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**Study of mutual influence between trait anxiety and risk of depression among older couples facing cancer**

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## **Abstract**

**Introduction:** The present study aims to examine the process of mutual influence in older couples with cancer diagnosis by studying their risk of depression.

**Materials and Methods:** 282 couples with one spouse diagnosed with cancer were selected from the Three-City cohort study. Dyadic analyses were used to determine whether trait anxiety affects the risk of depression and whether a mutual influence process occurs prior and post cancer diagnosis. Cross-sectional analyses were performed at two time-points: before and after receiving the diagnosis.

**Results:** A higher level of anxiety among cancer patients resulted in a decreased risk of depression among spousal caregivers. Moreover, a higher anxiety among spousal caregivers increased their own risk of depression, but it didn't influence depression risk among cancer patients. While there is an intra-individual relationship between a higher level of trait anxiety and a greater risk of depression prior to cancer diagnosis, there is no cross-influence between spouses.

**Discussion:** The study findings indicate that a dyadic psychological adjustment process might help older adults to cope with cancer by limiting the risk of depression among spousal caregivers.

## **Keywords**

Adjustment; anxiety; cancer; depression; older couples; mutual influence; oncology

## **1. Introduction**

Depression among patients with cancer is a major concern, as patients with cancer of all ages show a prevalence of depression at around 25% (1), at least twice as high as the corresponding number in the general population (2). Research on older patients with cancer is scarce (3), and the results are less clear. A decrease in the prevalence depression in older adults with cancer is reported (4). However, this decreased rate seems to be partly due to underestimation linked to diagnostic difficulties (5), and depression remains a major concern as it is the most common psychopathological comorbidity among older adults with cancer (6). In addition, depression and anxiety appear to be related among older people with cancer (8, 9). In a study of 500 patients aged 65 and over, Wiesel et al. reported prevalence rates of 20.9% for anxiety symptomatology and 12.6% for depression (9). In older adults, anxiety and depression are two distinct psychological disorders often considered on the same continuum as the level of anxiety could be a prodromal stage of depression or a vulnerability to depression (10). Trait anxiety defined as “a person’s disposition to respond with anxiety when faced with situations perceived as threatening” (11) is an independent predictor of incident and recurrent depressive symptomatology in older adults. While some studies found similar results on younger patients with breast cancer (12,13), to the best of our knowledge, no studies have been done on older cancer persons. Yet, when studying the risk of depression in older adults with cancer it is critical to consider trait anxiety as well, beyond other known sociodemographic and clinical factors associated with depression(14,15).

Detecting and treating depression is crucial as depression has harmful consequences for the patient including increased mortality risk (16), increase in the number of hospital days (17) and lower effectiveness of the treatment (14). Managing depression is also important from a dyadic point of view since the level of depression of patients not only impacts their well-being and their chances of recovery but also their spouse's psychological well-being. There is indeed

a strong relational closeness between spouses, especially important as patients get older, as advanced age increases in the importance of intimate relationships (18). The influence of close family (e.g., spouses) is important when evaluating mental health among older people (19,20). Emotional proximity among the spouses influences their mental health by facilitating the processes of mutual influence, especially with regard to fluctuations of positive and negative emotions during the time spent together (21–24). Mutual influence is understood here as a multi-determined process underpinned by the psychological interdependence inherent in the relational proximity between spouses (25). Emotional and psychological contagion processes predict the emotional distress and risk of depression in couples facing cancer (26–30). In addition, some studies suggest that being single and having low levels of social support significantly increase the risk of depression among older patients with cancer, while being married seems to have an opposite effect (31). To date, the underlying process of such a protective effect is poorly understood as the processes of mutual influence is rarely studied in older couples facing cancer.

Hagedoorn et al. suggest that couples react to the disease as a dyadic emotional system. Moreover, it seems that the distress is lower when the patient has a partner. One explanation could be that the marital relationship, through dyadic rather than individual emotional mechanism, acts as a protective factor (26). Spousal caregivers tend to have lower levels of anxiety, depression and higher levels of hope than patients with cancer (32). In other words, the spousal caregiver can provide significant support to the patient. To better understand this protective effect of the couple, the present study focuses on the process of mutual influence. Based on a sample of 282 couples from the Three-City (3C) cohort, this study aims firstly to determine whether the level of trait anxiety predicts the risk of depression in older spouses facing cancer. It is hypothesized that their higher level of trait anxiety will increase their risk of depression. The second goal is to examine spousal caregivers' response

to the psychological vulnerability of the cancer patient. It is hypothesized that a high level of trait anxiety among patients with cancer will decrease the risk of depression among spousal caregivers. Finally, it is hypothesized that the association between the spousal caregiver's depression risk and the spouse's anxiety level depend on the timing of the cancer diagnosis. Specifically, prior to cancer diagnosis the link between the spouse's anxiety level and their partner's risk of depression is minimal. To assess this hypothesis, we will study the process of mutual influence between the spouses during pre and post-cancer diagnosis stages.

## **2. Material and Methods**

### *2.1. Study population*

The present study relies on a subset sample from the 3C study which is a multicenter epidemiological cohort study aiming to assess the relationship between vascular diseases, dementia and cognitive impairment among people aged 65 and over, initially living at home. The study sample consisted in 9,294 people among which 1,817 couples. The participants were randomly selected from the voters' register of three French cities: Bordeaux, Montpellier and Dijon. The initial evaluation was conducted between 1999 and 2001 and is repeated approximately every two years. Trained nurses and psychologists collected a wide range of data including socio-demographics, educational level, cognitive assessment, psychological health, food habits, alcohol and tobacco consumption, lifestyle, family history of cardiovascular diseases, exhaustive medical history, medication use, disabilities, clinical measurements (blood pressure, height, weight...) and biological parameters, using a standardized questionnaire common to the three cities.

The ethics committee of the University Hospital of Kremlin-Bicêtre approved the 3C Study. For a detailed report of the 3C Study data collection methodology, refer to (33).

### *2.2. Sample*

Among the 1,817 couples included in the 3C cohort Study, 282 spousal dyads were selected according to the following inclusion criteria: couples living together, legally married or partners, and one of the spouses diagnosed with cancer within two years prior to the cohort follow-up. All the follow-up visits were considered in the present study. The exclusion criteria were: one of the spouses diagnosed with dementia during the same follow-up the cancer diagnosis was reported and couples diagnosed with cancer at the same follow-up as the presence of dementia in one partner or cancer in both partners could significantly alter the process of mutual influence between the spouses ; widowed couples and couples with missing data on anxiety or depression,. Our final sample included 282 couples (see flowchart, Figure1).

### **Insert Figure 1**

#### *2.3. Assessment*

*Outcome:* In order to consider the presence of a risk of depressive state related to cancer, we constructed a single outcome by taking into account both current depressive symptomatology and the use of antidepressants. Participants were considered to have depression when their CESD score was elevated and/or when antidepressant treatment was prescribed. The binary score was coded with 0 = absence of depressive symptomatology and no antidepressant treatment; 1 = presence of depressive symptomatology or antidepressant treatment.

The 20-item Center for Epidemiologic Studies Depression Scale (34) was used to assess the frequency of depressive symptoms on a four-point scale (0=rarely or never; 1=occasionally; 2=often; 3=most or always). The overall score (0 to 60) was dichotomized on the basis of cut-off points fixed at 17 for men and 23 for women, as previously validated in older population (35), with 1=high depressive symptomatology and 0=low depressive symptomatology.

The use of antidepressants was reported, as were all other treatments used by the patient at the time of the follow-up.

*Predictor:* Trait anxiety was evaluated during the initial visit with the 20-item Spielberger State-Trait Anxiety Inventory (STAI; 32), the scores ranging from 20 to 80, higher scores indicating higher anxiety. Couples in which one spouse had more than 2 missing items were excluded. When there was less than 3 missing items, we divided the total score by the number of items to which participants responded to obtain a score ranging from one to four, then we multiplied it by 20 as recommended by Spielberger.

*Covariates.* The covariates were selected from the literature based on their impact on the risk of depression in older patients with cancer. These variables were collected from both patients and their spousal caregivers.

- Sociodemographic variables included age, sex, and educational level classified in three categories (0=primary school education evidenced by a diploma, 1=short or long secondary education validated by a diploma, 2=higher educational level).

- To assess the specific impact of the cancer diagnosis on the risk of depression, depressive symptomatology and use of antidepressants were controlled at the prior follow-up visit to which the cancer diagnosis was reported. To take into account the effect of pre-existing mental health concerns beyond depression, use of anxiolytics and antipsychotic drugs at the prior follow-up visit to which the cancer diagnosis was reported were also controlled.

- To consider the effect of general health status beyond cancer, other health conditions were included. These conditions, considered as binary variables, included myocardial infarction, angina, stroke, dyspnea, heart failure, diabetes, and disability. The binary scores were coded with 0 = no medical history; 1 = medical history.

- To consider the effect of being a couple, we identify the 2 members of the same couple by using the couple's ID number, which is identical for each of the two partners.

#### *2.4. Statistical analysis*



In order to take into account the process of mutual influence between spouses the statistical methodology is based on Actor Partner Interdependence Model, APIM (36) which permits to distinguish: 1. the effect of each spouse's trait anxiety level on his/her own risk of depression (actor effect); 2: the effect of each spouse's trait anxiety level on each partner's risk of depression (partner effect) (for APIM design, see Figure2). In this study, the distinguishing variable is the fact of being the participant with cancer or the spousal caregiver.

### **Insert Figure 2**

The statistical methodology relied on several steps. In a first step, the descriptive analyses were conducted at the follow-up at which the cancer diagnosis was reported (see APIM design, Figure 2). Means and standard deviations were reported for continuous variables. Frequencies and percentages were reported for categorical variables. Differences between spouses were assessed using Student tests for continuous variables and Chi2 tests or Fisher's exact test for categorical variables. Categorical variables before and after cancer diagnosis were compared using Chi2 McNemar tests.

In a second step, the initial data set was reorganized to allow for dyadic mixed model analyses, with the couple as the unit of analysis. To do so, we referred to the APIM methodology (36). We performed two different models over two-time windows (at pre and post cancer diagnosis).

In both Model 1 and Model 2 the level of trait anxiety, considered as a global and stable measure of anxiety, was collected at the baseline of the study as were the socio-demographic variables.

Model 1 was performed on data collected at the follow-up at which the cancer diagnosis was reported. Mixed variables include the trait anxiety score as fixed effect predictor, and comorbidities (myocardial infarction, angina, stroke, dyspnea, heart failure,

diabetes, and disability) as fixed effect covariables. Individual intercept and couple I.D. were included as a random effect. Depressive symptomatology, use of antidepressants, use of anxiolytics and antipsychotic drugs were controlled at the prior follow-up visit to which the cancer diagnosis was reported.

Model 2 was performed on data collected at least two years prior to cancer diagnosis. Such a time window was used in order to study the process of mutual influence between spouses before the couple was faced with a cancer diagnosis or its first signs. Mixed variables include trait anxiety score as fixed effect predictor, and comorbidities as fixed effect covariate. Individual intercept and couple I.D. were included as random effects.

In a third step, in order to determine the most relevant adjustment variables for each model, we performed univariate logistical mixed regressions models of both own and partner health-related variables on own risk of depression. We kept all adjustment variables with  $p \leq .15$ .

Model 1 and model 2 were adjusted on socio-demographic variables (age, gender, education) as well as on retained health-related variables after a backward stepwise strategy. This backward stepwise strategy consisted in dropping the variable with the highest p-value (higher than 5%) out of the model to check the relative variation of the regression parameters (for anxiety, cancer and interactions). When the variation was smaller than 10%, we considered that the variable was not a confounding factor and we dropped it out of the model. We performed this backward stepwise strategy for each variable with p-value higher than 5%, until the model contains only variables with p-value under 5% as well as the variables that were confounding factors.

In a fourth step, we performed APIM analysis using two interactions between the distinguishing variable (cancer) and the predictors (actor and partner trait anxiety) to distinguish actor and partner effects.

Taking together the results of the two models will highlight the change in the process of mutual influence between spouses before and after facing a cancer diagnosis.

Analyses were performed using the Statistical Analysis System (SAS), software version 9.3 (SAS Institute, Inc., Cary, NC, USA) and R version 3.2.3.

### **3. Results**

#### *3.1. Sample characteristics*

The descriptive statistics for all study variables are presented in Table 1. Among the 282 participants with cancer, the level of depressive symptomatology does not differ before and after cancer diagnosis ( $p=.162$ ) but the use of antidepressants is significantly higher after the diagnosis ( $p=.020$ ). If we consider the combined score of high depressive symptomatology and use of antidepressants, it is not significantly higher after the diagnosis than before ( $p=.068$ ).

Among the 282 spouses of participants with cancer, neither the level of depression ( $p=.336$ ) nor the use of antidepressants ( $p=.083$ ) or the combined score ( $p=.095$ ) significantly differ before and after cancer diagnosis.

#### **Insert Table 1**

#### *3.2. Dyadic analysis*

Figure 3. presents the results of the dyadic mixed effects analysis in Model 1 and Figure 4. presents the results of the dyadic mixed effects analysis in Model 2 (for confidence intervals, see Table 2 in supplemental online materials).

#### **Insert Figure 3 and Figure 4**

This study first aimed to address the effect of the trait anxiety level of participants with cancer and spousal caregivers on their own risk of depression (actor effect). Regarding model 1, after the cancer diagnosis, the spousal caregiver's level of trait anxiety is positively associated with his/her own risk of depression (OR=1.09;  $p < .001$ ). There is no association between cancer participant's level of trait anxiety and his/her own risk of depression. Regarding model 2, at least two years prior to cancer diagnosis, the future cancer participant's level of trait anxiety is positively associated with his/her own risk of depression (OR=1.09;  $p = .004$ ). His/her spouse's level of trait anxiety is positively associated with his/her own risk of depression (OR=1.12;  $p < .001$ ).

This study secondly aimed to address the mutual effect of each spouse's trait anxiety level on his/her partner's risk of depression at the post cancer diagnosis stage (partner effect). Regarding model 1, after the cancer diagnosis, the cancer patient's level of trait anxiety is negatively associated with his/her spousal caregiver's risk of depression (OR=0.94;  $p = 0.034$ ) while there is no association between spouses' level of trait anxiety and cancer participant's risk of depression.

Regarding model 2, at least two years prior to cancer diagnosis, there is no partner effect.

#### **4. Discussion**

The purpose of this study was to examine the process of mutual influence in older couples facing a cancer diagnosis. We examined 1) the effect of the trait anxiety level of participants with cancer and spousal caregivers on their own risk of depression (actor effect) and, 2) the mutual effect of each spouse's trait anxiety level on his/her partner's risk of depression after a cancer diagnosis (partner effect). Accordingly, the impact of trait anxiety on the risk of depression was considered both at the individual level and between spouses, at two points of time (prior and during cancer diagnosis).

At the individual level (actor effect), the level of trait anxiety predicts the risk of depression prior to cancer diagnosis for both spouses. This finding is consistent with previous studies (10). The same holds true for spousal caregivers during the post-diagnosis stage. The absence of a link between anxiety and the risk of depression in older adults recently diagnosed with cancer could be explained by the fact that the risk of depression is mainly driven by cancer itself. Another possible explanation is that older adults with cancer perceive their marital relationship as reassuring support, thus limiting the negative impact of anxiety, while spousal caregivers perceive less marital support and rely on their own resources to face the situation (26). This account should be tested in a future study by comparing the relationship between trait anxiety and the risk of depression across married and unmarried patients. It would also be worthwhile to assess whether this relationship is partly mediated by the quality of care and support provided by the spouse. Moreover, patients who perceive that the spousal support is maladaptive or lacking are more likely to have a poor psychological adjustment to the disease (37). Therefore, as suggested by Berg & Upchurch (2007) the dyadic functioning between spouses might drive their adaptation to the disease (38).

At the dyadic level (partner effect), while there is no mutual influence between spouses prior to cancer diagnosis, our findings show that when the participant with cancer has a high level of trait anxiety, the spousal caregiver is less likely to be depressed. This finding is consistent with our hypothesis predicting the spousal caregiver's response to the psychological vulnerability of the participant with cancer. Older adults with cancer experiencing anxiety are likely to require the most emotional support from their partners, and to benefit from such support (39). The notion of spousal involvement facing cancer is important. The cancer patient expects the caregiver to take an active role in discussions, problem solving, and solution seeking, all of which are related to psychological adjustment (38,39). This type of engagement requires substantial availability of the spousal caregiver.

Therefore, in a process of dyadic influence, spousal caregivers tend to take it upon themselves. By limiting the impact of cancer on their own risk of depression, they could improve their ability to effectively support the patient. Furthermore, the absence of a partner effect between spousal caregiver and participant with cancer before and after the cancer diagnosis supports the hypothesis of the dyadic adjustment process. In other words, the mutual influence is not a passive process of emotional contagion from one spouse to the other, but an active process of adaptation of the spouse helping to meet the psychological needs of his or her partner with cancer.

Prior research shows that an active investment in discussion and collaboration with the cancer patient can lead to emotional contagion with a potential transmission of daily negative emotions (40–42). Thus, it would be worthwhile to examine the mental health of spousal caregivers and to study the process of emotional contagion in daily life. It is also important to examine whether the relationship between the cancer patient's anxiety and the caregiver's risk of depression persists over time. Such a relationship might be limited to a time close to the diagnosis. There might be a rebound effect with a subsequent risk of depression over longer periods of time following the diagnosis. The risk of depression in spousal caregivers should also be studied after remission and recovery, as the need for supportive behaviors is lessened. A dyadic study of the risk of depression over time based on the trait anxiety levels of the two parties is warranted. However, this would require the use of repeated measures over time, particularly after the cancer diagnosis. Unfortunately, due to attrition related to the number of deaths and the lack of participant's follow-up, we do not have the necessary data to conduct such analyses.

#### *4.1. Study limitations*

This study has several limitations. First of all, the exact date of diagnosis for all participants is not available. Only information about whether the cancer diagnosis occurred since the last

follow-up visit was available. Therefore, participants may not be at the same post-diagnosis period (diagnosis, treatment or end of treatment) which could influence their interactions and with spouses. Another potential limitation is the lack of information on cancer stage. It has been shown that the stage of the disease can influence the spouse's psychological state (43). However, we did control for the level of disability. In addition, in order to observe different dyadic relationships between trait anxiety and the risk of depression in the context of cancer and without major health events, we used data collected after the diagnosis and prior to the diagnosis. In this way, we were able to ascertain whether there was a difference in the relationship between anxiety and the risk of depression before and after the onset of the disease.

Finally, since the analyses were done on data from a cohort study, the study was not designed specifically to examine psychological distress in patients with cancer and their spouses. As a result, we did not have access to information that would have allowed us to better explain how this relationship might constitute a dyadic adjustment process to the disease. An assessment of dyadic coping or marital adjustment would have been of great value for this. Beyond these limitations, the appropriate tools were used to assess depression in older adults with cancer (39).

#### *4.2. Clinical implications*

As pointed out by Hagedoorn et al. (26) this study supports the view that couples react to the disease as a dyadic emotional system. Thus, the questions of the risk of depression in older adults with cancer needs to consider the patient's marital support. In a similar vein, the risk of depression in spousal caregivers can only be understood in the context of their interactions with the patient. From a clinical point of view, clinicians should first assess more systematically the tendency to anxiety of older adults with cancer, their risk of depression and their spouse's risk of depression. As our findings indicate that the spouse can be an important

source of support for anxious patients with cancer, it is necessary to take into account the spousal relationship. To the best of our knowledge, there are no studies on psychological interventions for older couples facing cancer. However, prior research suggests that interventions to support communication between the spouses have a positive impact on the couple's psychological balance and mutual influence processes (45). Thus, rather than considering the patient as an isolated unit, systematic interventions involving spouses and relying on dyadic psychological resources should be encouraged.

In conclusion, this study encourages both researchers and clinicians to consider the mental health of older spouses facing cancer through a dyadic approach, and to account not only for the experiences of each of the spouses, but also for the interdependence that exists between them.

### **Conflicts of interest**

None declared

### **Author Contributions**

Study Conception: SCR; VB

Study Design: SCR; VB; SG

Data Acquisition: CH

Analysis and Interpretation of Data: SG; SCR; VB

Manuscript Writing: SCR; VB; HA

Approval of Final Article: SCR; VB; HA; SG; CH

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## **Figures captions**

### **Figure 1. Title**

#### **Figure 1**

Flowchart summarizing the selection process for the 282 couples included in this study.

### **Figure 2. Title**

#### **Figure 2**

Actor Partner Interdependence Model design

#### **Figure 2. Captions**

U: residual portion of cancer patient's depression

U': residual portion for the spousal caregiver's depression

Single-headed arrows: causal/predictive paths

Double-headed arrows: correlated variables

Paths "a": actor effects

Paths "p": partner effects

### **Figure 3. Title**

#### **Figure 3.**

Dyadic effect of trait anxiety on risk of depression after a cancer diagnosis in one of the spouses, 3C Study

#### **Figure 3. Captions**

\* $p < .05$ ; \*\* $p < .01$  (for CI95% see table 2 in supplemental materials)

Adjusted on age, education, sex, before the cancer diagnosis: P's high depressive symptomatology, both P and SC's use of antidepressants, P's use of anxiolytics, SC's use of antipsychotics, and after the cancer diagnosis: dyspnea, stroke, both P and SC's disability

**Figure 4. Title**

**Figure 4.**

Dyadic effect of trait anxiety on risk of depression before a cancer diagnosis in one of the spouses, 3C Study

**Figure 4. Captions**

\* $p < .05$ ; \*\* $p < .01$  (for CI95% see table 2 in supplemental materials)

Adjusted on age, education, sex, P's use of antipsychotics, both P and SC's use of anxiolytics, P's disability, SC's myocardial infarction, SC's angina, SC's diabetes

## Tables

**Table1**

Sample characteristics of participants with cancer and their spousal caregivers (N=282 couples), 3C study

	Participants	Spousal caregivers	Comparisons p-value
Age, mean (SD)	74.8 (4.8)	75.0 (4.9)	.674
Men, n (%)	158 (56.0)	124 (44.0)	.004
Education, n (%)			.877
primary school	78 (27.7)	78 (27.7)	
short or long secondary education	89 (31.6)	92 (32.6)	
higher education	115 (40.8)	112 (39.7)	
Trait anxiety, mean (SD)	38.3 (9.0)	39.5 (9.7)	.127
<i><u>Before the cancer diagnosis</u></i>			
High depressive symptomatology, n (%)	23 (8.6)	18 (6.7)	.403
Use of antidepressants, n (%)	21 (7.4)	19 (6.7)	.743
<i><u>After the cancer diagnosis</u></i>			
High depressive symptomatology, n (%)	26 (9.2)	32 (11.4)	.406
Use of antidepressants, n(%)	29 (10.3)	21 (7.4)	.236
Dyspnea, n (%)	6 (2.2)	5 (1.8)	.734
Stroke, n (%)	4 (1.4)	6 (2.1)	.752
Angina, n (%)	20 (7.2)	16 (5.7)	.477
Myocardial infarction, n (%)	4 (1.4)	2 (0.7)	.686
Heart failure, n (%)	9 (3.4)	10 (3.6)	.854
Diabetes, n (%)	29 (10.3)	25 (8.9)	.586
Disability, n (%)	30 (11.2)	30 (11.1)	.951

**Figure 1.**

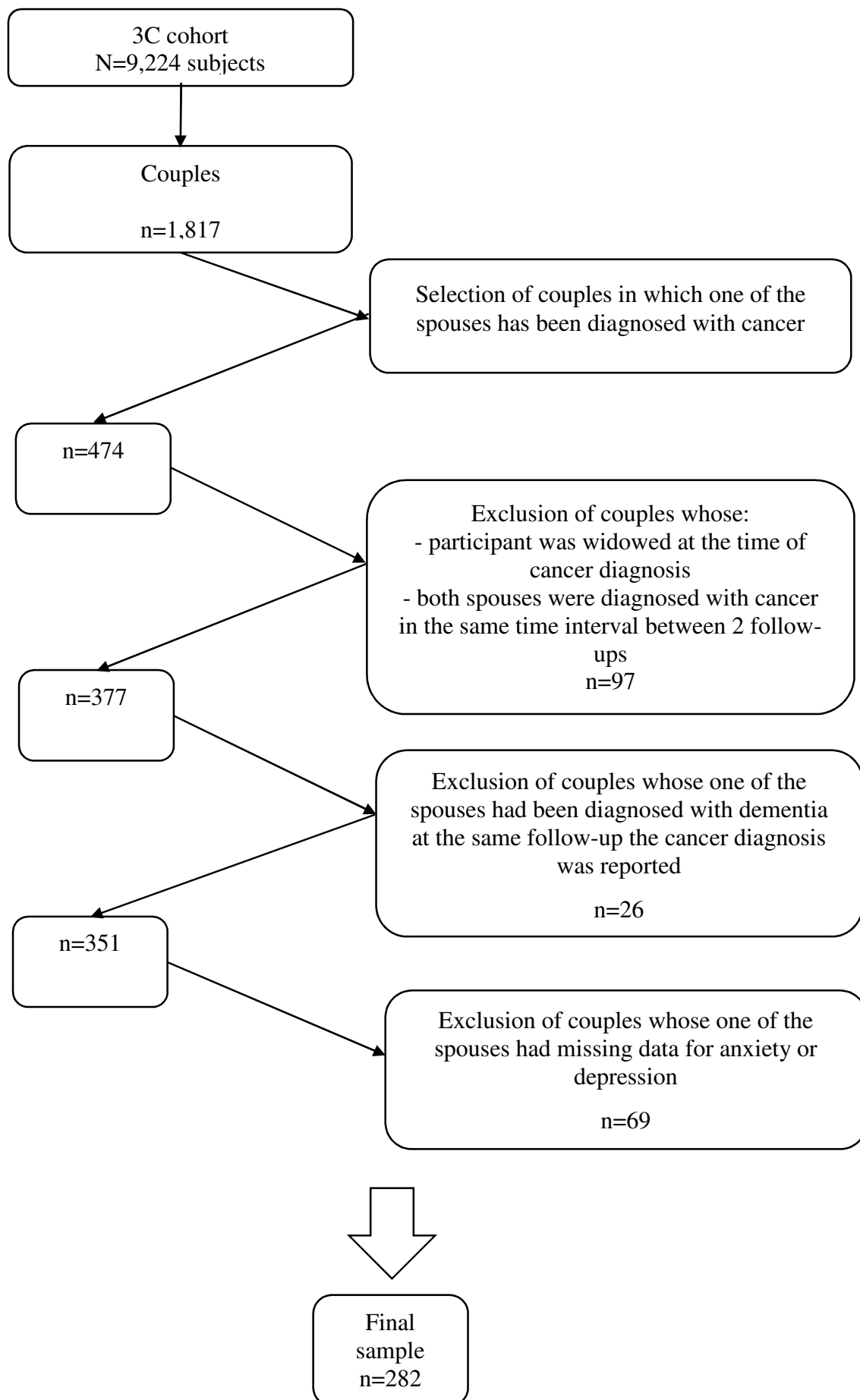


Figure 2.

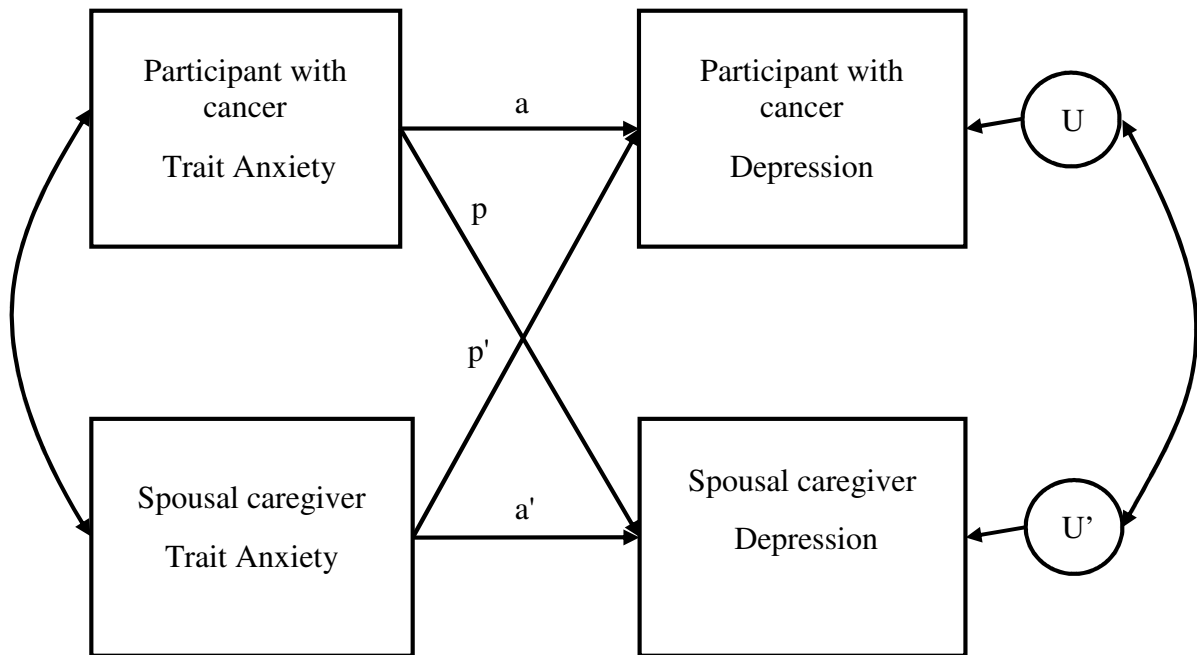


Figure 3.

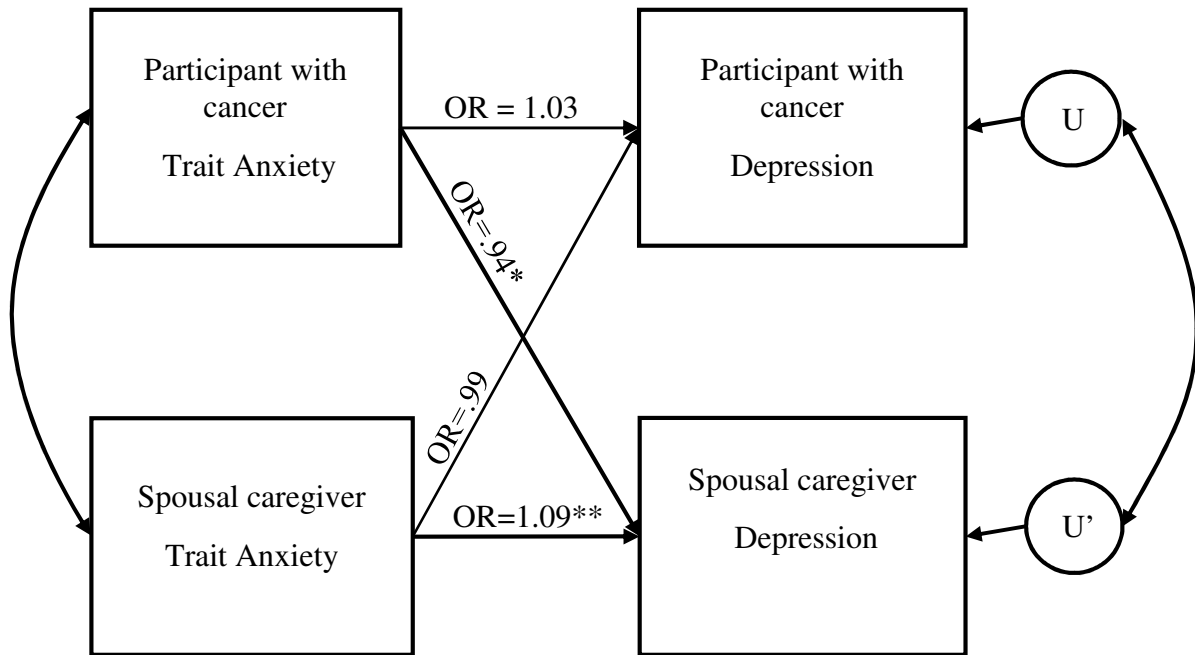
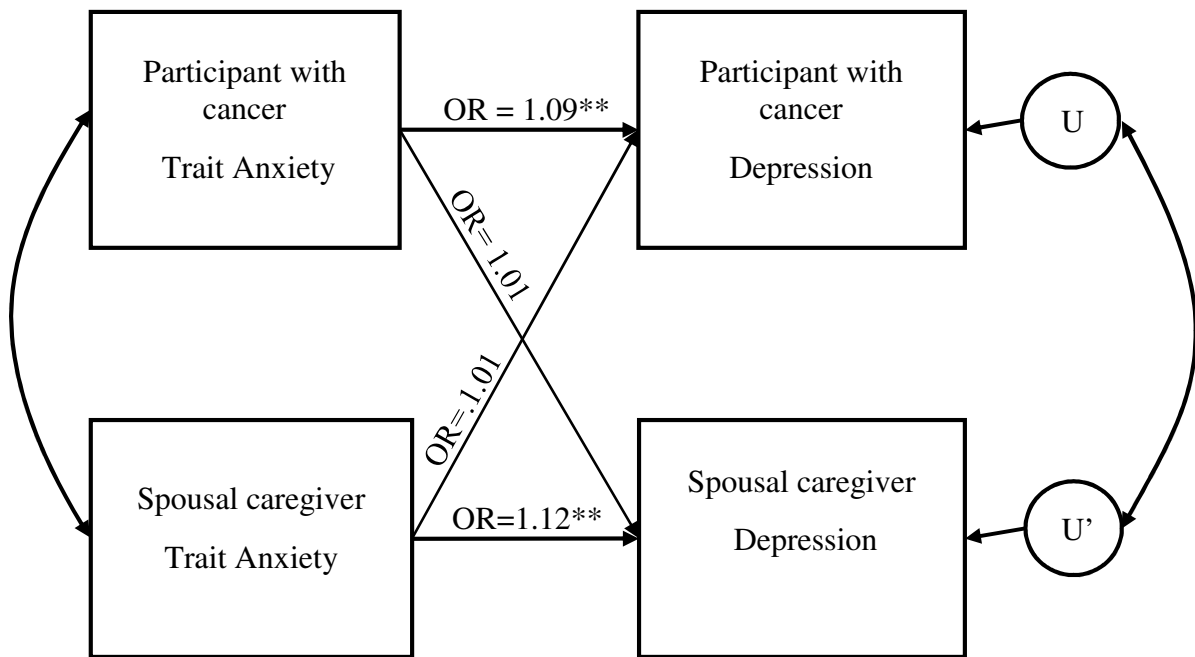


Figure 4.





## **Data references**

The availability of data from the Three City Cohort Study is subject to the agreement of the 3 City Cohort Study Scientific Committee (46). Investigators unaffiliated with any of the 3C-Study founding teams are welcome to propose new studies or new analyses (termed ancillary studies). 3C Study investigators are encouraged to work in collaboration with a senior investigator from one of the 3C-Study founding teams (listed in: Investigators, Study Sites, Collaborating Centres and Working Groups). The 3C-Study correspondent investigator can either be contacted directly by an investigator submitting an ancillary study or can be designated by the 3C-Study Steering Committee. Ancillary study proposals must be sent to the Coordinating Centre E3C.CoordinatingCenter@gmail.com

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