

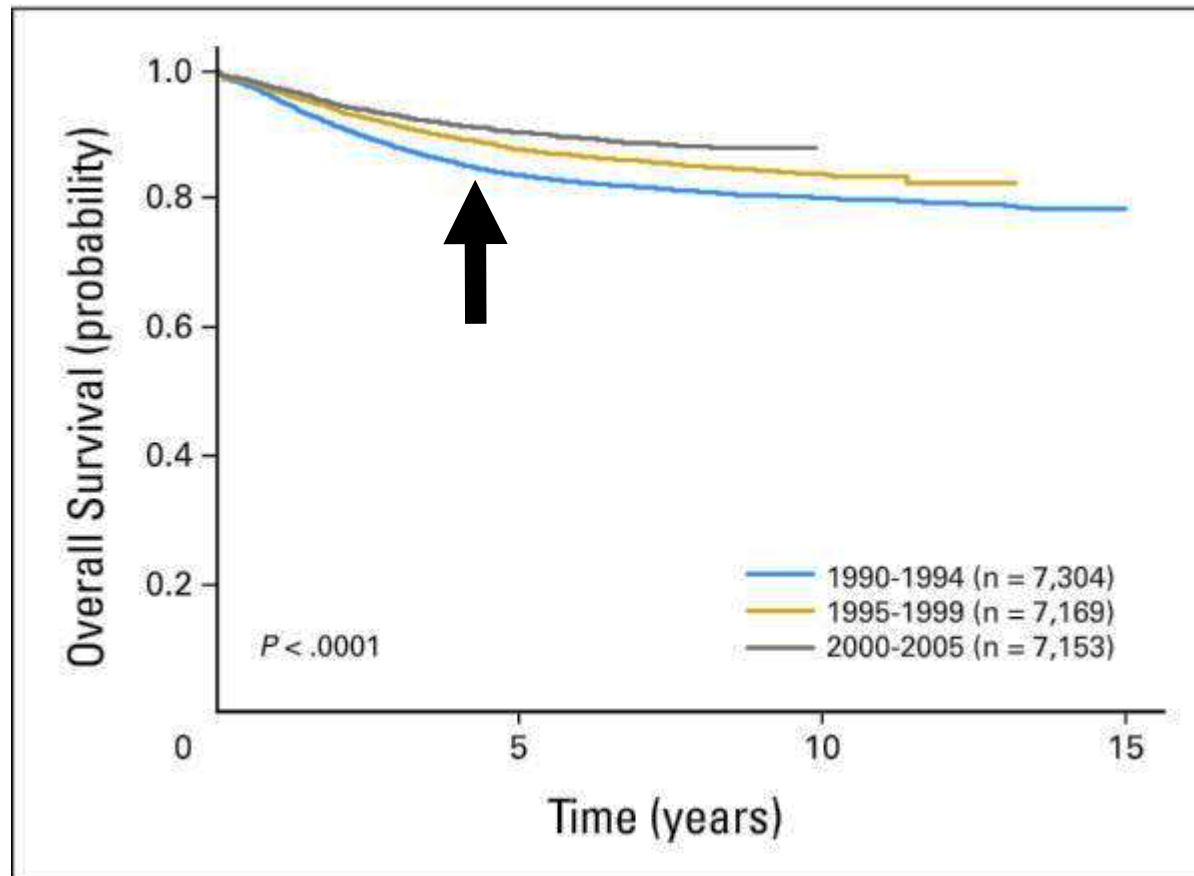
Managing Behavioral Changes During Treatment for Acute Lymphoblastic Leukemia (ALL)

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November 4, 2016



How *should* we measure outcomes?



Hunger et al., Journal of Clinical Oncology, 2012

Overview

- Results of multi-site prospective study
- Interventions
- Future directions

Design

- 31 sites in the U.S. and Australia
- Prospective and longitudinal
- Ancillary study within frontline therapeutic trial
- Parent surveys at 4 time points
- 170 patients enrolled

**CHILDREN'S
ONCOLOGY
GROUP**

The world's childhood cancer experts

OUR MISSION

To cure and prevent childhood and adolescent cancer through scientific discovery and compassionate care.



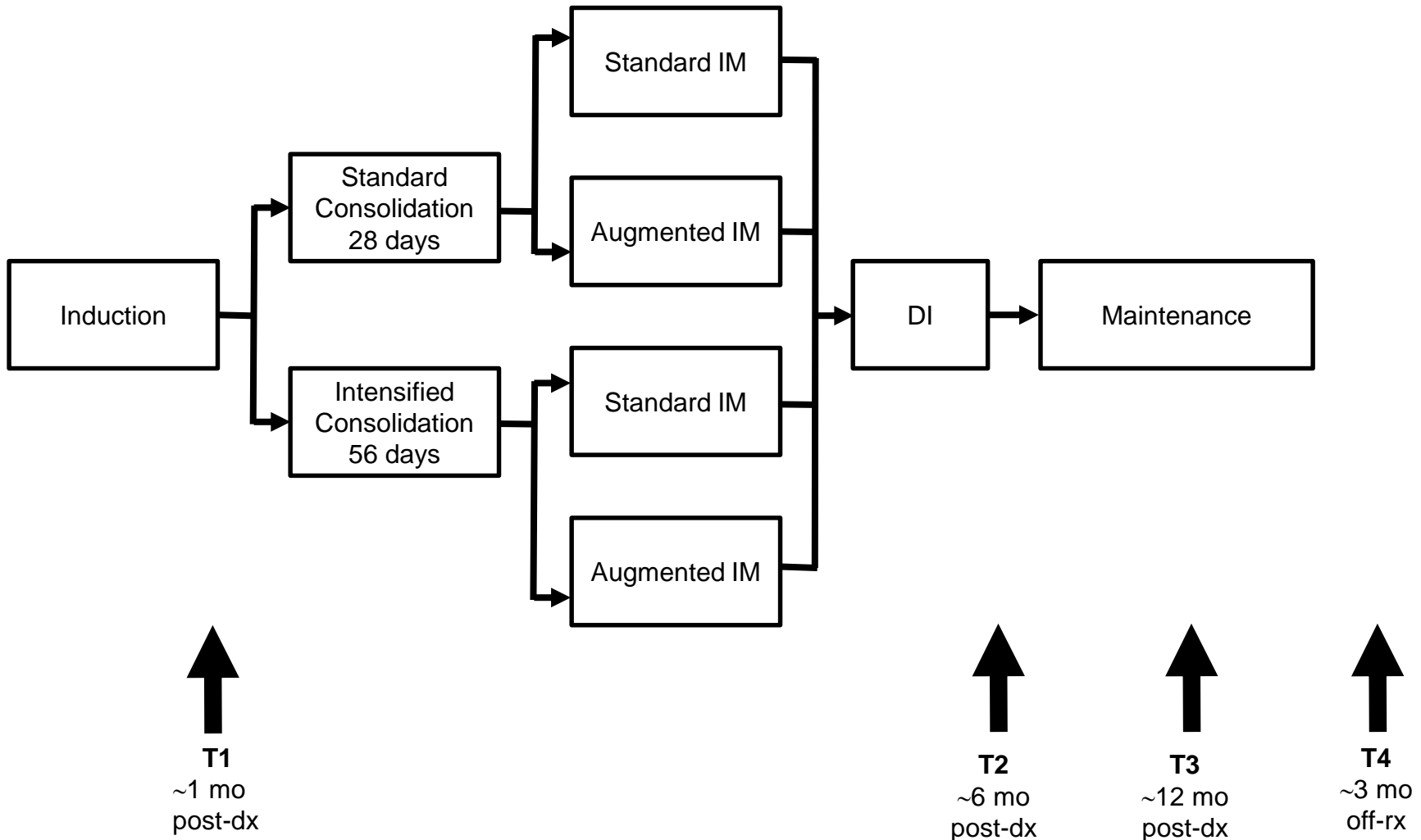
Eligibility

- Diagnosis of standard risk ALL
- Enrolled on COG AALL0331 at participating site
- Age at diagnosis 2.0-9.9 years
- Parent literate in English or Spanish

AIMS

- Determine how health-related quality of life (HRQOL) outcomes in children with ALL vary during therapy
- Identify predictors of HRQOL outcomes that will inform future intervention studies, and the critical time points when such interventions should occur

Children's Oncology Group AALL0331 Clinical Trial Schema



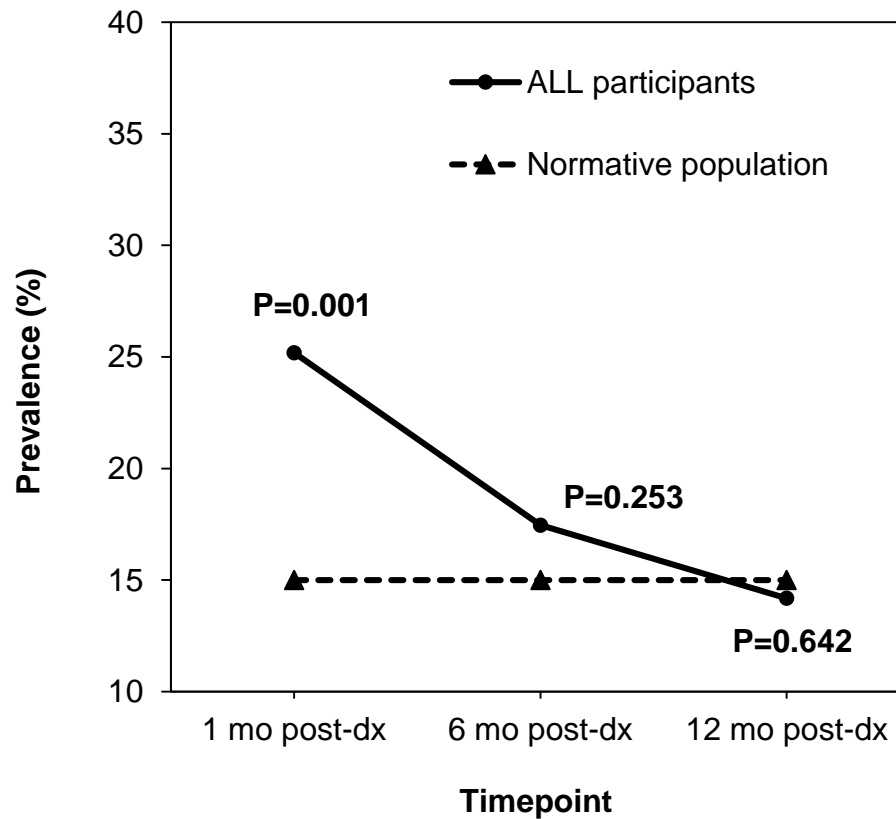
Patient Characteristics

	Participants (n = 160)	Nonparticipants (n = 34)	p
Age (years)	4.9 (SD: 2.9)	4.1 (SD: 2.2)	0.03
School Level			0.18
Preschool (2-4)	87 (54.4)	23 (67.7)	
School age (5-9)	73 (45.6)	11 (32.3)	
Sex			0.71
Male	83 (51.9)	16 (47.1)	
Female	77 (48.1)	18 (52.9)	
Race/Ethnicity			0.01
White, non-Hispanic	108 (67.5)	16 (47.1)	
Black, non-Hispanic	11 (6.8)	1 (2.9)	
Hispanic	27 (16.9)	8 (23.5)	
Other	14 (8.8)	9 (26.5)	
Treatment			0.71
Standard CS/standard IM-DI	43 (26.9)	8 (23.5)	
Intensified CS/standard IM-DI	51 (31.9)	11 (32.4)	
Standard CS/augmented IM-DI	37 (23.1)	6 (17.6)	
Intensified CS/augmented IM-DI	29 (18.1)	9 (26.5)	
Primary Language			
English	131 (81.9)		
Spanish	18 (11.3)		
Other	2 (1.3)		
Missing	9 (5.5)		
Maternal Education			
Less than college	55 (34.4)		
At least some college	93 (58.1)		
Missing	12 (7.5)		
Family Income			
<\$50,000	72 (45.0)		
≥ \$50,000	55 (34.4)		
Missing	33 (20.7)		

Survey Instruments

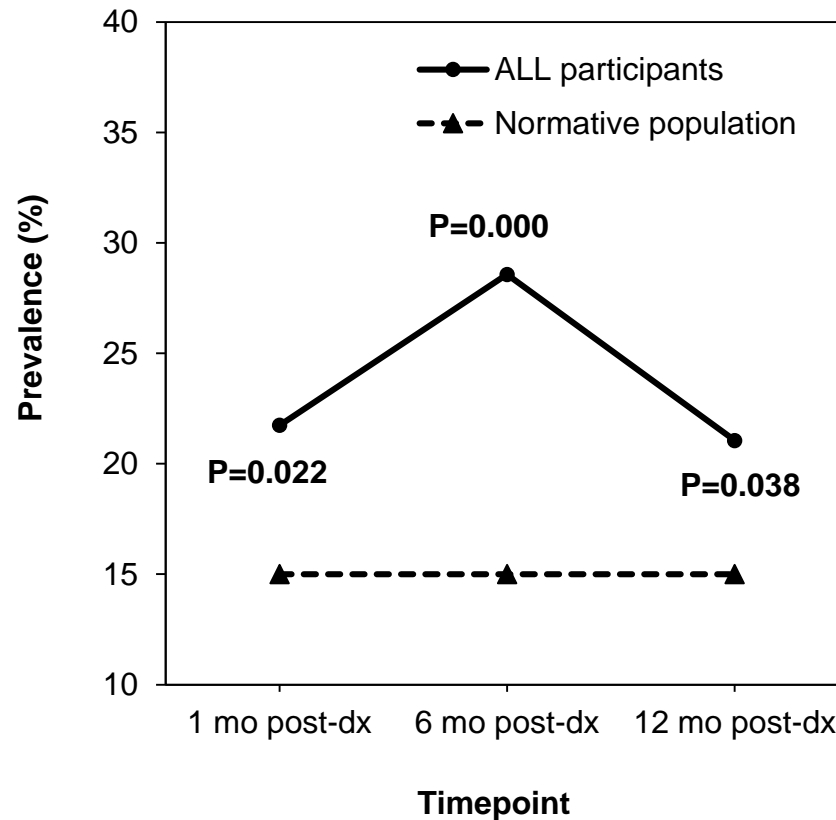
- **Behavioral Assessment System for Children- 2nd Ed (BASC-2)**
 - *Anxiety and depression*
- **Pediatric Quality of Life Inventory (PedsQL 4.0)**
 - *Physical, emotional, and social functioning*
- **Pediatric Quality of Life Inventory 3.0 Cancer Module**
 - *Nausea, pain, procedure anxiety, treatment anxiety during therapy*
- **Family Assessment Device-General Functioning scale (FAD-GF)**
 - *Family functioning*

First Year: Anxiety in at risk/clinical range



Myers et al., Cancer, 2014

First year: Depression in at risk/clinical range



Myers et al., Cancer, 2014

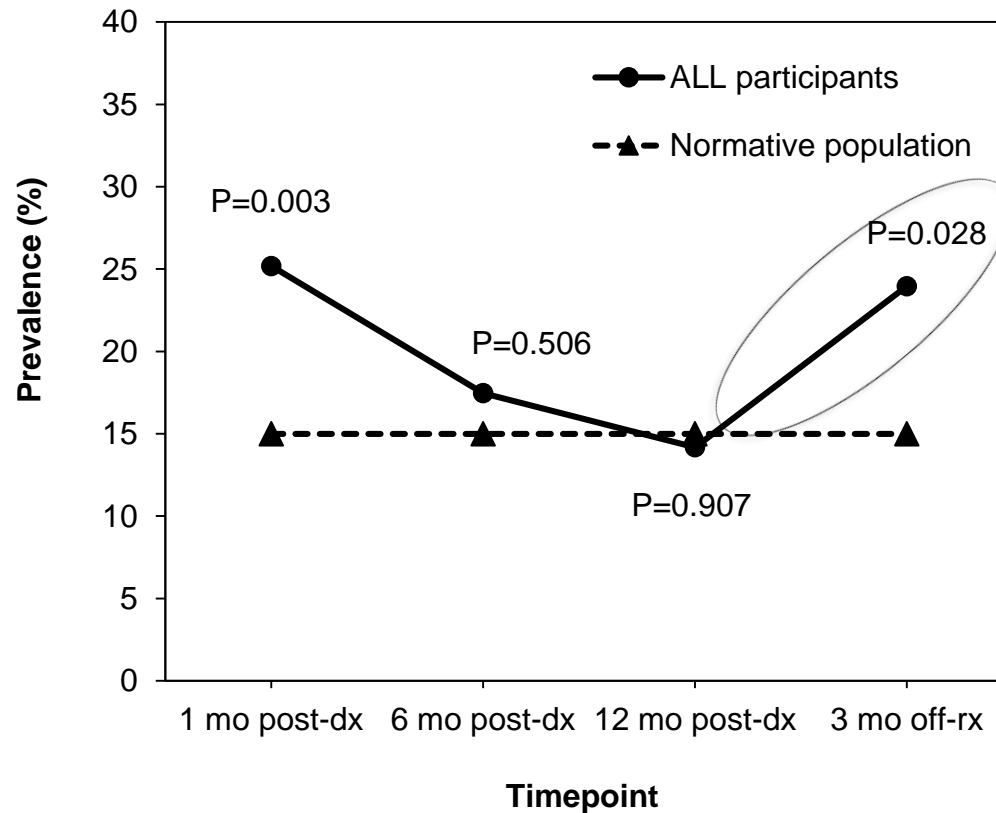
Predictors of emotional distress in the first year in multivariate analysis (repeated measures analysis)

Anxiety	Unhealthy family functioning	OR=2.24, p=0.03
	Hispanic ethnicity	OR=3.35, p=0.009

Depression	Unhealthy family functioning	OR=2.40, p=0.008
	Unmarried parents	OR=2.36, p=0.02

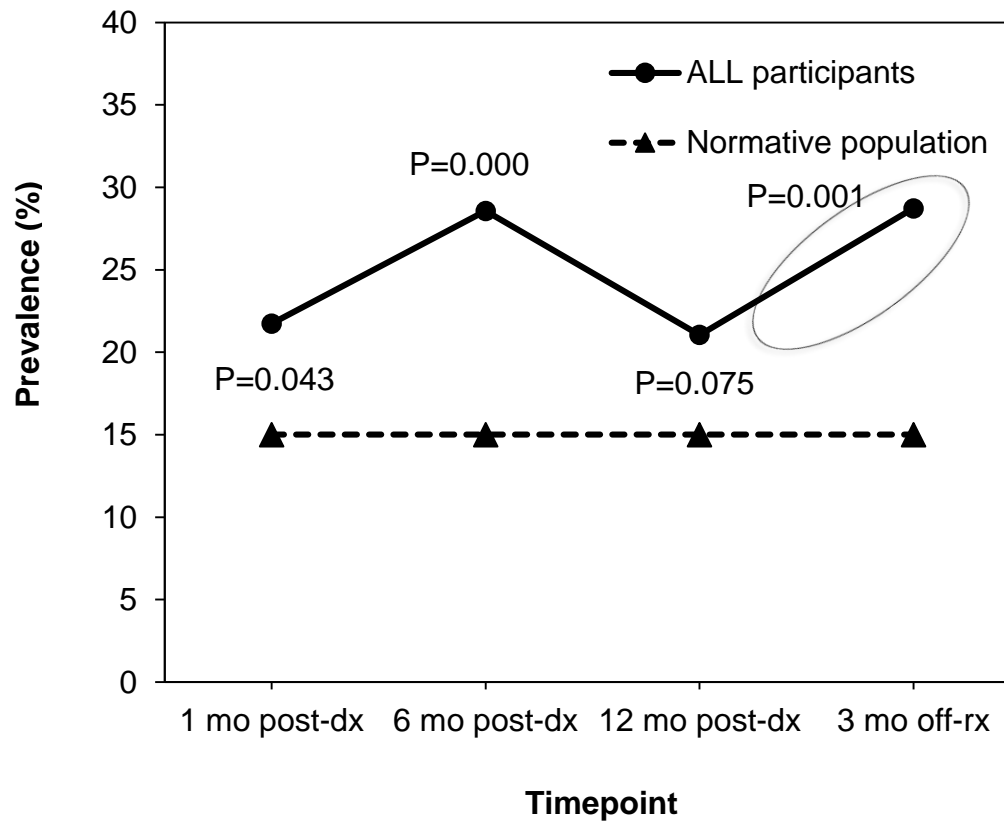
Not significant: sex, age, income, maternal education, treatment arm

Anxiety in at risk/clinical range three months post-therapy



Kunin-Batson et al., Cancer, 2016

Depression in at risk/clinical range three months post-therapy



Kunin-Batson et al., Cancer, 2016

Predictors of emotional distress 3 months post-therapy (multivariate analysis)

Anxiety	none	
Depression	Unhealthy family functioning	OR=2.62, p=0.02
Both	Unhealthy family functioning	OR=4.43, p=0.03
	Spanish speaking	OR=6.28, p=0.047

Not significant: sex, age, ethnicity, income, maternal education, treatment

Kunin-Batson et al., Cancer, 2016

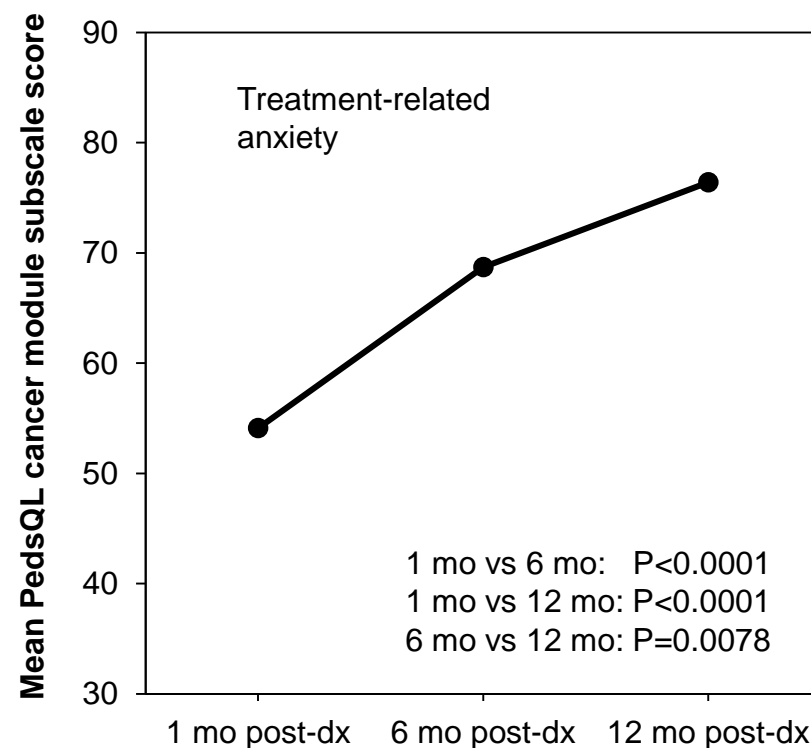
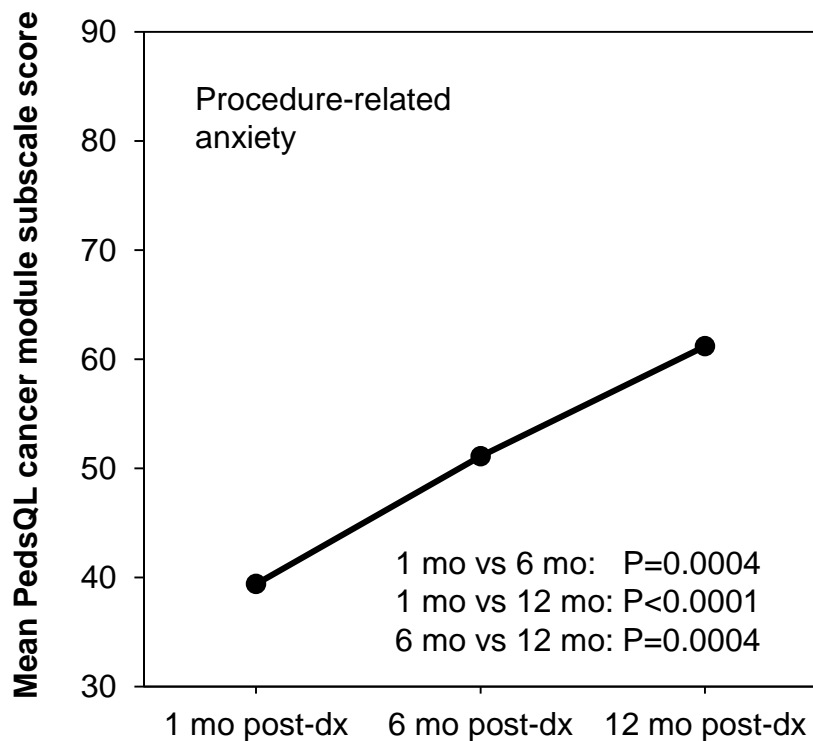
Earlier emotional distress predicts post-therapy distress

- **Anxiety symptoms in at risk/clinical range at 3 months post-therapy predicted by:**
 - Anxiety at 1 month (OR= 4.1, p=0.02)
 - Anxiety at 6 months (OR=5.5, p=0.009)
 - Anxiety at 12 months (OR=6.2, p=0.005)

- **Depression symptoms in at risk/clinical range at 3 months post-therapy predicted by:**
 - Depression at 6 months (OR=7.9, p=<0.001)
 - Depression at 12 months (OR=3.7, p<0.01)

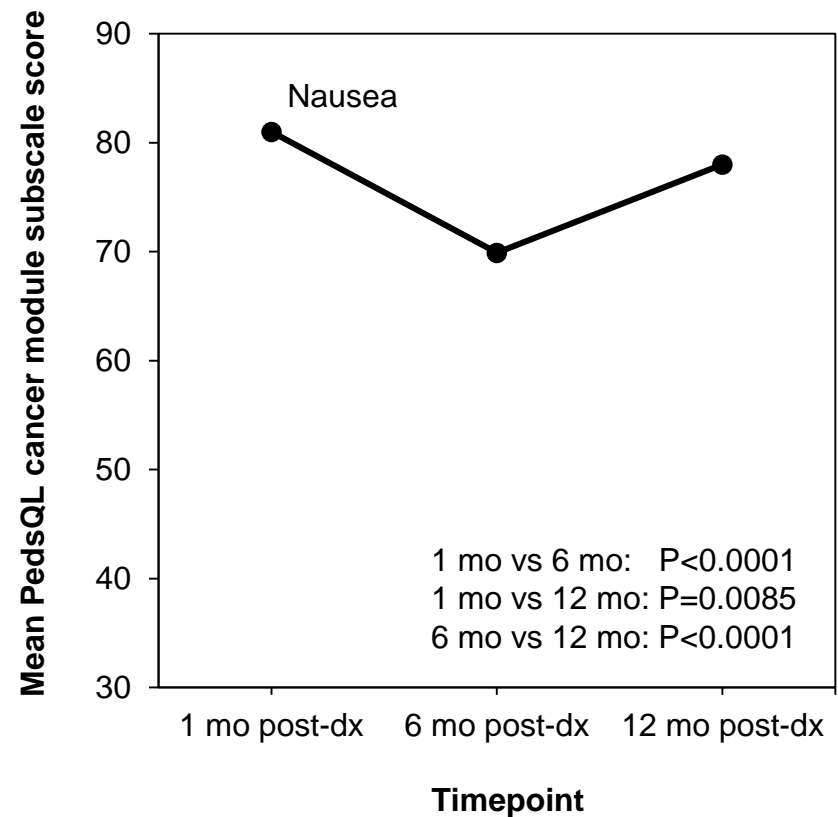
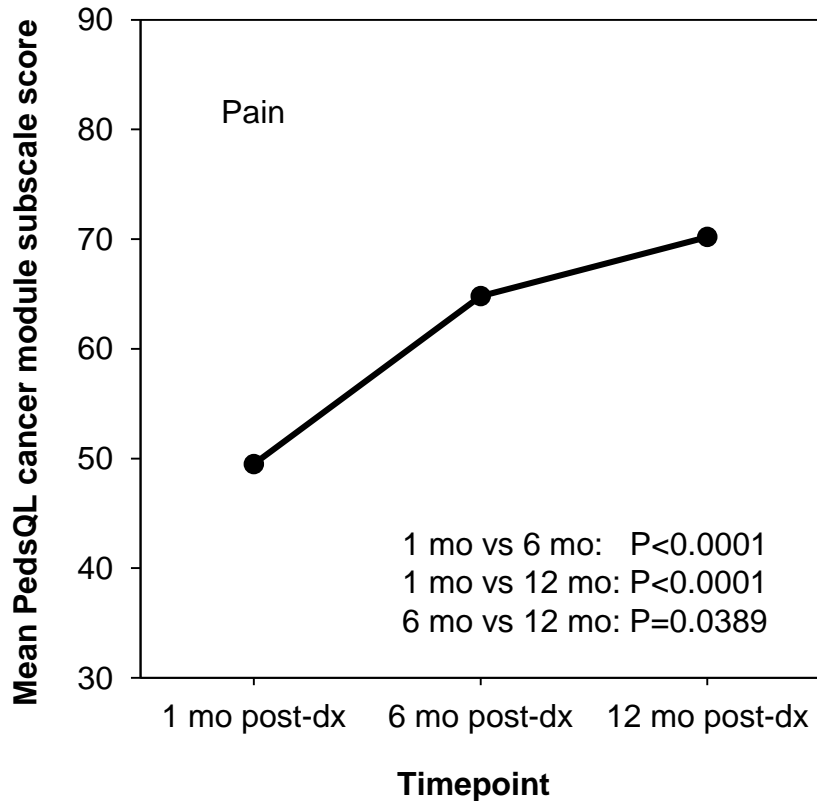
Kunin-Batson et al., Cancer, 2016

Cancer PedsQL scale scores in the first year



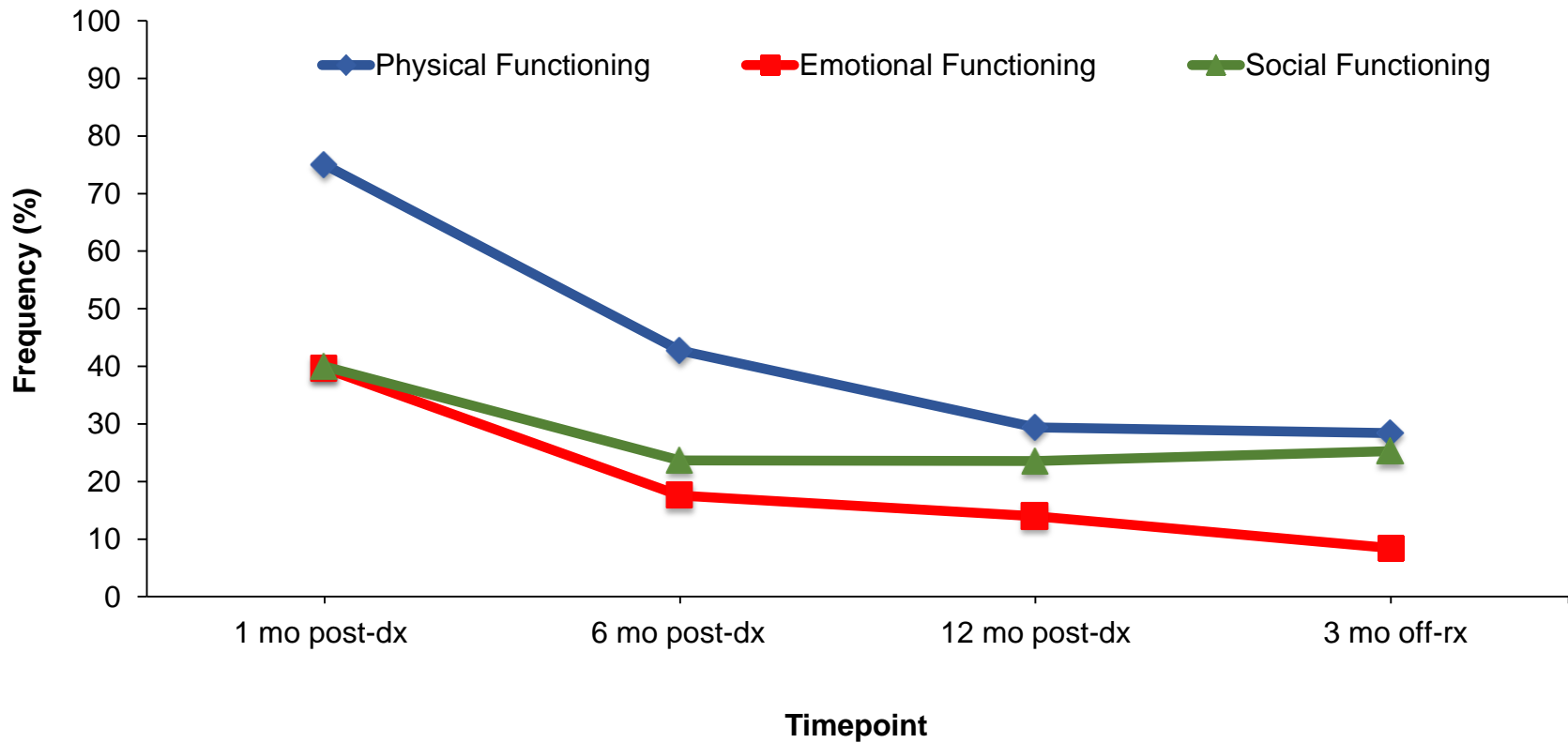
Dupuis et al., Cancer, 2016

Cancer PedsQL scale scores in the first year



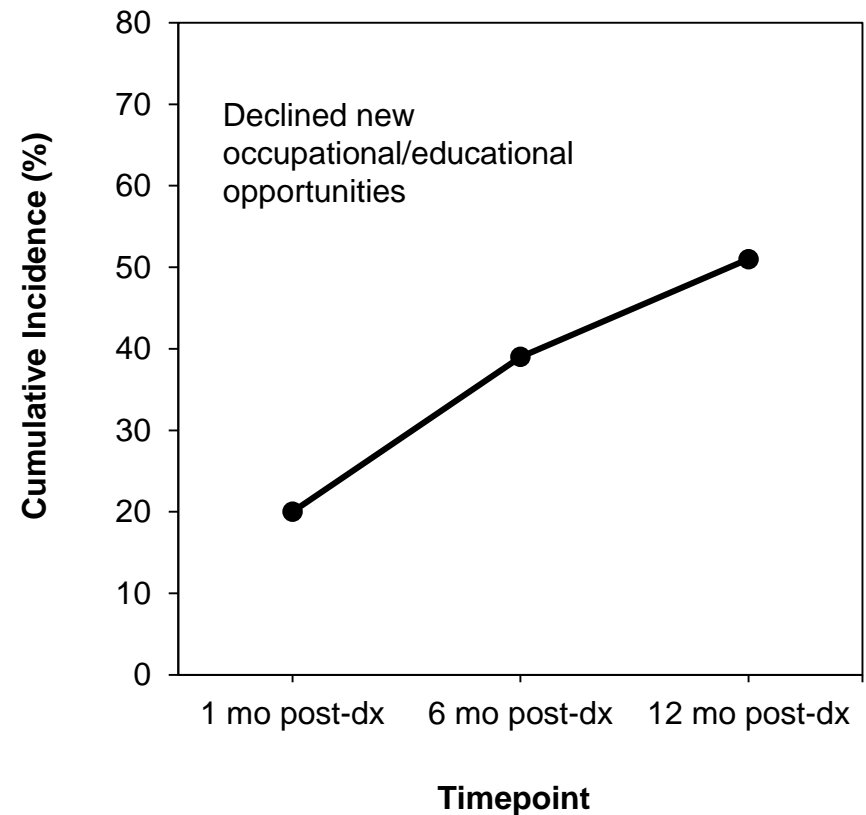
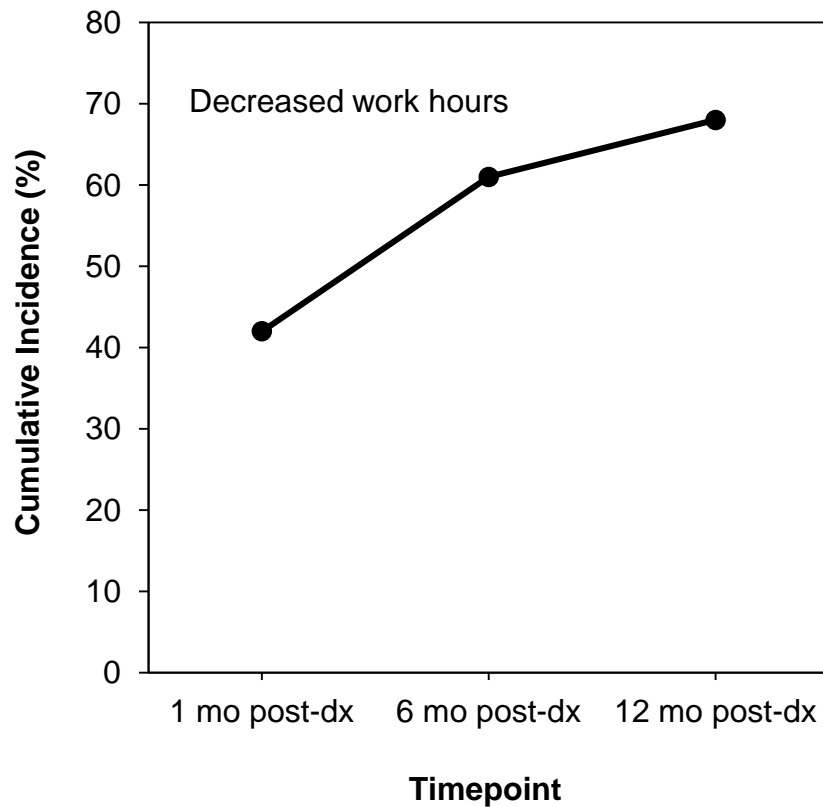
Dupuis et al., Cancer, 2016

Quality of Life: Trends in Impaired Functioning



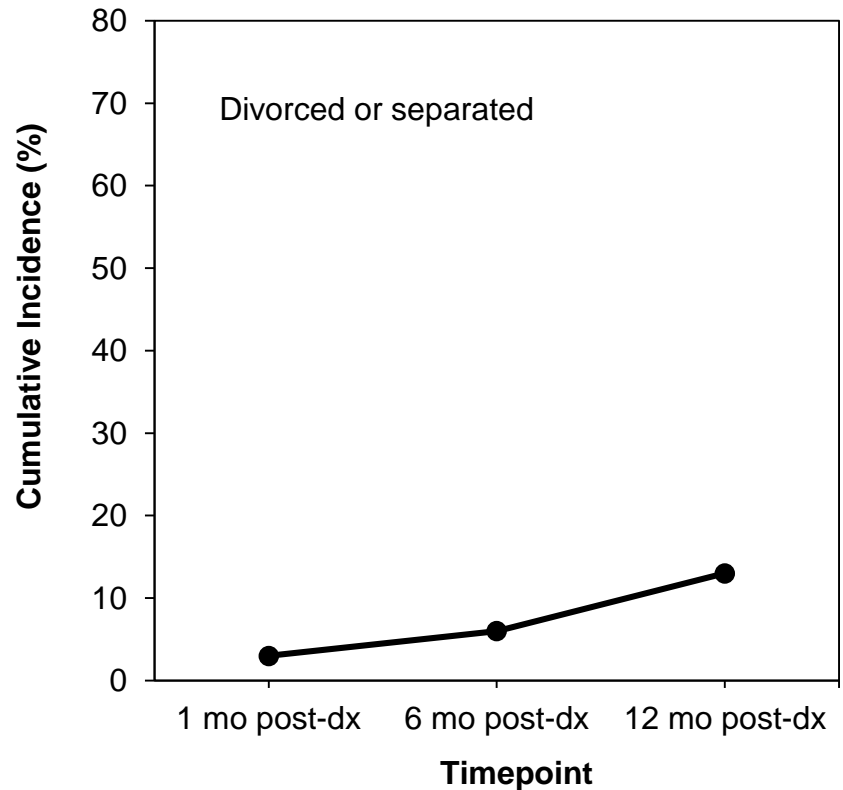
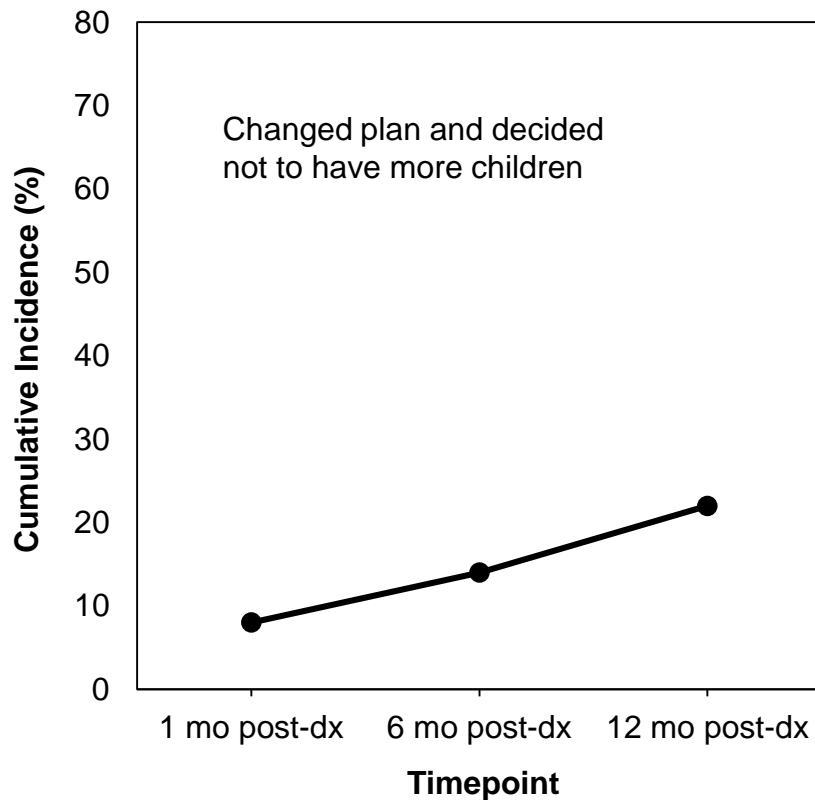
Mitchell et al., International Journal of Cancer, 2016

Stresses in first year: parents' work



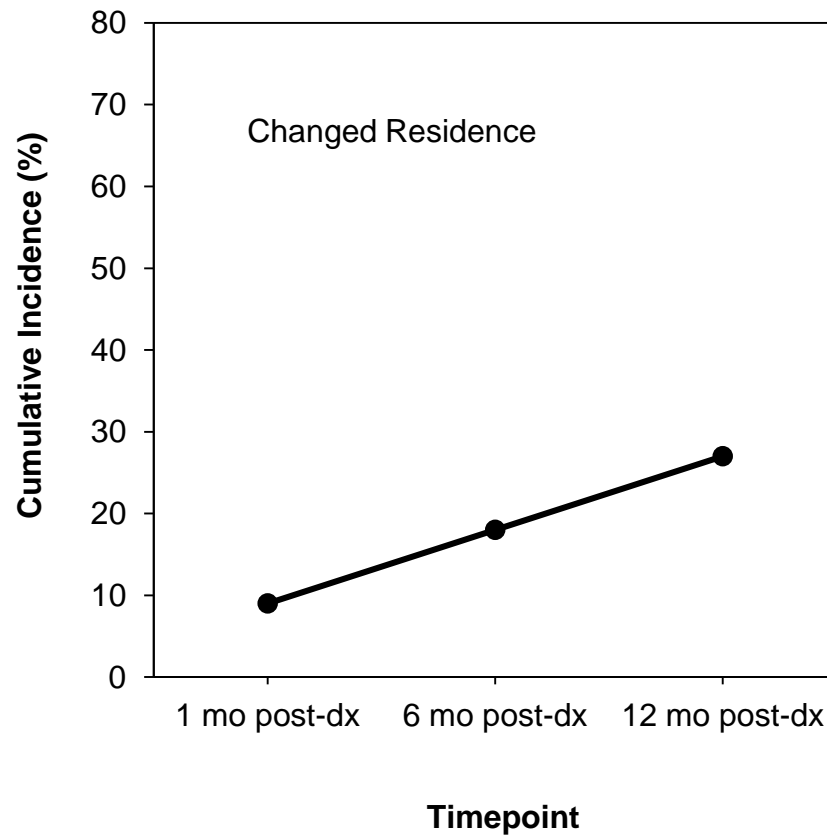
Lau et al., Pediatric Blood and Cancer, 2014

Stresses in first year: family life



Lau et al., Pediatric Blood and Cancer, 2014

Stresses in first year: Housing



Lau et al., Pediatric Blood and Cancer, 2014

Summary of findings

- **Substantial proportions of children with ALL experience emotional distress**
- **Treatment for ALL is disruptive to the entire family**
- **Unhealthy family functioning and Hispanic ethnicity are associated with greater emotional distress**
- **Patient experience elevated levels of anxiety and depression symptoms post-therapy**
- **Early emotional distress predicts later distress**

INTERVENTIONS



Psychosocial support is already part of our treatment culture

- **Social workers**
- **Child life specialists**
- **Nurses**
- **Chaplaincy**
- **Art therapy**
- **Therapy dogs**
- **Psychologists**
- **Psychiatrists**
- **Health Educators**
- **“Buddy” programs**
- **Complementary therapy**
- **Specialty camps**
- **Hospital schools**
- **Support groups**




... And Clowns!

Eur J Pediatr (2016) 175:1353–1360
DOI 10.1007/s00431-016-2764-0



ORIGINAL ARTICLE

Therapeutic clowns in pediatrics: a systematic review and meta-analysis of randomized controlled trials

Kannan Sridharan¹  • Gowri Sivaramakrishnan²



Challenges to effective interventions

- **Access to mental health expertise**
- **Cost of supportive care services**
- **Scheduling conflicts due to competing medical care priorities**
- **Different developmental needs**
- **Feasibility and generalizability across sites**

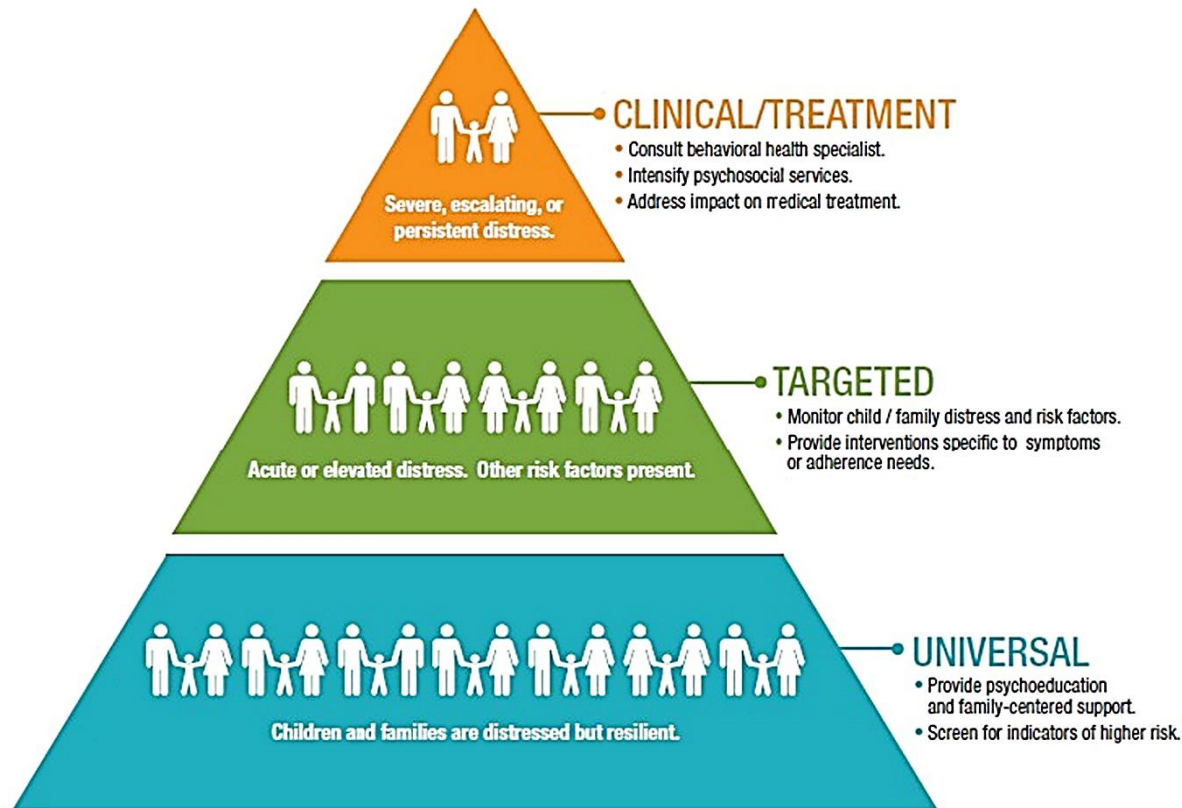
The Psychosocial Assessment Tool (PAT) by Kazak and colleagues

- **5-10 minutes by parent**
- **Web-based or paper and pencil**
- **4th grade reading level**
- **Multiple languages**
- **Categorizes family psychosocial risk**
 - **Universal (low)**
 - **Targeted (medium)**
 - **Clinical (high)**

Acta Oncologica, 2015; 54: 574-580

Conceptual framework for the PAT

Pediatric Psychosocial Preventive Health Model



©2011 Center for Pediatric Traumatic Stress

Impact of the PAT on psychosocial care

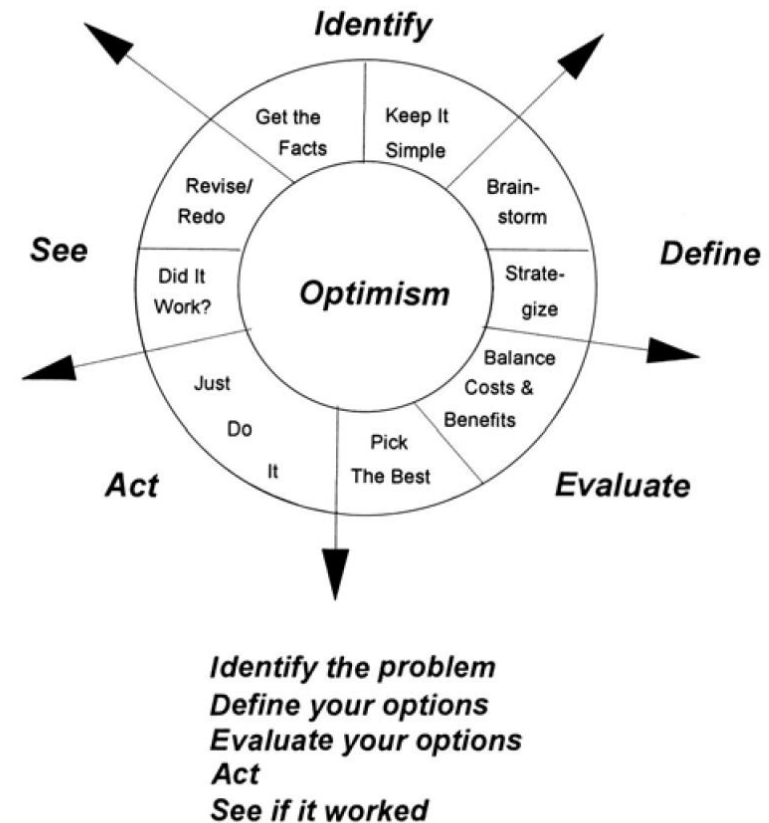
- **Identified 7.2 risks/family compared to 2.7/family after “usual” psychosocial screening at Children’s Hospital of Philadelphia (n=96 patients)**
Kazak et al. Psychooncology 2011
- **Providing PAT results to the medical team improved risk levels, parental anxiety, child behavior, and quality of life 6 months later in RCT (n=67 patients)**
Barrera et al. Psychooncology 2014

Cognitive Behavioral Therapy

- **Hands-on, practical approach to problem-solving**
- **Goal is to change patterns of thinking or behavior that are behind people's difficulties**
- **Efficacy in children and parents**
- **Usually in person and by trained mental health professionals**
- **Board game “ShopTalk” (Weiner et al. 2011)**

Problem-Solving Skills Training for mothers by Sahler and colleagues

- **Cognitive-behavioral approach**
- **8 one-hour individual in person sessions with mothers**
- **Associated with less negative emotions in mothers in 2 randomized trials**
- **Efficacy: Spanish > English speaking mothers**
- **Maintained 3 months post-intervention**



E-health interventions in children with cancer

- **Smartphone in addition to traditional therapy**
Smartphone training (n=197) did not enhance Problem-Solving Skills Training in mothers (Askins et al. 2009)
- **Videotelephone support for newly diagnosed patients and families**
Ongoing randomized control trial (n=162) of 12 week intervention (Bensink et al. 2007)
- **Online group-based cognitive behavioral therapy**
Three 90 minute sessions in parents (n=47) showed feasibility but not efficacy (Wakefield et al. 2016)

Strategies at your site

- **Systematically triage patients**
- **Identify a champion who leads the psychosocial program**
- **Psychosocial multidisciplinary conference**
 - **Care planning and coordination**
 - **“Matchmaker” of needs with resources**
 - **MDs, nurses, child life, SW, mental health experts**

Future Directions

- **Ongoing prospective study of 600 children on current ALL trial to replicate findings and understand impact of reducing maintenance therapy**
- **Planning intervention study for upcoming therapeutic study in Childrens Oncology Group**
- **Education and advocacy to champion expanded psychosocial support in clinical practice**

Acknowledgements

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Stephen Hunger	L. Lee Dupuis
Lillian Sung	Hannah-Rose Mitchell
Alicia Kunin-Batson	Regina Myers
- **Statisticians:** Meenakshi Devidas and Xiaomin Lu

Participating Sites for COG AALL0331 HRQOL Ancillary Study

- Children's Hospital Medical Center, Akron, OH
- Children's Hospital at the Cleveland Clinic, Cleveland, OH
- Children's Hospital Colorado, Aurora, CO
- Children's Hospital of Central California, Madera, CA
- Children's Hospital and Clinics of Minnesota, Minneapolis and St. Paul, MN
- Children's Hospital, New Orleans, LA
- Children's Hospital of Pittsburgh, Pittsburgh, PA
- Seattle Children's Hospital, Seattle, WA
- Helen DeVos Children's Hospital, Grand Rapids, MI
- Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE
- East Tennessee Children's Hospital, Knoxville, TN
- Hackensack University Medical Center, Hackensack, NJ
- Randall Children's Hospital at Legacy Emanuel, Portland, OR
- Loma Linda University Medical Center, Loma Linda, CA
- Midwest Children's Cancer Center, Milwaukee, WI
- Nevada Cancer Research Foundation
- Princess Margaret Hospital for Children, Perth, Australia
- St. Vincent Hospital, Regional Cancer Center, Green Bay, WI CCOP
- Packard Children's Hospital at Stanford, Stanford, CA
- SUNY Upstate Medical University, Syracuse, NY
- St. Joseph's Children's Hospital of Tampa, Tampa, FL
- University of Alabama at Birmingham Hospital, Birmingham, AL
- University of Florida Academic Health Center, Gainesville, FL
- University of Minnesota Medical Center, Fairview, Minneapolis, MN
- Children's Hospital, University of Mississippi Medical Center, Jackson, Mississippi
- University of New Mexico Children's Hospital, Albuquerque, New Mexico
- University of Texas Southwestern Medical Center, Dallas, TX
- American Family Children's Hospital, University of Wisconsin Children's Hospital, Madison, WI
- Children's Hospital at Vanderbilt, Nashville, TN