Dyadic Study of Cancer Patients & Caregivers: Depressive Symptoms and Stress Biomarkers

Kelly M. Shaffer, Armando Mendez, Maria L. Llabre, Michael Antoni, Neil Schneiderman, Stephany Giraldo, & Youngmee Kim

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Dyadic Study of Cancer Patients & Caregivers: Stress Biomarkers and Depressive Symptoms

**PAPER 1**

Dyadic Study of Cancer Patients’ and Caregivers’ Depressive Symptoms with their Own and their Partners’ Inflammation and Endocrine Functioning

**PAPER 2**

Cancer Patients’ and their Caregivers’ Stress Biomarkers are Positively Related at the Early Phase of Survivorship
Support

- Shaffer: NCI NRSA F31 CA189431-01A1
- Kim: ACS 121909-RSG-12-042-01-CPPB
Background
Stress

Physiological Response

Cancer

Depressive Symptoms

- Inflammation
  - Interleukin-6
  - C-Reactive Protein

- HPA axis
  - Diurnal cortisol variation

Figure from: Miller et al., 2008
Stress

Physiological Response

Cancer

Depressive Symptoms

THE METABOLIC SYNDROME

HEART DISEASE  LIPID PROBLEMS  HYPERTENSION  TYPE 2 DIABETES

Figure from: Grivennikov et al., 2010
• 3 million cancer caregiver in 2015\(^1\)
• Provide care an average of 9 hours per day\(^2\)
• 35-40% clinically significant depressive symptoms\(^3-4\)

1 National Alliance for Caregiving, 2015; 2 Kim & Spillers, 2010; 3 Braun et al., 2007; 4 Rhee et al., 2008;
• Elevated inflammation:
  - Hyperinflammatory response to stress\(^1\)
  - Linear rise in CRP\(^2\)
  - Flatter cortisol slope\(^1\)
  - Greater risk for stroke and cardiovascular diseases\(^3\)

\(^1\) Miller et al., 2002; \(^2\) Rohleder et al., 2009; \(^3\) Ji et al., 2012
Stress
Depressive Symptoms
Physiological Response

Cancer
Stress
Physiological Response

Patient

Depressive Symptoms

Stress
Physiological Response
Disease

Caregiver

Antoni et al., 2006; 2 Spiegel & Giese-Davis, 2003
3 Miller et al., 2002; 4 Rohleder et al., 2009; 5 Ji et al., 2012
6 Hagedoorn et al., 2008; 7 Hodges et al., 2005
8 Kim et al., 2014; 9 Beach et al., 2005
Actor Partner Interdependence Model

- **Patient Depressive Symptoms**
- **Depressive Symptoms**
- **Patient Stress Biomarkers**
- **Physiological Response**
- **Caregiver Stress Biomarkers**

**Actor Effect**

**Partner Effect**
Actor Partner Interdependence Model

Paper 1

Patient Stress Biomarkers

Patient Depressive Symptoms

Caregiver Depressive Symptoms

Caregiver Stress Biomarkers

Paper 2
Dyadic Study of Cancer Patients’ and Caregivers’ Depressive Symptoms with their Own and their Partners’ Inflammation and Endocrine Functioning

PAPER 1
Participants

PATIENTS
- > 21 years old
- English or Spanish
- Dx colon or rectal cancer
  - Stage I through V
  - Past 3 months
- Have a family-like individual assisting with their care

$N_{pt} = 84$

CAREGIVERS
- > 21 years old
- Non-Hispanic White, Black, or Hispanic
- English or Spanish
- Providing support to the cancer patient

$N_{cg} = 86$
# Measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measured Via</th>
<th>Processed Via</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive Symptoms</td>
<td>Center for Epidemiological Studies-Depression</td>
<td>Self-report</td>
<td>Sum score after reverse coding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cronbach $\alpha = .82-.90$</td>
</tr>
</tbody>
</table>

1 Sephton et al., 2000; 2 Smyth et al., 1997; 3 Turner-Cobb et al., 2000; 4 Kraemer et al., 2005;
5 Nicholson, 2008; 6 Sephton et al., 2000
## Descriptives: Covariates

<table>
<thead>
<tr>
<th>Descriptive</th>
<th></th>
<th>Patient</th>
<th>Caregiver</th>
<th>Paired $t / \chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-</td>
<td>54.20 (9.88)</td>
<td>50.70 (14.43)</td>
<td>2.08*</td>
</tr>
<tr>
<td>BMI</td>
<td>-</td>
<td>26.28 (6.12)</td>
<td>28.30 (6.93)</td>
<td>-1.68†</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>57%</td>
<td>73%</td>
<td>4.87*</td>
</tr>
</tbody>
</table>

* $p < .05$  † $p < .10$
Descriptives: Depressive Symptoms and Stress Biomarkers

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Caregiver</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>CES-D</td>
<td>13.24 (8.03)</td>
<td>15.31 (11.02)</td>
<td>Both samples &gt; prior studies&lt;sup&gt;1-3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> Cohen et al., 2012; <sup>2</sup> Kurtz et al., 2004; <sup>3</sup> Rohleder et al., 2009; <sup>4</sup> Dymicka-Piekarska et al., 2007; <sup>5</sup> Kaminska et al., 2005; <sup>6</sup> von Känel et al., 2006; <sup>7</sup> Gimeno et al., 2009; <sup>8</sup> Sephton et al., 2013; <sup>9</sup> Turner-Cobb et al., 2000; <sup>10</sup> Kraemer et al., 2006
Paper 1: Bivariate Results

- Patient and caregiver depressive symptoms $r = .06$

<table>
<thead>
<tr>
<th></th>
<th>Own Depressive Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient IL-6</td>
<td>.08</td>
</tr>
<tr>
<td>Patient CRP</td>
<td>.02</td>
</tr>
<tr>
<td>Patient Cortisol Slope</td>
<td>.04</td>
</tr>
</tbody>
</table>

No significant associations between patients’ and caregivers’ depressive symptoms with own or partner stress biomarkers
Paper 1: Dyadic Results

- Patient age, gender, BMI, treatment, stage
- Patient Depressive Symptoms
- Caregiver Depressive Symptoms
- Caregiver age, gender, BMI
- Pt Stress Biomarker
- Cg Stress Biomarker

Relationships indicated with arrows and symbols:
- $e_1$
- $e_2$

Crossed arrows indicate no significant relationship.
Paper 1

conclusions
Timing of data collection during acute diagnosis/treatment phase

Elevated depressive symptoms in both samples warrant (individualized) intervention

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#### Report Clinically Significant Depressive Symptoms (CESD>16)

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Caregivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>28%</td>
<td>38%</td>
</tr>
</tbody>
</table>

Figure from: Tuinstra et al., 2004
**Howren et al., 2009**

Patient Stress Biomarkers

Caregiver Stress Biomarkers

Patient Depressive Symptoms

Caregiver Depressive Symptoms

<table>
<thead>
<tr>
<th>Analysis</th>
<th>IL-6 Effect Size</th>
<th>CRP Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI Adjusted</td>
<td>0.08**</td>
<td>0.11***</td>
</tr>
<tr>
<td>BMI Unadjusted</td>
<td>0.50***</td>
<td>0.32***</td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td>0.08**</td>
<td>0.12***</td>
</tr>
<tr>
<td>Clinical interview</td>
<td>0.52***</td>
<td>0.26***</td>
</tr>
<tr>
<td><strong>Community sample</strong></td>
<td>0.09**</td>
<td>0.11***</td>
</tr>
<tr>
<td>Clinical sample</td>
<td>0.71***</td>
<td>0.40***</td>
</tr>
</tbody>
</table>

** p < .01      *** p < .001

Patients: .04
Caregivers: .07

Patients: .08
Caregivers: .12
Salivary Cortisol (nmol/L)

IL-6 (pg/mL)

Pre-Surgery

Caregivers
Controls

IL-6 (pg/mL)

CRP (mg/L)

~ month f/u  12 month f/u

Time (weeks)
Future Directions

- Alternative psychosocial correlates/predictors
- Moderating factors

Diagram:
- Patient’s Disease
- Physiological Response
- Caregiving Stress
- Social Support
- Patient Stress
- Physiological Response
- Caregiver Disease
- SES
- Shared Social Environment
- Culture

Relationship Factors
Cancer Patients’ and their Caregivers’ Stress Biomarkers are Positively Related at the Early Phase of Survivorship

PAPER 2
• Inflammation
• Interleukin-6
• C-Reactive Protein

• HPA axis
• Diurnal cortisol variation

Figure from: Miller et al., 2008
Stress → Depressive Symptoms → Physiological Response → Disease

Figure from: Grivennikov et al., 2010

THE METABOLIC SYNDROME
- Heart Disease
- Lipid Problems
- Hypertension
- Type 2 Diabetes
Cancer

Stress

Physiological Response

Stress

Physiological Response

Disease

Beach et al., 2005; Hagedoorn et al., 2008; Hodges et al., 2005; Kim et al., 2014; Shaffer et al., 2015
Participants

**PATIENTS**
- > 21 years old
- English or Spanish
- Dx colon or rectal cancer
  - Stage I through V
  - Past 3 months
- Family-like individual assisting with care

**CAREGIVERS**
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\[N_{pt} = 84 \quad N_{dyads} = 81 \quad N_{cg} = 86\]
# Measures

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<tr>
<th>Variable</th>
<th>Measured Via</th>
<th>Processed Via</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6</td>
<td>Blood Sample</td>
<td>R&amp;D Systems Quantikine ELISA kit</td>
<td>Natural log transformed</td>
</tr>
<tr>
<td>CRP</td>
<td>Blood Sample</td>
<td>High-sensitivity Luminex 200 xMap</td>
<td>Natural log transformed</td>
</tr>
<tr>
<td>Cortisol Slope</td>
<td>Salivettes from waking, afternoon, &amp; evening (2 days)</td>
<td>Chemiluminescence immunoassay</td>
<td>Natural log transformed Cortisol’ = (cortisol slope)(time) + error</td>
</tr>
</tbody>
</table>

**Covariates:**

- Patients – age, BMI, gender, treatment status, cancer stage, own & partner depressive sx
- Caregivers – age, BMI, gender, own & partner depressive sx

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1 Sephton et al., 2000; 2 Smyth et al., 1997; 3 Turner-Cobb et al., 2000; 4 Kraemer et al., 2005; 5 Nicholson, 2008; 6 Sephton et al., 2000
## Descriptives: Stress Biomarkers

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Patient</th>
<th>Caregiver</th>
<th>Paired t</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 pg/mL</td>
<td>3.14 (2.56)</td>
<td>1.83 (1.71)</td>
<td>4.21***</td>
<td>Both samples ≈ prior studies\textsuperscript{1-4}</td>
</tr>
<tr>
<td>CRP mg/L</td>
<td>6.49 (11.56)</td>
<td>3.60 (4.71)</td>
<td>1.83†</td>
<td>Patients &lt; prior studies\textsuperscript{2}</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Caregivers ≥ prior studies\textsuperscript{1,4-3}</td>
</tr>
<tr>
<td>Cortisol Slope μg/dL/hour</td>
<td>-0.09 (0.06)</td>
<td>-0.12 (0.07)</td>
<td>1.37</td>
<td>Both samples ≈ prior studies\textsuperscript{6-8}</td>
</tr>
</tbody>
</table>

\[ \text{† } p < .10 \quad \text{*** } p < .001 \]

\textsuperscript{1} Rohleder et al., 2009; \textsuperscript{2} Dymicka-Piekarska et al., 2007; \textsuperscript{3} Kaminska et al., 2005; \textsuperscript{4} von Känel et al., 2006; \textsuperscript{5} Gimeno et al., 2009; \textsuperscript{6} Sephton et al., 2013; \textsuperscript{7} Turner-Cobb et al., 2000; \textsuperscript{8} Kraemer et al., 2006
### Paper 2: Bivariate Results

<table>
<thead>
<tr>
<th></th>
<th>Pt IL-6</th>
<th>Pt CRP</th>
<th>Pt Cort Slope</th>
<th>Cg IL-6</th>
<th>Cg CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient CRP</td>
<td>.70**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Cortisol Slope</td>
<td>.32*</td>
<td>.35*</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver IL-6</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>.80***</td>
</tr>
<tr>
<td>Caregiver CRP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Caregiver Cortisol Slope</td>
<td>.23†</td>
<td>.20</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† $p < .10$  * $p < .05$  ** $p < .01$  *** $p < .001$

Small-to-moderate correlation in stress biomarkers between patients and their caregivers.
Paper 2: Multivariate Results

- Patient age, gender, BMI, treatment, stage
- Patient Depressive Symptoms
- Caregiver Depressive Symptoms
- Caregiver age, gender, BMI
- Pt Stress Biomarker
- Cg Stress Biomarker
- $e_1$
- $e_2$
Paper 2
conclusions
- Shared risk factors & cross-over effects
- Dyadic health-promotion interventions
- Future use of dyadic framework warranted
Future Directions

Cross-sectional → Longitudinal

Diagnosis

Figures from: Berg & Upchurch, 2007; Currier & Nemeroff, 2014
Thank you!

Youngmee Kim, Ph.D.

Stephanie Giraldo, M.P.H.

Armando Mendez, Ph.D.

Maria L. Llabre, Ph.D.

Michael Antoni, Ph.D.

Neil Schneiderman, Ph.D.

& many wonderful research assistants of the FAMILY Lab

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