International Journal of Public Health (2018) 63:811–821
https://doi.org/10.1007/s00038-018-1131-5

ORIGINAL ARTICLE

How does the social environment during life course embody in and influence the development of cancer?

Ming Chen[1,2] · Huiyun Zhu[1] · Yiqi Du[1] · Geliang Yang[3]

Received: 27 June 2017 / Revised: 19 May 2018 / Accepted: 1 June 2018 / Published online: 11 June 2018

Abstract

Objectives This review assessed the complex longitudinal processes involved in cancer etiology during life course to understand how the social inequality may be embodied in and influence cancer risk.

Methods A narrative literature review was performed with a keyword search conducted using PubMed, Scientific Electronic Library Online and Google. Three aspects of literatures were mainly included: social environmental mechanisms of cancer, life course of cancer development and social inequality of cancer risk. This review was complemented with manual searches of relevant journals and reference lists of primary articles.

Results Social inequality is mostly embodied in genetic susceptibility and early childhood development, the duration and intensity of exposures and the access to medical resources, which influence the timing and accumulation of cancer risk during life course.

Conclusions The individuals with lower socioeconomic status are more likely to have higher cancer risk because of more frequency of timing and quantity of accumulation of adverse exposures and greater impact on epigenetic mechanisms. Primary prevention is the best prevention strategy to reduce cancer risk.

Keywords Social inequality · Socioeconomic status · Exposure · Life course · Cancer · Cancer risk

Introduction

The influence of life course on the risk of developing cancer mostly depends on an individual's socioeconomic status (SES), which directly determines one's environmental exposures over time (Fig. 1) (Adler and Stewart 2010). As intermediate variables of cancer development, exposure to carcinogenic agents may come from behavioral, social, psychological and biological pathways related to occupational, residential and lifestyle factors which mainly depend on SES (Hemminki et al. 2003). Meanwhile, social inequality in cancer is embodied in these various exposures to risk factors in different SESs during life course. For example, stomach, lung and rectal cancers are typically more common in lower SES, whereas breast and colon cancers are more common in higher SES (Nordahl et al. 2014a). A life course approach to cancer development highlights the importance of the timing of exposures and the multiple pathways in understanding the developmental process of cancer and distinguishing the determined or triggered genesis of cancer.

Ming Chen and Huiyun Zhu contributed as co-first author to this article.

This article is part of the special issue 'Life course influences and cancer risk.'

✉ Yiqi Du
duyiqi006@126.com

✉ Geliang Yang
yanggeliang@hotmail.com

[1] Department of Gastroenterology, Changhai Hospital, Second Military Medical University (Naval Medical University), 168 Changhai Road, Shanghai 200433, China

[2] Company Eleven, Students Brigade, Second Military Medical University (Naval Medical University), Shanghai 200433, China

[3] Department of Integrative Oncology, Changhai Hospital, Second Military Medical University (Naval Medical University), 168 Changhai Road, Shanghai 200433, China

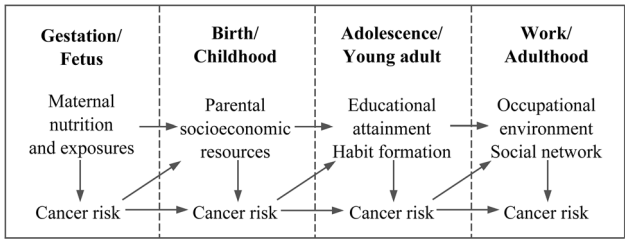

Fig. 1 Dynamic relationship between socioeconomic status and cancer risk during life course: different exposures in different periods of life course can increase cancer risk, which is accumulated over time influencing the development of cancer (Adler and Stewart 2010)

In this review, a life course approach on cancer epidemiology relies on comprehensive analysis of studies for understanding how early- and later-life behavioral, biological, social and psychological pathways affect cancer risk and incidence, which helps to understand the genesis of cancer associated with SES. As the first review focusing on this theme, we are mostly concentrated on summarizing and integrating all of the available literatures, especially taking into account the timing of exposures and the multiple pathways. We believe that the most important value of this review is to summarize different fields of scientific studies to help understand how a life course approach to the study of cancer can help achieve a better understanding of the genesis of cancer. What's more, we creatively make longitudinal collation and interpretation from macroscopical to microcosmic angles and horizontal comparison of multiple pathways.

Method

This narrative review followed the general steps of identifying research related to social environmental mechanisms of cancers, life course of cancer development, social inequality of cancer risk, locating relevant studies, selecting references from those studies and summarizing the findings. The main search engines used to source literature were PubMed and Scientific Electronic Library Online. The keywords used to conduct the search included a combination of ('social environment' OR 'social status' OR 'social inequality' OR 'life course') AND ('cancer' OR 'cancer risk' OR 'cancer mechanism'). Duplicated papers were excluded. Studies were screened for inclusion in two phases, and the process was carried out in duplicate by reviewers. In Phase 1, records were selected by reviewing the title and/or the published abstract. In Phase 2, the full-text article was reviewed (Fig. 2). In case of any disagreement, researchers discussed the problems, trying to reach consensus. When consensus was not reached, a third co-author read the paper.

Articles were included if:

(a) The study focused on all cancer research, not on certain specific cancer;
(b) The study was relevant to the social environmental mechanisms of cancers, the life course of cancer development, or the social inequality of cancer risk. The reference lists for each of the selected articles were also reviewed in full to identify other relevant papers;
(c) This review concentrated on summarizing and integrating all of the available literatures, especially taking into account the timing of exposures and the multiple pathways. If some pathways involved certain specific cancer, relevant literatures searched again in PubMed and Scientific Electronic Library Online were also included;
(d) The study was written in English.

Articles were excluded if:

(a) The study focused on certain specific cancer, not on all cancer research;
(b) The study was not related to this theme, including cancer treatment, cancer mortality, cancer survival, cancer complications, cancer recurrence and other irrelevant articles;
(c) The research object or region of study was not representative, such as specific race or unusual district.

The quality of each study was addressed taking into account internal validity (risk of bias), as well as the external and ecological validity of the study. Qualitative studies were not given an overall rating or score as there is no consensus in this area. We have followed some criterions to assess the result of included studies, including reach and representativeness, methodological implementation and adaptation, outcomes veracity and reliability and conclusion correlation.

Results

Behavioral pathways

Smoking

The extent to distinct mutational processes caused by smoking operate differs between tissue types (at least partially depending on the degree of direct exposure to tobacco smoke), and their mechanisms range from misreplication of DNA damage caused by tobacco smoke constituents to activation of more generally operative mutational processes (Alexandrov et al. 2016). A study on

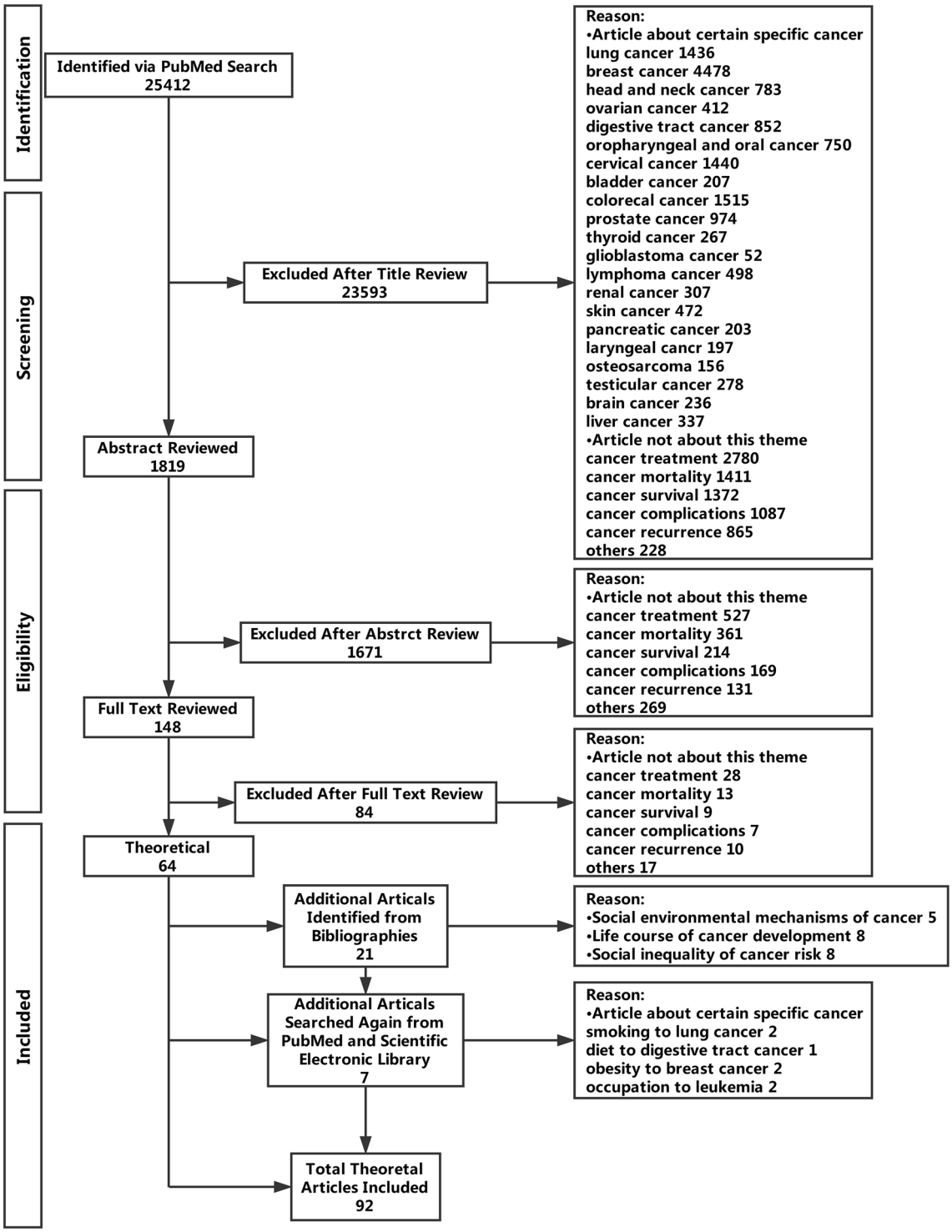

Fig. 2 Study flow diagram showing that the abstracts and/or full texts of 25,412 articles identified via PubMed search (top box) were reviewed, with boxes on the right detailing reasons for exclusion. A total of 92 articles were included in the review (bottom box)

social inequality indicated that both men and women with lower education appeared to be more vulnerable to the effects of smoking than those with higher education, since they are least informed about the cancer risk though smoking and the less likelihood to have access to smoking cessation services, finally increasing the incidence of cancer (Nordahl et al. 2014b). In childhood, passive smoking from maternal and paternal cigarette smoking has short-term health effects as well as setting the stage for diseases which arise later in life (Barnoya and Glantz 2005;

Harwood et al. 2007; Nordahl et al. 2014b). Moreover, children who grow up in less affluent households are more likely to have smoking parents and thus are more likely to imitate to be smokers (den Exter Blokland et al. 2004; Leonardi-Bee et al. 2011; Vohra et al. 2016).

Diet

Nutrition absorbed from diet, as a determinant of growth and body composition, also influences cancer risk, directly due to carcinogens in foods or indirectly by the hormonal and metabolic response to growth and obesity (Uauy and Solomons 2005). Hullar et al. presented examples of microbially mediated pathways, which involve both (1) direct contact of the pathogen with human host and (2) indirect effects of microbial metabolism of exogenous and endogenous substrates (Hullar et al. 2014). These pathways alter inflammation, modify DNA leading to mutations or influence epigenetics and gene silencing. It is an accepted fact that people with lower SES have less economic capability to afford for eating fresh vegetables and fruit. Therefore, children and adolescents with lower SES will likely have greater exposure to harmful foods and have more risk to diet-related cancers (Cohen et al. 2010). These early dietary exposures can have continuous and long-term influences on adult health by forming poor dietary habits that remain throughout adulthood, as well as by resulting in poor childhood health (high cholesterol, obesity, poor immunity) which ultimately can lead to elevated cancer risk later in life (Cohen et al. 2010). For example, dietary salt, nitrite and smoked food are thought to be risk factors mainly for the intestinal type of gastric cancer; dietary fat and red meat consumption during adolescence and body fatness at childhood increases risk for breast cancer later in life (Baer et al. 2010; Ekstrom et al. 2000; Linos et al. 2008, 2010; Mahabir et al. 2012; Palli et al. 1997).

Physical activity

Physical activity is a modifiable lifestyle factor that has been associated with a reduced risk of colon, endometrial and pre- and postmenopausal breast cancer (Friedenreich et al. 2010a; Jung et al. 2011). It is reported that the intensity, duration and frequency of physical activity and whether it is part of housework, occupational tasks or sport and recreation may influence its cancer risk (Bauman 2004; Thune and Furberg 2001; Uauy and Solomons 2005). Physical activity may influence cancer risk by reducing circulating levels of sex hormones and decrease inflammation by reducing amplification of inflammatory mediators and initiating cytokine inhibitors, which is an important factor in DNA methylation and tumor progression (Bertone-Johnson et al. 2009; Friedenreich et al. 2010b; Hodge et al. 2005; Kang et al. 2003; Korniluk et al. 2017; McTiernan 2008; White et al. 2013). Children with lower SES tend to have lower levels of physical activity. The absence of parent role modeling of regular physical activity and subsequent habits for sedentary activities make children have increased risk for obesity and increased incidence of cancers (Cohen et al. 2010; Morrow et al. 1999; Rowlands et al. 1999; Ruiz et al. 2006). All of these bad conditions in childhood may generate health-damaging trajectories that persist through adolescence and adulthood (Cohen et al. 2010).

Biological pathways

Obesity

Obesity is an unhealthy medical condition mostly caused by excessive food intake. Obesity increases the risk of developing cancer through a panoply of pathophysiological alterations including systemic inflammation, dysregulation of adipokines, insulin resistance with hyperinsulinemia and hyperglycemia, dysbiosis and immune system alterations (Font-Burgada et al. 2016). Obesity can cause a metabolic syndrome: elevated blood pressure, high levels of blood sugar and cholesterol, as well as increased circulating insulin levels, increased inflammatory cytokines, etcetera. Aforementioned abnormal hormonal regulation of growth may be the key factor of cancer incidence within an individual. For example, girls who are heavier experience menarche earlier than leaner girls, and the more exposure of accumulated estrogen is associated with higher risk of breast cancer (Jeffreys et al. 2004). Many findings from current research support Sobal and Stunkard's early review of 144 studies: Income is inversely associated with obesity risk among adult women in economically developed countries, but inconsistently associated with obesity among men (Ogden et al. 2010; Pavela et al. 2016; Sobal and Stunkard 1989). As obese adults are less likely successful in long-term weight control, prevention of obesity in childhood is crucial to reduce cancer risk (Uauy and Solomons 2005).

Chronic infection

Various infectious agents have been associated with the incidence of cancer, such as HP to gastric cancer, HPV to cervical cancer, HBV and HCV to liver cancer and Epstein–Barr virus (EBV) to nasopharynx cancer (Vohra et al. 2016). At the cellular level, human viruses promote proliferation and expansion of pre-neoplastic cells which predispose to cancer (Dobbelaere and Heussler 1999). At the level of the whole organism, infection can also set up chronic inflammatory conditions that predispose to cancer. The predominant view is that tumorigenesis occurs in areas

of chronic inflammation stemming from cell-mediated immune responses (Thomas-Tikhonenko and Hunter 2003). Therefore, an exaggerated immune response could be a risk factor for cancer. Some studies showed that characteristic of lower SES families' homes, such as lower family income, lower parental education and more residential crowding, may increase children's risk of exposure to infectious agents (Barr et al. 2001; Cohen et al. 2010; Dowd et al. 2009). More importantly, early life infections in infant or childhood are at greater risk for developing relevant cancer in later life. For stomach cancer, the mechanism is likely to be a more direct effect related to exposure to and acquisition of HP infection in less advantaged families during childhood (Lawlor et al. 2006; Vohra et al. 2016).

Social pathways

Occupation

Occupational cancers are concentrated among manual workers and in the lower socioeconomic areas, because of more accumulation and stimulation of carcinogens. For example, agriculture-related exposures, such as pesticides, could increase leukemia morbidity in rural areas (Infante-Rivard and Weichenthal 2007; Kong et al. 2010). Occupational exposures of parents might be related to cancer in their offspring (Bailey et al. 2014). The strongest evidence is for childhood leukemia and paternal exposure to solvents, paints and employment in motor vehicle-related occupations and childhood nervous system cancers and paternal exposure to paints (Metayer et al. 2016). Children may be exposed to carcinogenic substances that relevant to the cancer process occur prior to conception (i.e., germ cell effects), during pregnancy (i.e., transplacentally, from exposures experienced by the mother at the workplace or from paternal transfer of substances from the workplace to the home) or after birth (i.e., substances carried home by either parent) (Colt and Blair 1998; Febvey et al. 2016; Omidakhsh et al. 2017; Zhang et al. 2016).

Psychological pathways

Psychological dispositions

Mental depression and other negative emotions act on the central nervous system, causing autonomic function and endocrine dysfunction, so the cells lose their normal state and function, constantly changing, ultimately resulting in cancer cells (Cohen et al. 2010). On the other hand, subdued immune system accelerates the growth and formation of cancer. Psychosocial exposures from family and social experience in the life act as upstream influences on cancer risk (Cohen et al. 2010). People with lower SES experience a higher frequency of stressful events at home and work, and they have fewer social resources to deal with these stresses (Hatch and Dohrenwend 2007; Marmot et al. 2008; von Wagner et al. 2011). Chronic stress associated with lower SES is consistent with the view that SES-related exposures result in an acceleration of the aging process at the cellular level as indicated by shorter telomeres (Adler and Stewart 2010). Studies have revealed that telomeres can facilitate cancer formation: Cells with too short telomeres can lose capping function leading to a cellular catastrophe and genetic instability which are the origin of many cancers (Meena et al. 2015).

Discussion

Actually, the influence of SES on cancer risk is mostly embodied in the timing and accumulation of exposures through multiple pathways, which may cause epigenetic alteration and eventually induce cancer. Therefore, the most important element is the timing and accumulation of exposures through multiple pathways in different levels of SES, not the rich or the poor while the social equality increases or reduces the probability of exposures.

Theoretical models

The theoretical models to measure dose of cancer risk associated with life course exposures are summarized in Table 1.

Table 1 Theoretical life course models of cancer risk (Ben-Shlomo and Kuh 2002; Lynch and Smith 2005)

Timing model
(Focus on the greater influence due to exposures in a specific period)
Critical period
A limited time window when an exposure can influence development
Sensitive period
A relative broad period when an exposure can have greater effect
Accumulation model
(Focus on the total amount and/or sequence of exposures over time)
Amount of exposures
By measuring the ever-increasing intense of exposures
Sequence of exposures
By measuring the ever-increasing duration of exposures
Interaction of exposures
By analyzing chains of risk or clustering of risk

Timing model

Social timing focuses on the role of specific period in the occurrence, continuity and consequences, as well as the relevant age expectations and beliefs. Timing model indicates that the time of the event is more meaningful than the incident itself. Exposure to carcinogenic agents in the critical or sensitive period is more likely to have a great influence on developing cancer. A critical period is defined as a limited time window when an exposure can have harmful or protective effects on development and later disease outcome (Ben-Shlomo and Kuh 2002). Unalterable biological development caused by prenatal infections or drug exposure in a period time has long-lasting effects on physiological function or anatomical structure that may ultimately result in cancer (Lynch and Smith 2005). For example, very early postnatal infection with hepatitis B directly having a great damage to liver's function or anatomical structure increases the risk of adulthood liver cancer (Chang 2014). A sensitive period is defined as when an exposure has a greater effect on development and disease risk than it would at other times. For example, children who eat a lot of fat food are more likely to be obese and thus have a higher obesity-related cancer risk. Critical periods may have a higher cancer risk associated with developmental mechanisms in biological subsystems, whereas sensitive periods are more evident in behavioral development (Ben-Shlomo and Kuh 2002). The influence of exposures acting during critical or sensitive periods of susceptibility may also be modified by later-life exposures (Lynch and Smith 2005). Timing model emphasizes the crucial effect of the timing of exposures in the development of cancer to help us understand the relationship between life course influences and cancer risk (Fenton and Birnbaum 2015).

Accumulation model

Accumulation model is another life course model focusing on the total amount and/or sequence of exposures by measuring the ever-increasing intense and/or duration of exposures as well as cumulative damage to biological systems, ultimately causing cancers (Ben-Shlomo and Kuh 2002; Lynch and Smith 2005). The accumulation model indicates that the higher cancer risk of lower SES accrues throughout the life course with more increasing intensity and/or duration of exposures to socioeconomic disadvantage (Cohen et al. 2010). Different risk factors at different life stages may have an interaction with each other like chains of risk where one adverse exposure or experience tends to lead to another reciprocally (Ben-Shlomo and Kuh 2002). For example, becoming obese in childhood may cause reduced physical activity in adolescence and adulthood and also less physical activity in childhood may cause obesity in later life. Therefore, the trajectory or sequence of accumulation is also important, as they may be influenced by critical or sensitive periods' exposures and by each other (Lynch and Smith 2005). In addition, accumulation of risk can also be caused by clustering of exposures (Mahabir et al. 2012). For example, children with lower SES are also more likely to be of lower birth weight, to have poorer diets, to have less physical activity, to be more exposed to second-hand smoking and some infectious agents, to be easily stressed or depressed and to have fewer opportunities for education, all of which can be associated with increase of cancer risk or indirectly influenced by each other to facilitate developing cancer (Ben-Shlomo and Kuh 2002).

In conclusion, cancers seem to result from the complex interaction of critical and sensitive periods and accumulation and trajectory processes (Lynch and Smith 2005). For instance, the major risk factors of breast cancer—parental past history, younger age at menarche, early life at parturition, lower parity and later age at menopause—are temporally consistent with the basic understanding that breast cancer is related to cumulative and/or interactive exposures over the life course of active ovarian function (Fenton and Birnbaum 2015; Lynch and Smith 2005).

Theoretical mechanisms

The process and mechanism of environmental exposures during life course to develop cancer is concluded in Fig. 3.

Genetic susceptibility and poor early childhood development

The fetal origins hypothesis suggests that suboptimal maternal nutrition and harmful exposures during gestation may have detrimental effects on fetal growth, particularly by initiating persistent changes in metabolic, physiological and structural parameters (Barker 1997; Cohen et al. 2010). Poor fetal growth and genetic mutations in utero can cause genetic susceptibility and poor fetal development and hence increase cancer risk (Ozanne et al. 2004). In addition, infants after birth go into a rapid growth period as well as some critical or sensitive periods in which they are more vulnerable to carcinogenic exposures. Infants born to mothers with lower SES are at a higher risk to experience intrauterine growth restriction, be born prematurely and have a lower birth weight (Adler and Stewart 2010; Kramer et al. 2000). These disadvantages set them on trajectories of poorer development and higher disease risk, but also of lower adulthood SES as childhood illness influences academic achievement that, in turn, shapes adulthood SES

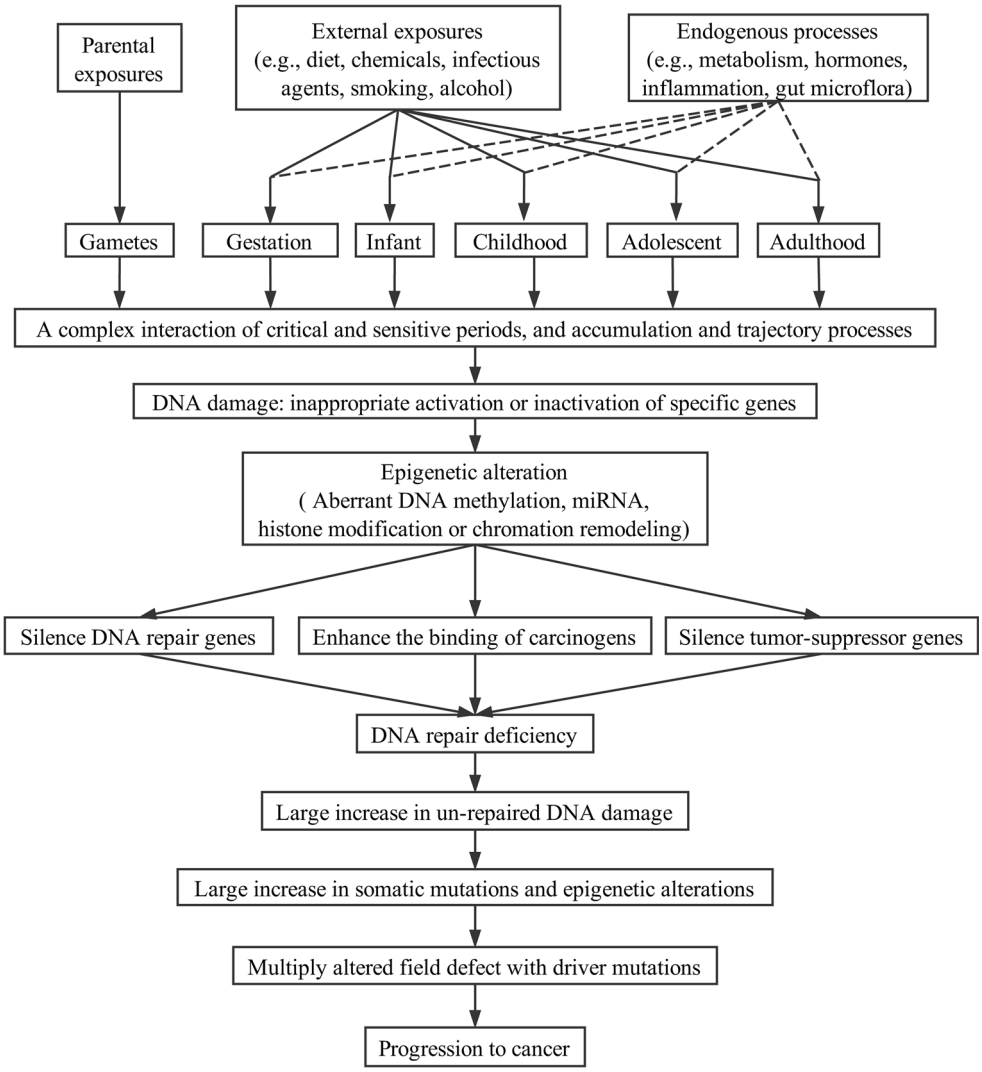

Fig. 3 Process of environmental exposures during life course to develop cancer: parental and external exposures and endogenous processes during life course, which are accumulated over time, cause epigenetic alteration and DNA repair deficiency and promote the development of cancer

(Adler and Stewart 2010; Case et al. 2005; Smith 1999). Human studies have showed the clear increases in cancer after prenatal exposure to ionizing radiation, and some evidence demonstrates that leukemia and brain tumors may contribute to parental exposure to chemicals or drugs (Uauy and Solomons 2005). These findings indicate that long-term cancers or susceptibility to cancer may result from developmental exposures rather than exposures existing at or near the time of cancer detection (Uauy and Solomons 2005). In terms of early childhood nutrition, the gut microbiome in infancy and childhood could be a crucial link between nutrition and cancer development later in life (Mahabir et al. 2012). However, the recognition of important early childhood influences on cancers should not neglect the possibility of later-life intervention (Wise 2003). For instance, gastric cancer caused by HP infection is mainly associated with later lifestyles and occurrences rare below age 50 (Lynch and Smith 2005).

Increasing duration and intensity of adverse exposures

A majority of adulthood cancers are unlikely to be explained as the predetermined consequence of inevitable trajectories of exposures in utero or early childhood, but rather as longer-term outcomes of the albeit complicated interaction and accumulation, across generations, of early- and later-life exposures (Lynch and Smith 2005). Greater accumulation of family indicators of lower SES was associated with greater possibility that children would have poorer health, would have a chronic condition or would have a higher risk of cancer (Adler and Stewart 2010; Evans 2003; Evans and Marcynyszyn 2004). Evidence from literatures shows that the greatest period with health disparities is middle adulthood (age 40–65), in which disparities may reflect the cumulative and interactive effects of differential exposures associated with socioeconomic disadvantage over the prior life course (Adler and Stewart 2010). Examples include HP for stomach cancer,

HBV for liver cancer and HPV for cervical cancer (Mahabir et al. 2012). These development processes of chronic diseases to cancers are life course processes with accumulation of increasing duration and intensity of adverse exposures, which eventually may act as a trigger to cancer formation (Cohen et al. 2010). Lower SES tends to have higher cancer incidence and poorer cancer survival overall rates than higher SES with more duration and intensity of adverse exposures during life course (Ben-Shlomo and Kuh 2002).

Less access to medical resources

Health-conscious behavior, participation in health screening programs and seeking and affordability of healthy food are linked to education and SES (Hemminki et al. 2003). It has been argued that health promotion strategies may not be effective for people with lower SES because of their bigger challenges to meet their basic needs, such as earning a living and providing a home for their family members (Garcia 2006; von Wagner et al. 2011). Lower SES communities are subjected to more hazards and have access to fewer medical resources to ameliorate their effects and hence have a higher risk of cancer (Adler and Stewart 2010). Lower SES has been proven to be associated with less awareness of the dangerous of cancer risk factors and the benefits of participating in screening, increased worry following a screening invitation and more fatalistic beliefs about cancer, likely due to less access to health recommendations and high-quality healthcare (Berenson et al. 2012; Lindholm et al. 1997; Niederdeppe and Levy 2007; Schroy et al. 2008; von Wagner et al. 2011; Wardle et al. 2004). Therefore, over time, lower SES individuals tend to expose and accumulate more adverse risk factors, increasing the risk to develop cancer (Ben-Shlomo and Kuh 2002). Some studies have demonstrated that smoking tends to be concentrated among the poor and uneducated individuals, as they are least informed about the health risk of smoking and less likely to have access to smoking cessation services (Akinyemiju et al. 2017; Hosseinpoor et al. 2012; Teo et al. 2013). Regular checkups and screening can find and treat precancerous lesions in time and hence reduce the occurrence of cancers. The only widely applied cancer screening programmers are those for cervical cancer (pap smear) and female breast cancer (X-ray mammography) (Memon et al. 2015; Saslow et al. 2012). Participation in cancer screening has been shown to depend on income and education, health insurance and type of health service (von Wagner et al. 2011). People with lower SES tend to have lower screening participation rates (Kong et al. 2010).

Biological mechanisms and their social determinants

There are several mechanisms through which obesity, in either childhood or adulthood, may affect subsequent cancer development: firstly, obesity is associated with altered sex hormone profiles through conversion of androgens into estrogens in adipose tissue and estrogen concentrations may influence either the initiation or the promotion of hormone-related cancers; secondly, obesity is associated with hyperinsulinemia, which itself is related to increased bioactivity of IGF-I and IGF-binding proteins, which in turn may facilitate cancer formation (Jeffreys et al. 2004). Breast cancer is shown to be related to high life course exposure to free estrogen. The earlier a girl starts menarche, the more menstrual cycles she will have, and the greater will be her accumulation and exposure to estrogen, and taller or heavier girls generally start menstruating earlier than shorter or lighter girls (Uauy and Solomons 2005). Nutrition and physical activity can affect the timing and rate of growth and the endocrine responses which interact with genetic factors that define cancer risk (Uauy and Solomons 2005). Specific dietary and environmental exposures-related hormones and growth factors regulated by signal and receptor transduction systems finish adjusting the expression of genes responsible for cell growth and replication (Cai et al. 2004; Davis and Milner 2004; Harris 2005; Uauy and Solomons 2005). Therefore, long-term adverse exposures and interaction may cause cell mutation and cancer formation through changing cell growth and replication.

Epigenetic programming

Environmental exposures may influence biochemical modifications to the nucleotides that contain DNA or to the histone proteins that package DNA, a key process of cancer formation known as epigenetic programming (Cohen et al. 2010). Cancers are the consequence of combined genetic and epigenetic changes and environmental exposures that induce inappropriate activation or inactivation of specific genes causing neoplastic transformation (Herceg and Vaissiere 2011; Lima et al. 2010). Epigenetic mechanisms indicate that aberrant DNA methylation (hypermethylation and hypomethylation), histone modifications, noncoding RNAs (micro-RNAs) or chromosomal architecture caused by environmental exposures may trigger the tumorigenic process. Exactly, all critical changes in cancer cells, such as silencing of tumor suppressor genes, activation of oncogenes and defects in DNA repair, are caused an interaction of genetic and epigenetic mechanisms (Herceg and Vaissiere 2011). A new generation of exposure biomarker is demanded to detect the role of epigenetic changes in carcinogenesis and

to reveal what type and frequency exposures have most impact in influencing those mechanisms and cancer risk, such that prevention strategies can be formulated by a strong scientific rationale (Wild 2009).

Prevention

Exploring trends for specific cancers and their inequalities can inform the extent to which social efforts to improve equity have been successful or not, and also they can guide prevention strategies for cancer development (Teng et al. 2017). The current inadequacy of cancer screening programs for people with lower SES and poor treatment facilities ensures that primary prevention through the elimination of cancer risk factors is the most efficient way of reducing the cancer incidence (Akinyemiju et al. 2017). For lower SES individuals, prevention efforts should focus on providing more information on the cancer-related risk and more medical resources to improve quality of life. For higher SES individuals, prevention efforts should concentrate on strengthening the awareness to keep away from adverse exposures and taking full advantages of medical resource to improve health conditions.

Conclusion

This review adopts a life course approach to the study of cancer to help achieve a better understanding of the genesis of cancer. We considered the timing of exposures and the multiple pathways to analyze how early- and later-life behavioral, social, psychological and biological factors affect cancer incidence based on current scientific studies linked to social inequality. By discussing the theoretical models and mechanisms of environmental-related cancer in the life course, we made the findings that social inequality is mostly embodied in genetic susceptibility and early childhood development, the duration and intensity of exposure and the access to medical resources. Epigenetic programming associated with environmental exposures may help explain the occurrence of cancer at a molecular level. The individuals with lower SES are more likely to have higher cancer risk because of more frequency of timing and/or more quantity of accumulation of adverse exposures and greater impact on epigenetic mechanisms. Primary prevention is the best prevention strategy to reduce cancer risk through a life course approach.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

Adler NE, Stewart J (2010) Health disparities across the lifespan: meaning, methods, and mechanisms. Ann N Y Acad Sci 1186:5–23. https://doi.org/10.1111/j.1749-6632.2009.05337.x

Akinyemiju T, Ogunsina K, Okwali M et al (2017) Lifecourse socioeconomic status and cancer-related risk factors: analysis of the WHO study on global ageing and adult health (SAGE). Int J Cancer 140:777–787. https://doi.org/10.1002/ijc.30499

Alexandrov LB, Ju YS, Haase K et al (2016) Mutational signatures associated with tobacco smoking in human cancer. Science (New York, NY) 354:618–622. https://doi.org/10.1126/science.aag0299

Baer HJ, Tworoger SS, Hankinson SE et al (2010) Body fatness at young ages and risk of breast cancer throughout life. Am J Epidemiol 171:1183–1194. https://doi.org/10.1093/aje/kwq045

Bailey HD, Fritschi L, Metayer C et al (2014) Parental occupational paint exposure and risk of childhood leukemia in the offspring: findings from the Childhood Leukemia International Consortium. Cancer Causes Control CCC 25:1351–1367. https://doi.org/10.1007/s10552-014-0441-z

Barker DJ (1997) The fetal origins of coronary heart disease. Acta Paediatr (Oslo, Norway: 1992) 86(Supplement 422):78–82

Barnoya J, Glantz SA (2005) Cardiovascular effects of secondhand smoke: nearly as large as smoking. Circulation 111:2684–2698. https://doi.org/10.1161/circulationaha.104.492215

Barr RG, Diez-Roux AV, Knirsch CA et al (2001) Neighborhood poverty and the resurgence of tuberculosis in New York City, 1984–1992. Am J Public Health 91:1487–1493

Bauman AE (2004) Updating the evidence that physical activity is good for health: an epidemiological review 2000–2003. J Sci Med Sport 7:6–19

Ben-Shlomo Y, Kuh D (2002) A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol 31:285–293

Berenson J, Doty MM, Abrams MK et al (2012) Achieving better quality of care for low-income populations: the roles of health insurance and the medical home in reducing health inequities. Issue brief (Commonw Fund) 11:1–18

Bertone-Johnson ER, Tworoger SS, Hankinson SE (2009) Recreational physical activity and steroid hormone levels in postmenopausal women. Am J Epidemiol 170:1095–1104. https://doi.org/10.1093/aje/kwp254

Cai Z, Chiu JF, He QY (2004) Application of proteomics in the study of tumor metastasis. Genom Proteom Bioinform 2:152–166

Case A, Fertig A, Paxson C (2005) The lasting impact of childhood health and circumstance. J Health Econ 24:365–389. https://doi.org/10.1016/j.jhealeco.2004.09.008

Chang MH (2014) Prevention of hepatitis B virus infection and liver cancer. In: Chang M, Jeang KT (eds) Viruses and human cancer. Recent results in cancer research, vol 193. Springer, Berlin, pp 75–95. https://doi.org/10.1007/978-3-642-38965-8_5

Cohen S, Janicki-Deverts D, Chen E et al (2010) Childhood socioeconomic status and adult health. Ann N Y Acad Sci 1186:37–55. https://doi.org/10.1111/j.1749-6632.2009.05334.x

Colt JS, Blair A (1998) Parental occupational exposures and risk of childhood cancer. Environ Health Perspect 106(Suppl 3):909–925

Davis CD, Milner J (2004) Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention. Mutat Res 551:51–64. https://doi.org/10.1016/j.mrfmmm.2004.01.012

den Exter Blokland EA, Engels RC, Hale WW 3rd et al (2004) Lifetime parental smoking history and cessation and early adolescent smoking behavior. Prev Med 38:359–368. https://doi.org/10.1016/j.ypmed.2003.11.008

Dobbelaere D, Heussler V (1999) Transformation of leukocytes by *Theileria parva* and *T. annulata*. Annu Rev Microbiol 53:1–42. https://doi.org/10.1146/annurev.micro.53.1.1

Dowd JB, Zajacova A, Aiello A (2009) Early origins of health disparities: burden of infection, health, and socioeconomic status in U.S. children. Soc Sci Med (1982) 68:699–707. https://doi.org/10.1016/j.socscimed.2008.12.010

Ekstrom AM, Serafini M, Nyren O et al (2000) Dietary antioxidant intake and the risk of cardia cancer and noncardia cancer of the intestinal and diffuse types: a population-based case-control study in Sweden. Int J Cancer 87:133–140

Evans GW (2003) A multimethodological analysis of cumulative risk and allostatic load among rural children. Dev Psychol 39:924–933

Evans GW, Marcynyszyn LA (2004) Environmental justice, cumulative environmental risk, and health among low- and middle-income children in upstate New York. Am J Public Health 94:1942–1944

Febvey O, Schuz J, Bailey HD et al (2016) Risk of central nervous system tumors in children related to parental occupational pesticide exposures in three European case–control studies. J Occup Environ Med 58:1046–1052. https://doi.org/10.1097/jom.0000000000000852

Fenton SE, Birnbaum LS (2015) Timing of environmental exposures as a critical element in breast cancer risk. J Clin Endocrinol Metab 100:3245–3250. https://doi.org/10.1210/jc.2015-2848

Font-Burgada J, Sun B, Karin M (2016) Obesity and cancer: the oil that feeds the flame. Cell Metab 23:48–62. https://doi.org/10.1016/j.cmet.2015.12.015

Friedenreich CM, Neilson HK, Lynch BM (2010a) State of the epidemiological evidence on physical activity and cancer prevention. Eur J Cancer (Oxford, England: 1990) 46:2593–2604. https://doi.org/10.1016/j.ejca.2010.07.028

Friedenreich CM, Woolcott CG, McTiernan A et al (2010b) Alberta physical activity and breast cancer prevention trial: sex hormone changes in a year-long exercise intervention among postmenopausal women. J Clin Oncol Off J Am Soc Clin Oncol 28:1458–1466. https://doi.org/10.1200/jco.2009.24.9557

Garcia A (2006) Is health promotion relevant across cultures and the socioeconomic spectrum? Fam Community Health 29:20s–27s

Harris H (2005) A long view of fashions in cancer research. BioEssays News Rev Mol Cell Dev Biol 27:833–838. https://doi.org/10.1002/bies.20263

Harwood GA, Salsberry P, Ferketich AK et al (2007) Cigarette smoking, socioeconomic status, and psychosocial factors: examining a conceptual framework. Public Health Nurs (Boston, Mass) 24:361–371. https://doi.org/10.1111/j.1525-1446.2007.00645.x

Hatch SL, Dohrenwend BP (2007) Distribution of traumatic and other stressful life events by race/ethnicity, gender, SES and age: a review of the research. Am J Community Psychol 40:313–332. https://doi.org/10.1007/s10464-007-9134-z

Hemminki K, Zhang H, Czene K (2003) Socioeconomic factors in cancer in Sweden. Int J Cancer 105:692–700. https://doi.org/10.1002/ijc.11150

Herceg Z, Vaissiere T (2011) Epigenetic mechanisms and cancer: an interface between the environment and the genome. Epigenetics 6:804–819. https://doi.org/10.4161/epi.6.7.16262

Hodge DR, Peng B, Cherry JC et al (2005) Interleukin 6 supports the maintenance of p53 tumor suppressor gene promoter methylation. Cancer Res 65:4673–4682. https://doi.org/10.1158/0008-5472.can-04-3589

Hosseinpoor AR, Parker LA, Tursan d'Espaignet E et al (2012) Socioeconomic inequality in smoking in low-income and middle-income countries: results from the World Health Survey. PloS one 7:e42843. https://doi.org/10.1371/journal.pone.0042843

Hullar MA, Burnett-Hartman AN, Lampe JW (2014) Gut microbes, diet, and cancer. Cancer Treat Res 159:377–399. https://doi.org/10.1007/978-3-642-38007-5_22

Infante-Rivard C, Weichenthal S (2007) Pesticides and childhood cancer: an update of Zahm and Ward's 1998 review. J Toxicol Environ Health Part B Crit Rev 10:81–99. https://doi.org/10.1080/10937400601034589

Jeffreys M, Smith GD, Martin RM et al (2004) Childhood body mass index and later cancer risk: a 50-year follow-up of the Boyd Orr study. Int J Cancer 112:348–351. https://doi.org/10.1002/ijc.20423

Jung MM, Colditz GA, Collins LC et al (2011) Lifetime physical activity and the incidence of proliferative benign breast disease. Cancer Causes Control CCC 22:1297–1305. https://doi.org/10.1007/s10552-011-9803-y

Kang GH, Lee HJ, Hwang KS et al (2003) Aberrant CpG island hypermethylation of chronic gastritis, in relation to aging, gender, intestinal metaplasia, and chronic inflammation. Am J Pathol 163:1551–1556. https://doi.org/10.1016/s0002-9440(10)63511-0

Kong KA, Khang YH, Cha ES et al (2010) Childhood cancer mortality and socioeconomic position in South Korea: a national population-based birth cohort study. Cancer Causes Control CCC 21:1559–1567. https://doi.org/10.1007/s10552-010-9584-8

Korniluk A, Koper O, Kemona H et al (2017) From inflammation to cancer. Ir J Med Sci 186:57–62. https://doi.org/10.1007/s11845-016-1464-0

Kramer MS, Seguin L, Lydon J et al (2000) Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? Paediatr Perinat Epidemiol 14:194–210

Lawlor DA, Sterne JA, Tynelius P et al (2006) Association of childhood socioeconomic position with cause-specific mortality in a prospective record linkage study of 1,839,384 individuals. Am J Epidemiol 164:907–915. https://doi.org/10.1093/aje/kwj319

Leonardi-Bee J, Jere ML, Britton J (2011) Exposure to parental and sibling smoking and the risk of smoking uptake in childhood and adolescence: a systematic review and meta-analysis. Thorax 66:847–855. https://doi.org/10.1136/thx.2010.153379

Lima SC, Hernandez-Vargas H, Herceg Z (2010) Epigenetic signatures in cancer: implications for the control of cancer in the clinic. Curr Opin Mol Ther 12:316–324

Lindholm E, Berglund B, Kewenter J et al (1997) Worry associated with screening for colorectal carcinomas. Scand J Gastroenterol 32:238–245

Linos E, Willett WC, Cho E et al (2008) Red meat consumption during adolescence among premenopausal women and risk of breast cancer. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cospons Am Soc Prev Oncol 17:2146–2151. https://doi.org/10.1158/1055-9965.epi-08-0037

Linos E, Willett WC, Cho E et al (2010) Adolescent diet in relation to breast cancer risk among premenopausal women. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cospons Am Soc Prev Oncol 19:689–696. https://doi.org/10.1158/1055-9965.epi-09-0802

Lynch J, Smith GD (2005) A life course approach to chronic disease epidemiology. Annu Rev Public Health 26:1–35. https://doi.org/10.1146/annurev.publhealth.26.021304.144505

Mahabir S, Aagaard K, Anderson LM et al (2012) Challenges and opportunities in research on early-life events/exposures and

cancer development later in life. Cancer Causes Control CCC 23:983–990. https://doi.org/10.1007/s10552-012-9962-5

Marmot M, Friel S, Bell R et al (2008) Closing the gap in a generation: health equity through action on the social determinants of health. Lancet (London, England) 372:1661–1669. https://doi.org/10.1016/s0140-6736(08)61690-6

McTiernan A (2008) Mechanisms linking physical activity with cancer. Nat Rev Cancer 8:205–211. https://doi.org/10.1038/nrc2325

Meena JK, Cerutti A, Beichler C et al (2015) Telomerase abrogates aneuploidy-induced telomere replication stress, senescence and cell depletion. EMBO J 34:1371–1384. https://doi.org/10.15252/embj.201490070

Memon ZA, Kanwal N, Sami M et al (2015) Risk of breast cancer among young women and importance of early screening. Asian Pac J Cancer Prev APJCP 16:7485–7489

Metayer C, Scelo G, Kang AY et al (2016) A task-based assessment of parental occupational exposure to organic solvents and other compounds and the risk of childhood leukemia in California. Environ Res 151:174–183. https://doi.org/10.1016/j.envres.2016.06.047

Morrow JR Jr, Jackson AW, Bazzarre TL et al (1999) A one-year follow-up to physical activity and health. A report of the Surgeon General. Am J Prev Med 17:24–30

Niederdeppe J, Levy AG (2007) Fatalistic beliefs about cancer prevention and three prevention behaviors. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cospons Am Soc Prev Oncol 16:998–1003. https://doi.org/10.1158/1055-9965.epi-06-0608

Nordahl H, Hvidtfeldt UA, Diderichsen F et al (2014a) Cohort profile: the social inequality in cancer (SIC) cohort study. Int J Epidemiol 43:1750–1758. https://doi.org/10.1093/ije/dyu003

Nordahl H, Lange T, Osler M et al (2014b) Education and cause-specific mortality: the mediating role of differential exposure and vulnerability to behavioral risk factors. Epidemiology (Cambridge, Mass) 25:389–396. https://doi.org/10.1097/ede.0000000000000080

Ogden CL, Lamb MM, Carroll MD et al (2010) Obesity and socioeconomic status in adults: United States, 2005–2008. NCHS Data Brief 50:1–8

Omidakhsh N, Bunin GR, Ganguly A et al (2017) Parental occupational exposures and the risk of childhood sporadic retinoblastoma: a report from the Children's Oncology Group. Occup Environ Med. https://doi.org/10.1136/oemed-2017-104404

Ozanne SE, Fernandez-Twinn D, Hales CN (2004) Fetal growth and adult diseases. Semin Perinatol 28:81–87

Palli D, Caporaso NE, Shiao YH et al (1997) Diet, Helicobacter pylori, and p53 mutations in gastric cancer: a molecular epidemiology study in Italy. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cospons Am Soc Prev Oncol 6:1065–1069

Pavela G, Lewis DW, Locher J et al (2016) Socioeconomic Status, risk of obesity, and the importance of Albert J. Stunkard. Curr Obes Rep 5:132–139. https://doi.org/10.1007/s13679-015-0185-4

Rowlands AV, Eston RG, Ingledew DK (1999) Relationship between activity levels, aerobic fitness, and body fat in 8- to 10-yr-old children. J Appl Physiol (Bethesda, Md: 1985) 86:1428–1435

Ruiz JR, Rizzo NS, Hurtig-Wennlof A et al (2006) Relations of total physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. Am J Clin Nutr 84:299–303

Saslow D, Solomon D, Lawson HW et al (2012) American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. Am J Clin Pathol 137:516–542. https://doi.org/10.1309/ajcptgd94evrsjcg

Schroy PC 3rd, Glick JT, Robinson PA et al (2008) Has the surge in media attention increased public awareness about colorectal cancer and screening? J Community Health 33:1–9. https://doi.org/10.1007/s10900-007-9065-5

Smith JP (1999) Healthy bodies and thick wallets: the dual relation between health and economic status. J Econ Perspect J Am Econ Assoc 13:144–166

Sobal J, Stunkard AJ (1989) Socioeconomic status and obesity: a review of the literature. Psychol Bull 105:260–275

Teng AM, Atkinson J, Disney G et al (2017) Changing socioeconomic inequalities in cancer incidence and mortality: cohort study with 54 million person-years follow-up 1981–2011. Int J Cancer 140:1306–1316. https://doi.org/10.1002/ijc.30555

Teo K, Lear S, Islam S et al (2013) Prevalence of a healthy lifestyle among individuals with cardiovascular disease in high-, middle- and low-income countries: the prospective urban rural epidemiology (PURE) study. JAMA 309:1613–1621. https://doi.org/10.1001/jama.2013.3519

Thomas-Tikhonenko A, Hunter CA (2003) Infection and cancer: the common vein. Cytokine Growth Factor Rev 14:67–77

Thune I, Furberg AS (2001) Physical activity and cancer risk: dose-response and cancer, all sites and site-specific. Med Sci Sports Exerc 33:S530–S550 **(discussion S609-510)**

Uauy R, Solomons N (2005) Diet, nutrition, and the life-course approach to cancer prevention. J Nutr 135:2934s–2945s

Vohra J, Marmot MG, Bauld L et al (2016) Socioeconomic position in childhood and cancer in adulthood: a rapid-review. J Epidemiol Community Health 70:629–634. https://doi.org/10.1136/jech-2015-206274

von Wagner C, Good A, Whitaker KL et al (2011) Psychosocial determinants of socioeconomic inequalities in cancer screening participation: a conceptual framework. Epidemiol Rev 33:135–147. https://doi.org/10.1093/epirev/mxq018

Wardle J, McCaffery K, Nadel M et al (2004) Socioeconomic differences in cancer screening participation: comparing cognitive and psychosocial explanations. Soc Sci Med (1982) 59:249–261. https://doi.org/10.1016/j.socscimed.2003.10.030

White AJ, Sandler DP, Bolick SC et al (2013) Recreational and household physical activity at different time points and DNA global methylation. Eur J Cancer (Oxford, England: 1990) 49:2199–2206. https://doi.org/10.1016/j.ejca.2013.02.013

Wild CP (2009) Environmental exposure measurement in cancer epidemiology. Mutagenesis 24:117–125. https://doi.org/10.1093/mutage/gen061

Wise PH (2003) Framework as metaphor: the promise and peril of MCH life-course perspectives. Matern Child Health J 7:151–156

Zhang JW, Zeng Q, Zhao L et al (2016) [Association between parental exposure to environmental risk factors and the risk of childhood acute lymphoblastic leukemia]. Zhonghua liu xing bing xue za zhi Zhonghua liuxingbingxue zazhi 37:1413–1416. https://doi.org/10.3760/cma.j.issn.0254-6450.2016.10.019