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# 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; PIs: 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).



# EXPERT ADVISORY BOARD

- Nicola Longo, MD, PhD
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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.



# METHODS



- 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.

# METHODS



- 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- No contact with authors was initiated and there was no inclusion of unpublished abstracts/studies.

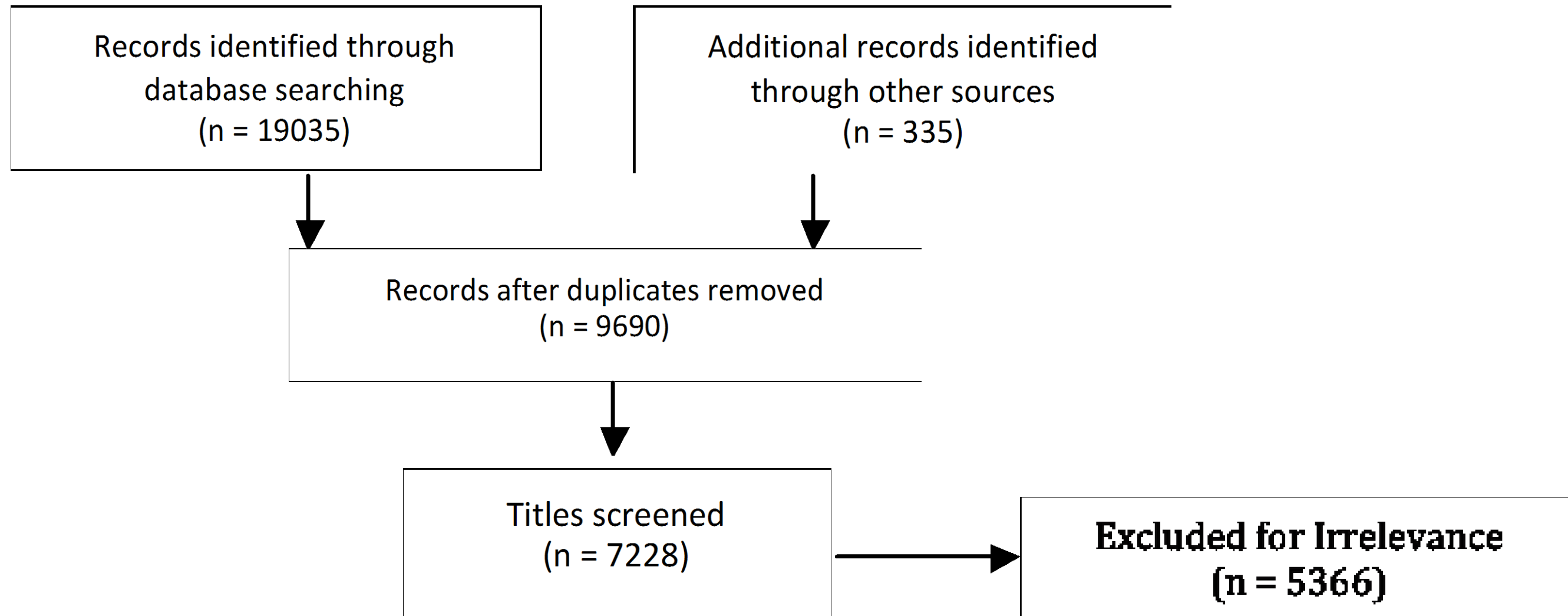


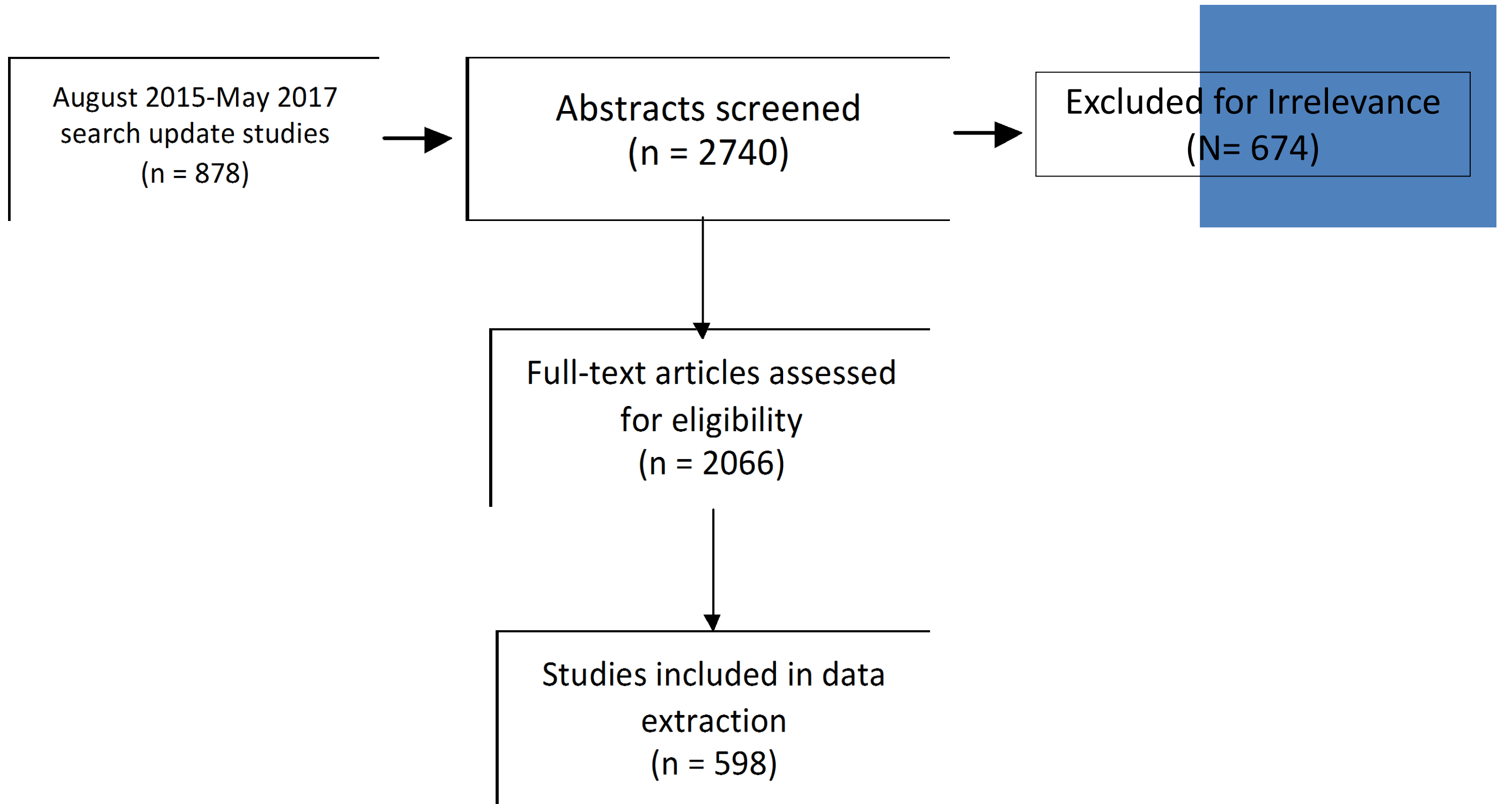
# METHODS

- 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.



# METHODS



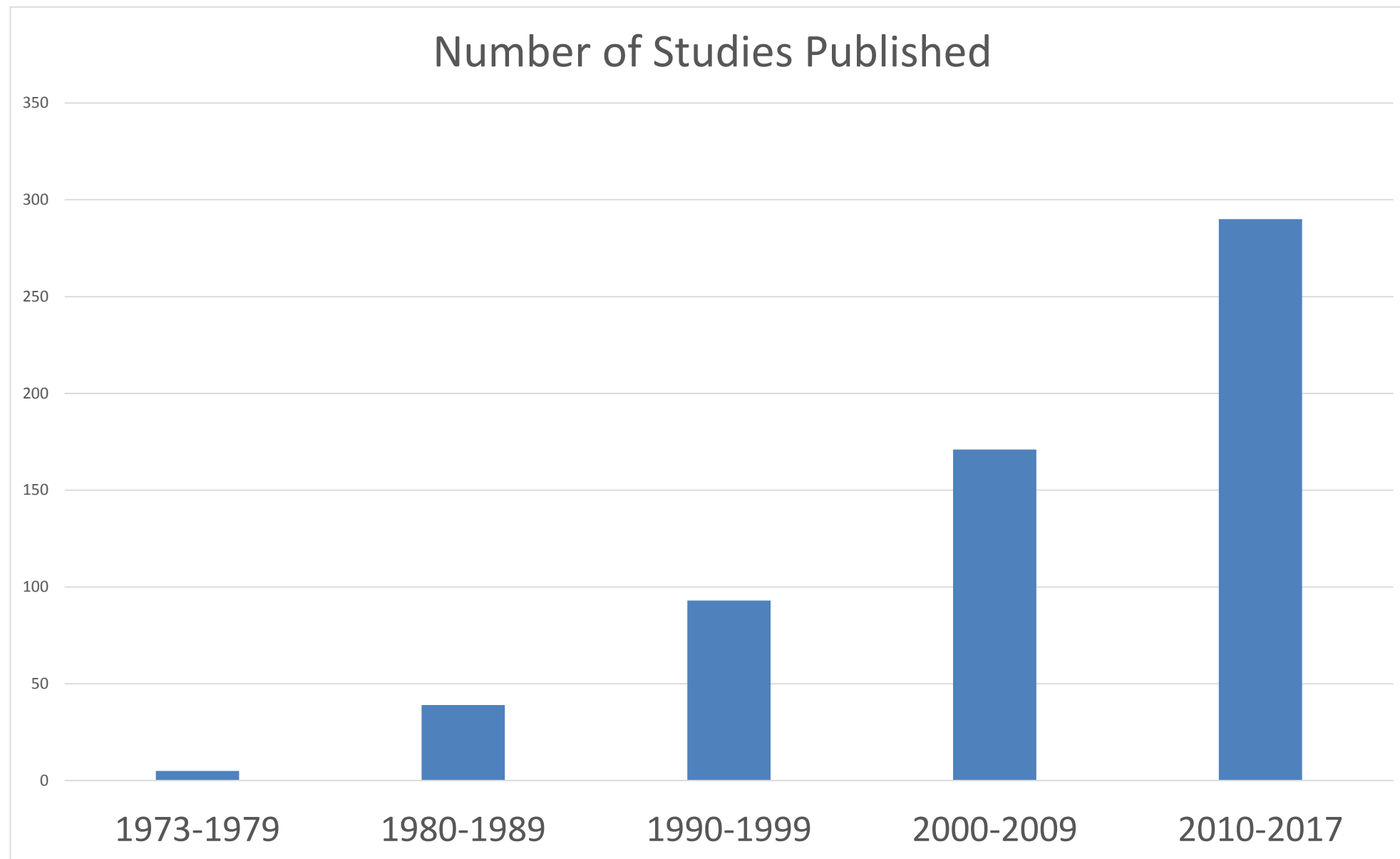


# METHODS

- 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 data reviewed by 2 independent reviewers for 10% of the data.




# RESULTS



# RESULTS

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

# RESULTS



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



# RESULTS



- 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

# RESULTS



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

# RESULTS



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%

# RESULTS

Was this a quality improvement study?	N = 598	Percent of total
Yes	120	20.6%
No	478	79.4%


Quality improvement only	N = 120	Percent of total
Yes	89	74.2%
No	31	25.8%

# RESULTS

Was this a pilot study?	N = 598	Percent of total
Yes	224	37.5%
No	374	62.5%

Test not part of the screening program at time of analysis	N = 598	Percent of total
Yes	428	71.6%
No	170	28.4%

<b>Studies in each State</b>	<b>State</b>	<b>Total</b>	<b>Unknown studies</b>
29	California	1,492,868	
1	Colorado	279,399	
1	Florida	3101	
3	Georgia	43,205	
1	Iowa	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

# RESULTS



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

# RESULTS

Was permission, consent or assent collected?	N = 598	Percent of total
Yes	193	33.6%
No	27	4.5%
Unknown	362	62.0%

Was data de-identified or anonymized?	N = 598	Percent of total
Yes	96	37.0%
No	60	10.5%
Unknown	306	52.5%



# RESULTS

## All Studies (n=598)

De-Identified/Anonymized		Parental Permission/Consent obtained		
		Yes (n=201)	No (n=27)	Unknown (n=370)
Yes	40 (19.9%)	20 (74.1%)	161 (43.5%)	
No	32 (15.9%)	2 (7.4%)	29 (7.8%)	
Unknown	129 (64.2%)	5 (18.5%)	180 (48.6%)	

## US Studies Only (n=182)

De-Identified/Anonymized		Parental Permission/Consent obtained		
		Yes (n=41)	No (n=6)	Unknown (n=135)
Yes	12 (29.3%)	5 (83.3%)	85 (63.0%)	
No	6 (14.6%)	1 (16.7%)	7 (5.2%)	
Unknown	23 (56.1%)	0 (0%)	43 (31.9%)	

# RESULTS

What type of medical condition was studied?	N = 598	Percent of total
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 disorder	97	
Endocrine disorders	20	

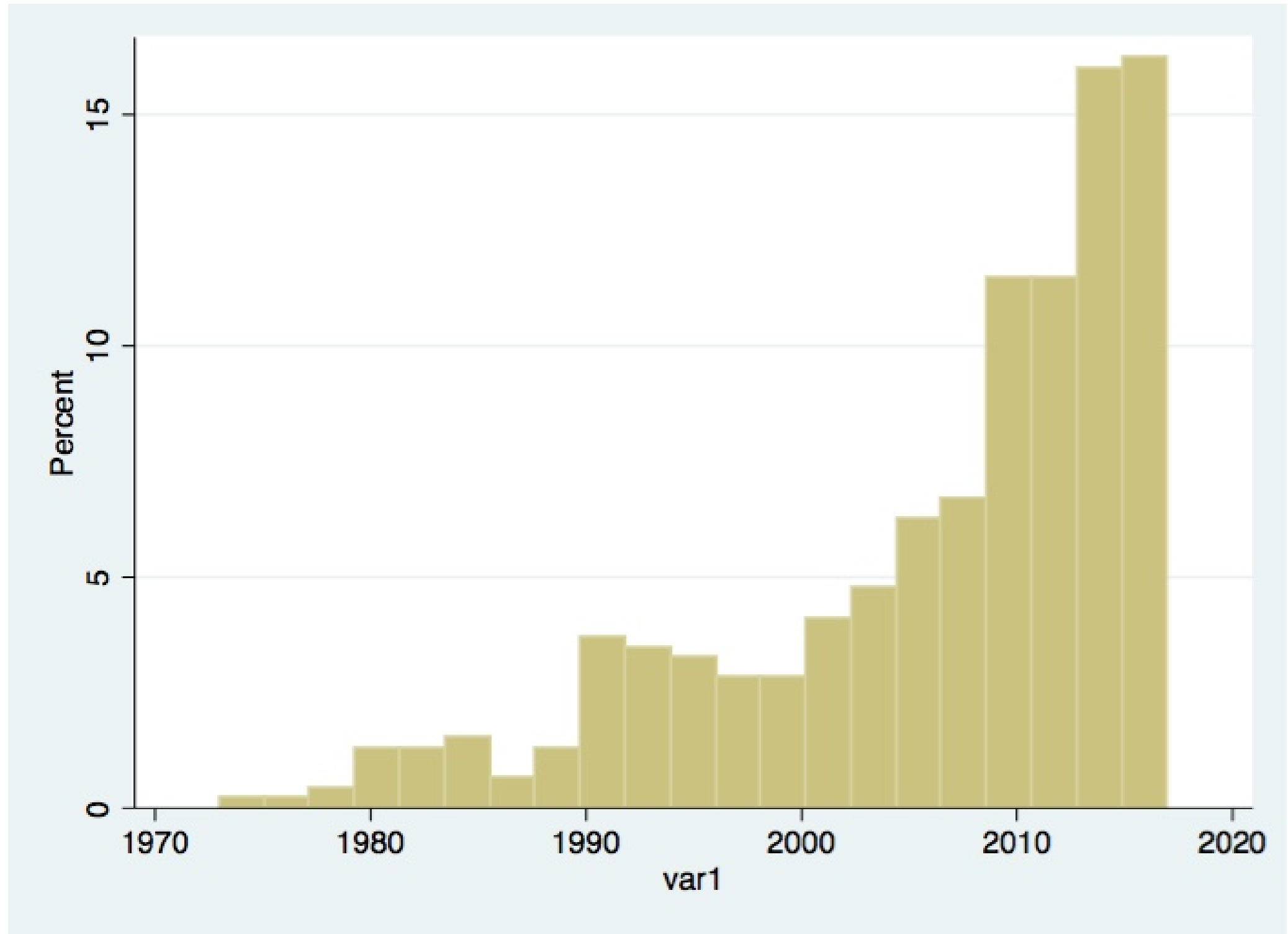
# CONCLUSIONS

- 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)