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Personality and the risk of cancer: A 16-year follow-up study of the GAZEL cohort.

Short title: Personality and the risk of cancer.

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Abstract

Objective: Large-scale prospective studies do not support an association between neuroticism and extroversion with cancer incidence. However, research on other personality constructs is inconclusive. This longitudinal study examined the associations between four personality measures, Type 1 "suppressed emotional expression," Type 5 "rational/anti-emotional," hostility and Type A with cancer incidence.

Methods: Personality measures were available for 13,768 members in the GAZEL cohort study (baseline assessment in 1993). Follow-up for diagnoses of primary cancers was obtained from January 1, 1994 to December 31, 2009. Associations between personality and cancer incidence were evaluated using Cox proportional hazards analyses and adjusted for potential confounders.

Results: During a median follow-up of 16.0 years [range: 9 days-16 years], 1,139 participants received at least one diagnosis of primary cancer. The mean duration between baseline and cancer diagnosis was 9.3 years. Type 1 personality was associated with a decreased risk of breast cancer [hazard ratio (HR) per standard deviation: 0.81, 95% confidence interval (CI) = 0.68-0.97, p=.02]. Type 5 personality was not associated with prostate, breast, colorectal or smoking-related cancers, but was associated with other cancers (HR per standard deviation: 1.17, 95% CI = 1.04-1.31, p=.01). Hostility was associated with an increased risk of smoking-related cancers, which was explained by smoking habits, and Type A was not associated with any of the cancer end-points.

Conclusions: Several personality measures were prospectively associated with the incidence of selected cancers. These links may warrant further epidemiological studies and investigations about potential biobehavioral mechanisms.

Key words

Emotion; Epidemiology; Incidence; Personality; Risk; Cancer.

Acronyms

BMI: Body Mass Index;

CI: Confidence Interval;

EDF-GDF: “Electricité de France-Gaz de France”;

HR: Hazard Ratio;

PSI: Personality Stress Inventory;

SD: Standard Deviation.

Introduction

Personality has long been hypothesized to predispose individuals to cancer initiation or progression. The early observation by Kissen and Eysenck (1) that patients with lung cancer may show high levels of extroversion and low levels of neuroticism led to posit a "cancer-prone" personality. However, well-designed large-scale prospective studies have convincingly dismissed this initial hypothesis (2-6). According to the International Agency for Research on Cancer (7), excluding a risk factor as carcinogenic warrants 1) several methodologically sound studies that 2) are mutually consistent in not showing a positive association. Whereas these two criteria may be considered as fulfilled as regards extroversion and neuroticism (8), most of studies that addressed other personality constructs had serious methodological limitations: a retrospective or cross-sectional design, a focus on cancer mortality rather than cancer incidence, a lack of comprehensive adjustment on confounding variables, a short follow-up period or a relatively small sample size, resulting in insufficient statistical power to analyze specific cancer sites. Overall, these studies have mostly produced negative results or mixed results at best (9-12). The present study took advantage of the large-scale prospective French GAZEL cohort (13) to examine the association between cancer incidence and four measures of personality.

Type 1 personality, characterized by suppressed emotional expression in the context of interpersonal relationships, and Type 5 personality, characterized by rational/anti-emotional tendencies, were proposed by Grossarth-Maticek and Eysenck (14) to account for the early observation of a negative association between neuroticism and cancer (1). These two personality types were claimed to be associated with poor stress coping strategies, resulting in high levels of cortisol and related immune deficiencies (14). Owing to serious methodological and ethical issues, it was suggested that the early reports by these authors, supporting a strong

link with cancer, should be withdrawn from the literature (8, 15, 16), making these personality constructs unfashionable for psychosomatic research. As a consequence, the hypothesis of their association with cancer incidence remains to be properly tested, whereas these early, questionable results still influence the results of recent impactful meta-analyses (16). The primary aim of the present study was to challenge these results focusing on cancer incidence rather than mortality. Type 5 personality was found to predict poor survival among lung cancer patients (17) but some prospective studies failed to find significant associations between other measures of rational/anti-emotional tendencies and cancer incidence (18-21) or mortality (22). However, none specifically examined Type 5 personality and cancer incidence and most well-designed studies considered only breast cancer (19, 21) or were underpowered to properly analyze specific cancer sites (18, 20). Finally, there is evidence linking related constructs such as alexithymia with deficiencies in cell-mediated immunity (23), suggesting possible causal pathways between Type 5 and cancer onset.

Here, we examined the associations between cancer incidence and Type 1 and Type 5 personality measures in the GAZEL cohort study, considering several main sites of cancer separately. In addition, we report exploratory analyses regarding two other personality constructs more widely accepted in psychosomatic research: Type A behavior pattern and hostility. Statistical analyses specifically addressed the potential role of several health behaviors, such as smoking habits, in mediating any association between personality and the risk of cancer (11, 12).

Material and Methods

Participants

Details of the GAZEL cohort study are available elsewhere (13). The target population consisted of 44,992 employees of the French national gas and electricity company "Electricité de France-Gaz de France" (EDF-GDF): 31,411 men aged 40-50 and 13,511 women aged 35-50. The study protocol was approved by the French authority for data confidentiality ("Commission Nationale Informatique et Liberté") and by the Ethics Evaluation Committee of the "Institut National de la Santé et de la Recherche Médicale" (INSERM) (IRB0000388, FWA00005831). In 1989, 20,625 employees (45.8%) (15,011 men and 5,614 women) gave written informed consent to participate in the GAZEL cohort study. Since then, participants were followed by means of an annual mailed questionnaire, as well as through administrative databases. The 1993 questionnaire, which was mailed to the 20,488 alive cohort members, included the Personality-Stress Inventory (PSI), the Buss and Durkee Hostility Inventory (BDHI) and the Bortner Type A Rating Scale (BTARS).

Personality measures

The PSI is a 70-item questionnaire with 'true-false' answers that aims to identify 6 personality types, each claimed to be specifically associated with increased or decreased morbid risks (14). Five of the personality scales are measured by 10 items each (sum of the 'true' responses), and one (Type 4) is measured by 20 items (sum of the 'true' responses, divided by 2). Six personality scores ranging from 0 to 10 are thus calculated. A pilot study in 1991 among a random sample of 408 male GAZEL cohort members examined the 3-month

retest reliability of the French version of the PSI (24). The 6 subscales of the PSI assess the following constructs: Type 1 = dependence on withdrawing objects (i.e. either persons or situations), leading to suppressed emotional expression in the context of interpersonal relationships; Type 2 = dependence on disturbing objects, leading to hostile thoughts and feelings; Type 3 = dependence on objects that are both withdrawing and disturbing, leading to ambivalent behaviors oscillating between the positive and negative aspects of the objects; Type 4 = autonomy and self-regulation; Type 5 = rational/anti-emotional tendencies ; Type 6 = antisocial tendencies. Here, we focused on Type 1 and Type 5 subscales for three main reasons: first, we aimed to limit multiple comparisons as much as possible; second, we nonetheless aimed to challenge previous results linking Type 1 and Type 5 with cancer; third, a principal component analysis suggested that Types 1, 2, 3 and, inversely, Type 4 may indeed relate to the same latent construct, whereas Types 5 and 6 may represent independent constructs (25).

Type 1 personality (Cronbach's α = 0.61 in the GAZEL cohort, 3-month retest r coefficient = 0.65, p<.001), is close to the type C personality proposed by Temoshok (26). It is characterized by a tendency to suppress negative emotions, especially anger, and to be unassertive in order to seek harmony with others (e.g. "I often feel inhibited when it comes to openly showing negative feelings such as hatred, aggression, or anger"). Type 1 correlates positively with emotion-oriented coping strategies, neuroticism and alexithymia, and negatively with extraversion (27).

Type 5 personality (Cronbach's α = 0.57 in the GAZEL cohort, 3-month retest r coefficient = 0.63, p<.001), once referred to as "rational/anti-emotional", shares a tendency to suppress emotion with Type 1 personality but also features non-emotional and rational tendencies such as inhibited emotional reactions and lack of confidence in one's own feelings (e.g. "I can only express feelings when they have a rational basis"). Type 5 correlates

positively with task-oriented coping strategies and alexithymia, and negatively with psychoticism. It does not correlate with neuroticism or extraversion (27).

Hostility was assessed with the French version of Buss and Durkee Hostility Inventory (BDHI) (24, 28). The BDHI is composed of 75 items with 'true-false' answers. It has eight subscales, seven of which are designed to measure different components of hostility: assault, verbal aggression, indirect hostility, irritability, negativism, resentment, and suspicion. The sum of these seven sub-scales leads to a 'total hostility' score with a high 3-month test-retest reliability (r = 0.87, p<.001) (24). In order to limit multiple comparisons, we focused on the total hostility score (Cronbach's α = 0.88 in the GAZEL cohort).

Although the 1991 pilot study (24) considered the Jenkins Activity Survey as index of Type A personality, the 1993 questionnaire included the Bortner Type A Rating Scale (BTARS) (29). It consists of 14 items each comprising two statements with a graded scale between the two statements (24-point scale in the original version, 6-point scale in the version adapted for the GAZEL cohort). Examples of statements include 'never late' versus 'casual about appointments'. Importantly, the BTARS captures time urgency, job involvement, hard driving, need for achievement, ambition and competitiveness, but not hostility. The sum of the 14 items yields a global score ranging from 14 to 84 (Cronbach's α = 0.64 in the GAZEL cohort). This scale was translated and validated for the French population against the Friedman and Rosenman (30) structured interview for assessing Type A, agreement observed 71.5% (31).

Cancer cases

All participants were followed-up for diagnoses of primary cancers from January 1, 1994 to December 31, 2009. Diagnoses of primary cancer came from two sources. Diagnoses

during the period of employment came from a registry kept by the medical departments at EDF-GDF and that has been validated for accuracy and completeness (32). Diagnoses after retirement came from the systematic validation of each self-reported primary cancer through a diagnosis validation survey that began in 2009. Each annual questionnaire asked participants to report whether or not they were hospitalized or diagnosed with several diseases; including cancer. All participants who self-reported a cancer at least once during the follow-up were contacted (if alive) to give consent for a detailed diagnostic investigation with their physician.

In a first set of analyses, we considered as cases all participants with a validated diagnosis as well as participants who reported a diagnosis of primary cancer but who died from a cancer before the onset of the diagnosis validation survey. Living status and the date of death were obtained annually for all participants from EDF-GDF itself as it pays out retirement benefits. Causes of death were available from baseline (i.e. January 1, 1994) to December 31, 2009 and were coded by the French national cause-of-death registry (CépiDc, INSERM) using the ICD 9th and 10th Revision.

We planned to examine the four most frequent types of cancer in France, separately: prostate cancer in men, breast cancer in women, smoking-related cancers (i.e. cancer of the oral cavity and pharynx, esophagus, larynx, trachea, bronchi and lungs, and bladder) and colorectal cancer (33). A fifth category encompassing all other sites was also examined. Non-melanoma skin cancers and *in situ* neoplasms were not considered as cancer cases.

Covariates

Age, sex, and occupation grade (blue-collar workers or clerks, first-line supervisors or sales representatives, management) were obtained from employer's human resources files at baseline. Alcohol consumption, smoking, fruits and vegetables consumption (<1, 1-2, >2

times per week), height, weight, physical activity (at least one time per week, occasionally, none) and perceived health status were self-reported at baseline. Alcohol consumption, as drinks per week, was categorized as non-drinkers, occasional and moderate drinkers (1–27 for men, 1–20 for women) or heavy drinkers (≥28 for men, ≥21 for women). Smoking in the same period was categorized into 5 classes: never-smokers, ex-smokers of fewer than 20 pack-years, current smokers of fewer than 20 pack-years, ex-smokers of more than 20 pack-years and current smokers of more than 20 pack-years. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared and categorized as < 18.5, 18.5–24.9, 25–29.9 or ≥30 kg/m^2. Perceived health status was reported with an 8-point Likert scale ranging from 1 ('very bad') to 8 ('very good').

Statistical analyses

All statistical analyses were computed with PASW 18.0.0 software (SPSS Inc.). Personality scores had a normal distribution. Coefficients of correlation and ANOVAs were computed to examine the relation of personality scores with continuous and discrete covariates, respectively. The association of personality scores and covariates with cancer incidence was estimated with Hazard Ratios (HR) and 95% confidence intervals (CI) computed in Cox regressions. The follow-up ran from January 1, 1994 to the date of cancer diagnosis, death, refusal to receive further questionnaire, or December 31, 2009, whichever occurred first. For participants who reported a diagnosis of cancer after retirement, but who died from a cancer before the onset of the diagnosis validation survey, the estimated date of diagnosis was the date of the first self-report minus 180 days (i.e. the mean interval between two annual questionnaires). Discrete covariates were considered as nominal variables. Each

personality score was considered as a continuous variable as we did not have *a priori* hypotheses to posit a more sophisticated relationship than a linear one.

To test the hypothesis that some personality features might increase the risk of cancer through their influence on health behaviors (e.g. smoking habits), unadjusted analyses and two multivariate models were computed. Model 1 was adjusted for all covariates except for health behaviors, whereas model 2 was further adjusted for health behaviors (i.e. alcohol consumption, smoking, fruits and vegetables consumption and physical activity). Whenever a personality measure was significantly associated with cancer in model 1, the contribution of health behaviors to this association was appreciated by the percentage of change in the HR from model 1 to model 2, calculated with the following formula: $100 \times (HR_{model\ 2} - HR_{model\ 1}) / (HR_{model\ 1} - 1)$.

Model 2a included all the cancer cases for which we had a date of diagnosis (see above). In sensitivity analyses, we also considered two additional models. In model 2b, which aimed at optimizing the diagnosis sensitivity, all the participants who died from a cancer were considered as cases, including those who did not report a diagnosis of cancer during the follow-up. The estimated date of diagnosis was the date of death minus 886 days (i.e. the mean survival time among participants with an ascertained date of diagnosis and who subsequently died from a cancer). In model 2c, which aimed at optimizing the diagnosis specificity, only participants with a validated diagnosis of cancer were considered as cases, excluding participants who reported a cancer during the follow-up but died from a cancer before the diagnosis validation survey.

Results

All personality scores (i.e. Type 1, Type 5, hostility and Type A) were available for 14,522 GAZEL cohort members (70.8%). Compared with non responders, responders were more likely to be male, older, to have a higher occupational grades, to eat fruits and vegetables more than twice a week and to have physical activity at least once a week, and were less likely to be heavy or non drinkers or current smokers and to have extreme BMI (all $p<.05$).

Among the responders, 754 (5.2%) were excluded from this study: 18 died and one asked to receive no further questionnaire before the beginning of the follow-up (i.e. January 1, 1994); 203 had previously had a cancer diagnosis at baseline; 408 self-reported either a cancer or an hospitalization for cancer but these cases were not confirmed owing to the following reasons: lack of written consent to participate in the diagnosis validation survey (N=296 volunteers including 17 who died before the onset of the survey), death of the volunteer (N=7), refusal to respond to the survey when contacted (N=2) or failure to contact the volunteer and his or her physician (N=103); 124 died from a cancer without having reported a diagnosis of cancer or an hospitalization for cancer during the follow-up. These 124 individuals were excluded from subsequent analyses to increase the specificity of cancer diagnoses, except in model 2b, which aimed at optimizing the diagnosis sensitivity (see above). The study population included 13,768 participants whose characteristics are displayed in Table 1.

Associations between personality scores and discrete and continuous variables are displayed in Table 2 and 3, respectively.

During a median follow-up of 16.0 years [range: 9 days-16 years], 1139 (8.3%) participants (881 men, 258 women) received at least one diagnosis of a primary cancer (other

than nonmelanoma skin cancer), including 121 participants (103 men, 18 women) who self-reported a cancer or a hospitalization for cancer during follow-up but died from a cancer before the diagnosis validation survey. Among participants who received at least one diagnosis of a primary cancer, the mean duration of follow-up prior to the first cancer diagnosis was 9.3 years. There were 413 prostate cancer cases among men, 146 breast cancer cases among women, 124 colorectal cancer cases (106 men, 18 women), 137 smoking-related cancer cases (132 men, 5 women), and 352 cases of other cancers (256 men, 96 women). Among this residual category, the most frequent cancers were lymphoid and hematopoietic cancers (N=95), cancers of the urinary organs (N=49), non colorectal digestive cancers (N=45) and melanomas (N=44). Associations between covariates and cancer incidence in multivariate analyses are displayed in Table 4.

Associations between personality scores and cancer incidence are displayed in Table 5. Type 1 personality was not associated with an increased risk of cancer, regardless of cancer site, and was even associated with a decreased risk of breast cancer in women. Type 5 personality score was associated with an increased risk of other cancers. Hostility was associated with an increased risk of smoking-related cancers in model 1, but no longer in model 2a (HR change: -56%). Indeed, this association was no longer significant when further adjusting model 1 with smoking only (HR for one standard deviation: 1.14, 95% CI: 0.96-1.35, p=.13, HR change: -38%). Type A was not associated with the risk of cancer, regardless of cancer site. Including participants who died from a cancer without having reported a cancer during the follow-up (model 2b) or excluding those who reported a cancer during the follow-up but died from a cancer before the diagnosis validation survey (model 2c) yielded similar results. There was no interaction between gender and Type 5 personality as regards its association with other cancers (Wald's statistic = 0.717, degree of freedom = 1, p=.40).

Some post hoc analyses were also performed.

To examine a potential dose-response relationship between Type 1 and the risk of breast cancer, and between Type 5 and the risk of other cancers, we divided these personality scores into quartiles. As regards Type 5 personality, we found that the highest quartile (versus the lowest) was significantly associated with an increased risk of other cancers, with intermediate HR for the second and third quartiles (Table 6). As regards Type 1 personality, we did not find evidence for a clear dose-response relationship, the lowest HR being associated with the third quartile, with intermediate HR for the second and the fourth quartiles (Table 6).

To examine whether Type 1 and Type 5 were associated with biases in reporting diseases, we examined the correlations between the total number of diseases reported by each participant in the 1993 questionnaire and these personality scores. It was positively associated with Type 1 personality (r = 0.129, p<.001) and negatively associated with Type 5 personality (r = -0.055, p<.001), suggesting that Type 1 was not associated with under-reporting diseases and that Type 5 personality was not associated with over-reporting diseases.

To examine the validity and the independence of Type 1 and Type 5 measures, we performed a principal component analysis over the 20 items of the two personality subscales. The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.78 and the Bartlett's test of sphericity was significant (χ^2=28124.742, df=190, p<.001). As expected, the scree test was clearly consistent with a two-factor solution. After varimax rotation, all except two items of the Type 1 subscale were selectively loading on the first factor and all except two items of the Type 5 subscale were selectively loading on the second factor. Computing the two personality scores without these items yielded slightly higher alpha coefficients for both Type 1 (Cronbach's α = 0.63) and Type 5 (Cronbach's α = 0.58). Type 1 was still associated with a decreased risk of breast cancer (HR for one standard deviation: 0.83, 95% CI: 0.69-1.00, p=.047) and Type 5 was still associated with an increased risk of other cancers (HR for one standard deviation: 1.19, 95% CI: 1.06-1.34, p=.004).

Discussion

To our knowledge, this is the first large-scale prospective study to examine the association between the PSI personality types and the incidence of cancer. Adjusting for an extensive set of covariates, we found no evidence for an association between Type 1 personality and an increased risk of cancer, regardless of cancer site. Type 1 personality was indeed associated with a decreased risk of breast cancer. This association remained significant in sensitivity analyses but there was no evidence for a clear dose-response relationship. Type 5 personality, which is characterized by rational/anti-emotional tendencies, was associated with an increased risk of other cancers. Post hoc analyses with a quartile approach suggested a dose-response relationship. Type 5 personality, however, was not associated with the risk of breast, prostate, colorectal or smoking-related cancers. In addition, there was a positive association between hostility and the risk of smoking-related cancers, which was explained by smoking habits. Finally, Type A personality was not associated with the risk of cancer, regardless of cancer site.

Strengths of the present study include its large sample size, the long duration of follow-up (i.e. 15.2 years on average), the wide set of covariates, the study of different cancer sites and the study of cancer incidence rather than mortality. Cancer diagnoses were carefully ascertained and validated and sensitivity analyses yielded similar results. Our data are consistent with known associations for established risk factors such as age, alcohol consumption and smoking, as well as for social and demographic variables and protective factors (33). They are also consistent with the lack of association between rational/anti-emotional tendencies and the incidence of breast cancer (19, 21). In comparison with previous studies that failed to find significant associations between other measures of rational/anti-emotional tendencies and cancer incidence (18, 20), the present study had more statistical

power owing to a five to ten-fold greater number of events. Indeed, one of these studies found a positive association between control of depressive feelings and cancer mortality, with a similar trend for cancer incidence (20).

Several limitations should nevertheless be acknowledged. Although most of the cancer cases were thoroughly ascertained and validated, thus making false positives unlikely, there may have been false negatives for cancer cases that were diagnosed after retirement. Indeed, 124 individuals died from a cancer without having self-reported a diagnosis of cancer or a hospitalization for cancer during the follow-up. Several of them died from a cancer with poor prognosis (e.g. lung cancer) and the lack of self-reported cancer incidence data may be due to the short time period between diagnosis and death. However, including these participants in the analysis yielded similar results. Owing to the possibility of false negatives, our results may partially result from reporting biases. For instance, the tendency to report cancer or to engage in screening procedures could have been lower in Type 1 and higher in Type 5. Theses hypotheses are, however, unlikely. First, the number of self-reported diseases tended to be positively associated with Type 1 and negatively with Type 5. Second, Type 1 and Type 5 were not associated with an increased risk of prostate cancer diagnosis, which may capture both real incidence and excessive screening based on the prostate specific antigen, or with colorectal cancer, for which routine screening is recommended for everyone over 50 years in France (33).

Since our study is observational, our findings should be interpreted with caution. For instance, our results might have been partially confounded by some unmeasured variables, such as genetic factors or early socioeconomic adversity, or mediated by unmeasured health behaviors, such as adherence to medical recommendations or preventive measures. For instance, the inverse association between Type 1 and the risk of breast cancer may have been partially explained by some specific risk factors such as exposure to estrogen, history of full-

term pregnancies or breastfeeding. As regards potential mediators, personality factors have been found to be associated with behavioral risk factors such as smoking status or alcohol consumption. In the present study, the association of hostility with the incidence of smoking-related cancers vanished after adjustment for health behaviors, as did similar trends regarding Type 1 and Type 5. Such findings could be of some relevance for cancer prevention. For instance, smoking cessation programs may benefit from taking into account the potential role of smoking in coping with hostile thoughts and feelings. Given the considerable role of smoking as a risk factor, one may argue that residual confounding due to inadequate adjustment may account for previous findings linking personality with smoking-related cancers (10). It is thus noteworthy that smoking-related cancers were not included in the other sites category, which was significantly associated with Type 5 personality. Likewise, although Type 5 personality appeared to be connected with alcohol consumption, the risk of cancers at other sites was not. However, the measure of some health behaviors, such as diet or physical exercise, may have been too crude to rule out residual confounding.

Our results may also have been confounded by shared biological processes. For instance, immune and inflammatory processes that are involved in cancer onset and progression may also influence psychological processes that are eventually captured by personality measures (34-36). Direct evidence linking personality with cancer risk through immune mechanisms is sparse in humans (37, 38). However, the activity of some brain regions involved in the neural underpinnings of personality, such as the medial prefrontal cortex (39), has been found to mediate the bi-directional relationships between immune and psychological processes among healthy subjects (40, 41). Immune processes may therefore shape both cancer vulnerability and some aspects of personality, potentially accounting for the present results without any causal link between personality and cancer. Since combined analyses across cancer sites may blur associations, site-specific analyses are needed. Further

studies may look for a specific association between Type 5 personality and cancer sites for which immune mechanisms are central, such as those associated with viral infection (e.g. B-cell lymphomas or cervical cancers) (34) or those in which immune therapy have proven efficacy (e.g. malignant melanomas, kidney cancers) (42). Interestingly, most of theses cancers were included into the "other sites" category, suggesting promising research avenues for future studies with a greater number of incident cases of these cancers. Our study was indeed underpowered to further test this hypothesis, as a result of the rather young age of study participants at the end of the follow-up.

Other limitations should be considered. First, although the GAZEL cohort covers all regions of France, various areas ranging from small villages to large cities and a wide range of socioeconomic status and occupations, it is not representative of the general population as it includes only middle-aged working individuals with employment security and excluded certain categories of the population (e.g. agricultural workers, self-employed, foreigners) (13). Furthermore, cancer incidence among the employees of the French national gas and electricity company was found to be lower in those who participated in the GAZEL Cohort Study than in those who did not (43). Although we believe that this selection is unlikely to have systematically biased our results, we cannot formally rule out this hypothesis. Third, Type 1 and Type 5 personality measures had low internal consistency and 3-month retest coefficients and Type A personality measure also had a low internal consistency. Poor measurement of these personality constructs might have contributed to the generally null pattern of results observed. Fourth, owing to the number of statistical tests performed, we cannot rule out a role of chance in our results. This might especially apply to the unexpected association between Type 1 and a reduced risk of breast cancer, as it did not demonstrate a clear dose-response relationship.

Although there is strong evidence to dismiss the relationships between general personality constructs and cancer risk (8), several personality constructs have not been properly tested yet. To our knowledge, our study is the first that examined the association between cancer incidence and the personality types posited to be "cancer-prone" by Grossarth-Maticek and Eysenck (14). Although one might have expected negative results, especially given the serious concerns surrounding the early reports by these authors (15, 16), we found some support for a link between rational/anti-emotional tendencies and the risk of at least some cancers. Should these findings be replicated, further studies would be needed to explore the underlying mechanisms of this association, as potential prevention strategies should address the processes through which psychological processes may be associated with cancer, rather than these processes *per se* (44).

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Table 1. Characteristics of the participants.

	MEN (N=10,136		WOMEN (N=3,632)	
CONTINUOUS VARIABLES	**Mean (SD)**	**Missing: N (%)**	**Mean (SD)**	**Missing: N (%)**
Age (years)	48.5 (2.9)	0 (0.0)	45.7 (4.2)	0 (0.0)
Perceived health status	5.7 (1.3)	0 (0.0)	5.5 (1.3)	1 (0.0)
CATEGORICAL VARIABLES	**N (%)**	**Missing: N (%)**	**N (%)**	**Missing: N (%)**
Occupational grade		5 (0.0)		5 (0.1)
Blue-collar workers, clerks	1092 (10.8)		787 (21.7)	
First-line supervisors, sales representatives	5221 (51.5)		2452 (67.6)	
Management	3818 (37.7)		388 (10.7)	
Alcohol consumption		295 (2.9)		88 (2.4)
Non-drinkers	818 (8.3)		806 (22.7)	
Occasional and moderate drinkers	7472 (75.9)		2596 (73.3)	
Heavy drinkers	1551 (15.8)		142 (4.0)	
Smoking		64 (0.6)		12 (0.3)
Never-smokers	3729 (37.0)		2450 (67.7)	
Ex-smokers < 20 pack-years	2792 (27.7)		527 (14.6)	
Ex-smokers ≥ 20 pack-years	976 (9.7)		362 (10.0)	
Current smokers < 20 pack-years	1399 (13.9)		97 (2.7)	
Current smokers ≥ 20 pack-years	1176 (11.7)		184 (5.1)	
Fruits consumption		516 (5.1)		252 (6.9)
< 1 × / week	733 (7.6)		197 (5.8)	
1-2 × / week	1367 (14.2)		316 (9.3)	
> 2 × / week	7520 (78.2)		2867 (84.8)	
Vegetables consumption		586 (5.8)		269 (7.4)
< 1 × / week	242 (2.5)		56 (1.7)	
1-2 × / week	3400 (35.6)		949 (28.2)	
> 2 × / week	5908 (61.9)		2358 (70.1)	
BMI		38 (0.4)		25 (0.7)
<18.5	30 (0.3)		139 (3.9)	
18.5-24.99	4451 (44.1)		2700 (74.9)	
25-29.99	4895 (48.5)		594 (16.5)	
≥30	722 (7.1)		174 (4.8)	
Physical activity		592 (5.8)		308 (8.5)
≥ 1 × / week	3493 (36.6)		1129 (34.0)	
Occasionally	3234 (33.9)		884 (26.6)	
None	2817 (29.5)		1311 (39.4)	

BMI: Body Mass Index; SD: Standard Deviation.

Table 2. Associations between personality variables and discrete covariates.

	Type 1			Type 5			Hostility			Type A		
	Mean	**SD**	***p***	**Mean**	**SD**	***p***	**Mean**	**SD**	***p***	**Mean**	**SD**	***p***
Gender			<.001			<.001			<.001			<.001
Male	3.7	2.1		6.3	1.9		28.2	10.0		52.8	7.7	
Female	4.0	2.2		5.6	2.1		29.5	9.7		54.4	7.5	
Occupational grade			<.001[a]			<.001[a]			<.001			<.001[a]
Blue-collar workers, clerks	4.1	2.2		6.0	1.9		30.5	10.4		51.8	7.9	
First-line supervisors, sales representatives	3.8	2.1		6.1	2.0		29.1	10.0		52.9	7.7	
Management	3.5	2.1		6.2	2.1		26.7	9.3		54.4	7.3	
Alcohol consumption			.03			.004[a]			<.001			.005
Non-drinkers	3.9	2.1		6.0	2.0		28.4	10.4		53.3	7.9	
Occasional and moderate drinkers	3.7	2.1		6.1	2.0		28.2	9.7		53.3	7.6	
Heavy drinkers	3.8	2.1		6.2	2.0		30.0	10.4		52.6	7.7	
Smoking			<.001			.24			<.001			.04
Never-smokers	3.9	2.2		6.1	2.0		27.5	9.9		53.2	7.6	
Ex-smokers < 20 pack-years	3.6	2.0		6.1	2.0		28.7	9.7		53.3	7.4	
Ex-smokers ≥ 20 pack-years	3.7	2.0		6.1	2.0		29.0	9.8		53.3	7.8	
Current smokers < 20 pack-years	3.7	2.0		6.1	2.1		30.7	9.9		53.6	7.8	
Current smokers ≥ 20 pack-years	3.9	2.1		6.2	2.0		30.2	10.2		52.8	8.1	
Fruits consumption			.02[a]			.32			<.001[a]			.68
< 1 × / week	4.0	2.1		6.1	2.0		29.8	10.2		53.4	8.1	
1-2 × / week	3.8	2.1		6.1	2.0		29.1	10.1		53.1	7.5	
> 2 × / week	3.7	2.1		6.1	2.0		28.2	9.8		53.2	7.6	
Vegetables consumption			.045			.16			<.001			.99
< 1 × / week	4.1	2.2		6.2	2.1		31.2	10.4		53.3	8.5	
1-2 × / week	3.7	2.1		6.2	2.0		28.9	10.0		53.2	7.5	
> 2 × / week	3.8	2.1		6.1	2.0		28.2	9.8		53.2	7.7	
BMI			.001			<.001			<.001			.16
<18.5	4.2	2.5		5.7	2.1		29.1	9.3		53.5	8.0	
18.5-24.99	3.8	2.1		6.1	2.0		28.1	9.9		53.3	7.6	
25-29.99	3.7	2.1		6.2	2.0		28.8	10.0		53.2	7.7	
≥30	3.9	2.1		6.1	2.0		30.0	10.1		52.7	8.0	
Physical activity			<.001			.08[a]			<.001[a]			.12
≥ 1 × / week	3.6	2.1		6.1	2.0		28.0	9.8		53.0	7.5	
Occasionally	3.7	2.1		6.1	2.0		28.4	9.7		53.4	7.5	
None	4.0	2.2		6.2	2.0		29.0	10.3		53.2	8.0	

BMI: Body Mass Index; SD: Standard Deviation.
ANOVAs were computed to examine the relation of personality scores with continuous and discrete covariates.
[a] $p<.05$ for linearity and $p\geq.10$ for deviation from linearity.

Table 3. Pearson's correlation coefficients between personality variables and continuous variables.

	Type 1	Type 5	Hostility	Type A	Age
Type 5	0.194***				
Hostility	0.091***	-0.006			
Type A	-0.137***	-0.071***	0.309***		
Age	0.027**	0.095***	-0.042***	-0.074***	
Perceived health status	-0.145***	0.017*	-0.211***	-0.079***	0.008

* $p<.05$; ** $p<.01$; *** $p<.001$.

Table 4. Associations between cancer incidence and covariates in multivariate analyses (Hazard Ratios and 95% confidence interval).

	Prostate (men) N = 368 / 8,877	**Breast (women)** N = 125 / 3,094	**Colorectal** N = 114 / 11,973	**Smoking-related** N = 113 / 11,968	**Other sites** N = 301 / 11,973
Age	**1.11*** [1.07-1.15]**	**1.05* [1.00-1.09]**	**1.08** [1.02-1.15]**	0.96 [0.90-1.03]	**1.04* [1.00-1.07]**
Gender					
Male	-	-	1.00	1.00	1.00
Female	-	-	0.62 [0.35-1.11]	**0.11*** [0.04-0.32]**	1.21 [0.89-1.65]
Occupational grade					
Blue-collar workers, clerks	1.00	1.00	1.00	1.00	1.00
First-line supervisors, sales representatives	**1.56† [0.98-2.49]**	0.97 [0.62-1.52]	1.14 [0.60-2.17]	**0.59* [0.36-0.96]**	0.99 [0.69-1.43]
Management	**2.17** [1.36-3.45]**	1.20 [0.64-2.25]	1.17 [0.59-2.31]	**0.40** [0.23-0.71]**	1.35 [0.91-2.00]
Alcohol consumption					
Non-drinkers	1.00	1.00	1.00	1.00	1.00
Occasional and moderate drinkers	1.19 [0.78-1.80]	1.19 [0.75-1.89]	1.54 [0.74-3.19]	0.99 [0.52-1.88]	0.99 [0.69-1.42]
Heavy drinkers	1.34 [0.83-2.16]	**2.39* [1.11-5.16]**	1.38 [0.57-3.33]	1.07 [0.52-2.18]	1.05 [0.65-1.68]
Smoking					
Never-smokers	1.00	1.00	1.00	1.00	1.00
Ex-smokers < 20 pack-years	1.19 [0.93-1.51]	0.97 [0.57-1.64]	0.86 [0.54-1.37]	1.79 [0.88-3.66]	0.84 [0.62-1.14]
Ex-smokers ≥ 20 pack-years	0.99 [0.68-1.44]	1.09 [0.61-1.97]	0.70 [0.33-1.47]	**2.31† [0.97-5.52]**	1.14 [0.78-1.67]
Current smokers < 20 pack-years	0.74 [0.52-1.06]	0.84 [0.26-2.67]	1.14 [0.65-2.00]	**4.41*** [2.19-8.89]**	1.00 [0.68-1.48]
Current smokers ≥ 20 pack-years	**0.60* [0.39-0.93]**	0.74 [0.30-1.87]	0.65 [0.30-1.40]	**12.33*** [6.70-22.67]**	0.93 [0.61-1.42]
Fruits consumption					
< 1 × / week	1.00	1.00	1.00	1.00	1.00
1-2 × / week	1.18 [0.73-1.90]	0.98 [0.35-2.70]	1.14 [0.50-2.60]	**0.44* [0.23-0.87]**	1.13 [0.66-1.94]
> 2 × / week	1.01 [0.66-1.54]	1.29 [0.56-2.97]	0.93 [0.45-1.91]	**0.62† [0.38-1.03]**	1.01 [0.63-1.62]
Vegetables consumption					
< 1 × / week	1.00	1.00	1.00	1.00	1.00
1-2 × / week	0.72 [0.39-1.30]	2.52 [0.35-18.44]	**0.29** [0.13-0.64]**	1.45 [0.45-4.70]	1.14 [0.50-2.62]
> 2 × / week	0.69 [0.38-1.25]	2.05 [0.28-14.80]	**0.32** [0.15-0.69]**	1.22 [0.38-3.96]	1.15 [0.51-2.62]
BMI					
<18.5	0.90 [0.12-6.43]	1.00 [0.37-2.75]	2.42 [0.58-10.15]	2.76 [0.64-11.78]	0.85 [0.27-2.70]
18.5-24.99	1.00	1.00	1.00	1.00	1.00
25-29.99	0.91 [0.74-1.13]	1.01 [0.63-1.60]	1.08 [0.73-1.60]	0.87 [0.59-1.28]	0.96 [0.75-1.23]
≥30	1.01 [0.66-1.55]	0.32 [0.08-1.32]	0.52 [0.19-1.46]	**0.26* [0.08-0.84]**	1.00 [0.61-1.62]
Physical activity					
≥ 1 × / week	**0.76* [0.59-0.99]**	0.92 [0.60-1.39]	0.89 [0.56-1.41]	**0.58* [0.34-0.99]**	1.09 [0.82-1.46]

Occasionally	0.97 [0.76-1.25]	0.82 [0.52-1.29]	0.96 [0.60-1.52]	1.00 [0.66-1.52]	1.15 [0.86-1.53]
None	1.00	1.00	1.00	1.00	1.00
Perceived health status	1.02 [0.94-1.11]	0.98 [0.86-1.13]	1.07 [0.92-1.24]	0.94 [0.82-1.08]	**0.89** [0.81-0.97]**

BMI: Body Mass Index; N: number of events / number of participants at risk.
Hazard ratios and 95% confidence interval were computed through Cox regressions.
† $p<.10$; * $p<.05$; ** $p<.01$; *** $p<.001$.

Table 5. Associations between cancer incidence and personality variables (Hazard ratio per standard deviation and 95% confidence interval).

	All sites	Prostate (men)	Breast (women)	Colorectal	Smoking-related	Other sites
Unadjusted	N = 1,139 / 13,767	N = 413 / 10,134	N = 146 / 3,631	N = 124 / 13,767	N = 137 / 13,759	N = 352 / 13,767
Type 1	1.01 [0.96-1.07]	1.01 [0.92-1.12]	0.86 [0.74-1.01]	0.94 [0.78-1.12]	1.17 [0.99-1.37]	1.01 [0.91-1.12]
Type 5	**1.08** [1.02-1.15]**	1.01 [0.92-1.12]	1.01 [0.86-1.18]	1.07 [0.90-1.28]	**1.21* [1.02-1.44]**	**1.15** [1.04-1.28]**
Hostility	1.05 [0.99-1.11]	1.05 [0.96-1.16]	0.91 [0.77-1.08]	0.88 [0.74-1.06]	**1.29** [1.09-1.52]**	1.07 [0.97-1.19]
Type A	1.00 [0.94-1.06]	1.03 [0.94-1.14]	1.01 [0.85-1.19]	0.91 [0.77-1.09]	0.85 [0.72-1.00]	1.09 [0.98-1.21]
Model 1	N = 1,133 / 13,694	N = 412 / 10,091	N = 145 / 3,601	N = 124 / 13,694	N = 136 / 13,687	N = 348 / 13,694
Type 1	1.00 [0.94-1.06]	1.03 [0.93-1.13]	**0.84* [0.71-0.99]**	0.95 [0.79-1.14]	1.15 [0.97-1.36]	0.98 [0.88-1.09]
Type 5	**1.06* [1.00-1.13]**	1.00 [0.91-1.11]	0.98 [0.84-1.15]	1.02 [0.85-1.22]	1.13 [0.95-1.35]	**1.16** [1.04-1.29]**
Hostility	1.06 [0.99-1.12]	1.09 [0.98-1.20]	0.92 [0.77-1.09]	0.91 [0.76-1.09]	**1.23* [1.04-1.45]**	1.06 [0.95-1.18]
Type A	1.00 [0.95-1.07]	1.01 [0.92-1.12]	1.03 [0.87-1.21]	0.95 [0.79-1.13]	0.92 [0.78-1.09]	1.07 [0.96-1.20]
Model 2a	N = 995 / 11,973	N = 368 / 8,877	N = 125 / 3,094	N = 114 / 11,973	N = 113 / 11,968	N = 301 / 11,973
Type 1	0.97 [0.91-1.04]	1.01 [0.91-1.12]	**0.81* [0.68-0.97]**	0.90 [0.74-1.09]	1.07 [0.88-1.29]	0.96 [0.86-1.08]
Type 5	1.06 [0.99-1.13]	1.02 [0.92-1.13]	0.96 [0.81-1.14]	1.05 [0.87-1.26]	1.04 [0.86-1.26]	**1.17** [1.04-1.31]**
Hostility	1.03 [0.96-1.10]	1.08 [0.97-1.20]	0.90 [0.75-1.09]	0.89 [0.73-1.08]	1.10 [0.91-1.33]	1.06 [0.94-1.19]
Type A	1.01 [0.95-1.08]	1.02 [0.92-1.13]	1.07 [0.89-1.28]	0.92 [0.76-1.11]	0.95 [0.79-1.14]	1.08 [0.96-1.21]
Model 2b	N = 1,055 / 12,033	N = 369 / 8,923	N = 127 / 3,108	N = 118 / 12,033	N = 133 / 12,028	N = 334 / 12,033
Type 1	0.96 [0.90-1.02]	1.01 [0.91-1.12]	**0.80* [0.67-0.96]**	0.90 [0.75-1.09]	0.99 [0.83-1.18]	0.95 [0.85-1.06]
Type 5	1.05 [0.98-1.11]	1.02 [0.92-1.13]	0.96 [0.81-1.13]	1.07 [0.89-1.29]	1.01 [0.85-1.20]	**1.12* [1.01-1.26]**
Hostility	1.04 [0.97-1.10]	1.08 [0.97-1.20]	0.89 [0.74-1.08]	0.90 [0.74-1.09]	1.11 [0.94-1.32]	1.08 [0.96-1.20]
Type A	1.01 [0.95-1.08]	1.02 [0.92-1.14]	1.06 [0.88-1.27]	0.92 [0.76-1.11]	1.00 [0.85-1.18]	1.06 [0.95-1.19]
Model 2c	N = 887 / 11,865	N = 360 / 8,785	N = 122 / 3,078	N = 95 / 11,865	N = 79 / 11,860	N = 258 / 11,865
Type 1	0.97 [0.91-1.04]	1.01 [0.91-1.12]	**0.81* [0.67-0.97]**	0.91 [0.74-1.12]	1.13 [0.90-1.41]	0.93 [0.82-1.05]
Type 5	1.06 [0.99-1.13]	1.02 [0.91-1.13]	0.97 [0.81-1.15]	1.11 [0.90-1.37]	1.00 [0.80-1.25]	**1.18* [1.04-1.33]**
Hostility	1.05 [0.98-1.12]	1.08 [0.97-1.21]	0.88 [0.73-1.07]	0.89 [0.72-1.10]	1.15 [0.92-1.44]	1.11 [0.98-1.26]
Type A	1.01 [0.95-1.08]	1.02 [0.92-1.14]	1.05 [0.87-1.27]	0.91 [0.74-1.11]	0.96 [0.77-1.20]	1.08 [0.95-1.22]

N: number of events / number of participants at risk.

Hazard ratios and 95% confidence interval were computed through Cox regressions.

* $p<.05$; ** $p<.01$.

Model 1 was adjusted for age, gender, occupational grade, BMI and perceived health status.

Model 2a = model 1 further adjusted for health behaviors (i.e. alcohol consumption, smoking, fruits and vegetables consumption and sport).

Model 2b = model 2a including participants who died from a cancer without having reported a cancer during the follow-up.

Model 2c = model 2a excluding participants who reported a cancer during the follow-up but died from a cancer before the diagnosis validation survey.

Table 6. Associations between Type 1 quartiles and breast cancers and between Type 5 quartiles and other cancers (Hazard Ratios and 95% confidence interval).

	Type 1 and breast cancers (women)		**Type 5 and other cancers**	
	Model 1	**Model 2a**	**Model 1**	**Model 2a**
	N = 145 / 3,601	**N = 125 / 3,094**	**N = 348 / 13,694**	**N = 301 / 11,973**
Quartile 2 vs. 1	0.68 [0.43-1.09]	0.63 [0.38-1.04]	1.20 [0.83-1.74]	1.22 [0.82-1.81]
Quartile 3 vs. 1	**0.48** [0.29-0.80]**	**0.42** [0.24-0.73]**	1.28 [0.93-1.75]	1.25 [0.89-1.75]
Quartile 4 vs. 1	0.64 [0.38-1.06]	**0.56* [0.33-0.97]**	**1.53** [1.11-2.12]**	**1.51* [1.07-2.14]**

N: number of events / number of participants at risk.
Hazard ratios and 95% confidence interval were computed through Cox regressions.
* $p<.05$; ** $p<.01$.
Model 1 was adjusted for age, gender, occupational grade, BMI and perceived health status.
Model 2a = model 1 further adjusted for health behaviors (i.e. alcohol consumption, smoking, fruits and vegetables consumption and sport).