

NOSLEEPatALL

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POGO Aftercare Education Day

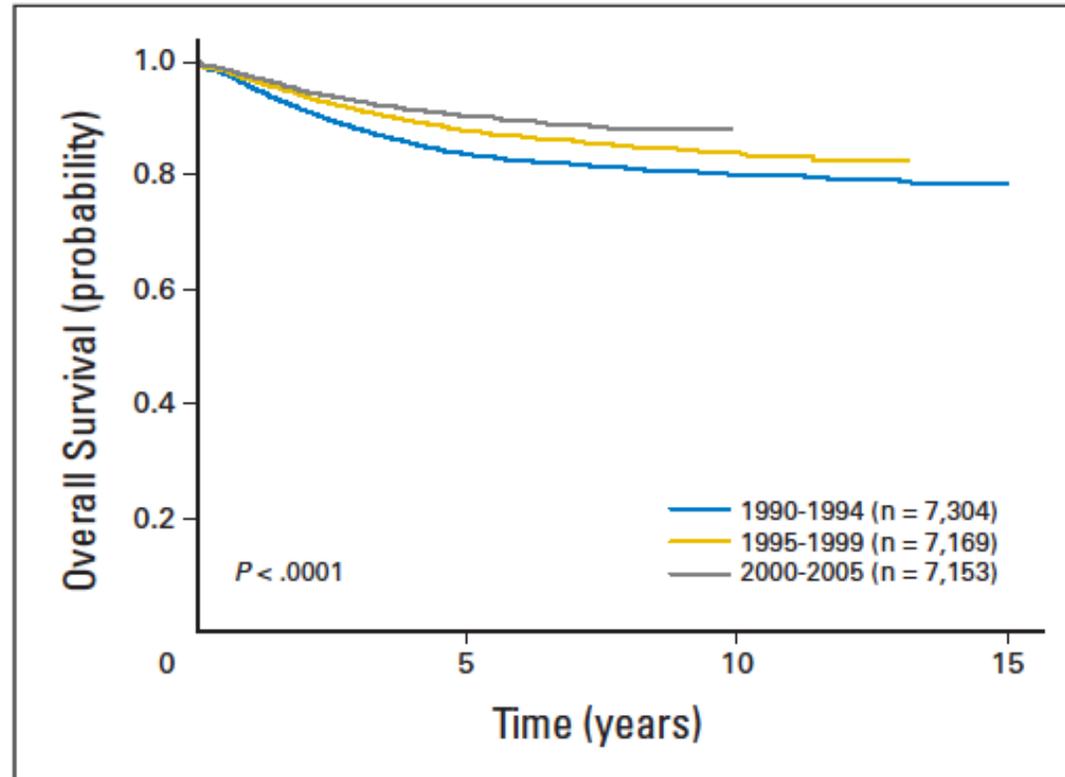
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SickKids





- Priority for ALL is Neurocognitive Outcomes (NO)
- Emerging evidence suggests association between sleep, fatigue, and neurocognitive outcomes in childhood ALL survivors
- Children with ALL (on maintenance) have evidence of disturbed sleep
- Sleep not an easy thing to fix
- Next Steps: We need interventions!

Neurocognitive Outcomes and ALL



- 20-40% NO reported in ALL survivors
- Problems in core functional domains
 - Attention
 - Executive Function
 - Processing speed
 - Working memory
 - Visual-motor integration
- Compromises quality of life, social and academic performance

1. Janzen, L. Spiegler, B. (2008) Neurodevelopmental sequelae of pediatric acute lymphoblastic leukemia and its treatment, *Dev Disability Res Rev.* 14(3) 185-195
2. Nathan, P. et al. (2007) Guidelines for identification of, advocacy for, and intervention in neurocognitive problems in survivors of childhood cancer: a report from the Children's Oncology Group. *Arch Pediatric Medicine* 161(8) 798-806

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Jacula et al. (2016)

St Jude Total XV (n=243) – **No Cranial Radiation**

- **Neurocognitive testing at 2 years post EOT**

“As a group, survivors performed within age expectations on several neurocognitive measures 2 years after completing therapy, confirming that omission of prophylactic CRT from childhood ALL therapy results in improved cognitive outcomes”

“Despite this notable improvement, our data show that survivors continue to demonstrate elevated risk for ATTENTION deficits”

Conklin et al. (2012)

- Neurocognitive outcomes in pediatric patients treated for ALL without radiation St Jude Total XV (n=243)
- Tested at week 120 post consolidation (same sample but earlier)

“statistically significantly elevated rate of impairment on a computerized measure of sustained attention, coupled with parent report of attention and learning problems, suggests that **ATTENTION difficulties are of noteworthy magnitude** and affect real-world functioning”

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True Functional Impact



- Patient, parent and teacher reports:
 - Children spending excessive time on homework yet having poor acquisition and retention
 - Often in reading, spelling and math
- Self monitoring skills and peer relationships can be compromised
- Post-traumatic stress common
- Families must advocate

1. Janzen, L. Spiegler, B. (2008) Neurodevelopmental sequelae of pediatric acute lymphoblastic leukemia and its treatment, *Dev Disability Res Rev.* 14(3) 185-195
2. Nathan, P. et al. (2007) Guidelines for identification of, advocacy for, and intervention in neurocognitive problems in survivors of childhood cancer: a report from the Children's Oncology Group. *Arch Pediatric Medicine*

Elimination of Cranial Radiation

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- It is clear the Neurocognitive Outcomes are better....but maybe not as much as we expected...and hoped!
- Success of ALL therapy = No expected significant modifications in the future
 - Ex. Elimination of Methotrexate, steroids
- We need to better understand host factors
- We need to better understand other potential contributors
 - Sleep?

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Sleep, fatigue and Neurocognitive Outcomes in Survivors

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- Cranky (emotional dysregulation)
- Can't think, less productive (cognitive fatigue)
- Feeling uncoordinated (prone to accidents)

Poor Sleep in Otherwise Healthy Children

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- Inadequate sleep correlates with poor attention, impulse control and behaviour regulation
- Limited experimental sleep deprivation studies in children (8)
 - Show more inattentive behaviour
 - Increased daytime sleepiness
 - Report less positive affect
 - Show diminished creativity, reasoning skills and executive functioning
 - Display diminished classroom performance
- Does this look familiar to the profile of Neurocognitive Outcomes??

Emerging Sleep and Neurocognitive Outcomes in CCS (Childhood Cancer Survivors)

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Clanton et al. (2011):

“Neurocognitive function in long-term survivors of childhood cancer appears particularly vulnerable to the effect of fatigue and sleep disruption. These findings suggest sleep hygiene should be emphasized among survivors, as it may provide an additional mechanism for intervention to improve neurocognitive outcomes”

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Will a sleep hygiene intervention work? Motivation? Readiness to make change? Dose Intensity?

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1. Clanton et al. (2011) Fatigue, vitality, sleep and neurocognitive functioning of adult survivors of childhood cancer: A Report from the Childhood Cancer Survivor Study, *Cancer*, 117(11)

SickKids CCS – Sleep and Neurocognitive Outcomes



Survivor Data

Cheung et al. (2017)

“Approximately two thirds of survivors reported delayed sleep onset and 30% to 40% had frequent nighttime and premature awakenings”

“Female survivors with frequent nighttime awakening displayed more inattention ($p = .01$), hyperactivity ($p = .03$), and aggression ($p = .01$). Worse executive function, processing speed, and behavioral symptoms were observed in female survivors with higher levels of IL-6, IL-1b, and hsCRP ($p < .05$)”

1. Cheung et al. (2017) Impact of Sleep, Fatigue, and Systemic Inflammation on Neurocognitive and Behavioral Outcomes in Long-term Survivors of Childhood Acute Lymphoblastic Leukemia

More Questions than Answers



- Neurocognitive Outcomes – sleep problems in disguise?
- What is the trajectory of sleep patterns and neurocognitive outcomes across ALL therapy?
- When should we intervene?
- How should we intervene?
- Do we have any clues now?

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A (quick) look at Sleep and Kids with ALL....

1. Zupanec, S., Jones, H., Stremler, R. (2010) Journal of Pediatric Hematology Oncology Nursing, 27, 217
2. Zupanec, S, Jones, H, McRae, L, Papaconstantinou, E, Weston, J, Stremler R. A Sleep Hygiene and Relaxation Intervention for Children with Acute Lymphoblastic Leukemia: A Pilot Randomized, Controlled Trial; Cancer Nursing, in press.



Mean (\pm SD)			
Actual sleep mn			
Off Dex	On Dex	<i>P</i>	
433.13 (55.61)	474.12 (88.39)	<.01*	
403.66 (109.27)	412.18 (146.74)	.61	
520.89 (61.46)	566.49 (161.32)	.23	
437.88 (87.81)	487.67 (97.85)	.001*	
Mean (\pm SD)			
Nocturnal Awakenings			
<i>P</i>	Off Dex	On Dex	<i>P</i>
.002*	18.74 (7.44)	16.52 (6.21)	.03*
.002*	16.43 (6.16)	15.38 (7.19)	.32
.23	11.47 (6.05)	12.71 (7.58)	.16
.001*	13.07 (6.42)	11.80 (5.10)	.38

- Night sleep time: Range 6.8 hours – 9.4 hours
- Average: 8 hours/night
- Night Awakenings: 11-18 per night

****Recommended 10-12 hours/night

SickKids Descriptive Sleep Results



- CHSQ scores > 41 indicate poor or problematic sleep habits (ROC sensitivity 0.80 and specificity 0.72) (Owens, Spirito, McGuinn, Sleep 2000)

CHSQ >41	Frequency	Percent
No	8	12.70
Yes	55	87.30

- 87% of our sample of children had scores indicating problematic sleep habits



Zupanec, S., Jones, H., Stremler, R. (2010)
Journal of Pediatric Hematology Oncology Nursing, 27, 217

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SHARI: Number of Night Awakenings

Reported normal night awakenings for children is 1-5*

	Sleep intervention	Control
Baseline	16.7	16.5
Follow-Up	18.5	20.0
Difference	Increased by 1.9	Increased by 3.5

- Consistent with Hinds et al (2007)

Evidence of Sleep Disruption/Poor Sleep Quality

Zupanec, S, Jones, H, McRae, L, Papaconstantinou, E, Weston, J, Stremmer R. A Sleep Hygiene and Relaxation Intervention for Children with Acute Lymphoblastic Leukemia: A Pilot Randomized, Controlled Trial; Cancer Nursing, in press.



SHARI: Results – Nighttime Sleep

Nighttime Sleep Minutes by Actigraphy

Group	Baseline	Follow-up
Sleep Intervention (n=9)	449 min (7.4 hours)	492 min (8.2 hours)
Sleep Control (n=9)	475 min (7.9 hours)	500 min (8.3 hours)

Age	Recommended number of sleep*
4-7	11-12 hours
8-12	10-11 hours

All children slept less than the recommended number of sleep hours

*Mindell & Owens (2003) A clinical guide to pediatric sleep: Diagnosis and management of sleep problems



- Evidence of Disturbed Sleep
- 7-8 hours of Nighttime Sleep Hours
 - Chronic Sleep Deprivation?
- 16-20 Night Awakenings
 - Impact on Restorative Sleep?
- Fixing Sleep might be harder than we think!

Williams et al. (2014)

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“Results revealed that the ALL group parents reported higher lax parenting and more spoiling and bribing of their child than the healthy control group”

“Results from regression models indicated that, after controlling for the significant contribution of illness status and child age on child emotional and behavioral difficulties, parental laxness and parental overprotection were significantly associated with child emotional and behavioral difficulties”

SickKids Parenting Child with ALL and Sleep



McCarthy et al. (2016):

“Parents of children undergoing ALL treatment reported significantly more child sleep problems; **48% of children with ALL** compared to **23% of healthy children** had clinical levels of sleep disturbance”

“Parents of the ALL group also reported significantly more **lax parenting practices** and strategies associated with their child’s sleep including co-sleeping, comforting activities, and offering food and drink in the bedroom”

“Results of multivariate regression analysis indicated that, after controlling for illness status, **parent–child co-sleeping was significantly associated with child sleep difficulties**”



Neurocognitive Assessment – Sleep Assessment too?

- Sleep not routinely screened as part of the Neurocognitive Assessments
- Recent evidence that daytime functioning and behaviour improves with improved sleep for other pediatric populations
 - ADHD
 - ASD
 - Evidence remains limited – somewhat controversial
- Sleep not routinely screened in oncology clinical visits

Despite lack of evidence should we still try?

- Reasonable to discuss that poor sleep, both decreased quantity and quality, might contribute to daytime functioning and behavior but maybe not promise that fixing the sleep will improve daytime functioning
- Potential benefits for the entire family!

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What's Next?



- Measure Neurocognitive scores across High Risk ALL therapy (COGState)
- Map trajectory of deficits!
- Need for Interventions
 - Medications
 - Remedial Cognitive Training
 - Sleep??
- Stay tuned!

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