Newborn Screening Analytical Tools Survey Results

Susan Tanksley, PhD

Present to the Advisory Committee on Heritable Disorders in Newborns and Children

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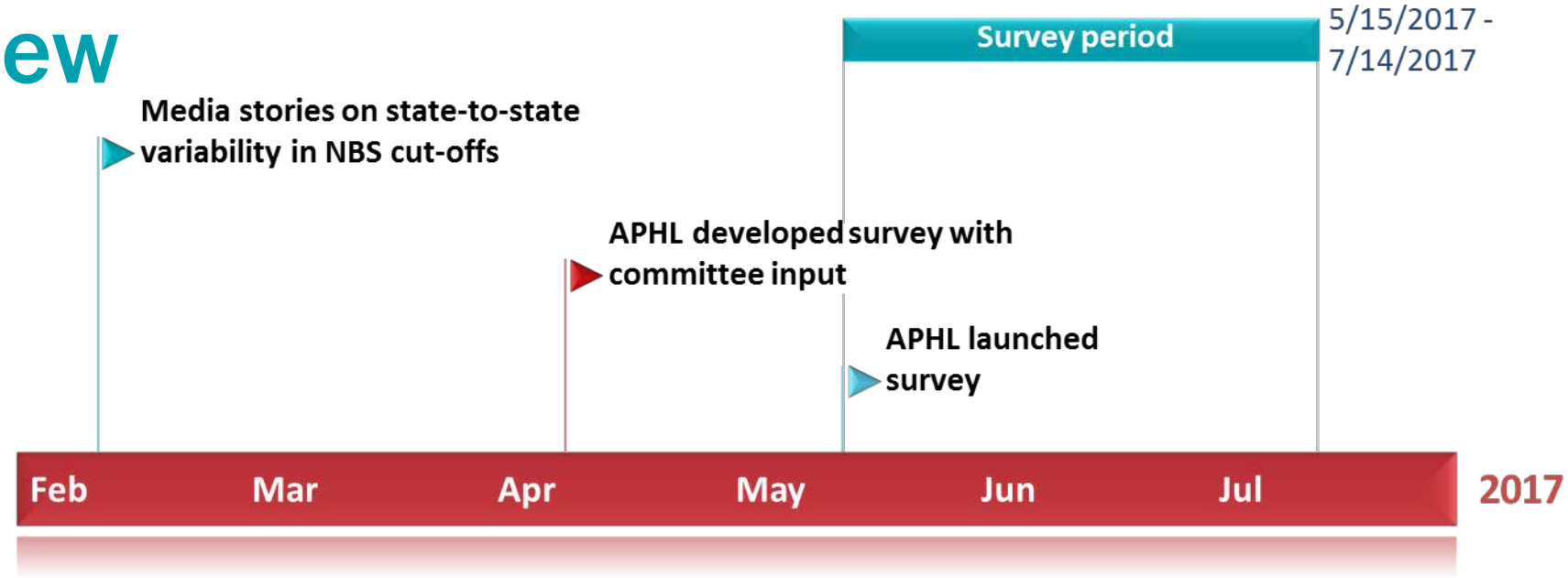
Overview



- Survey developed by APHL with input from Newborn Screening and Genetics in Public Health Committee (NBSGPH)
  - Field tested with small group of volunteers from NBSGPH committee
  - Questions further refined based on feedback
- Survey audience: NBS laboratory directors, follow-up managers, clinicians, any other personnel involved in NBS who use analytical tools.
- Response rate: 38 of 53 NBS programs (72%)

How do states establish their cut-offs?

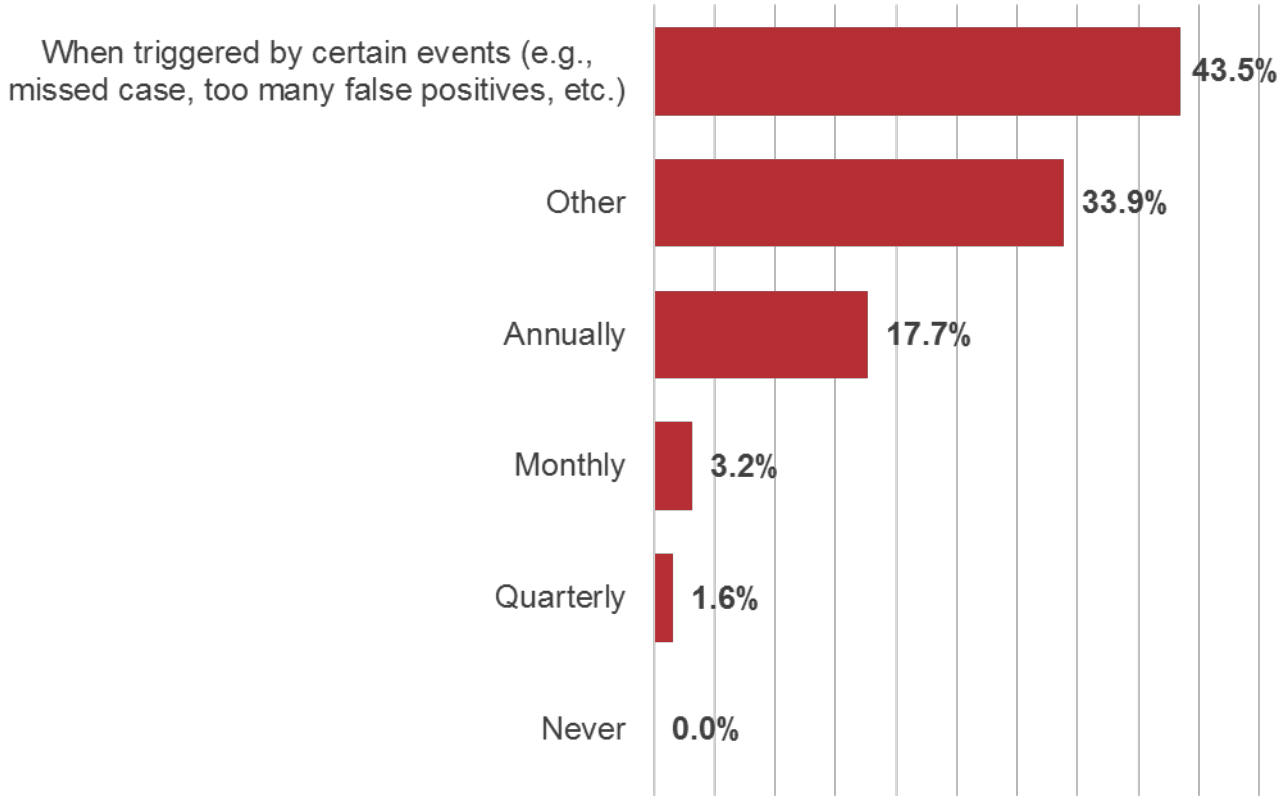
- Vendor recommendation (kit insert)
- Population data from screening DBS of normal and affected babies
  - Considerations for age and weight (sub-populations)
- Consultants/clinical specialists/NBS advisory committee input
- Published literature
- Other state NBS program experiences

Which software/tools do states use in establishing cut-offs?

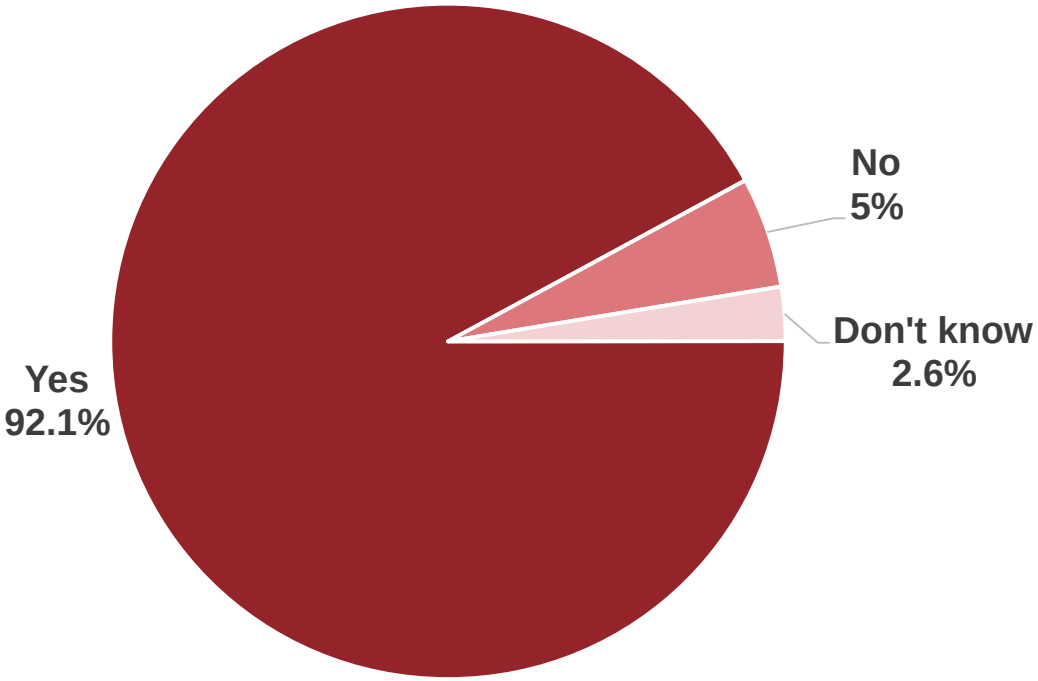
- Excel
- R4S
- SAS
- SpecimenGate / Cutoff Analyzer

How often does your program re-evaluate cut-off values or the process to determine the cut-off values for follow-up testing or referrals?

(n= 38)

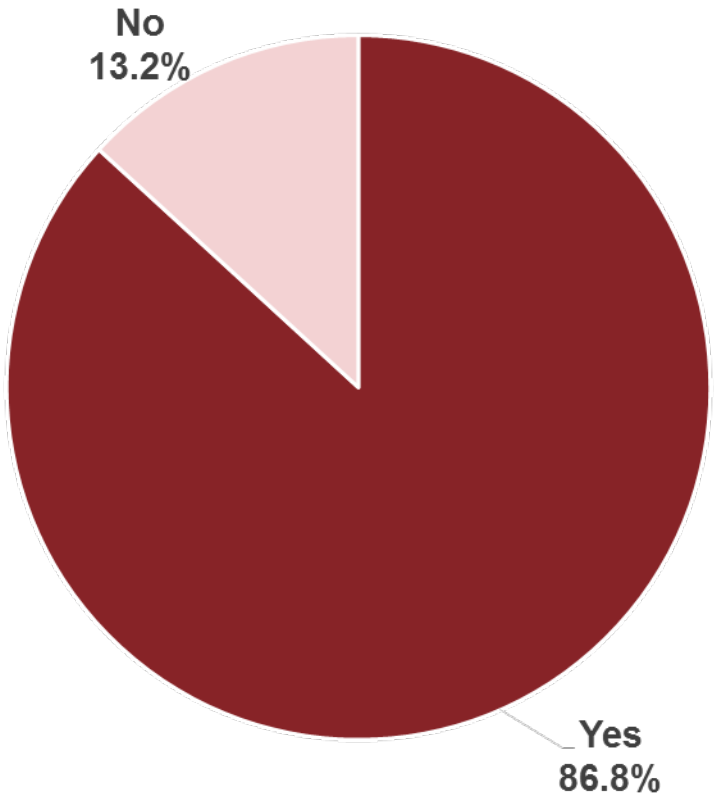


Does your state have a process to communicate reference range or referral protocol changes to healthcare providers/others outside of DOH? (n=38)



Does your NBS results report include a risk assessment (e.g., normal/abnormal, slightly/highly elevated, or heterozygous/disease)?

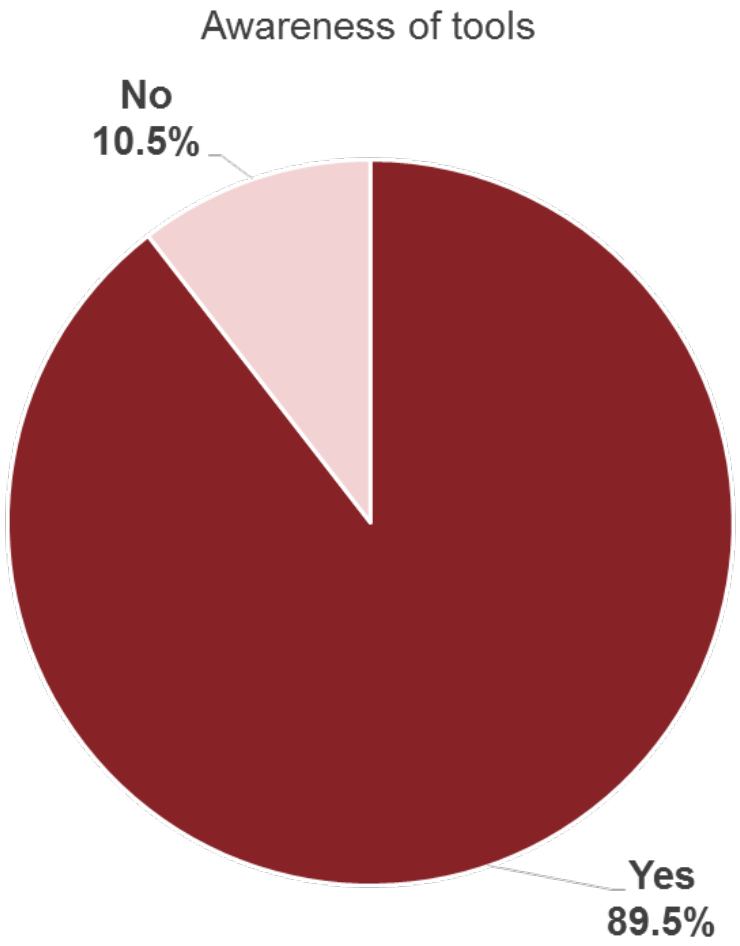
(n=38)



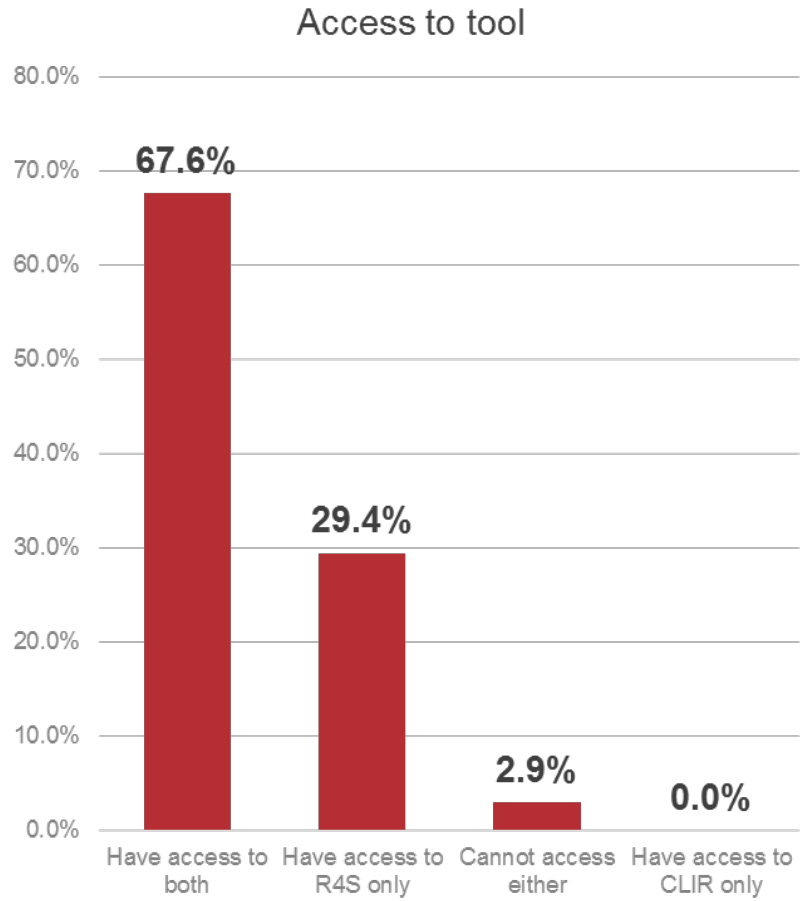
What challenges do you encounter by integrating risk into your NBS results report (e.g., limitations of data system, etc.)?

“Our LIMS reporting system is set up to report out abnormal analyte ranges, not disorders. This kind of a change may require a reworking of the whole system: time, personnel and money are all factors.”

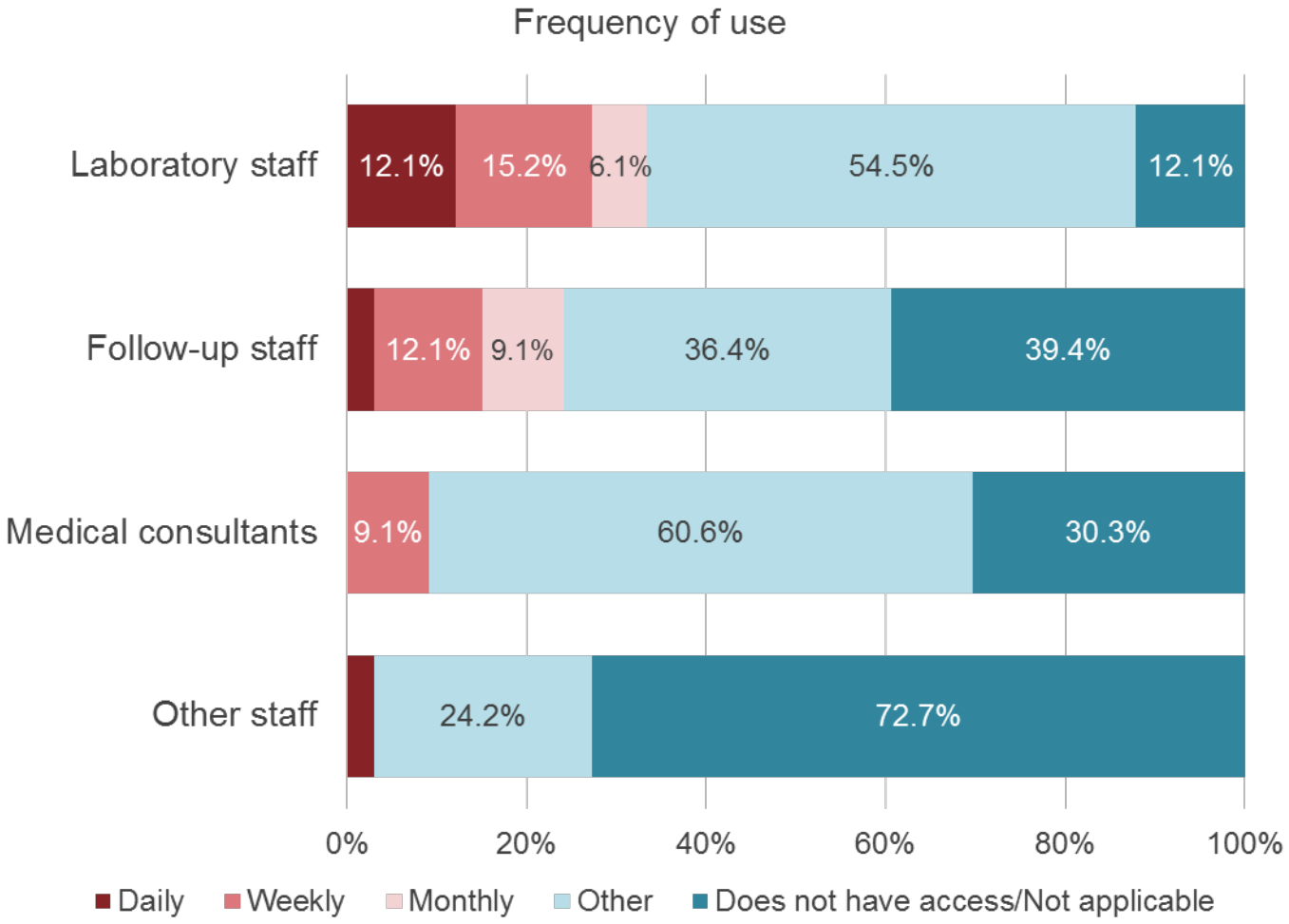
Do you know what R4S/CLIR is? (n=38)



Does your program have access to R4S/CLIR? (n=34)

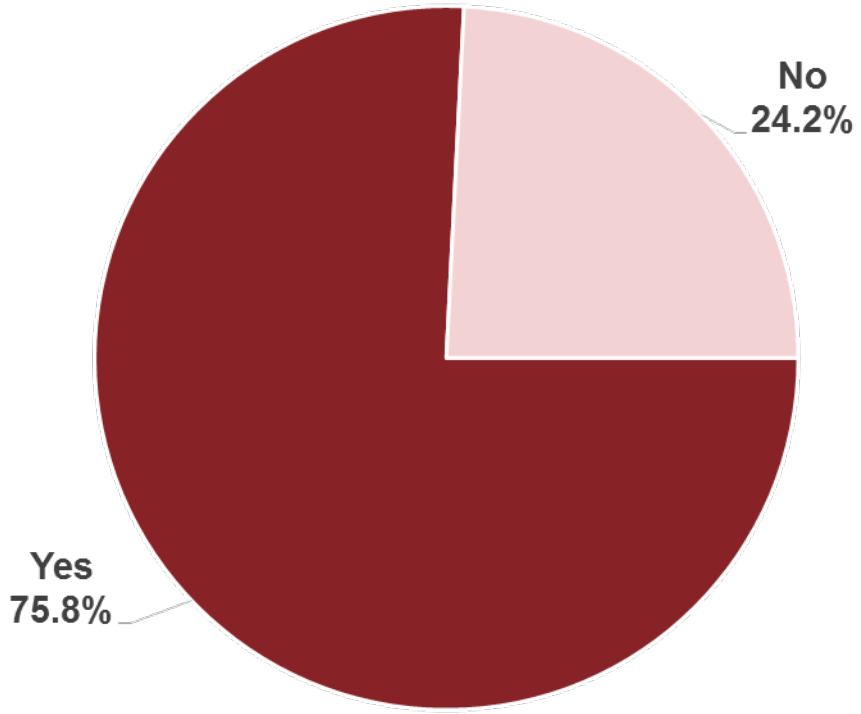


How often do the following staff use the R4S/CLIR?

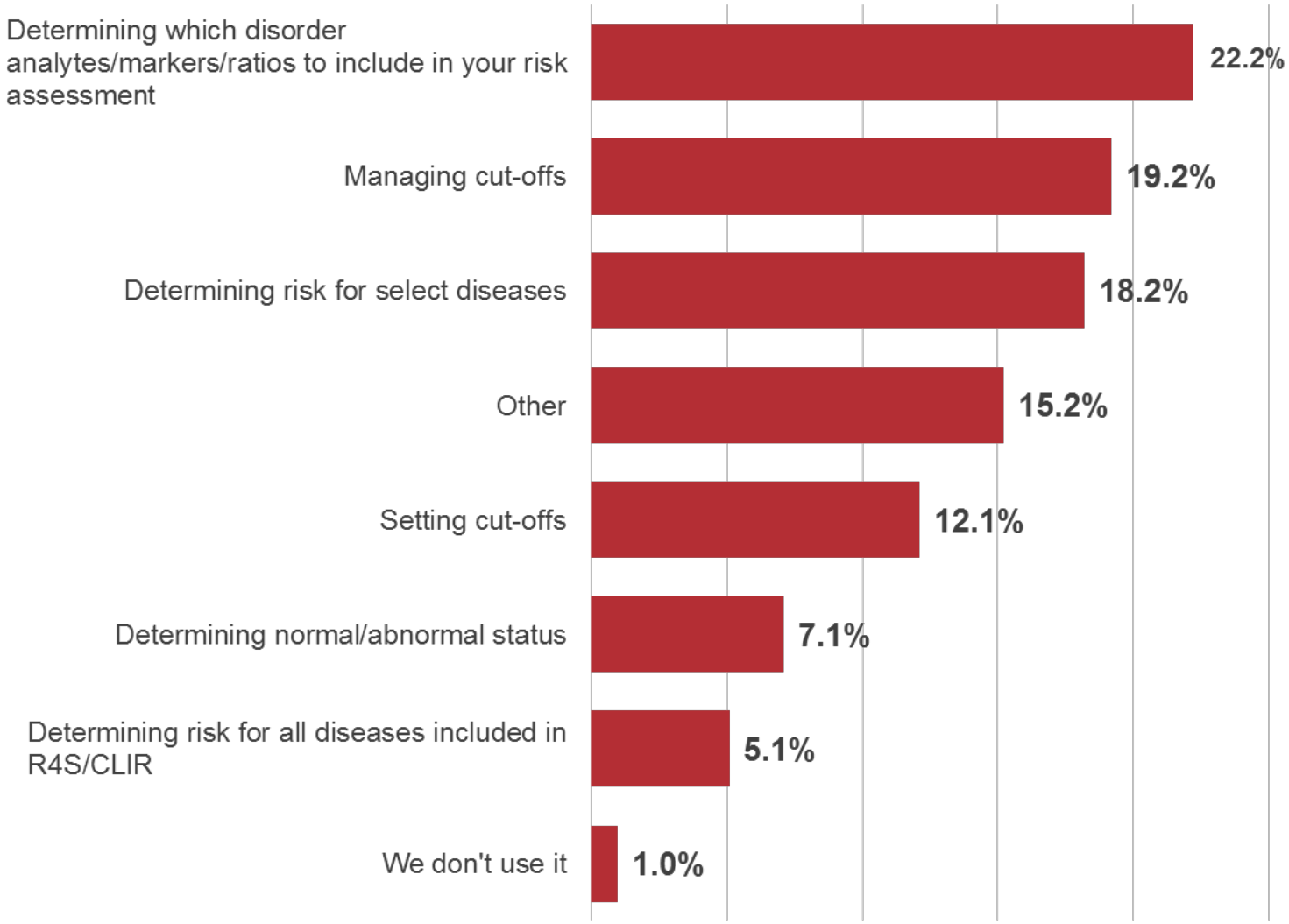


Have you been trained on how to use the R4S/CLIR databases?

(n=33)



How does your program use the R4S/CLIR?



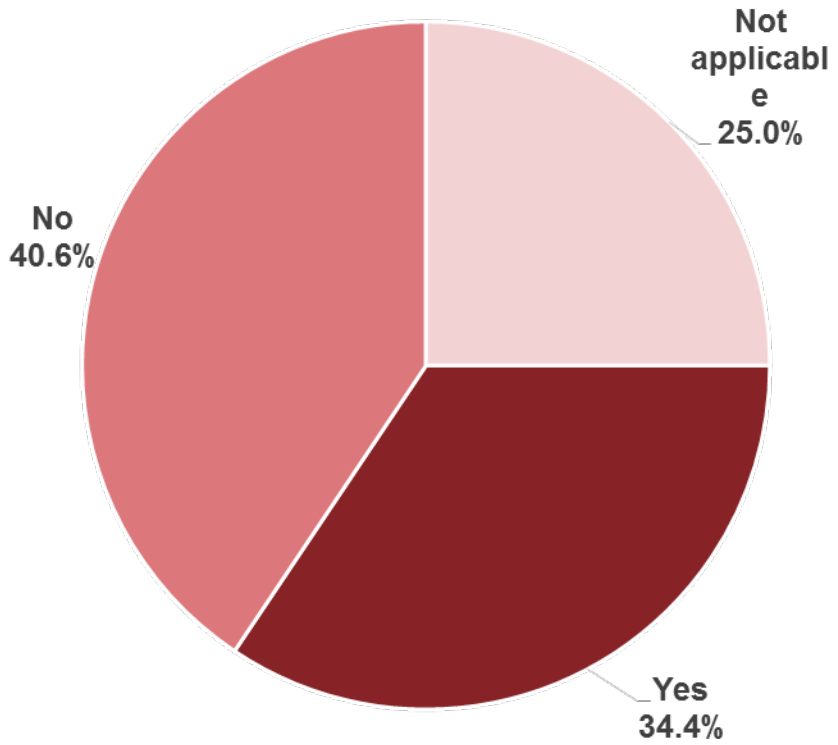
If your program does not use R4S/CLIR to determine risk or normal/abnormal status, why not?

“R4S has not been subjected to peer review with published results clearly supporting use for risk determination. In addition, the algorithms have not been validated and are subject to change which does impose a risk on a clinician.”

If your program does not use R4S/CLIR to determine risk or normal/abnormal status, why not?

“Not enough evidence that the tools work better than cut-offs to convince us to do so. For R4S the tool risk determination continuously evolves every time someone is adding data. You never know how well the tools were performing in the past. Not good integration with state LIMS resources. Lack of normalization.”

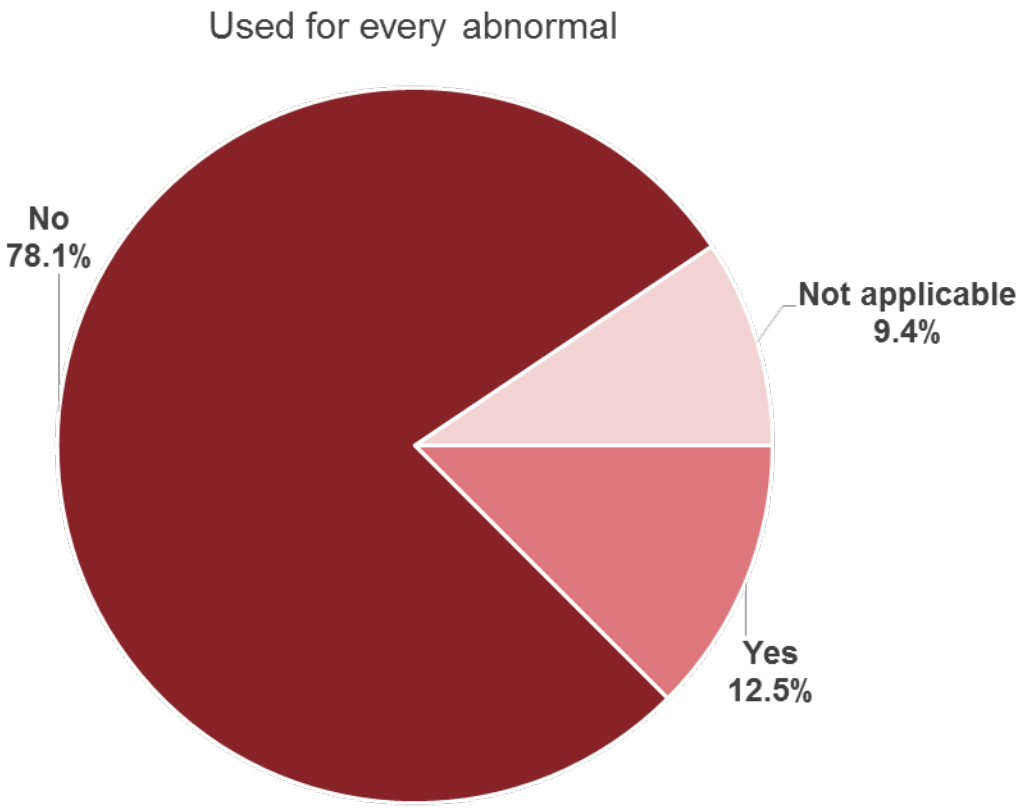
Do you have examples that using R4S/CLIR data resulted in false negatives or false positives? (n=32)



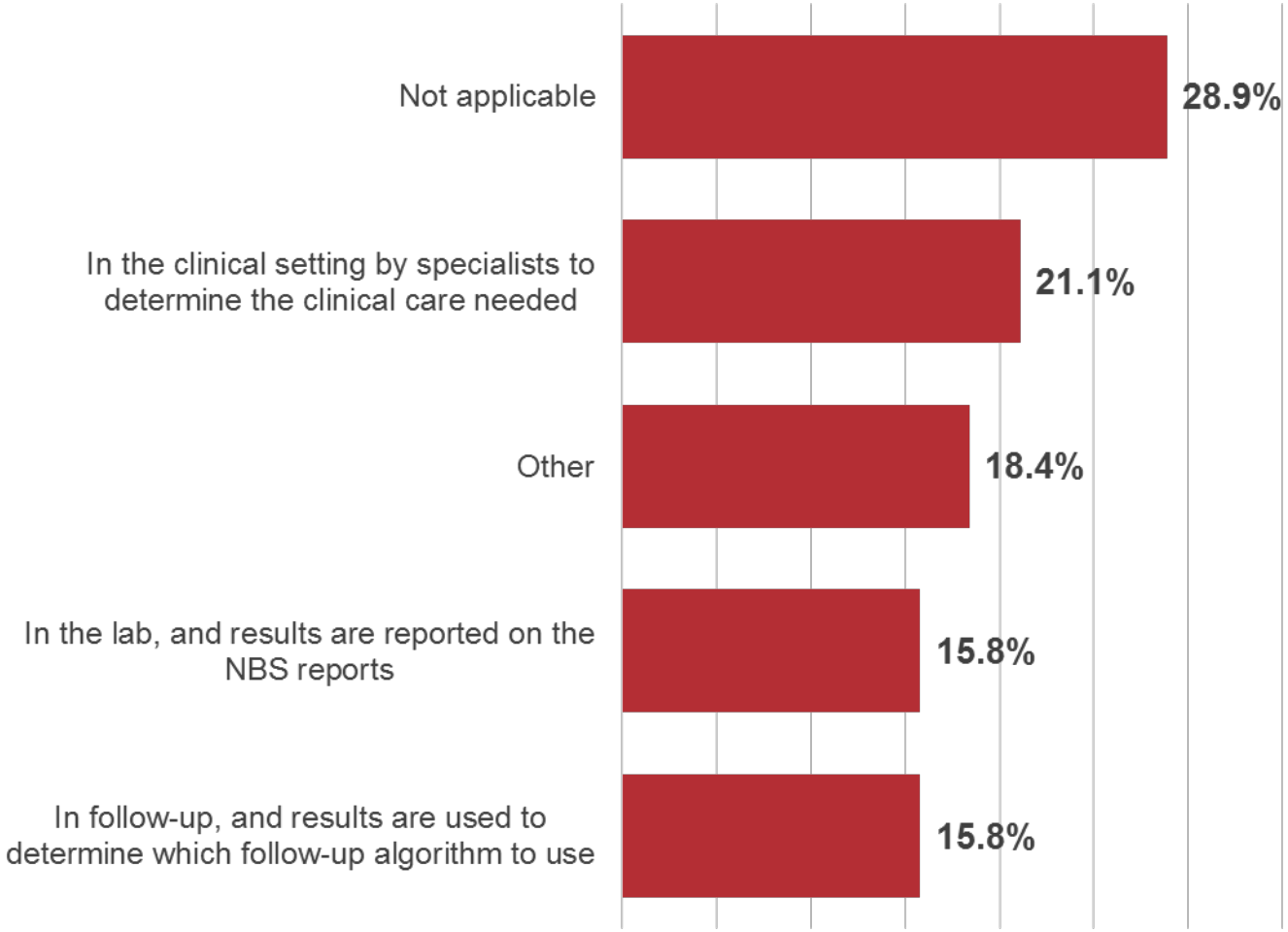
- False (+) for MSUD and CPT1
- Case of BKT was a false (-) both by state's tools and CLIR
- Two false (-); there have been 2 known cases of babies diagnosed with MSUD through our program that would not have been reported out for follow-up using R4S/CLIR
- CPTII, MSUD; concern with some disorders for positives that do not overlap the positive range significantly enough to get a positive score. As more data is added to the tool we have observed significant change can occur.

Does your program use R4S/CLIR for every abnormal result?

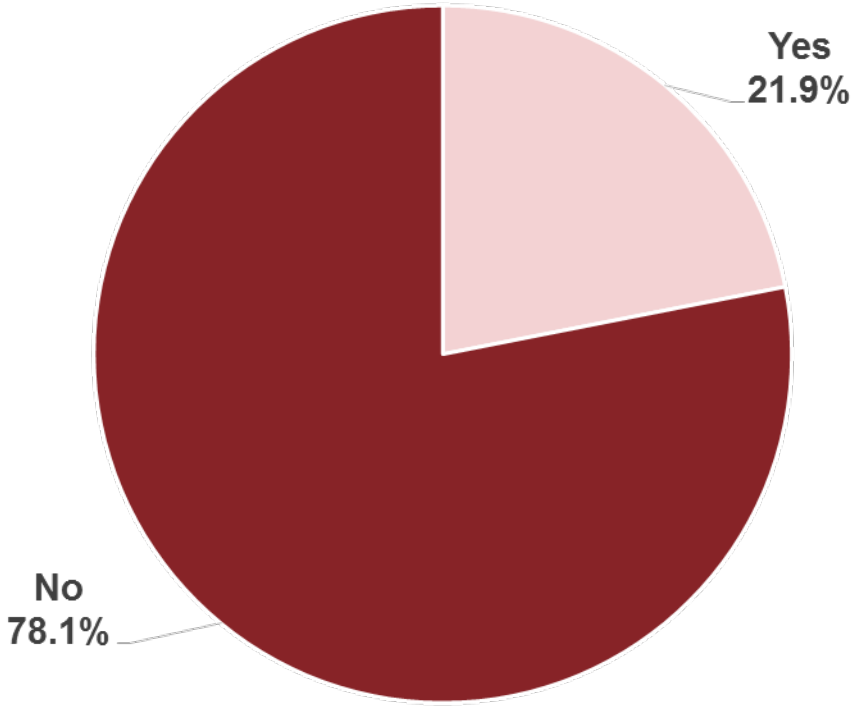
(n=32)



When using data from R4S/CLIR to determine risk or normality status, where are determinations made?



When using R4S/CLIR data to determine risk, has your program re-run values to obtain a new risk assessment on previously reported cases? (n=32)



What are the strengths of the R4S/CLIR?

Strengths of R4S/CLIR

“There is a lot of information about disorders and primary markers and also the ability to make sure the cutoffs are set appropriately. There are also ways of comparing results/cutoffs with other programs that use the system so that is helpful as well.”

What are the weaknesses of the R4S/CLIR?

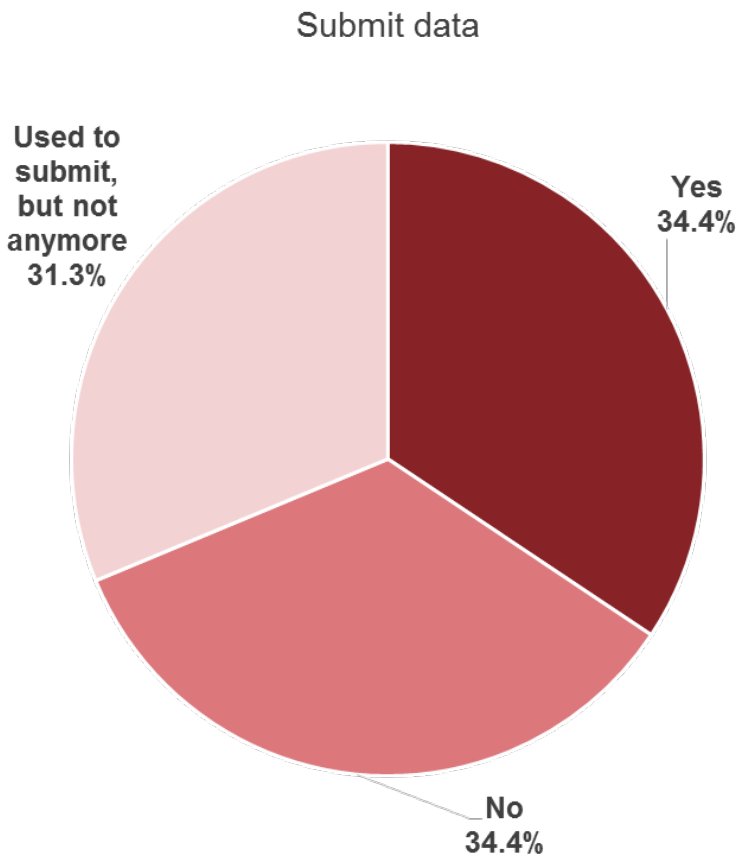
- Algorithms not validated
- Need to customize algorithm for each state
- Lack of transparency
- Better integration needed with LIMS
- Data/tools are not method/instrument specific
- Tool changes as more data is entered
- Variability in case definitions
- Training is lacking/not accessible when needed

Weaknesses of R4S/CLIR

“No clinical data available about false positives (specificity/PPV). Tools give ‘very likely’, ‘likely’, ‘possibly’, and ‘not informative’. These are very subjective interpretations. If system were tied to results from false positives, more information could be provided to clinicians when diagnostic testing is recommended for babies with positive screening results.”

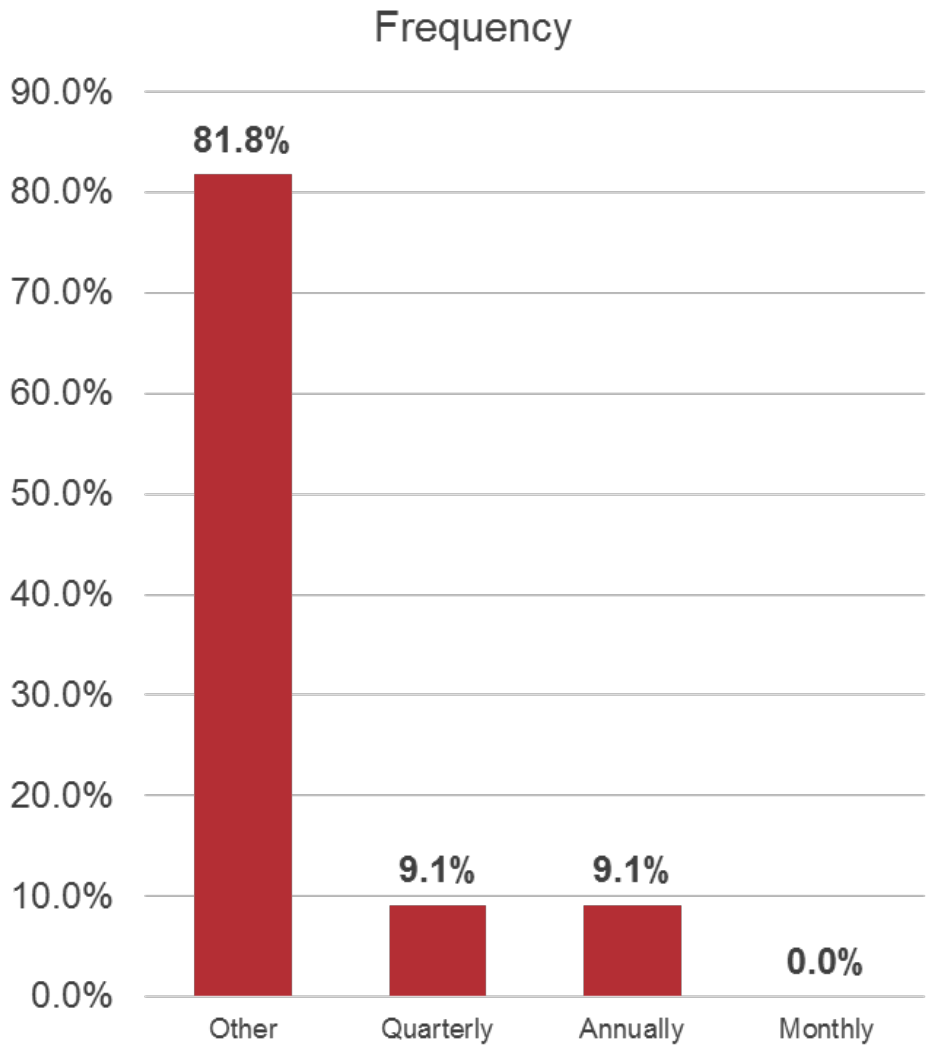
Do you submit normal population data results to R4S/CLIR?

(n=32)

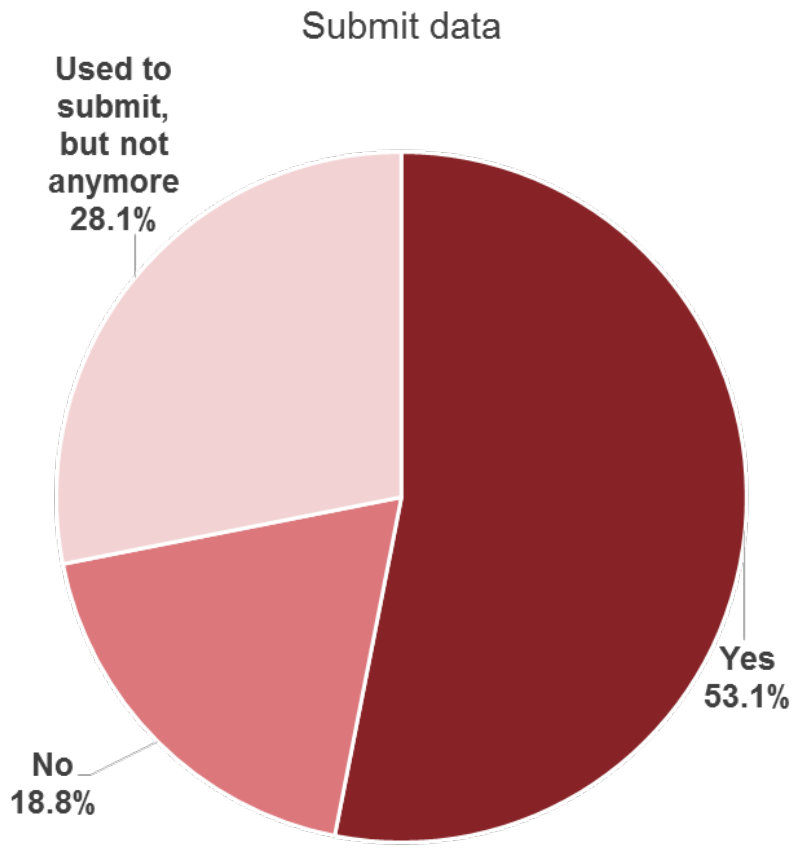


How often?

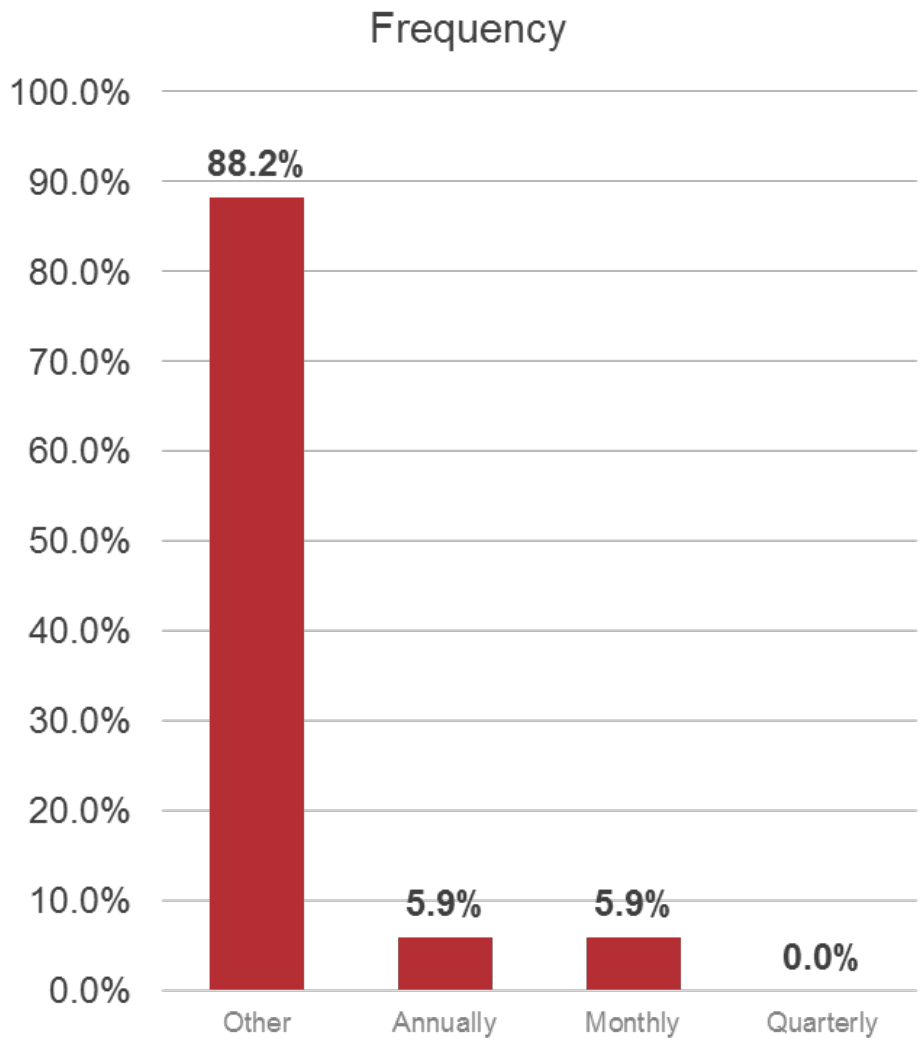
(n=11)



Do you submit case data to R4S/CLIR? (n=32)



How often? (n=11)



Why did your program stop submitting data?

- Lack of staff time
- Difficulty collating data from LIMS
- DOH concerned about potential data security issues
- Concern with managing, storing and sharing NBS data without a parental consent structure within the program's NBS process
- Legal concerns

What benchmarks are used to define a case prior to adding it to R4S/CLIR? (n=32)

- Positive diagnosis confirmed by
  - clinical specialist
  - follow-up program
  - genetic referral centers

Conclusions

- Limitations of survey:
  - Did not receive responses from all states
  - Follow-up with states for clarification or additional information did not result in timely response for inclusion in presentation
- Use of tools in NBS community:
  - Approximately 97% of states that completed the survey have access to R4S and/or CLIR

Conclusions, continued

- States have varied processes in determining cut-offs which involves
  - Analyzing state population data derived from screening of normal and affected babies
  - Incorporating feedback from specialists
  - Consulting published literature and/or R4S/CLIR
  - Consulting other state NBS programs
- States have mechanisms in place to re-evaluate cut-offs and do so on a regular basis

Questions/Comments