

# Follow-Up of Metabolic Cases for the First Three Years of Life: Results from a Population-Based Multi-State Pilot Project

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## **Project Overview**

- **3 year pilot, year 2 data**
- **2005-2007 population-based birth cohort**
- **CA: metabolic centers reporting to NBS program**
- **IA, NY, UT: partnership birth defect surveillance with NBS, multiple sources (including metabolic centers)**
- **19 conditions (TMS, core panel minus tyrosinemia)**

## Public health surveillance:

- ❑ **Ongoing, systematic**
- ❑ **collection, analysis, and interpretation of health data**
- ❑ **essential to the planning, implementation, and evaluation** of public health practice,
- ❑ **closely integrated with the timely dissemination** of these data to those responsible for prevention and control.

## DHHS definition of research (from 45 CFR 46.102) :

“A **systematic investigation**, including research development, testing and evaluation, **designed to develop or contribute to generalizable knowledge**. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.”

- attempt to make comparisons or draw conclusions from the gathered data;
- attempt to reach for generalizable principles of historical or social development;
- seek underlying principles or laws of nature that have predictive value and can be applied to other circumstances for the purpose of controlling outcomes;
- create general explanations about all that has happened in the past; or
- predict the future.

# **Core functions of public health in NBS: assessment, policy development, assurance**

Uses of public health surveillance	<b>Assessment: what is going on?</b> <b>Assurance: are we doing things right?</b>
Magnitude of problem	Prevalence (VLCAD), mortality (MCAD), morbidity, disability (GA1), cost, QoL
Health disparities	Rates of complication by race/ethnicity, SES, geography, rural/urban, insurance status
Epidemics, clusters of adverse events	Deaths (MCAD), neurologic complications (GA1), developmental delays
Effectiveness of control measures	<i>Variations</i> in frequency and severity of outcomes over time
Changes in health practices	Screening flow (# screens), diagnostic tests
Stimulate research	Genotype and GE interactions, diagnosis, treatment, education



**Informing Policy Development**

# Why birth defects surveillance programs?

- ❑ **Population-based, nationwide, ongoing**
  - Present already in most US states (and many countries),
  - typically population-based,
  - under the public health authority.
  - Also, integrated into health department and national network (NBDPN)
- ❑ **Data sources**
  - Many connections already made (hospitals, clinics, labs, administrative databases).
  - Will need to integrate NBS program, metabolic clinics, possibly additional labs.

## **Why birth surveillance (cont.)?**

### **❑ Data domains**

- **Already collecting usually extensive demographic and medical record information.**
- **Will need to define specific elements for diagnosis and outcomes (longitudinal)**

### **❑ Data quality**

- **Several programs (not all) with active case ascertainment,**
- **trained abstractors,**
- **case tracking, clinical case review, and quality assessment procedures in place.**

## **4 States for Pilot Project**

- ❑ California, Iowa, New York, Utah**
- ❑ Number of births at least 100,000 per state over pilot period**
- ❑ Legal authority to collect newborn screening data**
- ❑ Linkage in place with Vital Records**



# **Year 1 spent defining Data Elements: General Categories Collected on Confirmed Cases**

- ❑ Demographics**
- ❑ Basic diagnostic information**
- ❑ Morbidity/mortality**
- ❑ Service encounters**
- ❑ Treatments**
- ❑ Hospitalizations**
- ❑ Developmental assessments**

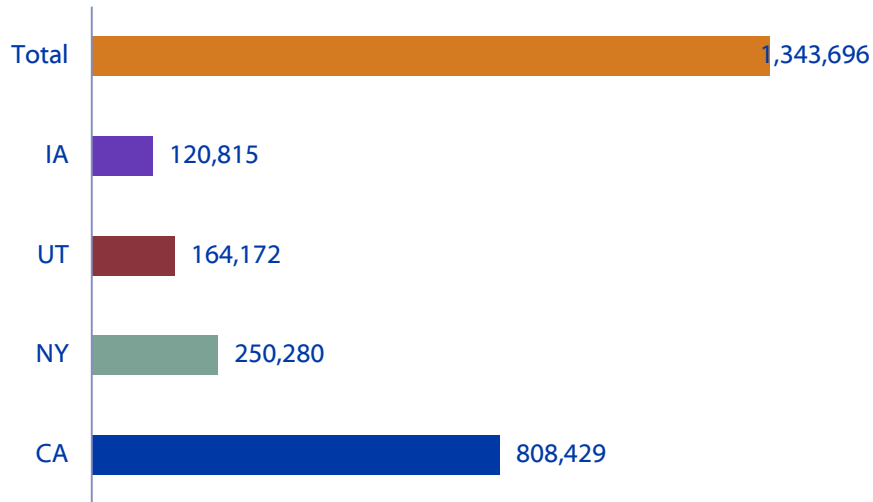
## **“Confirmed Cases”**

- ❑ **As designated by each state program**
  - An project to define cases for public health surveillance purposes is ongoing
- ❑ **Clinical geneticists reviewed the cases of VLCAD and 3MCC**
  - Devised standard case definition template
  - Evaluated cases status
  - Resulted in reclassification of cases, particularly for 3MCC

# Pilot study of metabolic surveillance: 4 states, 1.35 million births, 261 cases

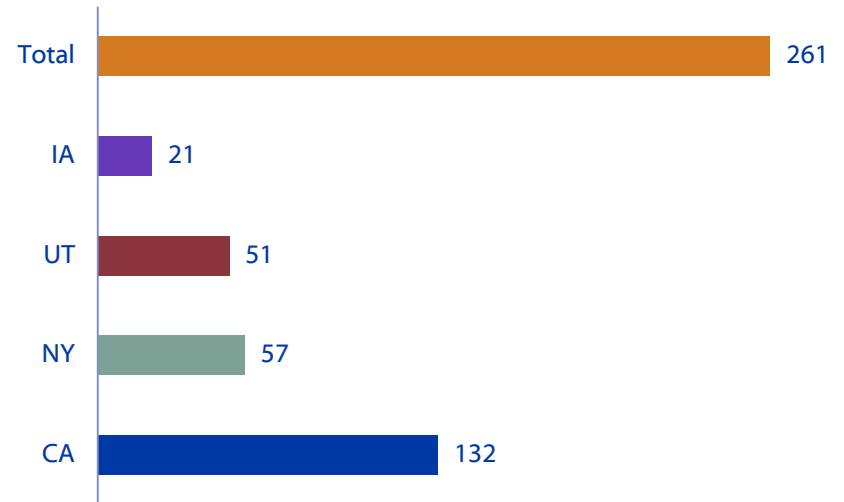
## Births

■ CA ■ NY ■ UT ■ IA ■ Total



## Cases

■ CA ■ NY ■ UT ■ IA ■ Total

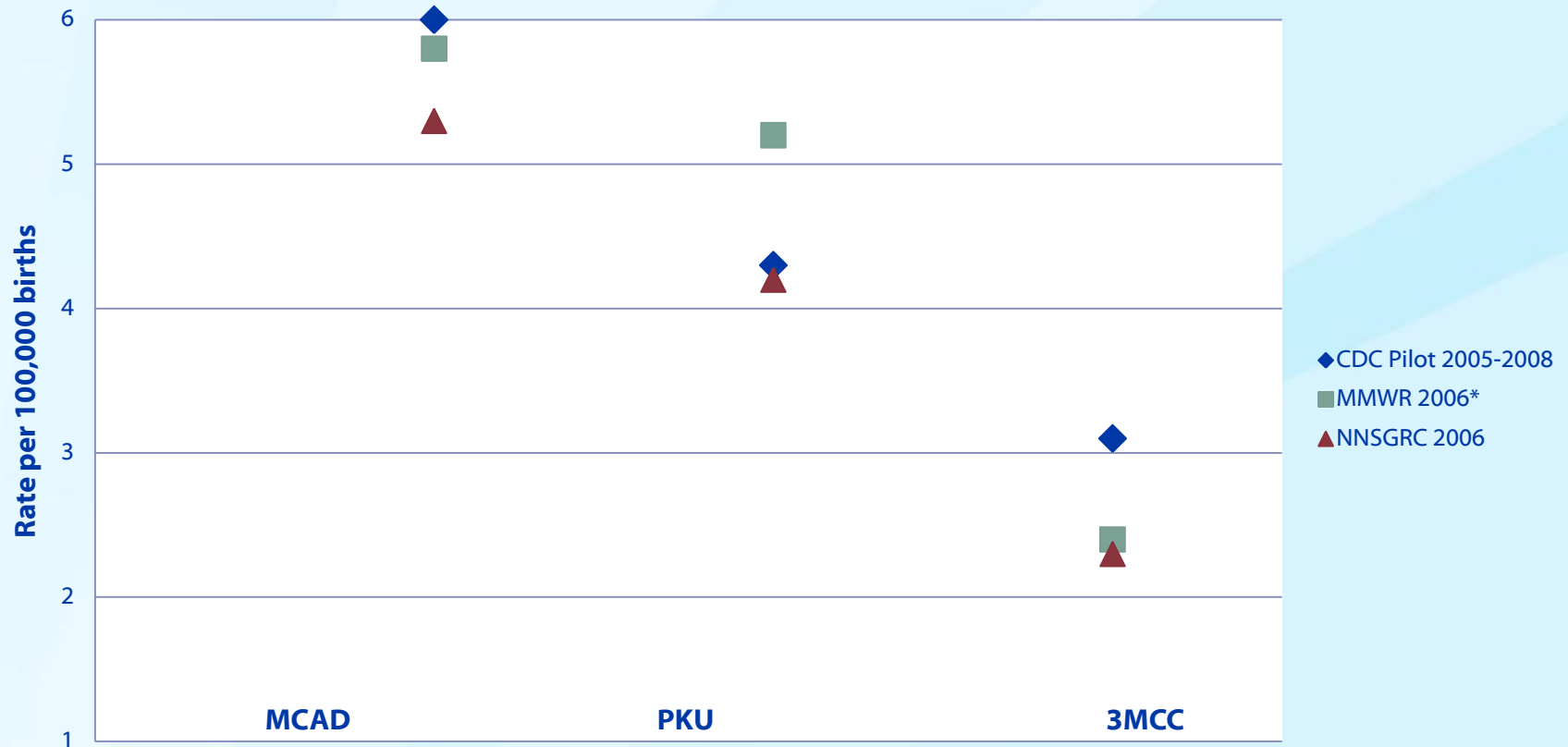


\*\* excluding New York City

# Confirmed cases of the 19 selected conditions from Newborn Screening, by type

	Disorder	Cases	%	Rate/100,000
TOTAL		261		19.4
Organic Acid Disorders	IVA	4	1.5	0.3
	GA1	11	4.2	0.8
	MUT	15	5.7	1.1
	3MCC	42	16.1	3.1
	MMA	4	1.5	0.3
	PROP	2	0.8	0.1
Fatty Acid Disorders	MCAD	80	30.7	6.0
	VLCAD	19	7.3	1.4
	LCHAD	1	0.4	0.1
	CUD	12	4.6	0.9
Amino Acid Disorders	PKU	58	22.2	4.3
	MSUD	7	2.7	0.5
	CIT	2	0.8	0.1
	ASA	4	1.5	0.3

# Birth prevalence compared to other studies



\*CA, WI, MA, NC. Includes Significant Hyperphe.

## **Follow-up Status Variable**

- Active**
- Lost-to-follow-up**
- Moved out of catchment area**
- Parents refused follow-up**
- Treatment deemed not necessary by clinician**
- Died**
- Unknown**

## What constitutes “active” status?

- ❑ **“Taken for grantedness” of what is meant by “active” and “lost”**
- ❑ **The variable is from an administrative perspective versus a “censored” status from an epidemiologic perspective**
  - How do we operationalize “follow-up status”?
- ❑ **At what point is status measured?**
  - At birthday
- ❑ **Does it reflect what happened during the year?**
- ❑ **What about states that can link to hospital discharge data?**
  - Child is still living in catchment area versus child is in care at metabolic center

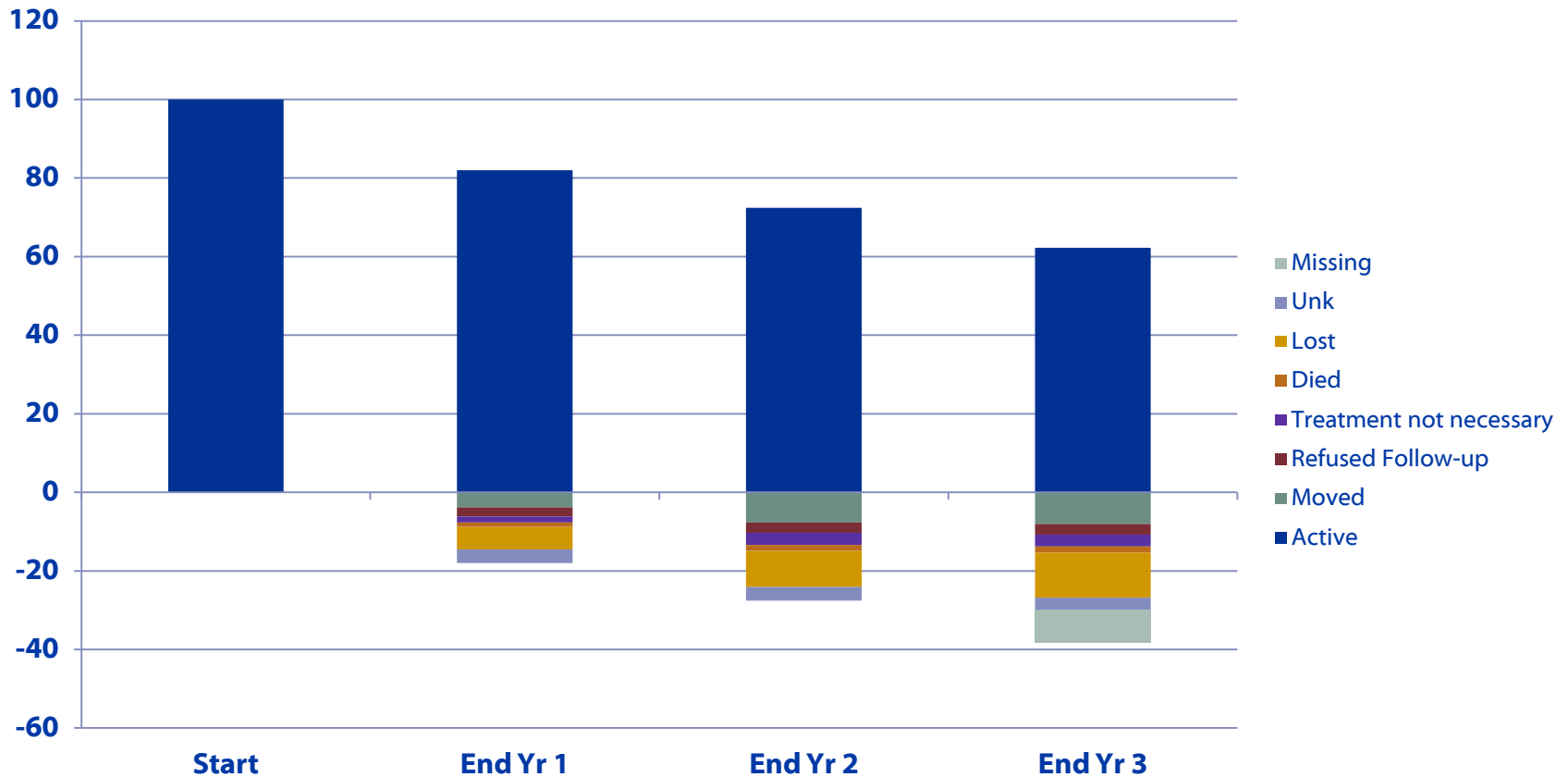
## **Follow-Up Variable defined:**

- ❑ **Active Status:**
  - Seen in genetics clinic at least once during the year
  - Does not include hospitalizations without genetics clinic visit during the year
- ❑ **Death, move, refuse, “treatment not needed” status reflected even if there was a clinic visit**
- ❑ **No clinic visit during year = lost to follow-up**
  - Grace period of a year

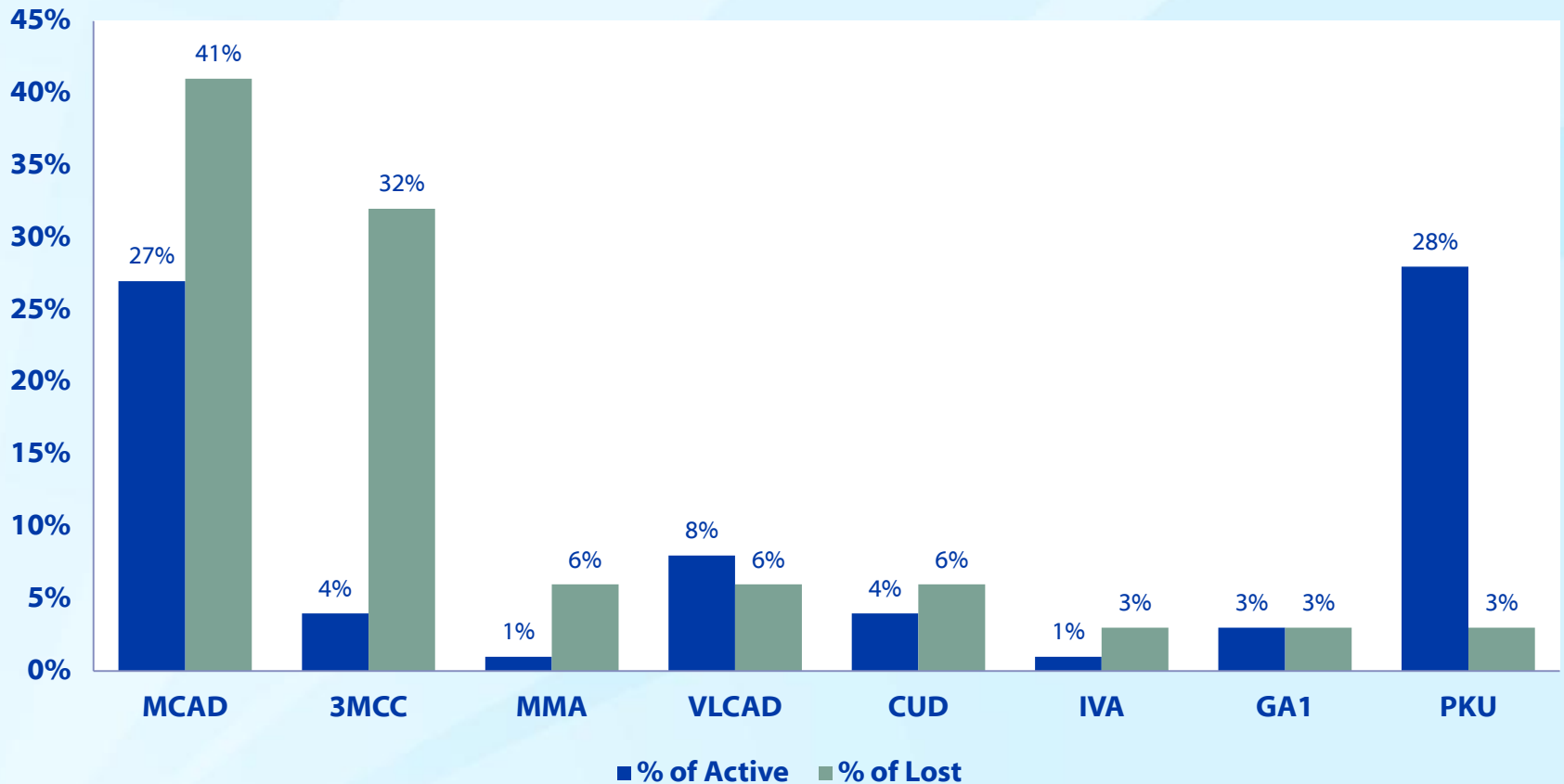


# Where did they go?

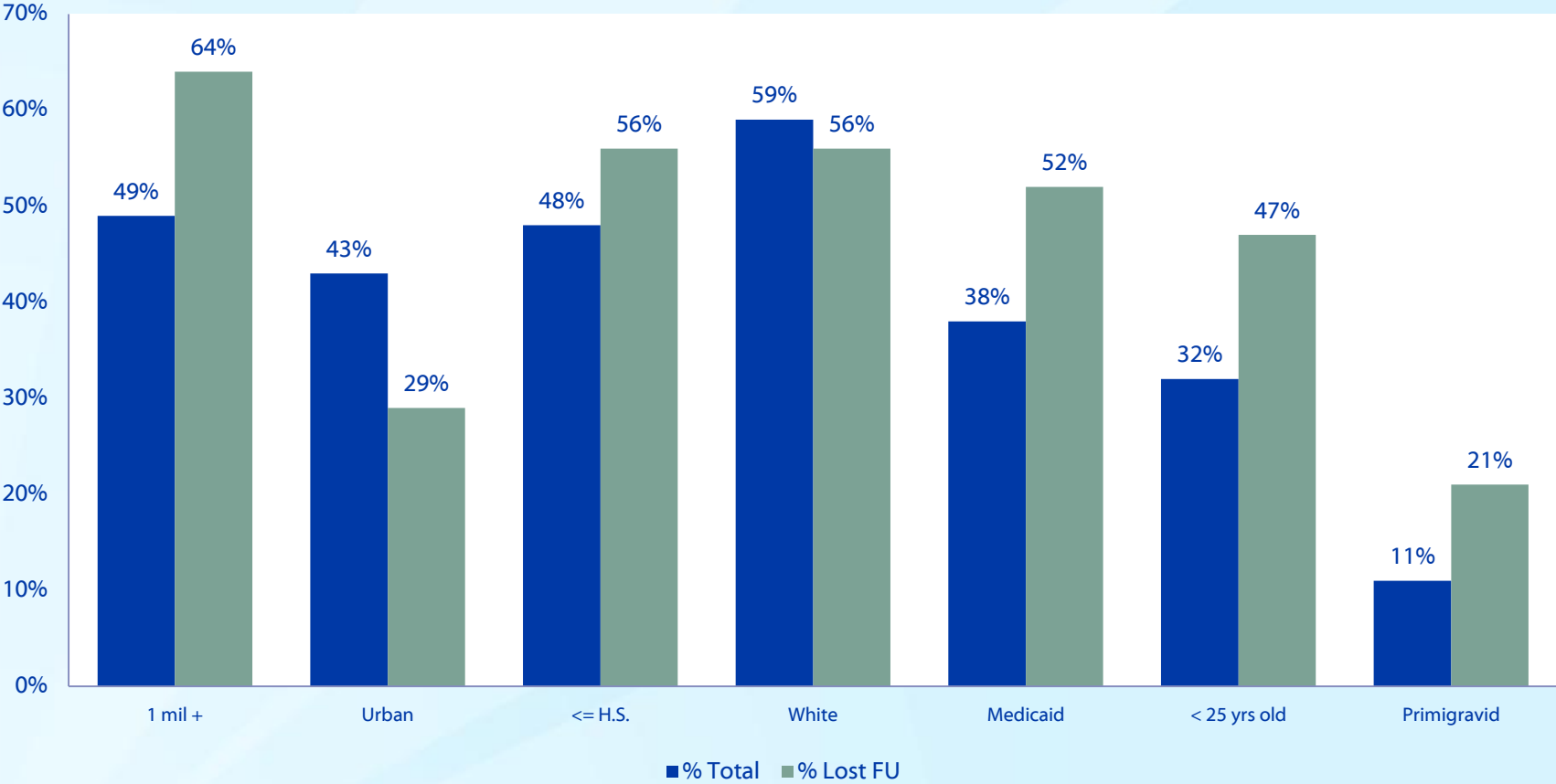
## Percent change from birth to end of Year 3.



# “Active” cases compared to “Lost to follow up”: Diagnosis



# Maternal Characteristics of All Cases versus Lost to Follow-Up Cases



## **Most likely to be Lost-to Follow-up:**

- ❑ MCADD, 3MCC**
- ❑ Mothers live in metro areas, 1 million pop +**
- ❑ Medicaid**
- ❑  $\leq$  High School Education**
- ❑  $< 25$  years of age**
- ❑ Primigravid**

## **In Conclusion:**

- ❑ **A four-state pilot project compiled three years of follow-up data on 261 newborns diagnosed with metabolic conditions**
- ❑ **Follow-up status needs to be carefully defined across states**
- ❑ **Recommend using individual variables to compute follow-up status**
  - Death
  - Move
  - Clinical encounters
  - Hospitalizations
  - Etc.



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