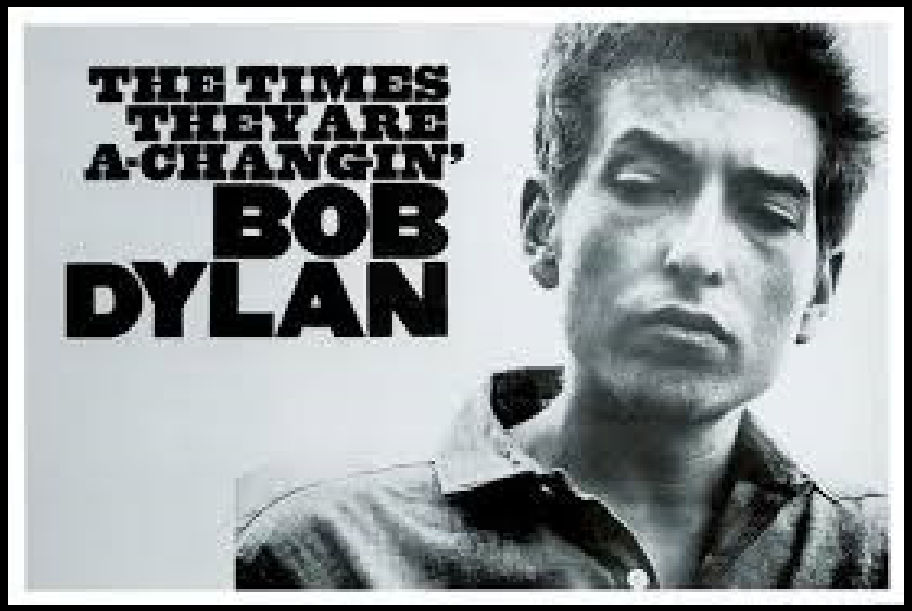
SCID Screening – Changes Are Inevitable



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New York State Department of Health
Newborn Screening Program

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COUNTDOWN TO SCID

- Automated assay developed and validated 12/2009-9/2010
- Validation package submitted 9/08/2010
- CLEP and emergency regulation approved 9/27/2010
- SCID screening started 9/29/2010
- 1st "True SCID" baby detected 12/27/2010
- New presumptive positive action category added 1/25/2011; second 8/8/2011
- Commissioner of Health officially adds SCID to NSP panel 4/12/2011

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SCID SCREENING ALGORITHM

Dried Blood Spot Specimen

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Multiplex PCR (TREC/RNaseP)

TREC values are copies/mL whole blood
RNaseP values are Cq

TREC ≥200
and
RNase P WAL <36.5

SCREEN NEGATIVE

RNase P ≥ 36.5

Sample is retested in duplicate

TREC<200

2 of 3 RNaseP WAL
AND
2 of 3 TREC ≥ 200
OR
Average of 3 TREC ≥200

SCREEN NEGATIVE

2 of 3 RNaseP WAL
AND
2 of 3 TREC < 200
AND
Average of 3 TREC ≥125<200
AND
Gestational age ≥37
AND
Has never been a PP before

PRESUMPTIVE POSITIVE

2 of 3 RNaseP WAL
AND
2 of 3 TREC <200
AND
Average of 3 TREC <200
AND
Gestational age <37

REPEAT PREMATURE

2 of 3 RNaseP WAL
AND
2 of 3 TREC <125
AND
Gestational age ≥37
OR
Average of 3 TREC <200 if a previous PP
OR
Average of 3 TREC <125 if an initial specimen

REFERRAL

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In the Beginning……

TREC ≥ 200 and RNase P WAL (<35)

RNase P ≥ 35 Cq

TREC <200

- 9/29/2010 to 1/25/2011
- No PP category
- Every baby < 200 TRECs referred to flow
- 166 babies referred to flow cytometry

~39 referrals per month (1 in 480)

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In the Middle……

TREC ≥ 200 and RNase P WAL (<35)

RNase P ≥ 35 Cq

TREC< 150

- 1/26/2011 to 8/8/2011
- PP category introduced; ≥150 ≤200 repeat sample
- Every baby < 150 TRECs referred to flow
- 102 babies referred to flow cytometry
  ~15 referrals per month (1 in 1,333 babies)

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Current (almost)…

TREC ≥ 200 and RNase P WAL (<36.5)

RNase P ≥ 36.5 Cq

TREC <125 (initial)

- 8/8/2011 to 3/21/2014
- PP category altered; ≥125 ≤200 repeat sample
- Every baby < 125 TRECs referred to flow
- 592 babies referred to flow cytometry
  ~17 referrals per month (1 in 1,180 babies)

Assay Changes

- Detected SNPs under one of our primers (c.999390 C>T)
- Redesigned reverse primer and probes
- Extractions on Janus replaced Biomek NXs (higher throughput)
- QuantStudio 12K Flex 12 replaced 7900HTs
- Overall number of referrals and PPs decreased

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Current (post move)…..

TREC ≥ 200 and RNase P WAL (<36.5)

RNase P ≥ 36.5 Cq

TREC <125 (initial)

- 3/22/2014 to 7/15/2015
- PP category remains; ≥125 ≤200 repeat sample
- Every baby < 125 TRECs referred to flow
- 79 babies referred to flow cytometry
  ~4.5 referrals per month (1 in 4,444 babies)

SCID Testing Summary

- **Number Infants Screened** 1,150,796
- **Non-Normal Results** 4005
  - **Full Term** 2721
    - Flow requested 939
    - Repeat NBS 1782
  - **Premature *(<37 weeks GA)*** 1284
- **Confirmed Cases**
  - SCID 20

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Case Dispensation

- **SCID:** 20
- **Variant, leaky SCID:** 3
- **Syndrome with TC impairment:** 59
- **Secondary TC impairment:** 36
- **Other disease:** 33

*** some disease, not NBS, B-cell etc*

- **FU incomplete, other:** 63

*** expired, parent refusal, in care, ltfu, open, algorithm changes etc*

Changes to Referral Rates

- March 2013 – March 2014
  - Mean referrals per month: 19.8
  - Range of referrals: 8-31
- April 2014 – mid-July 2015
  - Mean referrals per month: 6
  - Range of referrals: 2-11

Changes to TREC Values

GA >37 weeks

- Jan 2013 – Jan 2014
- Mean: 1701 v. 1748
- Median: 1488 v. 1550

- May 2013 – May 2014
- Mean: 1769 v. 1312
- Median: 1573 v. 1146

GA<37 weeks

- Jan 2013 – Jan 2014
- Mean: 1421 v. 1402
- Median: 1224 v. 1226

- May 2013 – May 2014
- Mean: 1407 v. 1082
- Median: 1192 v. 936

Avg <37 weeks: 9%

So What's The Incidence?

Pure SCID:	**1 in 57,539**
Pure and Leaky SCID:	**1 in 50,034**
Immunodeficiency:	**1 in 14,207**

excludes: 2ndry, ITCL, other conditions

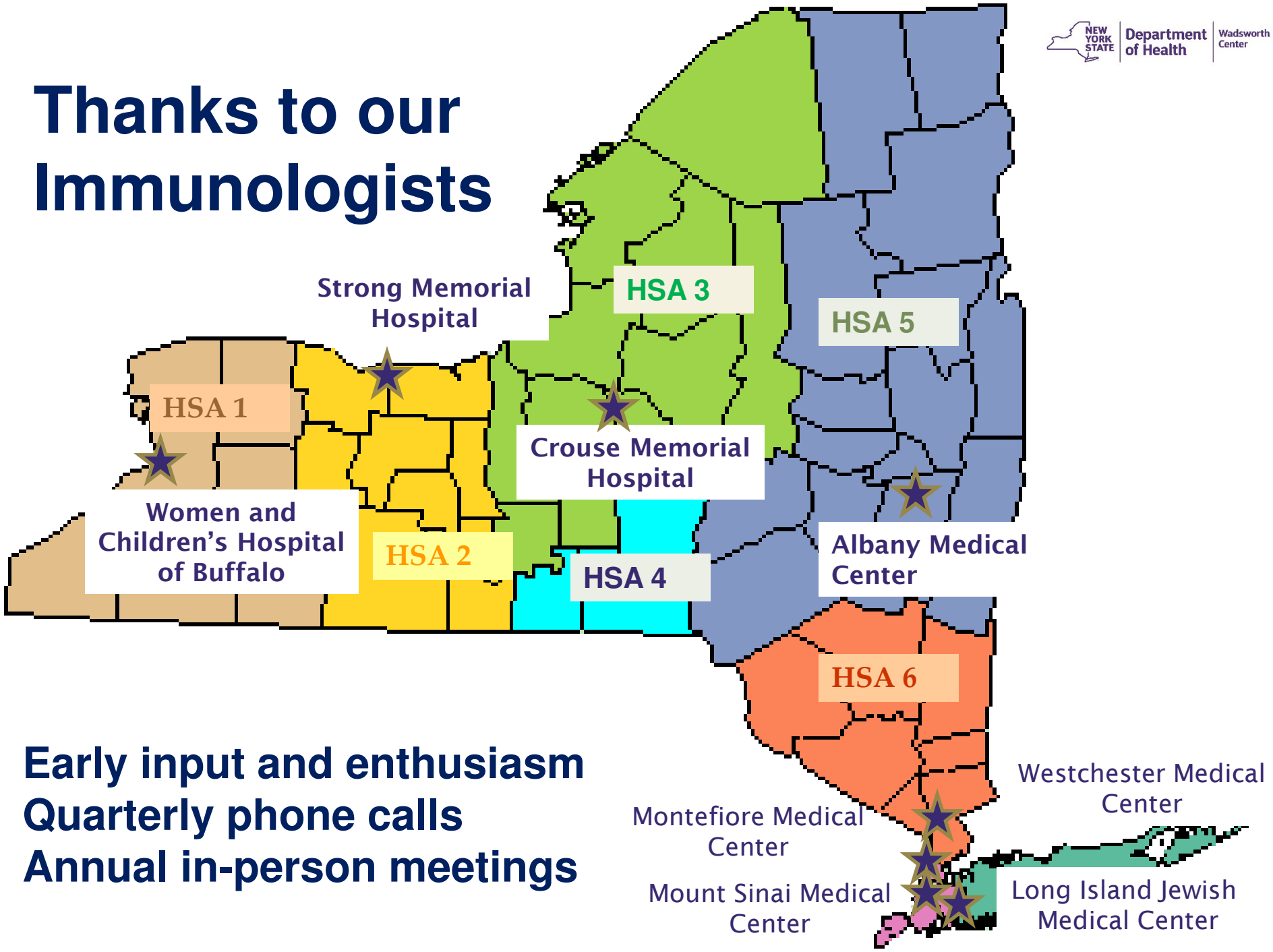
Anything:	**1 in 5,782**

includes: SCID, leaky, syndrome, 2ndry, ITCL

Issues and Insights

- PP category and assay changes reduced referrals by 87%
- PPV went from 0.6% to 5.1% for SCID
- Zero TREC rule for premature infants
- Further adjustment of cutoff and PP category
- Resolve with molecular to decrease TTDx??

Thanks to our Immunologists



Early input and enthusiasm
Quarterly phone calls
Annual in-person meetings

SCID Newborn Screening Staff

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