

SECONDARY RESEARCH USES OF **RESIDUAL NEWBORN SCREENING DRIED BLOOD SPOTS: A SCOPING REVIEW**

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DISCLOSURES

- National Institute of Child Health and Development (NIH/NICHD HD082148; Pls: Rothwell/Botkin).
- University of Utah Center for Clinical and Translational Science (NIH/NCATS 1UL1TR001067)
- Utah Center in Excellence for Ethical, Legal and Social Implications Research (NIH/NHGRI HG009037).



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BACKGROUND

- Newborn Screening
- Residual Dried Blood Spots from NBS
- Lack of explicit parental permission
- Public Awareness
 - Law Suits
 - Newborn Screening Saves Lives Reauthorization Act of Dec. 2014
 - Updated Common Rule Changes
- Lack a systematic review of the research evidence about extent and type of use



METHODS

- How much research has been undertaken using DBS?
- What type of research has been conducted using DBS?
- What study designs are employed in research using DBS?



DEFINITION

• Secondary research is defined as research unrelated to the original purpose (newborn screening) of blood spot collection.



MFTHODS

Scoping review is a type of research evidence synthesis that aims to 'map the literature on a particular topic or research area and provide an opportunity to identify key concepts; gaps in the research; and types and sources of evidence to inform practice, policymaking, and research'.

> Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology 2005;8:19-32.



MFTHODS

- Ovid Medline; Embase (via Embase.com); CINAHL (Ebsco); and Science and Social Sciences Citation Indices (via Web of Science). Search strategies were reviewed by a second librarian using the PRESS Checklist.
- Any lists of included and excluded studies from related systematic reviews or meta-analyses identified during database searches were evaluated.



METHODS

- Search terms used included: 1) blood spot OR bloodspots OR bloodspot OR blood samples OR Guthrie; AND 2) archived OR archive OR dried OR residual. A draft OVID Medline strategy is provided as an appendix.
- No contact with authors was initiated and there was no inclusion of unpublished abstracts/studies.



METHODS

- All study designs as well as quality assurance or quality improvement studies using DBS not directly related to NBS were included.
 - Conference abstracts, posters and non-English reports were excluded.







Excluded for Irrelevance (n = 5366)



Excluded for Irrelevance (N= 674)

METHODS

- Covidence for full text review
- 2 trained PhD research assistants
 - 94% inter rater reliability
 - Team conflicts resolved by lead author
- 598 coded by one of the PhD RAs
 - Consistency and accuracy of the coded date reviewed by 2 independent reviewers for 10% of the data.







Study design	N = 598	Percent of total
Observational	248	42.6%
Case-control	224	38.6%
Cross-sectional	89	15.2%
Case Report	21	3.5%
Randomized control trial	0	0
Clinical trial	0	0





USA state of DBS origin	N =182	Percent of total
California	28	23.6%
New York	31	20.9%
Multiple	36	20.3%
Washington	14	11.5%
Minnesota	13	8.2%
Texas	11	6.4%
Unknown	4	2.3%

What states never come up?

Alabama, Alaska, Idaho, Indiana, Nebraska, North Dakota, South Dakota, Vermont, West Virginia



• Multi-State Collaborations

- Some are "unknown"
- Other lists of states range in number from 2-39 states involved:
- (Gwinn 1991): Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Illinois, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, Washington, Wisconsin.
- (Tuuminen 1998): Texas, Massachusetts, Georgia



Funding source	Number
State health department	105
Federal agency	282
Non-profit company	208
For-profit company	54
Other	5
Unknown	145



Federal Funding for U.S. DBS Secondary Research		
National Institutes of Health	57.4%	
Centers for Disease and Control	23.8%	
Multiple Agencies	19.8%	
Other Federal	5.0%	





Was this a quality improvement study?	N = 598	Percent of total
Yes	120	20.6%
Νο	478	79.4%

Quality improvement only	N = 120	Percent of total
Yes	89	74.2%
Νο	31	25.8%



Was this a pilot study?	N = 598	Percent of total
Yes	224	37.5%
Νο	374	62.5%

Test not part of the	N = 598	Percent of total
screening program at time of analysis		
Yes	428	71.6%
Νο	170	28.4%



Studies in each State	State	Total	Unknown
			studies
29	California	1,492,868	
1	Colorado	279,399	
1	Florida	3101	
3	Georgia	43,205	
1	lowa	762	
1	Louisiana	71	
6	Maryland	38,137	
4	Massachusetts	49,124	
8	Michigan	919	
12	Minnesota	10,3499	
1	Missouri	43,701	
39	Multiple states	1,647,463	1
1	New Jersey	279	
29	New York	184,788	1
7	North Carolina	506	1
2	Ohio	30,600	
1	Pennsylvania	21	
11	Texas	3,832	1
4	Unknown	7,773	
1	Utah	10,000	
2	Virginia	296	1
15	Washington	45,211	
3	Wisconsin	810,790	



of DBS used in US secondary research

Target method used	N = 582	Percent of total
Analyte	339	58.2%
DNA	207	35.6%
Enzyme	36	6.2%



Was permission, consent or assent collected?	N = 598	Percent of total
Yes	193	33.6%
Νο	27	4.5%
Unknown	362	62.0%

Was data de-identified or	N = 598	Percent of total
anonymized?		
Yes	96	37.0%
Νο	60	10.5%
Unknown	306	52.5%





All Studies (n=598)

Parental Permission/Consent obtained

De-Identified/Anonymized	Yes (n=201)	No (n=27)	Unkno
Yes	40 (19.9%)	20 (74.1%)	161 (4
No	32 (15.9%)	2 (7.4%)	29 (7.
Unknown	129 (64.2%)	5 (18.5%)	180 (4

US Studies Only (n=182)

Parental Permission/Consent obtained

De-Identified/Anonymized	Yes (n=41)	No (n=6)	Unknov
Yes	12 (29.3%)	5 (83.3%)	85 (63.
No	6 (14.6%)	1 (16.7%)	7 (5.2%
Unknown	23 (56.1%)	0 (0%)	43 (31.



own (n=370) 43.5%) .8%) 48.6%)

own (n=135) 3.0%) %) ..9%)

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What type of medical	N = 598	Percent of total
condition was studied?		
Genetic disease	336	56.2%
Other *	123	20.6%
Infectious disease	89	14.9%
Toxicological	22	3.7%
Cancer	18	3.0%
Diet	4	0.7%
Metabolic (non-DNA based)	2	0.3%
Maternal disease	0	0%
Placental transmission	1	0.2%
Epigenetic	3	0.5%
*Other minus endocrine	97	
disorder		
Endocrine disorders	20	



CONCLUSIONS

- Residual DBS used extensively and worldwide
- Valuable source for a broad range of research
- Majority of studies did not report consent or identification
- There are limitations (missed articles, broad coding template), but this evidence synthesis significantly captures the nature, type and extent of the secondary research uses of DBS
- Suggestions for more detailed meta-analyses with more focused areas



Thank you!

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% of publications for biomedical research (not quality improvement)