School of Nursing
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Comparison of Symptom Reports Among Children with Advanced Cancer and Their Parents

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Objectives

1

To review current evidence of symptomatology in children with cancer and the role of parent-proxy reports

2

To outline findings of a sub-analysis comparing symptom experiences reported by children with advanced cancer and their parents

3

To discuss implications for clinical practice and future research

Significance

- Approximately 2,000 children aged 0-18 die of cancer annually in the US
- Increases in mortality associated with:
  - Treatment factors (intensity)
  - Disease factors (risk or stage of disease)
  - Diagnosis of “advanced cancer” – disease that has relapsed or progressed

- Children with advanced cancer experience high symptom burden
  - Physical and psychological symptoms
  - Children experience distressing symptoms at end of life
- Children suffering from poorly controlled symptoms can impact outcomes
  - Decreases in health-related quality of life
  - Increases in parental psychological distress

Noone et al. (2018) *SEER Cancer Statistics Review, 1975-2015;* Nguyen et al. (2008) *Leukemia;* Ceschel et al. (2006) *Pediatric Blood Cancer;* Wolfe et al. (2015) *J Clinical Oncology*; Heath et al. (2010) Med J Aust; Rosenberg et al. (2016) *J Pain and Symptom Management*; Rosenberg et al. (2012) *Pediatric Blood Cancer*

Gaps & Opportunities

- Patient reported outcomes (PROs) are the gold standard yet under-utilized in clinical and research settings for pediatrics
  - Limited use of PROs outside of the clinical setting (e.g. home)
- Use of parent proxy-report to capture child symptom experiences is not uncommon in the clinical setting

- Parent proxy-reports may be necessary or appropriate for some children
  - Lack of psychometrically tested symptom measures for very young children
  - Acute illness or changes in cognition (e.g. intubation, end-of-life)
- Inconsistency in parent-child agreement in symptom and health-related quality of life reporting has been demonstrated
  - Children undergoing cancer treatment, children with advanced cancer, adolescent survivors

Leahy, Feudtner, Basch (2018) *Patient;* Baggott et al. (2014) *Cancer Nursing;* Hinds et al. (2007) *J Pediatric Psychology*; Brock, Wolfe, Ullrich (2018) *Children;* Erickson et al. (2017) *J Health Psychol;* Tomlinson et al. (2017) *Supportive Care Can*; Russel et al. (2006) *Cancer*; Upton et al. (2008) *Qual Life Res*; Zhukovsky et al. (2015) *Cancer*

Overview of Primary Study

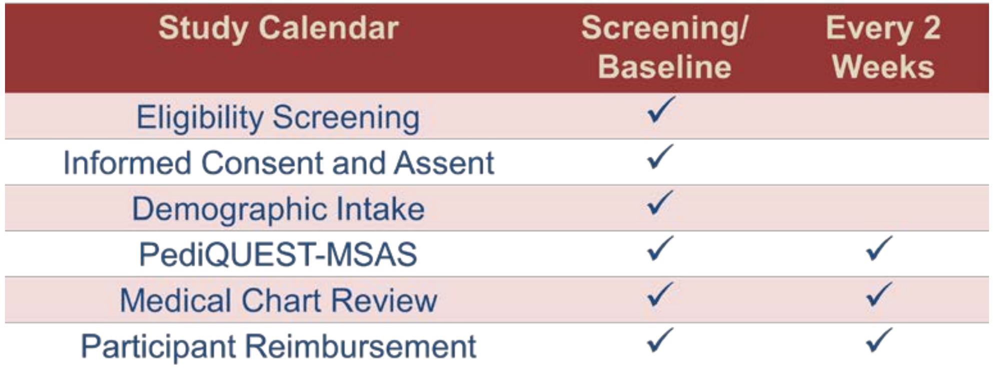
Symptom Assessment Study (SAS) 1.0

- SA 1: To evaluate the feasibility of electronic data collection in the hospital, clinic, and home settings
- SA 2: To describe symptom frequency, severity, and distress in children with advanced cancer

Montgomery, Raybin, Ward, Balian, Gilger, Murray, & Li (2020) *Cancer Nursing*

SAS 1.0 Design, Setting, & Sample

- Prospective cohort study using repeated measures
  - Multi-site within US
  - Five pediatric cancer centers
- Eligibility
  - 7-18 years of age, English-speaking, Diagnosis of advanced cancer
- Advanced Cancer
  - 2-week history of progressive, recurrent, or non-responsive disease or a decision not to pursue curative-focused therapy
- Sample
  - Target: 60 child/parent dyads (n=120)
  - Final: 46 child/parent dyads (n=92)



Study Calendar	Screening/ Baseline	Every 2 Weeks
Eligibility Screening	✓	
Informed Consent and Assent	✓	
Demographic Intake	✓	
PediQUEST-MSAS	✓	✓
Medical Chart Review	✓	✓
Participant Reimbursement	✓	✓

PediQUEST-MSAS: Abbreviated Pediatric Quality of Life and Evaluation of Symptoms Technology (PQ) – Memorial Symptom Assessment Scale (MSAS)

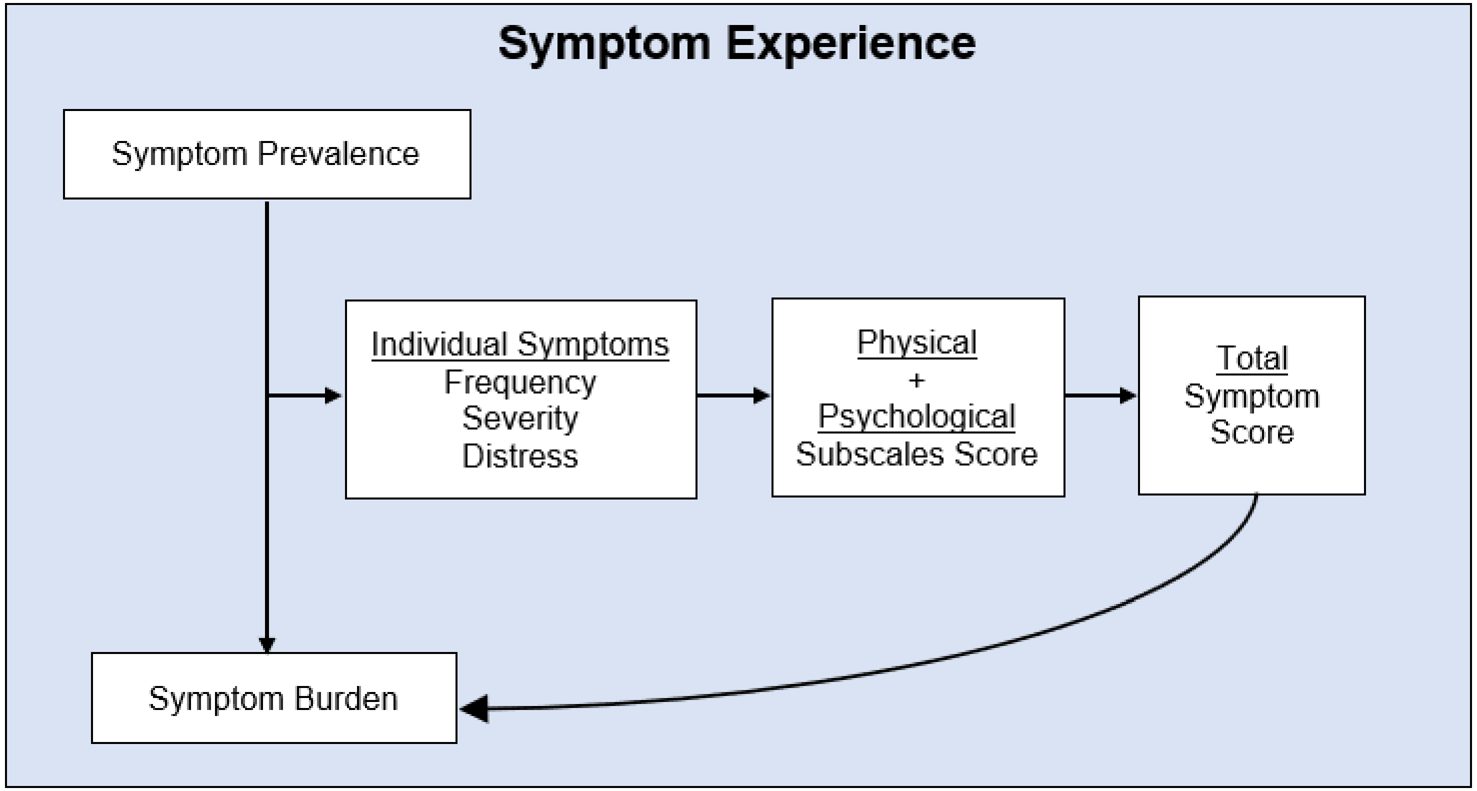
Montgomery, Raybin, Ward, Balian, Gilger, Murray, & Li (2020) *Cancer Nursing*

Overview of Sub-analysis

Objectives

1. To compare reports of symptom prevalence, symptom burden, and symptom frequency, severity, and distress between groups of children and their parents
2. To describe concordance of symptom reports within individual child-parent dyads

Study Constructs



Symptom Experience

Symptom Prevalence

Individual Symptoms
Frequency
Severity
Distress

Physical
+
Psychological
Subscales Score

Total
Symptom
Score

Symptom Burden

Analytic Approach

Symptoms were measured using the abbreviated PQ-MSAS scales (self-report and parent-proxy)

Prevalence → symptom frequency, severity, and distress (Likert scale)

Symptom burden → mean scores for frequency severity, and distress

Objective 1: Symptom prevalence, frequency, severity, distress, and symptom burden for individual symptoms and symptoms scales were analyzed using descriptive statistics

Differences in children's and parents' symptom reports were analyzed using a general linear mixed effects model adjusting for repeated measures

Objective 2: Concordance between symptom prevalence reports from children and parents were analyzed using percent agreement and Cohen's kappa coefficient

Results: Sample Characteristics

Characteristic	Children (*n* = 46)		Parents (*n* = 46)	
	n	Percent	*n*	Percent
Gender				
Male	24	52	5	11
Female	22	48	41	89
Ethnicity				
Hispanic or Latino	10	22	6	13
Not Hispanic or Latino	36	78	40	87
Race				
American Indian	0	0	0	0
Asian	3	7	2	4
Black	4	9	3	7
White	35	76	37	80
Other	4	9	4	9

- Parent participants were mostly female, not Hispanic or Latino, and White
- The mean age of parent participants was 44 years (SD ± 7.98)
- Approximately half of child participants had a diagnosis of a solid tumor, while the remainder had a diagnosis of a central nervous system tumor or hematological malignancy

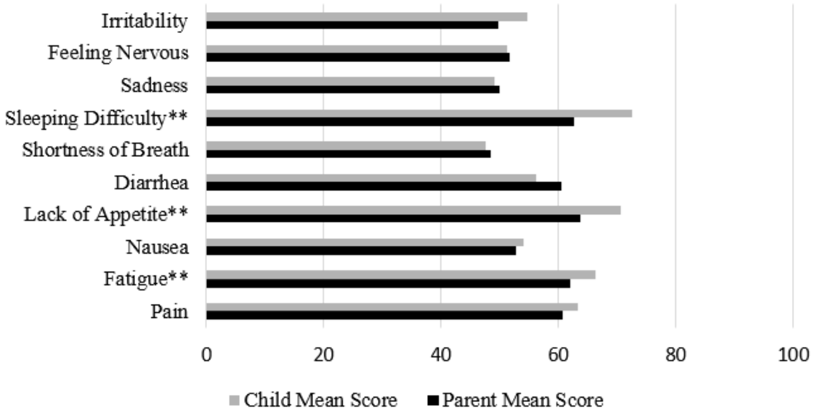
Results: Objective 1 (Prevalence)

	Child Survey responses n = 563		Parent survey responses[a] n = 575		
	n	Percent	n	Percent	p[b]
Pain	195	35	219	38	.2881
Fatigue	186	33	271	47	<.0001
Nausea	156	28	211	37	.0003
Lack of appetite	98	18	136	24	.0109
Shortness of breath	33	6	31	5	.7002
Diarrhea	53	15	100	17	.9469
Constipation	36	10	73	13	.3544
Sleeping difficulties	131	24	142	25	.5481
Feeling nervous	59	10	109	19	<.0001
Sadness	74	13	152	26	<.0001
Irritability	58	17	124	22	.5734

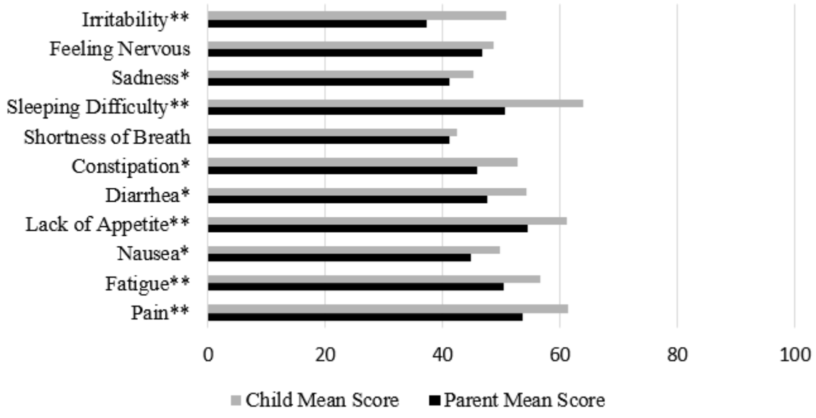
[a] A higher number of parent responses were reported because of circumstances when the child was unable to self-report or data was missing.
[b] A p value of < .05 is significant

- Children and parents both reported pain, fatigue, nausea, and sleeping difficulties as the most frequently occurring symptoms
- Parents' reports of higher symptom prevalence compared to children was significant for almost half of symptoms, including:
  - Fatigue ($p < .0001$)
  - Nausea ($p = .0003$)
  - Lack of appetite ($p = .0109$)
  - Feeling nervous ($p < .0001$)
  - Sadness ($p < .0001$)

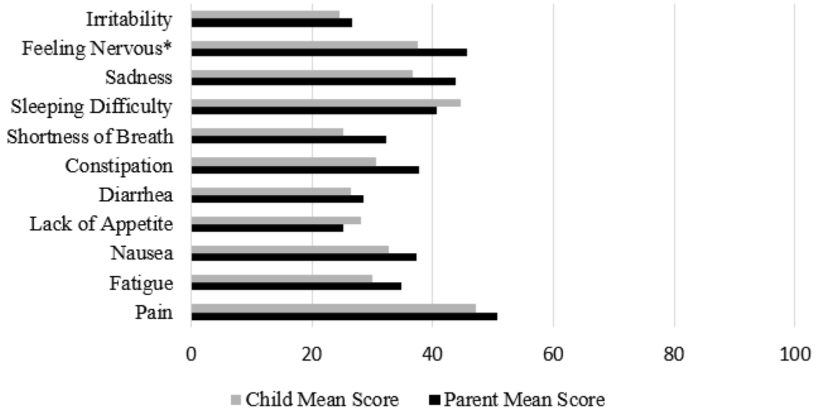
Results: Objective 1 (Frequency, Severity, and Distress)



2a. Symptom Frequency



2b. Symptom Severity



2c. Symptom Distress

- Comparison of mean scores for symptom frequency (2a), severity (2b), and distress (2c) between children’s and parents’ responses
- * = *p*-values of < .05
- ** = *p*-values of < .01
- The symptom measure did not include frequency of constipation

Results: Objective 1 (Symptom Burden)

	All child survey responses ($n = 563$)	All parent survey responses[a] ($n = 575$)	
	M ± SD	M ± SD	p[b]
Total Scale	9.01 ± 11.39	11.23 ± 12.84	.0004
Physical Subscale	10.28 ± 13.47	11.91 ± 14.33	.0381
Pain	19.59 ± 30.07	20.57 ± 28.83	.6754
Fatigue	16.43 ± 26.33	21.94 ± 26.55	.0005
Nausea	10.96 ± 20.2	16 ± 24.57	<.0001
Lack of appetite	7.65 ± 18.68	10.73 ± 22.12	.0093
Shortness of breath	2.22 ± 9.54	2.07 ± 9.3	.7566
Diarrhea	6.73 ± 18.34	6.9 ± 17.64	.5993
Constipation	4.23 ± 14.23	5.29 ± 15.98	.4403
Psychological Subscale	6.86 ± 11.05	10.04 ± 13.65	<.0001
Sleeping difficulties	10.88 ± 23.04	12.34 ± 23.11	.0984
Feeling nervous	4.63 ± 14.97	9 ± 19.81	<.0001
Sadness	5.72 ± 15.86	11.75 ± 21	<.0001
Irritability	7 ± 17.39	7.2 ± 15.68	.2490

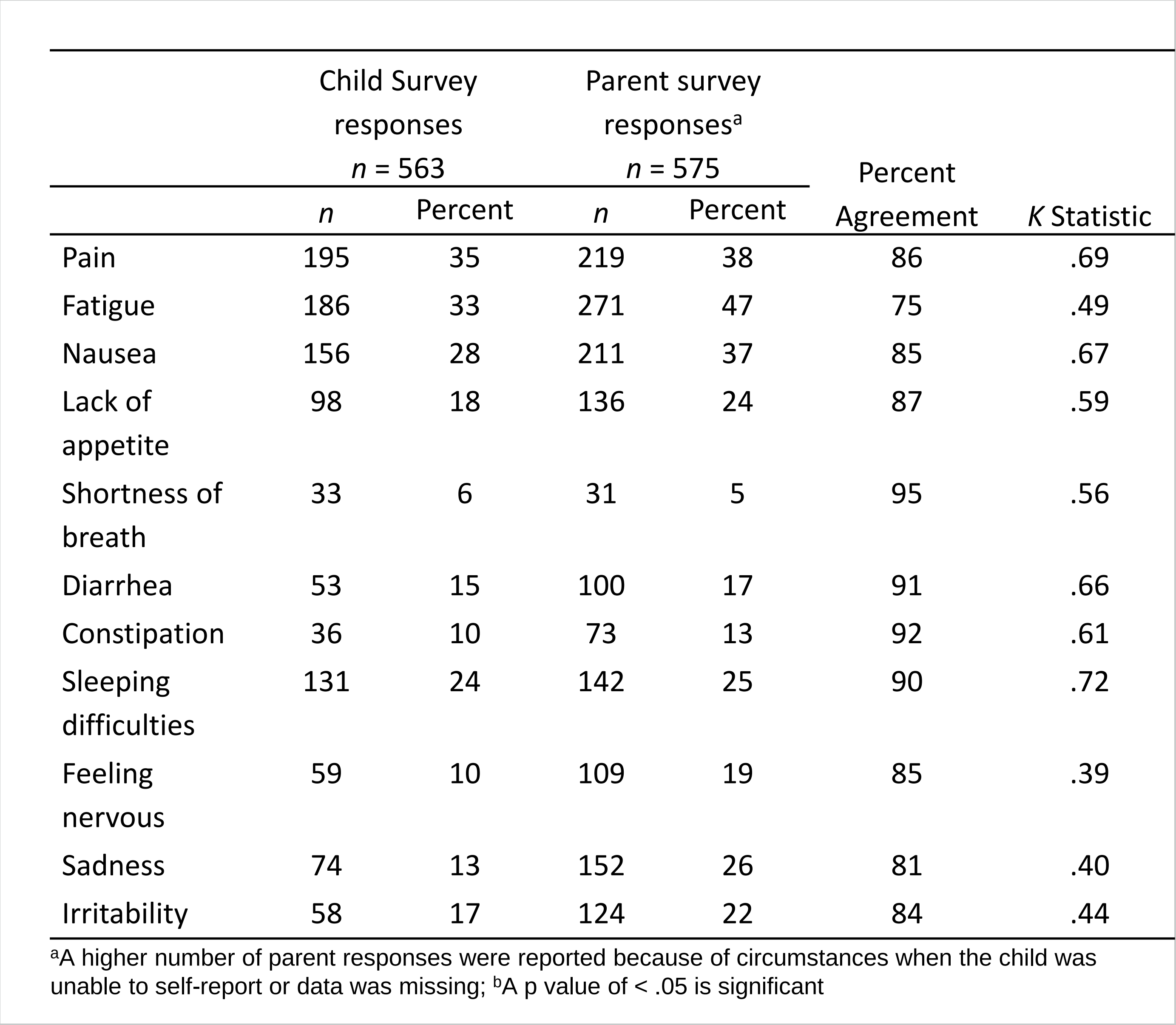
[a] A higher number of parent responses were reported because of circumstances when the child was unable to self-report or data was missing.

[b] A p value of < .05 is significant

- Parents reported higher symptom burden scores compared to children for all individual symptoms except shortness of breath
- Symptom burden scores for fatigue, nausea, lack of appetite, feeling nervous, and sadness reported by parents were significantly higher than corresponding scores reported by children
- Symptom burden scores for the total scale ($p = .0004$), and physical ($p = .0381$) and psychological ($p < .0001$) subscales were also significantly higher for parents' ratings compared to those of children

Results: Objective 2 (Agreement and Concordance)

- Symptoms that demonstrated the strongest percent agreement between dyad members included shortness of breath, constipation, diarrhea and sleeping difficulties
- Fatigue had the lowest percent agreement
- Sleeping difficulties, pain, nausea, and diarrhea yielded the highest concordance
- Feeling nervous, sadness, irritability, and fatigue yielded the lowest concordance



	Child Survey responses *n* = 563		Parent survey responses[a] *n* = 575			
	n	Percent	*n*	Percent	Percent Agreement	*K* Statistic
Pain	195	35	219	38	86	.69
Fatigue	186	33	271	47	75	.49
Nausea	156	28	211	37	85	.67
Lack of appetite	98	18	136	24	87	.59
Shortness of breath	33	6	31	5	95	.56
Diarrhea	53	15	100	17	91	.66
Constipation	36	10	73	13	92	.61
Sleeping difficulties	131	24	142	25	90	.72
Feeling nervous	59	10	109	19	85	.39
Sadness	74	13	152	26	81	.40
Irritability	58	17	124	22	84	.44

[a] A higher number of parent responses were reported because of circumstances when the child was unable to self-report or data was missing; [b] A p value of < .05 is significant

The following scale was used to interpret the strength of concordance and results of the *K* statistic: poor, *K* < 0; slight, *K* = 0-.20; fair, *K* = .21-.40; moderate, *K* = .41-.60; substantial, *K* = .61-.80; almost perfect, *K* = .81-1.0

Discussion

- Validates that pain, fatigue, nausea, and sleeping difficulties continue to be the most prevalent symptoms in children with advanced cancer
- Confirms previous findings that parents perceive children are experiencing more symptoms compared to children's self-report and that over-estimation of symptom prevalence was most significant for the physical symptoms of fatigue, nausea, lack of appetite, and the psychological symptoms of feeling nervous, and sadness
- Children's symptom scores were higher for frequency and severity, while parents' scores were higher for distress, suggesting that when symptoms are present, children may score the symptom as occurring more frequently and more severely, compared to parents'
- Confirms previous findings that several symptoms demonstrated moderate to poor agreement and psychological symptoms demonstrated the lowest degree of concordance

Baggott et al. (2014) *Cancer Nursing;* Eiser & Varni. (2014) Eur *J Pediatrics; Varni et al.* (2015) *Qual Life Res;* Zhukovsky et al. (2015) *Cancer*

Limitations

- Small sample size, thus not powered to analyze clinically-relevant variables and their influence on agreement or concordance
- Caution should be used when generalizing to the broader pediatric oncology population or other disease-specific populations
- PQ-MSAS is not an established symptom measurement tool, with limited data demonstrating validity and reliability
- Symptoms are dynamic and are likely to change within a symptom assessment recall period, which may contribute to differences between the report of symptom prevalence from a child and their parent

Implications for Clinical Practice

- Important for pediatric nurses to query the patient first (when appropriate) before eliciting information from a proxy rater
- Nursing assessment should consider the domains of frequency, severity, and distress which can add insight to the overall symptom experience of the child and identify symptoms of most concern to target for intervention
- When children are unable to self-report due to age, developmental level, or clinical status, nurses can partner with parents or caregivers to discuss how symptoms may present in their child, signs of controlled or poorly controlled symptoms, and monitoring effects of symptom management interventions
    - Psychological symptoms may be most difficult for proxy raters to identify due to the absence of a “visual cue”

Implications for Research

- Physical and psychological symptoms continue to be prevalent over time throughout cancer treatment, suggesting an opportunity to investigate the effectiveness of targeted symptom management interventions
- Few empirical studies have specifically compared symptom burden and symptom frequency, severity, and distress caused by symptoms between children's and parents' reports, thus there is an opportunity to validate and further explore differences between child self-report and parent-proxy reports
- Additional research is warranted to understand if discrepancies in symptom reporting between children and parents results in clinically meaningful outcomes (e.g. over-treatment of symptoms, suffering, etc.)

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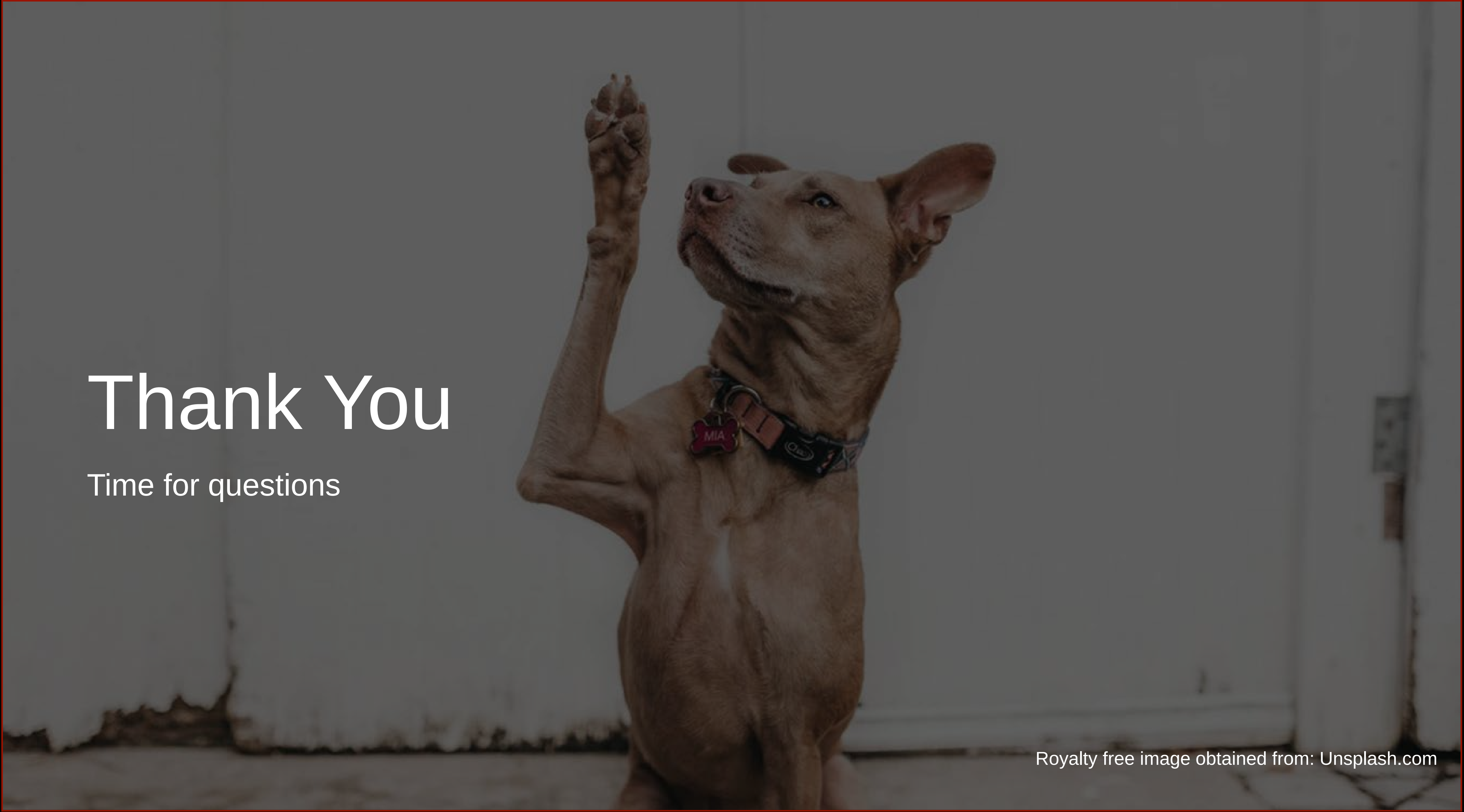
Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Wisconsin Institution for Clinical and Translational Research.



Thank You

Time for questions

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