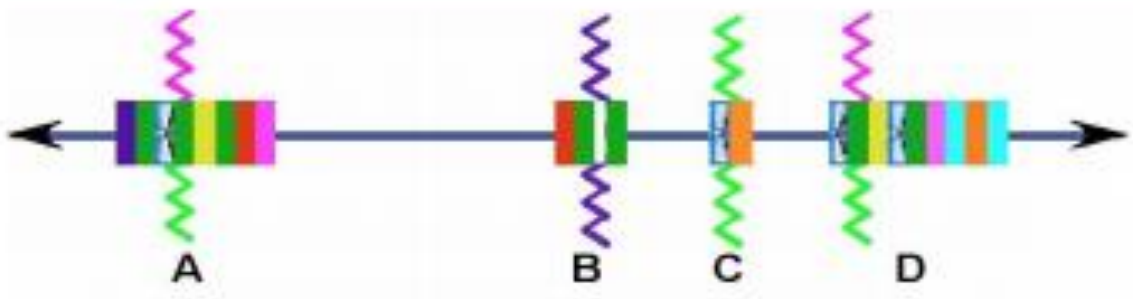
22q11.2 Duplication Syndrome

We have evaluated 150 patients with a 22q11.2 Duplication

- Age range – 20 weeks in the pregnancy to 63 years
- Mean age – 8.1 years
- 63% males

Majority of duplications are A-D but there are more nested duplications than deletions

Duplication Size (N=121)	Prevalence
A-D	67%*
A-B	5%
A-C	2%
B-D	7%
C-D	12%
Dups extending beyond LCR D (A-F [2], A-H, C-E [2]**)	6%
Dups within LCR A	2%



Clinical indications for testing most frequently include developmental differences

Reasons for referral (N=121)	Percentile
Developmental delay	56%
Heart defects (TOF, HLHS, VSD)	16%
Autism	13%
Growth differences (LGA, FTT, short stature)	9%*
Neurologic issues (seizures, microcephaly, macrocephaly)	6%
Palate abnormalities (VPI, cleft palate, cleft lip and palate)	5%
Mild differences in facial features	5%
Hearing loss	2%
ADHD	1%
Family history of 22q11.2 duplication	28%

Associated features overlap with 22q11.2 deletion syndrome but with less frequency

Feature	Prevalence
Neurologic (seizures, hypo/hypertonia, macrocephaly, microcephaly, balance and coordination difficulties, structural brain differences)	62%
GI (GERD, dysphagia, chronic constipation, FTT, hepatomegaly, splenomegaly, colitis, eosinophilic esophagitis, mega colon, hiatal and umbilical hernia)	62%
ENT (chronic otitis, sensorineural/conductive hearing loss, laryngomalacia, chronic epistaxis, complete tracheal ring, tracheal stenosis, pyriform aperture stenosis)	58%
Endocrine (short stature, overgrowth, obesity, hypocalcemia, hypothyroid)	48%
Heart (TOF, truncus arteriosus, ASD, VSD, HLHS, subvalvular aortic stenosis)	41%
Bones (Hemihypertrophy, joint laxity, C-spine anomalies, scoliosis, patellar dislocations, radioulnar dysostosis, pectus excavatum, clinodactyly, 2-3 syndactyly, broad digits)	32%
Immune (chronic infection, low immunoglobulins) and **GU** (cryptorchid, hypospadias, inguinal hernia, reflux, duplicated collecting system, hypoplastic kidneys)	32%
Palate (overt cleft palate, CLP, SMCP, VPI, bifid uvula, high narrow palate)	28%
Blood (easy bruising, thrombocytopenia (low platelets), leukocytopenia, lymphocytopenia)	20%

Growth appears to be an important feature

Measure	Percentile
Height >90th	22%
Height <10th	22%
Weight >90%	24%
Weight <10%	19%

~50% of patients were above or below the average curve for height and weight

Most patients who were diagnosed first in their families had developmental differences (86%)

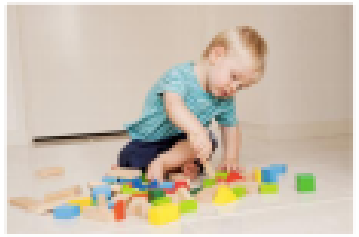
Finding	Percentage
Overall Developmental Issues	86%
Speech/Language	76%
Motor	70%
Overall Behavioral	76%
Autism	24%
ADHD	26%
PDD	16%
Anxiety	10%
Sleep Disturbance	7%
Other (depression, psychosis, ODD, OCD)	Single patients

Males were more likely to have developmental delay and autism

Gender	Overall developmental differences	Overall behavioral differences	PDD	Autism
Males	94%	77%	25%	38%
Females	78%	82%	18%	8%

A subset of patients had formal IQ testing (N = 22)

- Mean FSIQ – 92.8 +/- 16.3
- Falling primarily in the average range (a FSIQ of 100)

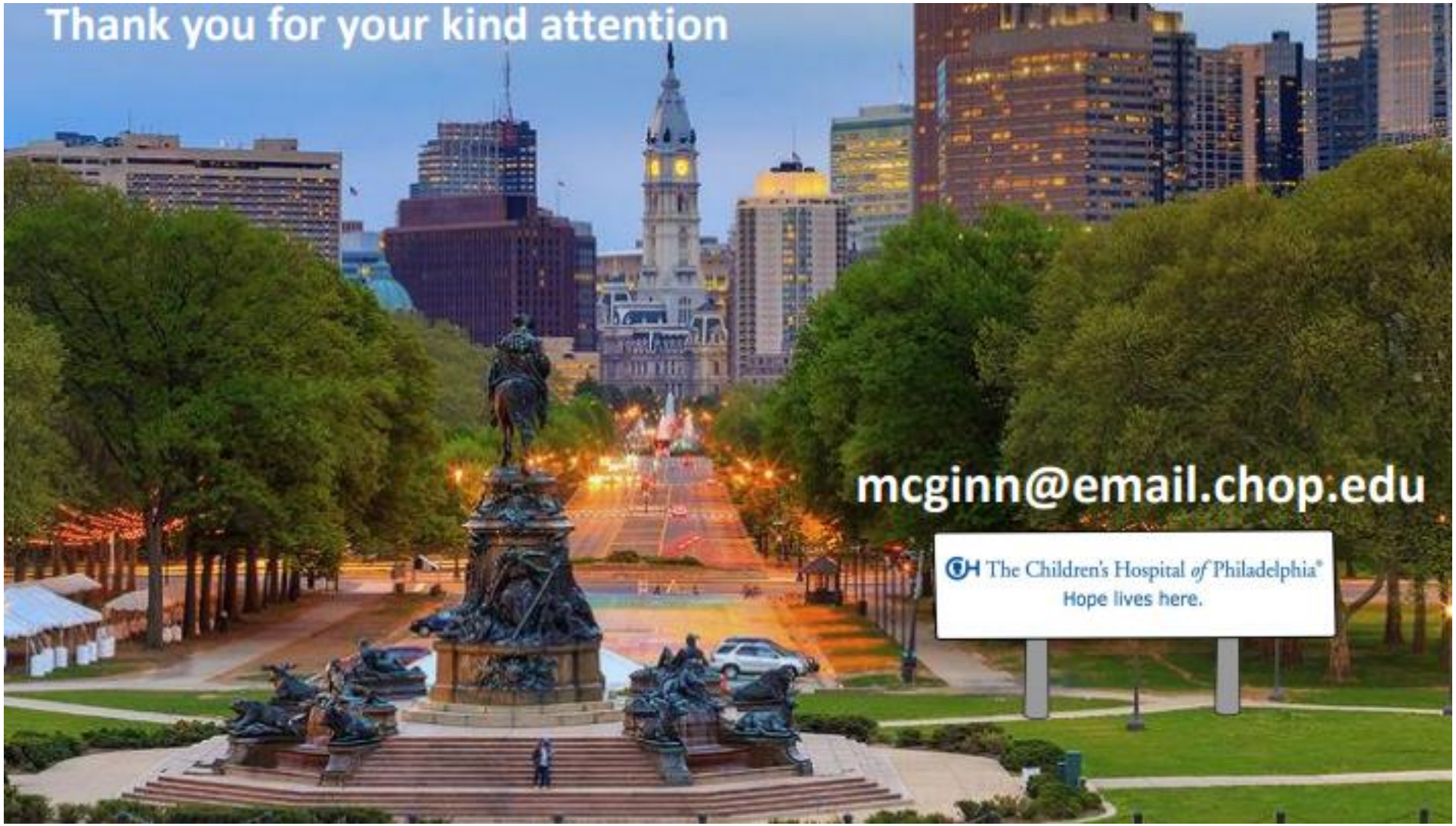


Most 22q11.2 duplications are familial

- 76/121 (where we had both parents available to test) **(63%)**
- 51% - paternally inherited
- Most parents had no associated features
- *Making it difficult to prognosticate for the child or make a consistent plan for follow-up*

In summary

- Patients with 22q11.2 duplications are being referred to 22q centers for care
- Often with features of 22q11.2 deletion syndrome
- Often with growth differences
- But without any published guidelines as to how the patients should be followed
- We are currently following patients like those with the deletion until more data becomes available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