Duke University School of Nursing

Symptom Research in Children with Cancer: One Researcher's Journey

1994 → 2016

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Objectives

1. Share the journey of the last 22 years exploring symptoms experienced by children and adolescents during cancer treatment.
2. Describe oxidative stress measures that reflect the severity of cancer treatment symptoms.
3. Discuss future directions for continued symptom exploration.

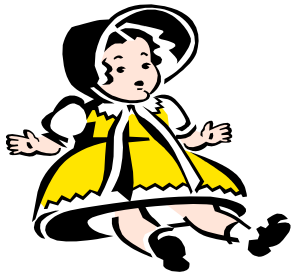
The Journey
Searching for Evidence

- Resilience and Vulnerability
- Protective Factors
- Cancer Treatment Stressors
- Fatigue
- Sleep
- Depression
- Anemia
- Symptom Clusters
- CNS Toxicity
- CNS Tissue Injury
- Neurocognitive Function
- Measures of CNS Toxicity
  - Phospholipids
  - Fatty Acids
  - Genetic Polymorphisms
- Math Interventions

The Evidence: Vulnerability and Resiliency in Children

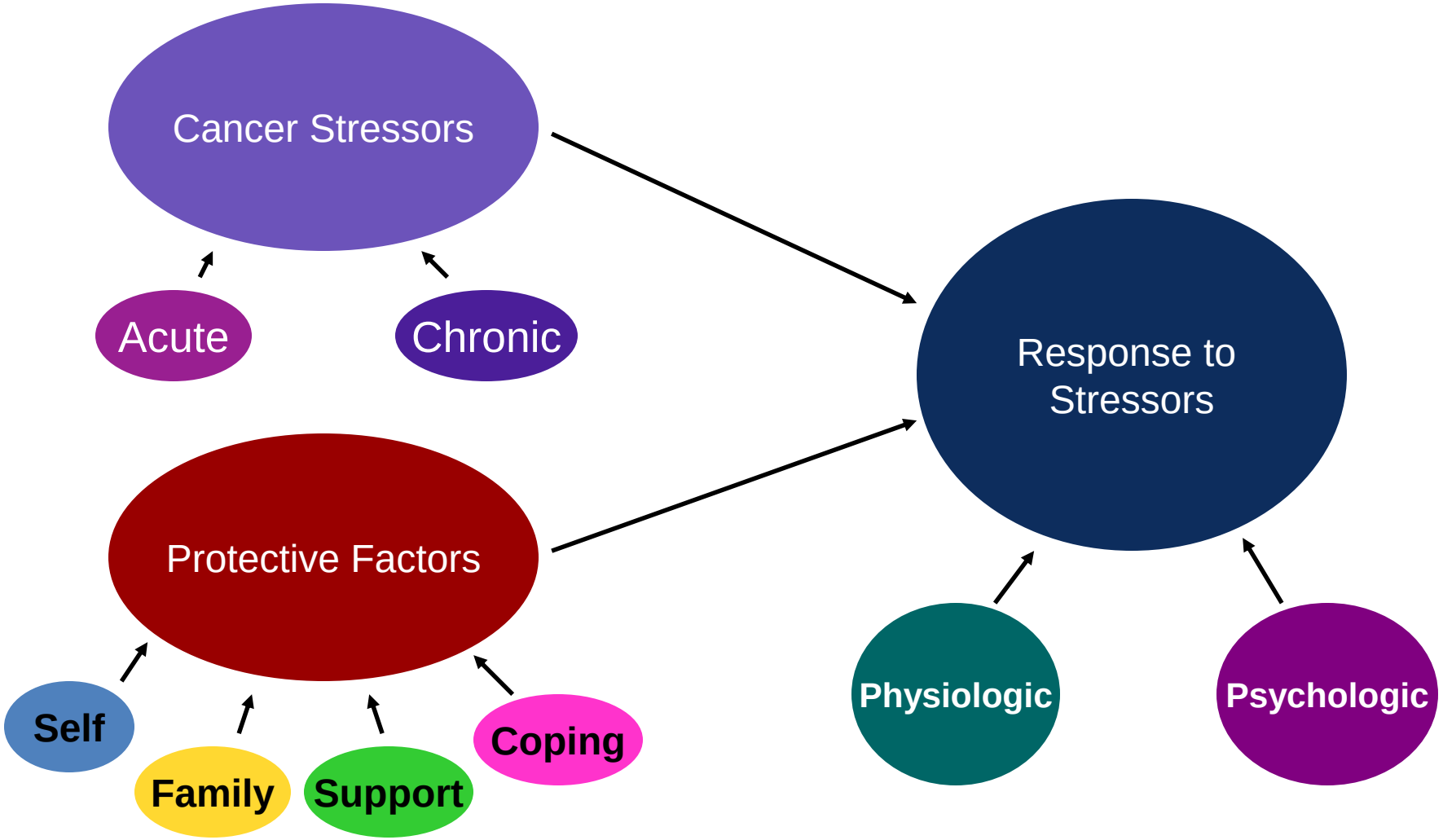
- Resilience acquired through competencies in the individual, family and environment
- Resilience is a process of overcoming adversity
- Vulnerability- risk of attack or damage
  - The “glass doll” analogy

Anthony and Koupernick, 1974

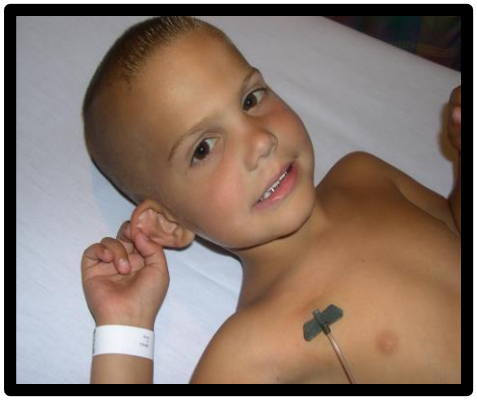


Protective Factors and Stressors Experienced by Children with Cancer

Hockenberry, Kemp, DiIorio, 1994



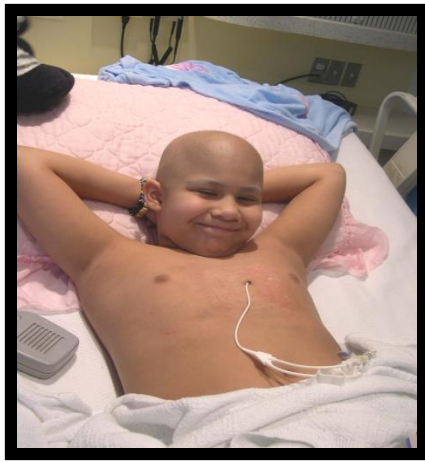
Childhood Cancer Stressors



Cancer Stressors

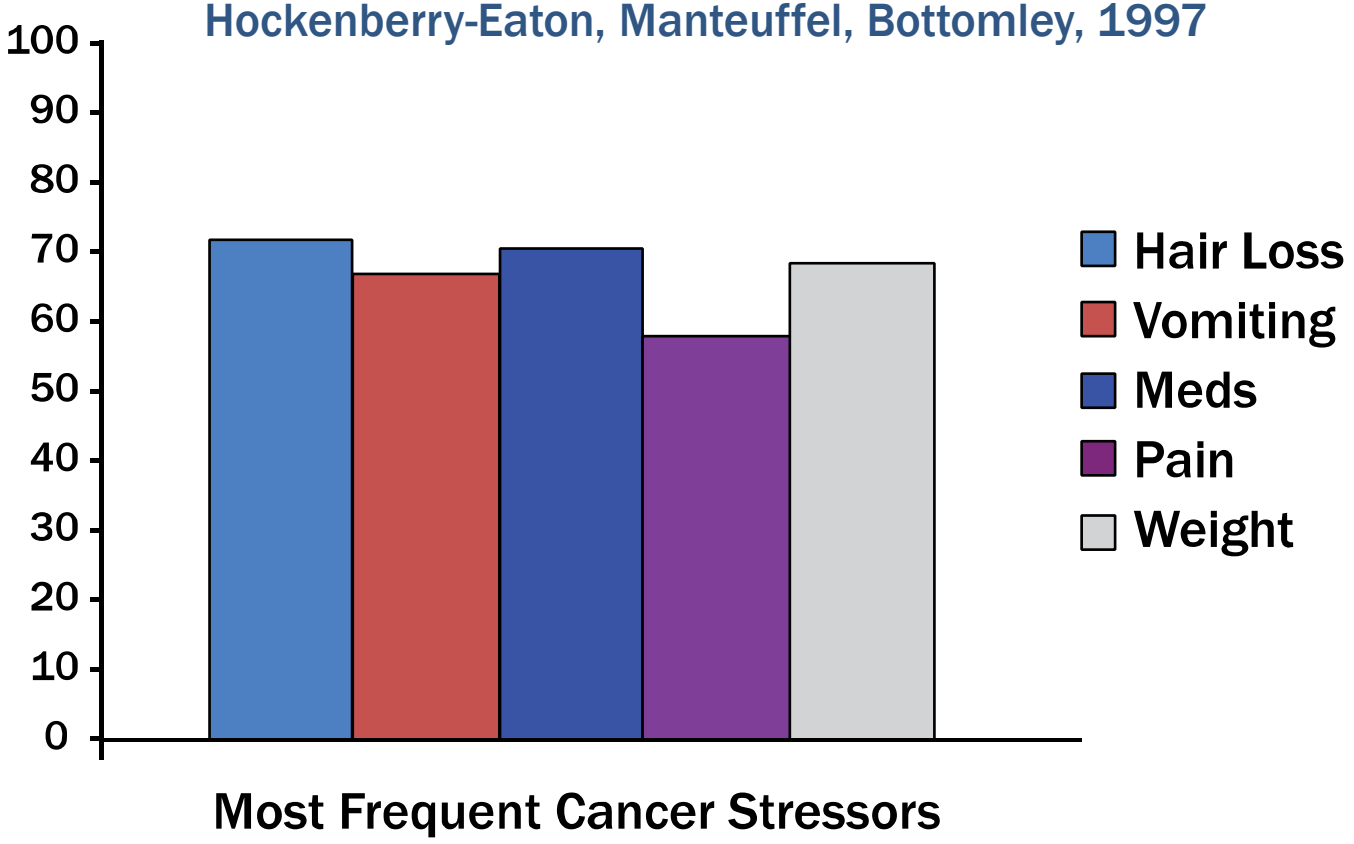
Acute

Chronic



Childhood Cancer Stressors in Children with Cancer

Hockenberry-Eaton, Manteuffel, Bottomley, 1997



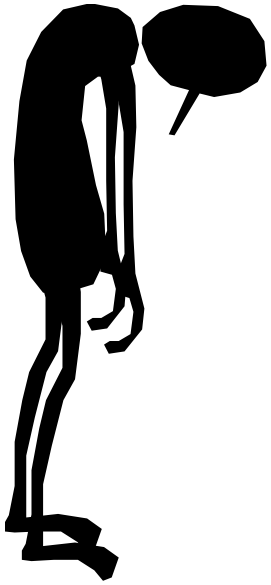
The Evidence: Childhood Cancer Stressors: Physical Symptoms

- Physical Stressors associated with childhood cancer
  - Tired
  - Nausea and vomiting
  - Sleep changes
  - Hair loss

Fatigue in Children with Cancer

- Established fatigue as a significant symptom in children with cancer through qualitative and quantitative research designs
- Identified the need to measure fatigue in children with cancer

ONS FIRE grant, 1996- Hockenberry and Hinds

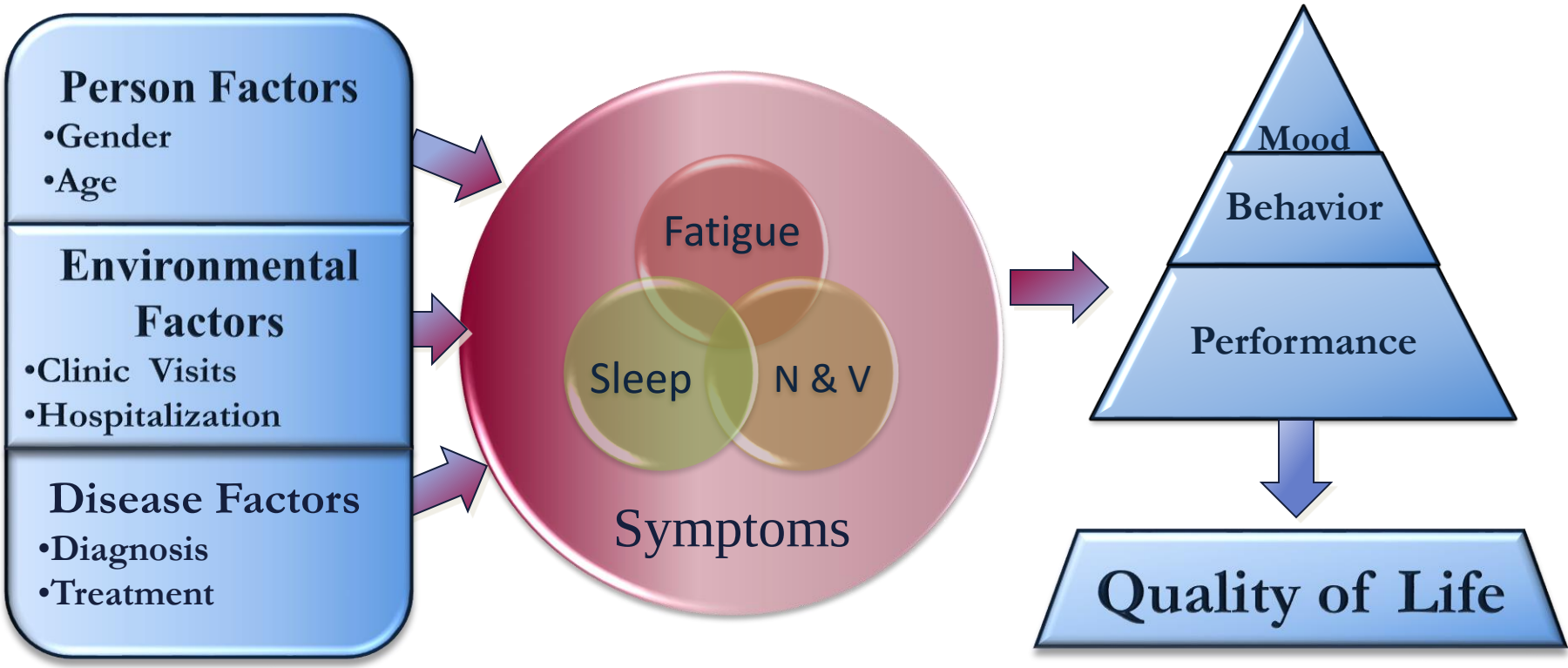


The Evidence: Factors Associated with Fatigue

- Sleep disturbances
- Medications
- Nausea and Vomiting
- Hospital Environment
- Mood
- Treatment phase
- Disease status

Childhood Cancer Symptoms Model

Adapted from Armstrong, 2003; Dodd and Others 2001; Hockenberry and Others, 1999; 2000



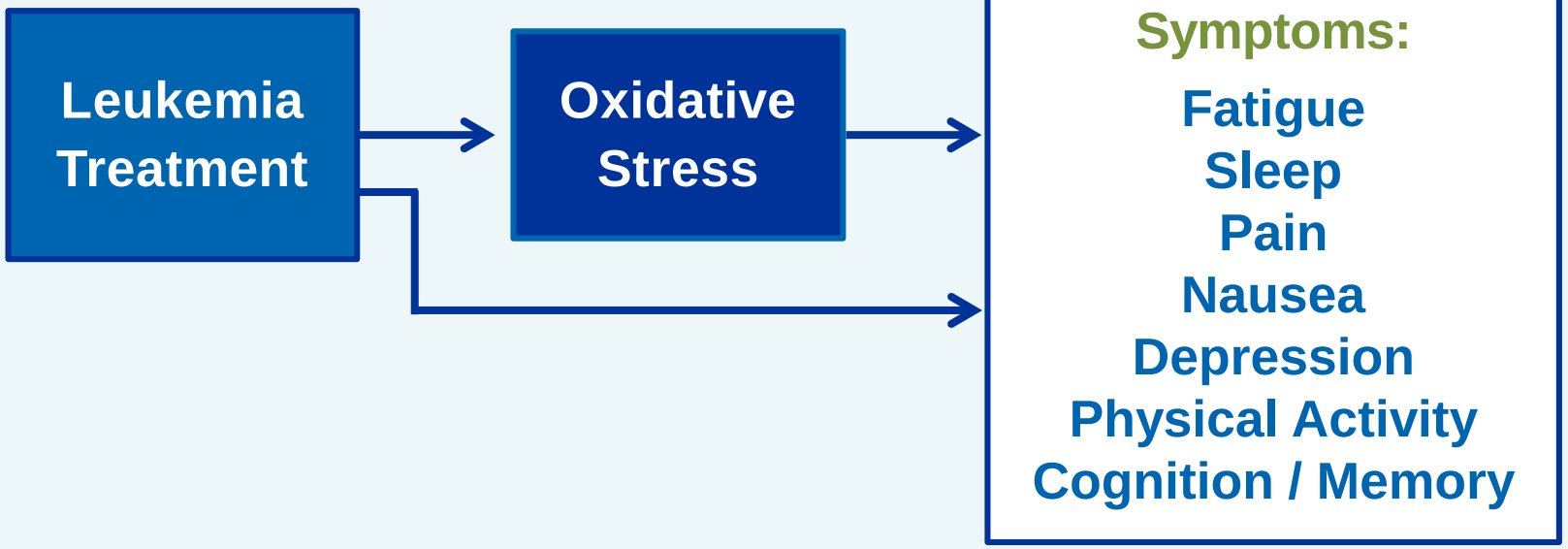
Exploring Symptom Trajectories

- Explore the symptom trajectory in children during their first 16 months of childhood leukemia treatment.
- Explore the influence of the oxidative stress pathway on symptom occurrence, severity, and distress during this time period, using F_2-Iso-P in children's CSF to measure oxidative stress levels.

Children with cancer experience multiple symptoms resulting from the disease and its treatment. The oxidative stress pathway may play a role because:

1) High oxidative stress increases risk of cellular and tissue damage
2) Chemotherapy administered in the course of treatment promotes formation of reactive oxygen species and increases the level of oxidative stress
3) Damage occurs and leads directly or indirectly to development and/or exacerbation of chemotherapy-related symptoms

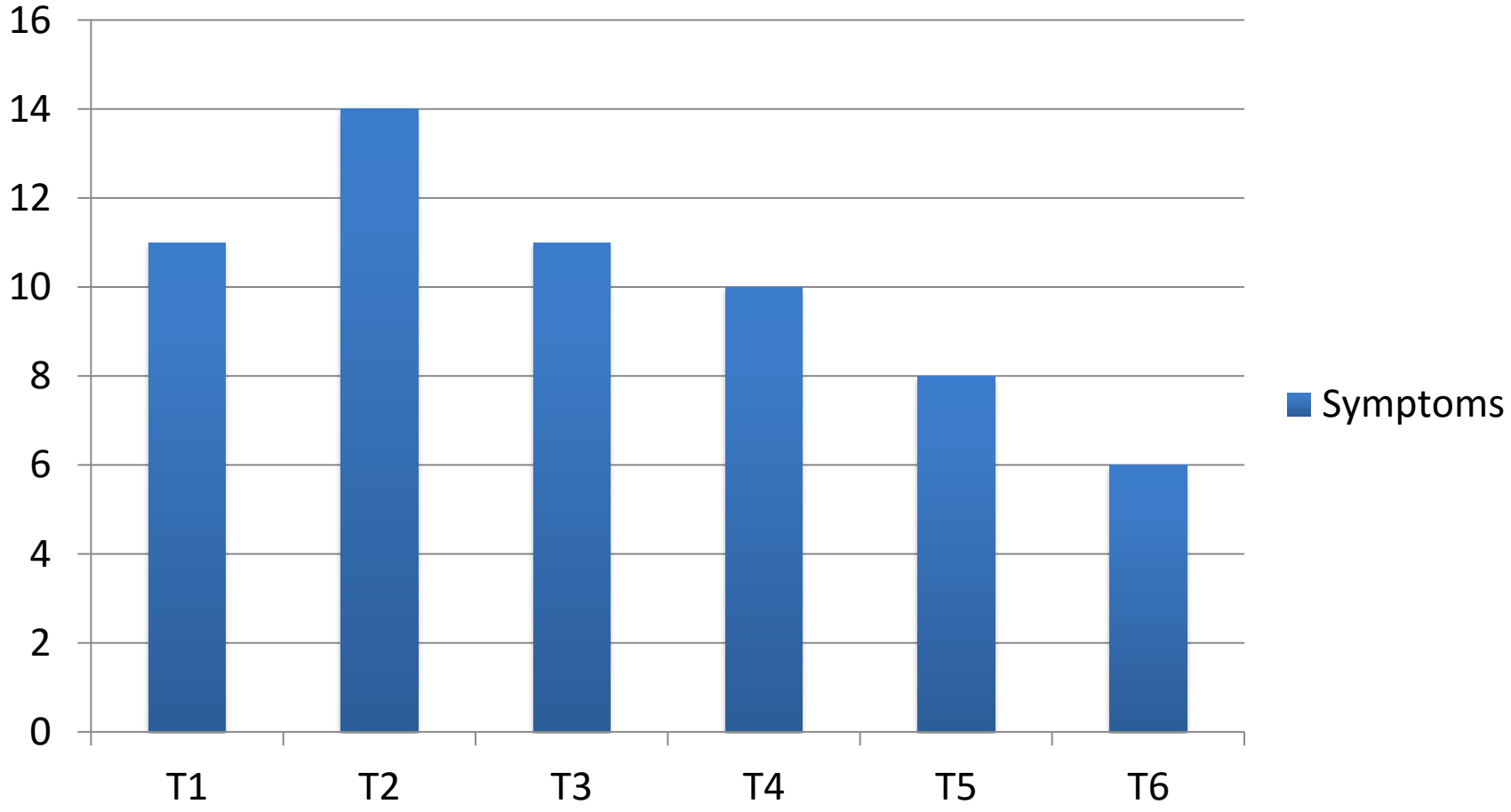
Oxidative Stress Pathway and Symptom Distress



During all 6 time periods, the most frequently reported symptoms (occurred in >30% of the children) were: lack of energy, pain, being irritable, nausea, feeling nervous, lack of appetite, difficulty

Time Period	Mean # of Days from Diagnosis	# Sx Reported in >30% of Children	Comments
1	45	11	Reported in >50% of children: hair loss, lack of energy, pain, being irritable, sweats, and feeling of sadness
2	142	14	Symptoms more frequent than in T1: nausea, lack of appetite, weight loss, changes in food tastes, vomiting, mouth sores, feeling nervous, difficulty concentrating, cough
3 - 5	241 to 424	11, then 10, then 8	# of symptoms decreased over time
6	510	6	The 6 symptoms were: cough, lack of appetite, being irritable, difficulty concentrating, difficulty sleeping, pain

Trajectory of Symptoms over Leukemia Treatment



F_2-ISOPROSTANES AND SYMPTOMS

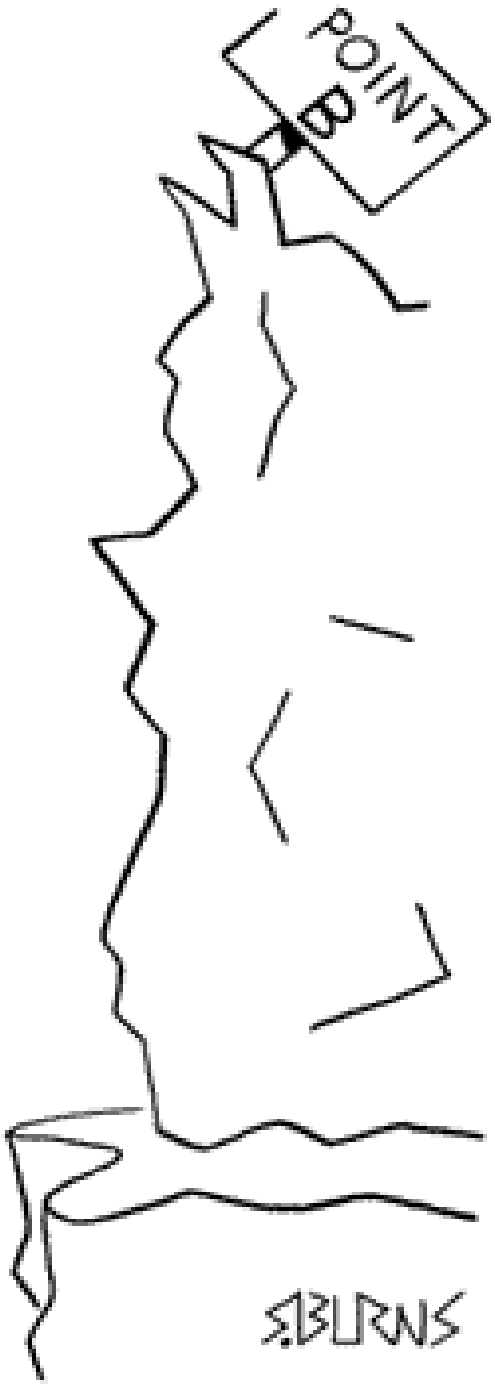
- **F_2-Iso-P and Symptoms: Post-Induction Phase of Chemotherapy**
  - The highest F_2-Iso-P concentration during post-induction (at Time 3) was significantly correlated with total number of symptoms ($r = 0.528$; $p = 0.035$) and with mean symptom severity ($r = 0.661$; $p = 0.005$).
  - The highest F_2-Iso-P concentration during post-induction (at Time 3) was correlated with mean symptom distress at trend level ($r = 0.471$; $p = 0.066$).

RESULTS: F_2-ISOPROSTANES AND SYMPTOMS

- **F_2-Iso-P and Symptoms: Continuation Phase of Chemotherapy**
  - The highest F_2-Iso-P concentration of during continuation was significantly correlated with total number of symptoms at Time 5 ($r = 0.516$; $p = 0.041$) and at Time 6 ($r = 0.526$; $p = 0.036$).

This work is the first to reflect symptom trajectory changes over 16 months of childhood leukemia treatment and examine the influence of the oxidative stress pathway on symptom frequency, severity and distress.

Our findings contribute to the evidence that pediatric leukemia chemotherapy drugs can trigger reactive oxygen species (ROS) production as byproducts of cellular destruction.



The Journey Continues

- Combining what we know about oxidative stress and symptom severity and clusters into a currently funded grant
- Associating symptom severity with level of oxidative stress and presence of genetic variations in children with ALL
- Exploring genetic variations associated with the oxidative stress and inflammatory pathways