



# Association of cancer caregiver stress and negative attribution style with depressive symptoms and cortisol: a cross-sectional study

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Received: 1 October 2021 / Accepted: 24 January 2022 / Published online: 18 February 2022  
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## Abstract

**Purpose** We examined the effect of informal cancer caregiver stress and negative attribution style (NAS) on depressive symptoms and salivary cortisol.

**Method** The sample came from a hospital bone marrow unit and caregiver support organizations and included 60 informal cancer caregivers (51.7% partners) of individuals with cancer (provided care for a median of 27.5 h per week for 12 months) and 46 non-caregiver participants. In this cross-sectional study, participants completed questionnaires assessing NAS and depressive symptoms and provided saliva samples to measure cortisol.

**Results** Linear regressions demonstrated that cancer caregiver stress ( $p=0.001$ ) and the cancer caregiver stress by NAS interaction ( $p=0.017$ ), but not NAS alone ( $p=0.152$ ), predicted depressive symptoms. Caregivers independent of their NAS and non-caregivers high in NAS reported high depression while non-caregivers low in NAS reported low depression. Neither cancer caregiver stress ( $p=0.920$ ) nor NAS alone ( $p=0.114$ ), but their interaction, predicted cortisol ( $p=0.036$ ). Higher NAS was associated with a higher cortisol in both groups while non-caregivers had *higher* cortisol than caregivers.

**Conclusions** If the findings can be replicated, consideration of NAS in existing interventions to support informal cancer caregivers in managing chronic stress appears warranted.

**Keywords** Informal cancer caregiving stress · Depressive symptoms · Negative attribution style · Salivary cortisol

Based on the 2020 Caregiving in the US report [1], cancer is one of the top five reasons for informal caregiving, the process by which family members and friends provide support to someone with cancer. About 2.9 million family members and friends list cancer as the main reason for informal caregiving [1]. Informal caregiving can require a significant time commitment, with an average caregiver providing care for 23.7 h a week over multiple years [1]. Given the chronicity of this emotional and demanding experience, it is unsurprising that informal cancer caregivers (hereafter referred to as cancer caregivers) report psychological stress [for a review see 2] and stress-related issues with psychological functioning including depression [3, 4]. In fact, cancer caregivers

experience high prevalence of depression and depressive symptoms ranging from 10 to 53% [for a review see 5].

Psychological stress among cancer caregivers is also expressed in physiological functioning such as elevated levels of cortisol [for a review see 6]. Elevated cortisol levels are critical because they are associated with depression [for a meta-analysis see 7] and physical health issues like cardiovascular disease (CVD [8, 9]). While the inclusion of measures of physiological functioning into research on cancer caregivers would provide a more comprehensive view of their health, unfortunately, research in this area is underdeveloped [10, 11]. To develop the most responsive interventions, identifying modifiable factors relevant to cancer caregivers' psychological and physiological health is critical. One such factor is maladaptive thought patterns, which can contribute to depressive symptoms in cancer caregivers [12]. Thus, studies assessing the role of modifiable factors on both psychological and physiological health outcomes among cancer caregivers are warranted.

Causal attributions of a stressful situation like caregiving can be modified in psychotherapy and are the mechanism

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underlying the effects of cognitive behavioral therapy on depressive symptoms with different populations [13]. Based on the reformulated helplessness theory [14], individuals attribute a stressful situation to a cause that is either global or specific, internal or external, and stable or unstable. When individuals have the tendency to attribute stressful situations to a global, internal, and stable cause, they demonstrate a negative attribution style (NAS). For example, a cancer caregiver might demonstrate a NAS and experience caregiving cancer as stressful. The caregiver might think that caregiving will negatively affect all aspects of their life (i.e., globality); that they are a bad caregiver (i.e., internality); and/or that the stress of cancer caregiving will never end (i.e., stability).

Empirical studies provide evidence for the impact of a NAS on depressive symptoms [for a review see 15]. Further, prior work has described associations of NAS with measures of physical health ranging from self-reported hypertension [16] and general health [17], to specific measures of physical functioning, like the T lymphocyte CD4/CD8 ratio (T-lymphocytes which are part of the immune system) and their response to stimulation by Phytohaemagglutinin [18], to incidents of CVD [19], and death caused by a coronary event [19, 20]. However, while both NAS and cortisol are associated with depression [15, 28] and CVD [8, 9, 19], no previous study examined the relation between stressful situations in general and NAS with cortisol nor between cancer caregiver stress and NAS with depressive symptoms and cortisol in particular. Considering the relevance of depression [for a review see 5] and cortisol [for a review see 6] and the importance of a modifiable factor like NAS [13] for interventions to improve health in this population, this seems a crucial gap in the literature.

In the current study, we examined the effect of cancer caregiving and NAS on depressive symptoms and salivary cortisol levels. Based on the reformulated helplessness theory [14] and empirical research, we predicted that (a) cancer caregivers would show elevated levels of depressive symptoms [4, 5] and salivary cortisol levels [for a review see 6]; (b) NAS is positively related to depressive symptoms [for a review see 15] and cortisol in both caregivers and non-caregivers; and (c) NAS serves as moderator [14] by increasing the effect of cancer caregiver stress on depressive symptoms and salivary cortisol. Specifically, we expected that NAS would relate to more self-reported depressive symptoms and higher cortisol levels in cancer caregivers.

## Methods

### Participants

The cancer caregiver group consisted of 60 caregivers of individuals with cancer. Recruitment efforts included

in-person requests at the Bone Marrow Unit of a local hospital (62.9%,  $n = 44$ ), email invitations to a local cancer support organization (20%,  $n = 14$ ) and members of a caregiver support group at a local cancer center (12.9%,  $n = 9$ ), and listserv announcements to a university community (4.3%,  $n = 3$ ). Caregivers identified as a partner (51.7%,  $n = 31$ ), parent (15%,  $n = 9$ ), child (13.3%,  $n = 8$ ), sibling (5%,  $n = 3$ ), friend (3.3%,  $n = 2$ ), or ‘other’ (8.3%,  $n = 5$ ) regarding their relationship with the care recipient. The remaining two caregivers (3.3%) did not specify their relationship to the individuals with cancer. Caregivers identified the cancer type of the care recipient as lymphoma/leukemia (30%,  $n = 18$ ), brain (10%,  $n = 6$ ), breast (11.7%,  $n = 7$ ), colorectal (11.7%,  $n = 7$ ), lung (8.3%,  $n = 5$ ), and other (e.g., bladder, skin, myeloma; 25%,  $n = 15$ ). The remaining two caregivers (3.3%) did not specify the type of cancer the care recipient had. Caregivers provided care for 1 week to up to 264 months, with a median of 12 months, and the number of hours per week of care ranged from about 1 to 168 h within a week, with a median of 27.5 h per week.

The mean age of the cancer caregiver group was 51.17 (SD of 15.22, range of 19 to 77). Regarding gender, 71.7% ( $n = 43$ ) of caregivers identified as female, and the racial/ethnic composition of the caregiver sample included 53 White (88.3%) four Black (6.7%), two multiracial (3.3%), and one Asian (1.7%) caregiver. The caregivers were primarily married (63.3%,  $n = 38$ ), with others identifying as single (16.7%,  $n = 10$ ), divorced (10%,  $n = 6$ ), living in a stable relationship (5%,  $n = 3$ ), widowed (3.3%,  $n = 2$ ), and being separated. (1.7%,  $n = 1$ ). Further caregivers reported to have < \$35,000 (33.3%,  $n = 20$ ), \$35,001 to \$50,000 (18.3%,  $n = 11$ ), \$50,001 to \$100,000 (26.7%,  $n = 16$ ), and > \$100,000 (18.3%,  $n = 11$ ) annual income, and two chose not to answer (3.3%).

The 46 non-caregiver control group participants were recruited using listserv announcements to a university community. The mean age of this group was 36.61 (SD of 12.80, range of 22 to 66). Regarding gender, 95.7% ( $n = 44$ ) of the control group identified as female, and the racial/ethnic composition of this sample included 45 White (97.8%) and one multiracial (3.3%) caregiver. The control group participants were primarily married (50%,  $n = 23$ ) with others identifying as single (32.6%,  $n = 15$ ), divorced (6.5%,  $n = 3$ ), living in a stable relationship (4.3%,  $n = 2$ ), widowed (2.2%,  $n = 1$ ), and two chose not to answer (4.3%). Further, non-caregivers reported to have < \$35,000 (17.3%,  $n = 8$ ), \$35,001 to \$50,000 (13%,  $n = 6$ ), \$50,001 to \$100,000 (50%,  $n = 23$ ), > \$100,000 (18.3%,  $n = 7$ ) annual income and two chose not to answer (4.3%).

No significant differences between the cancer caregiver group and the non-caregiver control group were found

for race/ethnicity,  $\chi^2(3) = 4.21$ ,  $p = 0.240$ , and income,  $\chi^2(7) = 11.84$ ,  $p = 0.106$ . However, the caregivers were significantly older,  $t(104) = 5.22$ ,  $p < 0.001$ , and less likely female,  $\chi^2(1) = 10.18$ ,  $p = 0.001$ .

## Procedure

The current study is a cross-sectional examination of cancer caregiver stress, NAS, depressive symptoms, and salivary cortisol, and is part of a larger study (for other relevant publications, see BLINDED). The study was approved by the University of BLINDED Institutional Review Board (IRB NUMBER: 13.0135) and informed consent was obtained from all participants; surveys were completed using an online program or on paper. Data from cancer caregivers were collected at the local hospital and during meetings of cancer caregiver support groups. The non-caregiver control group completed the study visit on the university campus. The data collection was completed before the COVID-19 epidemic.

## Measures

### Demographics

Self-reports of gender, weight, height, birthdate, socioeconomic status, and race/ethnicity were collected. Variables relevant for physiological measurement (e.g., allergies, date of last period, gum bleeding, smoking, shift work, time of most recent food, fluid, and other substances) were recorded.

### Negative attribution style (NAS)

To measure NAS, participants were presented with a hypothetical event (i.e., a caregiving situation for the cancer caregivers and a non-caregiving situation for the non-caregivers) and asked to write down one cause for the event. Participants then rate the degree to which the cause of the hypothetical event is (a) internal, (b) stable, and (c) global. Each rating uses a 7-point Likert scale, with higher scores representing a more NAS. Consistent with previous research measuring NAS, the internal consistency in the current study was  $\alpha = 0.60$ . This internal consistency is good considering that NAS is measured with only three items.

### Depressive symptoms

The 20-item Center for Epidemiologic Studies – Depression Scale (CES-D) measures depressive symptoms over the past week [21]. The Cronbach's alpha of the CES-D in a previous

caregiver study was  $\alpha = 0.90$  [22], which is consistent with the internal consistency in the current study ( $\alpha = 0.91$ ).

## Cortisol

Saliva samples were collected between 4:00 PM and 6:00 PM. The passive drooling method was used for collecting a single saliva sample over a period of 5 min while the participants responded to the survey questions. Saliva was collected in Salivette sampling devices (Sarstedt, Rommelsdorf, Germany) and kept frozen until it was analyzed. Salivary cortisol was measured using the Salivary Cortisol ELISA kit (Salimetrics, Carlsbad, CA, USA). The assay is based on a competitive immunoassay (ELISA) method. The minimal detectable concentration of the method is 0.007 ug/dL. The intra- and inter-assay coefficient of variations are 3–7% and 3–11%, respectively.

## Data analysis

We z-transformed the NAS scores and calculated the group (cancer caregiver = 1 vs. non-caregiver participants = 0) by z-transformed NAS scores interaction scores. Using these scores as predictors, we conducted two linear regression models with depressive symptoms and cortisol as outcome variables, respectively. None of the above listed health variables that have contributed to cortisol levels (e.g., allergies, caffeine, date of last period, gum bleeding, hormones, shift work, smoking) in the literature were significant in our sample. Because age and gender were significantly different between cancer caregivers and non-caregiver control participants, we included those variables as covariates in both regression models. Control variables were entered in step 1 of the regressions. In step 2, the main effects of group and z-transformed NAS scores were entered as predictors. In step 3, the group by z-transformed NAS scores interaction was entered. To further examine significant group by attribution interaction effects, we constructed model-implied graphs. Finally, we calculated the observed power in our study.

## Results

The descriptive statistics and correlations for the cancer caregiver group and the non-caregiver control participants are presented in Table 1, and the regression results are reported in Table 2. As expected, the main effects of group ( $p = 0.001$ ) and the group by NAS interaction ( $p = 0.017$ ) significantly predicted depressive symptoms. However, the main effect of NAS was not significant ( $p = 0.152$ ). Contrary to our hypotheses, the model-implied graph (Fig. 1) demonstrated that all caregivers, independent of their NAS, and only non-caregivers high in NAS reported

**Table 1** Descriptive statistics and correlations for cancer caregivers (n = 60) and non-caregiver control participants (n = 43)

	Attribution	Depressive symptoms	Cortisol	Mean	SD
Attribution	–	.00	-.19	8.81	4.35
Depressive symptoms	.41**	–	-.12	18.60	10.82
Cortisol	.27+	.22	–	0.082	0.052
Mean	11.00	14.60	0.109		
SD	4.21	10.72	0.069		

*Note.* Data of the cancer caregiver group are presented above the diagonal, data of the non-caregiver control participants are presented below the diagonal. Attribution = CSQ scores; depressive symptoms = CES-D scores; Cortisol = cortisol level (ug/dl)

+  $p < .10$ ; \*  $p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$

high depression scores. Only non-caregivers low in NAS reported low depression scores. In other words, while non-caregivers low in NAS reported lower depression scores, the other three groups exhibited similar levels of depressive symptoms. The observed power with depressive symptoms as dependent variable was 0.801.

Unexpectedly, the main effects of group ( $p = 0.920$ ) and NAS ( $p = 0.114$ ) did not significantly predict salivary cortisol. However, as hypothesized, the group by NAS interaction ( $p = 0.036$ ) was significantly associated with salivary cortisol

levels. Consistent with our hypotheses, the model-implied graph (Fig. 2) demonstrated that higher NAS was associated with higher salivary cortisol levels in both groups. However, unexpectedly, non-caregivers had *higher* salivary cortisol levels than caregivers and the impact of NAS on cortisol appears larger in non-caregivers than in cancer caregivers. The observed power with cortisol as dependent variable was 0.888.

## Discussion

Following the reformulated helplessness theory [14] and empirical research, we predicted that (a) cancer caregiver stress would be associated with elevated levels of depressive symptoms [4, 5] and salivary cortisol [for a review see 6]; (b) NAS would be positively related to depressive symptoms [for a review see 15] and cortisol independent of cancer caregiver stress; and (c) NAS serves as moderator [14] by increasing the effect of cancer caregiver stress on depressive symptoms and salivary cortisol. Our results demonstrated that cancer caregivers experienced more depressive symptoms than non-caregivers. Additionally, NAS was associated with elevated depressive symptoms and cortisol levels in non-caregivers and with cortisol levels in cancer caregivers. However, unexpectedly, the cortisol levels in caregivers seem to be lower than in

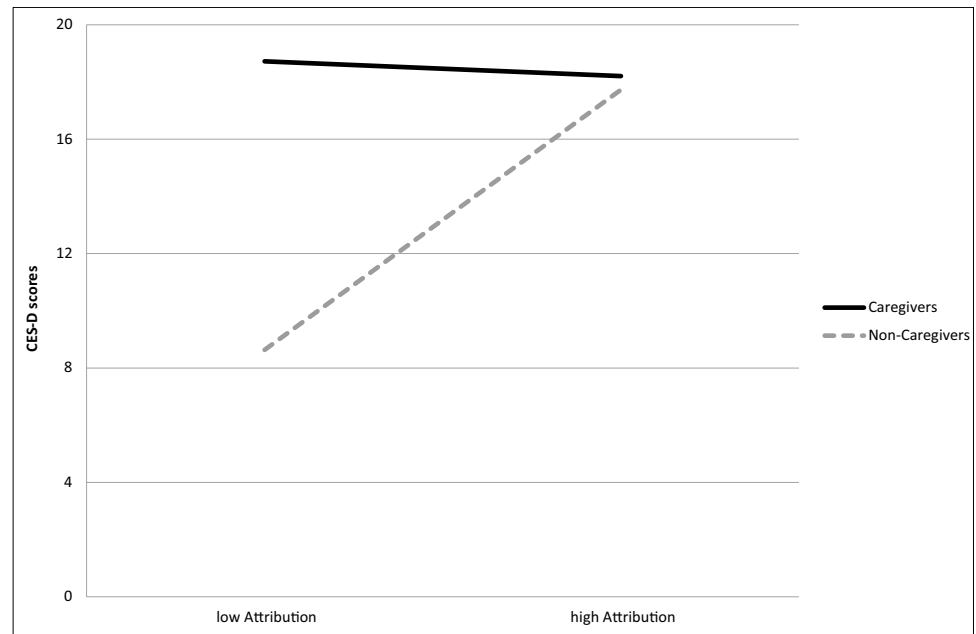
**Table 2** Linear regressions with group, attribution style, and their interaction as predictors of depressive symptoms and cortisol

Dependent variable	Depressive symptoms					
	Step 1		Step 2		Step 3	
	$R^2$	$\beta$	$R^2$	$\beta$	$R^2$	$\beta$
Age		-.121		-.243*		-.266*
Gender		.051		.063		-.057
Group				.349**		.407***
Attribution				.174+		-.333
Group $\times$ Attribution						.569*
$R^2$ change	.016		.094**		.011*	
Total $R^2$	.016		.111		.166	
Dependent variable	Cortisol					
	Step 1		Step 2		Step 3	
	$R^2$	$\beta$	$R^2$	$\beta$	$R^2$	$\beta$
Age		-.210+		-.173		-.198
Gender		-.080		-.071		-.064
Group				-.040		.016
Attribution				.131		-.535
Group $\times$ Attribution						-.720*
$R^2$ change	.055		.019		.066*	
Total $R^2$	.055		.074		.140	

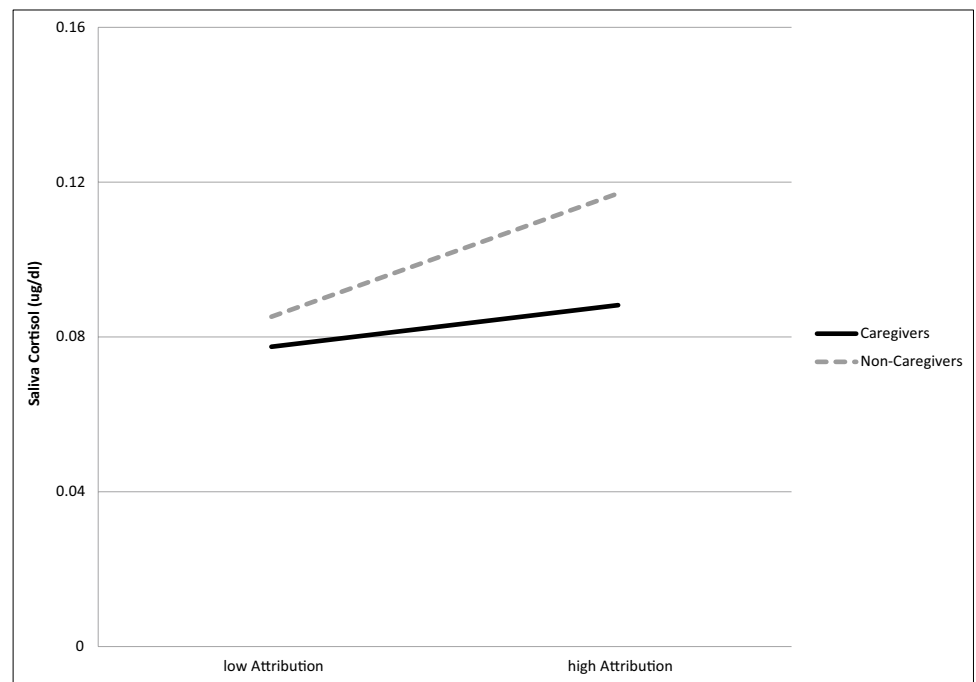
*Note.* Group = cancer caregiver vs. non-caregiver control participants; Attribution = z-transformed CSQ scores; Depressive Symptoms = CES-D scores; Cortisol = cortisol level (ug/dl)

+  $p < .10$ ; \*  $p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$

**Fig. 1** Model-implied graph for the interaction effect of group by negative attribution style on depression scores



**Fig. 2** Model-implied graph for the interaction effect of group by negative attribution style on salivary cortisol



non-caregivers, and NAS seems to be more relevant in non-caregivers than in cancer caregivers, regardless of the outcome variable (i.e., depressive symptoms, cortisol level).

The fact that we observed effects of NAS on depressive symptoms and cortisol levels in non-caregivers is noteworthy. These findings are consistent with previous literature demonstrating the impact of NAS on psychological (i. e., depressive symptoms [for a review see 15]) and physical health [16–20] in the general population. This literature is

informative for research examining possible mechanisms by which psychological and physical health can be improved in the general population.

Our findings that NAS is associated with elevated depressive symptoms and cortisol levels in non-caregivers makes the unexpected finding that cancer caregivers report elevated levels of depressive symptoms independent of their NAS even more surprising. This finding might reflect the significant psychological stress of cancer caregiving. This aligns

with the chronicity associated with caregiving in the current sample: an average of 1 year (median: 12 months, range: 1 week to 264 months) for roughly 30 h each week (median: 27.5 h per week, range: 1 to 168 h per week). In other words, the chronic stress associated with cancer caregiving overrides any contribution of NAS. To examine this possible explanation, a future longitudinal study should attempt to follow cancer caregivers from the time of the diagnosis. If our prediction is correct, one would expect that NAS impacts depressive symptoms at the time of the diagnosis and for some time after but that NAS loses its effect with time as caregiving remains a stressor.

One of cortisol's roles is to prepare individuals for the demands of an acute stressor and that, following exposure to an acute stressor, cortisol levels rise to accommodate the increased taxation on the body [23, 24]. However, in response to chronic stress, cortisol becomes dysregulated [23, 24]. Thus, the severity and chronicity of cancer caregiver stress could explain our unexpected finding of *higher* cortisol levels in non-caregivers than cancer caregivers as well as why NAS is associated with elevated cortisol levels in both groups but has a stronger impact in non-caregivers than in cancer caregivers. Our finding is consistent with some previous studies in which non-caregivers had higher cortisol levels than cancer caregivers [3]. Bevans et al. [3] found that cortisol levels in non-caregivers increased over time, while cortisol levels in cancer caregivers decreased. The authors interpret their results as indication that, over time, cancer caregiver stress wears and tears on the hypothalamic–pituitary–adrenal (HPA) axis to which cortisol belongs. That is, over time, cancer caregiving might be so stressful that the HPA axis cannot keep producing excess cortisol. Instead, even the levels of cortisol are reduced. In other words, the severity and chronicity of cancer caregiver stress likely influence the impact of association between cancer caregiver stress and cortisol. As described above, a longitudinal study following cancer caregivers from the time of the diagnosis appears crucial to test this. In addition, researchers might focus on one particular type of cancer to control for the intensity of care provided and durations of care (e.g., an allogeneic bone marrow transplant recipient vs. an early-stage breast cancer).

## Limitations

Some limitations of our study need be considered. We already highlighted the cross-sectional design as limitation. Thus, the above discussed three-wave longitudinal study design would strengthen the conclusions of our study. Another limitation is the homogeneity of our sample; most participants identified as female (> 70%) and White (> 85%). Given that previous research has identified psychological and physical differences regarding distress depending on gender and race/ethnicity [5,

25], authors of future research should recruit more diverse samples to broaden the generalizability of findings or consider the role of oppression and privilege in understanding these relationships.

Given the burden already placed on caregivers, collecting only one cortisol sample, as opposed to multiple samples, seemed important. Nevertheless, this decision also precluded examination of changes in cortisol secretion throughout the day. Some studies have found changes in the diurnal cortisol profile of caregivers, but not at individual time points [for a review see 6]. Thus, it is possible that there are associations between cancer caregiving and cortisol we were not able to detect and it may be meaningful to consider this in future research.

The outcomes of our study are limited to depressive symptoms and salivary cortisol. Depression is highly prevalent in cancer caregivers (53% [for a review see 5]), and cortisol is a commonly used biomarker in measuring the physiological stress response [for a review see 6], which has been associated with physical health issues including CVD [8, 9]. Beyond those two outcomes, NAS is related to other physiological measures, like cell-mediated immunity (i.e., T cell CD4/CD8 ratio, T-lymphocyte response to mitogen challenge [18]) and blood pressure [26]. Based on these additional associations, the exclusive use of only one mental health outcome and one biomarker of physical health could be interpreted as a limitation. Thus, the inclusion of other mental health outcomes and biomarkers should be considered by authors of future studies when evaluating the impact of cancer caregiver stress and NAS.

## Conclusions

Cancer caregiving is associated with depressive symptoms [for a review see 5] and physiological functioning like elevated levels of cortisol [for a review see 6]. Our study demonstrated that while NAS might not impact depressive symptoms in cancer caregivers, it is associated with an increase in their cortisol levels. In other words, NAS appears to exacerbate the relationship between cancer caregiver stress and cortisol levels. Cancer caregivers are crucial members of the treatment team who provide care; however, they are also in need of care [27]. By being better able to care for themselves, cancer caregivers can optimize the care they provide for their loved ones [27], reducing both the likelihood of hospital readmission and related costs for the providing medical facilities [28]. Thus, our findings have relevant implications. Prioritizing interventions, like cognitive behavioral therapy, that support cancer caregivers in managing chronic stress and

consideration of NAS could positively affect the quality of life for caregivers and their patients.

In sum, despite the limitations of our study, our findings demonstrate the effects of cancer caregiver stress and NAS on depressive symptoms and salivary cortisol. To expand on our findings, future studies following cancer caregivers from the time of diagnosis using a three-wave longitudinal design and including multiple biomarkers of physical health in a diverse sample appear crucial. If replicated, our findings demonstrate that considering NAS in the implementation of interventions to support cancer caregivers in managing chronic stress appears warranted.

**Author contribution** Patrick Pössel – co-conceptualized and designed the study, calculated the statistical analysis, and interpreted the findings, drafted the manuscript, agreed to be accountable for all aspects of the manuscript to ensure that questions related to the accuracy or integrity of any part of the manuscript are appropriately investigated and resolved.

**Amanda M. Mitchell**—co-conceptualized and designed the study, co-collected data, revised previous drafts of the manuscript, approved the submitted version of the manuscript.

**Brooks Harbison**—co-collected data, revised previous drafts of the manuscript, approved the submitted version of the manuscript.

**G. Rafael Fernandez-Botran**—co-conceptualized and designed the study, analyses the biological outcome data, wrote the parts of the manuscript to the biological outcome data, revised previous drafts of the manuscript, approved the submitted version of the manuscript.

**Data Availability** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Code availability** Not applicable.

## Declarations

**Ethics approval and consent to participate** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the IRB of the University of BLINDED (No. 13.0135). Informed consent was obtained from all individual participants included in the study.

**Consent for publication** Not applicable.

**Conflict of interest** The authors declare no competing interests.

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