Reduction in Infant Cardiac Deaths in US States that Implemented Mandates to Screen Newborns for Critical Congenital Heart Disease

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Outline of Presentation

- JAMA article on effectiveness
  - Background and study objectives
  - Study design
  - CCHD screening policies
  - Unadjusted results
  - Adjusted results
  - Discussion
- IJNS article on cost-effectiveness

JAMA | Original Investigation

Association of US State Implementation of Newborn Screening Policies for Critical Congenital Heart Disease With Early Infant Cardiac Deaths

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Background

- When CCHD was added to the RUSP in 2011, it was uncertain how many lives would be saved with universal screening
- Estimates varied of how many diagnoses of CCHD were delayed and how often delayed diagnoses resulted in death
  - Potentially avoidable deaths through CCHD screening thought to range from 20 to 100 per year
  - Cost-effectiveness analysis by Peterson et al. (2013) conservatively projected 20 deaths would be avoided each year

Peterson C, Grosse SD, Oster ME, Olney RS, Cassell CH. A cost-effectiveness analysis of routine screening to detect critical congenital heart disease among U.S. newborns. *Pediatrics*. 2013;132:e595-603.

Objectives

- To estimate the association of state CCHD newborn screening policies with relative reductions in numbers of infant deaths from congenital heart defects (CHDs) in the United States
  - Distinguish mandatory policies from voluntary recommendations
  - In states which adopted mandates distinguish births before and after implementation of mandates at the level of the birthing center
  - Distinguish deaths coded for CCHD and deaths coded for other CHDs
- To project the number of deaths that would be avoided if CCHD screening policies were to be universally implemented in the United States

What the Study Was NOT Able To Do

- Could not assess outcomes of CCHD screening per se
- That would require linked data on diagnoses among live-born infants
  - Data on which infants were screened
  - Data on CCHD diagnoses
  - Information on numbers of delayed diagnoses
- Study could only evaluate impact of CCHD screening policies
  - How policies affect outcomes can vary
    - Direct effect of screening on timely diagnoses
    - Indirect effects through increased clinical awareness

Study Design (1)

- Difference-in-difference analysis of impact of state screening policies on numbers of early infant deaths caused by CCHD or other cardiac causes
- This method compares changes in outcomes following the introduction of a policy in jurisdictions which did not did not introduce the policy
  - Can be used to assess outcomes of policies adopted at different times by state or local governments
  - The method presumes similar pre-policy trends in outcomes between jurisdictions which did or did not adopt the policy
  - It attributes different post-policy trends, after controlling for state-specific factors (fixed effects and time-varying variables), to the policy

Study Design (2)

- Data source – Period Linked Birth-Infant Death Data files from National Center for Health Statistics, 2007-2013
  - Restricted version with state identifier
  - Births through June 30, 2013 linked to infant deaths through December 31, 2013 by state of birth
  - 2013 was most recent year of data available in restricted version at time of study
- Data grouped by state of birth and month-year
  - Numbers of deaths in infants born in a state during a month when a CCHD screening policy was in place at the beginning of the month

Study Design (3)

- Outcome measures – counts of infant deaths from 24 hours after birth to less than 6 complete months
  - Underlying cause of death on death certificates and associated ICD-10 codes
  - Two categories of deaths as primary outcomes (dependent variables)
    - CCHD (codes on next slide)
    - Other/unspecified congenital heart disease (CHD) (following slide)
- Secondary outcomes – counts of deaths associated with other leading causes of infant death (codes on subsequent slide)
  - Used in placebo analyses – were CCHD screening policies significantly associated with other causes of early infant death?

CCHD Types and Associated *ICD-10* Codes

CCHD Types	ICD-10 Codes
Aortic interruption or atresia or hypoplasia	Q25.4, Q25.2
Coarctation or hypoplasia of the aortic arch	Q25.1
D-transposition of the great arteries	Q20.3
Double-outlet right ventricle	Q20.1
Ebstein anomaly	Q22.5
Hypoplastic left heart syndrome	Q23.4
Pulmonary atresia	Q22.0
Single ventricle	Q20.4
Teratology of Fallot	Q21.3
Total anomalous pulmonary venous connection	Q26.2
Tricuspid stenosis and atresia	Q22.4
Truncus arteriosus	Q20.0

Other/Unspecified CHDs and Associated *ICD-10* Codes

- All CHD ICD-10 codes
  - Q20.0-Q21.0
  - Q21.2-Q24.5
  - Q24.7-Q24.9
  - Q25.1-Q26.9
  - Q21.1 & Q25.0 excluding preterm births
- Other/unspecified CHDs defined as the above codes minus the 13 ICD-10 codes listed on the previous slide
  - Q24.9 is used for unspecified CHDs

Leading Non-cardiac Underlying Causes of Death and Associated *ICD-10* Codes

Sudden infant death syndrome	R95
Bacterial sepsis of newborn	P36
Maternal and placental complications	P01, P02
Short gestation and low birth weight	P07

Study Design (4)

- State screening policies
  - Mandate implemented
    - Reviewed state legislation and websites to confirm initial dates on which providers were required to screen newborns
  - Non-mandatory
    - Mandate adopted but not yet implemented
    - Voluntary screening policy
- Poisson regression models of numbers of deaths to infants in birth cohort
  - Log of number of births in month in state
  - Adjusted for state factors

CCHD Screening Policies as of June 1, 2013

- Birth months through June 2013 included to allow for 6 months of death records
- States first adopted CCHD screening policies in mid-2011
  - 8 states implemented mandates by June 1, 2013
    - 2 states implemented mandates during August 2011-January 2012
    - 6 implemented mandates during July 1, 2012-June 1, 2013
  - 13 states had adopted but had not yet implemented mandates by June 1, 2013
  - 5 other states adopted voluntary screening policies by June 1, 2013

States That Implemented Screening Mandates by June 1, 2013

State	Enactment Date	Implementation Date
Mandatory		
Connecticut	May 2012[b]	January 1, 2013
Delaware	May 1, 2013	May 1, 2013
Indiana	May 2011[b]	January 1, 2012
Maryland	May 19, 2011	September 1, 2012
New Hampshire	June 2012[b]	August 11, 2012
New Jersey	June 2, 2011	August 31, 2011
Tennessee	March 1, 2012	May 31, 2013
West Virginia	April 5, 2012	September 1, 2012

Nonmandatory		
Alabama	February 22, 2012	February 22, 2012
California	September 15, 2012	July 1, 2013
Iowa	August 2012[b]	August 2012[b]
Massachusetts	May 10, 2013	May 10, 2013
Pennsylvania	December 1, 2012	March 1, 2013
Mandatory enacted but not yet implemented		
Alabama	May 17, 2013	June 21, 2013
Arkansas	April 5, 2013	July 1, 2015
Kentucky	March 19, 2013	January 1, 2014
Minnesota	May 23, 2013	August 2013[b]
North Carolina	May 8, 2013	July 25, 2014
North Dakota	April 2013[b]	August 2013[b]
Oklahoma	April 18, 2013	July 1, 2013
South Dakota	March 2013[b]	July 2013[b]
Utah	March 2013[b]	October 1, 2014

Unadjusted Results

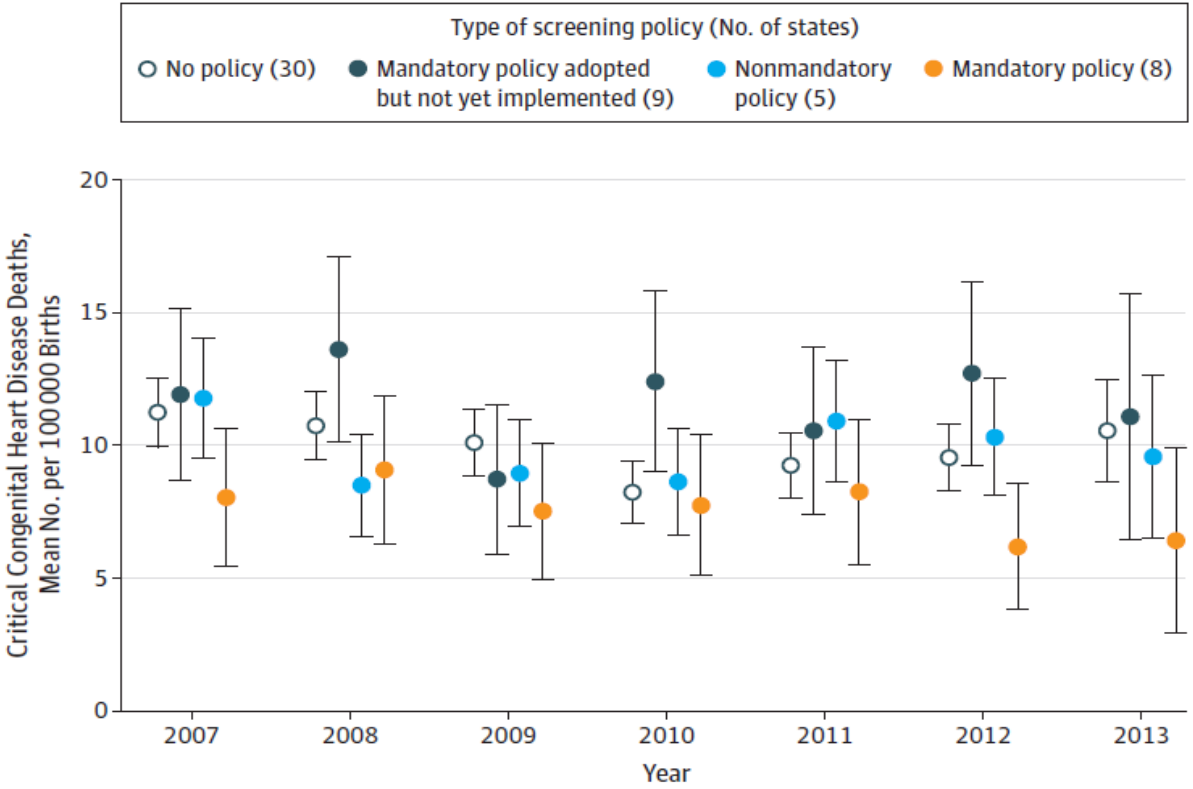
- Changes over time in CCHD and other/unspecified CHD death rates per 100,000 births
- Stratified by state screening policies as of June 1, 2013
- States with mandates as of June 1, 2013 stratified by times of enactment and implementation of screening mandates

Changes in Early Infant Deaths from CCHD or Other/ Unspecified CHDs During 2007-2013

Characteristic	All states	States with no policy implemented	States with mandatory policy			States with voluntary policy	
			Before enactment	Between enactment and implementation	After implementation	Before enactment	After enactment
CCHD deaths[a] per 100,000 births	9.8 (9.2-10.4)	10.0 (9.1-10.9)	8.3 (6.4-10.3)	7.8 (3.9-11.8)	4.5 (2.3-6.6)	10.6 (9.5-11.8)	10.0 (6.1-13.9)
Other/Unspecified CHD deaths[a] per 100,000 births	13.5 (12.7-13.4)	13.4 (12.4-14.4)	12.0 (10.0-14.0)	11.5 (5.5-17.5)	8.5 (5.3-11.6)	14.8 (13.3-16.3)	13.8 (9.8-17.8)

a. Deaths from 24 hours to <6 months of age

Figure. Mean Critical Congenital Heart Disease Early Infant Death Rates by Year, 2007-2013, for States With No Screening Policy, States With Mandatory Screening Policy Not Yet Implemented and Implemented by June 1, 2013, and States With Only Nonmandatory Screening Policies as of June 1, 2013



Adjusted Results

- Results of statistical analyses that controlled for
  - Time fixed effects
  - State fixed effects
  - State time-varying covariates
- Poisson regression coefficients with 95% confidence intervals reported in online supplement (next slide)
- Poisson coefficients were converted to relative reductions in deaths and reported in manuscript (following slide)

eTable 2. Poisson Regression Coefficients for the Association of Explanatory Variables With Deaths Due to Critical Congenital Heart Disease or Other/Unspecified Congenital Heart Disease

Explanatory variable	(1) Mean of explanatory variable (95% confidence interval)	(2) Poisson regression coefficient (95% confidence interval) Critical congenital heart disease deaths	(3) Poisson regression coefficient (95% confidence interval) Other/unspecified congenital heart disease deaths
Mandatory CCHD screening	0.021 (0.017, 0.026)	-0.406 (-0.699, -0.112)*	-0.241 (-0.410, -0.071)*
Non-mandatory CCHD screening	0.033 (0.027, 0.038)	-0.065 (-0.244, 0.114)	-0.016 (-0.233, 0.201)
Percentage of births from Black mothers	14.278 (13.862, 14.654)	0.020 (-0.038, 0.077)	-0.002 (-0.044, 0.040)
Percentage of plural term births	1.374 (1.361, 1.387)	0.036 (-0.154, 0.227)	-0.066 (-0.239, 0.108)
Log(real income in 2013 $)	10.668 (10.663, 10.673)	3.097 (-0.066, 6.261)	1.009 (-1.544, 3.562)
Log(unemployment rate)	1.892 (1.881, 1.903)	0.061 (-0.401, 0.524)	0.266 (-0.259, 0.791)

Table 4. Adjusted Percentage Declines in Rates of Deaths Due to Critical Congenital Heart Disease and Other Congenital Heart Disease Associated With State Mandatory Screening Policies, 2011-2013[a]

Age Range of Deaths	Decline in Death Rate, % (95% CI)	
	Critical Congenital Heart Disease Deaths	Other or Unspecified Congenital Heart Disease Deaths
24 h to <6 mo	33.4 (10.6 to 50.3)	21.4 (6.9 to 33.7)
Sensitivity analyses of timing of mandate (age at death 24 h to <6 mo)		
Implemented Aug 1, 2011–June 30, 2012	19.7 (3.1 to 37.1)	21.7 (8.7 to 32.9)
Implemented July 1, 2012–June 1, 2013	53.6 (36.0 to 66.3)	21.0 (0.3 to 37.4)
Sensitivity analyses of timing of deaths (screening implemented Aug 1, 2011–June 1, 2013)		
Birth to <6 mo	30.7 (9.3 to 47.1)	27.0 (15.1 to 37.3)
Birth to <12 mo	28.4 (8.5 to 44.0)	17.9 (3.0 to 30.6)
24 h to <12 mo	30.5 (12.9 to 44.5)	11.2 (−4.8 to 24.9)
24 h to <6 mo, restricted to infants born at >32 wk	29.5 (5.0 to 50.1)	20.1 (2.3 to 34.7)

Key Findings – Effects of Screening Policies

- Mandatory screening relative to months with no mandate in place
  - CCHD deaths fell by one-third (33.4%)
  - Other/unspecified CHD deaths fell by one-fifth (21.4%)
  - Both changes were statistically significant
- Non-mandatory screening relative to no screening policy
  - No reductions in CCHD deaths or other CHD deaths (<5% difference, not statistically significant)

Sensitivity Analyses – Time Window for Infant Deaths

- Base case analysis included deaths from 24 hours to <6 months
  - CCHD screening at 24 hours should not affect deaths <24 hours
  - Most infant deaths from CHDs occur <6 months
  - Restriction to <6 months allowed for inclusion of births during first half of 2013
- Inclusion of deaths <24 hours attenuates the associations modestly
- Exclusion of 2013 births due to 12 month end point has similar effect
- Excluding very preterm births also slightly lowers the associations

Sensitivity Analyses

- Placebo tests
  - No changes in other leading causes of infant deaths associated with CCHD screening policies
    - Sudden infant death syndrome (SIDS), sepsis, maternal complications, preterm or low birthweight
- Tests of non-parallel trends hypothesis
  - Regression analysis excluding birth-months following implementation of mandatory screening – interaction of screening mandate and time
    - Mandatory screening * time: -0.001 (95% CI: -0.008 to 0.006)

Extrapolation of Key Findings on Primary Outcomes from 2013 Sample to United States

- Potential reduction in annual deaths for US as a whole if results could be extrapolated to all states
  - Recognized CCHD deaths: 120 (95% confidence interval (CI): 38–181)/year
  - Other/unspecified CHD deaths: 117 (95% CI: 38-185)/year
    - Most of those deaths had an ICD-10 code for unspecified CHD and may represent undiagnosed or unrecorded CCHD deaths

Limitations and Next Steps

- Small numbers of state birth-months exposed to state mandates
  - 84 months of births exposed to mandates
  - 125 months of births exposed to voluntary screening policies
  - 3769 months of births with no screening policies
- We used the most recent data that were available to us
  - 2014 and 2015 linked birth-death files have been requested and additional analyses will be undertaken
  - Will also examine racial/ethnic differentials in CCHD and other CHD deaths

Implications for Cost-Effectiveness of CCHD Screening

- A US cost-effectiveness analysis in 2013 concluded that CCHD screening would likely be cost-effective
  - Approximately $40,000 per life-year saved
  - Assumed screening 4 million infants would avoid 20 deaths per year
- Implications
  - If universal screening avoids 120 infant deaths per year (or more), universal CCHD screening is even more likely to be cost-effective

Peterson C, Grosse SD, Oster ME, Olney RS, Cassell CH. A cost-effectiveness analysis of routine screening to detect critical congenital heart disease among U.S. newborns. *Pediatrics*. 2013;132:e595-603.

International Journal of
Neonatal Screening

MDPI

Review

Cost and Cost-Effectiveness Assessments of Newborn Screening for Critical Congenital Heart Disease Using Pulse Oximetry: A Review

Scott D. Grosse [1,*], Cora Peterson [2], Rahi Abouk [3], Jill Glidewell [1] and Matthew E. Oster [1,4]

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Cost Estimates of CCHD Screening in Birthing Centers

Table 2. Summary of data assumptions of micro-costing studies of critical congenital heart disease screening.

Study	Country and Jurisdiction	Screening Time (Minutes)	Screening Staff Type and Labor Cost per Infant	Type of Probes, and Equipment/Supply Cost per Infant	Total Screening Cost per Infant
Knowles et al. [13,14]	United Kingdom	2.0	Senior house officer £1.54 $2.20 (USD)	Reusable £1.28 $1.83 (USD)	£2.82 (2000–2001 prices) $4.03 (USD)
Roberts et al. [12]	United Kingdom	6.9	Midwives Not reported	Reusable Not reported	£6.24 (2009 prices) $8.80 (USD)
Peterson et al. [21]	United States New Jersey	9.1	Registered nurses $7.36	Mixed types $6.83	$14.19 (2011 prices)
Kochilas et al. [22]	United States Minnesota	5.5	Nursing staff $3.32	Reusable $1.82	$5.10 (2012 prices)
Reeder er al. [23]	United States Utah (two hospitals)	8.4	Medical assistants and nurses $2.60	Disposable $21.92	$24.52 (2014 prices)
		9.8	Nursing assistants $2.35	Reusable $0.25	$2.60 (2014 prices)

Note: all currency conversions were calculated using the purchasing power parity exchange rate for the year of the original cost estimate. Source: https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm.

Updated Cost-Effectiveness Estimates

- Peterson et al. (2013) cost-effectiveness model updated in several ways
  - Replaced estimate of 20 deaths averted with 110 deaths averted
    - Cost-effectiveness ratio decreased from $40,000 per life-year saved to $10,000 per life-year saved
  - Shorter life expectancy of children with CCHD who survive infancy
    - If life expectancy is lower by 6 years, cost-effectiveness ratio would be $12,000 per life-year saved
  - CHD-related medical costs in future years
    - If future costs equal $450,000 (with 3% discount rate), cost-effectiveness ratio would be $31,000 per life-year saved

Future Research on Costs and Cost-Effectiveness of CCHD Screening

- Better information on costs of medical follow-up after screening
  - How many infants need to be transferred to another hospital for echocardiogram?
  - Cost of transport
  - Cost of clinical evaluation for non-cardiac causes
- Inclusion of costs and outcomes for non-cardiac conditions detected
- Costs to public health system to support CCHD screening
  - Policy and health communications support
  - Data systems and surveillance
- Research using linkages to birth defects surveillance systems

Thank you for listening!

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