Gotta love New England! Feb 2015

In Our Own Words

some state perspectives on Public Health Service, Research and Public Trust

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February 2015

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Disclosures and Disclaimers

- Nothing to disclose
- Data presented are a sampling and do not represent a comprehensive set of states' experiences
- Any opinions expressed outside of those printed on the slides are the sole responsibility of the speaker and do not necessarily reflect those of colleagues or institutions who contributed to this dataset or of the DACHDNC Pilot Study Working Group.

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MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES
RESEARCH REVIEWS *12: 293–300 (2006)*

PILOT PROGRAMS IN NEWBORN SCREENING

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Pilot Program / Pilot Study

Evaluation of the clinical aspects

- *Clinical validity – Does the test / strategy find the infants who have the condition?*
- *Clinical utility– Is there benefit (minimal harm) to early detection of infants with the condition? - What is the window of opportunity?*

Pilot Phase

Evaluation of the laboratory screening test

- *Proof of analytic validity – can the test detect the marker?*
- *Proof of analytic utility– is the test scalable?*

Pilot Studies –
sampling of early statewide to national expansions

Begun	State	Pilot	Outcome
1982	Colorado	CF NBS	Statewide CF NBS
1985- 94	Wisconsin	CF NBS Clinical Trial	Statewide CF NBS; data -> national
1999 - 08	Massachusetts	CF NBS – verbal consent	Statewide CF NBS; data -> national
1999 - 08	Massachusetts	MS/MS – Verbal consent	Statewide NBS “expanded metabolics”; ->national
1999	Wisconsin	MS/MS- develop reporting cutoffs	Statewide NBS “expanded metabolics”; ->national

Pilot Studies –
critical continuations expansions

Begun	State	Pilot	Outcome
2003	California	MS/MS	50 %, later statewide
2005	Missouri	MS/MS	4 month pilot then live
2006	Texas	MS/MS	Statewide

Kits becoming available…
Borrowing cutoffs from colleagues using similar technology…
Training courses at Duke and Baylor….Publications….invaluable

Accessing startup funding
Fending off unfounded criticisms
Justifying new hires, dealing with staffing competencies….

Some Pilot Phase Technology Evaluations

Begun	State	Pilot	outcome
1994	Massachusetts	GALT 2nd tier DNA	Implemented MA and others
1995	Texas	Hgb 2nd tier DNA	Implemented TX
1999	Massachusetts	MCAD 2nd tier DNA	Implemented national
2001	Texas	Tgal vs GALT	Workaround for kit recall
2006	Texas	Biotinidase QI	Implemented
	Massachusetts Wisconsin	PAP as replacement for IRT	Set aside, no clear advantage
2007	Texas	GALT 2nd tier DNA	Implemented
2007-08	Wisconsin and Massachusetts	TREC	PILOT STUDY
2008	Missouri	GSP beta site FDA, parallel	FDA CLEARANCE
2008	Florida	GSP beta site FDA, parallel	FDA CLEARANCE
2011	Texas	CAH 2nd tier LC MS/MS	Ongoing – fit into workflow?
2012	Texas	MCAD 2nd tier DNA	Implemented
2013	Washington	Anonymized LSDs	Preliminary data for linked
2015	Texas	VLCADD 2nd tier DNA	Ongoing

Some Pilot Phase Technology Evaluations

Begun	State	Pilot	outcome
	Texas	Sanger Sequence Hgb	Implemented in TX
	California	Sanger Sequence CF 1 mut	Implemented in CA
	New York	Sanger Sequence Krabbe	Implemented/gold standard
	New York	Sanger Sequence Pompe other LSDs	
	Wisconsin	Next Gen Sequence CF	Data for validation

Pilot Studies – SCID

Begun	State/region	Pilot	Outcome
2008	Wisconsin	Waiver	Routine SCID screening
2009	Massachusetts	Verbal consent	Statewide offering
2010		SCID added to RUSP	
2011	New York California Louisiana by WI Puerto Rico by MA		Large numbers Large numbers Regional possible but start and stop
	More done and more to come		

Pilot Studies – LSD's

Begun	State/region	Pilot	Outcome
2010	Illinois	3-plex	Cutoff and referral determinations restart later with new technology
2013	Missouri	4-plex, waive consent	Ongoing evaluation, referral optimization
2013	Wisconsin	Pompe waive consent	In pilot phase development
2013	NY (select hospitals)	Select LSDs With consent	Ongoing
2014	New York	Pompe by regulation	Statewide by regulation and contributing to national pilot study
Spring 15	Georgia	Pompe	Concurrent with SCID

Interest in moving forward…

We are investigators from a group of state newborn screening programs who collectively possess strong capabilities, have worked together successfully, and who offer you this joint response to your request for a capabilities statement with regard to Pilot Newborn Screening Studies. We note that in contrast to the more conventional offering of a series of independent competitive RFP's as specific projects are budgeted, Solicitation NIH-NICHD-CDBPM-2013-13 appears to be in search of a single reliable resource that can function effectively in response to specific projects that are yet to be defined. To that end, we recognize value of the versatility inherent in a consortium of states with demonstrated experience and expertise with pilot newborn screening studies.

Our vision is to bring forward the varied expertise from a core group of investigators in collaborating states to provide the scientific grounding for future pilots. Our preference is for a structure that leaves open the possibility of inviting additional expertise and participation from other states on a project-by-project basis. We

In our own words…

- “You have to begin somewhere. Some like to test the waters and some like to swim in tested waters, and that’s ok. We have a strong history of sharing our experiences while improving.”

- “Funding from (…) supported the work on development of the strategies to generate preliminary data to apply for pilot studies.”
- “pilot studies are often conducted with lab-developed tests, which are harder and more costly to validate.”
- “there is frequently a lack of quality control and PT materials (for new tests), which means that you have to be able to produce and verify your own materials.”

In our own words…

- “the biggest challenge was the absence of experience with NBS for LSDs by other states…”
- “because of the size of our newborn population, grant funding is usually not enough to cover everyone.”
- “…In practice, this pilot did not work out as well as I had hoped. Our follow-up program had issues since cases are usually created automatically when a positive result is accepted by the lab…”
- “…Our attorney also felt that all the [] negative results should be sent to the hospitals for inclusion in the babies’ medical records. Since we were working off-line from our LIMS, this became problematic for us…”

In our own words…

- "Budgets are generally very tight, which makes it difficult to hire staff with the proper expertise to design and carry out pilot studies, or to even pay for the entire study. In the case of XX, NIH is not paying all of our costs. State money will be used…."
- "while not generally a problem in XX, there is often a lack of clinical specialists to ensure that infants who screen positive get appropriate confirmatory testing and are properly diagnosed."
- "We had to obtain a full IRB review to approve an exemption from parental consent for our pilot…"

In our own words…

- "We would have liked more time to implement…[legislative mandates]…"
- "We would have liked training courses…[like we had for MS/MS, for SCID]…"
- "We would have liked to have brought on SCID…"
- "we did not have enough money to integrate software, so we had a stand-alone database for SCID that was not integrated with the rest of NBS…"
- "Hospitals refused to participate, only 50% of infants were screened and we decided to never do a consented pilot again. We went almost two years with no MS/MS…"

Implications of NBS Saves Lives Act

SEC. 12. INFORMED CONSENT FOR NEWBORN SCREENING RESEARCH.

(a) In General.--Research on newborn dried blood spots shall be considered research carried out on human subjects meeting the definition of section 46.102(f)(2) of title 45, Code of Federal Regulations, for purposes of Federally funded research conducted pursuant to the Public Health Service Act until such time as updates to the Federal Policy for the Protection of Human Subjects (the Common Rule) are promulgated pursuant to subsection (c). For purposes of this subsection, sections 46.116(c) and 46.116(d) of title 45, Code of Federal Regulations, shall not apply.