

Establishing Follow-up Protocols for Low Frequency Events in SCID NBS: working with Specialists New to Newborn Screening

**2011 Newborn Screening and
Genetics Testing Symposium
San Diego, CA**

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Current Work-up Algorithm

Flow Cytometry:

CD3, CD4, CD8, CD16/56, CD19
naïve T cell determination

Clinic Referral if:

total T cell number <2500
naïve % <50%
any other abnormality

Clinic Referral inclusive of :

Functional testing
Physical Exam

Genotyping/Karyotyping if:

Suspected SCID
Suspected DiGeorge, other

Referral to Transplant Center for:

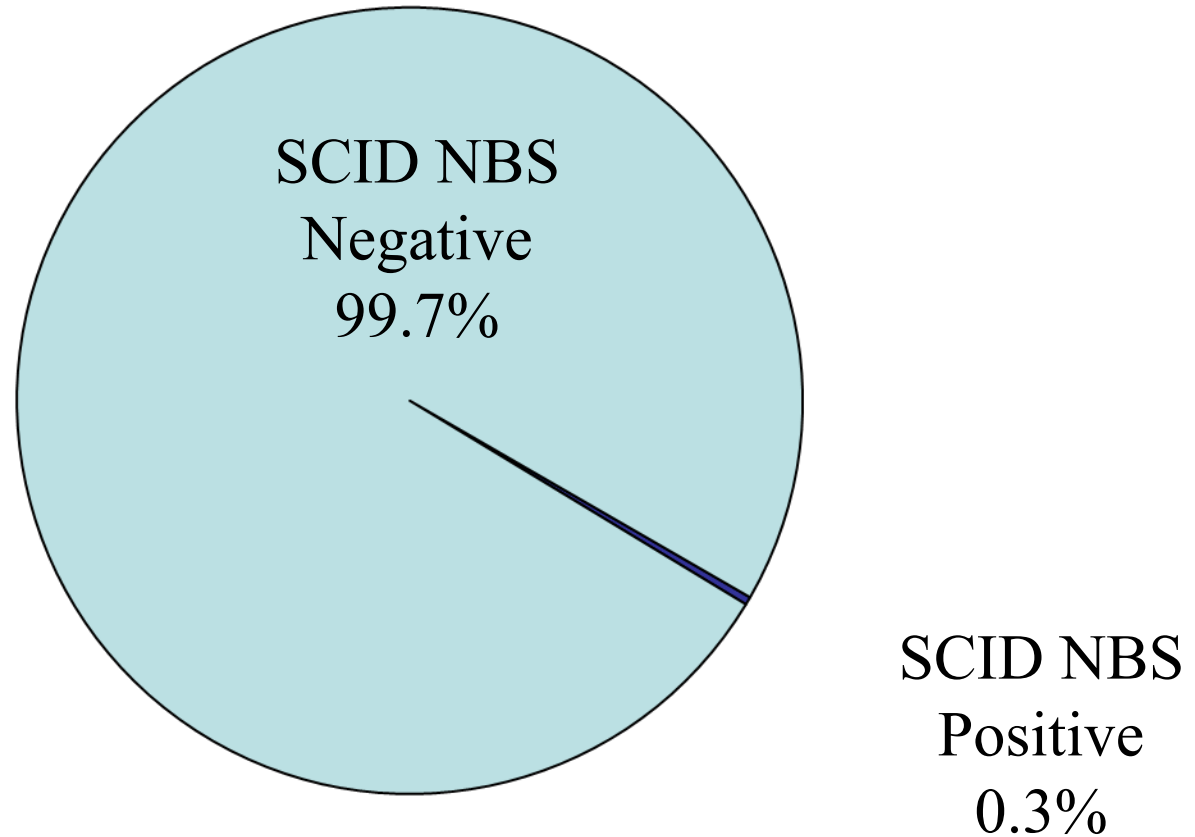
SCID

202,298 infants screened for SCID

- 644 infants with positive SCID NBS result on **any** specimen

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202,298 infants screened for SCID

- 644 infants with positive SCID NBS result on **any** specimen
 - 44 infants referred to Flow Cytometry*

*by current algorithm

Quality Improvements to Referral and Work-up Algorithms

First

TREC <252, refer for flow

Flow at any of 4 qualified centers

Current

Undetectable TREC on initial specimen
→ immediate flow

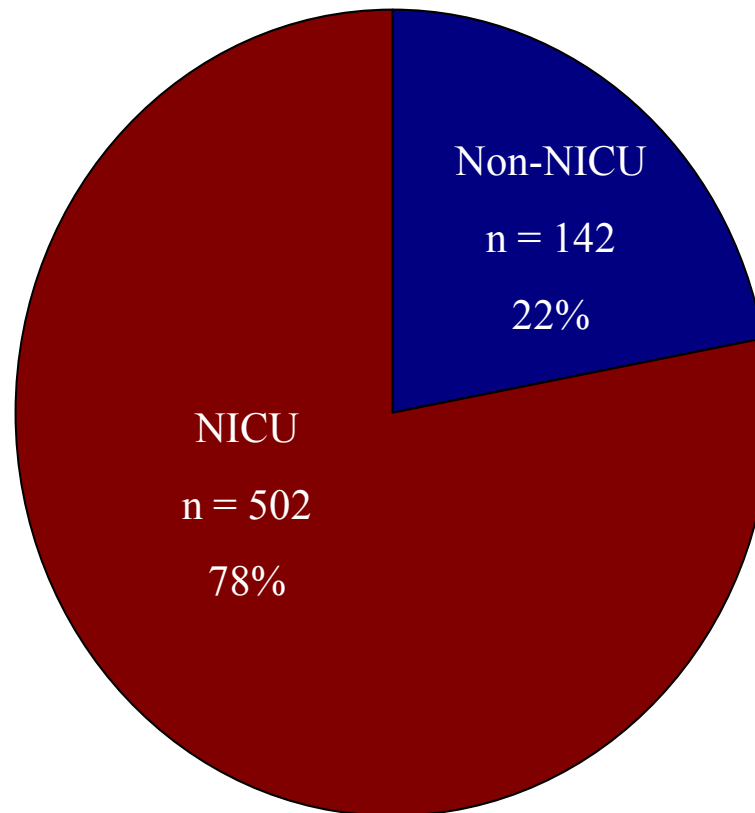
TREC <252 on initial → request repeat DBS

Serial TREC <252 and
no interim in-range TREC → flow

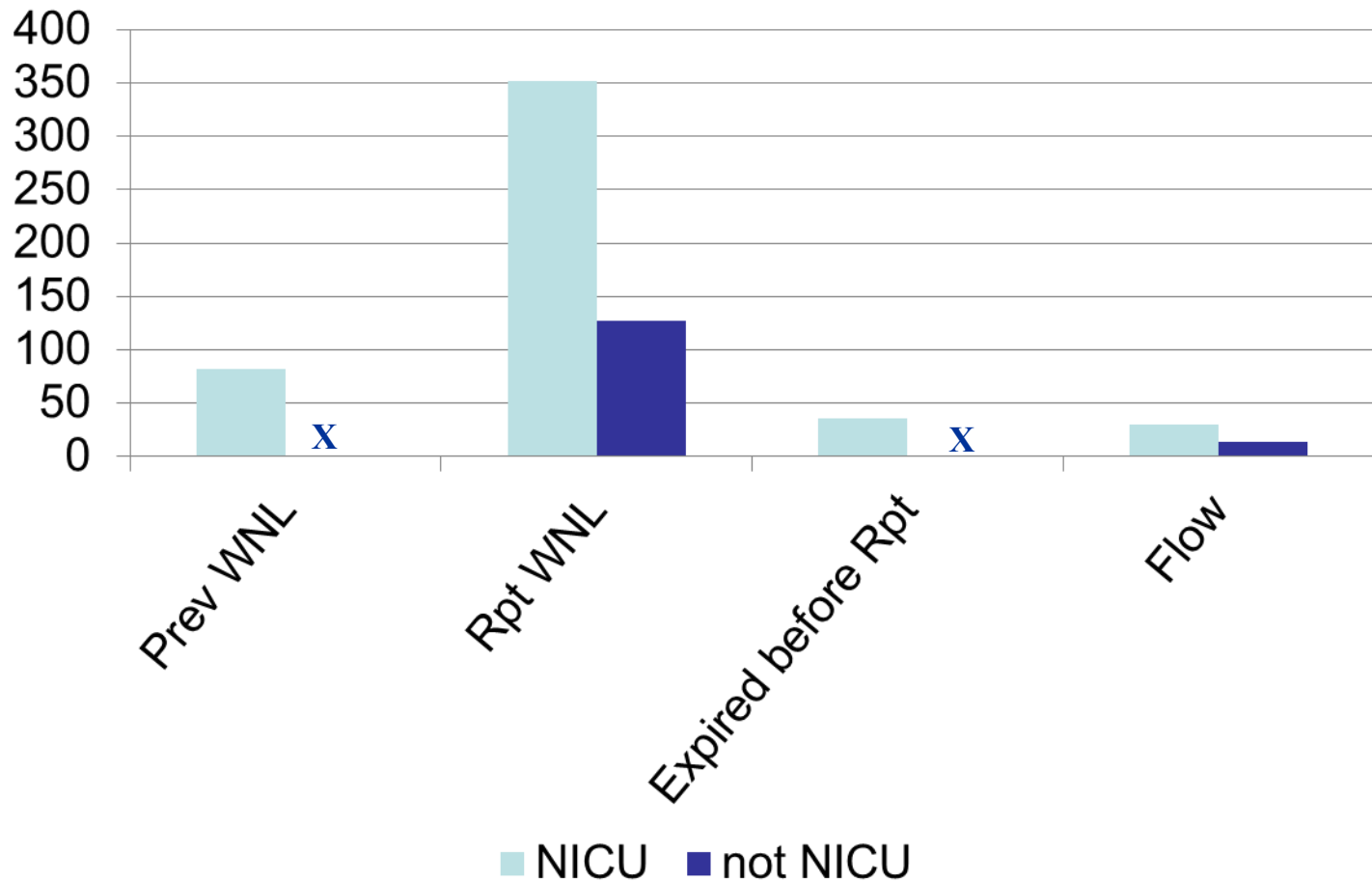
Any in-range TREC on a specimen from same
infant → no flow

Flow at any of 4 qualified centers
Specifications for use of gold standard pediatric
functional testing

NICU vs. non-NICU status
in 644 infants with a positive SCID NBS
on any NBS specimen



Outcomes of 644 infants with any positive SCID NBS result



US PILOT STUDIES

INTERIM FINDINGS

Combined data from CDC and NICHD-funded pilots
(through April 2011)

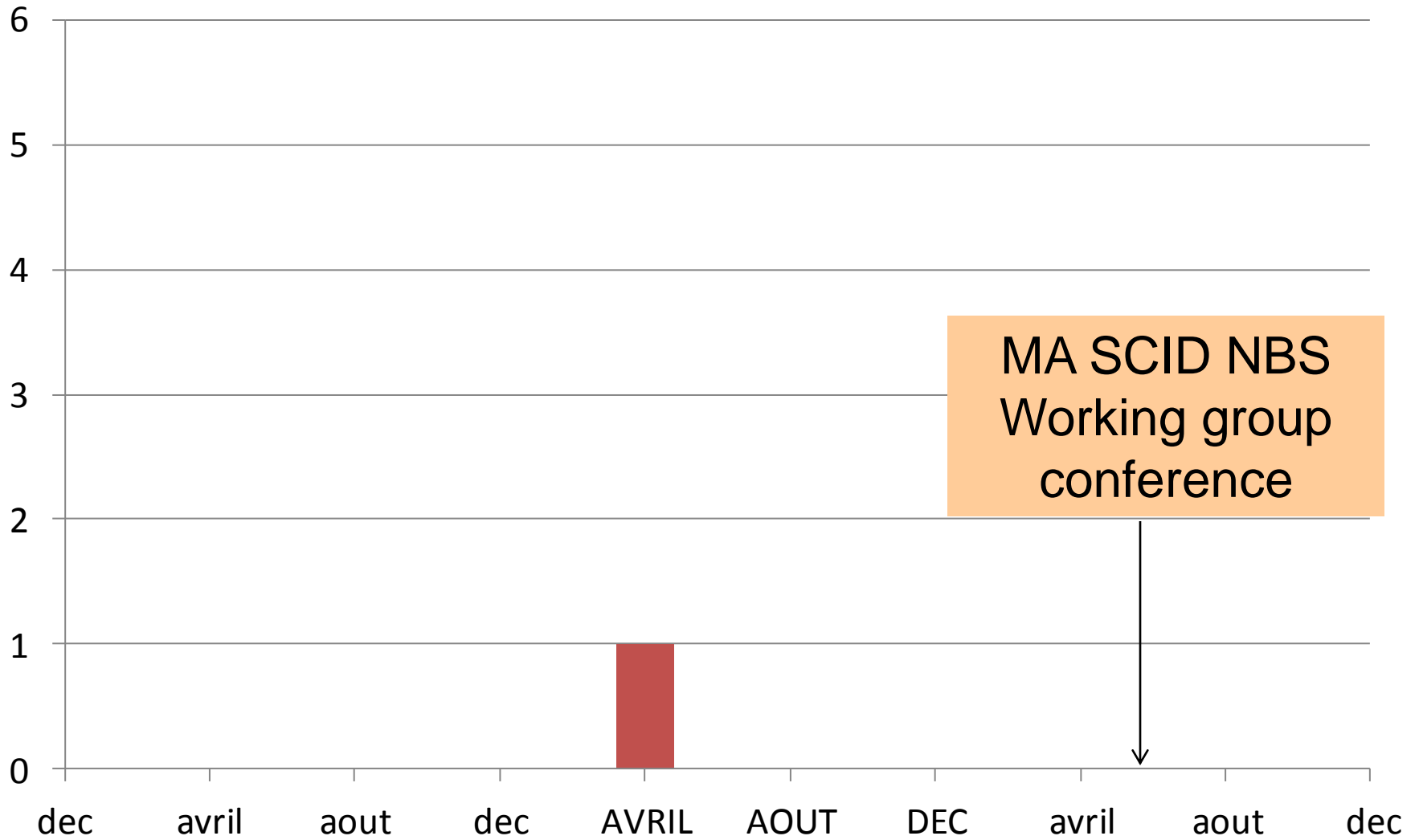
State	WI	MA	NY	CA	PR	LA	TOT
screened	243,707	161,707	136,635	358,000	29,000	31,464	960,513
SCID	4	1	4	5	0	0	14
rate (1/x)	61,000	161,707	34,000	72,000			69,000

Increased incidence extent?

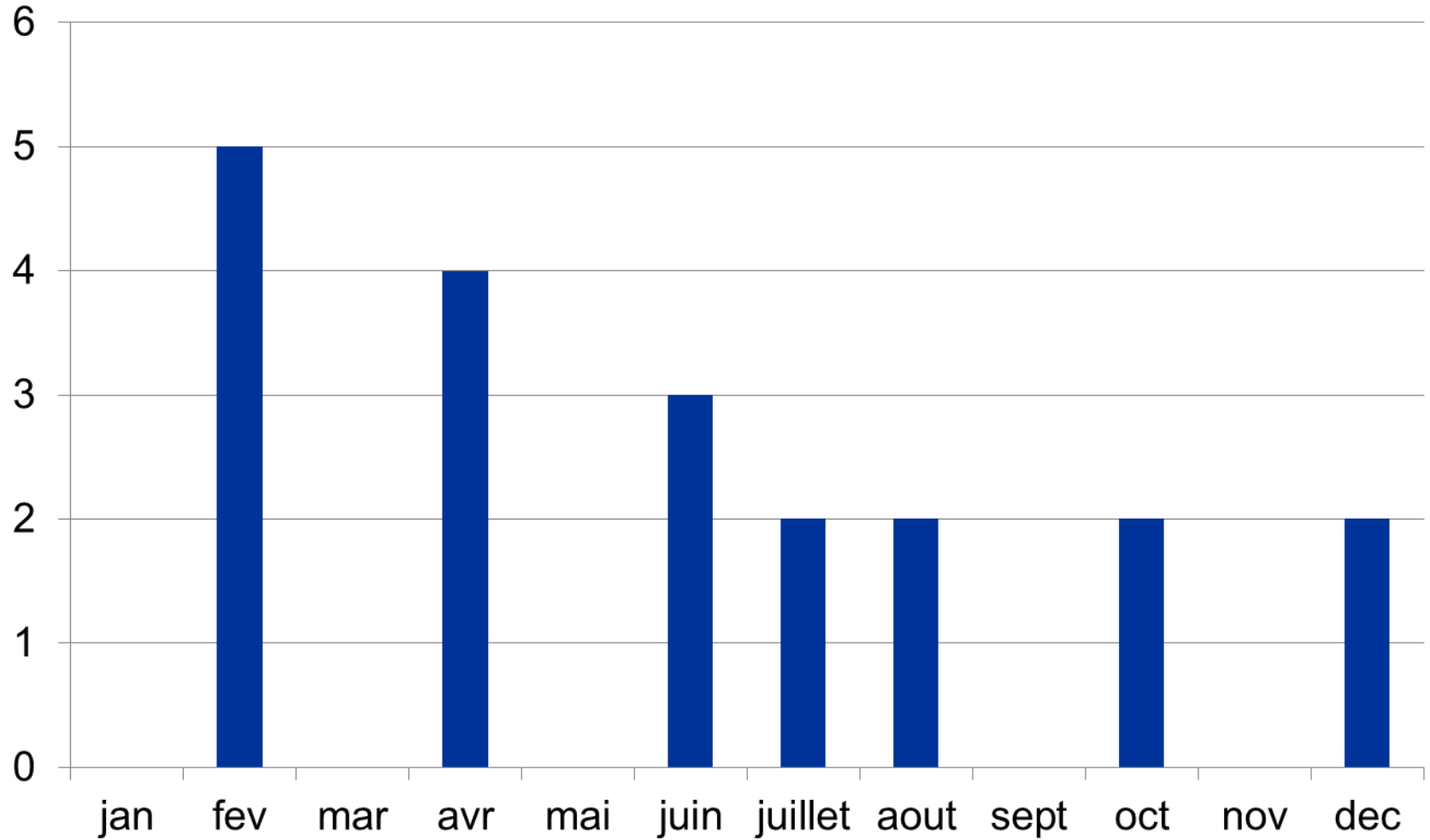
48% → 10% X-linked?

6% → 65% Hispanic?

SCID NBS Diagnoses



CF Diagnoses 2010



Sampling...when even a million might not be enough to give all the answers

Cystic fibrosis		SCID
1/3,000	← 30 →	1/100,000

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30 months timeline

Sampling...when even a million might not be enough to give all the answers

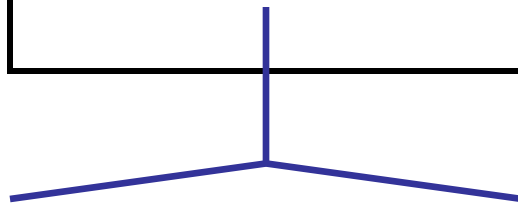
Cystic fibrosis		SCID
1/3,000	← 30 →	1/100,000

30 days timeline

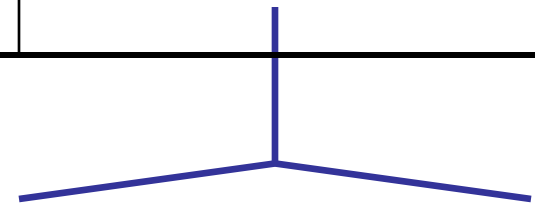
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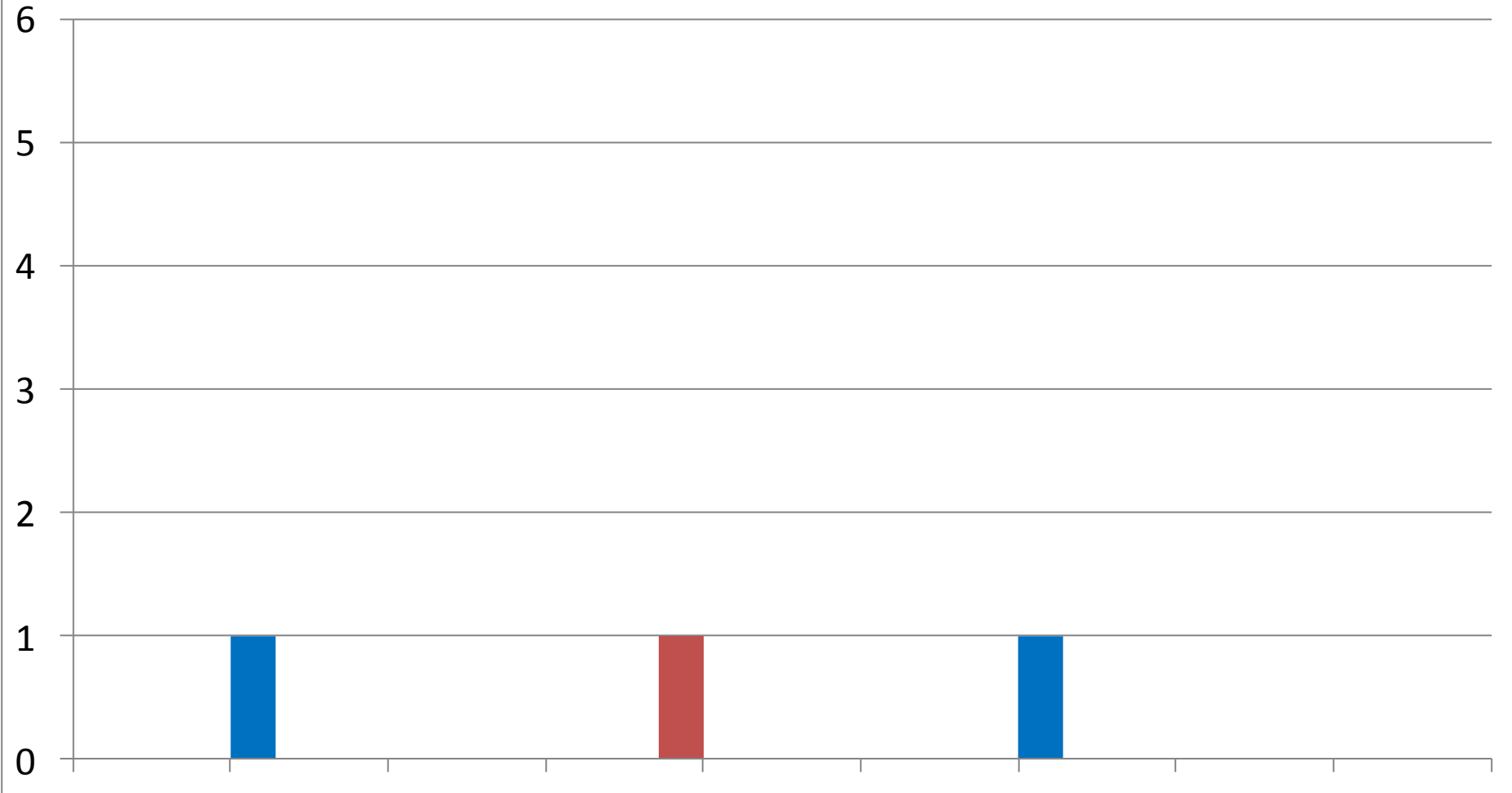


30 months timeline

MERGE TIMELINES?

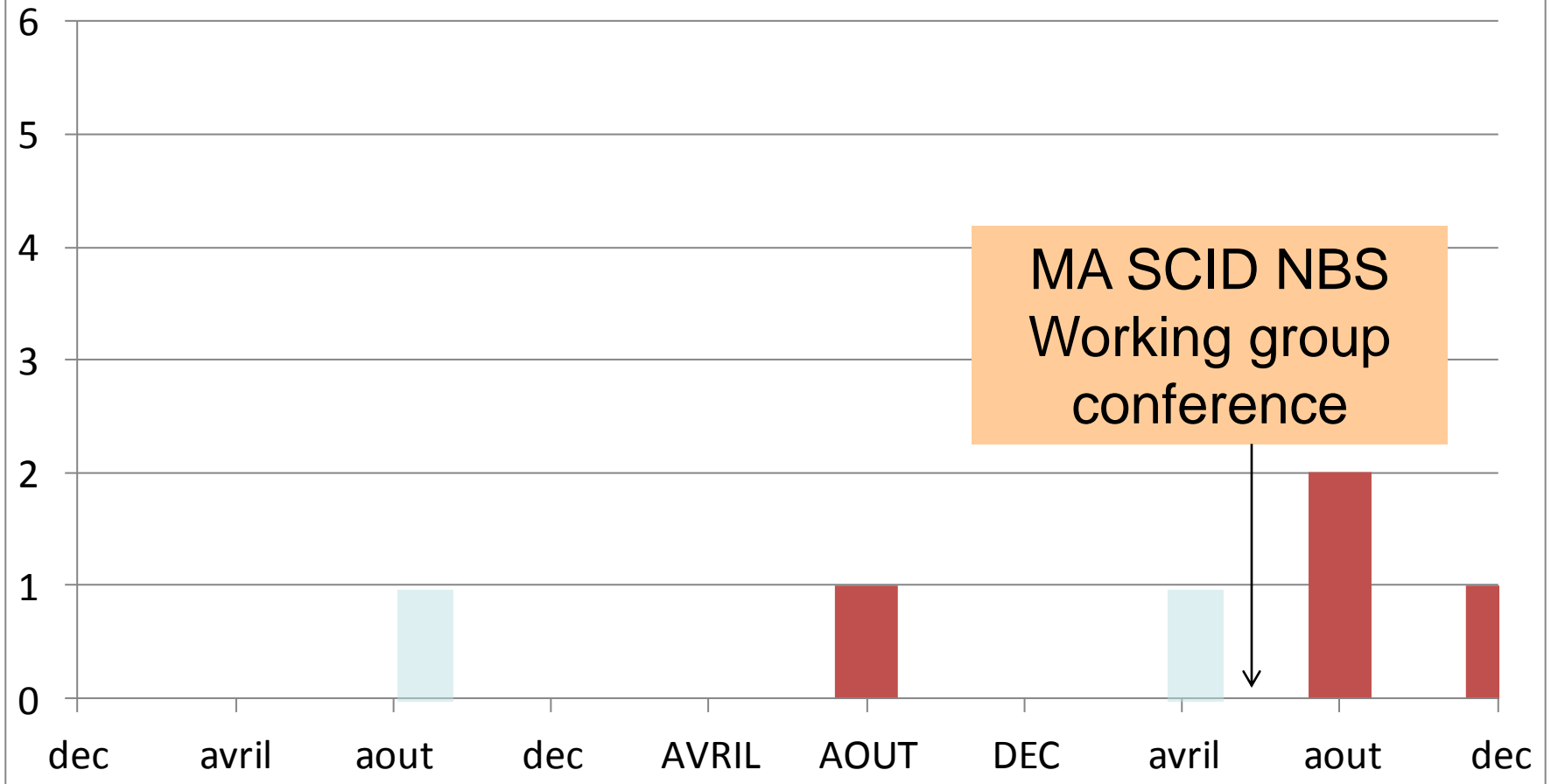
30 days
30 months

NBS Diagnoses



SCID NBS

Fev 2009-Sept 2011



Summary of MA SCID cases detected by NBS

Lymphocyte Profile	SCID type	Donor/Regimen	Status
T- B+ NK-	<i>JAK3</i>	9/10 mismatched unrelated Busulfan, cyclophosphamide ATG	Transplanted At home, well
T- B+ NK+	MIA; sub-type unknown	9/10 rej; 10/10 GVHD sibling ATG	Transplanted, at home, engrafting
T- B+ NK-	<i>IL2RG</i>	10/10 unrelated Busulfan, fludarabine, ATG	Transplanted
T- B+ NK+	<i>CD3D</i>	pending	Awaiting transplant

Pearls from...experience



- Continuous quality measures
 - For the screening laboratory
 - For the diagnostic workup
 - For what we can do about communications
- Projections...are only projections...

Status of 44 Infants with Out Of Range SCID NBS Prompting Flow Cytometry

