CF-NBS Quality Improvement & Timeliness Meeting
Algorithm Breakout Session: Challenges & Goals
June 21, 2016

Challenges (and proposed solutions) related to timely newborn screening related both the IRT/DNA algorithm and the IRT/IRT or IRT/IRT/DNA algorithms

IRT/DNA—Stout (Facilitators: Marci & Suzanne)

FOLLOW-UP

- Loss to follow-up due to lack of coordination of care.
    - **Solution**: developing good relationships and communication with appropriate teams.
    - **Solution**: key contact at CF center who takes all calls.
    - Insurance/payment issues, especially with Medicaid, and identifying the appropriate care center/sweat testing lab for follow-up.
- Sweat test delays:
    - Limited number of accredited CF sweat testing centers
    - Limited number of genetic counselors to follow-up with appropriate counseling at the time of sweat test.

- Not knowing cut-offs and algorithms from other state NBS programs so that information can be delivered to the family appropriately (i.e. issue with border babies)
- Timely diagnosis of babies with one mutation (i.e. inconclusive). Scheduling sweat appointments with clinicians for babies with an inconclusive CF screen (high IRT or one mutation) is not seen as a priority due to high clinic volume.
    - For babies with 1 CF mutation that get sent to PCP vs. CF Center could delay diagnosis especially in rural areas (timeliness can be related to urgency with 1 mutation babies and follow-up)
        - Triage: (1) 2 mutations CF causing; (2) 1 CF causing, 1 unknown or mild; (3) 1 mutation (only sweat).
    - IRT/DNA/IRT: PCP asking for 2nd specimen for 1 mutation babies to see if IRT goes down. If decreases, then assume carrier and PCP monitors growth.
    - **Solution:** Change culture so understand that baby with 1 CF mutation could actually have CF
    - **Solution:** Utilize PCP with assistance of genetic counselors and CF centers to make sure babies with 1 mutation are not delayed.
    - **Solution:** Leave slots open each week at CF Centers for sweat tests to avoid delays since cannot predict when baby will show up (KY)
- Lack of coordinated care between PCP and CF Center-- if tests get sent to pediatrician vs. CF center (and not both) can delay follow-up and diagnosis.

- **Solution:** Standardization of reporting out (i.e. standardizing the actual report for pediatricians on what's actionable)
- **Solution:** NBS program assists the pediatrician by connecting them to genetic counselors and CF centers
- **Solution**: development of educational materials for PCPs and parents on inconclusive screen results and sweat testing

LAB

- Most labs confirm DBS mutations, so DNA lab test of 1 or 2 mutations takes 2x as long
- Batching DNBA tests—DNA testing does not occur daily, it could be weekly or every other day due to cost
- Technology—some methods are faster than others in terms of frequency and efficiency. Further, if run small number of samples then cost will increase.
  - **Solution:** regional approach to DNA testing (i.e. reference lab) so can be run daily and maximize test cost. However, there would be barriers with transport delays and repeats.
- NICU babies and delayed diagnosis – IRT is often elevated in NICU babies/preemies, requiring repeat testing
  - **Solution:** DNA testing right away?
- IRT isn't necessarily elevated in newborns with meconium ileus
  - **Solution:** DNA testing right away? Some states include MI on DBS card, others do not – there are challenges in the appropriate interpretation

<u>Parking Lot Items</u>

- How to deal with special issues of twin DNA testing (VT)
- Resources for carriers/providers on sweat testing
- DBS card—PCP info incorrect or missing
- Transit time of DBS card from hospital to lab
- Centralized DNA labs in the future?
- Primary DNA testing to lower false negatives?
- Hispanic CF babies do not have panel mutations and sometimes no mutations in CFTR—need to be treated differently
- NICU babies are delayed—should NICU babies go straight to DNA testing?
- Payment issues, especially related to Medicaid babies

IRT/DNA—Ballroom (Facilitators: Yvonne & Susanna)

- Arizona
  - Challenges: QNS/unsat on 1st screen – need to manually track arrival of 2nd screen and risk delays and/or missing adding CF to 2nd screen
  - Solutions: safety nets in place to find babies missing IRTs (run queries to ensure babies do not miss IRT, standalone 2nds), education on collection process to reduce eliminate QNS/unsats, one-on-one meetings with specialists twice a year to discuss challenges/successes, encourage only those who have a relationship with family to contact with abnormal results
- Georgia
  - Challenges: screening results getting to PCP and CF not timely - follow-up is contracted out to Emory
  - Solutions: identify the barrier (why is it taking average of 17 days?), identify what is going on with other centers, re-institute CF workgroup for Georgia (monthly calls)
- Iowa/North Dakota
  - Challenges: change in platform, limited days for mutation analysis, delays in PCP to family to referral center
  - Solutions: move to new platform, run more days with new platform, consider direct notification from STFU to families, education
- Kansas
  - Challenges: lab schedule for PCR, improving timeliness of receipt at lab for testing
  - Solutions: increase 2x per week for PCR, CoIIN project
- Michigan
  - Challenges: Hospitals are not packaging specimens correctly, home delivery, sometimes reporting results to CF center for hospitals might not occur, saves money testing 3 days/week, but delays reporting
  - Solutions: Monitor pick-up and delivery times, any specimens collected 5 hours before pick up time should go out that day, Title IV program can pay for diagnostic evaluation and assist with transportation, do molecular screen 3 times a week
- North Carolina
  - Challenges: halogic recall and alternate DNA analysis into lab, missing information on DBS cards (correct PCP, name changes, unsatisfactory specimen), batching specimens, engaging PCP to contact family, state law mandates collection time, coordination between CF Center and PCP (i.e. contacting family, not pursuing, no phone), sweat testing (QNS and no shows), state lab hours, CF centers wait to do sweat test to decrease QNS, staff shortages to support weekend testing
  - Solutions: Establish new system in lab with training and validation, need back-up plan for when things fall apart (ex. Halogic recall), retrain nursery staff, create training module for new staff, publish a transparent report to hospitals on timeliness and unsat rates (has prompted competition among hospitals), periodic calls with CF Centers and PCPs to review calls and solutions
- Nebraska:
  - Challenges: meconium ileus not always reported appropriately, premies—QNS, if zero copies of Delf508, but increased IRT, repeat IRT (should we wait until 2 weeks of age?)

  - Solutions: continued reinforcement through education, repeat DNA if appropriate, consult CF Team sooner, further research
- New York
  - Challenges: different ethnicities, lack of identification of 1 mutation, high % of specimens from premies, delay in sweat test appointments, lower NY have clinics with multiple docs
  - Solutions: NextGen sequencing coming soon, special UPS envelopes that identify as NB specimen, Saturday staff, have clinicians talk to NICU staff to ensure specimens are collected, educate clinicians that babies can undergo sweat test before they are 10 lbs.
- South Carolina
  - Challenges: no DNA component in current algorithm, specimen quality on initial or subsequent specimens, incomplete/incorrect demographic info, funding for the DNA component
  - Solutions: add DNA—change algorithm to IRT/DNA, currently re-educating hospitals in regional trainings, raise NBS panel fee
- Tennessee
  - Challenges: personnel training, short term follow-up—LIMs does not capture enough data for presumptive diagnosis; need baseline data. There are 5 CF Centers, but only 4 are accredited. Rare CF mutations cause higher percentage of African Americans and Hispanics babies missed because mutations common to those groups are not on panels
  - Solutions: hire/train more people, make database changes to capture information in case management, bring care centers and genetics together to share state data, get 5th center accredited, survey all sties to capture baseline data on barriers or pitfalls which delay diagnosis
- Virginia
  - Challenges: notification/follow-up on one mutation results, relay results to parents (explain cutoffs etc.), Friday results (preliminary screen – waiting for confirmation)
  - Solutions: identify staff resources, wanted feedback on how to communicate results with parents—possible solutions that are working for other states?

2-Screen States—`IRT /IRT/DNA or IRT/IRT (Facilitators: John & Kathy)

FOLLOW-UP

Screening Protocols

- Takes too long to get 2nd DBS if abnormal 1st IRT
- Variation in military screening protocols
- Crossing state borders
- Not getting 2nd screen due to transfers
- Ultrahigh IRT algorithm (i.e. 1st IRT is high then notify CF Center who notifies PCP to expedite/prioritizes 2nd IRT); how to set standard for high IRT for 1st specimen

POTENTIAL SOLUTIONS:

- Educational materials for PCP regarding time critical nature of CF diagnosis, standardized scripts
- Elevate 2nd/repeat specimens to faster delivery (courier service)
- Collect 2nd screen anywhere (not just PCP); send to birth hospital
- Standardize language on 1st high IRT report (stronger language)
- Change timeline for getting second screen
- Improve linking algorithm and share
- Change algorithm to consider population/genetics
- Courier service to expedite delivery of cards

Communication with PCP

- Misinformation; PCP not listed correctly
- PCP has to contact family first
- Phone tree at PCP office, time lag, hold time
- Lag to get into PCP office and lack of response
- Upkeep of contact information
- NICU delayed diagnosis
- High false + IRT/IRT and not followed up

POTENTIAL SOLUTIONS:

- Handout faxed to PCP on date of testing with instructions for next steps
- Providing information on the importance of transit time for 2nd specimens

Communication with CF Center

- Variation in CF Center response (e.g. won't see w/o sweat)
- Communication between lab and CF center
- Small CF center with limited provider availability

POTENTIAL SOLUTIONS:

- Proactivity of CF centers to make sweat test referral and/or appointment
- CF center holds reserved time slots for NBS sweat testing

Sweat Testing

- Infant too small to sweat
- Multiple labs doing sweat testing
- Unaccredited labs doing sweat testing
- Geographical and financial barriers to getting sweat
- Challenges in CEUs for tech with low rates of testing leading to delays in testing and proficiency issues
- Training staff/staff turnover in sweat techs
- Delay in getting sweats scheduled
- Variations in sweat procedures
- HMO/insurance issues
- Ethnic differences in amount of sweat
- Sweat test offered at 2 weeks vs. 4 weeks

LAB

- Location of genetic testing (in house vs. external)
- Second screen
    - Delay/absence of 2nd screen
    - Linking algorithm of 1st and 2nd screens for name of baby
- CFTR Mutation Testing
    - Frequency of CFTR genetic testing (number of times/week)
    - Choice of mutation panel/platform
    - Limited number of CFTR vendors
- IRT
    - Time of IRT Testing
    - Poor sensitivity/specificity of primary IRT Assay
- Lab to follow-up communication
- Perception CF NBS is non time-critical
- Weekend/holidays

POTENTIAL SOLUATIONS

- Discussion/development of core/regional lab services
- In-house genetic testing

Parking Lot Items

- IRT cutoff on ultrahigh protocols
- QNS rate reporting (reluctance to do sweat testing on young infants which could increase this rate)
- Higher QNS rates for sweat tests in African Americans