

Newborn Screening for Cystic Fibrosis

IRT is Lower in Infants with Meconium Ileus

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and

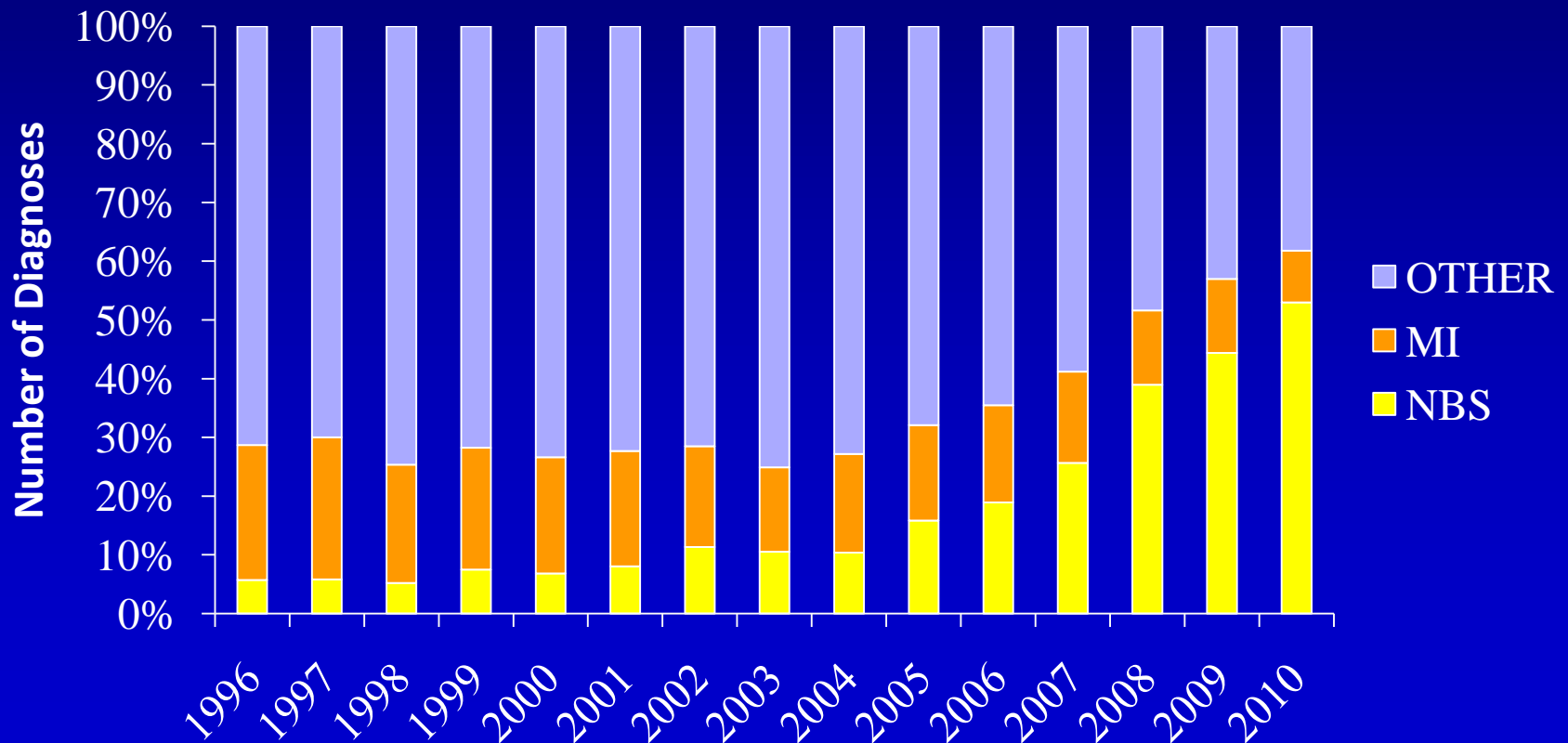
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By 2010, newborn screening was the most common diagnostic indication

U.S. CF Foundation Registry

All new diagnoses reported to CFF in each year

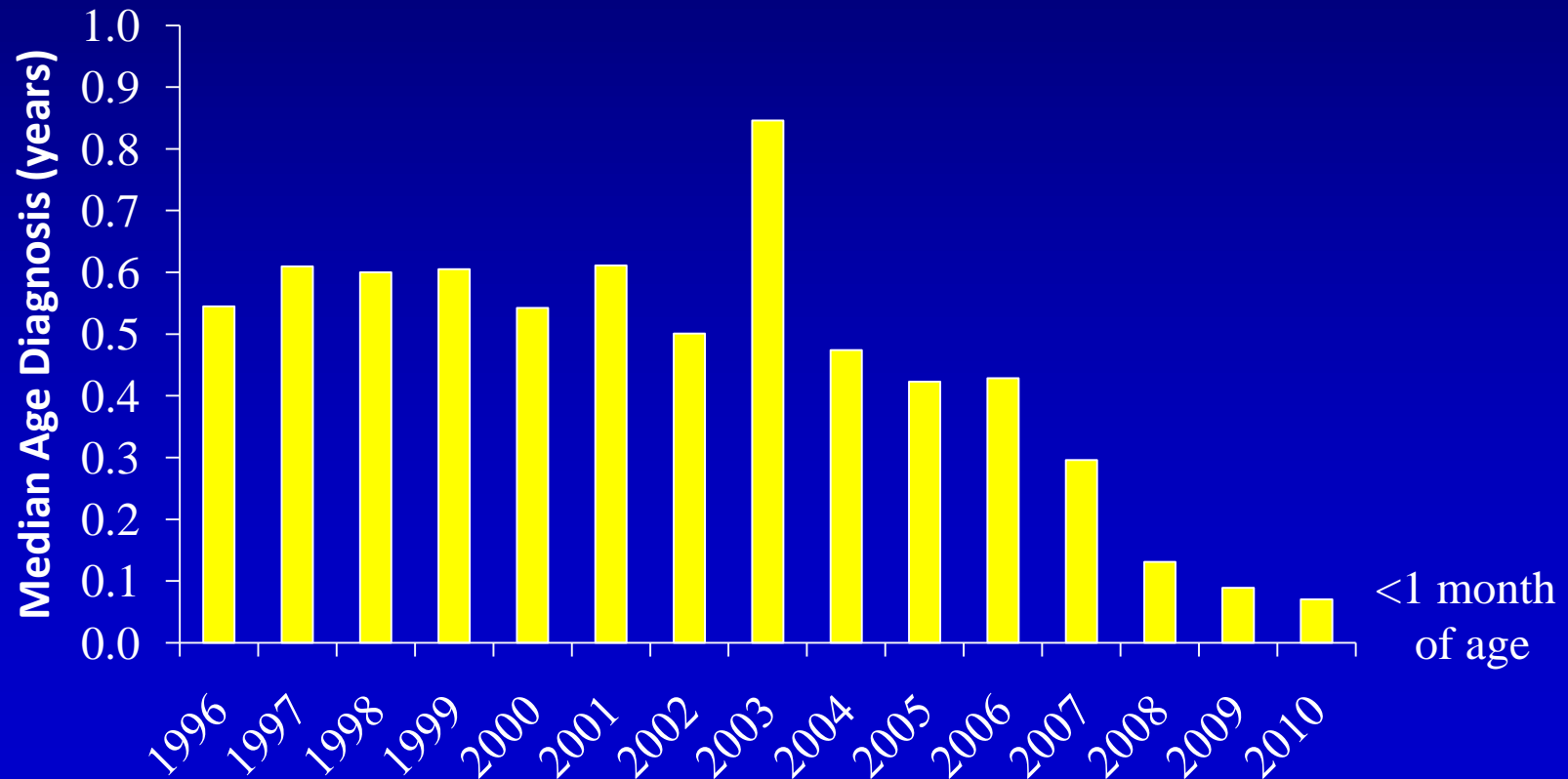


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Age of diagnosis has decreased with newborn screening

U.S. CF Foundation Registry

All new diagnoses reported to CFF in each year



Quick overview of IRT

- Identifies infants before severe malnutrition
- Screening program is part of standard newborn screening panel
- Immunoreactive Trypsinogen (IRT)
 - Pancreatic enzyme precursor
 - Elevated in the blood as pancreas is being damaged
 - Elevated IRT is the first biochemical evidence that an infant has CF

IRT Declines throughout early childhood in CF

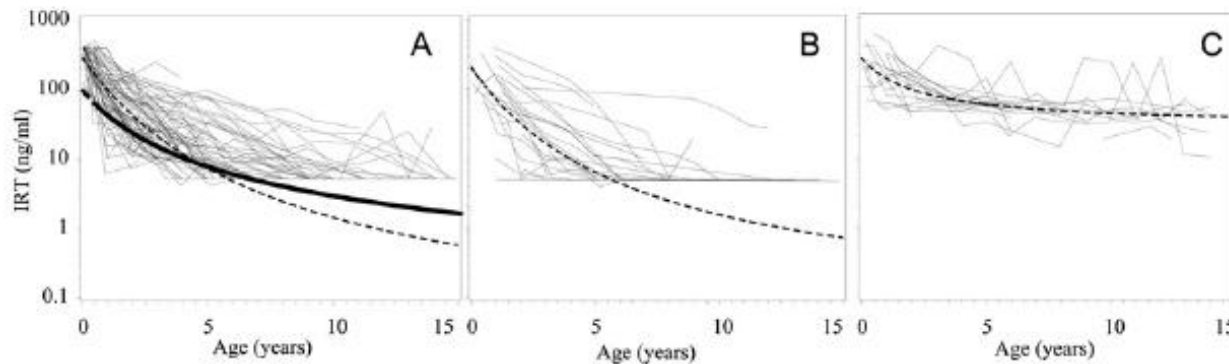
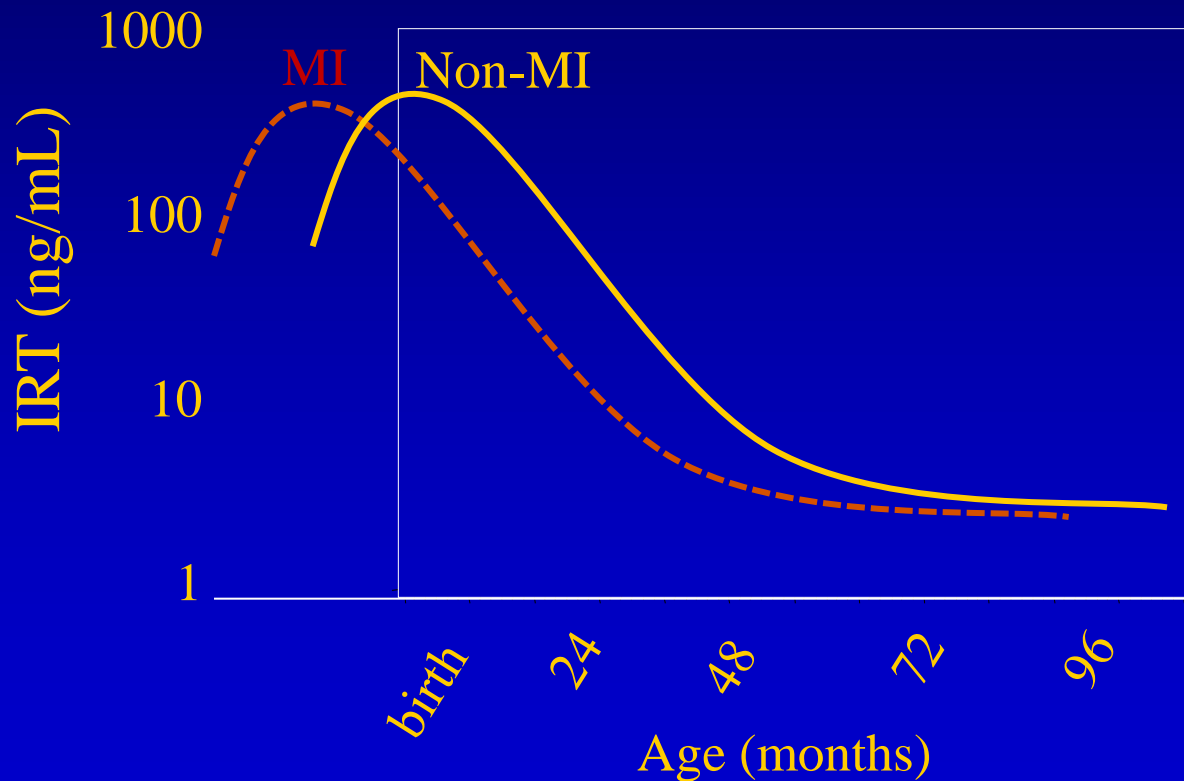


Figure 2. Log IRT declines in a predictable manner in children with CF. Longitudinal IRT levels on individual children are represented and overall predicted model for IRT decline. A, Subjects with severe disease (dashed line), with Couper et al's model overlaid (solid line). B, Infants with meconium ileus (MI). C, Subjects with pancreatic sufficiency. Longitudinal mixed effects modeling with likelihood modified for censored values was used to develop the statistical decline models.

Hypothetical difference in MI and NBS IRT values



IRTs are Lower in Infants with Meconium Ileus, but stable across first four days

Data from 1982 - 2002

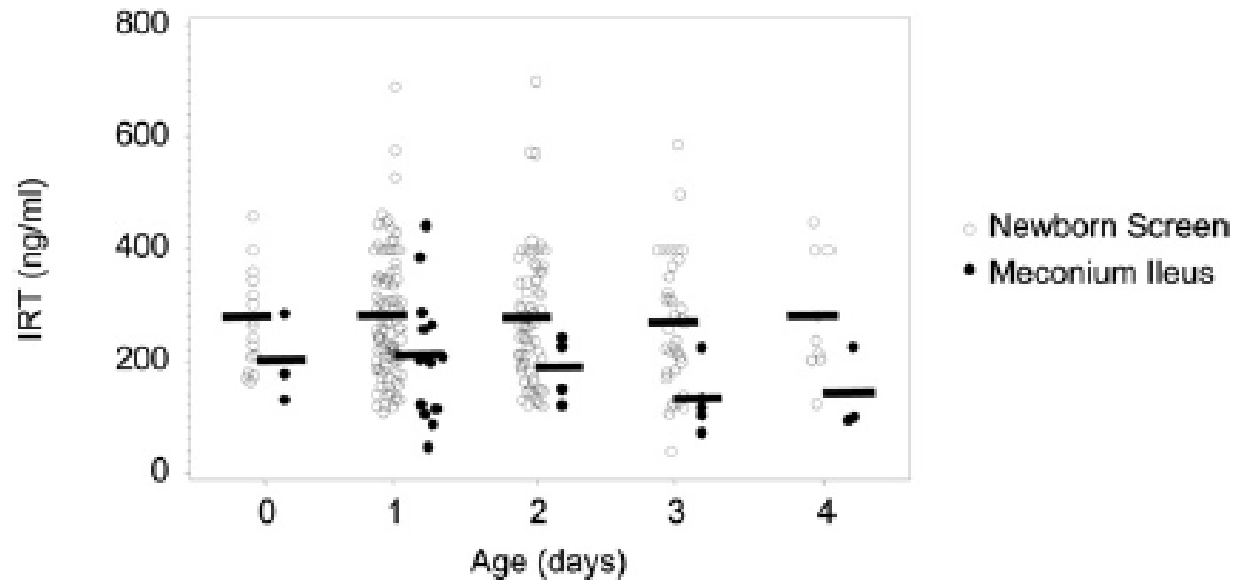


Figure 3. IRT levels are lower in infants with meconium ileus (MI) but do not show significant variability day to day. Measurements on different infants with CF on each of the first 4 days of life demonstrate that infants with MI have lower IRT levels than infants without MI ($P < .01$).

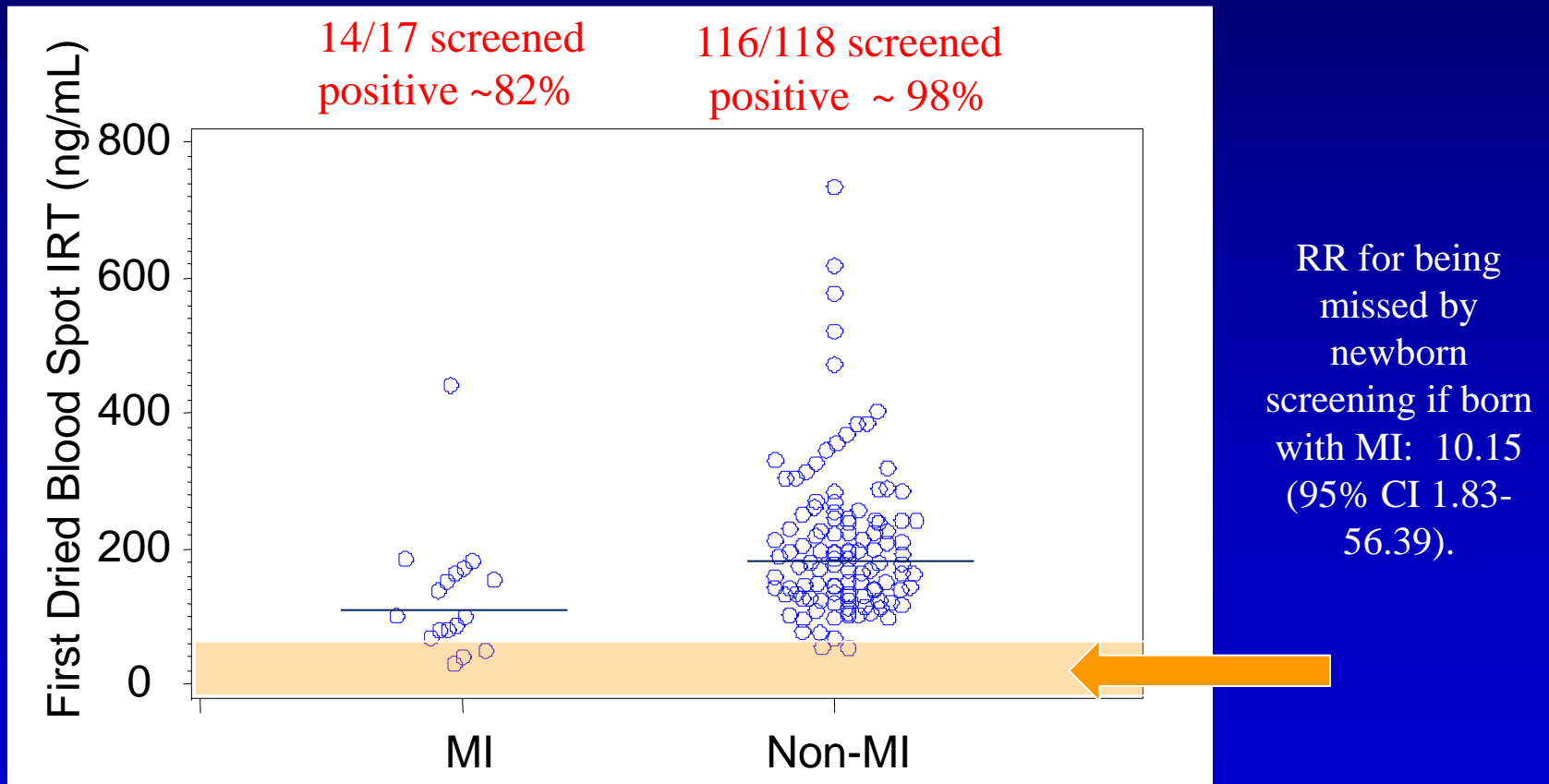
Questions

- Do infants with CF and meconium ileus have lower IRTs than those with CF without MI?
- How many babies with CF would be 'missed' based on newborn screening alone?

Identification of babies

- January 2003 – May 31 2008 – IRT/IRT
 - Cutoffs 105 ng/mL and 75 ng/mL
- June 1 2008 – June 1, 2011 – IRT/IRT/DNA
 - Cutoffs 60 ng/mL and 60ng/mL
 - ~32 mutation panel
- 132 Babies identified
 - 17 with meconium ileus
 - 118 non-meconium ileus (NBS, Prenatal, FN)

Infants with meconium ileus are at higher risk of being missed by NBS



Does MI matter?

- YES!
- Babies with MI *MAY* have lower IRT levels than those without MI – but not all will.
- The newborn screen is another way to catch the babies with MI.
- For comparisons of missed cases across states we must have the same definitions.

Pros and Cons of knowing MI Status

Pros

- Can accurately calculate statistics for newborn screening program
- Could adjust cut-off for MI babies

Cons

- Difficult to collect on newborn screening card
- Can be misdiagnosed or misclassified

Infants with CF and MI may have lower IRT values than infants with CF without MI and are more likely to be missed by IRT based newborn screening.

The clinical presentation of infants with MI needs to be considered in conjunction with IRT values.