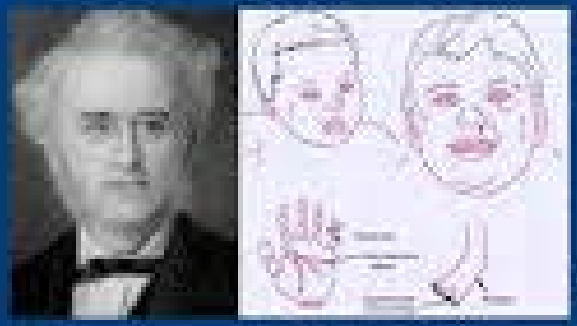
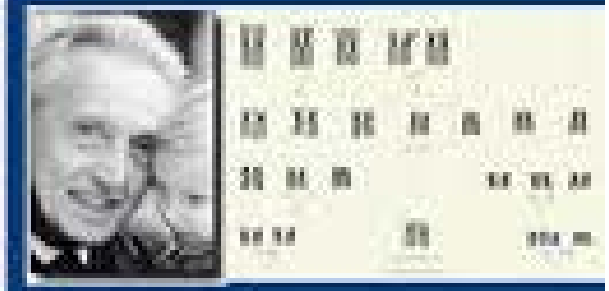
Anna & John J. Sie Center for Down Syndrome Affiliates

Down Syndrome is caused by Trisomy 21





1866: Langdon Down describes the clinical features of Down syndrome

1959: Jerome Lejeune describes trisomy 21 in association with DS

Types of Medical Research

Bench or basic research: done in a controlled laboratory setting using nonhuman subjects

Clinical research: answer questions regarding the effectiveness of treatments, medications, preventative measures, and more with human subjects

- ex: studying patients over time to see who had the best outcomes

Clinical trials (type of clinical research): explore whether a medical strategy, treatment, or device is safe and effective for humans

- ex: testing a new medication before it is made available

Translational research: aims to "translate" findings in bench research into medical practice and meaningful health outcomes

Health Supervision for Children with Down Syndrome: AAP, August 2011 *Pediatrics 2011*

- These guidelines are designed to assist the pediatrician and Subspecialties in caring for children with a diagnosis of Down syndrome

AAP Guidelines Chart

Children's Hospital Colorado
Anna and John J. Sie Center for Down Syndrome

Down Syndrome Healthcare Guidelines (2011 Revision) Record Sheet*

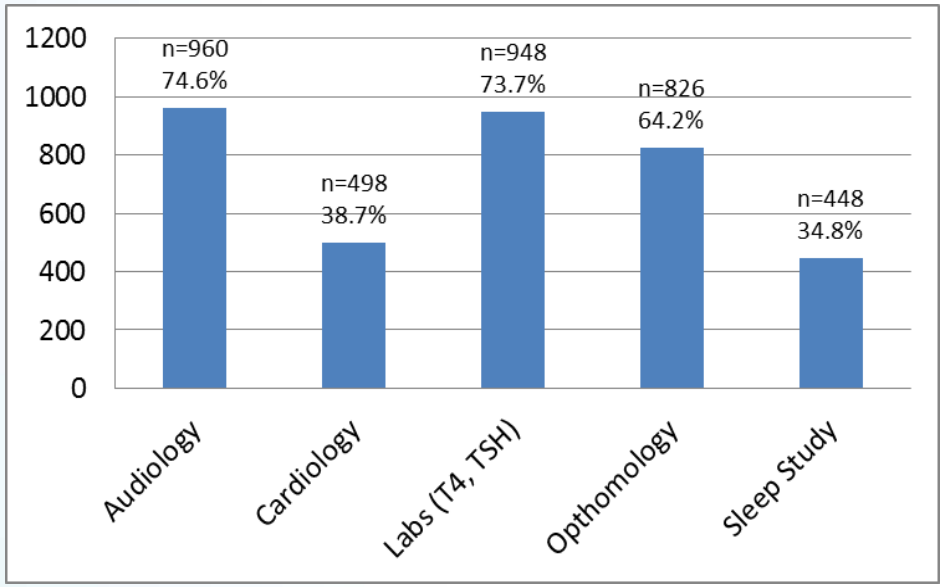
	Birth	6 mo	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Genetic Counseling[1], Karyotype																						
Parent Group Info and Support																						
CBC to R/O transient myeloproliferative disorder, polycythemia	Parent-to-parent contact, support groups, current books and pamphlets																					
Swallowing assessment if feeding problems or aspiration																						
Hemoglobin			Hemoglobin annually beginning at 1 year old. If Hg<11, do (a) CRP and ferritin, or (b) Reticulocyte Hemoglobin Content (CHr). If possible risk for iron deficiency, do (a) or (b) regardless.																			
23-valent pneumococcal vaccine[2]																						
Cardiology	Echo[4]														Screen for acquired mitral or aortic valvular disease							
Audiological Evaluation	ABR or OAE	Every 6 months till 3 years of age. Annually thereafter.																				
Ophthalmologic Evaluation	Red Reflex	Optho Appt	Annual ophthalmology appt					Q2 Ophthalmology appointment							Q3 Ophthalmology appointment							
Celiac Disease Screening					(Only test if signs and symptoms present)																	
Thyroid – TSH, T4	State Screen	Test	Test	Test TSH and T4 annually																		
Neck X-ray (AAI)[3]					✓[3]																	
Dental Exam			Annual Dental Exams. Reassure parents that delayed or irregular eruption, hypodontia are common.																			
Sleep Study by age 4 years	Done prior to 4 years of age																					
Early Intervention																						
Childhood					Discuss self-help, ADHD, OCD, wandering off, transition to middle school																	
Puberty															Discuss physical and psychosocial changes through puberty, need for gynecologic care (pelvic exams) in pubescent female							
Facilitate transition															Guardianship, financial planning, behavioral problems, school placement, vocational training, independence with hygiene and self-care, group home, work settings							
Sexual development and behaviors															Discuss Contraception, STDs, recurrence risk for offspring							
Preventive care	Annually monitor for signs and symptoms of constipation, OSA, and aspiration.																					

1. Discuss Recurrence Rate of future pregnancies with parents
2. 23-valent pneumococcal vaccine if chronic or pulmonary disease.
3. AAI: See AAP Guidelines page 399 - X-rays only if myopathic signs or symptoms
4. Follow up to be determined by Cardiologist

* Peds 2011 ;128 :393-406 Chart by Sie Center for Down Syndrome

Updated 09/2013

Impact on Compliance to AAP Down syndrome Guidelines at Sie Center



74.6% referred to **Audiology**

38.7% referred to **Cardiology**

73.7% referred to get **labs (TSH, T4)**

64.2% referred to **Ophthalmology**

34.8% referred to get a **Sleep Study**

2016

Total Unique Patients: 1,287

Total Referrals: 8,745

2015

Total Unique Patients: 1,125

Total Referrals: 6,000+

Sleep Study Recommended in 2011 Guidelines

Sleep studies (start at 4yo per guidelines) N=678 61.2%

Abnormal sleep studies (out of n=678) N= 482 71.1%

Obstructive sleep apnea (out of n=678) N=448 66.1%

Predisposing Factors for OSA

Anatomic

- Maxillary Hypoplasia
- Relative Macroglossia
- Obesity
- Smaller Airways
- Pulmonary Hypoplasia: poorer gas exchange

Neurologic

- Hypotonia; airway hypotonia

Reflux /Aspiration

- Inflammation; Hypoxia

Morbidity of OSA

Neuropsychological

Cognitive

- Learning
- Executive Function

Behavior

Cardiovascular

OSA may compromise long term CV health

PAH in DS

Cardiac dysfunction

Growth issues

Pulmonary Issues in Down Syndrome

- 1 in 700 live births
- 6000 births per year in the US
- High risk of morbidity and mortality from pulmonary disease.
- **Pneumonia is the most common cause of death in Down Syndrome**
  - Causes 23-40% of deaths depending on age

Bittles, *Eur J of Public Health* 2006
Weijerman, *J Pediatr*, 2007
Yang *The Lancet*. 2002
Watts, *Arch Dis Child*, 2013
Joffre, *J Paediatr Child Healthm* 2016

Pulmonary Hypertension in T21

Sie Center for T21 Database (n=1252)

- Pulmonary Hypertension (28%)

Aerodigestive Presenting Symptoms

Comorbid Condition	Number with Condition	Relative Risk
Congenital Heart Disease	269	8.62
Obstructive Sleep Apnea	146	**3.22**
Thyroid Dysfunction	86	0.64
Abnormal Swallow Study	76	**2.08**
Recurrent Pneumonia	72	**2.06**
Intermittent Hypoxemia	136	3.56
Airway Malacia	140	**21.3**

Data from Sie Center Article Submitted recently

Anatomy contributes to morbidity and mortality

Structural Airway:
- Mid-face hypoplasia
- Relative macroglossia
- Small airways
- Malacia

Congenital heart disease

Pulmonary hypoplasia

Pulmonary vascular disease

Dental issues

Immune abnormalities

Structural GI tract:
- duodenal atresia
- pyloric stenosis
- Hirschsprung's disease
- esophageal atresia/ stenosis
- malrotation

Endocrine issues
- Thyroid, Obesity, DM

Low muscle tone

Neurocognitive development

Weijerman, *J Pediatr*, 2007
Watts, *Arch Dis Child*, 2013
Joffre, *J Paediatr Child Healthm* 2016

Respiratory Illness: Morbidity and Mortality

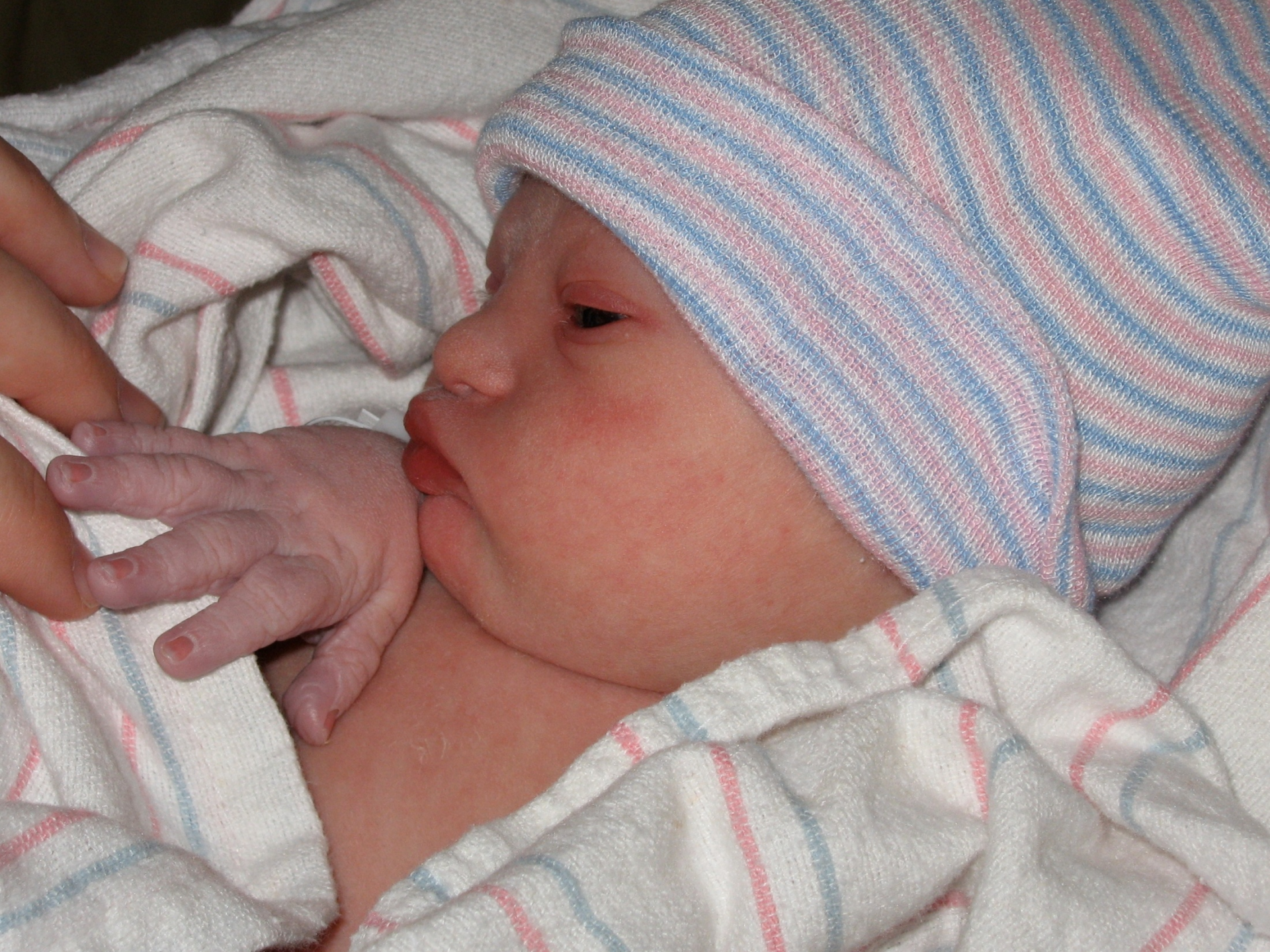
- Respiratory illnesses are the cause of 80% of admissions to the hospital for children with DS
- Leading cause of mortality in published studies
- Aspiration issues:
  Recurrent Pneumonias, Laryngeal clefts

  High Referral Rate to Aerodigestive Team-Pulm,GI,ENT,Feeding

McDowell 2011 Yang 2002

SIE CENTER ETHNIC SUBGROUPS

Ethnicities	n	%
White, non-Hispanic	833	57.3%
Hispanic/Latino	415	**28.6%**
More than one race, non-Hispanic	28	1.9%
Black or African American, non-Hispanic	48	3.3%
Other race, non-Hispanic	33	2.3%
Asian	25	1.7%
American Indian/Alaska Native	6	0.4%
Native Hawaiian/Pacific Islander	1	0.0%
Unknown	64	4.4%
Total	**1453**	100%



High Rate of Neonatal Complications

70.6% requiring NICU stay as newborns, indicating the importance of appropriate medical readiness and intervention from birth to discharge

Oxygen in over 60% of admits and 60% required phototherapy.

These numbers are higher in comparison to the largest NICU dataset for DS published from the United Kingdom (n=725, NICU admission rate=46%; require oxygen=31%).

PAH 15%

Feeding Problem 48%

Comorbidities and medical complications of children treated in the SCDS Clinic

Results		n	%
GI diagnosis		766	**69.1%**
	GERD	424	38.3%
	Feeding problem	319	28.8%
	GI malformations	134	12.1%
	G-tube	99	8.9%
	Esophageal stricture	9	1.6%
Ophthalmologic anomalies		722	**65.2%**
	Strabismus	190	17.1%
	Nasolacrimal duct obstruction surgery	89	8.0%
	Strabismus surgery	59	5.3%
	Cataracts	43	3.9%
Cardiac defects		712	**64.3%**
	Heart defects requiring surgery	343	**31.0%**
Sleep: Sleep study		678	61.2%
	Abnormal sleep studies (out of n=678)	482	71.1%
	Obstructive sleep apnea (out of n=678)	448	66.1%

Comorbidities and medical complications of children treated in the SCDS Clinic

Results (continued)		n	%
ENT: Tonsillectomy and/or adenoidectomy		522	47.1%
ENT: **Laryngomalacia**		65	**5.9%**
Audiology: PE tube		468	42.2%
Audiology: Hearing aid		100	9.0%
Autoimmune diagnosis		409	36.9%
	Hypothyroidism	302	27.3%
	Hyperthyroidism	15	1.4%
	Celiac disease	55	5.0%
	Alopecia	15	1.5%
	Juvenile Rheumatoid Arthritis	2	0.2%
Pulmonary: Aspiration		135	**12.2%**
Pulmonary hypertension		314	**28.3%**
Neurologic: Seizures		53	4.8%
	Infantile spasms	30	2.7%
Autism		38	3.4%
Leukemia		17	1.5%
Transient Myelodysplasia		12	1.1%

Audiology:

Guideline recommendations for testing every 6 months until three years of age and then annually .

Our highest noncompliant rate of all guideline recommendations is audiology at 74%, which is disconcerting.

A recent published paper * from our clinic and audiology dept at CHCO, indicates a high rate of hearing loss. In 2013, after increasing referrals from our clinic to audiology, **24.9%** of 308 children with DS were identified with permanent hearing loss at the average age of 6 years.

Autoimmune diagnosis:

Thyroid abnormalities (29.1%),hypothyroid (27.3%) and celiac disease (5.0 %) results may be an underestimation of the prevalence, since a large percentage of our clinic population is under four years of age.

* Nightengale 2017

Pediatricians and family practice physicians need to be aware of:

(1) The increased incidence of comorbidities, especially at birth

(2) the importance of appropriate evaluation and referral consistent with the compliance to the AAP's DS Guidelines for all children with DS

(3) establishing treatment plans with a developmental specialty team for identified comorbidities

(4) Considering implementing routine celiac screenings and swallow studies not currently outlined in the guidelines

Dysphagia and Aspiration Management in Children with Down Syndrome

Children's Ho
Here, it's different.™

Aspiration in Down syndrome

In the first few years of the clinic, a significant number of abnormal swallow studies were noted in our population data. The 2011 AAP DS Guidelines also recommended increased consideration of obtaining feeding assessments in children with DS if symptoms.

These two issues led to the following:

1) increase in ordering of swallow studies
2) starting a Feeding Clinic
3) initiating subsequent feeding research.

The research led to the finding of 158 patients studied- 56% had pharyngeal phase dysphagia;

90.2% of patients who aspirated did so silently without symptoms

Follow up studies are in process to better define at-risk infants.

Jackson et al. (2016)

Clinical Care Pathway (CCP) for Dysphagia in Down Syndrome

Better process for dysphagia management identified as an area of need by CHCO physicians, parents/caregivers, and community physicians

Goals:

- Guidelines for evaluation
- Physician management
- Therapeutics
- Standardization of care
- Centralized resource for information

What We Have Learned About Feeding

Routine screening of feeding/swallowing is essential during PCP visits

Aspiration is the most common symptom of dysphagia in children with DS, and is often silent

When dysphagia persists, coordinated subspecialty care with ENT, GI, and Pulmonary is recommended

Communication with feeding and swallowing specialists is critical to establish a developmentally supportive feeding plan when dysphagia is present

Research Projects N=25

Endostatin as a Biomarker of Risk for Pulmonary Hypertension in Down Syndrome

Abstract/Aims: To determine whether serum endostatin levels correlate to PAH disease onset or severity in patients with DS. We will compare patients who have DS with PAH, DS without PAH, non-DS with PAH and non-DS normal healthy controls.

Trisomy 21, Obstructive Sleep Apnea, & Airvo High-flow Nasal Cannula Algorithm -PULM

Abstract/Aims: We are looking at both "rescue" and "CPAP comparison" groups where the rescue kids will have attempted and failed CPAP, and the CPAP comparison group includes kids adherent to prescribed CPAP.

Immune -Neutropenia/Leukopenia in Trisomy 21

Abstract/Aims: Define average CBC panel results for children with Down syndrome.

Part II to assess Immune Function in Down Syndrome

Comparison of children with history of significant infection vs. a control group

Human Trisome Project

Working with Crnic Project

Ethnic Differences in Child Feeding Practices in Children with Down syndrome and Association with BMI

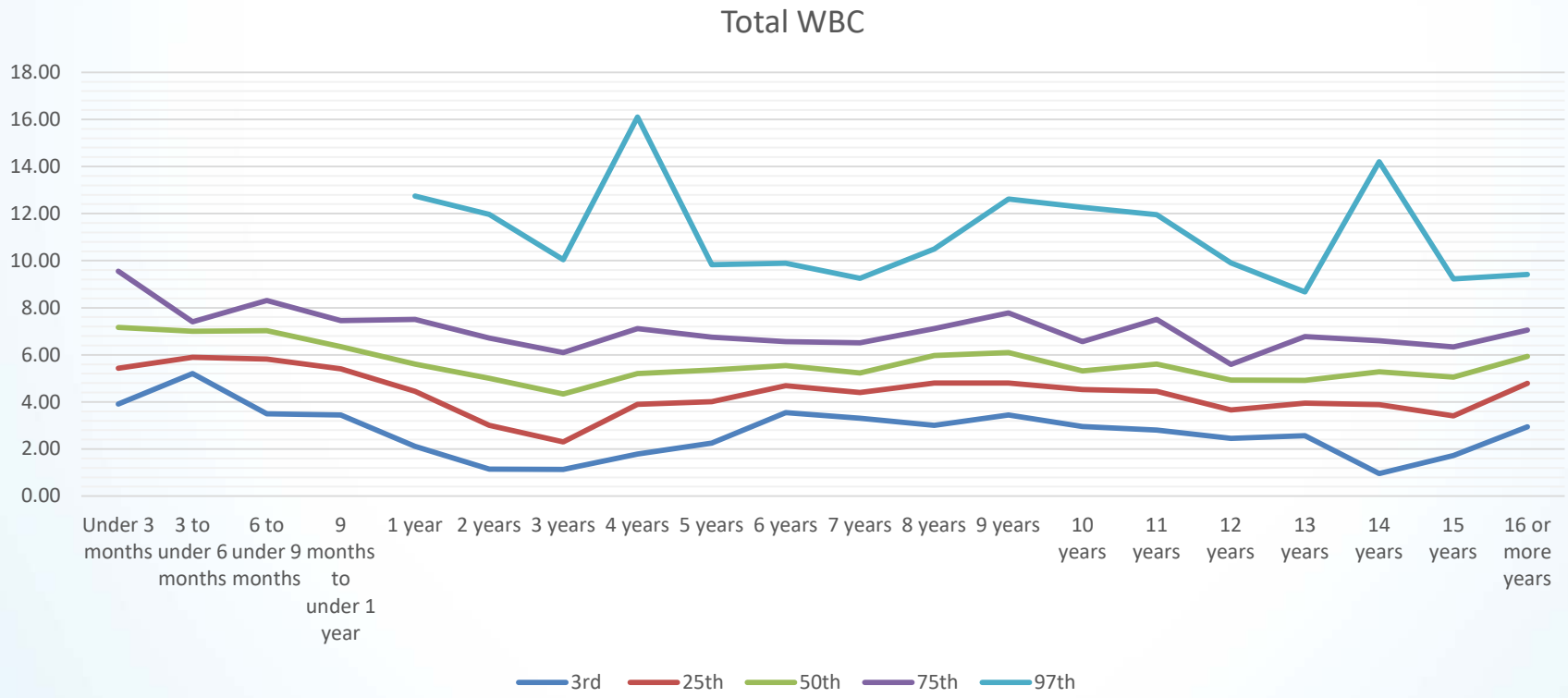
Abstract/Aims: Examining how ethnicity and demographics play a role in feeding practices and relationship of feeding to BMI

Accuracy of Welch Allyn Spot™ Vision Screener to Detect Amblyogenic Factors in Developmentally Delayed Children

Abstract/Aims: Assess whether the Welch-Allyn SPOT Vision Screener (SPOT) is effective at detecting various amblyogenic risk factors (ARFs) in developmentally delayed children. Fifty patients would be recruited from the Sie Center Clinic and 50 from SCC Special Care Clinic.

Status: Completed

Total tests in the sample (Sie Center patients) n=2,083
Unique Sie Center patients with results n=669



The End and Thanks