



MATERNAL* AND CHILD MORTALITY: ANALYSIS OF NURSE HOME VISITING IN 3 RCTS

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Disclosures

Dr. Olds has a contract with the Nurse Family Partnership (NFP) National Service Office to conduct research to improve the NFP program and its implementation; this contract covers part of Dr. Olds salary and parts of Dr. Donelan-McCall's and Mr. Knudtson's salaries.



ABBREVIATIONS

- **NVPI – Nurse visited pregnancy and infancy**
- **NVP – Nurse visited pregnancy**
- **PPV – Paraprofessional visited**
- **CC – Combined control group (Denver/Elmira)**
- **C – Combined control group Memphis**
- **C2 – Single control group Memphis**



INTRODUCTION

- **Racial and economic disparities in adult morbidity and mortality are substantial**
 - Toxic stress, health behaviors, access to health care
- **Overall mortality among US children has decreased over the decades, however substantial disparities exist**
 - Preventable causes of death (SIDS, unintentional injuries, homicide) prime candidates for prevention
- **Premature death is of significant public health importance**

Social Determinants of Health



NFP PROGRAM

- **Three Goals**
 - Improve pregnancy outcomes
 - Improve child health and development
 - Improve parents' health & economic self-sufficiency
- **NFP program effects (at least 2 trials)**
 - timing of subsequent pregnancies
 - child health and development
 - Pronounced among mothers least capable of coping with deep poverty
 - use of government benefits



Memphis NFP Trial Mortality Study

- **NFP program effects on mortality not initially hypothesized**
- **Memphis mortality study**
 - **NVP-Control differences in maternal all cause mortality; expected direction for NVPI-Control**
 - **Through child age 20, sig. lower rates for preventable causes in the NVPI group than control followed after birth.**



3 NFP RCTs

Elmira, NY 1977



N = 400

- **Low-income whites**
- **Semi-rural**
- **NVP & NVPI**

Memphis, TN 1987



N = 1,138 and N=742

- **Low-income blacks**
- **Urban**
- **NVP & NVPI**

Denver, CO 1994



N = 735

- **Low-income**
- **Large portion of Latino families**
- **PPV & NVPI**

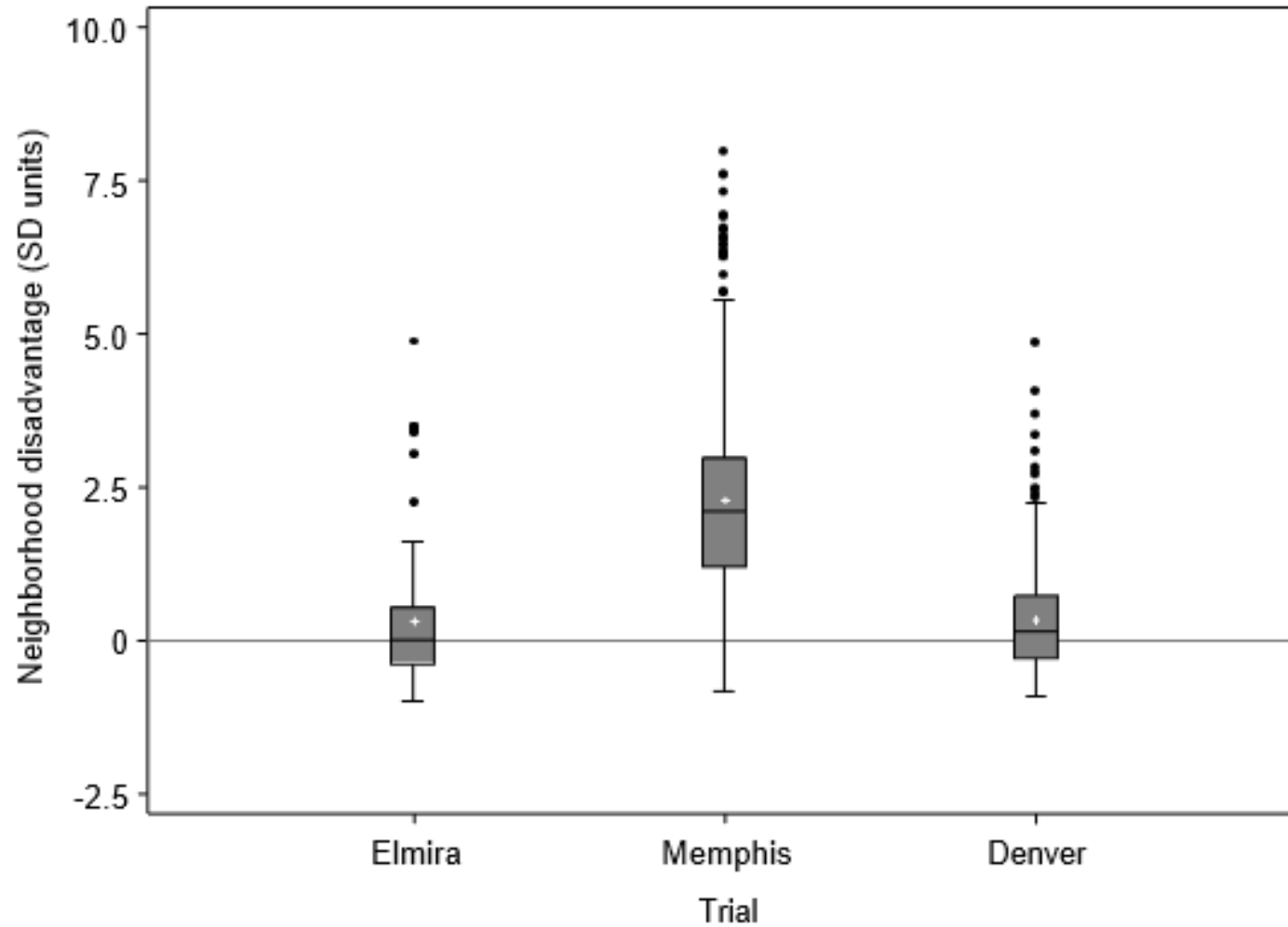


TRIAL SAMPLE CHARACTERISTICS AT BASELINE

	Memphis		Elmira		Denver	
	N	Mean(SD) or %	N	Mean(SD) or %	N	Mean(SD) or %
Maternal Age-years	1138	18.1 (3.15)	400	19.4 (3.17)	735	19.8 (4.01)
Education-years	1136	10.2 (1.95)	400	11.2 (1.59)	734	11.2 (1.92)
Married-%	1136	1.9%	400	38.5%	735	14.3%
White-%			400	88.5%	735	35.9%
Black-%	1138	92.4%			735	16.3%
Hispanic-%					735	44.8%
Neighborhood Disadvantage	698	2.3 (1.68)	400	0.3 (1.16)	735	0.3 (0.89)
IQ	1138	96.4 (10.31)			735	100.3 (9.50)
Smoker-% (5+ cigs/day)	1133	9.0%	400	43.5%	734	11.4%
Gestational Age at Registration	1138	16.4 (5.72)	370	17.7 (5.37)	735	18.6 (7.23)



DISTRIBUTIONS OF NEIGHBORHOOD DISADVANTAGE SCORES



CONSORT INFORMATION

	Memphis				Elmira			Denver		
Eligible Subjects Invited to Participate	1290				500			1178		
Number declined participation	151				100			443		
Number randomized	1138 ^a				400			735		
Treatment Group Assignment	C1	C2	NVP	NVP I	C1+C2	NVP	NVPI	C1	PPV	NVPI
Mothers allocated to each treatment	166	514	230	228	184	100	116	255	245	235
Mothers sent to NDI without SSN	9	1	10	2	32	21	18	0	2	0
Mothers included in All-Cause Mortality analyses	166	514	230	228	184	100	116	255	245	235
Mothers included in External-Cause Mortality analyses	166	514	230	228	184	100	116	254 ^b	245	235
Fetal demise (miscarriages, stillbirths)	6	24	9	10	5	3	4	9	7	10
Children Born alive	160	490	221	218	179	97	112	246	238	225
Children Missing Identifiers	5	1	6	1	5	1	2	2	0	0
Children sent to NDI without SSN	155	14	215	4	19	12	10	23	26	30
Children included in Preventable-Cause Mortality analyses	155	489	215	217	175 ^c	95 ^d	110	244	238	225

Abbreviations: C1 C2: control group; NVP: nurse visited through pregnancy/postpartum only; NVPI: nurse visited through child age 2; PPV: paraprofessional visited through child age 2; NDI: National Death Index.

^a One person was randomized a second time in to C2 following a miscarriage and was subsequently excluded. Earlier reports¹ of sample size showed 1139 participants and noted the exclusion of this case.

^b Cause of death for one mother in the Denver control group was not available.

^c Includes one child with death and cause of death confirmed through alternative source.

^d Minus one child with death confirmed through alternative source without a known cause of death.



METHODOLOGY

- **Identifying information for enrolled women and first live-born children sent to NDI**
 - 508 children missing SS#
 - 23 children missing identifiers not sent to NDI
- **NDI matching methodology**
 - Centralized database of death records
 - Deceased status based on match probability and class
 - Validation process
 - Deaths through 2015
- **Deceased status other sources**
 - National searches and family interviews
 - 2 women in Denver (C); 3 children in Elmira (1 C, 1 NVP, 1 NVPI)
 - 2 children not submitted to NDI (Elmira C, Denver C)



METHODOLOGY – CENSORING

- **Analyses with combined trials**
 - Randomly selected follow-up time
 - Match distribution of follow-up time in Denver



METHODOLOGY – CAUSES OF DEATH

- **Primary & secondary causes of death provided by NDI**
 - ICD-9 (prior to 1999) and ICD-10 (1999-2015) codes
- **Natural causes of death (women)**
 - neoplasms, HIV infection, heart attack and heart disease, sickle cell anemia, diabetes, endocarditis, stroke, renal disease, electrolyte imbalance, defects in the complement system, acidosis, mycoses, obesity, pneumonia, aortic dissection, and pulmonary embolism
- **External causes of death (women)**
 - drug overdose, suicide, unintentional injuries, and homicide
- **Preventable causes of death (children)**
 - sudden infant death syndrome*, unintentional injuries, and homicide
- **Exceptions**
 - 7 women & 6 children cause of death expert review
 - 1 women & 1 child - cause of death unknown



PRIMARY HYPOTHESES

Women assigned to NVPI in Memphis will exhibit lower rates of all-cause mortality than women assigned to a combined control group (C1+C2).

Women assigned to NVPI in Elmira and Denver (combined) will exhibit lower rates of all-cause mortality than women assigned to a combined control group (CC).

Children born alive in Memphis whose mothers had been assigned to the NVPI group will die less frequently of preventable causes than their counterparts assigned to C2.

Children born alive in Elmira and Denver (combined) whose mothers had been assigned to NVPI will die less frequently of preventable causes than those assigned to CC.



SECONDARY HYPOTHESES

The NVPI-Control (C1+C2) relative difference in maternal mortality in the Memphis trial will be most pronounced for external causes.

The NVPI-CC relative difference in maternal mortality in the combined Elmira and Denver trials will be most pronounced for external causes.

The NVP-Control all-cause and external-cause difference in maternal mortality in the Memphis trial will fall between the Control and NVPI groups

The Elmira NVP-CC relative difference in maternal all-cause mortality will fall between the CC and combined NVPI groups

The Denver PPV-CC relative difference in maternal all-cause mortality will fall between the CC and combined NVPI groups

The rate of death for preventable-cause mortality among Elmira children born alive in the NVP group will be between CC and the combined Elmira/Denver NVPI group.

Denver children whose mothers were assigned to the PPV group will have rates of preventable-cause mortality that fall between CC and the combined NVPI group.

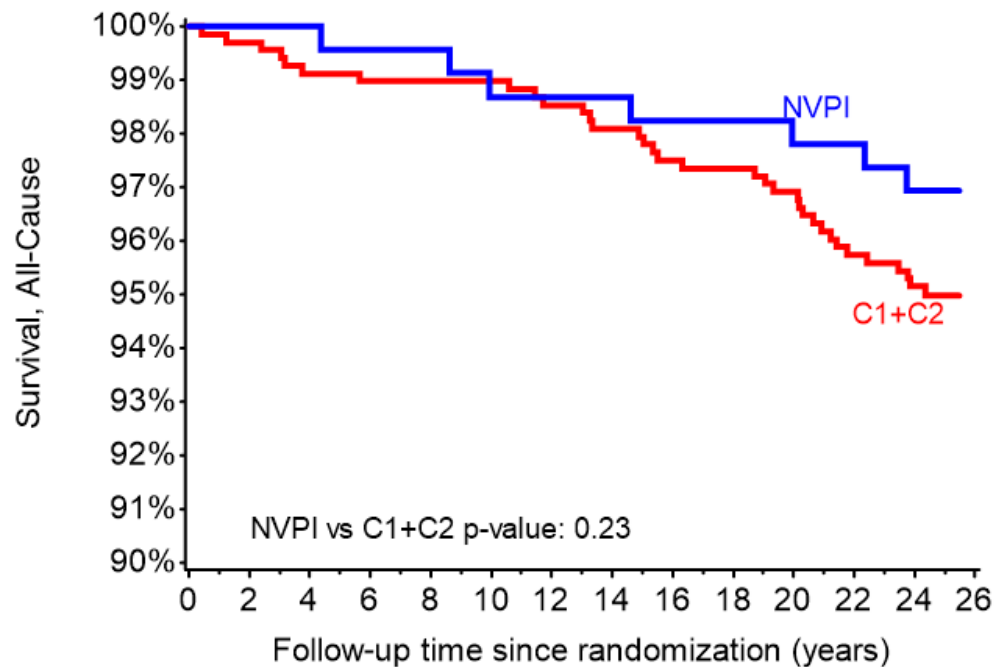


DEATHS AND CAUSE-OF-DEATH CATEGORIES BY TREATMENT CONDITION

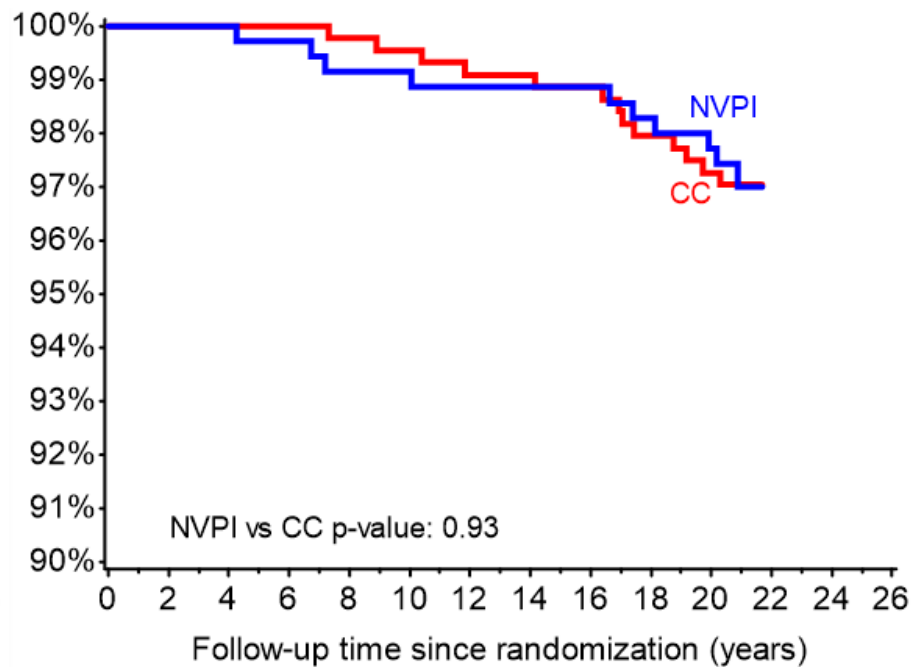
Cause of Death	Memphis				Elmira and Denver			
	Treatment							
	C1	C2	NVP	NVPI	CC	NVP (Elmira)	PPV (Denver)	NVPI
Maternal deaths, No.								
Natural (disease-related) ^a	7	15	4	6	5	1	1	8
External (unintentional injuries, suicides, drug overdose, homicide) ^a	0	12	0	1	7 ^b	0	2	2
Unknown	0	0	0	0	1 ^b	0	0	0
Total								
Deaths	7	27	4	7	13	1	3	10
Sample Size ^c	166	514	230	228	439 ^b	100	245	351
Child deaths, No.								
Non-preventable (disease related) ^d	3	5	2	2	4	2	1	6
Preventable (SIDS, unintentional injuries, homicide)	2	11	2	1	3	1	2	1
Unknown ^e	0	0	0	0	1	1	0	0
Total								
Deaths	5	16	4	3	8	4	3	7
Preventable Deaths Sample Size	155	489	215	217	419	95	238	335



SURVIVAL CURVE FOR MOTHERS ALL-CAUSE MORTALITY



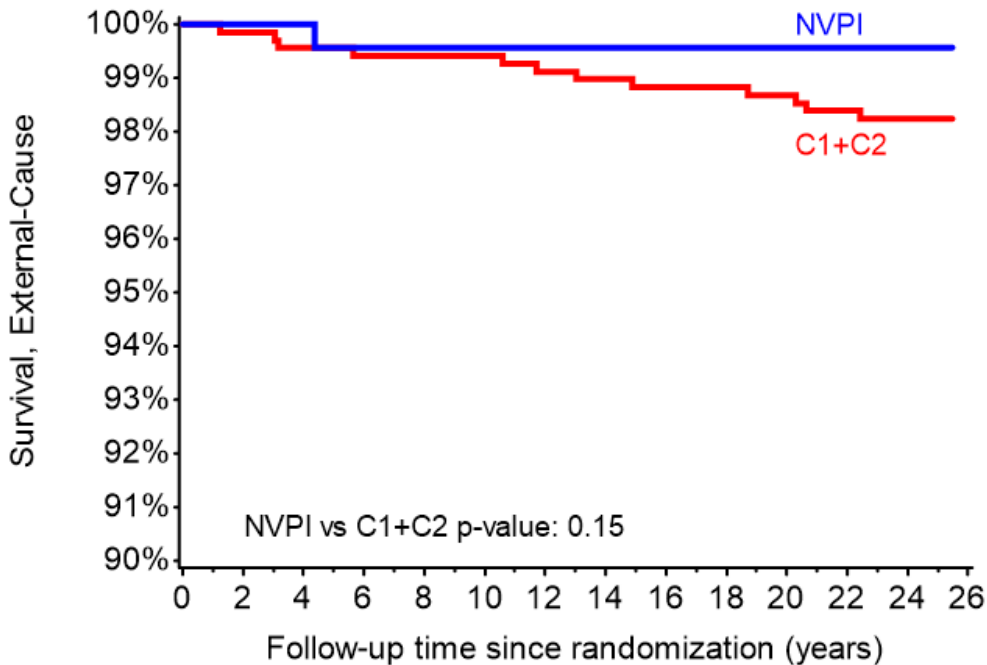
Memphis (NVPI vs. C1+C2)



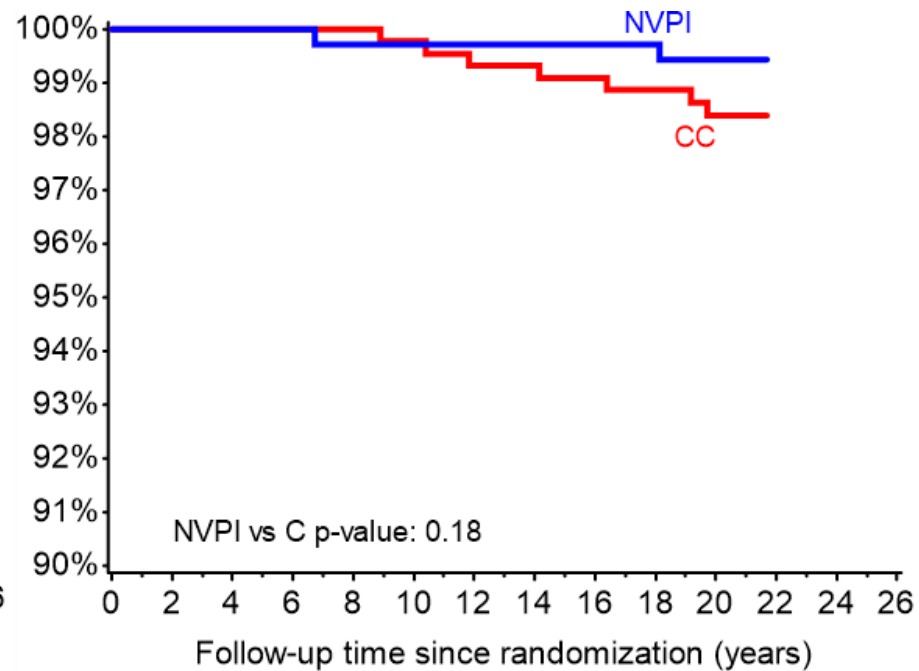
Elmira and Denver (NVPI vs. CC)



SURVIVAL CURVE FOR MOTHERS EXTERNAL-CAUSE MORTALITY



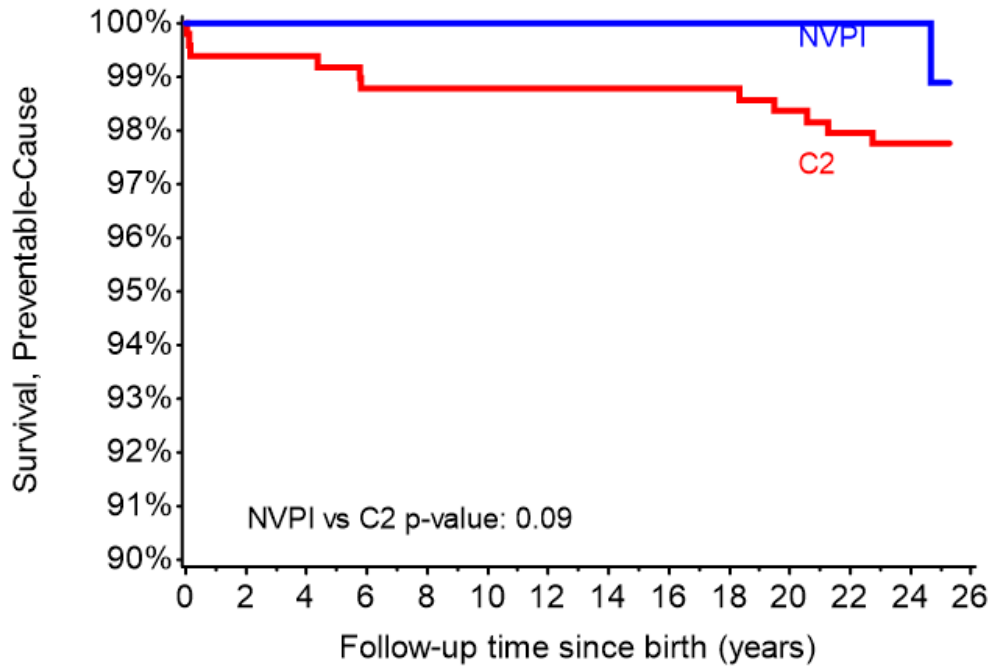
Memphis (NVPI vs. C1+C2)



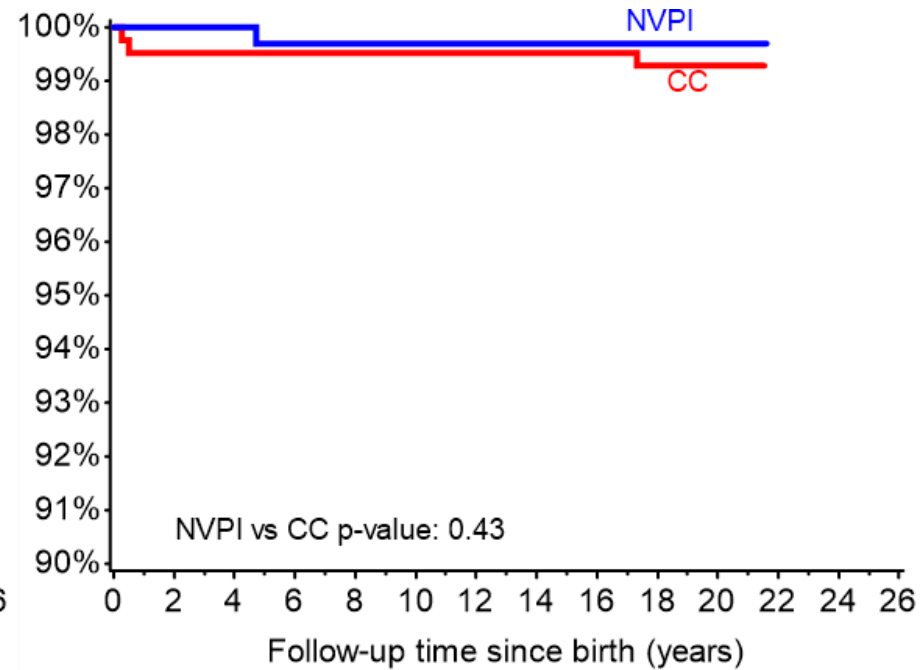
Elmira and Denver (NVPI vs. CC)



SURVIVAL CURVE FOR CHILD PREVENTABLE-CAUSE MORTALITY



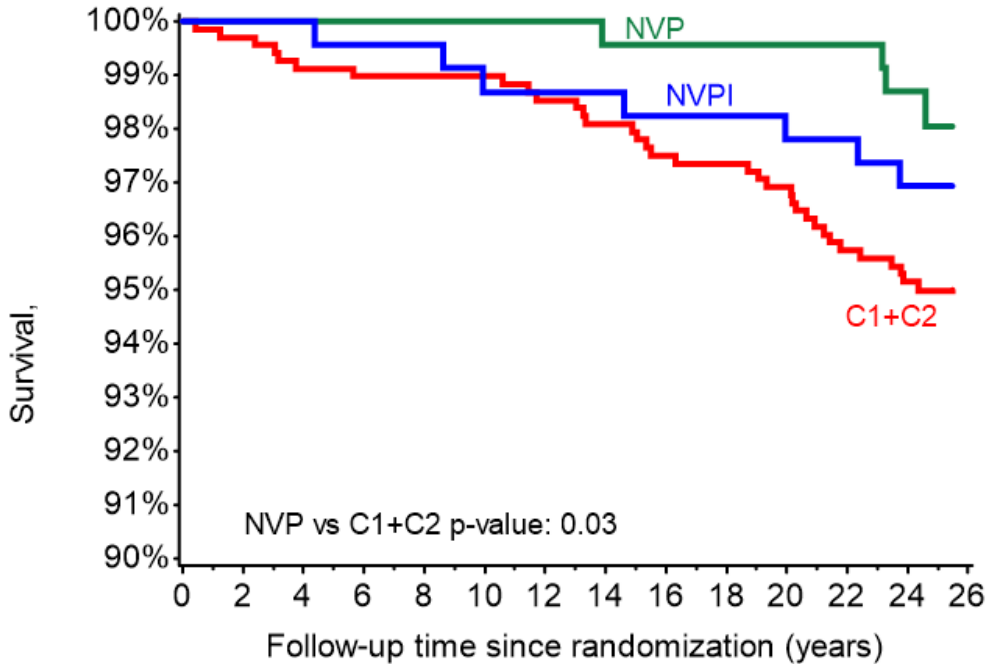
Memphis (NVPI vs. C1+C2)



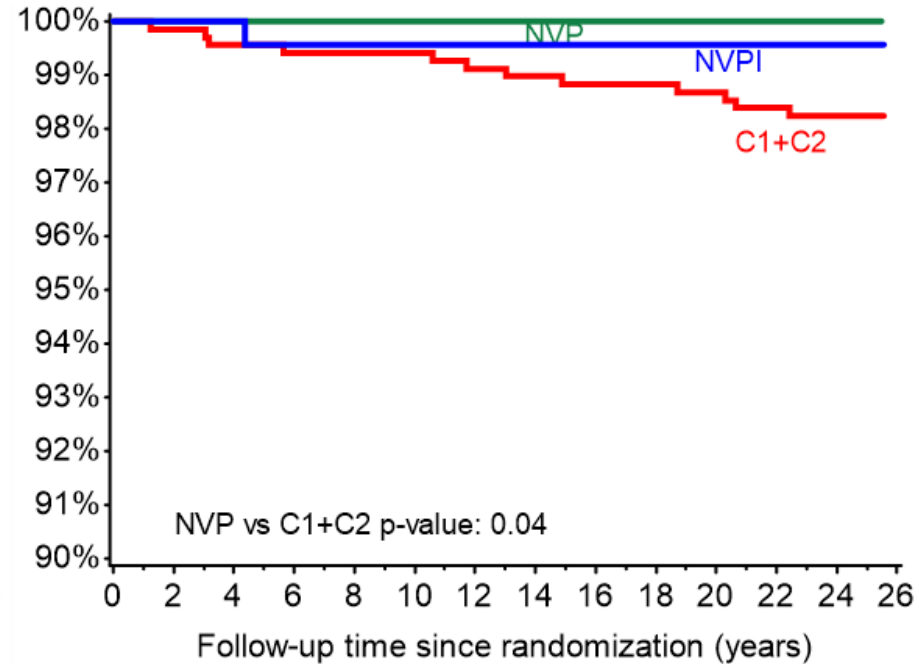
Elmira and Denver (NVPI vs. CC)



SURVIVAL CURVE FOR MEMPHIS MOTHERS MORTALITY

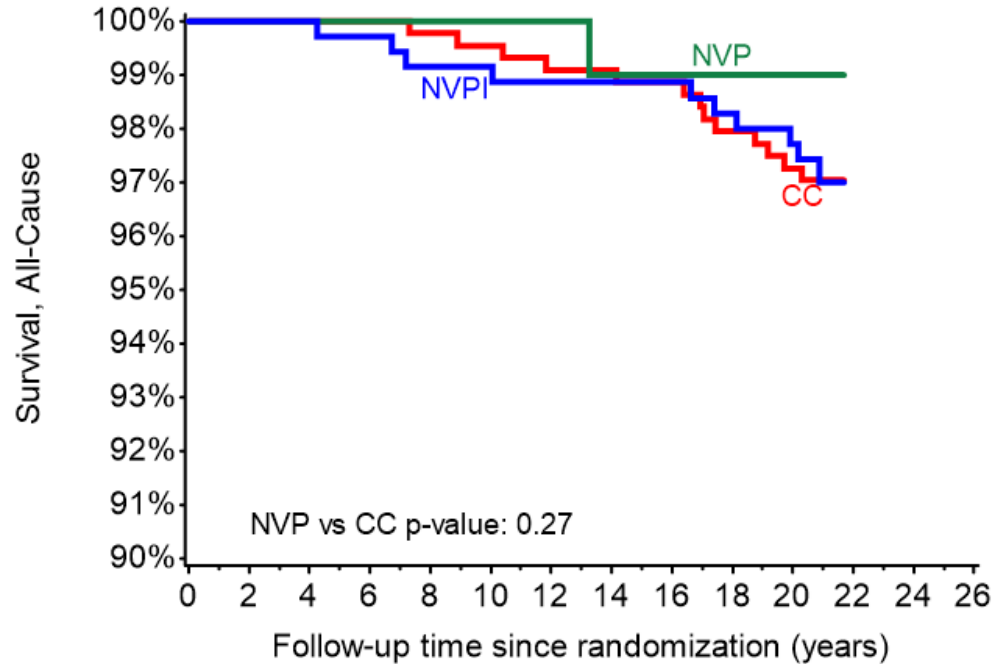


All-Cause (NVP vs. C1+C2)

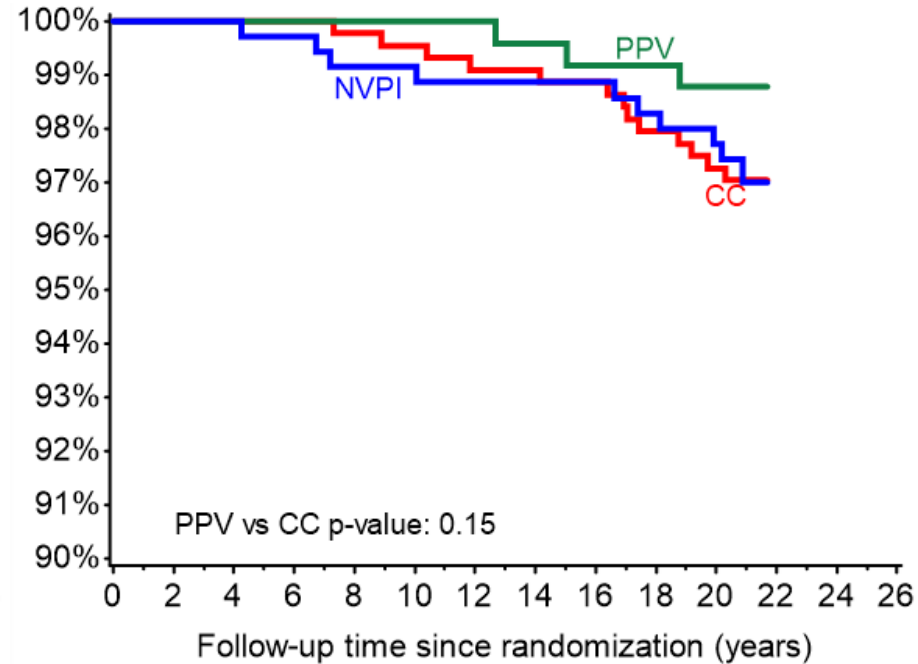


External-Cause (NVP vs. C1+C2)

SURVIVAL CURVE FOR MOTHERS ALL-CAUSE MORTALITY



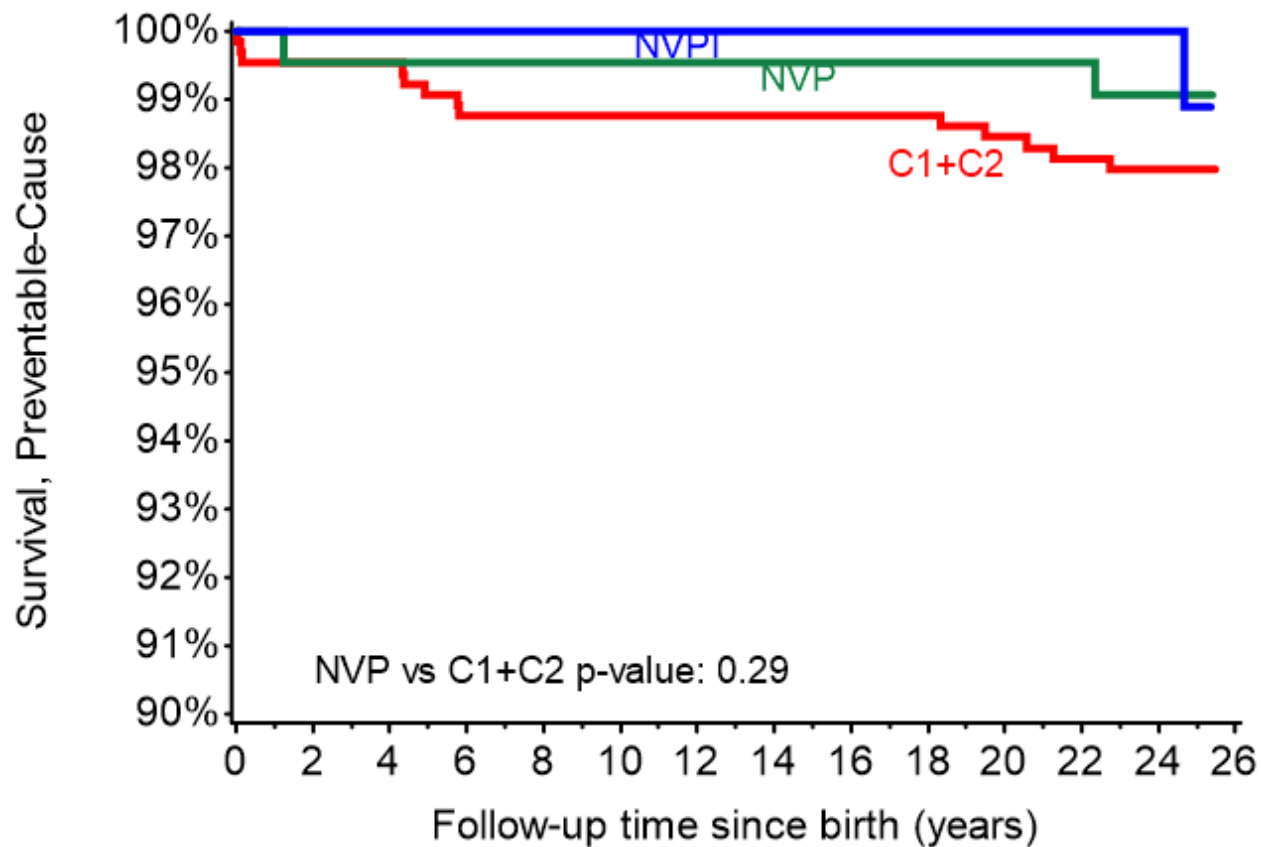
Elmira (NVP vs. CC)



Denver (PPV vs. CC)



SURVIVAL CURVE FOR MEMPHIS CHILDREN PREVENTABLE-CAUSE MORTALITY



(NVP versus C1+C2)

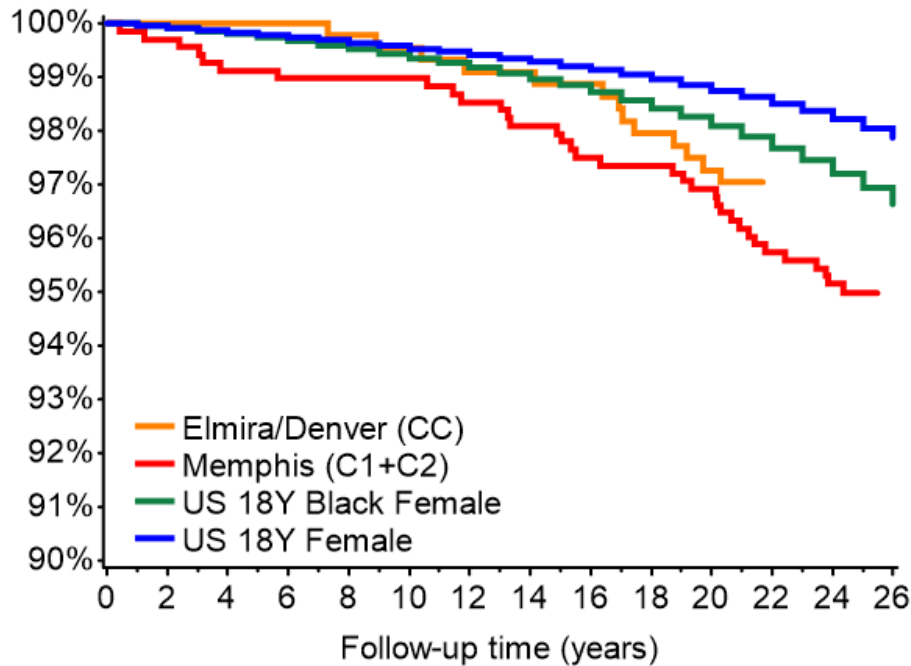


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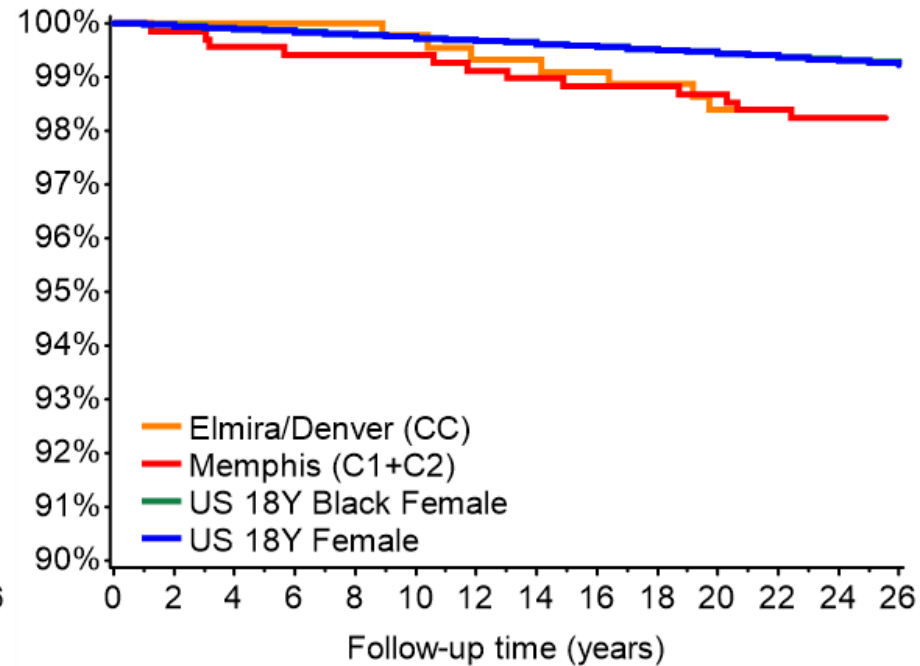
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US NATIONAL MORTALITY (18+ WOMEN) COMPARED TO CONTROL GROUP WOMEN IN THE TRIALS



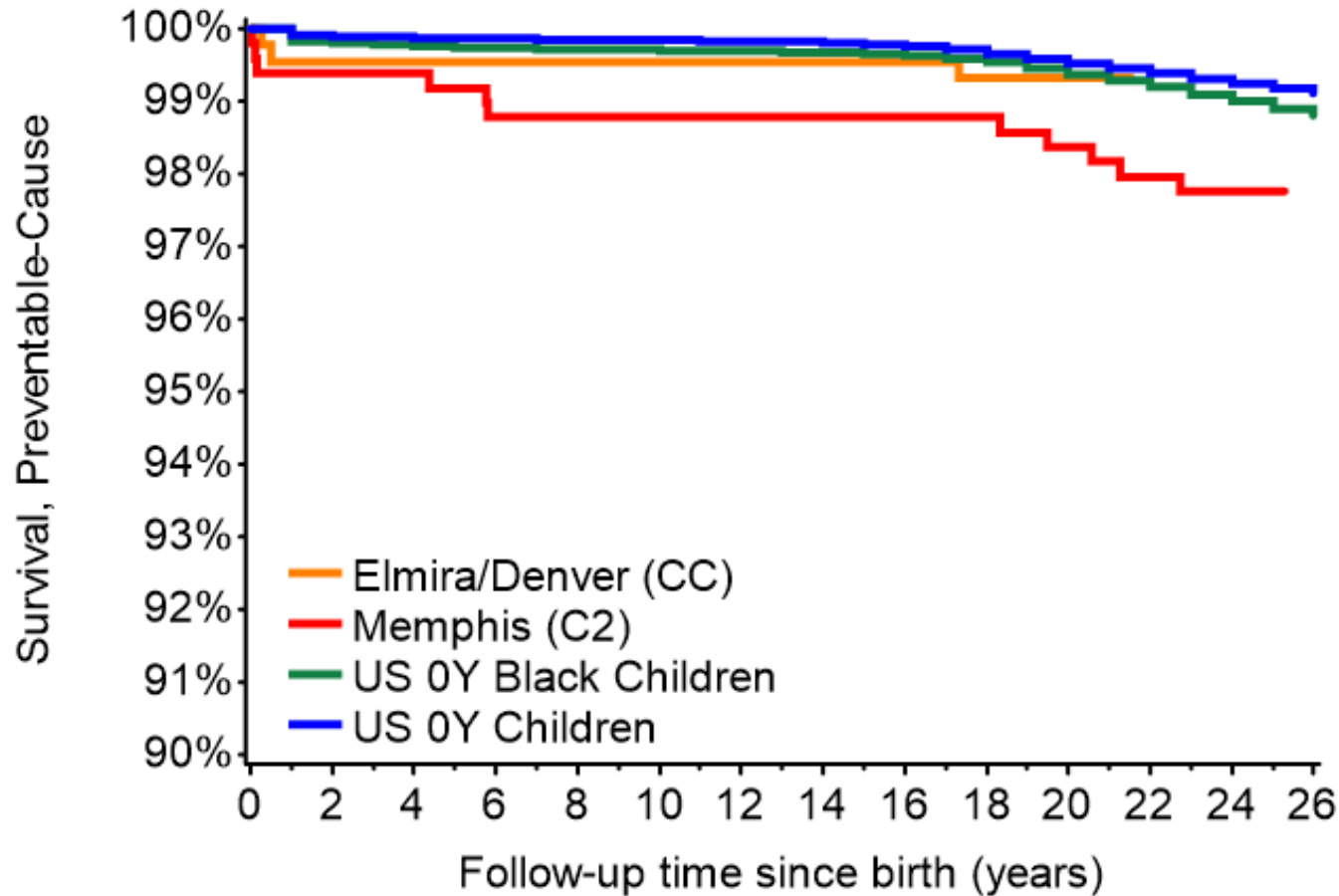
All-Cause



External-Cause



US NATIONAL PREVENTABLE-CAUSE MORTALITY COMPARED TO CONTROL GROUP CHILDREN IN TRIALS



Summary and Limitations

Summary

- **no significant NVPI–control differences in maternal mortality in Memphis or Elmira and Denver.**
 - **Posthoc (3 trials) – suggests reduction in external cause mortality for NVPI women**
- **marginally significant NVPI–Control difference in preventable-cause child mortality in Memphis.**

Limitations

- **Infrequently occurring event and statistical power**
- **Lower than expected rates of death in Denver and Elmira**
- **Findings sensitive to relatively small changes**



CONCLUSIONS AND FUTURE DIRECTIONS

- **Conclusions**

- Findings are noteworthy given the importance of mortality and its objective measurement
- Accumulating evidence of epigenetic effects of toxic stress in pregnancy and early development to health and long-term outcome
- Those at greatest risks receive greatest benefits

- **Future Directions**

- Continued follow-up from trials
- Call for studies that examine mortality across independent trials of the NFP and other prevention programs
 - Meta-analysis or harmonized data sets



QUESTIONS

