship exists between ACEs and self-reported sexually-transmitted disease (STD) history (Hillis, Anda, Felitti, Nordenberg, & Marchbanks, 2000). Furthermore, ACEs have been linked to risky sexual behaviors, which lead to an increased risk of acquiring STDs (Lu et al., 2008). In addition, because stress is associated with decreased immune response, stress-inducing childhood trauma could potentially increase susceptibility to infection (Anda et al., 2008). In the current review, we identified 12 articles that investigated associations between childhood adversity and exposure to infectious agents in adulthood. The studies measured various infectious agents, including HIV ($N = 10$), hepatitis B virus ($N = 1$), hepatitis C virus ($N = 3$), Epstein-Barr virus (EBV; $N = 2$), and cytomegalovirus (CMV; $N = 1$). Fourteen different types of ACEs were measured across the 12 studies, with the majority collecting information on CSA ($N = 10$). No studies utilized the original ACE questionnaire or BRFSS data.

Significant associations between adversity and HIV were most common, with exposure to adversity predicting increased risk of HIV infection in adulthood. For example, among African American couples, HIVpositive men were more likely to report CSA histories than HIVnegative men (Nimh Multisite HIV/STD Prevention Trial for African American Couples Group, 2010), although this association was not significant for women (Nimh Multisite HIV/STD Prevention Trial for African American Couples Group, 2010). Additional studies highlighted significant associations between CSA and HIV infection among men who have sex with men (MSM) (Arreola, Neilands, Pollack, Paul, & Catania, 2008; Brennan, Hellerstedt, Ross, & Welles, 2007; Friedman, Marshal, Stall, Cheong, & Wright, 2008; Mimiaga et al., 2009; Phillips et al., 2014). In addition, studies found that adversity scores were associated with an incremental increase in HIV risk (Reisner, Falb, & Mimiaga, 2011; Rosenberg, Lu, Mueser, Jankowski, & Cournos, 2007). For example, each additional exposure to childhood adversity was associated with a 32% increase in odds of HIV infection, and 17.8% of HIV infections were attributable to early adversity (Reisner et al., 2011). However, two studies that used the same dataset from substantiated CM records and matched controls did not find associations between CM and HIV infection (Widom, Czaja, Bentley, &Johnson, 2012; Wilson & Widom, 2008).

Associations between childhood adversity and adult hepatitis B and/or C were not significant across three studies (Nimh Multisite HIV/STD Prevention Trial for African American Couples Group, 2010; Rosenberg et al., 2007; Widom et al., 2012). However, among breast cancer survivors, childhood adversity was associated with elevated antibodies to two latent herpesviruses (e.g., EBV and CMV) (Fagundes, Glaser, Malarkey, & Kiecolt-

Glaser, 2013). Elevated EBV antibodies were also associated with repeated exposure to CSA, being exposed to CPA in preschool, and having parents with lower educational attainment and job status, but not with family income (Slopen, McLaughlin, Dunn, & Koenen, 2013).

Obesity

Obesity is a known risk factor for several forms of cancer, including endometrial, esophageal, pancreatic, breast, colorectal, ovarian, and renal cancer (International Agency for Research on Cancer, 2016), and people exposed to ACEs have an increased risk of becoming obese later in life (Gustafson & Sarwer, 2004). Obesity results from an energy imbalance between calories consumed and energy expenditure (e.g., physical activity). Forty-three obesity-related studies met inclusion criteria. The most common measurement of obesity or excess body fat and size was BMI ($N = 39$), followed by waist circumference/girth ($N = 5$), waist-to-hip ratio ($N = 4$), and body composition ($N = 1$). The majority of studies that measured BMI used a cutoff score of 30 kg/m^2 or more to indicate obesity; however, some studies measured increased BMI over time, which may or may not have made the cutoff for obesity. As such, articles included in this section may refer to obesity or excess body fat and size, and will heretofore be referred to as obesity-related measures. A total of 23 types of childhood adversity were measured across the 43 studies, with physical ($N = 35$), sexual ($N = 35$), and emotional ($N = 22$) abuse being the most common. Five studies utilized BRFSS ACE data (Campbell et al., 2016; Dube et al., 2010; Font & Maguire-Jack, 2016; Gjelsvik et al., 2013; McCauley et al., 2015).

Collectively, summed adversity scores (Afifi, Mota, MacMillan, & Sareen, 2013; Crowell et al., 2016; Davis, Usher, et al., 2014; Dube et al., 2010; Duncan, Sartor, et al., 2015; Font & Maguire-Jack, 2016; Friedman, Montez, Sheehan, Guenewald, & Seeman, 2015; Greenfield & Marks, 2009; Hostinar et al., 2015; Li, Chassan, Bruer, Gower, & Shelton, 2015; McCauley et al., 2015; Pederson & Wilson, 2009; Richardson, Dietz, & Gordon-Larsen, 2014; Spann et al., 2014), including early socioeconomic hardships (Bae, Wickrama, & O'Neal, 2014; Wickrama, Kwon, Oshri, & Lee, 2014) and academic adversity (Friedman, Montez, et al., 2015), were positively associated with obesity-related measures. These findings were upheld in female-only samples (Alvarez, Pavao, Baumrind, & Kimerling, 2007; Duncan, Sartor, et al., 2015; Midei, Matthews, & Bromberger, 2010; Shinozaki, Romanowicz, Kung, Rundell, & Mrazek, 2012; Tietjen et al., 2012). In the Missouri Adolescent Female Twin Study, CM was positively associated with both obesity and being underweight (Duncan, Sartor, et al., 2015).

Individually, exposure to harsh physical punishment (Afifi et al., 2013), CPA (Bentley & Widom, 2009; Duncan, Auslander, et al., 2015; Li et al., 2015), CSA (Campbell et al., 2016; Font & Maguire-Jack, 2016), mental illness or substance abuse in the household (Font & Maguire-Jack, 2016), and childhood SES (Lehman, Taylor, Kiefe, & Seeman, 2005) were positively associated with obesity measures. In a sample of AI/AN, verbal abuse was associated with obesity (Hodge, Stemmler, & Nandy, 2014), but other CM types were not. In studies with female-only samples, CSA (Boynton-Jarrett, Rosenberg, Palmer, Boggs, & Wise, 2012; Duncan, Sartor, et al., 2015; Noll, Zeller, Trickett, & Putnam, 2007; Rich-

Edwards et al., 2010; Rohde et al., 2008; Smith et al., 2010), CPA (Boynton-Jarrett et al., 2012; Francis, Nikulina, & Widom, 2015; Rich-Edwards et al., 2010; Rohde etal., 2008), emotional abuse (Mason et al., 2015), severity of neglect (Pederson & Wilson, 2009), and severity of abuse (Riley, Wright, Jun, Hibert, & Rich-Edwards, 2010) were positively associated with obesity-related measures.

Among lesbian and/or bisexual women, CSA (Aaron & Hughes, 2007; Lehavot & Simoni, 2011), CPA (Lehavot & Simoni, 2011), emotional abuse (Lehavot & Simoni, 2011), emotional neglect (Lehavot & Simoni, 2011), and physical neglect (Lehavot & Simoni, 2011) were associated with obesity-related measures. In addition, several studies found that differences in obesity prevalence between abused and non-abused women grew wider over time (Midei et al., 2010; Rich-Edwards et al., 2010).

Fifteen studies reported mixed findings between obesity and various measures of childhood adversity, and six studies found no significant direct associations (Davis, Dearing, etal., 2014; Grilo et al., 2005; McIntyre et al., 2012; Min, Minnes, Kim, & Singer, 2013; Ramirez & Milan, 2016; Schrepf et al., 2014). For example, childhood trauma was not associated with BMI among a sample of healthy adults; however, in mediation models, trauma was associated with distress, distress with use of food coping, and use of food coping with elevated BMI (Schrepf et al., 2014). Other studies found that adversity scores (Campbell et al., 2016; Davis, Dearing, et al., 2014; Grilo et al., 2005; McIntyre et al., 2012; Richardson et al., 2014), CSA (Bentley & Widom, 2009; Ramirez & Milan, 2016), neglect (Bentley & Widom, 2009), early family environment (Lehman et al., 2005), and severity of abuse (Min et al., 2013) were not associated with obesity-related measures.

Physical Activity

The relationship of ACEs to physical activity was assessed in five studies, and accompanied measurements of BMI or waist circumference. Studies investigating the relationship between early adversity and physical activity were less common, and had varied results. ACE score (Hostinar et al., 2015) and having an incarcerated household member (Gjelsvik et al., 2013) were significantly associated with less physical activity, but childhood adversity was unrelated to physical activity in a sample of middle-aged adults from Boston (Davis, Usher, et al., 2014). In women-only studies, CSA was associated with greater physical activity, although CPA (Bertone-Johnson et al., 2012) and severity of abuse (Riley et al., 2010) were not.

Radiation

Radiation occurring at certain wavelengths can damage DNA and increase cancer risk (El Ghissassi et al., 2009). Radiation occurs naturally in the environment (e.g., radon), but high-energy radiation such as X-rays and gamma rays is also released during nuclear power plant accidents and atomic weapons development, testing, and use. Given that people may be at higher risk for exposure to harmful radiation based on their geographic location (Cohen, 1995) and that exposure to early adversity varies across geographic regions (Stoltenborgh, Bakermans-Kranenburg, & van Ijzendoorn, 2013), it is possible that early adversity may be

more prevalent in areas where radiation exposure is also higher. Our search terms revealed 204 potential articles; however, none met our inclusion criteria.

Ultraviolet Radiation

Exposure to ultraviolet (UV) radiation from sunlight or artificial sources, including sunlamps and tanning booths, is associated with skin cancer (Boniol, Autier, Boyle, & Gandini, 2012; El Ghissassi et al., 2009; U.S. Department of Health and Human Services, 2014). Both intentional tanning (i.e., indoor tanning) and ACEs have been associated with mental health and substance abuse (Coups & Phillips, 2011; Felitti et al., 1998), and thus, it is possible that exposure to ACEs could influence sun protection behavior and intentional tanning. However, none of the identified articles ($N = 84$) met the inclusion criteria.

Tobacco

Tobacco smoking causes cancers of the lung, oral cavity, naso-, oro- and hypopharynx, nasal cavity and accessory sinuses, larynx, esophagus, stomach, pancreas, colorectal, liver, kidney (body and pelvis), ureter, urinary bladder, uterine cervix and ovary (mucinous), and myeloid leukemia (IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, 2012f; Warren, Alberg, Kraft, & Cummings, 2014). Furthermore, smoking can weaken the immune response, blocking the body's ability to fight cancer (U.S. Department of Health and Human Services, 2010). ACEs have been associated with smoking status whereby higher ACE scores correspond to greater odds of being a current smoker (Felitti et al., 1998) and being nicotinedependent (Xie et al., 2012). Furthermore, long-term tobacco use has been identified as a coping strategy for the negative effects of ACEs (Anda et al., 1999). Forty-one articles met inclusion criteria. Various tobacco-related behaviors were measured, including tobacco/nicotine use ($N = 5$), smoking status (Current $N = 16$; Lifetime $N = 18$; Past year $N = 1$; Quit $N = 1$), and other tobacco-related behaviors ($N = 11$). Twenty-one types of ACEs were assessed across the 41 studies. Ten studies used data from the BRFSS ACE module (Campbell et al., 2016; Chapman et al., 2013; Dube et al., 2010; Font & Maguire-Jack, 2016; Ford et al., 2011; Fuller-Thomson et al., 2013; Gjelsvik et al., 2013; Vander Weg, 2011; Walsh & Cawthon, 2014; Yeoman et al., 2013), and four used data from the original ACE study (Brown et al., 2010; Dong et al., 2005; Edwards et al., 2007; Strine et al., 2012).

Summary adversity scores were positively associated with tobacco-related behaviors (Brown et al., 2010; Campbell et al., 2016; Chapman et al., 2013; Dong et al., 2005; Edwards et al., 2007; Elliott et al., 2014; Font & Maguire-Jack, 2016; Ford et al., 2011; Hostinar et al., 2015; Lehavot & Simoni, 2011; Mersky, Topitzes, & Reynolds, 2013; Mingione, Heffner, Blom, & Anthenelli, 2012; Morton, Mustillo, & Ferraro, 2014; Su et al., 2015; Topitzes, Mersky, & Reynolds, 2010; Vander Weg, 2011; Walsh & Cawthon, 2014; Wu et al., 2010; Yeoman et al., 2013). This positive association was found in a sample of lesbian and bisexual women (Lehavot & Simoni, 2011) and ethnic/racial minority samples (Mersky et al., 2013), including Hispanics (Allem et al., 2015) and African Americans (Slopen et al., 2012). Both severity (Bertone-Johnson et al., 2012; Sacco et al., 2007; Spratt et al., 2009; Taha, Galea, Hien, & Goodwin, 2014) and frequency (Sacco et al., 2007; Taha et al., 2014) of trauma exposures were associated with smoking status.

Individually, CSA (Campbell et al., 2016; Chapman et al., 2013; Elliott et al., 2014; Font & Maguire-Jack, 2016; Ford et al., 2011), CPA (Chapman et al., 2013; Elliott et al., 2014; Ford et al., 2011; Taha et al., 2014), emotional abuse (Allem et al., 2015; Campbell et al., 2016; Chapman et al., 2013; Elliott et al., 2014; Ford et al., 2011; Taha et al., 2014), mental illness (Allem et al., 2015; Chapman et al., 2013; Font & Maguire-Jack, 2016; Ford et al., 2011) or substance abuse (Allem et al., 2015; Campbell et al., 2016; Chapman etal., 2013; Fordet al., 2011) in the household, witnessing domestic violence (Chapman et al., 2013; Ford et al., 2011), family disruption/separation by age 15 (Larson & Halfon, 2013), having an incarcerated household member (Chapman et al., 2013; Font & Maguire-Jack, 2016; Ford et al., 2011), foster care history (Thompson & Hasin, 2011), and parental divorce/separation (Allem et al., 2015; Campbell et al., 2016; Chapman et al., 2013; Font & Maguire-Jack, 2016; Ford et al., 2011; Larson & Halfon, 2013) were all positively associated with tobacco-related behaviors, but emotional neglect was associated with less nicotine dependence in one study (Elliott et al., 2014). Having an incarcerated household member was positively associated with smoking status among Hispanics and non-Hispanic Whites, but not among non-Hispanic Blacks (Gjelsvik et al., 2013). Among patients utilizing services at Indian Health Service clinics in California, both neglect and CPA were associated with smoking, but CSA was not (Hodge & Nandy, 2011).

Among female-only samples, alcohol abuse (Fuller-Thomson et al., 2013) or drug abuse (Fuller-Thomson et al., 2013) in the household, parental separation/divorce (Fuller-Thomson et al., 2013; Strine et al., 2012), having an incarcerated household member (Strine et al., 2012), CSA (Bertone-Johnson et al., 2012; Fuller-Thomson et al., 2013; Jessup, Dibble, & Cooper, 2012; Pederson et al., 2008), CPA (Bertone-Johnson et al., 2012; Fuller-Thomson et al., 2013; Jessup et al., 2012; Pederson et al., 2008; Strine et al., 2012), any abuse (De Von Figueroa-Moseley, Landrine, & Klonoff, 2004), physical neglect (Strine et al., 2012), and verbal/emotional abuse (Fuller-Thomson et al., 2013; Pederson et al., 2008; Strine et al., 2012) were all associated with tobacco use and related behaviors. For men, alcohol abuse or drug abuse in the household, parental separation/divorce, and CPA were associated with smoking status (Fuller-Thomson et al., 2013), and among MSM, CSA was associated with smoking (O'Cleirigh et al., 2015).

Several studies found no significant associations ($N = 5$) or mixed associations ($N = 5$). For example, CM was not associated with smoking among never-deployed young male Marines (Agorastos et al., 2014), nor in a sample of primarily poor, urban dwelling African American women with a history of substance use during pregnancy (Min et al., 2013). In other studies, significant associations between smoking status and related behaviors were not found for individuals exposed to CPA (Francis et al., 2015; Kristman-Valente, Brown, & Herrenkohl, 2013), CSA (Kristman-Valente et al., 2013), or CM (Kim & Williams, 2009). ACE score from Wave 2 of the original ACE study was not associated with smoking status, and among men, individual ACE categories were not associated with smoking (Strine et al., 2012). Using BRFSS ACE data, exposure to any child abuse was not associated with smoking status (Dube et al., 2010), but exposure to any household challenges was positively associated (Dube et al., 2010).

Discussion

The purpose of this review was to describe the scope and nature of the published evidence on associations between ACEs and behaviors and exposures in adulthood that are associated with increased risk for cancer. We identified 155 quantitative, peer-reviewed, US-based articles published between 2005 and 2015 that examined associations between childhood adversity and the presence of cancer risk factors in adulthood. The majority of articles investigated associations between ACEs and alcohol, obesity/excess body fat or size, and tobacco. Fewer studies investigated the links between ACEs and chronic inflammation or infectious agents. No publications met our inclusion criteria and investigated associations between ACEs and environmental carcinogens, hormones, immunosuppression, radiation, or ultraviolet radiation, highlighting gaps in the literature. Although not all of these connections are intuitive, ACEs and some of these risk factors share similar underlying risk factors. For example, research suggests that children living in poverty are at higher risk of exposure to both environmental carcinogens (Payne-Sturges & Gee, 2006; Powell & Stewart, 2001) and violence (Sedlak et al., 2010), which may both contribute, independently or cumulatively, to their adult cancer risk.

Associations varied by the ACE measure, the cancer risk factor, sample demographics, and study methodologies. Despite these variations, when taken together, the studies highlight the potential impact of childhood experiences on risk factors for cancer in adulthood, and may explain some of the association between ACEs and cancer found in previous reviews (Holman et al., 2016). As such, efforts to prevent ACEs or minimize their negative impact on individuals' lives may result in reductions in certain cancer risk factors, potentially contributing to decreases in cancer incidence over time. Implications for clinical practice, particularly for pediatric nurses are described below.

This scoping review uncovered notable research gaps and limitations, including inconsistencies in defining and measuring ACEs, the lack of diversity in study samples, and areas of research that have yet to be explored. Addressing these research gaps and limitations could expand our understanding of the associations between early adversity and cancer risk. Recommendations for future research, in the context of our findings, are expounded on below.

Limitations

This review is not without limitations. The diversity in ACE and cancer risk factor measurement and study methodologies resulted in an inability to analytically synthesize the results. Additionally, although our selected inclusion criteria excluded less rigorous studies, it was beyond the scope of this review to assess methodological quality. We also limited study selection to the US and to the previous 10 years; as such, more research may be available that was not included here, including grey literature. The selected search terms may not have picked up important associations between ACEs and cancer risk. For example, the hormone search criteria were limited to words specific to sex hormones, and thus we did not capture articles related to cortisol or other hormones that may significantly contribute to associations between ACEs and cancer risk. Additionally, the selected risk factors may have over simplified the relationship between ACEs and cancer risk. For example, the complex

relationship between physical activity, obesity and cancer risk was beyond the scope of this review. Sociodemographic considerations were also limited in this review. However, studies with restricted demographic samples were identified; 12 studies specifically focused on LGBT populations; seven studies included Black participants only; two studies included American Indian/Alaskan Native participants only; and three studies included Hispanic participants only. Finally, cancer risk factors were restricted to those present in adulthood, although many risk factors begin to develop before the age of 18.

Implications for Nursing Practice

Pediatric nurses see a wide range of health issues – both physical and emotional – that have short- and long-term effects on patients. Pediatric nurses are a trusted resource for children and families, and they are often the only service providers who come into contact with all children on a regular basis. As such, pediatric nurses can play an important role in both treating and preventing ACEs. Nurses can help identify children at risk of ACEs and connect families to appropriate services (e.g., social/economic services, parent training, and counseling). They are also ideally suited to break the intergeneration transmission between parents/caregivers, and the children/babies they see in their practice by engaging with parents/caretakers during the child's appointment. In doing so, they can identify parents who may need assistance and connect them to services. This can reduce the risk of children experiencing ACEs. Pediatric nurses may also be the first to identify symptoms related to exposure to ACEs (somatic complaints, mental health issues, behavioral problems) (American Academy of Pediatrics & Pediatric Orthopaedic Society of North America, 2008). Pediatric nurses who are knowledgeable about ACEs may be able to direct families to the services they need to address the root causes of health consequences related to ACEs. As such, being informed about ACEs and equipped with as many treatment options and resources as possible could reduce the number of children and adults that need treatment and care further downstream. It is also important to understand the ways in which ACEs extend beyond the patient populations. ACEs are a significant public health concern that inflict high individual and social costs on patients, their families, and communities at large. Pediatric nurses are ideally situated to educate others about the biology of adversity and healthy child development to improve outcomes for children who experience adversity, and to help decrease the heavy toll ACEs take on our society and collective health.

Recommendations for Future Research

Given the variability in the associations between ACEs and cancer risk factors, the field could benefit from more studies that utilize a uniform approach to measuring adversity and later health. One suggestion is to encourage the use of uniform definitions and best practices for measurement. For example, previous research suggests that behaviorally specific questions may increase disclosure of violence and victimization compared to checklist items (Cook, Gidycz, Koss, & Murphy, 2011); however, many of the included studies relied on checklist items only. Indeed, stronger associations between CSA and alcohol use were found using behavioral questions compared to checklist items (Sartor et al., 2012), which suggests that measurement of ACEs could have significant implications on reported associations, and may have contributed to the varied results in the present review.

Beyond question type, the diversity in ACE categories and dimensions of exposure warrants consideration. Over thirty different types of childhood adversity were measured by the studies included in this review. Some studies created a summed adversity scores and others relied on individual items, which likely contributed to variations in study findings, and made comparisons across studies challenging. In addition, few considered other important dimensions of ACEs, such as age of exposure, severity, frequency, relationship to perpetrator, and symptomology, which all likely contribute to later risk of poorer outcomes. Furthermore, although investigations of protective factors were not within the scope of this review, many studies lacked information on the effects of potential protective factors, such as access to a safe, stable, nurturing relationship with an adult. A thorough understanding of this critical dimension would help to inform novel prevention strategies. A deeper investigation of ACEs and cancer risk, through quantitative and qualitative studies, could better inform cancer risk reduction, and may contribute to innovative ways to change a person's cancer risk trajectory, starting in childhood.

Studies specific to women ($N = 43$) were more prevalent, particularly for alcohol and obesity outcomes. Future research is needed to better understand the distribution of ACE exposure across different sociodemographic groups and the differential impact of adversity on risk across one's lifetime. To understand the complex connections and interactions between childhood experiences and adult cancer risk, researchers could provide critical information to practitioners and policy-makers by consistently and systematically identifying how race/ethnicity, sexual orientation, gender identity, SES and other markers of advantage and disadvantage contribute to inequities in exposures and outcomes between groups. These explorations can equip researchers and practitioners with a better understanding of risk factors for early adversity and later health conditions, and may contribute to a broader evidence-base for prevention and intervention approaches for all sociodemographic backgrounds.

Despite no found associations between ACEs and sex hormones, the role of other hormones warrants attention in future work. For example, cortisol, an anti-inflammatory hormone that plays a key role in our stress response, has been associated with impaired immune response, which can complicate cancer risk and recovery (Schrepf et al., 2013). Cortisol and distorted physiological stress responses have been linked to childhood trauma (Shonkoff, 2016), and while these topics were beyond the scope of this review, they are an important consideration for future research. In addition, despite the paucity of research, the connection between ACEs and immune response, which likely confounds the relationship of ACEs to other risk factors, including infectious agents, is an important future direction of research. As noted above, researchers have found that childhood trauma is associated with prolonged activation of the stress response system (Shonkoff, 2016); this prolonged activation stimulates irregular cortisol production, which impairs the immune response and alters cancer risk and recovery (Schrepf et al., 2013).

It remains important to consider what contexts place children and families at greater risk of ACEs and cancer risk factors, as well as how context may contribute to the accumulation of adversity and cancer risk over time and compound the impact of exposure on risk of cancer. Twelve studies included measures of family poverty, but little is known about how this may

have put children and families at risk of additional adversity across their lives. More research is needed to understand the complexity of such relationships, including how social and structural determinants of health place individuals and families at increased risk of poverty, which then puts them at increased risk of ACEs and poorer health outcomes (Metzler et al., 2017; Sedlak et al., 2010) - cycles that can repeat across generations. To address and prevent ACEs, comprehensive strategies that work across the social ecological levels (individual, relational, community, and societal), generations and sectors are needed. Another important issue to consider is the accumulation of trauma over time. Exposure to ACEs heightens risk for additional violent exposures, which may then compound and accumulate cancer risk. For example, Eames et al. (2014) found that among men with high adult stress, those who experienced higher ACEs consumed more alcohol than men did with no or low ACEs. This suggests that ACEs may intensify the effect of adult stress on drinking behaviors, and possibly other modifiable risk behaviors. Similarly, ACEs can accumulate across and impact future generations (Schofield, Lee, & Merrick, 2013). Therefore, prevention strategies could consider a generational approach whereby parents exposed to childhood adversity are included in intervention strategies.

Conclusion

Despite limitations, this review has important implications for cancer research and health care practice. Given the breadth of the science and noted associations between ACEs and cancer risk, we encourage researchers to take ACEs into account when planning future studies of cancer risk and prevention. Practitioners, including nurses and mental health providers, may wish to implement ACE screening and prevention strategies using clinical interventions and treatment programs. Furthermore, the effective prevention of ACEs and management of subsequent health outcomes require programs and policies that assure that children and families have access to the essentials – safe, stable, nurturing relationships and environments – so that all children can reach their full health and life potential (Centers for Disease Control and Prevention, 2014; Fortson et al., 2016). Antecedents for adult cancer may be rooted in childhood experiences; therefore, the importance of preventing and treating exposure to ACEs before they occur can be innovative in upstream cancer prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ACEs	Adverse Childhood Experiences
AI/AN	American Indians and Alaskan Natives

BRFSS	Behavioral Risk Factor Surveillance System
CDC	Centers for Disease Control & Prevention
CM	child maltreatment
CPA	childhood physical abuse
CRP	C-reactive protein
CSA	childhood sexual abuse
HPV	human papillomavirus
IL-1β	interleukin-1 beta
IL-6	interleukin-6
LGB	lesbian, gay, bisexual
MIDUS II Study	the National Survey of Midlife Development in the United States
MSM	men who have sex with men
NCI	National Cancer Institute's
TNF-α	tumor necrosis factor-alpha
UV	ultraviolet

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Fig. 1.

Types of adverse childhood experiences included in studies. Note: The size of the word reflects its frequency of measurement in studies. The adversity type may have been measured as an individual item, included as part of a summary or score, or both. The shade of the word has no meaning.

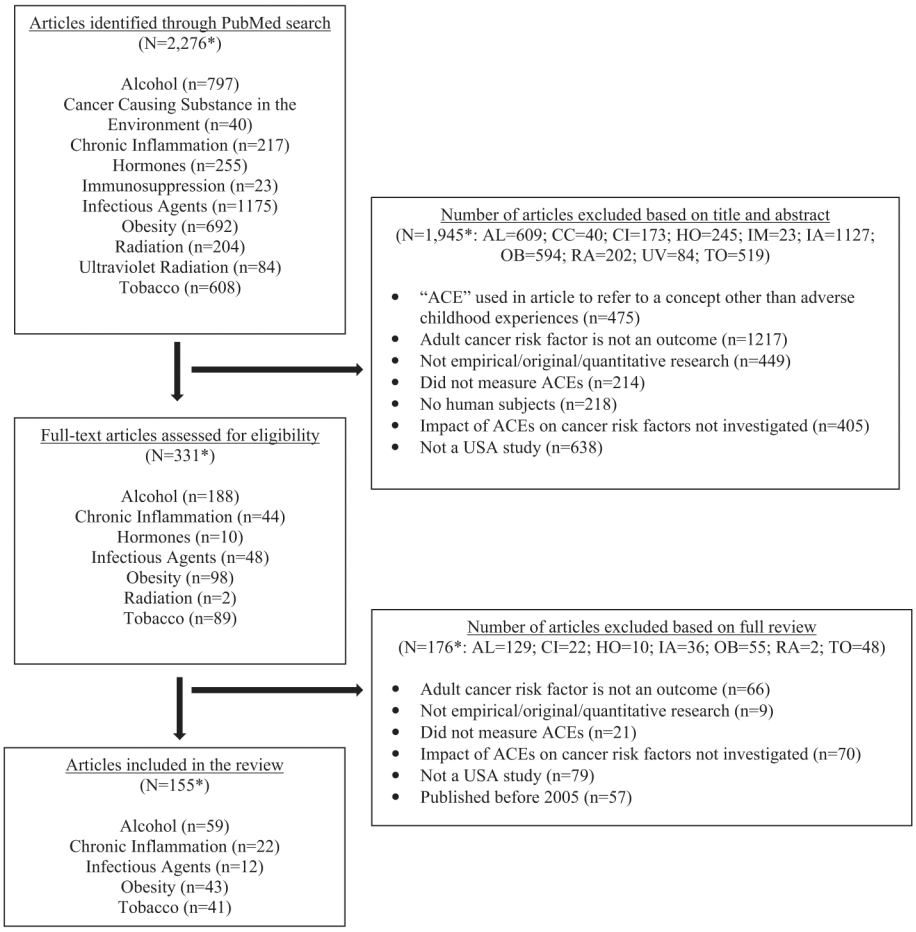

Fig. 2.

Flowchart of study selection. Note. Alcohol = AL; Cancer causing substances in the environment = CC; Chronic inflammation = CI; Hormones = HO; Immunosuppression = IM; Infectious agents (IA); Obesity = OB; Radiation = RA; Ultraviolet radiation = UV; Tobacco = TO; *N = total number of unique articles; some articles addressed multiple topics or were excluded for multiple reasons.

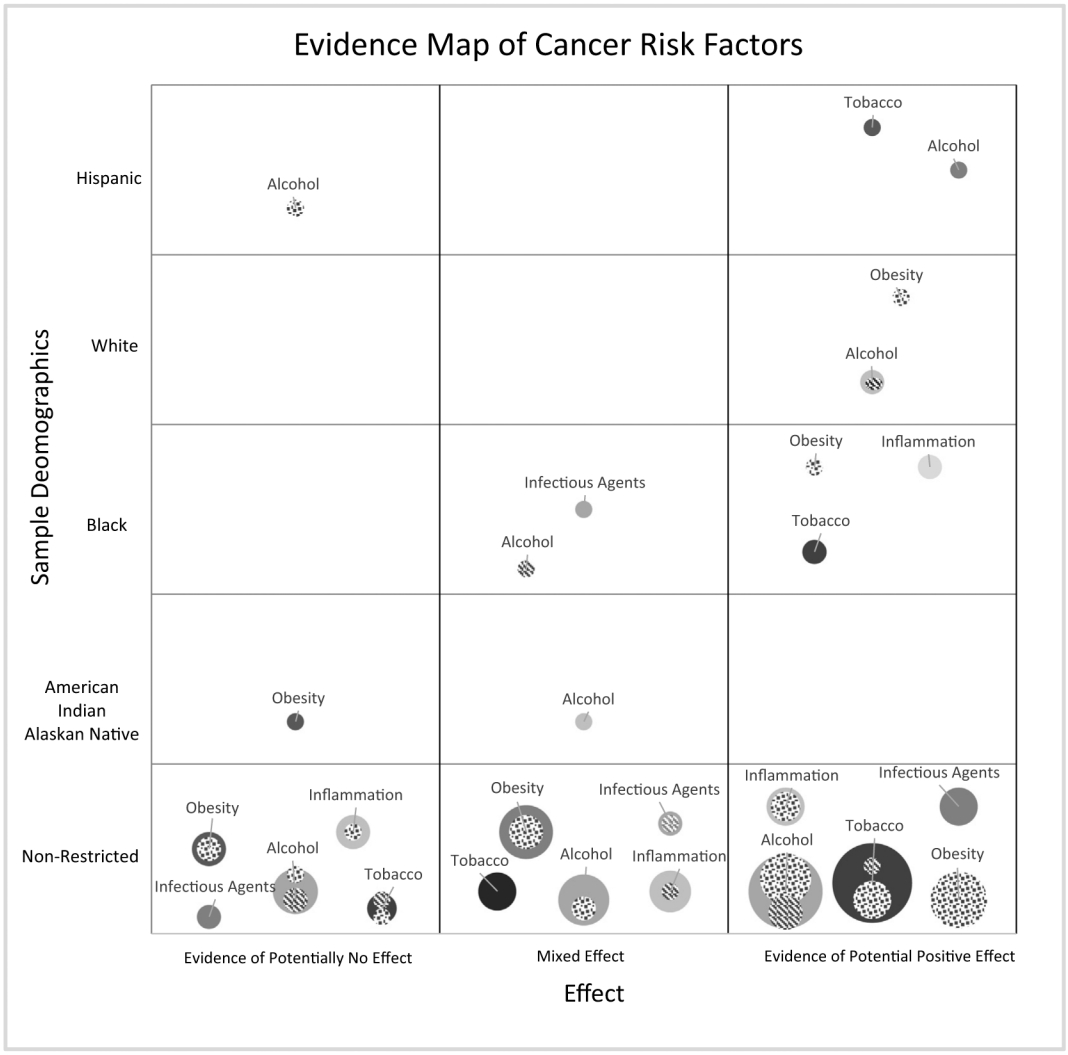

Fig. 3.

Bubble plot of reported associations between ACEs and cancer risk factors by effect and demographics. Key: Size of bubble = the number of articles looking at the association between ACEs and the identified cancer risk factor; ▨ = male-only participants ● = female-only participants. **Note:** Study samples were non-Hispanic unless noted.

Table 1

Summary of search terms used in the PubMed online database to identify articles reporting on the association between Adverse Childhood Experiences (ACEs) and cancer risk factors in adulthood.

Terms related to adverse childhood experiences	((“ACE”) OR (“ACEs”) OR (“adverse childhood experiences”) OR (“adverse childhood events”) OR (“childhood maltreatment”) OR (“child maltreatment”) OR (“childhood adversity”) OR (“child adversity”) OR (“childhood adversities”) OR (“child adversities”) OR (“early adversity”) OR (“early adversities”) OR (“physical abuse”) OR (“sexual abuse”) OR (“childhood neglect”) OR (“child neglect”) OR (“physical neglect”) OR (“child abuse”) OR (“childhood abuse”) OR (“emotional abuse”) OR (“child emotional neglect”) OR (“childhood emotional neglect”) OR (“child trauma”) OR (“childhood trauma”) OR (“emotional neglect”) OR (“parental incapacities”) OR (“family incapacities”) OR (“adverse family experiences”) OR (“adverse family events”))
AND	
Terms related to cancer riskfactor – Alcohol	((“alcohol consumption”) OR (“alcohol drinking”) OR (“consumption of alcoholic beverages”) OR (“consumption of alcohol”) OR (“alcohol dependence”) OR (“alcohol abuse”) OR (“excessive drinking”) OR (“binge drinking”) OR (“heavy drinking”) OR (“heavy alcohol drinking”) OR (“underage drinking”) OR (“drinking underage”))
OR	
Terms related to cancer risk factor – Environmental Cancer Causing Substance	((“environmental carcinogens”) OR (“aflatoxins”) OR (“aspergillus flavus”) OR (“aspergillus parasiticus”) OR (“aristolochic acids”) OR (“arsenic”) OR (“asbestos”) OR (“benzene”) OR (“benzidine”) OR (“beryllium”) OR (“1, 3-butadiene”) OR (“cadmium”) OR (“coal tar”) OR (“coal-tar pitch”) OR (“creosote”) OR (“coke-oven emissions”) OR (“crystalline silica”) OR (“erionite”) OR (“ethylene oxide”) OR (“formaldehyde”) OR (“hexavalent chromium compounds”) OR (“indoor emissions from the household combustion of coal”) OR (“indoor emissions”) OR (“household combustion of coal”) OR (“coal combustion”) OR (“mineral oils”) OR (“nickel compounds”) OR (“radon”) OR (“secondhand tobacco smoke”) OR (“secondhand smoke”) OR (“secondhand smoking”) OR (“environmental tobacco smoke”) OR (“soot”) OR (“inorganic acid mists containing sulfuric acid”) OR (“sulfuric acid”) OR (“acid mist”) OR (thorium) OR (“vinyl chloride”) OR (“wood dust”))
OR	
Terms related to cancer risk factor – Chronic Inflammation	((“inflammation”) OR (“CRP”) OR (“C-reactive protein”) OR (“inflammatory response”) OR (“inflammatory markers”) OR (“adiponectin”) OR (“resistin”) OR (“interleukin-6”) OR (“adipokines”) OR (“adipocyte-derived inflammation”) OR (“chronic inflammatory disease”))
OR	
Terms related to cancer risk factor – Sex Hormones	((“estrogen”) OR (“hormone therapy”) OR (“hormone replacement therapy”) OR (“estrogen plus progestin”) OR (“endogenous estrogen and progesterone”) OR (diethylstilbestrol) OR (“DES”) OR (“oral contraception”) OR (“oral contraceptive”) OR (“birth control”))
OR	
Terms related to cancer risk factor – Immunosuppression	((“immunosuppression”) OR (“immunosuppressive drugs”) OR (“immunocompromised”) OR (“compromised immune system”) OR (“transplant recipients”))
OR	
Terms related to cancer risk factor – Infectious Agents	((“human papillomavirus”) OR (“HPV”) OR (“human papilloma virus”) OR (“HPV infection”) OR (“human papilloma virus infection”) OR (“hepatitis B virus”) OR (“hepatitis C virus”) OR (“hepatitis B”) OR (“hepatitis C”) OR (“HBV”) OR (“HCV”) OR (“hepatitis”) OR (“hep C”) OR (“hep B”) OR (“T-cell leukemia”) OR (“T-cell lymphoma”) OR (“lymphoma virus type 1”) OR (“HTLV-1”) OR (“T-cell leukemia/lymphoma”) OR (“HIV”) OR (“human immunodeficiency virus”) OR (“HIV/AIDS”) OR (“AIDS”) OR (“acquired immune deficiency”) OR (“epstein-barr virus”) OR (EBV) OR (“human herpesvirus 8”) OR (“HHV8”) OR (“kaposi sarcoma-associated herpes virus”) OR (“KSHV”) OR (“merkel cell polyomavirus”) OR (“MCPyV”) OR (“helicobacter pylori”) OR (“H. pylori”) OR (“schistosoma haematobium”) OR (“opisthorchis viverrini”))
OR	
Terms related to cancer risk factor – Obesity, Physical Activity, Sedentary Behavior	((“obesity”) OR(“obese”) OR (“overweight”) OR (“over-weight”) OR (“metabolic syndrome”) OR (“BMI”) OR (“body mass index”) OR (“body fat percentage”) OR (“BFP”) OR (“waist-hip ratio”) OR (“waist-to-hip ratio”) OR (“WHR”) OR (“physical activity”) OR (“exercise”) OR (“sedentary behavior”) OR (“sedentary”) OR (“sedentary lifestyle”) OR (“sedentary time”) OR (“screen time”))

OR	
Terms related to cancer risk factor – Radiation	((“radiation”) OR (“ionizing radiation”) OR (“radon”) OR (“radium”) OR (“x-rays”) OR (“gamma rays”) OR (“high-energy radiation”) OR (“alpha particles”) OR (“beta particles”) OR (“neutrons”) OR (“accidents at nuclear power plants”) OR (“atomic weapons”) OR (“fallout”) OR (“iodine-131”) OR (“I-131”) OR (“NRI”) OR (“computed tomography scans”) OR (“CT scans”) OR (“positron emission tomography scans”) OR (“PET scans”) OR (“medical radiation”) OR (“radiation from medical imaging”))
OR	
Terms related to cancer risk factor – Ultraviolet Radiation	((“sunlamps”) OR (“tanning booths”) OR (“tanning”) OR (“ultraviolet radiation”) OR (“UV”) OR (“UVR”) OR (“sun exposure”) OR (“sun damage”) OR (“sunburn”))
OR	
Terms related to cancer risk factor – Tobacco	((“tobacco”) OR (“cigars”) OR (“smoking”) OR (“smoke”) OR (“cigarettes”) OR (“cigarette”) OR (“cigar”) OR (“cigars”) OR (“snuff”) OR (“dip”) OR (“snus”))
AND	
Language selection	“English”[Language]
AND	
Date-Publication	2005/01/01–2015/12/31
NOT	
Excluded search terms	((“angiotensin-converting enzyme inhibitors”) OR (“ACE inhibitors”) OR (“angiotensin”) OR (“acute care of the elderly”) OR (“ACE-27”) OR (“ACE 27”) OR (“adjuvant chemotherapy and endocrine therapy”) OR (“HPV4A ACE”) OR (“ACE serum”) OR (“acute care for the elderly”) OR (“agitation-calmness evaluation scale”) OR (“ACE polymorphism”) OR (“T-ACE”) OR (“angiotensin-converting enzyme”) OR (“central nucleus of the amygdala”) OR (“ACE inhibitor”) OR (“adverse clinical event”) OR (“ACE inhibitor-drug”) OR (“Auto-capillary Electrophoresis”) OR (“alternative cellular energy”) OR (“comment”[Publication Type]) OR (“meta-analysis”[Publication Type]) OR (“review”[Publication Type]))