

**1. Study Title:** Cognitive, behavior and learning problems in adolescent survivors of childhood acute lymphoblastic leukemia (ALL)

**2. Working Group:** Psychology/Neuropsychology

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**3. Background and Rationale:**

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, with a peak incidence of diagnosis between age 2 and 5 years.<sup>1</sup> Prognosis for children diagnosed with ALL has improved substantially over the past several decades, with 10-year overall survival rates reaching 90%.<sup>2</sup> One of the primary objectives of contemporary protocols is to maintain high cure rates while reducing treatment late effects, ultimately improving quality of life for survivors.

Survivors of childhood ALL are at increased risk for neurocognitive deficits, including problems with attention, reduced processing speed, and executive dysfunction.<sup>3-6</sup> These deficits reflect difficulty acquiring new skills at an age appropriate rate; as such, the functional impact may be heightened with increased time since treatment.<sup>7</sup> During adolescence, parents report increased symptoms of depression and anxiety and more social problems in survivors as compared with siblings.<sup>8</sup> Long-term adult survivors are at increased risk for learning difficulties<sup>9</sup> and decreased educational attainment<sup>10-11</sup> when compared with siblings.

Historically, cranial radiation therapy (CRT) was used for CNS prophylaxis in the majority of patients. Contemporary protocols have largely replaced CRT in favor of intrathecal (e.g., methotrexate alone or with cytarabine, and hydrocortisone) and intensified systemic chemotherapy (e.g., high-dose methotrexate, dexamethasone). Treatment intensity has been the most reliable predictor of increased risk,<sup>4,7,12-15</sup> although young age at treatment<sup>12,15-16</sup> and female gender<sup>17,18</sup> are frequently cited as risk factors. The majority of studies in survivors treated without CRT (i.e. chemotherapy only) demonstrate that survivors continue to be at risk for neurocognitive deficits, albeit at lesser magnitude than those survivors treated with CRT.<sup>5-6,19</sup> These existing studies are informative; however, they are limited by small sample sizes, single site data collection, and short time to follow-up. The CCSS survey data includes comprehensive information on >6000 survivors of childhood ALL treated at multiple sites over the past three decades. As such, these data allow for a detailed examination of the impact of treatment modifications on the emergence of late effects.

Adolescence is a developmental period when patterns of thinking and behavior become established; these characteristics often continue into adulthood.<sup>20-22</sup> The impact of neurocognitive late effects may be heightened during adolescence, as the expectations for planning, organization, and self-direction (i.e. executive function) are substantially increased. Studies demonstrate that adolescent survivors of childhood cancer with attention and executive function deficits more frequently engage in risky health behaviors (e.g., smoking).<sup>23</sup> Improved specification of cognitive, behavior, and learning problems in adolescent survivors can be used in efforts focused on the prevention and early detection of late effects that may ultimately lead to better functional outcomes and quality of life in adulthood. The longitudinal data available within CCSS provide a unique opportunity to quantify the impact of adolescent function on adult educational outcomes in order to identify and prioritize targets for intervention.

#### 4. SPECIFIC AIMS AND RESEARCH HYPOTHESES

The objective for the proposed project is to investigate the relationship between cognitive, behavior, and learning problems in adolescent survivors of childhood ALL, so as to target areas for intervention and improve overall quality of life for survivors. Using existing CCSS data, we will assess the prevalence and predictors of cognitive, behavior, and learning problems in adolescent survivors of ALL and examine the impact of adolescent problems on functional outcomes in adulthood. The detailed treatment information and extensive follow-up data available in CCSS will allow us to examine the functional impact of changes to ALL therapy over three decades.

##### Aims & Hypotheses

**4.1** To estimate the prevalence of parent-reported cognitive, behavior, and learning problems in adolescent survivors of childhood ALL.

**4.1.1** Cognitive and behavior problems are more frequent in survivors as compared to normative data.

**4.1.2** Cognitive, behavior, and learning problems are more frequent in survivors compared to siblings.

**4.2** To identify demographic and clinical predictors of parent-reported cognitive, behavior, and learning problems in adolescent survivors of childhood ALL.

**4.2.1** Survivors treated without CRT have less frequent cognitive, behavior, and learning problems when compared with survivors treated with CRT, but will have more frequent problems compared to siblings.

**4.2.2** Among survivors treated without CRT, cognitive, behavior, and learning problems are positively associated with higher-intensity chemotherapy (i.e., intrathecal [IT] therapy [total number of IT; IT methotrexate vs. triple IT, high-dose methotrexate - cumulative dose]; corticosteroid. [prednisone, dexamethasone, both]).

**4.2.3** Among survivors treated without CRT, cognitive, behavior, and learning problems are positively associated with young age at diagnosis and female gender.

**4.3** To examine the association among cognitive, behavior, and learning problems in adolescent survivors of childhood ALL.

**4.3.1** Survivors with parent-reported cognitive and/or behavior problems have a higher frequency of learning problems, as measured by parent-reported rates of participation in formalized academic services (e.g., special education).

**4.3.2** Among adolescent survivors with available follow-up data, parent-reported cognitive, behavior, and learning problems during adolescence are associated with self-reported educational outcomes in adulthood.

#### 5. ANALYSIS FRAMEWORK

##### 5.1 Study Population

**Aims 4.1, 4.2, and Hypotheses 4.3.1** will be investigated using pre-existing data from the following cohorts:

- Overall Cohort: Baseline data from ALL survivors and siblings who were 12-17 years old (Table 1).
  - Inclusion criteria: ALL survivors and siblings who were 12-17 years old at Baseline with completed parent-report measures of cognitive, learning, and behavior problems
  - Exclusion criteria: Down syndrome

**Hypotheses 4.3.2** will be investigated using pre-existing data from the following cohorts:

- Original Cohort: Baseline data from ALL survivors who 12-17 years old (Table 1).

- Original Cohort: Follow-up data for ALL survivors who were 12-17 years old at Baseline. We will use data from the 2003 or 2007 Follow-up survey, whichever is more recent (Table 1).
  - Inclusion criteria: ALL survivors who were 12-17 years old at Baseline with completed parent-report measures of cognitive, learning, and behavior problems and completed self-reported educational attainment at the 2003 or 2007 Follow-up, whichever is more recent
  - Exclusion criteria: Down syndrome

## 5.2 Variables of Interest

### Aims 4.1, 4.2, and Hypothesis 4.3.1

- Outcomes: Cognitive, behavior, and learning problems
  - Behavior Problem Index (BPI): Original Baseline, items J19-21; Expansion Baseline, items K3-6
  - School History: Original Baseline, items O1, O3-5; Expansion Baseline, items R1, R3-4
- Predictors/Covariates: Demographic, clinical, and treatment factors
  - Demographics: patient age at survey completion, sex (A2), race/ethnicity (A4/a), income (Original Baseline: O8, Expansion Baseline: T1).
  - Clinical/Treatment: medical record abstraction for ALL survivors between 12-17 years old
    - Age at diagnosis: continuous and categorical (<5 years old or >5 years old at diagnosis)
    - Chemotherapy: IT [total number of IT; IT methotrexate vs. triple IT]; high-dose methotrexate [cumulative dose]; corticosteroids [prednisone, dexamethasone, both].
    - CRT: None;  $\geq 20$  Gy;  $< 20$  Gy
    - We will assess whether the frequency of other medical conditions (e.g., hearing deficits, stroke, and epilepsy) impact findings. These variables will be included as covariates in analyses as needed.

### Hypothesis 4.3.2

- Outcome: Educational Attainment: 2003 Follow-up, item A1; 2007 Follow-up, item A3
- Predictors/Covariates: Cognitive, behavior, and learning problems
  - BPI: Original Baseline, items J19-J21; Expansion Baseline, items K3-K6
  - School History: Original Baseline, items O1, O3-5; Expansion Baseline, items R1, R3-4

## 5.3 Summary of Proposed Analyses

**Aim 4.1** Descriptive statistics will be calculated to characterize participants on demographic and treatment variables. Comparisons between survivors and siblings will be performed with generalized estimating equations, using a Poisson distribution. Comparisons between survivors with and without follow-up data will be made using frequency comparisons (e.g., Chi-Square). Please see Table 2.

The following factor scores will be calculated from the BPI: attention deficit, depression/anxiety, headstrong behavior, social withdrawal, and antisocial behavior, using previously established methods.<sup>8</sup> In order to examine the prevalence of cognitive and behavior problems, we will calculate the percentage of survivors with scores  $\geq 1.3$  standard deviations above the sibling group mean for each factor score. We will calculate Internalizing, Externalizing, and Total Problem Scores for survivors between the ages of 12 and 14 and compare these scores to normative expectations based on methods and data from the National Longitudinal Survey, Child Version (Table 3, Appendix 1).<sup>24</sup> We will compare frequencies of cognitive, behavior, and learning problems between survivors and siblings using analysis adjusted for intra-family correlation (e.g., Poisson regression with robust variances; Table 4).

**Aim 4.2** We will compare the frequency of cognitive, behavior, and learning problems between survivors and siblings using frequency comparisons adjusted for intra-family correlation (e.g., Poisson regression with robust variances; Table 4). We will compare the frequency of cognitive, behavior, and learning problems between survivors treated with and without CRT using Chi-square analyses (Table 4). We will assess the impact of demographic and categorical treatment variables on the frequency of cognitive, behavior, and learning problems in survivors treated

without CRT using univariate Chi-Square analyses (Tables 5 & 6). We will use multivariate analyses (e.g., logistic regression or Poisson regression) to assess the relative impact of these variables on rates of cognitive, learning, and behavior problems. Analyses will be adjusted for covariates as appropriate (Tables 7 & 8).

**Aim 4.3** We will use multivariate logistic regression to examine predictors of special education placement, including covariates as appropriate (Table 9). We will use multivariate analyses (e.g., logistic regression or Poisson regression) to assess the impact of cognitive, behavior, and learning problems on adult educational outcomes, including covariates as appropriate (Table 10).

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**Table 1. Characteristics of ALL survivors in the CCSS Original and Expansion Cohorts**

	Original Cohort		Expansion Cohort	
	N	%	N	%
Total Participants*	4329	100.0	1786	100.0
Gender (% male)	2302	53.2	989	55.4
Age at Diagnosis				
<1	57	1.3	65	3.6
1-3	1746	40.3	588	32.9
4-7	1417	32.7	429	24.0
8-10	440	10.2	162	9.1
11-14	436	10.1	340	19.0
15-20	233	5.4	202	11.3
<18 years old at Baseline	1552	37.4	--	--
Completed 2003 Follow-up	--	--	NA	NA
Completed 2007 Follow-up	--	--	NA	NA
Treatment				
Available data	4278	100.0	2453	100.0
Any radiation	2958	69.1	820	33.4
Dexamethasone	585	13.7	1109	45.3
Methotrexate - All routes	4129	96.5	2004	81.9
Methotrexate – IM	445	10.4	463	18.9
Methotrexate – IT	3831	89.6	1900	77.6
Methotrexate – IV	1725	40.3	1264	51.6
Methotrexate – PO	3098	72.4	815	33.3
Prednisone	3981	93.1	1662	67.9

\*Total participants eligible for Baseline survey in the ALL Original cohort = 5980 and ALL Expansion cohort = 2522.

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**Table 2. Participant Characteristics**

	<b>Baseline</b>					<b>Follow-up</b>				
	Survivors		Siblings		$p^a$	Participants		Non-participants		$p^b$
	<i>N</i>	%	<i>n</i>	%		<i>n</i>	%	<i>n</i>	%	
Sex										
Male										
Female										
Race										
White										
Black										
American Indian/Alaskan Native										
Asian or Pacific Islander										
Other										
Ethnicity										
Hispanic										
Non-Hispanic										
Age at Diagnosis (years)										
<1										
1-3										
4-7										
8-10										
11-14										
15-20										
CNS treatment										
Chemotherapy			.	.	.					
Radiation			.	.	.					
Chemotherapy and radiation			.	.	.					
CRT										
None			.	.	.					
< 18 Gy			.	.	.					
18 – 20 Gy			.	.	.					
20 - 24 Gy			.	.	.					
> 24 Gy			.	.	.					
Intrathecal chemotherapy (total # doses)										
None			.	.	.					
MTX			.	.	.					
Triple IT			.	.	.					
IV MTX**										
No			.	.	.					
Yes			.	.	.					
Corticosteroids										
None			.	.	.					
Prednisone only			.	.	.					
Dexamethasone only			.	.	.					
Prednisone and Dexamethasone			.	.	.					

Abbreviations: CRT, cranial radiation therapy, Triple IT, triple intrathecal chemotherapy (including methotrexate), MTX, methotrexate, IV, intravenous

<sup>1</sup>Baseline surveys for ALL survivors and all siblings 12-17 years old. <sup>2</sup>ALL survivors with completed self-report follow-up surveys from 2003 or 2005, whichever is later. <sup>3</sup> Follow-up non-participants ALL survivors who were 12-17 years old at Baseline with without completed follow-up surveys.

$p^a$ : *p-value is from frequency comparisons of survivors and siblings, adjusted for intra-family correlation (e.g., Generalized Estimating Equation).*

$p^a$ : *p-value is from frequency comparisons (e.g., Chi Square) between ALL survivors with completed Baseline with or without follow-up survey.*

**\*\* IV MTX may also be analyzed in dose ranges, depending on available data**

**Table 3. Mean score, standard deviation, and frequency of clinical elevations by BPI Internalizing, Externalizing, and Total Problem Scores**

	<u>Internalizing Symptoms*</u>			<u>Externalizing Symptoms*</u>			<u>Total Score*</u>		
	<i>M ± SD</i>	<i>n (%)</i>	<i>P</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>
Survivors									
Normative data									

\* Higher score indicates more difficulty. Data for both cohorts are from children between the ages of 12 and 14.

Frequency of participants with scores that are  $\geq 1.3$  SD above the mean factor score for the normative data

*p*-values are from frequency comparisons (e.g., Chi-Square) between survivors and normative expectations.



**Table 4. Univariate frequency comparisons of parent-reported cognitive, behavior, and learning problems**

	<b>Overall survivor cohort (N=X)</b>	<b>Siblings (N=649)</b>		<b>Survivors treated with CRT (N=X)</b>		<b>Survivors treated without CRT (N=X)</b>		
	<i>n (%)</i>	<i>n (%)</i>	<i>p</i> <sup>1</sup>	<i>n (%)</i>	<i>p</i> <sup>2</sup>	<i>n (%)</i>	<i>p</i> <sup>3</sup>	<i>p</i> <sup>4</sup>
Behavior Problems Index <sup>‡</sup>								
Depression/Anxiety*								
Headstrong Behavior*								
Attention Deficit*								
Peer Conflict/Social Withdrawal*								
Antisocial *								
Special Education Classes								
Yes								
No								

\* Higher score indicates more difficulty

<sup>‡</sup>Frequency of participants with BPI factor scores that are  $\geq 1.3$  SD above the mean score for the sibling cohort

*p*<sup>1</sup>: *p*-value from frequency comparisons between the overall survivor cohort and siblings, adjusted for with robust variances (e.g., Generalized Estimating Equation)

*p*<sup>2</sup>: *p*-value from frequency comparisons between survivors treated with CRT and siblings, adjusted for with robust variances (e.g., Generalized Estimating Equation)

*p*<sup>3</sup>: *p*-value from frequency comparisons between survivors treated without CRT and siblings, adjusted for with robust variances (e.g., Generalized Estimating Equation)

*p*<sup>4</sup>: *p*-value from frequency comparisons between survivors treated with and without CRT (e.g., Chi-Square)

**Table 5. Univariate frequency comparisons of parent-reported cognitive and behavior problems by demographic and treatment risk factors in ALL survivors treated without CRT**

	<u>Depression/Anxiety *</u>			<u>Headstrong Behavior *</u>			<u>Attention Deficit *</u>			<u>Peer Conflict/Social Withdrawal *</u>			<u>Antisocial Behavior *</u>		
	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>	<i>M ± SD</i>	<i>n (%)</i>	<i>p</i>
Sex															
Males ‡															
Females															
Age at diagnosis															
< 5 years															
≥ 5 years ‡															
Intrathecal therapy															
None ‡															
MTX															
Triple IT															
IV MTX															
None ‡															
Yes**															
Corticosteroids															
None ‡															
Prednisone															
Dexamethasone															
Prednisone & Dexamethasone															

Abbreviations: *M*, mean *SD*, standard deviation, *Triple IT*, triple intrathecal chemotherapy (including methotrexate), *MTX*, methotrexate, *IV*, intravenous

\* Higher score indicates more difficulty

*p*-values are from comparison of the frequency of clinical elevation by demographic and treatment factors (e.g. Chi-Square)

‡Reference group for statistical comparison

\*\* *IV MTX* may also be analyzed in dose ranges, depending on available data

**Table 6. Univariate frequency comparisons of special education placement by demographic and treatment factors in ALL survivors treated without CRT**

	<b>Special Education Placement</b>	
	<i>n (%)</i>	<i>p</i>
Sex		
Males <sup>‡</sup>		
Females		
Age at diagnosis		
< 5 years <sup>‡</sup>		
≥ 5 years		
Intrathecal therapy		
None <sup>‡</sup>		
MTX		
Triple IT		
IV MTX		
None <sup>‡</sup>		
Yes**		
Corticosteroids		
None <sup>‡</sup>		
Prednisone		
Dexamethasone		
Prednisone + Dexamethasone		

*Abbreviations: M, mean SD, standard deviation, Triple IT, triple intrathecal chemotherapy (including methotrexate), MTX, methotrexate, IV, intravenous*

*p-values are from comparison of the frequency of clinical elevation by demographic and treatment factors (e.g. Chi-Square)*

*<sup>‡</sup>Reference group for statistical comparison*

*\*\* IV MTX may also be analyzed in dose ranges, depending on available data*

**Table 7. Risk of cognitive and behavior problems among survivors treated without CRT by demographic and treatment characteristics**

	<u>Depression/Anxiety *</u>			<u>Headstrong Behavior *</u>			<u>Attention Deficit *</u>			<u>Peer Conflict/Social Withdrawal *</u>			<u>Antisocial Behavior *</u>		
	%	OR/ RR	99% CI	%	OR/ RR	99% CI	%	OR/ RR	99% CI	%	OR/ RR	99% CI	%	OR/ RR	99% CI
Sex															
Males <sup>‡</sup>															
Females															
Age at diagnosis															
< 5 years <sup>‡</sup>															
≥ 5 years															
Intrathecal therapy															
None <sup>‡</sup>															
MTX															
Triple IT															
IV MTX															
None <sup>‡</sup>															
Yes**															
Corticosteroids															
None <sup>‡</sup>															
Prednisone															
Dexamethasone															
Prednisone/Dexamethasone															

Abbreviations: SD, standard deviation, MTX, methotrexate, Triple IT, triple intrathecal chemotherapy (including methotrexate), IV, intravenous, RR standardized risk ratio, CI, confidence interval

\* Higher score indicates more difficulty.

<sup>‡</sup>Referent group for statistical comparison

RRs and 99% CIs for cognitive and behavior limitations from multiple variable models adjusted for variables including (e.g., sex, age at diagnosis, etc.)

\*\* IV MTX may also be analyzed in dose ranges, depending on available data

**Table 8. Risk of cognitive and behavior problems among survivors treated without CRT by demographic and treatment characteristics**

	<u>Special Education Placement</u>		
	(%)	OR/RR	p
Sex			
Males ‡			
Females			
Age at diagnosis			
< 5 years ‡			
≥ 5 years			
Intrathecal therapy			
None ‡			
MTX			
Triple IT			
IV MTX			
None ‡			
Yes**			
Corticosteroids			
None ‡			
Prednisone			
Dexamethasone			
Prednisone & Dexamethasone			

*Abbreviations: SD, standard deviation, MTX, methotrexate, Triple IT, triple intrathecal chemotherapy (including methotrexate), IV, intravenous, RR standardized risk ratio, CI, confidence interval*

*\* Higher score indicates more difficulty.*

*‡Referent group for statistical comparison*

*RRs and 99% CIs for cognitive and behavior limitations from multiple variable models adjusted for variables (e.g., sex, age at diagnosis, etc.)*

*\*\* IV MTX may also be analyzed in dose ranges, depending on available data*

**Table 9. Predictors of learning problems in survivors treated without CRT**

	<b>Special Education</b>		
	<b>%</b>	<b>OR/RR</b>	<b>99% CI</b>
Anxiety/Depression*			
Headstrong Behavior*			
Attention Deficit*			
Peer Conflict/Social Withdrawal*			
Antisocial*			

*Abbreviations: SD, standard deviation, MTX, methotrexate, Triple IT, triple intrathecal chemotherapy (including methotrexate), IV, intravenous, RR standardized risk ratio, CI, confidence interval*

*\* Higher score indicates more difficulty.*

*RRs and 99% CIs for cognitive and behavior limitations from multiple variable models adjusted for variables (e.g., age, sex, etc.)*

**Table 10. Self-reported educational outcomes for participants completing a follow-up survey**

	<u>Completed high school/GED</u>			<u>Training after high school</u>			<u>Some college</u>			<u>College graduate</u>			<u>Post-graduate level</u>		
	%	OR/RR	99% CI	%	OR/RR	99% CI	%	OR/RR	99% CI	%	OR/RR	99% CI	%	OR	99% CI
Males <sup>‡</sup>															
Females															
Age at diagnosis															
< 5 years															
≥ 5 years <sup>‡</sup>															
Special Education															
No <sup>‡</sup>															
Yes															
Behavior Problem Index															
Anxiety/Depression*															
Headstrong Behavior*															
Attention Deficit*															
Peer Conflict/Social Withdrawal*															
Antisocial*															

Abbreviations: SD, standard deviation, MTX, methotrexate, Triple IT, triple intrathecal chemotherapy (including methotrexate), IV, intravenous, RR standardized risk ratio, CI, confidence interval

\* Higher score indicates more difficulty

<sup>‡</sup>Referent group for statistical comparison

RRs and 99% CIs for cognitive and behavior limitations from multiple variable models adjusted for variables (e.g., sex, age at diagnosis, etc.)

**Appendix 1***Internalizing and Externalizing Symptom Domains from the Behavior Problem Index on the National Longitudinal Survey of Youth*

<b>Parent-report items for children <math>\geq 12</math> years</b>	<b>Scale*</b>
Does not seem to feel sorry after misbehaving	**
Feels others are out to get him/her	**
Hangs around with kids who get into trouble	**
Is secretive, keeps things to self	**
Worries too much	**
Cheats or tells lies	E
Bullies or is cruel/mean to others	E
Is disobedient at school	E
Has trouble getting along with teachers	E
Has sudden changes in mood or feeling	E
Is rather high strung, tense, and nervous	E
Argues too much	E
Is disobedient at home	E
Is stubborn, sullen, or irritable	E
Has strong temper and loses it easily	E
Is impulsive or acts without thinking	E
Has trouble getting mind off certain thoughts	E
Is restless, overly active, cannot sit still	E
Has trouble getting along with other children	E
Is not liked by other children	E
Is too fearful or anxious	E/I
Is unhappy, sad, or depressed	E/I
Is easily confused, seems in a fog	E/I
Feels/complains no one loves him/her	I
Feels worthless or inferior	I
Has difficulty concentrating/paying attention	I
Is withdrawn, does not get involved with others	I

\*E = Externalizing, I=Internalizing; \*\* Does not load on the E-I dimensions

**Methods**

- Parents of children between the ages of 4-14 who completed the National Longitudinal Survey, Child Version
- Scores are recoded such that higher scores indicate more problems
  - o Not True = 3 recoded to 0
  - o Sometimes True = 2 on survey, recoded to 1
  - o Often True = 1 on survey, recoded to 2
- Standard Scores and percentile ranks are available for 12, 13, and 14 year-old children



Age 12

Internalizing Subscale			Externalizing Subscale			Total Score		
Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score
0	246	90	0	175	86	0	178	86
1	436	98	1	221	88	1	217	88
2	643	105	2	273	91	2	262	90
3	814	113	3	330	93	3	310	93
4	922	121	4	392	96	4	363	95
5	974	129	5	456	98	5	418	97
6	993	137	6	522	101	6	474	99
7	999	145	7	587	103	7	531	101
8	1000	153	8	650	106	8	588	103
9	1000	161	9	708	108	9	642	105
>=10	1000	169	10	762	111	10	694	108
			11	810	113	11	742	110
			12	852	116	12	786	112
			13	886	118	13	826	114
			14	915	121	14	860	116
			15	938	123	15	889	118
			16	956	126	16	914	120
			17	969	128	17	934	123
			18	979	130	18	951	125
			19	986	133	19	964	127
			20	991	135	20	974	129
			21	994	138	21	981	131
			22	996	140	22	987	133
			23	998	143	23	991	136
			24	999	145	24	994	138
			25	999	148	25	996	140
			26	1000	150	26	997	142
			27	1000	153	27	998	144
			28	1000	155	28	999	146
			29	1000	158	29	999	148
			30	1000	160	30	1000	151
			31	1000	163	31	1000	153
			32	1000	165	32	1000	155
			33	1000	168	33	1000	157
			>=34	1000	170	34	1000	159
						35	1000	161
						36	1000	163
						37	1000	165
						>=38	1000	168

Age 13

Internalizing Subscale			Externalizing Subscale			Total Score		
Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score
0	244	90	0	163	85	0	166	85
1	441	98	1	207	88	1	204	88
2	654	106	2	257	90	2	247	90
3	826	114	3	313	93	3	294	92
4	931	122	4	373	95	4	345	94
5	979	130	5	437	98	5	399	96
6	995	139	6	502	100	6	455	98
7	999	147	7	567	103	7	512	100
8	1000	155	8	631	105	8	568	103
9	1000	163	9	691	107	9	624	105
10	1000	171	10	746	110	10	676	107
>=11	1000	179	11	796	112	11	726	109
			12	839	115	12	771	111
			13	876	117	13	812	113
			14	907	120	14	848	115
			15	931	122	15	879	118
			16	950	125	16	905	120
			17	965	127	17	927	122
			18	976	130	18	945	124
			19	984	132	19	959	126
			20	989	135	20	970	128
			21	993	137	21	979	130
			22	996	140	22	985	133
			23	997	142	23	990	135
			24	998	144	24	993	137
			25	999	147	25	995	139
			26	1000	149	26	997	141
			27	1000	152	27	998	143
			28	1000	154	28	999	145
			29	1000	157	29	999	148
			30	1000	159	30	1000	150
			31	1000	162	31	1000	152
			32	1000	164	32	1000	154
			>=33	1000	167	33	1000	156
						34	1000	158
						35	1000	160
						36	1000	162
						37	1000	164
						38	1000	166
						>=39	1000	169

Age 14

Internalizing Subscale			Externalizing Subscale			Total Score		
Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score	Raw Score	Percentile Score	Standard Score
0	245	90	0	176	86	0	178	86
1	453	98	1	222	89	1	218	88
2	675	107	2	274	91	2	262	90
3	848	115	3	331	93	3	311	93
4	945	124	4	393	96	4	363	95
5	985	133	5	458	98	5	418	97
6	997	141	6	523	101	6	475	99
7	1000	150	7	588	103	7	532	101
8	1000	158	8	651	106	8	589	103
9	1000	167	9	710	108	9	643	106
10	1000	176	10	764	111	10	695	108
11	1000	185	11	811	113	11	744	110
>=12	1000	193	12	853	116	12	788	112
			13	887	118	13	827	114
			14	916	121	14	861	116
			15	938	123	15	890	118
			16	956	126	16	915	121
			17	969	128	17	935	123
			18	979	131	18	951	125
			19	986	133	19	964	127
			20	991	135	20	974	129
			21	994	138	21	982	131
			22	996	140	22	987	133
			23	998	143	23	991	136
			24	999	145	24	994	138
			25	999	148	25	996	140
			26	1000	150	26	997	142
			27	1000	153	27	998	144
			28	1000	155	28	999	146
			29	1000	158	29	999	149
			30	1000	160	30	1000	151
			31	1000	163	31	1000	153
			32	1000	165	32	1000	155
			33	1000	168	33	1000	157
			34	1000	170	34	1000	159
			35	1000	173	35	1000	161
			36	1000	175	36	1000	164
			37	1000	178	37	1000	166
			>=38	1000	180	38	1000	168
						39	1000	170
						40	1000	172
						41	1000	174
						42	1000	176
						43	1000	178

Jacola LM

Cognitive, behavior, and learning problems in ALL

	44	1000	180
	45	1000	182
	>=46	1000	185