Public Health Impact Survey for X-ALD
Summary Data Report

Survey Participation

Sample	Completed Surveys	Response Rate
53	38	71.7%

1. Within the last 3 years, has your NBS program... Please check all that apply. (n=38)

Answer	Response	%
Included ALD as part of the routine NBS [END SURVEY]	1	2.6%
Included ALD as any type of pilot evaluation [END SURVEY]	0	0.0%
Received a mandate to screen for ALD [END SURVEY]	4	10.5%
None of the above	33	86.8%

2. If ALD was added to the Recommended Uniform Screening Panel (RUSP) tomorrow, how long would it take to get authorization to screen for ALD in your state? (n=33)

Answer	Response	%
Less than 1 year	5	15.2%
1 to 3 years	20	60.6%
More than 3 years	8	24.2%
Never	0	0.0%
Total	33	100.0%

3. Once you received authorization to screen, how long would it take to have funds allocated for ALD? (n=33)

Answer	Response	%
Less than 1 year	5	15.2%
1 to 3 years	19	57.6%
More than 3 years	7	21.2%
Never	2	6.1%
Total	33	100.0%

4. Please select the top 3 challenges related to ALD implementation. (n=33)

Answer	Response	%
Provide screening test	20	60.6%
Short-term follow-up of abnormals	20	60.6%
Increase of NBS fee	16	48.5%
Long-term follow up for carriers and individuals with peroxisomal disorders	15	45.5%
Support to ALD specialists	12	36.4%
Treatment support for ALD	8	24.2%
Other-please specify	3	9.1%
Other specified responses		
staffing, building infrastructure improvements		
Preparation of broad health care system (ie, pediatricians/other medical providers, hospitals, Medicaid) for screening/follow-up		
Hiring freeze, Laboratory Space, Advisory Committee review and approval (if not included in RUSP)		

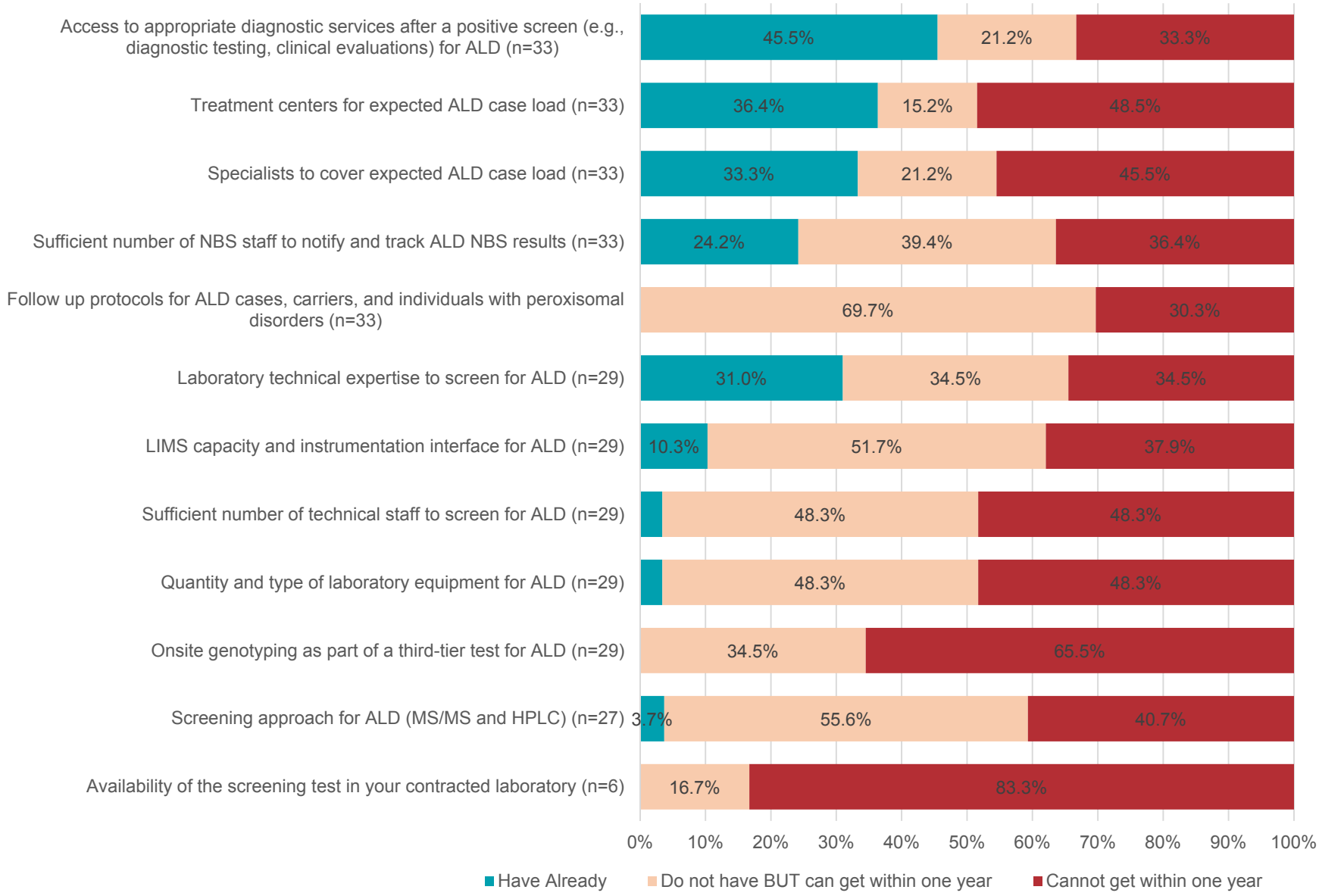
5. Please indicate your NBS program's readiness to implement screening for ALD by evaluating the following resources.

	Have Already		Do not have BUT can get within one year		Cannot get within one year	
	n	%	n	%	n	%
Access to appropriate diagnostic services after a positive screen (e.g., diagnostic testing, clinical evaluations) for ALD (n=33)	15	45.5%	7	21.2%	11	33.3%
Treatment centers for expected ALD case load (n=33)	12	36.4%	5	15.2%	16	48.5%
Specialists to cover expected ALD case load (n=33)	11	33.3%	7	21.2%	15	45.5%
Sufficient number of NBS staff to notify and track ALD NBS results (n=33)	8	24.2%	13	39.4%	12	36.4%
Follow up protocols for ALD cases, carriers, and individuals with peroxisomal disorders (n=33)	0	0.0%	23	69.7%	10	30.3%
Laboratory technical expertise to screen for ALD (n=29)*	9	31.0%	10	34.5%	10	34.5%
LIMS capacity and instrumentation interface for ALD (n=29)*	3	10.3%	15	51.7%	11	37.9%
Quantity and type of laboratory equipment for ALD (n=29)*	1	3.4%	14	48.3%	14	48.3%
Sufficient number of technical staff to screen for ALD (n=29)*	1	3.4%	14	48.3%	14	48.3%
Onsite genotyping as part of a third-tier test for ALD (n=29)*	0	0.0%	10	34.5%	19	65.5%
Screening approach for ALD (MS/MS and HPLC) (n=27)**	1	3.7%	15	55.6%	11	40.7%
Availability of the screening test in your contracted laboratory (n=6)***	0	0.0%	1	16.7%	5	83.3%

*Question only asked to labs with a state NBS program or commercial contract

**Question only asked to labs with a state NBS program.

*** Question only asked to labs with a regional contract or commercial contract.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Sufficient number of NBS staff to notify and track ALD NBS results (n=33)
24.2%
39.4%
36.4%
Follow up protocols for ALD cases, carriers, and individuals with peroxisomal disorders (n=33)
69.7%
30.3%
Laboratory technical expertise to screen for ALD (n=29)
31.0%
34.5%
34.5%
LIMS capacity and instrumentation interface for ALD (n=29)
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Sufficient number of technical staff to screen for ALD (n=29)
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Quantity and type of laboratory equipment for ALD (n=29)
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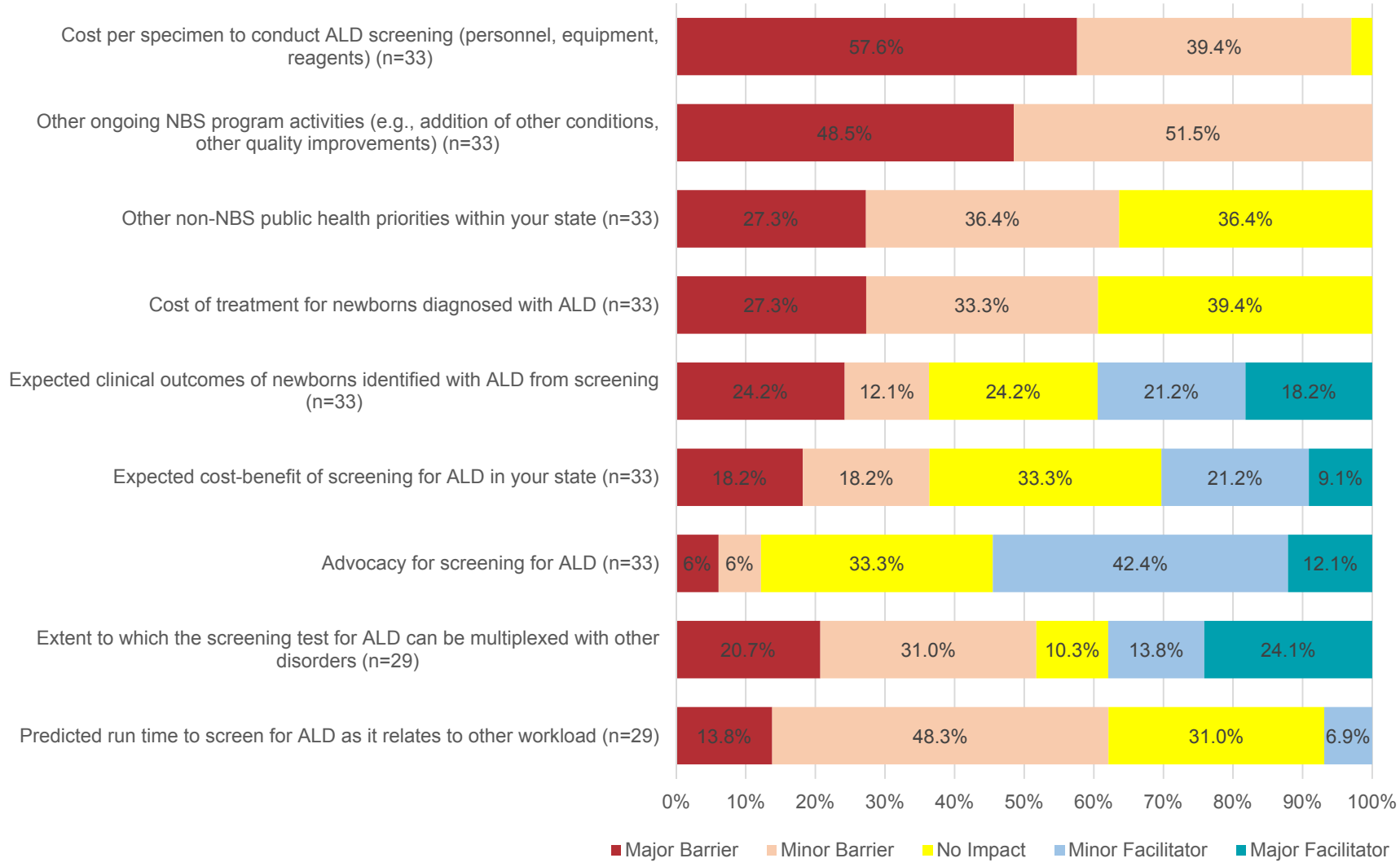
Onsite genotyping as part of a third-tier test for ALD (n=29)
34.5%
65.5%
Screening approach for ALD (MS/MS and HPLC) (n=27)
3.7%
55.6%
40.7%
Availability of the screening test in your contracted laboratory (n=6)
16.7%
83.3%
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Have Already
Do not have BUT can get within one year
Cannot get within one year

6. To what extent do the factors below impede or facilitate the adoption of screening for ALD in your NBS program?

	Major Barrier		Minor Barrier		No Impact		Minor Facilitator		Major Facilitator	
	n	%	n	%	n	%	n	%	n	%
Cost per specimen to conduct ALD screening (personnel, equipment, reagents) (n=33)	19	57.6%	13	39.4%	1	3.0%	0	0.0%	0	0.0%
Other ongoing NBS program activities (e.g., addition of other conditions, other quality improvements) (n=33)	16	48.5%	17	51.5%	0	0.0%	0	0.0%	0	0.0%
Cost of treatment for newborns diagnosed with ALD (n=33)	9	27.3%	11	33.3%	13	39.4%	0	0.0%	0	0.0%
Other non-NBS public health priorities within your state (n=33)	9	27.3%	12	36.4%	12	36.4%	0	0.0%	0	0.0%
Expected clinical outcomes of newborns identified with ALD from screening (n=33)	8	24.2%	4	12.1%	8	24.2%	7	21.2%	6	18.2%
Expected cost-benefit of screening for ALD in your state (n=33)	6	18.2%	6	18.2%	11	33.3%	7	21.2%	3	9.1%
Advocacy for screening for ALD (n=33)	2	6.1%	2	6.1%	11	33.3%	14	42.4%	4	12.1%
Extent to which the screening test for ALD can be multiplexed with other disorders (n=29)*	6	20.7%	9	31.0%	3	10.3%	4	13.8%	7	24.1%
Predicted run time to screen for ALD as it relates to other workload (n=29)*	4	13.8%	14	48.3%	9	31.0%	2	6.9%	0	0.0%

*Question only asked to labs with a state NBS program or commercial contract


Cost per specimen to conduct ALD screening (personnel, equipment, reagents) (n=33)
57.6%
39.4%
Other ongoing NBS program activities (e.g., addition of other conditions, other quality improvements) (n=33)
48.5%
51.5%
Other non-NBS public health priorities within your state (n=33)
27.3%
36.4%
36.4%
Cost of treatment for newborns diagnosed with ALD (n=33)
27.3%
33.3%
39.4%
Expected clinical outcomes of newborns identified with ALD from screening (n=33)
24.2%
12.1%
24.2%
21.2%
18.2%
Expected cost-benefit of screening for ALD in your state (n=33)
18.2%
18.2%
33.3%
21.2%
9.1%
Advocacy for screening for ALD (n=33)
6%
6%
33.3%
42.4%
12.1%
Extent to which the screening test for ALD can be multiplexed with other disorders (n=29)
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13.8%
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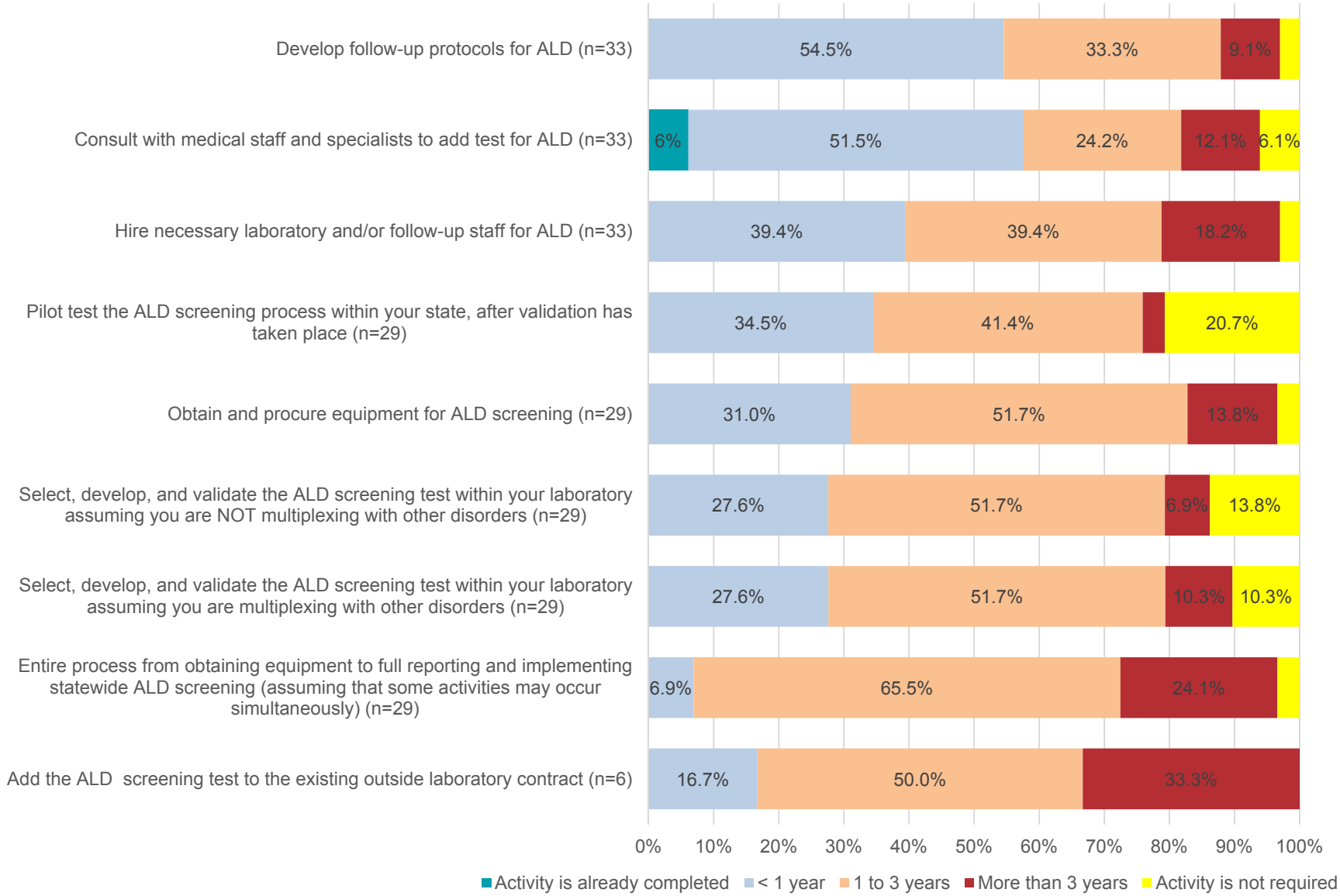
Predicted run time to screen for ALD as it relates to other workload (n=29)
13.8%
48.3%
31.0%
6.9%
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Major Barrier
Minor Barrier
No Impact
Minor Facilitator
Major Facilitator

7. How long would it take your NBS program to complete the following activities?

	Activity is already completed		< 1 year		1 to 3 years		More than 3 years		Activity is not required	
	n	%	n	%	n	%	n	%	n	%
Develop follow-up protocols for ALD (n=33)	0	0.0%	18	54.5%	11	33.3%	3	9.1%	1	3.0%
Consult with medical staff and specialists to add test for ALD (n=33)	2	6.1%	17	51.5%	8	24.2%	4	12.1%	2	6.1%
Hire necessary laboratory and/or follow-up staff for ALD (n=33)	0	0.0%	13	39.4%	13	39.4%	6	18.2%	1	3.0%
Pilot test the ALD screening process within your state, after validation has taken place (n=29)*	0	0.0%	10	34.5%	12	41.4%	1	3.4%	6	20.7%
Obtain and procure equipment for ALD screening (n=29)*	0	0.0%	9	31.0%	15	51.7%	4	13.8%	1	3.4%
Select, develop, and validate the ALD screening test within your laboratory assuming you are multiplexing with other disorders (n=29)*	0	0.0%	8	27.6%	15	51.7%	3	10.3%	3	10.3%
Select, develop, and validate the ALD screening test within your laboratory assuming you are NOT multiplexing with other disorders (n=29)*	0	0.0%	8	27.6%	15	51.7%	2	6.9%	4	13.8%
Entire process from obtaining equipment to full reporting and implementing statewide ALD screening (assuming that some activities may occur simultaneously) (n=29)*	0	0.0%	2	6.9%	19	65.5%	7	24.1%	1	3.4%
Add the ALD screening test to the existing outside laboratory contract (n=6)**	0	0.0%	1	16.7%	3	50.0%	2	33.3%	0	0.0%

*Question only asked to labs with a state NBS program or commercial contract

**Question only asked to labs with a regional contract or commercial contract.


Develop follow-up protocols for ALD (n=33)
54.5%
33.3%
9.1%
Consult with medical staff and specialists to add test for ALD (n=33)
6%
51.5%
24.2%
12.1%
6.1%
Hire necessary laboratory and/or follow-up staff for ALD (n=33)
39.4%
39.4%
18.2%
Pilot test the ALD screening process within your state, after validation has taken place (n=29)
34.5%
41.4%
20.7%
Obtain and procure equipment for ALD screening (n=29)
31.0%
51.7%
13.8%
Select, develop, and validate the ALD screening test within your laboratory assuming you are NOT multiplexing with other disorders (n=29)
27.6%
51.7%
6.9%
13.8%
Select, develop, and validate the ALD screening test within your laboratory assuming you are multiplexing with other disorders (n=29)
27.6%
51.7%
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Entire process from obtaining equipment to full reporting and implementing statewide ALD screening (assuming that some activities may occur simultaneously) (n=29)
6.9%
65.5%
24.1%
Add the ALD screening test to the existing outside laboratory contract (n=6)
16.7%
50.0%
33.3%
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Activity is already completed
< 1 year
1 to 3 years
More than 3 years
Activity is not required

8. What is the most significant barrier to implementing screening for ALD in your program?

The state nomination process and funding.
Please see the responses of the [state] program. Under current arrangements, [state] would wait for piloting, approval, and implementation by [state] before considering addition to our panel, since [state] would perform testing for [state].
Currently we contract with a out of state lab, and unless they take on ALD screening our program would not split spots to send to another lab for this piece
I have no comment to provide
Recommendation by the State Advisory Council and Approval by the Secretary of [state] Department of Health.
Identification of clinics/clinical specialists and followup protocol development
Funding, Hiring restrictions
I have no comment to provide
Space, cost, multiplexing
No current FDA-approved kit.
funding for staffing, equipment, LIMS update, and building infrastructure improvement; ability to recruit qualified staff
Lack of laboratory facilities to perform screening
Both human resource time and money associated with ALD testing, follow-up and community education
Cost/kit fee increase
Financing - requires NBS fee increase that must be legislatively approved.
The screening method. Once it becomes available in the PE Neobase II kits, it will be much easier. They say that will be over two years away.
Other Department priorities, lack of medical community support
Increased workload for staff due to carriers and peroxisomal disorders being detected in addition to ALD.
We are adding SCID to our panel in the fall.
The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children has not recommended adding to panel.
Appropriate laboratory staff to interpret screening results
Cost of screening and staffing issues
Kit availability and competing laboratory projects
Cost
The need for a viable screening method and the cost associated with screening implementation
1. RUSP approval / 2. Treatment protocols / 3. Prioritization of other disorders/deficiencies / 4. Funding-approval of newborn screening fee increase
? Obtaining funding, budget approvals and new staff to begin implementation activities. / ? Lack of validated treatment protocol and long-term follow-up and outcome data, including tested guidelines for management of NBS detected cases (as opposed to familial or clinical determined cases). /
Approval for increased funding and increased FTE's for follow-up, as well as funding for treatment (Medicaid)
The uncertainty of the appropriateness of including X-ALD as a mandated screened disorder. If evidence is clear (including the “certainty” of the evidence) decision making is straightforward; if evidence is not clear (including the “uncertainty” of the evidence) the decision making processes will repeatedly get de-railed and generating the “will” to move forward will be difficult. Other conditions recommended to the RUSP would compete for resources (Pompe, MPS-1, DMD, SMA, etc.)
-Recurrent funds for equipment, additional technitian and follow up personnel; in addition to cover for annual maintenance fees. / -Limited expertise of the service engineers who provide support to us locally which in the past has paralyzed the MSMS and S
I have no comment to provide
I have no comment to provide
Legislation approval/Rules Process

9. What is the most significant facilitator to implementing screening for ALD in your program?

Positive clinical outcomes from the early identification and treatment.
Please see the responses of the [state] program. Under current arrangements, [state] would wait for piloting, approval, and implementation by [state] before considering addition to our panel, since [state] would perform testing for [state].
unknown at this time
I have no comment to provide
Addition to RUSP
Ability to multiplex with current MSMS analytes once Perkin Elmer FDA approval is achieved
Funding, Legislation
I have no comment to provide
State Board of Health
Add to RUSP.
high positive predictive value of test with low false positive rate and availability of treatment that saves lives and improves quality of lives
None
Multiplex testing plus an FDA cleared testing platform
benefits of early detection
Capability of adding testing to existing instrumentation and processes.
The ability to multiplex ALD with our current Fatty Acid Disorder panel on the MS/MS by measuring C26.
Has met newborn screening criteria. Pilot screening in other state programs.
Having ALD experts suddenly move to our state.
Readiness of our regional laboratory in [state].
Reliable outside/contracted screening laboratory
Strong genetics/metabolic follow up system
If the ALD could be multi-plexed with other MS/MS analytes, then adding this test would not be prohibitive.
Ability to capitalize on existing infrstructure; e.g. expert advisory committees in place, SACHDNC evidence review. / Existing instruments will be used.
RUSP
addition to the RUSP
If it could be multiplexed with existing tests or other new tests
• [state] state law requires screening for conditions on the RUSP as funding allows. / • Existing newborn screening program and infrastructure are well established. /
Advocates
The possibility of multiplexing ALD is of benefit to the lab. Existing NBS staff and medical consultants are experienced in the process of adding conditions to the state's NBS panel.
-Our current MSMS technitians are all extremely competent thus adding a new assay would not be particularly troublesome for them. / / -In [state] we do not need formal individualized legislation to include XALD or other specific disorders. The curren
I have no comment to provide
I have no comment to provide
Ability to multiplex with other MS/MS disorders

10. Please share any additional information regarding implementation of screening for ALD.

Please see the responses of the [state] program. Under current arrangements, [state] would wait for piloting, approval, and implementation by [state] before considering addition to our panel, since [state] would perform testing for [state].
At this time our program still needs to implement the LSD's law was set in place in [year] due to the lack of our out of state lab ready to screen at this time , it may be the same case with the ALD. It would put hardship on our birthing hospitals to have to split bloodspots to several different labs. Plus we recently increased our bloodspot fee within the last year and at the rate of new screens requested to the panel makes it diffcult for implementation for states that relay soley on revenue from the bloodspots.
Will require training for short-term follow-up on how to communicate results to PCP about implications of abnormal NBS results - i.e. if diagnosed, many different manifestations of ALD without ability to predict clinical course.
We would need a fee increase, and the NBS fee would need to be dedicated to NBS. /
A multiplexed FDA cleared testing platform would be ideal for implementation. Also, in the unknown category, there is potential concern about secondary findings for which there is no known treatment.
I have no comment to provide
Another added challenge is that this is an X-linked disorder, which requires additional investigations of other family members, and their diagnoses, management, care and counseling.
Implementation of ALD will be considered by the Department as are all recommendations announced by the ACHDNC.
This is the first disorder in NBS that has intervention/treatment well outside the newborn period. It doesn't fit the established reasons to do NBS so will be more difficult to justify to advisory committee, providers, hospitals, and others.
I have no comment to provide
all additions are approved through the Advisory Committee
I have no comment to provide
I have no comment to provide
Want to add ALD to our existing MSMS testing process. Must wait until kits are available.
I have no comment to provide
Having analysis included in a multiplex assay would facilitate implementation
The X-ALD screening will identify carriers and individuals with peroxisomal disorders. There is no treatment for some and some are late onset disorders. Long-term follow up for these patients will be a big concern.

• Answers are based on knowledge of new method developed in NY that allows multiplexing with amino acids & acylcarnitines. If screening of the new condition cannot be multiplexed with existing disorders using current instrumentation, additional implementation activities will be needed to obtain and procure equipment. Lack of space for new staff and equipment will also be a major issue. / • LIMS updates and validation are convoluted and complicated, especially in the current electronic health information system used to collect, maintain, and transfer patient data. / • Addition of new condition and related implementation activities will hinder the progress of NBS quality improvement and other activities such as timeliness because NBS programs have limited staffing and resources. / • Since ALD is an X-linked condition, we would expect to detect carriers who are at risk. Guidelines and protocols for carriers as well as additional genetics expertise are needed. / • There is adequate capacity for treatment and long-term follow-up in the state (both specialists and treatment centers). However, there is a skewed geographic distribution of these resources. / • There is diversity of opinion about the adequacy of treatment and long-term follow-up at the current time by the metabolic physicians in our state. / • Given the current lack of evidence base, the metabolic physicians in the state felt that adequate long-term follow-up protocols for ALD cases, carriers and individuals with peroxisomal disorders could not be available within one year. However, short term follow-up protocols for potential ALD cases could be developed within one year. / • Diverse feedback received from clinicians: / o "Overall, I think X-ALD is not ready for inclusion because all of the issues have not been worked out. Even New York's guideline paper (Mol Gen Metab 114:599, April 2015), admits that long-term follow-up is needed to evaluate their presented guidelines. If they are the first state with any guidelines, and they do not know if the guidelines are truly evidence based, why are we going to do this?" / o "I like the idea of adding X-ALD to the panel. It is one of the more reliable conditions to confirm, and since it is X-linked recurrence risk is a big deal. Also, since stem cell transplant is being tried more consistently, I think this is a much more reasonable assay to add than Krabbe or others of the lysosomal storage disorders that other states have added." /
I have no comment to provide
The most significant thing ACHDNC can do to speed the rate of implementation of a recommended condition (that will be mandated for all newborns; thus impacting all newborns and families and healthcare systems) is to require valid evidence that Wilson and Jungner criteria are met before making the recommendation. The biggest factor influencing the time for implementing screening by the State once a recommendation is formally approved by the Secretary is the level of "uncertainty" associated with the recommendation. The degree to which the recommendation meets Wilson and Jungner criteria (and certainty of the evidence) will greatly influence the time for full implementation of the recommendation by a State. The less compelling the evidence and/or the greater the uncertainty of the evidence, the more difficult it will be to obtain consensus and the "will" to move forward. Although the issues addressed in this survey are important and will have impact on the speed for full implementation, they are minor compared to the larger issue of whether the recommendation is appropriate. / The lack of pilot data prior to adding a condition to the RUSP makes it very difficlut to decide what's appropriate. Data need to be made available to programs to present to legislators who may be influenced by constituents to mandate a condition. Disorders like Pompe, MPS-1 and ALD that have early and late onset phenotypes may not provide significant benefit since timing of interventions may not be able to be determined, so benefit of interventions are not known. Follow up would require funding for increased staff to conduct care coordination activities, including nursing time and social work time.
This survey summarizes the imput from the [state] [advisory] Council and the [state] NBS Program after discussion today. / The current biochemical assay as the one performed by New York State would offer the opportunity to test for both XALD as well as LSDs (including Pompe). Thus there is a benefit for using this type of assay for NBS. Nonetheless as with MSMS, it is laborious and also requires experts in the field to validate and troubleshoot. Perhaps considering a PhD or MD with Board Certifications in Biochemical Genetics should be considered to be part of the supervising teams in MSMS or HPLC-MSMS NBS laboratories. / In our case for the multiple reasons (barriers) explained above, in a condition such as XALD where most patients do not need a treatment in the first few days of life, perhaps sending the specimens to another state laboratory for testing might be a valid alternative.

I have no comment to provide
I have no comment to provide
Other barriers: / Cost, Space, Hiring Freeze / Other facilitators: / Implementation federal grants that allow capital purchases