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### Authors

Bergerot, Cristiane Decat  
Mitchell, Hannah-Rose  
Ashing, Kimlin Tam  
et al.

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# A prospective study of changes in anxiety, depression, and problems in living during chemotherapy treatments: effects of age and gender

Cristiane Decat Bergerot<sup>1</sup> · Hannah-Rose Mitchell<sup>2</sup> · Kimlin Tam Ashing<sup>3</sup> · Youngmee Kim<sup>2</sup>

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## Abstract

**Purpose** Monitoring distress assessment in cancer patients during the treatment phase is a component of good quality care practice. Yet, there is a dearth of prospective studies examining distress. In an attempt to begin filling this gap and inform clinical practice, we conducted a prospective, longitudinal study examining changes in distress (anxiety, depression, and problems in living) by age and gender and the roles of age and gender in predicting distress.

**Methods** Newly diagnosed Brazilian cancer patients ( $N = 548$ ) were assessed at three time points during chemotherapy. Age and gender were identified on the first day of chemotherapy (T1); anxiety, depression, and problems in living were self-reported at T1, the planned midway point (T2), and the last day of chemotherapy (T3).

**Results** At T1, 37 and 17% of patients reported clinically significant levels of anxiety and depression, respectively. At T3, the prevalence was reduced to 4.6% for anxiety and 5.1% for depression ( $p < .001$ ). Patients 40–55 years, across all time points, reported greater anxiety and practical problems than patients >70 years ( $p < .03$ ). Female patients reported greater emotional, physical, and family problems than their male counterparts ( $p < .04$ ).

**Conclusions** For most patients, elevated levels of distress noted in the beginning of treatment subsided by the time of treatment completion. However, middle-aged and female patients continued to report heightened distress. Evidence-based psychosocial intervention offered to at risk patients during early phases of the treatment may provide distress relief and improve outcomes over the illness trajectory while preventing psychosocial and physical morbidity due to untreated chronic distress.

**Keywords** Anxiety · Depression · Problems in living · Brazilian cancer patients · Longitudinal study · Age · Gender

## Introduction

Cancer diagnosis and treatment often bring heightened distress and disrupt daily routines [1]. Not surprisingly, considerable proportions of patients who are newly diagnosed with cancer report clinical levels of anxiety (10 to 58%) and depression (14 to 30%) [2, 3]. Numerous physical and psychological problems are caused by the tumor, and the side effects of treatment are commonly reported and can interfere with the patients' daily functioning and ability to maintain family and social relationships [4–6].

Studies have shown steady reductions in anxiety and depression symptoms [7–10], whereas others showed worsened depression [11] and stable, low levels of distress during the first year [12, 13]. Surprisingly, change patterns in problems in daily living are unknown. The investigation of factors associated with the trajectory of anxiety, depression, and problems in daily living across the course of treatment will provide crucial information for developing precise psychosocial care plans that are likely to yield immediate and long-term benefit for cancer patients.

✉ Cristiane Decat Bergerot  
crisbergerot@gmail.com; ykim@miami.edu

<sup>1</sup> Federal University of São Paulo (UNIFESP), Rua Napoleão de Barros, 754 –Vila Clementino, São Paulo, SP 04024-002, Brazil

<sup>2</sup> Department of Psychology, University of Miami, Coral Gables, FL 33146, USA

<sup>3</sup> Department of Population Sciences, City of Hope Medical Center, Duarte, LA 91010, USA

Further, age and gender have been consistently identified as significant correlates of anxiety, depression, and problems in daily living among cancer patients. For example, younger adults (18 to 40 years) have reported greater levels of anxiety and depression [14, 15] and significantly more difficulties with concentration, pain, nervousness, nausea/vomiting, sleep, worry, sadness, and sexual interest [16]. Female patients have also reported greater levels of anxiety and depression [15, 17, 18] and higher numbers of emotional and physical problems [4, 18]. Unknown is whether age and gender are equally significant predictors of *changes* in anxiety, depression, and problems in living during cancer treatment, above and beyond the natural tendency for adjustment as time proceeds.

Current knowledge about these concerns comes mainly from North America [2]. Such information for patients in South America is timely, particularly in Brazil, with a population of almost 210-million people experiencing a 500% increase in cancer incidence between 1995 and 2015 [19]. To date, the few studies conducted in Brazil have found that 21 to 39% of cancer patients displayed clinical levels of anxiety, and from 17 to 47% endorse depression [20–22]. However, these studies have substantial methodological limitations, such as use of cross-sectional design [20–22] and convenience sampling without specific eligibility criteria based on the time since diagnosis and treatment type or status [22, 24]. These limitations also preclude reliable, precise knowledge on the prevalence, trajectory, and predictors of distress and problems in daily living among newly diagnosed cancer patients in Brazil.

In an attempt to begin filling the scientific gap regarding the lack of longitudinal studies, research that includes patients from developing countries and inadequate age and gender consideration, we conducted a prospective study in examining distress. Thus, this study aimed (a) to document levels of anxiety, depression, and problems in living among newly diagnosed cancer patients in Brazil during the cancer treatment phase and (b) to predict changes in anxiety, depression, and problems in living by assessment time, age, and gender. We hypothesized anxiety, depression, and problems in living that would peak in the beginning of treatment and subside by completion of treatment (hypothesis 1). We also hypothesized that younger and female patients would report greater levels of anxiety, depression, and problems in living (hypothesis 2), for which the associations would be most prominent in the beginning of treatment (hypothesis 3).

## Methods

### Participants and procedure

A longitudinal and prospective study was conducted. Adult ambulatory patients with any cancer diagnosis requiring

chemotherapy treatment at a private cancer center in Brasilia, Brazil (the Centro de Câncer de Brasília–CETTRO) were invited to participate. Eligibility criteria included the following patients: (a) newly diagnosed with cancer and to be treated with chemotherapy, (b) 18-years old or older, (c) able to understand and provide voluntary informed consent to participate in the study, (d) physical functioning score better than “fair” ( $\leq 2$  on the Eastern Cooperative Oncology Group) [24], and (e) able to enroll to the study before chemotherapy begins.

Eligible participants provided the data on the first day of chemotherapy (T1), midway point (T2), and last day (T3) of initially planned chemotherapy treatment. The average interval between assessments was 3 months ( $M = 2.97$ ,  $SD = 0.38$ ), and the total duration of chemotherapy treatment was about 6 months ( $M = 5.97$ ,  $SD = 0.69$ , ranged from 4 to 8 months). A total of 642 patients enrolled to the study (100% response rate, as this study was presented as a distress screening with no additional cost for patients). Of those, 94 (14.6%) were excluded in subsequent analyses due to missing data at T2 or T3, leaving 548. Primary reasons for missing data include death ( $n = 72$ ; 76.4%), switching to different hospitals for treatment ( $n = 11$ ; 11.8%), incompleteness of recommended treatment regimen ( $n = 6$ ; 6.5%), or moving away to a different region ( $n = 5$ ; 5.4%). No compensation was given to participants and all patients consented to participate in the study. The study was conducted in compliance with the regulations of the Ethical standards of the Helsinki declaration and of the Brazilian National Health Council (CNS) Resolution No. 466/2012. The study was approved by the Research Ethics Committee of Faculdade de Ciências da Saúde of the Universidade de Brasília.

Participants who provided incomplete data, compared with those who provided complete data, were older (60.8 vs 54.5,  $p < .001$ ), more likely to be male and diagnosed with non-gender specific types of cancer ( $ps < .01$ ), reported higher mean scores of anxiety at T2 (5.7 vs 4.2,  $p < .01$ ), of depression at T1 and T2 (7.9 and 7.9 vs 5.6 and 4.2,  $ps < .001$ ), and overall problems at T1 and T2 (11.6 and 10.1 vs 8.7 and 7.2,  $ps < .001$ ).

### Measures

**Anxiety and depression** The 14-item Hospital Anxiety and Depression Scale (HADS) [25], a widely used measure to assess anxiety (HADS-A 7 items) and depression (HADS-D 7 items), was used. The HADS was translated and validated in Brazilian Portuguese [26]. The HADS-A and HADS-D range from 0 to 21, with higher scores indicating greater levels of anxiety and depression. Both the HADS-A and the HADS-D had good internal consistency with the current sample ( $\alpha = .83$ ,  $.72$ , and  $.68$  for the HADS-A and  $\alpha = .83$ ,  $.81$ , and  $.78$  for the HADS-D, at T1, T2, and T3, respectively). Scores

on the HADS-A  $\geq 8$  and the HADS-D  $\geq 9$  suggest clinical levels of anxiety and depression, respectively [25].

**Problems in living** The list of 35 problems in daily living [5], which was translated/back-translated in Brazilian Portuguese [27], was used to assess emotional (6 problems e.g., fears, nervousness), practical (5 problems e.g., housekeeping, transportation), physical (21 problems e.g., fever, pain), spiritual (1 problem), and family (2 problems e.g., dealing with partner, dealing with children) problems at T1, T2, and T3. Participants evaluated presence or absence of each problem. The number of problems endorsed as present was counted within sub-category.

**Demographic and medical variables** Self-reported age, gender, education, and marital status were assessed at T1. Cancer type and disease stage were retrieved from the hospital's medical records.

### Statistical analyses

Descriptive information about the sample and study variables is presented in Table 1. General linear modeling (GLM) analysis was employed to predict levels and changes in anxiety, depression, and problems in living during cancer treatment simultaneously in three steps. First set of GLM included education, marital status, and type of cancer as predictors, which served as covariates. Main effects of time (linear and quadratic), age, and gender were added in the second step; and time by age and time by gender interaction effects were added in the third step of GLM. Thus, the main effects tested were above and beyond the effects of covariates, and the interaction effects were above and beyond the effects of covariates and main effects (Table 3). The same analytic procedure was employed predicting sub-types of problems in living (Table 4). We repeated the same sets of analysis including disease stage (early vs advanced) as a covariate excluding 57 cases whose cancer stage information was missing. The results remained the same, thus, results without cancer stage as a covariate are presented below.

## Results

### Patient characteristics and changes in anxiety, depression, and problems in living over time

Patients were primarily female, married, aged 40–55 and with at least a high school degree (Table 1). Most were diagnosed with a non-gender-specific type of cancer (gastrointestinal, hematologic, lung, other 58.9%). Compared with a large non-clinical sample [28], broadly representative of the UK adult population ( $N = 1729$ ; 56.6% women;  $M = 41.5$  years

**Table 1** Demographic and medical characteristics ( $N = 548$ )

	Mean (SD) or frequency (%)
Age (overall mean)	54.4 (15.5)
<40 years	98 (17.9%)
40~<55	159 (29.0%)
55~<70	187 (34.1%)
>70	104 (19.0%)
Gender female	383 (69.9%)
Marital status	
Married	338 (61.7%)
Single	80 (14.6%)
Divorced	72 (13.1%)
Widow	58 (10.6%)
Education	
No or little education	7 (1.3%)
Elementary school	74 (13.5%)
High school	129 (23.5%)
College	273 (49.8%)
Beyond college	65 (11.9%)
Type of cancer	
Breast	160 (29.2%)
Gastrointestinal	117 (21.4%)
Genitourinary	23 (4.2%)
Gynecological	55 (10.0%)
Hematological	130 (23.7%)
Lung	32 (5.8%)
Other	31 (5.7%)
Stage of cancer	
Early	182 (33.2%)
Advanced	309 (56.4%)
Missing	57 (10.4%)

of age), levels of anxiety reported at T1 were significantly higher, as shown in Table 2, whereas those at T2 and T3 were significantly lower ( $ts > 11.21$ ,  $ps < .001$ ); and levels of depression at T1 and T2 were significantly higher ( $ts > 3.22$ ,  $ps < .01$ ), and those at T3 were comparable ( $t = 0.81$ ,  $p = .42$ ). Anxiety (HADS-A  $\geq 8$ ) and depression (HADS-D  $\geq 9$ ) were prominent, and clinical levels were reported at T1 by 37.0 and 16.8% of patients, whereas that at T2 and T3 subsided to normative levels (5.7 and 4.6% for anxiety; 7.3 and 5.1% for depression at T2 and T3, respectively).

The overall number of problems endorsed by our sample at T1 and T2 was significantly higher ( $ts > 5.54$ ,  $ps < .001$ ) but comparable at T3 ( $t = 0.17$ ,  $p = .86$ ), compared with that reported by a large sample of US cancer patients at their first clinic visit (Table 2) [5]. In our sample at T1, physical (93.1%) and emotional (87.4%) problems were reported most frequently, followed by practical (43.4%), family (40.9%), and spiritual (7.1%) problems.

**Table 2** Mean scores of anxiety, depression, and problems in living over time (*N* = 548)

	Possible range	T1	T2	T3
HADS-anxiety	0–21	7.54 (4.24)	4.20 (2.72)	3.66 (2.35)
HADS-depression	0–21	5.64 (4.07)	4.17 (3.25)	3.56 (2.84)
Problems-overall	0–35	8.73 (4.86)	7.24 (4.63)	5.88 (4.32)
Problems-emotional	0–6	3.11 (1.91)	1.79 (1.78)	1.42 (1.67)
Problems-family	0–2	0.49 (0.64)	0.30 (0.54)	0.23 (0.49)
Problems-physical	0–21	4.43 (2.94)	4.70 (2.86)	3.88 (2.63)
Problems-practical	0–5	0.63 (0.87)	0.41 (0.74)	0.33 (0.66)
Problems-spiritual	0–1	0.07 (0.26)	0.04 (0.20)	0.02 (0.15)

**Effects of education, marital status, and types of cancer on anxiety, depression, and problems in living**

Before testing effects of the primary predictors, effects of covariates (education, marital status, and types of cancer) were tested and showed at Block 1 of Tables 3 and 4. Married patients reported a greater number of overall problems in living, which was significant at T1 (9.08 vs 8.22 for non-married,  $t = 2.03, p = .04$ ); problems with family were the most reported across all three assessments ( $ts > 2.31, ps < .03$ ). Further, patients with gender-specific types of cancer (breast, gynecological, prostate, and testicle) reported greater anxiety, which was significant at T1 (7.95 vs 7.25,  $t = 2.02, p = .04$ ), and more overall problems in living, which was significant at T2 and T3 (7.31 and 6.54 for gender-specific types of cancer vs 6.80 and 5.43 for non-gender specific types of cancer at T2 and T3, respectively,  $ts > 2.04, ps < .04$ ), compared with those with non-gender specific types of cancer. Emotional problems were greater reported by patients with gender-specific types of cancer at T1 and T3 ( $ts > 2.08, ps < .04$ ) and physical problems at

T2 and T3 ( $ts > 2.60, ps < .01$ ). Education was not significantly related to any of the outcomes examined.

**Linear time effects on anxiety, depression, and problems in living**

Above and beyond the covariate effects (Block 2 of Table 3), linear time effects were significant on all three outcomes: anxiety, depression, and problems in living peaked at T1 to subside as time proceeded (Figure 1). In addition to the significant linear effects, both anxiety and depression had significant quadratic time effects—peaked at T1 to subside significantly at T2, then remaining at similar levels at T3. For types of problems, linear time effects were significant for emotional, family, practical, and spiritual concerns peaked at T1 and subsided as time proceeded. Quadratic time effects were also significant for emotional, physical, and practical problems, which displayed peaks at T1, significantly subsided at T2 and remained at similar levels at T3 ( $F_s > 4.64, ps < .03$ ). While the linear effect of physical problems was not significant, the

**Table 3** Predicting anxiety, depression, and overall problems during cancer treatment (*N* = 548)

	Anxiety			Depression			Overall problems		
	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$
Block 1: covariates									
Education	0.65	.42	.00	0.46	.50	.00	0.00	.99	.00
Marital status	0.56	.45	.00	0.50	.48	.00	4.26	.04	.01
Type of cancer	3.95	.05	.01	0.04	.84	.00	6.66	.01	.01
Block 2: main effect									
Time_linear	270.25	.001	.33	77.30	.001	.13	89.26	.001	.14
Time_quadratic	95.17	.001	.15	6.83	.009	.01	0.87	.35	.00
Age	3.20	.02	.02	1.45	.23	.01	2.20	.09	.01
Gender	3.61	.06	.01	2.55	.11	.01	10.48	.001	.02
Block 3: interaction effects									
Time_linear x age	3.09	.027	.02	0.63	.60	.00	1.90	.13	.01
Time_quadratic x age	0.29	.84	.00	1.48	.22	.01	0.39	.76	.00
Time_linear x gender	2.35	.13	.01	4.87	.03	.01	7.68	.006	.01
Time_quadratic x gender	2.04	.15	.01	0.11	.75	.00	0.24	.63	.00

Education 1 college or more education, 0 less than college education; Marital Status 1 married, 0 other; Type of cancer 1 gender-specific type of cancer (breast, gynecological, prostate, and testicle), 0 non-gender specific type of cancer; Time linear effect Age 1 <40, 2 40~<55, 3 55~<70, 4 >70; Gender 1 female, 0 male

**Table 4** Predicting types of problems during cancer treatment ( $N = 548$ )

	Emotional			Family			Physical			Practical			Spiritual		
	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$	<i>F</i>	<i>p</i>	$\eta^2$
Block 1: covariates															
Education	0.06	.80	.00	0.06	.80	.00	0.03	.87	.00	0.00	.95	.00	0.83	.36	.00
Marital status	1.03	.31	.00	23.98	.001	.04	3.42	.07	.01	0.23	.64	.00	0.00	.96	.00
Type of cancer	5.91	.02	.01	0.17	.68	.00	5.70	.02	.01	1.74	.19	.00	1.34	.25	.00
Block 2: main effect															
Time_linear	211.72	.001	.28	49.04	.001	.08	2.40	.12	.00	28.78	.001	.05	6.34	.01	.01
Time_quadratic	32.62	.001	.06	2.78	.10	.01	9.88	.002	.02	4.64	.03	.01	0.09	.77	.00
Age	1.78	.15	.01	0.80	.50	.00	1.91	.13	.01	6.29	.001	.03	0.36	.78	.00
Gender	7.66	.01	.01	5.05	.03	.01	11.12	.001	.02	0.02	.89	.00	0.02	.88	.00
Block 3: interaction effects															
Time_linear x age	1.71	.16	.01	0.79	.50	.00	2.83	.04	.02	1.87	.13	.01	0.35	.79	.00
Time_quadratic x age	1.35	.26	.01	0.21	.89	.00	0.31	.82	.00	0.11	.96	.00	0.63	.59	.00
Time_linear x gender	2.78	.10	.01	0.06	.81	.00	7.89	.005	.01	0.50	.48	.00	0.12	.73	.00
Time_quadratic x gender	0.10	.76	.00	0.52	.47	.00	0.89	.35	.00	0.09	.77	.00	0.03	.86	.00

Emotional, family, physical, practical, and spiritual are types of problems. Education 1 college or more education, 0 less than college education; Marital status 1 married, 0 other; Type of cancer 1 gender-specific type of cancer (breast, gynecological, prostate, and testicle), 0 non-gender specific type of cancer; Time linear effect; Age 1 <40, 2 40–<55, 3 55–<70, 4 >70; Gender 1 female, 0 male

quadratic effect was significant, displaying elevated levels of physical problems at both T1 and T2, which subsided at T3.

### Roles of age in predicting anxiety, depression, and problems in living over time

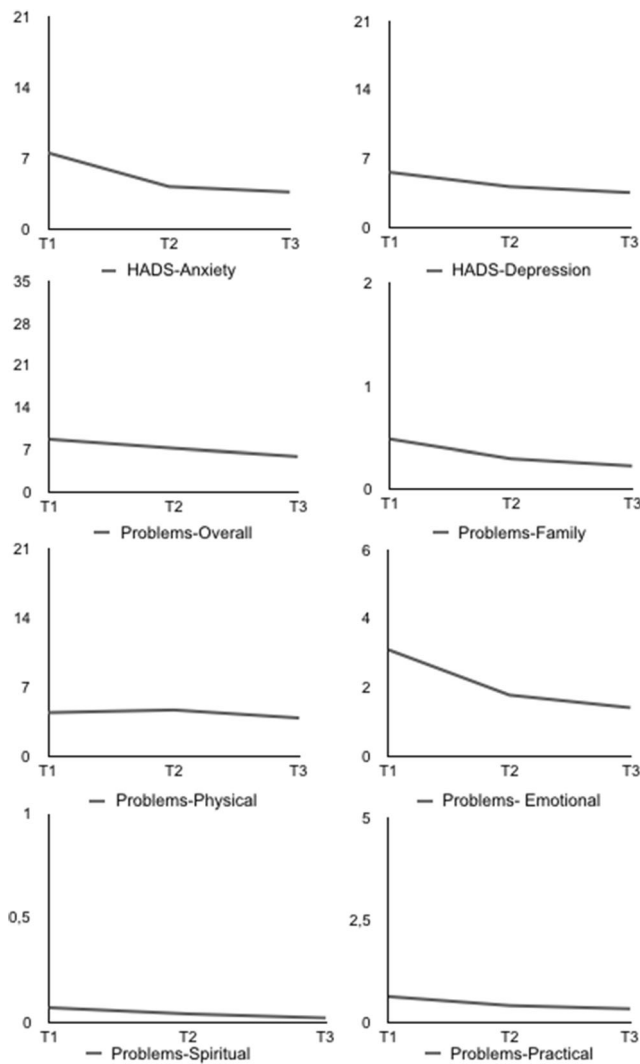
Age was a significant predictor of anxiety, particularly at T1 and T2. Patients who were 40 to 55-years old reported greater levels of anxiety ( $ts > 2.26$ ,  $ps < .03$ ), compared with patients >70-years old. The linear time by age interaction effect was significant on anxiety (Block 3 of Table 3). An ad hoc contrast test revealed that the difference in anxiety between patients who were 40 to 55-years old (8.14, 4.57, and 3.72 at T1 through T3) and those who were 55 and 70 (7.12, 4.02, and 3.53, respectively) reduced significantly as assessment time proceeded ( $F = 3.20$ ,  $p = .02$ , partial  $\eta^2 = .017$ ).

In addition, age was a significant predictor of problems with practical concerns. Patients younger than 55, compared with those 70 and older, reported greater problems with practical concerns at all three assessments ( $ts > 2.19$ ,  $ps < .03$ ). Furthermore, a significant interaction effect of the linear time effect with age on physical problems revealed that the age group differences in physical problems between patients 40 to 55-years old and those 55 to 70 became larger as time proceeded (0.13, 0.52, and 0.69, at T1 through T3) while patients who were 40 to 55-years old reported greater physical problems at all three assessment times (Block 3 of Table 4).

### Roles of gender in predicting anxiety, depression, and problems in living over time

Gender predicted significantly the number of overall problems endorsed and marginally significantly anxiety. Female patients, compared with male patients, reported more overall problems at T1 and T2 ( $ts > 2.93$ ,  $ps < .01$ ) and greater anxiety at T1 ( $t = 2.14$ ,  $p = .03$ ). The linear time by gender interaction effects were also significant on depression and overall problems (Block 3 of Table 3). The gender difference in depressive symptoms was significant at T1 ( $t = 2.18$ ,  $p = .03$ ) and became smaller and insignificant as time proceeded ( $ts = 1.25$  and  $0.28$ ,  $ps = .21$  and  $.78$ , at T2 and T3, respectively). The gender differences in overall problems in living also became smaller as time proceeded: gender differences at T1 and T2 ( $ts = 3.77$  and  $2.93$ ,  $ps = .001$  and  $.004$ , at T1 and T2, respectively) were significant, while that at T3 was not ( $t = 1.24$ ,  $p = .22$ ).

Gender also played a significant role predicting emotional, family, and physical problems. Female patients, compared with male patients, reported greater emotional problems at T1 and T2 ( $ts > 2.03$ ,  $ps < .04$ ), greater family problems at T3 ( $t = 2.39$ ,  $p = .01$ ), and greater physical problems at T1 and T2 ( $ts > 3.13$ ,  $ps < .002$ ). In addition, a significant interaction effect of the linear time effect with gender on physical problems revealed that the gender differences in physical problems became smaller as time proceeded (1.18, 0.96, and 0.23, at T1



**Figure 1** Changes in mean scores of anxiety, depression, and problems in living overtime

through T3) while female patients reported greater physical problems at all times (Block 3 of Table 4).

As the gender differences in overall problems in living were mainly driven by those in physical problems, we conducted a supplementary exploratory factor analysis with the 21 physical items, yielding a two-factor model—activities in daily living (12 problems e.g., getting around, congested nose, eating) and physical symptoms (9 problems: e.g., pain, sexual, nausea). Female patients reported greater problems in both factors at T1 and T2 ( $t_s > 2.22$ ,  $p_s < .03$ ) and marginally so at T3 ( $t_s > 1.77$ ,  $p_s < .09$ ), with slightly more problems reported with activities in daily living (difference scores between genders for problems with activities in daily living were 0.40, 0.62, and 0.25; and those with physical symptoms were 0.36, 0.38, and 0.27, at T1, T2, and T3, respectively).

## Discussion

This prospective, longitudinal study aimed to document levels of anxiety, depression, and problems in living among newly diagnosed cancer patients in Brazil and the changes in these variables at three time points during chemotherapy. The majority of patients reported elevated levels of anxiety and depression and encountered numerous problems in daily living at T1. Their levels of anxiety and depression were higher than those from a non-clinical sample [28] but comparable to those of cancer patients in North America and Northwest Europe [1–3]. Brazilian patients, however, reported greater problems in living than those in North America [5] at T1. Our findings support the view that cancer diagnosis and treatment is a major stressor that brings up substantial psychological turmoil [1, 2]. The findings extend current knowledge by documenting elevated levels of distress among newly and recently diagnosed cancer patients in South America. Furthermore, the findings highlight the need for psychosocial interventions that target helping patients cope with the psychological turmoil and problems in daily living brought up by cancer.

The second aim of the study was to test the effects of assessment time, age, and gender on changes in anxiety, depression, and problems in living. Our findings revealed that while anxiety subsided substantially by T2, both depression and problems in living did so only by T3. The majority of patients in our study displayed resilience by returning to normative levels of distress by T3, which supports our hypothesis 1 (anxiety, depression, and problems in living would peak in the beginning of treatment and subside by completion of treatment) and the general human tendency of adaptation to stressful events [29, 30]. Time alone likely plays a role in reduced distress, as the natural passage of time can lead to better adjustment.

Our findings also showed that both depression and physical problems remained elevated by T2, whereas anxiety and other types of problems in living subsided by that time. We speculate that depression and problems in living may be more closely related to the presence of side effects that is common while receiving treatment, than anxiety may be related to. Further studies should explore this relationship. Findings suggest that different timing of introducing interventions targeting different types of distress would be efficient. Future studies are also needed to test the degree to which the resilience seen in our sample during a relatively brief time window of the treatment phase would be extended for a longer period such as to the long-term survivorship phase.

An additional contribution of our findings is identifying subgroups of cancer patients who are vulnerable to distress and problems in living. We hypothesized that younger and female patients would report greater levels of anxiety, depression, and problems in living (hypothesis 2), which would be most prominent at T1 (hypothesis 3). Providing partial support

for hypotheses 2 and 3 regarding age, our findings showed that patients between 40 and 55-years old (mid-aged) were more likely to report greater levels of anxiety and practical problems, compared with those 70 and older, throughout the treatment phase but more prominently around the time of diagnosis and treatment's beginning. This is perhaps because mid-aged patients are still involved in managing multiple social roles and responsibilities, thus experiencing more disruptions in daily life by their cancer diagnosis and treatment, yet are unfamiliar with seeking health services and navigating healthcare systems for cancer. Findings suggest that developing interventions targeting mid-aged cancer patients that aim to mitigate anxiety, practical, and physical concerns would be warranted.

Our findings also showed that female patients reported greater emotional, family, and physical problems than male patients, providing again partial support for hypothesis 2, and the gender differences in depression and overall problems in living became smaller as time proceeded, supporting hypothesis 3. Our supplementary analysis with physical problems, which formed groups of activities in daily living and physical symptoms, showed that female patients' greater physical problems were not limited to a certain sub-group of physical domains. The findings rule out the possibility that greater physical problems in female patients might be attributed to menopausal symptoms [31], or are natural or cancer-treatment driven. The findings may rather reflect the fact that Brazil has traditionally been a patriarchal society where men in general have power and resources over women [32]. Beyond the gender inequality issues, as emotional and physical problems have been hallmarks of poor cancer treatment outcomes [6] and family is often central to women's self-identity, gender-based psycho-oncology interventions tailored to address specific concerns of the targeted subgroup would be a good practice towards precision medicine.

Limitations of this study should be noted, including that data were collected only from patients who were receiving chemotherapy; thus, generalizability of findings to other types of treatment is limited. The assessment time points were anchored by planned treatment schedules, and patients' actual treatment schedule could differ from planned due to various complications during the course of treatment. There were also differences in participants who provided incomplete data including older age, more likely to be male, diagnosed with non-gender specific cancer; and thus, generalizability may be limited. Those with incomplete data also reported higher distress, which could also reflect selection bias, but also may suggest higher risk patients were excluded. The study was conducted in a Brazilian private cancer center, where patients were more affluent and educated than those in public hospitals; thus, generalizability of current findings on those dimensions is limited. Finally, relevant sociocultural factors were not measured. Future studies examining those factors particularly

pertinent to Brazilian, such as machismo (strong sense of masculine pride) and marianismo (submissiveness and selflessness as the ideal female gender role), in cancer patients' adjustment outcomes would be fruitful.

Despite these limitations, this is to our knowledge one of the first large, prospective, longitudinal studies investigating distress in cancer patients in Brazil. Our findings suggest that for many patients, there is distress relief and adaptive coping over time. Therefore, clinically, these patients who experience natural course relief may not need supportive care intervention. However, our findings also indicate that specific subgroups of cancer patients—namely mid-aged (40–55-years old) and female patients—are at risk for elevated distress during cancer treatment. Thus, these at risk patients should be considered for early interventions that aim to facilitate adaptive coping processes to address anxiety, depression, and problems in living during and following cancer treatment.

Our investigation reveals that future distress and functional wellbeing studies and clinical care practice should attend to both distress (i.e., level and type) and vulnerable subgroups at risk for poorer outcomes. In addition, future research and practice may consider other appropriate healthcare factors that may influence patient outcomes including medical communication and treatment setting. As cancer diagnoses and expected deaths in Brazil continue to rise, it is important to increase the research to inform evidenced-based supportive care practice to enhance patient outcomes.

Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

We have full control of all primary data and we agree to allow the journal to review our data if requested.

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