

Psychosocial stress and cancer risk: A Narrative Review

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Declarations

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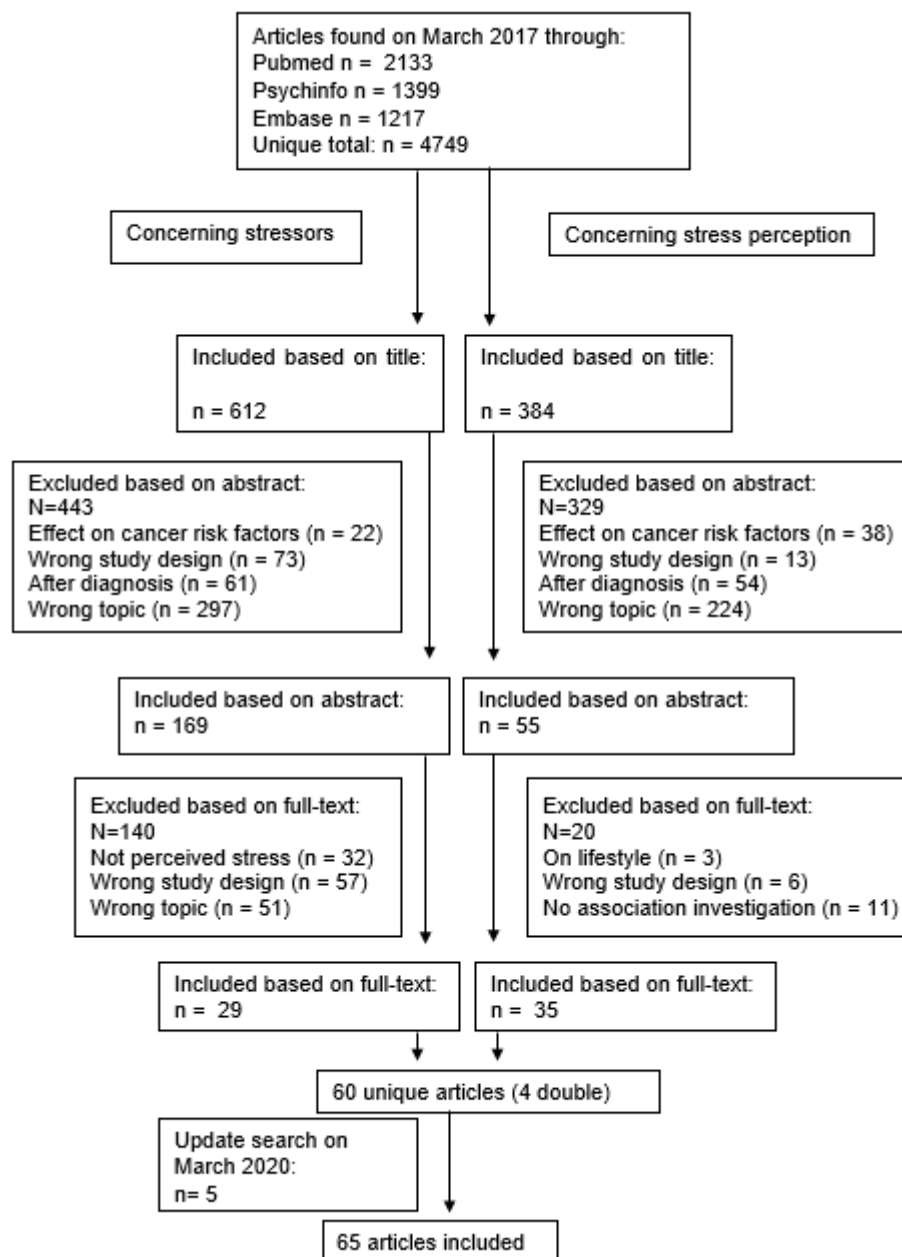
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Supplementary figure 1: Flowchart for study selection process

Supplementary text: Search strategy Pubmed

(cancer*[title/abstract] OR neoplasm*[title/abstract]) AND ("Stress, Psychological"[Mesh] OR psychological stress*[tw] OR "Life Change Events"[Mesh] OR life change events*[tw] OR "mental health"[mesh] OR mental health*[tw] OR "anxiety"[mesh] OR anxiety*[tw] OR "depression"[mesh] OR depressi*[tw] OR "workload"[mesh] OR workload*[tw] OR "job stress"[tw] OR psychosocial*[tw] OR psycho-social [tw] OR "grief"[MeSH Terms] OR "Mood Disorders"[Mesh] OR mood [title/abstract] OR emotion*[title/abstract] OR emotions [MESH] OR "Psychological Trauma"[Mesh] OR psychological trauma[Text Word] OR "happiness"[MeSH Terms] OR happiness[Text Word] OR well-being[Text Word]) AND ("Incidence"[Mesh] OR "epidemiology" [Subheading] OR "Causality"[MeSH] OR inciden*[tw] OR risk[tw] OR occur*[tw] OR onset[tw] OR neoplasms/etiology* OR caus*[TI] OR relation*[TI] OR associat*[TI]) NOT survivor*[tw] NOT "cancer patients" [TI] AND (cohort studies[Mesh:noexp] OR longitudinal studies[Mesh:noexp] OR follow-up studies[Mesh:noexp] OR prospective studies[Mesh:noexp] OR retrospective studies[Mesh:noexp] OR cohort[TIAB] OR longitudinal[TIAB] OR prospective[TIAB] OR retrospective[TIAB] OR "Case-Control Studies"[Mesh:noexp] OR "retrospective studies"[Mesh:noexp] OR "Control Groups"[Mesh:noexp] OR (case[TIAB] AND control[TIAB]) OR (cases[TIAB] AND controls[TIAB]) OR (cases[TIAB] AND controlled[TIAB]) OR (case[TIAB] AND comparison*[TIAB]) OR (cases[TIAB] AND comparison*[TIAB]) OR "control group"[TIAB] OR "control groups"[TIAB])

Supplementary Table 1: Characteristics of studies with psychological stress as cancer predictor

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Archer, G. (United Kingdom, 2015) ¹	6983	Mean: 44.4 Range: 33-55	17 years	Overall cancer	Whitehall II: London-based office staff aged 33-55 working in 20 civil service departments. (69.5% male)	The 30-item general health questionnaire was used at 3 phases. 4 groups: 1 st group with no depressive symptoms over 3 phases, 4 th group with depressive symptoms over all 3 phases.	Non-response (n=2176) Death before phase iii (n=125) Previous cancer incidence (151) No link to cancer registry (n= 11) Missing GHQ data (n= 987)
Batty, D. (United Kingdom, 2017) ²	163 363	Aged 16 or older	9.5 years (in 16 studies)	Colorectum, prostate, pancreas, and esophagus and for leukemia	Nationally representative samples drawn from the health survey for England (13 studies) and the Scottish health survey (three studies).	Self-reported psychological distress scores based on the general health questionnaire, GHQ-12	None mentioned
Brown, S. (United States, 2016) ³	71439	Mean: 61.8 Range: 50-79	17 years	Breast cancer	WHI-OS: Postmenopausal women recruited in 40 clinical centers throughout the US from 1993 to 1998.	Burnam eight-item scale for depressive disorders at baseline. 2 groups: depressive symptoms versus no depressive symptoms.	History of cancer of (except for non-melanoma skin cancer) at baseline (n=11726) Missing information on the Burnam depression scale (n=2546) Missing data or potential confounders (n=7965)
Butow, P. N. (Australia, 2015) ⁴	2739	Mean: 45 Range: 18-75	15 years	Breast cancer	Women with either BRCA1, BRCA2, other cancer predisposition genes, or a combination of a number of 1 st or 2 nd degree family members with breast cancer or breast cancer predisposition genes.	Life Events and Difficulties Schedule (LEDS), a semi-structured interview that assessed life stressors, psychosocial variables (social support, personality), optimism, Anti-emotionality, anger	History of cancer of (except for non-melanoma skin cancer) at baseline, non-English literacy, physical or mental illness affecting memory recall.

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
						control at baseline and repeated 3-yearly.	
Chang, H. Y. (South-Korea, 2015) ⁵	601775	Range: 30-64 years	20 years	Overall cancer. Hormone related cancer divided into cancer of the: breast, cervix, corpus uteri, ovary and prostate	The Korean Cancer Prevention Study: a cohort of South Korean workers and their dependents (5/1 ratio men/women)	In 1992 and 1994 a short depression questionnaire, based on DSM-IV and Patient Health Questionnaire 9 criteria was used. 546514 participants filled in the questionnaire 2 times, others only once.	Missing information (n=19050), history of cancer (n=2594) and subjects who died in the interval between questionnaire completion and start follow-up.
Chapman B.P. (United States, 2013) ⁶	729	Mean: 44	12 years	Overall cancer	The 1996-2008 General Social Survey-National Death Index (NDI) cohort of non- institutionalized adults age 18 and over more or less representative of US population.	The General Social Survey (GSS) Emotion Suppression Scale was taken by an interviewer at baseline.	Non mentioned
Chen Y.H. (Taiwan, 2011) ⁷	Predictor cohort: 778 Control cohort: 3890	Predictor: 18-29: 23.9%, 30-44: 30.7%, 45-54: 17.7%, 55-64: 12.2%, >64: 15.5% cohort: identical.	5 years	Oral cancer, gastrointestinal cancer, respiratory cancer, genitourinary cancer, hematological cancer	The Longitudinal Health Insurance Database (LHID) (Taiwan): from which patients hospitalized for depressive disorder 1998-2003 formed cohort 1 and patients who underwent femoral/inguinal hernia operation or appendectomy formed cohort 2	Hospitalization with a primary diagnosis of depression	Patients under 18 years (n=20), previous diagnosis of cancer (n=224), previous hospitalization for any mental disorder (n=183),
Denollet J. (The Netherlands, 2009) ⁸	5428	Mean: 50.4 Range: 46-54	10 years	Lung cancer death, breast cancer death	Eindhoven Perimenopausal Osteoporosis Study: women living in The	Three-item anxiety subscale of the EDS.	Personal history of cancer (n=274), cardiovascular disease (n=81)

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					Netherlands of perimenopausal age.		
Falkstedt D. (Sweden, 2013) ⁹	42192	Range: 40-57	17 years	Overall cancer	Swedish males who were conscripted into compulsory military service in 1969/1970.	Psychosocial functioning was assessed through a semi-structured interview by a certified psychologist. Willingness to assume responsibility, independence, having an outgoing character, persistence, emotional stability and power of initiative were assessed.	Death before baseline (n=1050), lacking of reliable information on IQ or psychosocial functioning (n= 428), absence of information on social class or crowded housing (n=804), absence of other data (n=908)
Feller, S. (Germany, 2013) ¹⁰	48411	Range: 35-65 Average: 50	Average: 8 years	Overall cancer	2 German cohorts of the European Prospective Investigation into Cancer and Nutrition (EPIC), randomly selected from the general population of Potsdam and Heidelberg	PC-guided face-to-face interview asking for individual characteristics concerning health and lifestyle + one-item question measuring global life satisfaction.	Missing information on life satisfaction (n=47), covariates (n=1082), diagnosis (n=15), death (n=3), or non-participation in follow-up (n=1583)
Gross, A. (United States, 2010) ¹¹	3481	Mean: 46	24 years	Breast cancer, colon cancer, lung cancer, prostate cancer, skin cancer	A cohort of the ECA program: a large-scale, multi-site, community-based epidemiologic survey of psychiatric disorders among a general population in the US including persons aged 18 years and older living in households.	The DIS was used in standardized interviews at baseline. DIS is composed of standardized questions which are used to make DSM-III diagnoses of mental disorders based on symptoms, co-occurrence of symptoms over time,	Lifetime history of cancer at baseline.

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
						and other relevant factors. Three groups: lifetime history of major depression, lifetime history of dysphoric episode, or neither.	
Hange, D. (Sweden, 2009) ¹²	1462	5 age groups: 60, 54, 50, 46, 38	32 years	Overall cancer	The Prospective Population Study of Women in Gothenburg, including 5 age groups representative of women in the community.	A self-administered questionnaire was used at baseline to assess moodiness or nervousness.	Women with CVD or with a history of cancer at start were excluded.
Huang, T. (United States, 2015) ¹³	77451 (NHS) 106452 (NHSII)	Range NHS: 30-55 Range NHSII: 25-42	18 years	Epithelial ovarian cancer	The Nurses' Health Study I and II cohorts were used for this study, with only female nurses aged 30-55 years and 25-42 years respectively.	Mental Health Index, antidepressant medication use, self-reported physician-diagnosed depression were assessed. Depressive symptoms were assessed with the 5-item Mental Health Index at 3 different points for both cohorts.	Women who died (n=5494), had bilateral oophorectomy (n=27526), menopause due to pelvic irradiation (n=509) or diagnosis of cancer other than non-melanoma skin cancer (n=7495), no assessment on depression (n = 14203)
Hung, Y.N. (Taiwan, 2014) ¹⁴	20033 patients with affective disorder.	<20: 1278 20-29: 4561 30-39: 4257 40-49: 3757 50-59: 2352 60-69: 1835 70-79: 1591 80/>80: 402	14 years	Overall cancer	Through the National Health Insurance Program in Taiwan, 98% of all people admitted to a hospital for any psychiatric affective disorder between 1998 and 2008 were included.	Admission for affective disorder: major depressive disorder or bipolar disorder.	Previous diagnosis with any cancer on first admission (n=474), ever diagnosed with schizophrenia (n=7923), unknown gender or birthdate (n=80)
Ikeda, A. (Japan, 2013) ¹⁵	44152	Range: 40-69 Mean: +/- 54	11 years	Cancer of the liver, lung, stomach, colorectal	The Japan Public Health Centre-Based Prospective Study	Self-administered questionnaire at baseline, including	Non-Japanese nationality (n=11), emigration

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					Cohort II, representative of the population, drawn from 6 public health centers.	personal and family history and psychosocial factors (e.g. perceived stress)	before start of follow-up (n=11).
Jokinen, J. (Sweden, 2013) ¹⁶	186627 in the exposed cohort.	30% younger than 25 (the youngest 15) years, 14% 60 years or older.	43 years	40 types of cancers	All Swedish persons aged 15 years or older ever hospitalized for self-inflicted injury or attempted suicide as recorded in the Swedish patient register between 1968 and 2011 (covering all Swedes from 1973). Control: all age-specific cancer incidences in Sweden.	Hospitalization for self-inflicted injury or suicide attempt. Stratifying by mode of suicide attempt (violent or non-violent, clear or unclear intent)	All persons with cancer occurrence before first hospitalization for self-inflicted injury or attempted suicide.
Karakus, M. C. (United States, 2011) ¹⁷	3645	Range: 50-62	12 years	Overall cancer (not specified)	The US Health and Retirement Survey: a representative sample of non-institutionalized men and women born between 1931 and 1941 inclusive, and their spouses or partners.	The eight-item version of the CES-D was used to generate a 0-1 indicator of participant's baseline depression.	Individuals with any of the 4 researched chronic conditions (cancer, heart problems, arthritis and diabetes) at baseline (n=5922). No participation in all 6 waves (n=2427). Less than 50 years old at baseline (n=623). Missing observations (n=35)
Kim, S. (United States, 2016) ¹⁸	45767	Range: 35-74 years	Average: 859 days	Breast cancer	The sister study: a prospective cohort of women with a sister with breast cancer.	Biennially optimism was assessed using the 6-timen Life Orientation Test – Revised (LOT-R)	No baseline assessment of optimism (n=4108). Breast cancer prior to the biennial survey (n=1009)
Lemogne, C. (United States, 2013) ¹⁹	13768	Range men: 40-50	16 years	Prostate cancer, breast cancer, colorectal cancer, smoking-	The GAZEL cohort: employees of the French national gas and	The PSI: a 70-item questionnaire with 'true-false' answers,	Unwillingness to participate in follow-up (n=1), death before

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
		Range women: 35-50		related cancer, cancer of the lymphoid and hematopoietic tissue, cancer at other sites	electricity company 'EDF-GDF'.	aiming to identify 6 personality types (Type 1= dependence on withdrawing objects, type 2= dependence on disturbing objects, type 3=dependence on objects that are both withdrawing and disturbing, type 4=autonomy and self-regulation, type 5= rational tendencies, type 6= antisocial tendencies.	follow-up (n=32), previous cancer diagnosis at baseline (n=224), death from cancer without a reported cancer diagnosis during follow-up (n=136), diagnosis of cancer or hospitalization for cancer without validation (n=434), lack of written consent to participate in diagnosis validation survey (n=322), death before beginning of follow-up (n=8), cancer diagnosis at baseline (n=203), refusal to respond to survey (n=1), failure to contact volunteer or their physician (n=103).
Lemogne, C. (United States 2015) ²⁰	14203	Range men: 40-50 Range women: 35-50	15 years	Prostate cancer, breast cancer, colorectal cancer, smoking-related cancer, cancer of the lymphoid and hematopoietic tissue, cancer at other sites	The GAZEL cohort: employees of the French national gas and electricity company 'EDF-GDF'.	Depressive mood was assessed in 1993, 1996 and 1999 with the CES-D.	Unwillingness to participate in follow-up (n=1), death before follow-up (n=32), previous cancer diagnosis at baseline (n=224), death from cancer without a reported cancer diagnosis during follow-up (n=136), diagnosis of cancer or hospitalization for cancer without validation (n=434), lack of written consent to participate in diagnosis validation survey

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
							(n=322), death before beginning of follow-up (n=8), cancer diagnosis at baseline (n=203), refusal to respond to survey (n=1), failure to contact volunteer or their physician (n=103).
Liang, J.A. (Taiwan, 2012) ²¹	24066 in the exposed cohort. 94104 in the control cohort.	Mean: 54.1 in the exposed cohort, 54 in the control cohort.	8 years	Oral cancer, colorectal cancer, liver cancer, lung cancer, breast cancer, cervical cancer, prostate cancer and other cancer	Exposed cohort: patients who had been diagnosed with Anxiety Disorder in 2000-2002 were retrieved from the National Insurance Research Database (NHIRD, covering 96% of all medical claims in Taiwan since 1996). Patients had to be admitted to the hospital for AD3 times to be included, to increase diagnosis accuracy. Control cohort: random selection of enrollees of the NHIRD without AD with the same age and sex distribution.	Patients diagnosed with AD and admitted to hospital 3 times for AD.	Patients with any type of cancer prior to the date of indexing.
Liu, B. (United Kingdom, 2016) ²²	719671	Median: 59 Range: 50-69	10 years	Overall cancer	The Million Women Study: recruiting women aged 50-69 years through the national Breast Screening Programmes of England and Scotland.	At baseline, women were asked about their happiness and subjective measures of wellbeing.	Women with heart disease, stroke, cancer, or chronic obstructive airways disease at baseline (n=125769)

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Nakaya, N. (Japan, 2014) ²³	30277 in Japanese cohort 59548 in Scandinavian cohort.	Not mentioned.	7 years for Japanese cohort. 30 years for Scandinavian cohort.	Overall cancer	Japanese cohort: residents of Miyagi Prefecture in northern Japan (of which 671 had cancer at baseline). Scandinavian cohort: Swedish and Finnish participants who completed a questionnaire.	Japanese cohort: the Eysenck Personality Questionnaire-Revised (EPQ-R) at baseline. Scandinavian cohort: Eysenck Personality Inventory (EPI) at baseline.	Japanese cohort: cancer cases within the first 3 years. Scandinavian cohort: not mentioned.
Nielsen, N.R. (Denmark, 2008) ²⁴	12128	Range: 20-93 Mean:57 for women 56 for men.	23 years	Overall cancer	The Longitudinal Copenhagen City Heart Study, an age-stratified, random sample of men and women in Denmark.	Participants were asked about stress in terms of intensity and frequency at baseline.	Missing of information on stress (n=42), other covariates (n=528).
Nielsen, N.R. (Denmark, 2008) ²⁵	11914	Range: 21-91 Mean:57 for women, 56 for men	19 years	Colon cancer, rectal cancer	The Longitudinal Copenhagen City Heart Study, an age-stratified, random sample of men and women in Denmark.	Study participants were asked two questions about their stress levels in term of intensity and frequency.	Colorectal cancer before baseline (n=49), lacking information on stress (n=42), or other covariates (n=605). Women lacking information on reproductive and hormonal factors (n=88).
Okely, J.A. (United Kingdom, 2016) ²⁶	8182	Mean: 63.2 Minimum age: 50	9 years	Overall cancer	The ELSA prospective cohort: a study of people 50 years and older recruited from the Health Survey for England database.	Well-being was assessed at baseline with the CASP-19 quality of life questionnaire that assesses the domains of control, autonomy, self-realization and pleasure.	Participation only in wave 1 (n=2121), incomplete or missing data on well-being (n=886) or on other covariates (n=910)
Poole, E.M.	148570	Range: 25-55 Mean NHS: 54	22 years	Ovarian cancer	The Nurses' Health Study I and II (NHS)	Symptoms of phobic anxiety were self-	Diagnosis with cancer (except non-melanoma)

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
(United States, 2016) ²⁷	(66396 NHS, 82174 NHSII)	Mean NHSII: 38			and NHS II). Two prospective cohorts of female registered US nurses respectively aged 30 to 55 and 25 to 42.	reported in the NHS and NHSII at two points with the Crown-Crisp phobic anxiety index (CCI).	skin cancer) prior to baseline (n: NHS= 6462; NHSII=1605), bilateral oophorectomy (n: NHS= 11843, NHSII=2977), menopause due to pelvic irradiation (n: NHS=54, NHSII=28), missing date of birth (n: NHS=36, NHSII=187).
Shen, C. (Taiwan, 2013) ²⁸	89485	Mean: 49.6 20-39: 5832 40-59: 8748 60-79: 4654 >80: 559	10 years	Cancer of the head and neck, digestive tract (esophagus, colon and rectum, anus), liver and biliary tract, pancreas, lung and mediastinum, bone and soft tissue, skin, breast, genitourinary (cervix, uterus, ovary, prostate, kidney, bladder), thyroid, hematologic malignancies, others	The NHI program, a mandatory universal health insurance program covering 98% of the Taiwanese population.	Newly-diagnosed patients with Generalized Anxiety Disorder (GAD) were recruited from the NHI program.	Not mentioned
Song, H. (Japan, 2017) ²⁹	101708	Range: 40-69	5 years and 10 years	Overall cancer	Japan Public Health Centre-based Prospective Study (JPHC Study). Records of individuals registered at registered at 11 public health center (PHC) areas nationwide from 1990–1994.	1 Item Questionnaire to determine stress	Subjects with a self-reported cancer, or who died or moved out their PHC area before baseline enrolment (study entry, defined as submission date of the baseline questionnaire).
Svensson, T. (Japan, 2016) ³⁰	55130	Range 55-79 Mean: 60	10 years	Breast cancer, rectal cancer, gastric cancer,	The third survey of the Japan Public Health	Coping was assessed with an adaptation of	Failing to provide complete answers on

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
				liver cancer, pancreatic cancer, lung cancer, prostate cancer, colon cancer	Centre-based Prospective Study (JPHCS). A cohort with registered Japanese inhabitants identified by population registries maintained by local municipalities.	the Stress and Coping Inventory, evaluating six coping behaviors (planning, consulting someone, fantasizing, positive reappraisal, self-blame and avoidance)) at baseline.	coping (n=27554), history of cancer before starting point (n=3469), a BMI less than 18.5kg/m ² (n=1781), non-Japanese nationality (n=51), duplicate enrolment (n=4), a late report of emigration before the start of the baseline study (n=392), incorrect birth date (n=7).
Wise, L.A. (United States, 2015) ³¹	15963	Mean: 36.5 Range: 21-69	16 years	Uterine leiomyoma	The Black Women's Health Study: a prospective cohort of African-American women aged 21-69 at baseline.	The 20-item Centre for Epidemiologic Studies Depression Scale was used to assess depressive symptoms.	Age >50 years (n=1576), loss to follow-up (n=890), no report of year of diagnosis (n=149), no report of method of confirmation of diagnosis (n=110), incomplete data (n=3043), or incomplete covariates (n=553)

Abbreviations: GHQ: general health questionnaire

Supplementary Table 2: Characteristics of case-control and longitudinal studies with stressors as cancer predictor

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Albert, M. A. (United States, 2010) ³²	48924	40.5 (21-69)	8 years	Overall cancer	Black women's health study: black women residing in the United States	8 item questionnaires adapted from questions by Williams et al	History of CVD or cancer at baseline
Azizi, H. (Iran, 2015) ³³	214 (207 cases & 207 controls)	Mean: 60 Range: (40-75)	N/A	Colorectal cancer	Cases: diagnosed no longer than six months before the interview, confirmed by pathology and colonoscopy findings at colonoscopy unit. Controls: free of neoplastic conditions and diet related chronic diseases at the same hospital at the same period	43-item self-reported Holmes and Rahe Life Events Questionnaire	Controls: age above 75 years old and below 40 years old, neoplastic conditions, history of depression/ mental/nervous diseases and diet related chronic diseases
Bahri (Iran, 2019) ³⁴	11 Studies	16-79 (Based on studies included)	18 Months - 40 years (Based on studies included)	Breast cancer	Not Mentioned	Interviews, Stress of daily activities questionnaire, Brown and Harris Life Event and Difficulties Schedule, A researcher made questionnaire	Review Articles, editorials, debates, letters, case reports, meeting abstracts, and non- peer-reviewed articles and studies examining the relation between breast cancer and anxiety and other psychological disorders.
Brown, D. (United States, 2010) ³⁵	17337	50-64	8-10 years	Lung cancer	ACE study: Kaiser Permanente's San Diego Health Appraisal Clinic	Questionnaire based upon prior research; questions adapted from Conflict Tactics Scale (CTS)	Incomplete information on race and educational attainment

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					(primary care clinic) - > members of the Kaiser Permanente Health Maintenance Organization		
Cabaniols, C. (France, 2011) ³⁶	144 (122 cases & 122 controls)	Mean:57 Range:(20.4-86.3)	N/A	Brain cancer	Cases: all new cases of malignant primitive brain cancer in public referral hospitals in Toulon and Marseille. Controls: patients of the neurosurgical departments of these hospital and hospitalized for reasons unrelated to cancer	Life events: Holmes and Rahe Stress Scale	Pilocytic astrocytoma's, recurrence of previous MPBT
De Vries, E. (Finland, Germany, Greece, Italy, Malta, Poland, Scotland and Spain, 2012) ³⁷	2921 (1371 cases & 1550 controls)	Controls: 58.5 (18-99); CMM: 62 (19-90); BCC: 72 (21-101); SCC: 76 (38-101)	N/A	Skin cancer	Cases: Patients recently diagnosed with SCC, BCC or CMM (histological confirmation and a maximum of 3 months since diagnosis was required); visiting one of the participating dermatology departments. Controls: patients visiting the hospital clinics for any condition unrelated to skin cancer	Self-administered questionnaire including one question about stress ("Do you have experienced stressful or traumatic events during the past year?")	Inability to complete the questionnaire; naturally pigmented skin (Fitzpatrick skin types V–VI); patients who received phototherapy; patients with photo allergies and/or lupus erythematosus. Additional for controls: history of invasive skin cancer or clearly UV-influenced disease.

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Eskelinen, M. (Finland, 2010) ³⁸	115 (34 breast cancer patients, 53 benign breast disease and 28 healthy patients)	BC patients: 51.5 BBD: 47.5 HSS: 45.7	N/A	Breast cancer	Kuopio Breast Cancer Study: individuals showing breast cancer symptoms or an abnormality of the breast	Semi-structured in-depth interview: patients were asked to draw their 'life lines' and to rate the life events according to the degree of threat or stress they experienced	None mentioned
Falkstedt, D. (Sweden, 2013) ⁹	42192	(40-57)	17 years	Overall cancer	Swedish males who were conscripted into compulsory military service in 1969/1970	Education: Longitudinal Database of Education, Income and Occupation (LOUISE -held by Statistics Sweden). Occupational level and income: National Population and Housing Census.	Lack of reliable information, people who could not be assigned a hierarchically defined SES on the basis of occupation (farmers for example)
Fang, F. (Sweden, 2011) ³⁹	4687073	Unexposed group: 47.4 exposed group: 66	14 years	Infection-related cancers	Swedish Multi-Generation Register (people born in 1932 or later): all parents who were born in Sweden and alive on January 1, 1990, and had at least 1 child recorded as alive on that day (if born earlier) or born thereafter	Causes of Death Register	Prevalent cancer diagnosis, inconsistencies discovered in record linkages (death or emigration), parent-child pairs with identical cancer diagnosis (parents) and underlying cause of death (children). In additional analysis: previous
Fischer, A (United States, 2018) ⁴⁰	664 female cases (Cancer Surveillance)	24-75 years	N/A	Breast cancer	Hereditary Breast and Ovarian Cancer (HBOC) study of the University of	Epidemiological risk factor questionnaire (RFQ) that included extensive information regarding personal, social,	

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
	Program of Orange County 203 female population-based controls				California. Cases were identified via the population-based cancer registry of the Cancer Surveillance Program of Orange County (CSPOC).	medical and family history in addition to a section querying about LEs	
Hougaard, C. O. (Denmark, 2017) ⁴¹	749617	(40-50)	Job mobility: 1992-2001; health outcomes: 2002-2006	Lung & colorectal cancer	All people aged 40–50 years in 2002, living in Denmark and economically active In the years 1992–2002		Those who had registered cases of the outcome during the previous five years
Huang, J. (Sweden, 2013) ⁴²	98629 (16522 cases & 82107 controls)	> 76	N/A	Pancreatic cancer	All persons included in the Swedish Population and Housing Census in 1990 who were born in Sweden and had at least 1 child recorded in the Swedish Multi-Generation Register	Multi-Generation Register	Death, diagnosed with a primary malignant cancer of emigrated out of Sweden before 1/1/1991, lost children who had pancreatic cancer, MEN1, HBOC syndrome, HNPCC, FAP, diabetes and congenital malformations
Ikeda, A. (Japan, 2013) ⁴³	44152	53 (40-69)	Median = 12 years	Liver, lung, colorectal, stomach and overall cancer	Japan Public Health Center-Based Prospective Study Cohort II (all residents of six public health center areas across Japan)	Self-administered questionnaire at baseline, including personal and family history and psychosocial factors (e.g. perceived stress)	Non-Japanese nationality, reports of emigration, previous history of myocardial infarction, angina pectoris, stroke, or cancer at study baseline

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Jakovljevic, G. (Croatia, 2010) ⁴⁴	263 (127 cases (PCC) & 136 controls (PHC))	Not mentioned	N/A	Overall cancer	Parents of children with different stages and different cancer diseases and parents of healthy children	Questionnaire: list of stressful life events	None mentioned
Jansson, C. (Sweden, 2009) ⁴⁵	1438 (618 cases & 820 controls)	60-79 (< 80)	N/A	Esophageal and cardia cancer	Native Swedish population (<80 years) and living in Sweden 1995–1997. Cases: all newly diagnosed patients with esophageal or cardia adenocarcinoma and half of the patients with esophageal squamous-cell carcinoma. Controls: randomly selected from the Swedish register of the total population and frequency-matched according to the age and sex distribution of the esophageal adenocarcinoma cases.	Validated psychosocial job-exposure matrix were applied on the data obtained by personal interviews by professional interviewer	None mentioned
Jokinen, J. (Sweden, 2015) ¹⁶	186627	25-59 (> 15)	Not mentioned	Overall cancer	All persons who were ever hospitalized for self-inflicted injury or attempted suicide as recorded in the	Hospitalization for self-inflicted injury or suicide attempt. Stratifying by mode of suicide attempt (violent or non-violent, clear or unclear intent)	All persons with cancer occurrence before first hospitalization for self-inflicted injury or attempted suicide, cancers detected at

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					Swedish patient register		autopsy only, non-melanoma skin cancers
Kantor, E. D (United States, 2019) ⁴⁶	26741	40-79	6.1 years	Prostate cancer	All persons were drawn from the SCCS, prospective cohort focused on cancer disparities	An 8-item SE adversity composite questionnaire covering socioeconomic status, residential environment, and social support/buffers. Two items from the Perceived Stress Scale were assessed.	CHC-recruited population to examine the association between SE adversity and PC risk
Kelly-Irving, M. (Great Britain, 2013) ⁴⁷	6138	All were 50	50 years	Overall cancer	1958 National Child Development Study (NCDS): all live births during one week in 1958 in Great Britain	Questionnaire answered by parent or teacher: 6 categories of possible adversities	If missing data on cancer or adverse child events
Kennedy, B. (Sweden, 2014) ⁴⁸	4705642	All were followed from birth until 40	40 years	Overall cancer	All individuals born in Sweden between 1961 and 2002 who had both parents identifiable in the Multi-Generation Register and both parents alive at the birth of the index individual	Swedish National Cancer Register, the Causes of Death Register	When not both of the parents were registered in a Population and Housing Censuse, same cancer as their parent, familial cancer syndromes
Kocic, B. (Serbia, 2015) ⁴⁹	240 (120 cases & 120 controls)	50.8 (30-69)	N/A	Breast cancer	Patients of Clinic of Physical Medicine and Orthopedic Clinic with non-occupational accidental injuries	Personal interview (Paykel Life Events Scale)	None mentioned
Kondo, N. (Japan, 2015) ⁵⁰	21031	(>65)	4 years	Overall cancer	Aichi Gerontological Evaluation Study	Yitzhaki Index	Physical or cognitive dependence

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					(AGES): community-dwelling older adults (>65y) residing in eight rural and suburban municipalities		
Korpimaki, S. K. (Finland, 2010) ⁵¹	19626	Cases: 50-54 Controls: 20-24 (20-54)	N/A	Overall cancer	Health and Social Support Study (HeSSup): Finnish working-age population	Six-item postal questionnaire: questions mentioned in article	None mentioned
Krishna Rao, S. (India, 2015) ⁵²	452 (180 cases & 272 controls)	54 (> 18)	N/A	Oral & oropharyngeal cancer	Cases: all patients diagnosed histopathological with oral and/or oropharyngeal cancer during the study period, attending the selected cancer hospitals and ages 18 years or more. Controls (same hospital): carers or visitors of cancer patients or those seeking medical care for medical conditions not related to tobacco and/or alcohol, memory loss, oral cancer.	Face-to-face interviews, semi-structured questionnaire, life grid (no details mentioned)	Sarcomas, secondary cancers, and skin cancers of external lip (due to pre-existing comorbidity or different etiopathology. Controls: upper aerodigestive tract, lung, and liver cancers
Kruk, J. (Poland, 2012) ⁵³	1943 (858 cases &	55 (28-79)	N/A	Breast cancer	Cases: women aged 28–79 years identified	Structured questionnaire based on the social readjustment rating scale	Not residing in the Region of Western

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
	1085 controls)				directly from the Szczecin Cancer Registry, newly diagnosed and surgically operated between July 1, 1999, and December 30, 2006. Controls: randomly recruited among the outpatients from ambulatories, clinics, the largest hospital in Szczecin, and four relatively smaller hospitals in the same region.	items developed by Holmes and Rahe	Pomerania; not able to complete a self-administered questionnaire; too much missing data
Kuper, H. (Sweden, 2007) ⁵⁴	36332	41 (30-50)	12-13 years	Breast cancer	Women's Lifestyle and Health Cohort Study: women aged 30–49 years and employed at baseline and residing in the Uppsala Health Care Region were randomly selected from the Swedish Central Population Registry at Statistics Sweden	Questionnaire (job demands: 5 questions, job control: 6 questions and social support at work: 6 questions)	History of invasive cancer before enrolment
Li, M. L. (China, 2014) ⁵⁵	750 (250 cases & 500 controls)	70.3 (33-90)	N/A	Prostate cancer	Cases: newly diagnosed patients with prostate cancer by histopathological verification after		Patients who could not answer the questionnaire for themselves

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					radical prostatectomy; 250 controls were non-tumor patients from pneumology or cardiology departments from the same hospitals as cases and the other 250 controls were non-tumor community people with normal value of PSA from different District in Shangai.		
Michael, Y. L. (United States, 2009) ⁵⁶	84334	63.5 (50-79)	7.6 years	Breast cancer	Women's Health Initiative Study: multi-ethnic cohort of postmenopausal women at 40 geographically diverse clinical centers and with at least a 3-year life expectancy	Life events: questionnaire containing a life events inventory + rating based on the amount of upset that it caused. Social support: nine items chosen from the Medical Outcomes Study questionnaire (MOS).	History of BC at baseline; BC cases diagnosed before the first follow-up visit; women with less than 1 year of follow-up; those missing information at baseline on stressful life events or social support
Nielsen, N.R. (Denmark, 2008) ²⁴	18932	Not mentioned (> 44)	7.2 years	Breast cancer	Danish Nurse Cohort: all registered Danish nurses above the age of 44	Questionnaire: one question about pressure of work, one question about tempo of work, one question about influence and work hours were asked about.	Women with breast cancer before baseline, who were censored before baseline, who were not working at baseline, who lacked information on work-related stressors or other covariates

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
Peled, R. (Israel, 2008) ⁵⁷	622 (255 cases & 367 controls)	Cases: 40 controls: 34.7 (25-45)	N/A	Breast cancer	Cases: newly diagnosed patients in six major oncology units. Controls: women free of any malignancy who visited the outpatient clinics of Shiba Medical center, a large hospital and Barzilai Medical Center, a relatively small hospital	Life event questionnaire including 10 events	None mentioned
Pudrovska, T. (United States, 2013) ⁵⁸	3682	All were 36	36 years	Breast cancer	Wisconsin Longitudinal Study (WLS): random sample of men and women who graduated from Wisconsin high schools in 1957	Interviewed questionnaire: one question per aspect, except job authority (4 questions) and hours worked per week.	None mentioned
Renzaho, A. M. (Australia, 2014) ⁵⁹	9222	47.1 (> 21)	8 years	Overall cancer	Household, Income and Labour Dynamics in Australia panel survey: national probability sample of all individual's resident in 7682 Australian households	Questionnaire using Cobb-Clark and Schurer classifications	Missing values on the life events; serious personal injury of illness to self
Schorr, L. (Israel, 2016) ⁶⁰	80015	Not mentioned	Average of 35.6 years	Overall cancer	Jerusalem Perinatal Study (JPS): population-based birth cohort of infants born from 1964 to 1976 to	Israeli Population Registry (IPR)	Parents with cancer diagnosed within 5 years after child loss

Author (Country, Year)	Sample size (After exclusion)	Age (Mean/range in years at start)	Maximum follow-up time	Cancer type	Study population	Method of stress assessment	Exclusion criteria
					residents of Jerusalem and their parents		
Toleutay, U. (Kazakhstan, 2013) ⁶¹	310 (114 cases & 196 controls)	(30-75)	N/A	Breast cancer	Cases: women from Karmakshy district registered on dispensary register. Controls: healthy women, who passed screening testing.	Specially developed anonymous questionnaire (no details mentioned)	None mentioned
Trudel-Fitzgerald, C. (Canada, 2013) ⁶²	828	18 - 80	18 months	Breast, prostate, gynecological, urinary and stomach cancer	Part of a larger longitudinal study on the epidemiology of insomnia in the context of cancer. Participants recruited at L'Hôtel-Dieu de Québec (Centre Hospitalier Universitaire de Québec; CHUQ) and Hôpital du St-Sacrement (Centre Hospitalier Affilié Universitaire de Québec; CHA), in Quebec City, Canada, from 2005 to 2007	Hospital Anxiety and Depression Scale, Insomnia Severity Index, Multidimensional Fatigue Inventory, Physical Symptoms Questionnaire.	Missing data, variable symptoms. Patients excluded widows, those receiving chemotherapy, to have cancer urinary and gastrointestinal.

Abbreviations: BMI: body mass index; SCC: squamous cell carcinoma; BSS: basal cell carcinoma; CMM: cutaneous malignant melanoma; UV: ultraviolet; BC: breast cancer; BBD: benign breast disease; HSS: healthy study participants; MEN1: multiple endocrine neoplasia type 1; HBOC: hereditary breast-ovarian cancer; HNPCC: hereditary nonpolyposis colorectal cancer; FAP: familial adenomatous polyposis; PCC: parents of cancer children; PHC: parents of healthy children; PSA: prostate-specific antigen. CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease; ACE: adverse childhood experience; SES: socioeconomic status; IQ: intelligence quotient; BMI: body mass index; BC: breast cancer.

Supplementary Table 3: Results of studies with psychological stress symptoms as cancer predictor

Supplementary Table 3.1: Perceived stress as predictor

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Hange, D. ¹²	Perceived nervousness, perceived moodiness + <u>yes.</u>	None.	Overall cancer + <u>yes.</u>	Smoking, hypertension, S-cholesterol, S-triglycerides, BMI, WHR, SES, education, number of children.	Perceived nervousness – cancer morbidity: no significant link before and after adjustments. Perceived moodiness – cancer morbidity: no significant link before and after adjustments.
Nielsen, N.R. ⁶³	Perceived stress + <u>yes.</u>	None.	Overall cancer mortality + <u>yes.</u>	Age, marital status, educational level, tobacco smoking, alcohol intake, physical activity during leisure time, body mass index, systolic blood pressure, serum cholesterol.	Women with high stress vs women with low stress – cancer mortality: inverse significant link after adjustments (HR 0.73 95%CI 0.57-0.93)
Nielsen, N.R. ²⁴	Perceived stress + <u>yes.</u>	Stress intensity, stress frequency.	Colorectal cancer + <u>yes.</u> Colon cancer, rectal cancer.	Age, education, income, cohabitation, physical activity during leisure time, alcohol consumption, tobacco smoking, body mass index, diabetes mellitus. In analyses for women, adjustments were also made for: hormone therapy, menopause, oral contraceptive use and number of children.	Women with moderate stress intensity vs women with no reported stress – colorectal cancer incidence: significant inverse link after adjustments (HR 0.60 95%CI 0.37-0.98). Women with reported daily stress – colorectal cancer incidence: significant inverse link before (HR 0.29 95%CI 0.12-0.71) and after adjustments (HR 0.28 95%CI 0.11-0.67). Men with high reported stress – colorectal cancer incidence: significant link before (HR 2.13 95%CI 1.14-3.99) and after adjustments (HR 1.96 95%CI 1.03-3.74)
Song, H. ²⁹	Perceived stress + <u>yes</u>	Stress intensity	Overall cancer+ <u>yes</u>	Perceived level of life enjoyment, sleep hours, type A behavioral, smoking status, alcohol intake level, BMI, occupation, physical activity, living arrangement, fruit and vegetable consumption, and family history of cancer.	Significant increase in risk of overall cancer is observed with medium and high perceived stress level (HR = 1.04 (95% CI 1.01–1.09) and HR = 1.06 (95% CI 1.00–1.11), respectively).

Supplementary Table 3.2: Depression as predictor

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
Archer, G. ¹	Affective/emotional depressive symptoms. + <u>yes</u>	Depression incidence or history during the 3 assessments.	Overall cancer + <u>yes</u>	Sex and age. Secondly, a group of potential confounders and mediators (employment grade, smoking, longstanding illness).	<u>Depression incidence/depression history – Overall cancer over 17 years: not significant with or without adjustments.</u> Borderline significant link between ‘new depressive symptoms’ and an increased risk of developing cancer as opposed to ‘never depressive symptoms. (HR = 1.89, 95% CI: 1.23-2.90
Batty, D. ²	Psychological distress + <u>No</u>	Depression and anxiety	Overall cancer + <u>yes</u> Esophagus, stomach, colorectal, liver, pancreas, lung, mesothelioma, breast (female), ovary (women), prostate (men), bladder, kidney, central nervous system (, non-Hodgkin’s lymphoma, multiple myeloma leukemia.	Sex and age. Along with physical activity, C reactive protein, area level deprivation, socioeconomic position (education) and health behaviors (cigarette smoking, alcohol intake).	After adjustments higher levels of distress was significantly associated with 32% greater risk (HR 1.32, 95% CI 1.18-1.48). Significant associations were observed for the following cancers- not related to smoking (HR 1.45, 95% CI 1.23-1.71), Colorectal cancer (HR 1.84, 95% CI 1.21-2.78), Prostate (HR 2.42, 95% CI 1.29-4.54), pancreas (HR 2.76, 95% CI 1.47-5.19), esophagus (HR 2.59, 95% CI 1.34-5.00), and leukemia (HR 3.86, 95% CI 1.42-10.5).
Brown, S. ³	Depressive symptoms. + <u>yes</u>	None.	Breast cancer. + <u>yes.</u> Invasive breast cancer. In situ breast cancer.	Any confounder that changed the estimate for the exposure by greater than 10%: age, BMI, alcohol use, smoking status, physical activity, parity, age at first birth, breastfeeding, oophorectomy,	<u>Depressive symptoms-breast cancer over 17 years: not significant with or without adjustments.</u>

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
			Estrogen receptor breast cancer (ER)+. (ER)-cancer.	postmenopausal hormone use, age at menopause and race.	
Chang, H.Y. ⁵	Depression. + <u>yes</u>	Major depression and minor depression, each divided into 2 categories according to severity.	Overall cancer. + <u>yes</u> . Overall cancer. Hormone related cancer divided into cancer of the: breast, cervix, corpus uteri, ovary and prostate.	Age, smoking status, drinking status, regular exercise, cancer family history.	Major depression, minor depression and chronic depression – overall cancer incidence in men: Significant after adjustments (major: HR 1.05, 95% CI 1.01-1.09, minor: HR 1.03, 95% CI 1.01-1.06, chronic: HR 1.08 95%CI 1.02-1.14). * Major depression – overall cancer incidence in women: Significant inverse after adjustments (major: HR 0.90, 95% CI 0.83-0.98) Minor depression-prostate cancer significant after adjustments. (major: HR 1.13, 95% CI 0.98-1.29, minor: HR 1.13 95%CI 1.05-1.23). Major depression – Cervical cancer: Significant inverse after adjustments (HR 0.63, 95%CI 0.45-0.90) Chronic depression and cervical cancer: significant inverse after adjustments (HR 0.51, 95%CI 0.28-0.93) Other specific types of cancer were not significantly associated with depression of any severity.
Chen, Y. ⁶⁴	Severe depressive disorder. + <u>Yes</u> .	None.	Overall + <u>yes</u> Oral, gastrointestinal, respiratory, genitourinary, hematological cancer	Geographic location, urbanization level of the community, monthly income.	Severe depressive disorder – overall cancer incidence: significant with (HR 1.44 95%CI 1.07-1.94) and without (HR 1.62 95%CI 1.12-2.34) adjustments. Severe depressive disorder-gastrointestinal cancer: significant (HR 1.80 95%CI 1.03-3.14). Severe depressive disorder- genitourinary cancer: significant (HR 1.92 95%CI 1.01-3.66). There was no significant link between the

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
					other types of cancer and severe depressive disorder.
Gross, A.L. ¹¹	Depression + <u>yes</u>	A lifetime history of major depression. A lifetime history of a dysphoric episode. Neither a history of major depression nor dysphoric episode.	Overall cancer + <u>yes</u> Breast cancer, colon cancer, lung cancer, prostate cancer, skin cancer.	Age self-reported race, sex, marital status at each wave, smoking status at each wave, socioeconomic status, history of alcohol abuse/dependence.	Depression – overall cancer incidence: no significant link before adjustments and significant link after adjustments (1.87 95%CI 1.16-3.01). Dysphoric episode – overall cancer incidence: significant link before (HR 1.30 95%CI 1.02-1.66) and after (HR 1.69 95%CI 1.30-2.19) adjustments. Due to small numbers of the subsets of cancer, there were trends, but no further significant links between dysphoria/depression and these specific subsets of cancer.
Huang, T. ¹³	Depression + <u>yes.</u>	Persistent negative depression status. Persistent positive depression status. Improved depression status. Worsening depression status.	Epithelial ovarian cancer + <u>yes.</u>	BMI, physical activity, smoking, intake of caffeine and lactose.	Depression assessed 2-4 years before diagnosis – ovarian cancer incidence: significant link before (HR 1.30 95%CI 1.05-1.60) and after (HR 1.26 95%CI 1.02-1.56) adjustments. Significant links were also found for: persistent positive depression status – ovarian cancer incidence (HR 1.34 95%CI 1.01-1.76) after adjustments. Depression at baseline or >4 years before diagnosis was not significantly linked to ovarian cancer incidence.
Hung, Y.N. ¹⁴	Affective disorder + <u>yes</u>	Bipolar disorder. Major depressive order.	Overall cancer + <u>yes</u> Tobacco- and/or alcohol related cancer (buccal cavity, esophagus, larynx, liver, lung, nasal cavity, pancreas, stomach, kidney, bladder, uterine	Adjustments were implemented in a table of HR's stratified by age, sex, tobacco or alcohol use by subdividing into alcohol- and/or tobacco-related cancers.	Bipolar disorder – cancer incidence: significant link in both genders (SIR 1.39 95%CI 1.26-1.53) not adjusted. Major depression – cancer incidence: significant link in both genders (SIR 2.01 95%CI 1.85-2.19). The risk was higher with lower age of affective disorder diagnosis. For bipolar disorder there were significant links with incidence of tobacco- and alcohol-related (SIR 1.75 95%CI 2.21-3.44), tobacco-related (SIR 1.29 95%CI 1.07-1.56), alcohol-

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
			cervix, myeloid leukemia, colorectal, breast). Non-tobacco-/alcohol-related (skin, brain, thyroid, other). Gender specific (breast, cervical, uterus, prostate).		related (SIR 1.25 95%CI 1.01-1.55) and sex-specific (SIR 1.6 95%CI 1.29-1.97) cancers. For major depression, there were significant links with incidence of tobacco- and/or alcohol related (SIR 2.01 95%CI 1.85-2.19), tobacco-related (SIR 1.94 95%CI 1.65-2.29), alcohol-related (SIR 2.11 95%CI 1.77-2.50), non-tobacco- or alcohol-related (SIR 1.51 95%CI 1.68-2.12) and gender-specific (SIR 2.16 95%CI 1.79-2.61) cancers. Bipolar disorder was also positively significantly linked to site specific cancer at the: buccal cavity, esophagus, uterine cervix, breast and uterus and major depression with cancer at the: buccal cavity, esophagus, larynx, liver, lung, pancreas, stomach, kidney, colon or rectum, breast, brain, thyroid and prostate.
Karakus, M.C. ¹⁷	Depression + <u>yes.</u>	None.	Overall cancer + <u>yes.</u>	Age at baseline, gender, race, marital status, education level, BMI and smoking were included in a multivariable analysis.	Depression – overall cancer incidence: no significant link.
Lemogne, C. (2) ⁶⁵	Depression + <u>yes.</u>	Sickness absence for depression (SAD), depression incidence, chronic depression, recurrent depression.	Overall cancer + <u>yes.</u> Prostate cancer, breast cancer, colorectal cancer, smoking-related cancer, cancer of the lymphoid and hematopoietic tissue, cancer at other sites.	Age, sex, occupational grade, smoking, fruit and vegetable consumption, height, weight, physical activity, perceived health status, alcohol consumption.	Sickness absence for depression – cancer at other sites: significant after adjustments (HR 1.76 95%CI 1.12-2.78) Chronic depression – prostate cancer: inverse significant after adjustments (HR 0.60 95% CI 0.38-0.96) Of 24 statistical tests, only 2 got a significant result.
Wise, L.A. ³¹	Depressive symptoms + <u>yes.</u>	CES-D scores of <16, 16-24 and >24, past or current	Uterine leiomyoma + <u>yes.</u>	Age at menarche, parity, age at first birth, years since last birth, age at first oral contraceptive use, history	CES-D score 16-24 vs <16 – uterine leiomyoma incidence: not significant

Author	Stress type + (<u>Primary independent variable?</u>)	Relevant subsets of stress types	Cancer type + (<u>primary dependent variable?</u>)	Adjustments	Results + HR compared to absent independent variable.
		physician diagnosed depression.		of oral contraceptive use, BMI, physical activity, smoking, current alcohol intake, participant's education, marital status, occupation, annual household income, region of residence.	CES-D score >24 vs <16 – uterine leiomyoma incidence: significant after adjustments (RR 1.16 95%CI 1.06-1.27) present physician-diagnosed depression – uterine leiomyoma: significant after adjustments (RR 1.32 95%CI 1.14-1.52)

Supplementary Table 3.3: Personality as predictor

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
Butow, P.N. ⁶⁶	Psychosocial variables + <u>no</u>	Satisfaction with social support. Optimism. Anti-emotionality. Anger control.	Breast cancer. + <u>yes</u> . Invasive breast cancer. Ductal carcinoma in situ.	Current anxiety or depression.	5 psychosocial variables-breast cancer over 15 years: not significant with or without adjustments.
Chapman, B.P. ⁶⁷	Emotion suppression. + <u>Yes</u>	None.	Death from overall cancer + <u>no</u>	Age, sex, minority race, education level, self-rated health.	Emotion suppression – cancer death (removing deaths within the 1 st year): significant after adjustments (HR between 1 st and 3 rd quartile of emotion suppression :2.08 95%CI 1.16-3.75).
Falkstedt, D. ⁹	Psychosocial functioning + <u>no</u> .	3 levels of psychosocial functioning from low to high.	Cancer death + <u>no</u> Lung cancer.	None	Low psychosocial functioning score – lung cancer death: significant (HR 1.87 95%CI 1.02-3.42). Low psychosocial functioning score – cancer death: no significant link .
Ikeda, A. ⁴³	Perceived social support + <u>yes</u>	Very high, high, medium and low social support.	Overall cancer + <u>yes</u> . Cancer of the liver, lung, stomach, colorectal cancer, colon cancer, rectal cancer.	Age, public health center area, smoking status, ethanol intake, body mass index, sports during leisure time, perceived stress, occupation, history of diabetes, participation status in any medical examinations or screening test performed within the past year.	Social support – overall cancer incidence: no significant link in women and men after adjustments. Low social support – colorectal cancer in men: significant link after adjustments (HR 1.48 95%CI 1.07-2.05). Low social support colon cancer in men: significant link after adjustments (HR 1.59 95%CI 1.07-2.39).
Jokinen, J. ¹⁶	Suicide attempt + <u>yes</u> .	None.	Overall cancer + <u>yes</u> 40 types of cancers.	To account for smoking status differences between the suicide-attempt group and controls, some cancer types were defined as ‘tobacco smoking-related cancers’ (cancer of the oral cavity, pharynx, larynx, esophagus, lung, pancreas, kidney, urine bladder).	Suicide attempt – overall cancer incidence: significant link in women (SIR 1.25 95% CI 1.22-1.28) and in men (SIR 1.30 95%CI 1.27-1.33). A significant link was also found for laryngeal (SIR 4.63), pharyngeal (SIR 2.93), lung (SIR 2.62), liver (SIR 2.61) cancer in

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
					women and for oral (SIR 3.29), liver (SIR 3.25), larynx and tongue cancer in men. A significant inverse link was found for suicide attempt and melanoma in men (SIR 0.69) and women (SIR 0.87). There were other smaller significant links for non-tobacco related cancer types.
Kim, S. ¹⁸	Optimism + <u>yes</u>	High, modest and low optimism.	Breast cancer + <u>yes</u> .	Sociodemographic, behavioral, reproductive and psychological variables.	High optimism (compared to modest optimism) – breast cancer incidence: significant after adjustments (HR 0.82 95%CI 0.72-0.93) This link was stronger for women aged <60 years (HR 0.69 95%CI 0.49-0.96)
Kennedy, B. 68	Stress Resilience+ <u>yes</u>	Willingness to assume responsibility, high independence, persistence, emotional stability and ability to take the initiative + mental energy, emotional control, social maturity and active/passive interests.	Overall cancer + <u>yes</u> Prostate cancer, liver cancer, kidney cancer, lung cancer urinary cancer.	Demographic factor, socioeconomic factors, parents' socioeconomic index, household crowding, cognitive function, BMI and physical fitness.	High resilience- 23.7%, Moderate resilience- 54.7%, low resilience-21.6%. After adjustment Moderate stress resilience significantly associated with moderate decrease in cancer risk (HR: 0.91; 95% CI 0.87 to 0.95) With low resilience significant increase in lung cancer risk, (HR:2.75; 95% CI 2.02 to 3.74), liver cancer risk (HR: 4.73;95% CI 2.73 to 8.19), kidney cancer risk (HR: 1.51; 95% CI 1.06 to 2.15) and urinary cancer risk (HR: 1.39; 95% CI 1.04 to 1.86) Significant Inverse association with prostate cancer (p<0.001) Significant risk reduction by 35% for high stress resilience (HR: 0.65; 95% CI 0.56 to 0.76)

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
Lemogne, C. (1) ¹⁹	Personality + <u>yes.</u>	6 aspects of personality: Dependence on withdrawing objects, leading to suppressed emotional expression in the context of interpersonal relationships (type 1). Dependence on disturbing objects, leading to hostile thoughts and feelings (type 2). Dependence on objects that are both withdrawing and disturbing, leading to ambivalent behaviors oscillating between the positive and negative aspects of the objects (type 3). Autonomy and self-regulation (type 4). Rational/anti-emotional tendencies (type 5). Antisocial tendencies (type 6). Also: hostility and type A personality (competitive, highly organized,	Overall cancer + <u>yes.</u> Prostate cancer, breast cancer, smoking-related cancer (oral cavity, pharynx, esophagus, larynx, trachea, bronchi, lungs, bladder), colorectal cancer and other cancer.	Age, sex, occupation grade, alcohol consumption, smoking, fruits and vegetables consumption, height, weight, physical activity, perceived health status were included in a multivariate analysis.	Type 1 personality – breast cancer: inverse significant link after adjustments (HR 0.81 95% CI 0.68-0.97). Type 5 personality – overall cancer, smoking related cancer, other cancer: significant before adjustments (HR respectively: 1.08 (1.02-1.15), 1.21 (1.02-1.44) and 1.15 (1.04-1.28)) but only significant after adjustments for other cancer (HR 1.16 95% CI 1.04-1.29). Hostility – smoking related cancer: significant before adjustments (HR 1.29 95% CI 1.09-1.52)

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Results + HR compared to absent independent variable.
		ambitious, impatient)			
Nakaya, N. ⁶⁹	Psychosocial factors + <u>yes.</u>	Extraversion, neuroticism.	Overall cancer + <u>yes.</u>	Sex, age, cigarette smoking, alcohol consumption, body-mass index, education, family history of cancer.	Neuroticism and/or extraversion – cancer incidence: no significant link.
Svensson, T. ³⁰	Coping strategies + <u>yes.</u>	Planning, consulting someone, fantasizing, positive reappraisal, self-blame, avoidance. (Planning, consulting and positive reappraisal were also combined as approach based, the others as avoidance based, having both approach and avoidance-based coping strategies, was called combined coping).	Overall cancer + <u>yes.</u> Breast cancer, rectal cancer, gastric cancer, liver cancer, pancreatic cancer, lung cancer, prostate cancer, colon cancer	Gender, age, alcohol consumption, smoking, a history of diabetes, total physical activity, use of prescribed medications, unemployment, having undergone screening examinations, living arrangements.	Avoidance-oriented coping strategy – cancer incidence: inverse significant link after adjustments (HR 0.69, 95% CI 0.50-0.94). Avoidance – breast cancer: significant link after adjustments (HR 1.91 95% CI 1.26-2.91). Approach coping strategies – rectal cancer: inverse significant link after adjustments (HR 0.64 95% CI 0.42-0.98). Combined coping strategy – breast cancer incidence: significant link after adjustments (HR 2.32 95% CI 1.15-4.70).

Supplementary Table 3.4: Anxiety as predictor

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Denollet, J. ⁸	Anxiety + <u>yes</u>	None.	Cancer death. + <u>no</u> Lung cancer death, breast cancer death.	Higher age, lower education living alone, smoking, excessive alcohol consumption, physical inactivity, BMI >30, hypertension diabetes, score of more than 12 on the Edinburgh Depression Scale.	Anxiety – breast cancer death: no significant link with or without adjustments. Anxiety – lung cancer death: no significant link after adjustments for smoking and significant link before adjustment for smoking (HR 2.21 95% CI 1.04-4.70).
Liang, J. ²¹	Anxiety disorder + <u>yes</u>	None.	Overall cancer + <u>yes</u> . Oral cancer, colorectal cancer, liver cancer, lung cancer, breast cancer, cervical cancer, prostate cancer and other cancer.	Urbanization level, comorbidities (hypertension, diabetes mellitus, hyperlipidemia). Life style factors could not be retrieved from NHI database.	Anxiety disorder – prostate cancer: significant after adjustments (HR 1.32 95% CI 1.02-1.71). No significant link was found between anxiety disorder and other types of cancer.
Poole, E.M. ²⁷	Phobic anxiety + <u>yes</u> .	None.	Ovarian cancer + <u>yes</u> .	Duration of oral contraceptive use, number of children, tubal ligation, family history of ovarian cancer, menopausal status, body mass index, smoking, alcohol intake, caffeine intake, total caloric intake, physical activity, census tract income, post-menopausal hormone therapy, beta blocker use, antidepressant medication use, anti-anxiety medication use, depression.	Phobic anxiety score – ovarian cancer incidence: no significant trends .
Shen, C.C. ⁷⁰	Generalized anxiety disorder + <u>yes</u> .	None.	Overall cancer + <u>yes</u> . Cancer of the: head and neck, digestive tract	None	Generalized anxiety disorder – overall cancer incidence: significant link (SIR 1.14 95% CI 1.05-1.24), this link was more outspoken in men (SIR 1.30 95% CI 1.15-1.46) and in patients aged 80 years and older (SIR 1.56 95% CI 1.35-2.39). Generalized anxiety –

Author	Stress type + (<u>Primary independent variable?</u>)	Relevant subsets of stress types	Cancer type + (<u>primary dependent variable?</u>)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
			(esophagus, colon and rectum, anus), liver and biliary tract, pancreas, lung and mediastinum, bone and soft tissue, skin, breast, genitourinary (cervix, uterus, ovary, prostate, kidney, bladder), thyroid, hematologic malignancies, others.		specific cancer type incidence: significant link for cancer of the: lung and mediastinum (SIR 1.53), prostate (SIR 2.17)

Supplementary Table 3.5: Positive state of mind as predictor

Author	Stress type + (Primary independent variable?)	Relevant subsets of stress types	Cancer type + (primary dependent variable?)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Feller, S. ⁷¹	Life satisfaction + <u>yes.</u>	Very satisfied. Rather satisfied. Unsatisfied.	Overall cancer + <u>yes.</u>	Smoking, alcohol intake, physical activity education, WHR consumption of fruits and vegetables, red meat and whole-grain bread.	Life satisfaction – overall cancer incidence: no significant link . Low life satisfaction – increased cancer risk in men consuming less than 10g alcohol per day: significant (HR 1.19 95%CI: 1.01-1.41). Unsatisfied (vs very satisfied) women – overall cancer risk: significant (HR 1.45 95%CI 1.18-1.78).
Liu, B. ²²	Happiness + <u>yes.</u>	Self-reported happiness (happy most of the time, usually or rarely/never/sometimes). Self-reported feeling in control (rarely, usually, most of the time). Self-reported feeling relaxed (rarely, usually, most of the time), self-reported feeling stressed (rarely, usually, most of the time).	Overall cancer mortality + <u>no.</u>	Age, area deprivation, body-mass index, qualifications, strenuous exercise, smoking, alcohol, living with a partner, parity, participation, in group activities, sleep duration.	Happiness – cancer mortality: no significant link before and after adjustments.
Okely, J.A. ⁷²	Well-being + <u>yes.</u>	None.	Overall Cancer + <u>no.</u>	Age, sex, depressive symptoms, socioeconomic status, education, relationship status, physical activity, alcohol consumption, smoking status, body mass index.	Well-being – cancer incidence: no significant link .

Supplementary Table 4: Results of studies with stressors as cancer predictor

Supplementary Table 4.1: Stressful life events as stressor

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Stressful Life-Events					
Azizi, H. ⁷³	Stressful life events, death of dears	N/A	Colorectal cancer	Age, sex, family history of colorectal cancer, history of diabetes, smoking, physical activity and BMI.	<u>Life events & death of dears - colorectal cancer: SIGN.</u> The result of T-test showed that there is significant relationship between scores of stressful life events in case and control groups (p<0.011). Multivariate logistic regression shows that death of dears increased the risk of CRC 2.5 times (OR: 2.49; 95% CI: 1.41-5.13). Other types of stressful life events (family and husband disputes, serious occupational problems, unemployment of > 6 months, and serious financial problems) were associated with CRC, but not statistically significant.
Bahri, N. ³⁴	Stressful Life events	N/A	Breast Cancer	None.	<u>Life Events-Breast cancer: SIGN.</u> Significant Q test for heterogeneity ($\chi^2 = 21.47$, p = 0.01) History of stressful events significantly increases risk of breast cancer (RR: 1.11 (95% CI 1.03 to 1.19))
Brown, D. ³⁵	Adverse childhood experiences	N/A	Lung cancer	Smoking and other co-factors associated with an increased risk of lung cancer (COPD, history of tuberculosis...), age at baseline, sex, race/ethnicity, education, marital status and current financial problems.	<u>Adverse childhood experiences - lung cancer: SIGN.</u> Graded relationships between the ACE score and the risk of lung cancer were observed. Moreover, relationships between a high ACE score and lung cancer were particularly strong for those who died from lung cancer at younger ages. The increase in risk of lung cancer was only partly due to relationships between aces and an intermediate causal factor, smoking.
Cabaniols, C. ³⁶	Major life events	N/A	Brain cancer	Age, sex and other specific adjustments when focused on stress.	<u>Life events – brain cancer: SIGN.</u> A significant positive association of major life events occurred over the last 5 years before MPBT diagnosis (or = 1.90, 95% CI 1.13–3.20).
de Vries, E. ³⁷	Stressful life events	N/A	Skin cancer	Age, sex, self-reported photo type and country.	<u>Life events: skin cancer: SIGN.</u> 'Any traumatic event' was always significantly associated with a higher risk of BCC, SCC and CMM (p<0,001). For BCC, the stressful events that were statistically significant in multivariate analysis were loss of a family member or close friend (p=0,002 OR=2,19 95% CI: 1,34-3,57), personal major illness (p=0,023 OR=2,23 95% CI: 1,12-4,43) or 'other trauma' (p=0,002 OR=8,28 95%

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
					CI: 2,12-32,43). For SCC, the stressful events were loss of a family member or close friend (p<0,001 OR=3,24 95% CI: 1,81-5,80) and personally having a major illness (p=0,01 OR=3,03 95% CI: 1,31-7,04). Loss of a family member or friend (p<0,001 OR=3,02 95% CI: 1,74-5,26), loss of job (p=0,017 OR=4,62 95% CI: 1,32-16,20), having a major illness (p=0,033 OR=4,62 95% CI: 1,07-4,77), and 'other trauma' (p=0,009 OR=6 95% CI: 1,54-20,30) were all related to increased risk of CMM. These associations remained significant after Bonferroni correction for multiple testing, excluding loss of job (CMM), personal major illness and 'other trauma' (CMM).
Eskelinen, M. ⁷⁴	Life events	N/A	Breast cancer	None	<u>Breast cancer - life events: SIGN.</u> Findings of a weak relationship between life stress due to severe losses and severe deficit (p=0,02) in childhood and adolescence and breast cancer risk.
Eskelinen, M. ⁷⁵	Life events	N/A	Breast cancer	None	<u>Breast cancer - loss of social status: SIGN. Breast cancer - other life events: NS.</u> Only significant relation between loss of social status and breast cancer (p<0,05). There is a significant relation between the stress due to severe losses and breast cancer (p<0,01), but no significant relationship between the losses themselves and breast cancer.
Fang, F. ³⁹	Loss of a child	N/A	Infection-related cancers	Sex, age at follow-up, calendar year of follow-up, educational level, civil status.	<u>Loss of a child - infection-related cancer: SIGN (except EBV, H. Pylori, non-melanoma skin cancer)</u> Parents who lost a child did not have a significantly altered risk for EBV- and H. Pylori-related cancers overall, whereas they had a higher risk of liver cancer (RR: 1.14; 95% CI: 1.00-1.30), especially primary hepatocellular carcinoma (RR: 1.22; 95% CI: 0.99-1.52). Among the HPV-related cancers, the risks of cancer in the cervix uteri, vulva and vagina, as well as anus appeared to be associated with child loss, although some of the excess risks were based on small numbers and not statistically significant. Among possibly HPV-related cancers, statistically significant associations were observed for cancers in oral cavity and pharynx, esophagus, larynx, and eye (RR: 1.43, 1.25, 1.49, and 1.58 respectively). Non-melanoma skin cancer was not associated with the loss of a child. The increased risk was seen only during the first 5 years after loss overall.

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Fischer, A. ⁴⁰	Stressful life events	N/A	Breast cancer	Age (age at diagnosis for cases and age at RFQ completion for controls), smoking history (ever smoked/never smoked), race/ethnicity (non-Hispanic white/all other groups), education (less than college/some college or more), family history (yes/no) (determined based on family history of breast cancer in first degree relative), hormone replacement therapy (HRT) (ever use/never use), age at menarche (≤ 11 , 12-13 and ≥ 14), age at first full term pregnancy (FFTP): (< 25 , 25-29 and ≥ 30), menopausal status (pre-menopausal/peri-menopausal/post-menopausal) and physical activity (not active/moderately active/very active).	<u>Stressful Life Events-Breast cancer, SIGN</u> -Perceived stressful life event was associated with increased risk of breast cancer incidence (OR = 1.63, 95% CI = 1.00-2.66, Ptrend = 0.045). While abortion and relocation were observed to have a protective effect on risk of breast cancer if perceived as stressful (OR = 0.54, 95% CI = 0.32-0.92; OR = 0.63, 95% CI = 0.43-0.93, respectively).
Huang, J. ⁴²	Loss of a child	N/A	Pancreatic cancer	Education, socioeconomic status, region of residence, total number of children.	<u>Loss of a child - pancreatic cancer: SIGN</u> . They found a slightly increased risk of pancreatic cancer among women who had previously lost a child. The risk increment was noted only within the first 5 years after the child's death. Loss due to suicide appeared to be most clearly associated with the risk increase. A stronger association was also suggested for early onset pancreatic cancer and for persons with coexisting psychiatric illnesses.
Jakovljevic, G. ⁴⁴	Stressful life events, family quarrels	N/A	Overall cancer	None	<u>Stressful life events - overall cancer: SIGN. Family quarrels - overall cancer: SIGN.</u> PCC reported they had more family stressful life events than PHC ($p < 0,01$); PCC reported that their children had more stressful life events compared to healthy children ($p < 0,01$); In FHC there was less arguing (verbal fights) than in FCC ($p < 0,05$); Cumulative effect of family stress, children's stress and family quarrels ($p < 0,001$).
Kelly-Irving, M. ⁴⁷	Adverse childhood experiences	N/A	Overall cancer	Mother's age at birth, overcrowding, mother's partner's social class (or mother's father's if unavailable), mother's education level, maternal smoking during pregnancy, sex, gestational age at birth, parity, birth weight, fetal distress, problems during pregnancy, breastfeeding and childhood pathologies (congenital	<u>Adverse childhood experiences - overall cancer: SIGN.</u> Psychosocial adversity in childhood was related to cancer incidence before 50 y among women, after adjusting for prior confounding factors and potential mediators. Women who experienced two or more ACE doubled their risk of having a cancer before 50 relatives to women who had had no childhood adversities (OR: 2.1, 95% CI: 1.42-3.21, $p < 0.001$). The strength of the relationship between adversity and cancer

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
				conditions, moderate/severe disabilities, chronic respiratory or circulatory conditions, sensory impairments and special schooling). Mediators across the life course (at 23y): respondent's educational attainment and occupational social class, symptoms of depression/anxiety, alcohol, smoking, BMI, first pregnancy.	was of the same magnitude as that observed between age at first pregnancy and cancer, a well-known risk factor for breast cancer.
Kennedy, B. ⁴⁸	Loss of a parent	N/A	Overall cancer	Age at follow-up, sex, calendar period of follow-up and socioeconomic status of the family.	<u>Loss of a parent - overall cancer: NS. Loss of a parent - specific cancer sites: some SIGN. No overall association</u> between loss of a parent through death and the risk of cancer before the age of 40 was found. Individuals who experienced parental death during childhood had an increased risk for HPV-related cancers and pancreatic cancer. A parental death during early adulthood was associated with higher risks of early onset stomach, lung, rectal, pancreatic, and breast cancers. As of note, loss of a parent due to death was associated with a higher risk of pancreatic cancer, regardless of age at loss.
Kocic, B. ⁴⁹	Stressful life events	N/A	Breast cancer	None	<u>Stressful life events - breast cancer: SIGN.</u> Patients were statistically more likely to have stressful life events (p=0,0000) in the years prior to diagnosis, severe life events (p=0,0390) and severe and moderate life events (p=0,000), compared to controls. Also, this study found that experience of severe and moderate threats, death of close family member and son's military service increase the risk for breast cancer development. The stress most strongly associated with increased breast cancer risk appears to be stress induced by major life events.
Korpimaki, S. K. ⁷⁶	Childhood adversities	N/A	Overall cancer	Age, sex, education, health behavior (smoking, alcohol, BMI).	<u>Childhood adversities - overall cancer: NS.</u> Working-aged cancer patients did not report significantly more childhood adversities than cancer free controls. Some differences were nonetheless found. Those reporting parental divorce had decreased risk of cancer and those reporting conflicts increased risk.

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Kruk, J. ⁵³	Life events	N/A	Breast cancer	Age at enrolment, age at menarche and age at first birth, BMI, education level, parity, months of breast-feeding, menopausal status, use of oral contraceptives, postmenopausal hormonal replacement therapy use, family history of breast cancer in first-degree relatives, ever a regular cigarette smoker, ever exposure to cigarette smoking, adult alcohol consumption, diet during adult life, screening mammography or ultrasonographic examination of breast within the past 2 years, total physical activity.	<u>Life events - breast cancer: SIGN.</u> We found that the total life event scores accumulated over lifetime was, on average, higher for breast cancer cases than for controls. Women with the highest scores were five times more likely to develop the disease than those at the baseline level. Women with four to six major life events had about 5 times increased risk. Death of a close family member, personal illness or injury, imprisonment/trouble with the law, and retirement were each significantly related to increased risk.
Michael, Y. L. ⁵⁶	Life events	N/A	Breast cancer	Age, education, ethnicity, income, insurance status; history of CVD, diabetes, cancer diagnosis other than BC, BMI; Gail model score (risk of BC using parameters such as age, hyperplasia, number of biopsies...); parity, length of breast feeding, oral contraceptive use and duration of hormone therapy use; amount of exercise, alcohol use, smoking status, fat intake, and mammography adherence.	<u>Life events - breast cancer: NS.</u> No significant association of breast cancer with life events was found.
Michael, Y. L. ⁵⁶	Stressful life events + social support	N/A	Breast cancer	Age, education, ethnicity, income, insurance status; history of CVD, diabetes, cancer diagnosis other than BC, BMI; Gail model score (risk of BC using parameters such as age, hyperplasia, number of biopsies...); parity, length of breast feeding, oral contraceptive use and duration of hormone therapy use; amount of exercise, alcohol use, smoking status, fat intake, and mammography adherence.	<u>Interaction social support and life events – breast cancer: SIGN.</u> A marginally significant interaction (p=0,07) between life events and social support was observed. Compared with women with no life events and lower social support, women with lower social support who reported one life event experienced increased risk of breast cancer (HR 1.20, 95% CI 1.00-1.43), although an increasing number of life events (above one) were significantly protective against breast cancer (p=0,04).

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Primary results and significant subset results. + HR compared to absent independent variable.
Peled, R. ⁵⁷	Life events	N/A	Breast cancer	Age and family status.	<u>Life events - breast cancer: SIGN.</u> A significant difference was found when comparing the groups according to the cumulative number of events (two or more events) (OR =1.62 95% CI: 1.09–2.40).
Renzaho, A. M. ⁵⁹	Family-related life events, positive life events	N/A	Overall cancer	Demographic and health-related factors, hypertension, BMI, disability, equalized household income, SES.	<u>Family-related stress - overall cancer: NS. Positive life events - overall cancer: NS.</u> Work-related stress (OR= 1.51, P< 0.01) and personal stress (OR=1,52, P<0,05) were positively associated with the onset of cancer.
Schorr, L. ⁶⁰	Loss of a child	N/A	Overall cancer	Parents' education level, parents' age at child's birth and death, and child's age at death.	<u>Loss of a child - overall cancer: NS.</u> No association was observed between offspring's death and parent's cancer morbidity (HR=0.89-0.98).
Trudel-Fitzgerald, C. ⁷⁷	Life-events- Social Integration, Marital Status	N/A	Ovarian Cancer	Participant's age, education level, marital, employment, and socioeconomic status, cancer site and stage, and adjuvant treatments received.	<u>Social Integration, Marital Status: SIGN</u> social isolation versus integration was Significantly associated with increased ovarian cancer risk 8 to 12 years later (HR = 1.51, 95% CI = 1.07–2.13) but not 4-8 years period. Additionally, Widowed women were significantly at higher risk of ovarian cancer compared to separated and divorced individuals when the results were adjusted. (HR = 1.57 [95% CI = 1.15–2.14])

Supplementary Table 4.2: Job strain as stressor

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Results
Job Strain					
Cabaniols, C. ³⁶	Job stress	N/A	Brain cancer	Pilocytic astrocytoma, recurrence of previous MPBT	<u>Job stress - brain cancer: NS.</u> Intensity of stress at work had no apparent effect.
Hougaard, C. O. ⁴¹	Job mobility	N/A	Lung cancer, colorectal cancer	Those who had registered cases of the outcome during the previous five years.	<u>Job mobility - lung & colorectal cancer: NS.</u> No effect was seen for colorectal cancer.
Jansson, C. ⁷⁸	Job strain	N/A	Esophageal and cardia cancers	None	<u>Job strain - esophageal and cardia cancer: SIGN (except cardia adenocarcinoma).</u> Job strain was positively associated with risk of esophageal adenocarcinoma in the most exposed patients (OR = 3,2). Job strain was also associated with an increased risk of squamous-cell carcinoma (OR = 4,0). Job strain was, however, not associated with cardia adenocarcinoma. No associations were observed between demands, control or support and risk of esophageal or cardia adenocarcinoma or esophageal squamous-cell carcinoma, except for a positive association between high control and risk of esophageal squamous-cell carcinoma (OR 1.5).
Kuper, H. ⁵⁴	Job strain	N/A	Breast cancer	Age at baseline, education, parity, age at first birth, age at menarche, oral contraceptive use, family history of breast cancer, duration of breast-feeding, BMI, physical activity, education, alcohol consumption and cigarette smoking.	<u>Job strain - breast cancer: SIGN.</u> A small increased risk of breast cancer among women working full-time who experience job strain, high job demands, or low job control was found.

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Results
Nielsen, N.R. ⁶³	Work-related stressors	N/A	Breast cancer	Age at baseline, age at menarche, parity, age at first birth, family history of breast cancer, oral contraceptive use, body mass index, physical activity in leisure time, physical activity at work, work shifts, alcohol consumption, postmenopausal hormone use, age at menopause and height.	<u>Work-related stressors - breast cancer: NS.</u> Women who experienced high pressure of work did not have higher risk of breast cancer compared to women with low work pressure. Women who reported either too low (HR = 1.46, 95% CI: 0.68, 3.12) or too high (HR = 1.25, 95% CI: 1.02, 1.54) tempo of work seemed to have a slightly higher risk of breast cancer than women who felt that the tempo of their work was suitable. No association between influence or work hours and breast cancer incidence was found. No clear associations between work-related stressors and incidence of breast cancer were found.
Pudrovska, T. ⁵⁸	Job strain	N/A	Breast cancer	None	<u>High-status occupation - breast cancer: SIGN. Job strain - breast cancer: NS.</u> Women who were in professional and managerial occupations had a substantially higher risk of breast cancer compared to housewives and women in lower-status occupations. The risk of breast cancer associated with job authority accumulates with longer duration in the professional/ managerial occupations. Weekly work hours, time pressure, responsibility for things at work outside own control, job autonomy, and job satisfaction are not significantly related to breast cancer incidence. Responsibility for things outside one's own control, time pressure, and job satisfaction are more prevalent among higher-status women and are related negatively (although not significantly) to breast cancer risk.

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Adjustments	Results
Renzaho, A. M. ⁵⁹	Work-related life events	N/A	Overall cancer	Demographic and health-related factors known to be associated with chronic diseases, hypertension, BMI, disability, equivalized household income.	<u>Work-related stress - overall cancer: SIGN.</u> Work-related stress was positively associated with the onset of cancer. (OR= 1.51, P< 0.01)

Supplementary Table 4.3: Socioeconomic equity as stressor

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Method outcome	Results
Socioeconomic equity					
Krishna Rao, S. ⁵²	Childhood socioeconomic disadvantage	N/A	Oral cancer	Paternal alcohol drinking, smoking, chewing quid and/or tobacco, alcohol, adult socioeconomic measures.	<u>Childhood socioeconomic disadvantage - oropharyngeal cancer: SIGN.</u> When all the three mediators were controlled in a marginal structural model, the risk for developing oral cancer among those in low early life socioeconomic conditions was increased (RR=1.3 95% ci = 1.0, 1.6).
Falkstedt, D. ⁹	Socioeconomic inequity	N/A	Overall cancer	Lack of reliable information, people who could not be assigned a hierarchically defined SES on the basis of occupation (farmers for example).	<u>Socioeconomic inequity - overall cancer: SIGN.</u> Of the SES-related inequalities in total mortality, around 60–70% remained unexplained by IQ and psychosocial functioning as measured in the present study.
Jakovljevic, G. ⁴⁴	Financial issues	N/A	Overall cancer	None	<u>Financial issues - overall cancer: NS.</u> No significant result regarding financial issues was found.
Kondo, N. ⁵⁰	Relative deprivation in income	N/A	Overall cancer	Health behaviors and depressive symptoms. In addition: socioeconomic status including absolute income.	<u>Relative deprivation in income - overall cancer: NS.</u> Among older Japanese men, relative deprivation may be associated with increased risk for mortality from CVD (but not cancer or other causes), independent of absolute income. Nevertheless, relative deprivation was not independently associated with mortality from tobacco-related cancers.

Supplementary Table 4.4: Living conditions and racial discrimination as stressor

Author	Stressor type (=predictor)	Relevant subsets of stress types	Cancer type (= outcome)	Method outcome	Results
Living Condition and Racial Discrimination					
Albert, M. A. ³²	Racial discrimination	N/A	Overall cancer	Age/age and education level/age, education level, body mass index, family history of myocardial infarction at age younger than 50 years, physical activity, smoking status, neighborhood, racial composition, level of urbanization, marital status, occupation, health insurance status, and histories of hypertension, diabetes, and hyperlipidemia.	Overall cancer- racial discrimination: NS. Cancer mortality was not associated with reports of unfair treatment on the job (HR, 1.0; 95% CI, 0.8-1.3), in housing (HR, 1.2; 95% CI, 0.91.5), or by the police (HR, 1.0; 95% CI, 0.7-1.4). Likewise, there was no relationship between cancer death and everyday racism (HR for category 4 relative to category 1, 1.2; 95% CI, 0.8-1.7).
Kantor, E. D. ⁴⁶	Socio-environmental adversities	N/A	Prostate cancer	Race/ethnicity. Time since last doctor visit (≤ 3 months, 3 to ≤ 12 months, > 12 months), family history of PC (0 first-degree relatives, 1 + first-degree relatives, missing), history of digital rectal exam (DRE) screening (never, > 2 years since last screen, ≤ 2 years since last screen), and history of prostate-specific antigen (PSA) screening (never, > 2 years since last screen, ≤ 2 years since last screen).	Prostate cancer-socio-environmental adversity Sign Each one unit increase in socio-environmental adversity composite was associated with significant increase in prostate cancer risk among non-Hispanic white men (HR 1.23; 95% CI 1.02–1.48) and reduced risk among non-Hispanic Black men (HR 0.89; 95% CI 0.82–0.95).
Toleutay, U. ⁶¹	Poor living conditions	N/A	Breast cancer	None	Poor living condition - breast cancer: SIGN. Significant factors that increase the risk of breast cancer in women were unfavorable living conditions increases the risk of breast cancer significantly (OR=22.17 p<0,001).

Abbreviations: n/a: not applicable; SIGN: significant; NS: non-significant; p: probability; OR: odds ratio; CI: confidence interval; PCC: parents of cancer children; PHC: parents of healthy children; FHC: families of healthy children; ACE: adverse childhood experience; HPV: human papillomavirus; HR: hazard ratio; EBV: Epstein–Barr virus; H. pylori: Helicobacter pylori; RR: relative risk; SCC: squamous cell carcinoma; BSS: basal cell carcinoma; CMM: cutaneous malignant melanoma; CRC: colorectal carcinoma; PCa: prostate carcinoma; aOR: adjusted odds ratio; MPBT: malignant primitive brain tumour; IQ: intelligence quotient; CVD: cardiovascular disease; MRR: mortality rate ratio.

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