Prenatal and Infancy Nurse Home Visiting and 18-Year Outcomes of a Randomized Trial

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abstract

OBJECTIVES: Given earlier effects found in randomized clinical trials of the Nurse-Family Partnership, we examined whether this program would improve 18-year-old first-born youths' cognition, academic achievement, and behavior and whether effects on cognitive-related outcomes would be greater for youth born to mothers with limited psychological resources (LPR) and on arrests and convictions among females.

METHODS: We enrolled 742 pregnant, low-income women with no previous live births and randomly assigned them to receive either free transportation for prenatal care plus child development screening and referral (control; n = 514) or prenatal and infant home nurse visit (NV) plus transportation and screening (n = 228). Assessments were completed on 629 18-year-old first-born offspring to evaluate these primary outcomes: (1) cognitive-related abilities (nonverbal intelligence, receptive language, and math achievement) and (2) behavioral health (internalizing behavioral problems, substance use and abuse, sexually transmitted infections, HIV risk, arrests, convictions, and gang membership).

RESULTS: Compared with control-group counterparts, NV youth born to mothers with LPR had better receptive language (effect size = 0.24; 95% confidence interval [CI]: 0.00 to 0.47; P = .05), math achievement (effect size = 0.38; 95% CI: 0.14 to 0.61; P = .002), and a number of secondary cognitive-related outcomes. NV females, as a trend, had fewer convictions (incidence ratio = 0.47; 95% CI: 0.20 to 1.11; P = .08). There were no intervention effects on other behaviors.

CONCLUSIONS: The program improved the cognitive-related skills of 18-year-olds born to mothers with LPR and, as a trend, reduced female convictions but produced no other effects on youth behavioral health.

WHAT'S KNOWN ON THIS SUBJECT: Two randomized trials of prenatal and infant home visit by nurses found effects on children's behavioral problems, early adolescent substance use, and among children born to mothers with limited psychological resources, cognitive outcomes. One trial found fewer convictions among females.

WHAT THIS STUDY ADDS: This trial extends earlier estimates of intervention impact: compared with control-group counterparts, nurse-visited 18-year-olds born to mothers with limited psychological resources exhibited better cognitive functioning; females, as a trend, had fewer convictions. There were no significant effects on behavioral health.

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The potential of early intervention to improve the lives of children born into disadvantaged families has gained considerable attention.[1,2] Pregnancy and the early years of life are opportune times to intervene because of significant neuroendocrine changes in mothers, developing fetuses, and young children.[3,4] Prenatal and early childhood exposures to toxicants, maltreatment, and stress are thought to amplify one another over time, contributing to compromised life-course development and making this an opportune time to intervene to improve vulnerable children's development.[5] Our team has been conducting a series of pragmatic randomized clinical trials (RCTs) of a program of prenatal, infant, and toddler home visiting by nurses for low-income mothers and their children known as the Nurse-Family Partnership (NFP).[6–20] The current study assesses 629 primarily African American first-born 18-year-old youth whose mothers participated in the second RCT of NFP in Memphis, Tennessee.[11–17]

Findings from the current trial[11–16] and NFP trials conducted earlier in Elmira, New York,[6–10] and later in Denver, Colorado,[18–20] led us to hypothesize that NFP would improve 18-year-old youth language, cognition, and math achievement and that effects in this broad domain would be most pronounced for youth born to mothers with limited psychological resources (LPR) to cope with adversity: in the lower half of the distribution on an index composed of maternal intellectual functioning,[21] mental health,[22] and sense of mastery[23] plus self-efficacy (mothers' beliefs about the importance of and her confidence in accomplishing key NFP behavioral objectives)[24] measured at baseline.[11]

Given NFP effects on substance use and antisocial behavior through age 15 among youth born to disadvantaged mothers in the Elmira trial[9] and substance-use and internalizing disorders in the current trial at age 12,[15] we hypothesized that the program would reduce 18-year-olds' internalizing disorders, substance use, and abuse disorders. In light of intervention effects on the number of lifetime sex partners through age 15 among youth born to disadvantaged mothers in Elmira[9] and anticipated effects on substance abuse disorders in the current trial, we hypothesized that nurse visited (NV) 18-year-olds would have fewer pregnancies and births and a lower risk for HIV. Given NFP effects on arrests, convictions, and violations of probation among 15-year-olds born to disadvantaged mothers in the Elmira trial[9] and substance use at age 12 in the current trial,[15] we hypothesized that the program would reduce rates of gang membership, arrests, and convictions among 18-year-olds.

Before analysis of intervention-control differences, we found that program effects on arrests and convictions in Elmira were limited to females through age 19,[10] leading us to hypothesize the presence of corresponding female effects in Memphis. Also, given the presence of little meaningful variation in neighborhood disadvantage (2.4 SDs above the national mean[25]), we eliminated, before analysis of intervention effects, a hypothesis that program effects would be greater among youth whose mothers lived in the most distressed neighborhoods at registration.

METHODS

The basic features of this study have been reported earlier.[11] We conducted this RCT in a public system of obstetric and pediatric care in Memphis, Tennessee, with registration of the original sample completed between June 1990 and August 1991. Given that program effects were more pronounced for mothers and children from more disadvantaged families in the preceding trial,[6–10] we focused sampling in Memphis on those with overlapping sociodemographic risks. We enrolled women <29 weeks' gestation with no previous live births and at least 2 sociodemographic risks (unmarried, <12 years of education, or unemployed). Ninety-two percent of the women were African American, and at enrollment, 98% were unmarried, 64% were <18 years of age, and 85% were from households with incomes below the federal poverty guidelines. For the current follow-up, participating mothers, other caregivers, and youth completed informed consent procedures approved by the University of Rochester Institutional Review Board.

Table 1 summarizes the Consolidated Standards of Reporting Trials information. Eighty-eight percent (n = 1138) of 1289 eligible pregnant women who were offered participation completed informed consent and were randomly assigned to 1 of 4 treatment conditions following a procedure that concealed assignment from individuals involved in gathering participant data.[11] We assigned 742 participants to 2 treatment conditions created to estimate program effects on postnatal outcomes: 514 to Treatment 2 (control) and 228 to Treatment 4 (NV), both described below. Sample size and assignment ratios were derived from statistical power calculations in the original phase of the trial.[11] Table 1 shows those lost to follow-up because of miscarriage or child death, maternal or child refusal to participate at earlier phases, and the number evaluated with youth assessments and maternal and/or other-custodian interviews at youth age 18.

Interviews for this follow-up were conducted between October 2008 and September 2014, and reviews of school records were conducted by

TABLE 1 Consolidated Standards of Reporting Trials Information for Youth Enrolled in the Trial Through 18-Year Follow-up

Treatment Group Assignment	T1[a]	T2[b]	T3[c]	T4[d]	Total (T2 + T4)
No. allocated to each treatment	166	514[e]	230	228	742
Miscarriages	6	19	6	8	27
Stillbirths	0	5	3	2	7
Child death before age 18	—	10	—	2	12
Mother declined participation after randomly assigned	—	14	—	11	25
Child declined participation before age 18	—	1	—	0	1
Available for 18-y follow-up[f]	—	465	—	205	670
Completed age-18 youth assessment[g]	—	435	—	194	629
Completed maternal and/or other-custodian interview for youth arrests[h]	—	429	—	192	621
Completed maternal or other-custodian interview for CBCL externalizing and total behavior problems[i]	—	428	—	187	615
Completed maternal or other-custodian interview for SSI (disability)	—	429	—	190	619
Collected youth urine[j]	—	419	—	187	606
Completed review of high school graduation records	—	431	—	188	619

There were 1290 subjects eligible to participate; 151 declined participation, and 1138 were randomly assigned. CBCL, Child Behavior Checklist; —, not applicable.

[a] Treatment 1: prenatal transportation.

[b] Treatment 2: prenatal transportation plus developmental screening and referral.

[c] Treatment 3: prenatal transportation plus developmental screening and referral and prenatal nurse home visits.

[d] Treatment 4: prenatal transportation plus developmental screening and referral and prenatal and infant and/or toddler nurse home visits.

[e] Note that 1 mother was enrolled and randomly assigned twice by mistake after a miscarriage. We included her only once, with her original assignment, in the control group.

[f] Some outcomes reported in Tables 4 and 5 show higher numbers than indicated in this table because they include repeated estimates of outcomes from earlier phases of follow-up, as indicated by "all" under "age at assessment" in those tables.

[g] Some youth were unable or unwilling to complete the standardized psychological or achievement assessments or to provide urine to screen for STIs or substances, reducing the numbers shown in Tables 4 and 5.

[h] Youth arrests were derived from a detailed examination of self-report, maternal, and other-caregiver report, synthesizing data from all 3 data sources (when available); this shows the number of cases for which data were gathered from maternal and/or other-caregiver report. Estimates of arrest-related outcomes were made even if maternal and other-caregiver reports were unavailable.

[i] Youth CBCL externalizing and total behavioral problems (borderline or clinical) were derived from a combination of youth self-report and either maternal or other-caregiver report. Maternal report was given priority over other-caregiver report.

[j] Some youth were unable or refused to provide urine for substance-use or STI screening. One sample was unusable for STI screening.

December 2015 by staff masked to treatment assignment. Most assessments were conducted after youth 18th birthdays (mean age 18.67 years; SD = 0.95; range: 17.5–23.9). Repeated measures of some outcomes over time increased the numbers and are noted by "all" under the column "Child Age ge at Assessment" in Tables 3 and 4.

Interviews were completed with 629 of the 669 available youth. Interviews were conducted with mothers and other caregivers to augment youth report of arrest outcomes (n = 621) and externalizing and total behavior problems (n = 615) and to determine Supplemental Social Security Income (SSI) for disability (n = 619). High school graduation records were collected for 619 youth, and urine was collected for 606 youth.

Treatment Conditions

Women in the control group (n = 514) were provided with free transportation for scheduled prenatal care plus developmental screening and referral for children at 6, 12, and 24 months of age. Women in the NV condition (n = 228) were provided with the same services as the control group plus prenatal and infant home visitation through age 2.

NFP was designed to (1) improve pregnancy outcomes by promoting women's prenatal health behaviors, (2) improve children's health and development by promoting parents' care of their children, and (3) enhance parents' health and life course by encouraging women to plan the timing of subsequent pregnancies, complete their educations, and find work. Nurses linked families with needed services and, when possible, involved other family members (especially children's fathers and grandmothers).[5] Program protocols were grounded in developmental epidemiology and theories of human attachment, human ecology, and self-efficacy and adjusted to families' individual needs.[5]

The program was implemented by the Memphis and Shelby County Health Department during a nursing shortage, leading to nurse turnover for 37% of the families.[11] Nurses carried a maximum caseload of 25 families each and relied on detailed visit-by-visit guidelines structured around 62 home visits. It is impossible for nurses to complete 62 visits for all families, and most families do not need this level of service. Nurses used their clinical judgment to adjust dosage and visit content, as well as telephone communications when in-person visits were not possible, to address individual needs revealed in the conduct of visits.

All families were scheduled to receive 4 weekly visits at the beginning of the program to facilitate nurses' and

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TABLE 2 Outcome Domains, Variables Measured, and Bases for Hypotheses

Outcome Domains and Variables Measured	Basis for Hypotheses[a]			
	Earlier Effect in Current Trial	Effect in Other Trial	Predicted From Earlier Phases or Trials	Conditional Effect
Primary cognitive-related outcomes				
Nonverbal intelligence[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
Kaufman Brief Intelligence Test 2, matrices subtest[28,d]	X[13]	—	—	—
Receptive language[b]	—	X[18–20]	X[5–9,11–16,18–20]	LPR[c]
Peabody Picture Vocabulary Test III[30]	X[13]	—	—	—
Math achievement[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
Peabody Individual Achievement Test, math subtest[31]	X[13,15]	—	—	—
Secondary cognitive-related outcomes				
Sustained attention[b]	—	X[19,20]	X[5–9,11–16,18–20]	LPR[c]
Leiter-R sustained attention test[32]	—	—	—	—
Verbal Working Memory Index[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
WAIS No. recall sequences[33]	—	—	—	—
Emotion recognition[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
Facial Emotion Recognition Task, No. correct[34]	—	—	—	—
Risky decision-making[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
Cambridge Decision-Making Test[35]	—	—	—	—
High school graduation, %[b]	—	—	X[5–9,11–16,18–20]	LPR[c]
Administrative records and self-report	—	—	—	—
Exploratory cognitive-related outcomes				
High school graduation with honors[b,e], %	—	—	X[5–9,11–16,18–20]	LPR[c]
Administrative records	—	—	—	—
SSI: disability[b,f]	—	—	X[5–9,11–16,18–20]	LPR[c]
Maternal and/or caregiver report of enrollment	—	—	—	—
Primary behavioral health outcomes				
Internalizing behavioral problems (borderline or clinical)[b]	—	—	X[5–9,11–16,18–20]	—
Youth self-report ages 11–18: Achenbach system[36]	X[15]	—	—	—
Current substance use[b]	X[15]	X[9]	X[5–9,11–16,18–20]	—
Drug Use Screening Inventory (adolescent version)[37] plus urine screens for cotinine, phencyclidine, benzodiazepines, cocaine, amphetamines, tetrahydrocannabinol, opiates, and barbiturates (coded yes or no)	—	—	—	—
Substance-use disorder[b]	—	—	X[5–9,11–16,18–20]	—
CIDI-SAM[38]	—	—	—	—
STIs[b]	—	—	X[5–9,11–16,18–20]	—
Neisseria gonorrheae, *Chlamydia trachomatis*, and *Trichomonas vaginalis*[39–41]	—	—	—	—
HIV risk[b]	—	—	X[5–9,11–16,18–20]	—
Risky sexual behaviors, STIs, and pregnancies[42]	—	—	—	—
Arrests and convictions[b]	—	X[9,10]	X[5–16,18–20]	Females
Counts of self- and maternal and/or caregiver-reported arrests and convictions before age 18 for all offenses and interpersonal violence	—	—	—	—
Gang membership[b]	—	—	X[5–9,11–16,18–20]	—
Self-report	—	—	—	—
Secondary behavioral health outcomes				
Externalizing and total behavioral problems (borderline or clinical)[b]	X[13]	—	X[5–9,11–16,18–20]	—
Achenbach assessment[36]: self- and maternal and/or caregiver report both crossing the borderline or clinical threshold	—	X[20]	—	—

CIDI-SAM, Composite International Disease Interview–Substance Abuse Model; WAIS, Wechsler Adult Intelligence Scale; —, not applicable.

[a] We show the bases for hypotheses in 3 categories: (1) an earlier effect on the same specific measure or construct in an earlier phase of the trial, (2) an effect on the same measure or construct in other trials, and (3) effects in earlier phases or trials that predict the current outcomes on theoretical or epidemiological grounds. When the prediction was made from the same measure, the basis for the hypothesis is shown on the same row; otherwise, it is shown on the construct row. Note that those outcomes hypothesized to be greater for particular subgroups are shown in the last column.

[b] Outcome domain. Specific variables assessed are shown under each outcome domain. Outcomes were selected on the basis of their being affected in earlier phases of this trial or the preceding trial or on theoretical and epidemiological grounds, with attention paid to those aspects of functioning that are of clinical or public health importance and that could be assessed without overburdening respondents.

[c] Subgroup defined by youths' mothers at registration[11] falling into the lower half of the distribution of an index composed of the average z scores of women's intellectual functioning,[21] mental health,[22] and sense of mastery[23] plus self-efficacy (based on mothers' confidence in their ability to accomplish key NFP behavioral objectives).[24]

[d] The intervention effect on nonverbal intelligence at age 6 was a trend overall and for the LPR group, derived from the Kaufman Assessment Battery for Children Mental Processing Composite.[29] The analysis of the whole-scale Kaufman Assessment Battery for Children Mental Processing Composite was significantly different for the treatment-control contrast, both overall and for the LPR group at age 6.[13] The nonverbal subscale trend was not reported in the earlier publication.[13] The Kaufman Brief Intelligence Test 2 administered at age 18 is a shortened version of intellectual functioning based on the full-scale Kaufman Assessment Battery for Children.

[e] Exploratory outcome. Graduating with honors was not part of the original measurement design per se. The original plan called for gathering school records of grade point averages and disciplinary records, which were incomplete, leading us to eliminate them as part of the final measurement design. We discovered, however, that states sent information on graduation with honors, which aligns with the original measurement design and thus is included in this report. Note that all states to where participants moved record graduating with honors, with the exception of Mississippi. Seventeen participants graduated from Mississippi schools (10 control; 7 NV); they are included in the analysis as not having graduated with honors.

[f] Exploratory outcome. SSI (disability) was based on parent and/or caregiver report and not included in the original measurement design. The question is relevant to this report and thus is included here.

TABLE 3 Background Characteristics at Randomization of Those Participants for Whom 18-Year Assessments Were Completed

Variable	Group	Control, T2		NV, T4	
		N	Result	N	Result
Male sex, %	Whole	435	48.3	194	49.0
	LPR[a]	230	43.9	108	51.9
Mother married, %	Whole	435	1.8	194	1.0
	LPR[a]	230	1.3	108	1.9
Maternal race: African American, %	Whole	435	93.6	194	90.7
	LPR[a]	230	95.2	108	90.7
Head of household employed, %	Whole	434	56.5	193	49.2
	LPR[a]	229	52.4	107	48.6
Drank alcohol in last 14 d, %	Whole	434	4.4	194	5.2
	LPR[a]	229	5.7	108	7.4
Smoked cigarettes in last 3 d, %	Whole	434	8.5	194	10.8
	LPR[a]	229	7.9	108	13.0
Used marijuana in last 14 d, %	Whole	434	1.6	194	1.0
	LPR[a]	229	1.7	108	1.9
Any sexually transmitted disease before random assignment, %	Whole	432	33.3	194	37.6
	LPR[a]	227	33.0	108	38.9
Maternal age, y, mean (SD)	Whole	435	18.10 (3.20)	194	18.08 (3.32)
	LPR[a]	230	18.13 (3.31)	108	18.30 (3.85)
Gestational age, wk, mean (SD)	Whole	435	16.56 (5.74)	194	16.72 (5.71)
	LPR[a]	230	16.39 (5.79)	108	16.68 (5.63)
PR index,[b,c] y, mean (SD)	Whole	434	99.87 (9.92)	194	99.36 (10.69)
	LPR[a]	229	92.34 (5.80)	108	91.85 (6.71)
Highest grade completed: mother, y, mean (SD)	Whole	435	10.26 (1.88)	194	10.08 (2.04)
	LPR[a]	230	9.93 (1.94)	108	9.62 (2.06)
Discretionary annual household income (per $1000),[d] y, mean (SD)	Whole	435	1.57 (6.99)	194	−0.18 (6.45)
	LPR[a]	230	−0.19 (6.50)	108	−1.07 (6.16)
% of census tract below poverty, y, mean (SD)	Whole	435	34.85 (21.34)	194	35.30 (20.48)
	LPR[a]	230	36.40 (21.08)	108	34.49 (21.31)
Housing density,[e] y, mean (SD)	Whole	435	0.95 (0.50)	194	1.04 (0.57)
	LPR[a]	230	1.04 (0.53)	108	1.12 (0.52)
Conflict with mother,[f] y, mean (SD)	Whole	434	3.99 (0.90)	194	4.03 (0.74)
	LPR[a]	229	4.15 (1.09)	108	4.09 (0.80)
Conflict with partner[f]	Whole	434	3.97 (0.83)	194	4.07 (0.83)
	LPR[a]	229	4.08 (0.96)	108	4.21 (0.96)
Attitudes toward child-rearing predictive of CA,[g] y, mean (SD)	Whole	435	99.88 (7.64)	194	101.08 (8.48)
	LPR[a]	230	102.33 (7.06)	108	103.34 (7.70)
Household poverty index,[c,h] y, mean (SD)	Whole	435	99.63 (10.16)	194	102.19 (9.91)
	LPR[a]	230	101.94 (10.09)	108	103.72 (9.82)
Neighborhood disadvantage index,[i] y, mean (SD)	Whole	435	2.33 (1.64)	194	2.38 (1.82)
	LPR[a]	230	2.50 (1.60)	108	2.24 (1.72)

T2, prenatal transportation plus developmental screening and referral.; T4, prenatal transportation plus developmental screening and referral and prenatal and infant and/or toddler nurse home visits.

[a] Subgroup defined by youths' mothers falling into the lower half of the distribution for PR (LPR) described in the following footnote.

[b] Average z scores of women's intellectual functioning,[21] mental health,[22] and sense of mastery[23] plus self-efficacy[24] (mastery and self-efficacy measures were standardized and averaged; self-efficacy is based on participants' beliefs about the importance of and confidence in accomplishing key NFP behavioral objectives).

[c] Standardized to sample: mean = 100; SD = 10.

[d] Annual household discretionary income is based on income subsistence standards for Medicaid eligibility, reported household income, and number of individuals in the household at registration.

[e] Persons per room.

[f] Locally developed scale that assesses degree to which the mother experiences conflict in her relationship with this person.

[g] Adult-Adolescent Parenting Inventory.[43]

[h] Average z scores of household discretionary income, housing density, and whether the head of household was employed.

[i] Average of variables calculated in SD units from the national means of components that comprise the index of concentrated social disadvantage (percentage of block group residents: [1] below federal poverty level, [2] receiving public assistance, [3] unemployed, [4] headed by single women, [5] age <18, and [6] African American).[25]

mothers' getting to know one another as early in the pregnancy as possible and to develop a trusting relationship founded on nurses' understanding of mothers' aspirations and concerns about their prenatal health, the developing fetus, birth, and the challenges of caring for a newborn. Newborn health and mother's adjustment to caregiving were critical factors in nurses' decisions about visit dose and content. Nurses recorded features of program implementation on every attempted and completed visit.[5,26,27]

TABLE 4 Estimates of Cognitive, Language, Academic, and Executive Functioning Outcomes and SSI Benefit Received Among 18-Year-Old Youth in the Intervention and Control Conditions

Variable	Group	Child Age at Assessment,[a] y	Control, T2		NV, T4		T4–T2	
			N	LS Mean[b] or % (SE)	N	LS Mean[b] or % (SE)	ES[c] or aOR (95% CI)	P
Primary outcome								
Nonverbal intelligence	Whole	18	431	LS mean 88.25 (0.62)	192	LS mean 88.47 (0.93)	ES 0.02 (−0.17 to 0.20)	.85
	LPR[d]	18	227	LS mean 86.37 (0.86)	106	LS mean 87.41 (1.26)	ES 0.09 (−0.16 to 0.34)	.49
	Whole	All[e]	454	LS mean 88.65 (0.47)	204	LS mean 89.58 (0.71)	ES 0.08 (−0.06 to 0.22)	.27
	LPR[d]	All[e]	237	LS mean 87.16 (0.66)	111	LS mean 88.69 (0.98)	ES 0.13 (−0.06 to 0.32)	.19
Receptive language	Whole	18	427	LS mean 81.60 (0.69)	194	LS mean 82.34 (1.03)	ES 0.05 (−0.12 to 0.23)	.55
	LPR[d]	18	223	LS mean 79.02 (0.96)	108	LS mean 82.32 (1.39)	ES 0.24 (0.00 to 0.47)	.05**
	Whole	All[e]	454	LS mena 82.08 (0.56)	204	LS mean 83.33 (0.83)	ES 0.09 (−0.05 to 0.23)	.21
	LPR[d]	All[e]	237	LS mean 79.91 (0.78)	111	LS mean 82.79 (1.14)	ES 0.21 (0.02 to 0.40)	.03**
Math achievement score	Whole	18	428	LS mean 80.38 (0.59)	193	LS mean 82.22 (0.88)	ES 0.15 (−0.02 to 0.32)	.08*
	LPR[d]	18	225	LS mean 78.18 (0.82)	108	LS mean 82.73 (1.19)	ES 0.38 (0.14 to 0.61)	.002***
	Whole	All[f]	454	LS mean 85.22 (0.47)	205	LS mean 86.54 (0.71)	ES 0.11 (−0.03 to 0.25)	.12
	LPR[d]	All[f]	237	LS mean 82.89 (0.66)	111	LS mean 86.70 (0.98)	ES 0.31 (0.13 to 0.50)	.001***
Secondary outcome								
Sustained attention	Whole	18	432	LS mean 8.68 (0.13)	194	LS mean 8.77 (0.19)	ES 0.03 (−0.13 to 0.20)	.67
	LPR[d]	18	227	LS mean 8.22 (0.18)	108	LS mean 8.60 (0.26)	ES 0.14 (−0.08 to 0.36)	.22
	Whole	All[g]	443	LS mean 8.68 (0.12)	199	LS mean 8.67 (0.18)	ES −0.00 (−0.15 to 0.15)	.97
	LPR[d]	All[g]	232	LS mean 8.45 (0.17)	110	LS mean 8.57 (0.24)	ES 0.04 (−0.16 to 0.24)	.67
Working memory index	Whole	18	432	LS mean 8.33 (0.13)	194	LS mean 8.66 (0.19)	ES 0.12 (−0.04 to 0.29)	.15
	LPR[d]	18	227	LS mean 7.90 (0.18)	108	LS mean 8.51 (0.26)	ES 0.23 (0.01 to 0.46)	.04**
Emotion recognition, no. correct	Whole	18	427	LS mean 52.55 (0.37)	190	LS mean 53.75 (0.56)	ES 0.14 (−0.01 to 0.30)	.08*
	LPR[d]	18	225	LS mean 52.32 (0.52)	104	LS mean 54.19 (0.77)	ES 0.22 (0.01 to 0.44)	.04**
Risky decision-making	Whole	18	430	LS mean 5.23 (0.19)	193	LS mean 4.92 (0.29)	ES −0.08 (−0.25 to 0.10)	.38
	LPR[d]	18	227	LS mean 5.02 (0.27)	107	LS mean 4.95 (0.39)	ES −0.02 (−0.25 to 0.21)	.88
High school graduation	Whole	18	431	71.8% (2.22)	188	75.5% (3.26)	aOR 1.21 (0.81 to 1.82)	.35
	LPR	18	227	70.3% (3.14)	106	71.4% (4.51)	aOR 1.06 (0.63 to 1.76)	.83
Graduate with honors[h]	Whole	18	431	4.4% (1.05)	188	8.8% (2.12)	aOR 2.12 (1.09 to 4.13)	.03**
	LPR	18	227	2.5% (0.99)	106	8.0% (2.70)	aOR 3.34 (1.19 to 9.34)	.02**
SSI: disability[h]	Whole	18	429	5.8% (1.30)	190	3.4 %(1.27)	aOR 0.58 (0.25 to 1.34)	.19
	LPR[d]	18	226	10.9% (2.21)	104	3.9% (1.70)	aOR 0.33 (0.13 to 0.84)	.01**

The estimates of intervention-control differences averaged over all other fixed classification variables, including those within subjects, and the same treatment effect were restricted to the group defined by LPR. This table shows the least-squares means at 18 y and repeated measures over time (labeled "all" under "age at assessment"), which also are averaged over other fixed classification effects. For estimates of treatment effects based on repeated measures, we assumed an error structure with different variances at each time for a given child and a different covariance between pairs of times within each child. These were assumed to be the same for all children, and covariance between children was assumed to be negligible. Contrasts at specific, earlier time points are presented in earlier publications.[11–16] LS, least squares; T2, prenatal transportation plus developmental screening and referral.; T4, prenatal transportation plus developmental screening and referral and prenatal and infant and/or toddler nurse home visits.

[a] Age 18 assessment denoted by 18 y; repeated-measures assessment denoted by "all." The exact ages aggregated for repeated-measures estimates are given in footnotes.
[b] Adjusted.
[c] Expressed in SD units.
[d] Subgroup defined by youth mothers falling into the lower half of the distribution for PR (LPR).
[e] Ages 6 and 18.
[f] Ages 6, 12, and 18.
[g] Ages 12 and 18.
[h] Exploratory outcome.
* P < .10; ** P < .05; *** P < .01.

Overall, nurses completed a mean of 7 home visits during pregnancy and 26 visits during the first 2 years postpartum.[11,27] Mothers in the lowest quartile of psychological resources (PR) at baseline received the highest number of home visits (mean = 37.67; SE = 2.38), those in the middle 2 quartiles had the fewest (mean = 32.02; SE = 1.68), and those in the highest quartile of PR received an intermediate number of visits (mean = 34.26; SE = 2.38).

Main Outcomes

Table 2 shows that outcomes were divided into 2 broad categories: (1) cognitive-related outcomes (nonverbal intelligence, language, math achievement, sustained attention, working memory, emotion recognition, risky decision-making, SSI for disability, high school graduation, and graduation with honors) and (2) behavioral health (mental health [internalizing, externalizing, and total behavioral problems], substance use and abuse, sexually transmitted infections [STIs], HIV risk, arrests and convictions, and

TABLE 5 Estimates of Youth Substance-Use Disorders, Drug or Alcohol Use, STIs, Pregnancies, Births, Behavioral Problems, Arrests, Convictions, and Gang Activity

Variable	Group	Child Age at Assessment, y	Control, T2		NV, T4		T4–T2	
			N	LS Mean[a] or % (SE)	N	LS Mean[a] or % (SE)	ES,[b] aOR, IR, or HR (95% CI)	P
Primary outcome								
Time to substance-use disorder[c,d]	Whole	18	435	10.5% (1.41)	194	13.2% (2.22)	HR 1.28 (0.85 to 1.93)	.24
Current drug use SR past month or positive laboratory test result[e]	Whole	18	423	48.4% (2.49)	190	51.1% (3.73)	aOR 1.11 (0.78 to 1.58)	.55
Time to first pregnancy[c,d]	Males	18	210	17.2% (2.56)	95	15.0% (3.30)	HR 0.86 (0.51 to 1.46)	.57
	Females	18	225	26.4% (2.92)	99	22.8% (3.95)	HR 0.85 (0.54 to 1.32)	.46
Time to first live birth[c,d]	Males	18	210	6.3% (1.60)	95	7.5% (2.37)	HR 1.20 (0.58 to 2.49)	.62
	Females	18	225	16.8% (2.45)	99	13.7% (3.21)	HR 0.80 (0.46 to 1.41)	.44
Any positive STI laboratory test result	Males	18	198	15.4% (2.58)	88	14.8% (3.82)	aOR 0.95 (0.47 to 1.94)	.89
	Females	18	220	22.8% (2.87)	99	25.5% (4.47)	aOR 1.16 (0.66 to 2.04)	.60
HIV risk (log transformed)	Whole	18	417	LS mean −13.50 (0.17)	187	LS mean −13.77 (0.26)	ES −0.08 (−0.25 to 0.10)	.38
Internalizing behavior problems[f,g]	Whole	18	431	17.7% (1.93)	194	16.5% (2.79)	aOR 0.92 (0.57 to 1.48)	.73
	Whole	All[j]	459	20.4% (1.35)	207	17.4% (1.85)	aOR 0.82 (0.61 to 1.11)	.19
No. arrests[c]	Whole	18	435	LS mean 0.35 (0.05)	194	LS mean 0.36 (0.08)	IR 1.02 (0.61 to 1.70)	.93
	Females	18	225	LS mean 0.23 (0.05)	99	LS mean 0.19 (0.06)	IR 0.84 (0.39 to 1.81)	.65
No. convictions[c]	Whole	18	435	LS mean 0.28 (0.04)	194	LS mean 0.24 (0.06)	IR 0.86 (0.50 to 1.47)	.59
	Females	18	225	LS mean 0.21 (0.04)	99	LS mean 0.10 (0.04)	IR 0.47 (0.20 to 1.11)	.08*
No. interpersonal violence arrests[c]	Whole	18	435	LS mean 0.14 (0.03)	194	LS mean 0.19 (0.05)	IR 1.39 (0.73 to 2.65)	.32
	Females	18	225	LS mean 0.09 (0.03)	99	LS mean 0.14 (0.05)	IR 1.48 (0.57 to 3.86)	.42
No. interpersonal violence convictions[c]	Whole	18	435	LS mean 0.10 (0.02)	194	LS mean 0.13 (0.04)	IR 1.33 (0.66 to 2.65)	.43
	Females	18	225	LS mean 0.08 (0.02)	99	LS mean 0.07 (0.03)	IR 0.81 (0.28 to 2.34)	.69
Ever in a gang[c]	Whole	18	432	8.5% (1.44)	193	11.2% (2.31)	aOR 1.35 (0.80 to 2.28)	.27
Secondary outcome								
Externalizing behavior problems[h]	Whole	18	424	7.4% (1.31)	187	8.3% (2.08)	aOR 1.13 (0.59 to 2.17)	.72
	Whole	All[j]	459	14.1% (1.20)	206	14.4% (1.80)	aOR 1.02 (0.72 to 1.44)	.91
Total behavior problems[g,h]	Whole	18	424	4.4% (1.01)	187	6.8% (1.89)	aOR 1.60 (0.75 to 3.39)	.22
	Whole	All[j]	459	8.2% (0.95)	206	7.7% (1.48)	aOR 0.94 (0.58 to 1.51)	.79

The estimates of intervention-control differences averaged over all other fixed classification variables, including those within subjects, and the same treatment effect was restricted to the group defined by females for arrest and conviction outcomes. This table shows the least-squares means at 18 y and repeated measures over time, which also are averaged over other fixed classification effects. For estimates of treatment effects based on repeated measures (labeled "all" under "age at assessment"), we assumed an error structure with different variances at each time for a given child and different covariance between pairs of times within each child. These were assumed to be the same for all children, and covariance between children was assumed to be negligible. Contrasts at specific, earlier time points are presented in earlier publications.[11–16] HR, hazards ratio; LS, least squares; SR, self-report; T2, prenatal transportation plus developmental screening and referral; T4, prenatal transportation plus developmental screening and referral and prenatal and infant and/or toddler nurse home visits.

[a] Adjusted.
[b] Expressed in SD units.
[c] Arrest-related outcomes were based on self-report combined with maternal and other-caregiver report (when available).
[d] Survival rate at age 18 from Cox proportional hazard model.
[e] Based on both self-report for all substances and urine assays for specific substances: phencyclidine, benzodiazepines, cocaine, amphetamines, tetrahydrocannabinol, opiates, and barbiturates.
[f] Internalizing problems were based on youth self-report at ages 12 and 18 and maternal and/or other-caregiver report at child age 6, indicated by values exceeding the borderline or clinical threshold.
[g] Ages 6, 12, and 18.
[h] Externalizing and total problems were based on reports in which mothers and/or other caregivers (age 6); mothers and/or other caregivers, teachers, and children (2 of 3 at age 12); and youth and mothers and/or other caregivers (age 18) reported scores that exceeded the borderline or clinical threshold.
* $P < .10$.

gang membership). Within these broad categories, we separated primary from secondary outcomes. Table 2 shows the specific measures used and bases for hypotheses.

Primary outcomes were predicted from previous intervention effects on the same measures or constructs in earlier phases of the current trial or other NFP trials and, for some

outcomes, from effects found at earlier phases. Secondary outcomes were selected on the basis of their epidemiological and theoretical associations with earlier effects in the

Elmira, Memphis, or Denver trials.[5–9,11–16,18–20] We included 2 exploratory outcomes: high school graduation with honors and mother and/or caregiver report of youth receipt of SSI for disability.

Statistical Models and Methods of Analysis

Data analyses are reported on all cases randomized insofar as outcome data were available. The analysis adhered to a statistical analysis plan established before examination of data from the intervention group.

The primary statistical model for cognitive-related outcomes consisted of a 2-level treatment factor (control versus NV) and a 2-level factor reflecting mothers' PR (above versus below the sample median), focusing on treatment differences for the LPR group, in models that included 3 covariates (household poverty index, maternal attitudes predictive of child abuse [CAA],[43] and youth sex). The first 2 covariates, consistent predictors of a range of outcomes, adjusted for treatment nonequivalence at registration; the third was added because of its strong relationship with some outcomes. The household poverty index incorporates 3 variables: discretionary household income, housing density, and head-of-household employment. For emotion-recognition analyses, we added age-18 nonverbal intelligence to the model to reduce the likelihood that intervention effects would simply reflect differences in intelligence.

For arrest and conviction outcomes, we examined NV-control differences in a model that included sex as a classification factor, examining treatment differences separately for females and males, in models that included 3 covariates: maternal PR, household poverty, and CAA.[43]

Given that rates of pregnancies, births, and STI outcomes were operationalized differently for males and females, we examined NV-control differences separately for males and females and included 3 covariates: maternal PR, household poverty, and CAA.[43]

For analysis of HIV risk, we examined NV-control differences in a model that included covariates for maternal PR, youth sex, youth age at assessment, household poverty, and CAA.[43]

For all remaining behavioral health outcomes, we examined NV-control differences in models that included covariates for maternal PR, youth sex, household poverty, and CAA.[43]

For continuous and dichotomous outcomes on which we had repeated assessments for each child over time, we analyzed outcomes using generalized mixed models that included, in addition to variables from the primary model, children as levels of a random factor, a fixed repeated-measures classification factor for time of assessment, and all interactions of time with the other fixed classification factors.

Continuous dependent variables were analyzed in the general linear model, and dichotomous outcomes were analyzed in the logistic linear model. For low-frequency count outcomes, we analyzed data in generalized linear models with negative binomial error assumptions. We examined low-frequency outcomes with rerandomization tests to determine model fit[44] and truncated 1 outlier for the count-of-convictions outcome. Substance-use disorders and timing to first pregnancy and birth were analyzed over time by using Cox proportional-hazards models. We present survival rates at age 18 along with hazard ratios.

Supplemental Tables 6 and 7 show estimates of NV-control differences without covariate adjustments.

RESULTS

The NV and control groups were similar on background characteristics for participants for whom 18-year follow-up assessments were conducted (Table 3), with these exceptions: at intake, NV women, compared with controls, lived in households with less discretionary income, higher person-per-room density, higher scores on a household poverty index, and higher scores on CAA.[43]

Cognitive, Language, Achievement, and Executive Functioning Outcomes

Table 4 summarizes estimates of youth functioning in the cognitive, language, achievement, and executive functioning domains for the sample as a whole and for youth born to mothers with LPR. With the exception of NV youth having higher rates of graduation with honors (adjusted odds ratio [aOR] = 2.12; 95% confidence interval [CI]: 1.09 to 4.13; $P = .028$) and trends ($P < .10$) of NV youth having higher math scores and better emotion recognition, there were no intervention-control differences for the sample as a whole. NV children born to mothers with LPR, on the other hand, had better receptive language (effect size [ES] = 0.24; 95% CI: 0.00 to 0.47; $P = .048$) and math achievement (ES = 0.38; 95% CI = 0.14 to 0.61; $P = .002$) at age 18. For both of these outcomes, there were longitudinal effects over time. There were no intervention-control differences in nonverbal intelligence.

NV children born to mothers with LPR also had better working memories (ES = 0.23; 95% CI = 0.01 to 0.46; $P = .045$) and emotion-recognition abilities (ES = 0.22; 95% CI: 0.01 to 0.44; $P = .040$), lower SSI for disability (aOR = 0.33; 95% CI: 0.13 to 0.84; $P = .011$), and higher rates of high school graduation with honors (aOR = 3.34; 95% CI: 1.19 to 9.34; $P = .022$) than their control-group counterparts.

There were no intervention-control differences in children's sustained attention, risky decision-making, or high school graduation.

Behavioral Health

Table 5 shows that NV females, as a trend, had fewer criminal convictions than control females (incidence ratio [IR] = 0.47; 95% CI 0.20 to 1.11; P = .080). There were no intervention-control differences in internalizing, externalizing, or total behavioral problems or in substance use or substance use disorders. There was a marginally significant difference for NV males, compared with control males, to report more convictions for interpersonal violence (IR = 2.15; 95% CI 0.90 to 5.27; P = .082; data not shown). There were no overall NV-control differences in STIs, timing to first pregnancy, timing to first live birth, HIV risk, gang participation, counts of arrests, convictions, and arrests or convictions for interpersonal violence.

DISCUSSION

There were no overall intervention-control differences for any of the behavioral health outcomes, but the program improved the receptive language and math achievement of 18-year-olds born to mothers with LPR and, as a trend, reduced convictions among females. In addition, NV youth graduated with honors more frequently, and those born to mothers with LPR, compared with control-group counterparts, had better working memories and emotion-recognition skills and fewer disabilities leading to receipt of SSI. High rates of sample retention increase the validity of these findings.

The program effect on cognitive-related outcomes was, with the exception of graduation with honors, limited to youth born to mothers with LPR, conditional effects consistent with earlier phases of this trial,[11–15] and a subsequent trial.[18–20] Most of these effects, except for the twofold increase in graduation with honors overall and threefold reduction in SSI for disability in the LPR group, are

small by conventional standards[45] but important because they reflect different aspects of cognition, disability, and academic success relevant to adult functioning. Moreover, most of these outcomes are based on directly measured abilities.

Program effects on emotion-recognition abilities and working memory, although not examined in other NFP trials, are consistent with a reduction in child maltreatment[46,47] and earlier program effects on maltreatment-related outcomes.[11,13,17] By age 2, for example, control children, compared with those visited by nurses, were hospitalized for fewer days for injuries and ingestions[11]; all admissions for fractures and/or head trauma occurred in control infants born to mothers with LPR.[5,11] Control children born to mothers with LPR were less communicative and responsive to their mothers than those visited by nurses through 24 months[11]; and through age 18, they exhibited more compromised development and achievement.[13,15] All preventable child mortality through age 20 occurred in the control group.[17]

The improvements in cognitive outcomes and reductions in disability in the LPR group at age 18 suggest that the intervention may lead to additional functional and societal savings for this group, including possible reductions in Alzheimer disease and related disorders, given their relationship with adolescent cognitive functioning.[48,49]

In interpreting the more pronounced program effect on the cognitive-related outcomes of children born to mothers with LPR, it is important to note that nurses visited the most vulnerable mothers more frequently, a consistent feature of NFP program design beginning with the Elmira trial.[26] Moreover, children born to mothers with LPR had greater room for improvement.

Note that families were not randomly assigned to different visitation schedules, so discerning the role of visit patterns on outcomes is challenging. In exploratory latent class analyses of home visits in the current trial, 3 patterns were uncovered: low attendance (33% of those visited), high attendance (48%), and increasing attendance (18%). Those in the low-visit group had the highest educations at baseline; those in the increasing group had low education, the lowest number of prenatal visits, and high rates of preterm delivery; and those in the high-visit group also had low education at baseline. These findings highlight the role that mothers, in addition to nurses, play in shaping visit attendance patterns and the methodologic challenges involved in estimating intervention effects for those with different visitation patterns.[27]

In using the visit patterns found here to guide community replication,[5] it is important to emphasize that the dosage metric that the NFP is designed to achieve is the one actually delivered in the original RCTs and that nurses adjusted visit frequency and content in an effort to ensure that they address specific risks and guide responsive caregiving in the most vulnerable subgroups.

The program effect on convictions among females, although a trend, is consistent with a corresponding finding in the Elmira trial,[10] reduced physical aggression among females at age 2 in the current trial,[50] and intervention effects on trajectories of externalizing problems in the subsequent Denver trial among females, but not males, at ages 2, 4, 6, and 9.[51] These female-limited beneficial effects may be connected to females' particular susceptibility to the effects of prenatal stress on androgen activity during gestation[52] and hormone-dependent endpoints, including conduct disorder.[53] Moreover, females, compared with

males, are particularly susceptible to the effects of harsh parenting on health,[54,55] including the development of aggression.[56]

There were no beneficial intervention effects in the current trial on 18-year-olds' substance-use disorders, substance use, or internalizing disorders despite significant intervention effects in these domains at age 12 in the current trial[15] and on substance use, arrests, and convictions through age 15 in the Elmira trial.[9] The trend for NV males to report higher rates of conviction for interpersonal violence was not predicted. The absence of overall beneficial intervention effects on antisocial behavior at the end of adolescence, especially among males, is consistent with age-19 findings in the Elmira trial.[10] There are at least 2 possible explanations for this pattern of results.

The first is that NFP's promotion of sensitive, responsive care and avoidance of harsh treatment may have decreased parents' attention to setting effective limits, especially among noncompliant males.[56] The increase in NV males' self-reported convictions for interpersonal violence found here, although not hypothesized, suggests that greater attention may be needed to address effective limit setting in NFP and to link this program to effective toddler and preschool parenting interventions.[57–60]

Second, the nearly normative rise in male adolescent–limited antisocial behavior not linked to maltreatment or early adversity[61] may mask intervention effects on life-course–persistent antisocial behavior linked to early maltreatment that may become evident once adolescents assume adult roles. Note, however, that adolescents who become ensnared in substance abuse and criminal activity are at risk for long-term criminal involvement.[61–63]

The current report has limitations. The first is that nearly all of the behavioral health findings were based on self-report, and some evidence suggests that NV women become more accurate reporters of socially undesirable behavior, such as smoking.[6] Although a case might also be made that NV youth were more attentive listeners and reporters (given program effects on verbal working memory), measurement of STIs and use of substances included urine assays, so this form of treatment-related report bias does not account for the absence of an intervention effect for these outcomes.

Second, we included 2 exploratory outcomes (high school graduation with honors and SSI for disability) that were not part of the original measurement design, so these findings need to be treated with caution.

Third, the age range for completing 18-year assessments was larger than anticipated but not different by treatment. Adjusting for youth age at assessment does not alter the findings (data not shown).

The fourth limitation is that the number of outcomes analyzed raises challenges with multiple comparisons. We have not adjusted for multiple comparisons in NFP trials.[64–67] We have focused instead on determining if findings replicate with different populations living in different contexts in separate trials. The long-term program effect on cognitive-related outcomes through the end of adolescence has not yet been tested in other trials, so particular caution is warranted in interpreting these outcomes.

CONCLUSIONS

This study found enduring program effects on the cognitive functioning of youth born to the mothers least capable of coping with the adversities that come with living in poverty and a trend for reduced convictions among females but no effects on other adolescent health behavior.

ABBREVIATIONS

aOR: adjusted odds ratio
CAA: maternal attitudes predictive of child abuse
CI: confidence interval
ES: effect size
IR: incidence ratio
LPR: limited psychological resources
NFP: Nurse-Family Partnership
NV: nurse visit
PR: psychological resources
RCT: randomized clinical trial
SSI: Supplemental Social Security Income
STI: sexually transmitted infection

REFERENCES

1. Shonkoff JP, Boyce WT, McEwen BS. Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. *JAMA.* 2009;301(21):2252–2259

2. Garner AS, Shonkoff JP; Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. Early childhood adversity, toxic stress, and the role of the pediatrician: translating developmental science into lifelong health. *Pediatrics.* 2012;129(1). Available at: www.pediatrics.org/cgi/content/full/129/1/e224

3. Kinsella MT, Monk C. Impact of maternal stress, depression and anxiety on fetal neurobehavioral development. *Clin Obstet Gynecol.* 2009;52(3):425–440

4. Rauh VA, Margolis AE. Research review: environmental exposures, neurodevelopment, and child mental health – new paradigms for the study of brain and behavioral effects. *J Child Psychol Psychiatry.* 2016;57(7):775–793

5. Olds DL. Prenatal and infancy home visiting by nurses: from randomized trials to community replication. *Prev Sci.* 2002;3(3):153–172

6. Olds DL, Henderson CR Jr, Tatelbaum R, Chamberlin R. Improving the delivery of prenatal care and outcomes of pregnancy: a randomized trial of nurse home visitation. *Pediatrics.* 1986;77(1):16–28

7. Olds DL, Henderson CR Jr, Chamberlin R, Tatelbaum R. Preventing child abuse and neglect: a randomized trial of nurse home visitation. *Pediatrics.* 1986;78(1):65–78

8. Olds DL, Eckenrode J, Henderson CR Jr, et al. Long-term effects of home visitation on maternal life course and child abuse and neglect. Fifteen-year follow-up of a randomized trial. *JAMA.* 1997;278(8):637–643

9. Olds D, Henderson CR Jr, Cole R, et al. Long-term effects of nurse home visitation on children's criminal and antisocial behavior: 15-year follow-up of a randomized controlled trial. *JAMA.* 1998;280(14):1238–1244

10. Eckenrode J, Campa M, Luckey DW, et al. Long-term effects of prenatal and infancy nurse home visitation on the life course of youths: 19-year follow-up of a randomized trial. *Arch Pediatr Adolesc Med.* 2010;164(1):9–15

11. Kitzman H, Olds DL, Henderson CR Jr, et al. Effect of prenatal and infancy home visitation by nurses on pregnancy outcomes, childhood injuries, and repeated childbearing. A randomized controlled trial. *JAMA.* 1997;278(8):644–652

12. Kitzman H, Olds DL, Sidora K, et al. Enduring effects of nurse home visitation on maternal life course: a 3-year follow-up of a randomized trial. *JAMA*. 2000;283(15):1983–1989

13. Olds DL, Kitzman H, Cole R, et al. Effects of nurse home-visiting on maternal life course and child development: age 6 follow-up results of a randomized trial. *Pediatrics*. 2004;114(6):1550–1559

14. Olds DL, Kitzman H, Hanks C, et al. Effects of nurse home visiting on maternal and child functioning: age-9 follow-up of a randomized trial. *Pediatrics*. 2007;120(4). Available at: www.pediatrics.org/cgi/content/full/120/4/e832

15. Kitzman H, Olds DL, Cole RE, et al. Enduring effects of prenatal and infancy home visiting by nurses on children: age-12 follow-up of a randomized trial. *Arch Pediatr Adolesc Med*. 2010;164(5):412–418

16. Olds DL, Kitzman H, Cole R, et al. Enduring effects of prenatal and infancy home visiting by nurses on maternal life-course and government spending: age-12 follow-up of a randomized trial. *Arch Pediatr Adolesc Med*. 2010;164(5):419–424

17. Olds DL, Kitzman H, Knudtson MD, et al. Effect of home visiting by nurses on maternal and child mortality: results of a 2-decade follow-up of a randomized clinical trial. *JAMA Pediatr*. 2014;168(9):800–806

18. Olds DL, Robinson J, O'Brien R, et al. Home visiting by paraprofessionals and by nurses: a randomized, controlled trial. *Pediatrics*. 2002;110(3):486–496

19. Olds DL, Robinson J, Pettitt L, et al. Effects of home visits by paraprofessionals and by nurses: age 4 follow-up results of a randomized trial. *Pediatrics*. 2004;114(6):1560–1568

20. Olds DL, Holmberg JR, Donelan-McCall N, et al. Effects of home visits by paraprofessionals and by nurses on children: follow-up of a randomized trial at ages 6 and 9 years. *JAMA Pediatr*. 2014;168(2):114–121

21. Shipley WC. A self-administered scale for measuring intellectual impairment and deterioration. *J Psychol*. 1940;9:371–377

22. Ware JE, Veit CT, Donald CA. *Refinements in the Measurement of Mental Health for Adults in the Health Insurance Study*. Santa Monica, CA: Rand Corp; 1985

23. Pearlin LI, Schooler C. The structure of coping. *J Health Soc Behav*. 1978;19(1):2–21

24. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev*. 1977;84(2):191–215

25. Lauritsen JL. The social ecology of violent victimization: individual and contextual effects in the NCVS. *J Quant Criminol*. 2001;17(1):3–32

26. Olds DL, Korfmacher J. Maternal psychological characteristics as influences on home visitation contact. *J Community Psychol*. 1998;26:23–36

27. Holland ML, Xia Y, Kitzman HJ, Dozier AM, Olds DL. Patterns of visit attendance in the Nurse-Family Partnership program. *Am J Public Health*. 2014;104(10):e58–e65

28. Kaufman AS, Kaufman NL. *Kaufman Brief Intelligence Test*, 2nd ed. Bloomington, MN: Pearson Clinical; 2004

29. Kaufman AS, Kaufman NL. *K-ABC: Kaufman Assessment Battery for Children*. Circle Pines, MN: American Guidance Service; 1983

30. Dunn LM, Dunn LM. *Peabody Picture Vocabulary Test*, 3rd ed. Bloomington, MN: Pearson Clinical; 1997

31. Markwardt FC. *Peabody Individual Achievement Test-Revised (Normative Update)*. Circle Pines, MN: American Guidance Service; 1998

32. Roid GH, Miller LJ. *Leiter International Performance Scale–Revised: Examiner's Manual*. Wood Dale, IL: Stoelting Co; 1997

33. Wechsler D. *Wechsler Adult Intelligence Scale*, 3rd ed. San Antonio, TX: Psychological Corporation; 1997

34. Ekman P, Friesen WV. *Pictures of Facial Affect*. Palo Alto, CA: Consulting Psychologists Press; 1975

35. Fishbein DH, Eldreth DL, Hyde C, et al. Risky decision making and the anterior cingulate cortex in abstinent drug abusers and nonusers. *Brain Res Cogn Brain Res*. 2005;23(1):119–136

36. Achenbach TM, Rescorla LA. *Manual for ASEBA School-Age Forms & Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families; 2001

37. Tarter RE, Mezzich AC, Kirisci L, Kaczynski N. Reliability of the drug use screening inventory among adolescent alcoholics. *J Child Adolesc Subst Abuse*. 1994;3(1):25–36

38. Cottler LB, Robins LN, Helzer JE. The reliability of the CIDI-SAM: a comprehensive substance abuse interview. *Br J Addict*. 1989;84(7):801–814

39. Carroll KC, Aldeen WE, Morrison M, et al. Evaluation of the Abbott LCx ligase chain reaction assay for detection of Chlamydia trachomatis and Neisseria gonorrhoeae in urine and genital swab specimens from a sexually transmitted disease clinic population. *J Clin Microbiol*. 1998;36(6):1630–1633

40. Gaydos CA, Howell MR, Quinn TC, Gaydos JC, McKee KT Jr. Use of ligase chain reaction with urine versus cervical culture for detection of Chlamydia trachomatis in an asymptomatic military population of pregnant and nonpregnant females attending Papanicolaou smear clinics. *J Clin Microbiol*. 1998;36(5):1300–1304

41. Madico G, Quinn TC, Rompalo A, McKee KT Jr, Gaydos CA. Diagnosis of Trichomonas vaginalis infection by PCR using vaginal swab samples. *J Clin Microbiol*. 1998;36(11):3205–3210

42. Pinkerton SD, Abramson PR. The Bernoulli-Process Model of HIV Transmission. In: Holtgrave DR, ed. *Handbook of Economic Evaluation of HIV Prevention Programs*. New York, NY: Springer US; 1998

43. Bavolek SJ, Kline DF, McLaughlin JA, Publicover PR. Primary prevention of child abuse and neglect: identification of high-risk adolescents. *Child Abuse Negl*. 1979;3(3–4):1071–1080

44. Proschan MA, Dodd LE. Re-randomization tests in clinical trials. *Stat Med*. 2019;38(12):2292–2302

45. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988

46. Pollak SD, Cicchetti D, Hornung K, Reed A. Recognizing emotion in faces: developmental effects of child abuse and neglect. *Dev Psychol.* 2000;36(5): 679–688

47. Dodaj A, Krajina M, Sesar K, Šimić N. The effects of maltreatment in childhood on working memory capacity in adulthood. *Eur J Psychol.* 2017;13(4): 618–632

48. Huang AR, Strombotne KL, Horner EM, Lapham SJ. Adolescent cognitive aptitudes and later-in-life Alzheimer disease and related disorders. *JAMA Netw Open.* 2018;1(5):e181726

49. Russ TC. Intelligence, cognitive reserve, and dementia: time for intervention? *JAMA Netw Open.* 2018;1(5):e181724

50. Sidora-Arcoleo K, Anson E, Lorber M, et al. Differential effects of a nurse home-visiting intervention on physically aggressive behavior in children. *J Pediatr Nurs.* 2010;25(1):35–45

51. Lorber MF, Olds DL, Donelan-McCall N. The impact of a preventive intervention on persistent, cross-situational early onset externalizing problems. *Prev Sci.* 2019;20(5):684–694

52. Barrett ES, Swan SH. Stress and androgen activity during fetal development. *Endocrinology.* 2015; 156(10):3435–3441

53. Pajer K, Tabbah R, Gardner W, et al. Adrenal androgen and gonadal hormone levels in adolescent girls with conduct disorder. *Psychoneuroendocrinology.* 2006; 31(10):1245–1256

54. Thompson MP, Kingree JB, Desai S. Gender differences in long-term health consequences of physical abuse of children: data from a nationally representative survey. *Am J Public Health.* 2004;94(4):599–604

55. Suglia SF, Clark CJ, Boynton-Jarrett R, Kressin NR, Koenen KC. Child maltreatment and hypertension in young adulthood. *BMC Public Health.* 2014;14:1149

56. Keenan K, Shaw DS. The development of aggression in toddlers: a study of low-income families. *J Abnorm Child Psychol.* 1994;22(1):53–77

57. Pidano AE, Allen AQR. The Incredible-Years Series: a review of the independent research base. *J Child Fam Stud.* 2015;24(7):1898–1916

58. Dawson-McClure S, Calzada E, Huang KY, et al. A population-level approach to promoting healthy child development and school success in low-income, urban neighborhoods: impact on parenting and child conduct problems. *Prev Sci.* 2015;16(2):279–290

59. Breitenstein SM, Gross D, Fogg L, et al. The Chicago Parent Program: comparing 1-year outcomes for African American and Latino parents of young children. *Res Nurs Health.* 2012;35(5): 475–489

60. Côté SM, Orri M, Tremblay RE, Doyle O. A multicomponent early intervention program and trajectories of behavior, cognition, and health. *Pediatrics.* 2018; 141(5):e20173174

61. Moffitt TE. Male antisocial behaviour in adolescence and beyond. *Nat Hum Behav.* 2018;2:177–186

62. Mercer N, Farrington DP, Ttofi MM, et al. Childhood predictors and adult life success of adolescent delinquency abstainers. *J Abnorm Child Psychol.* 2016;44(3):613–624

63. Hussong AM, Curran PJ, Moffitt TE, Caspi A, Carrig MM. Substance abuse hinders desistance in young adults' antisocial behavior. *Dev Psychopathol.* 2004;16(4):1029–1046

64. Olds DL, Luckey D, Henderson C. Can the results be believed?: in reply. *Pediatrics.* 2005;115(4):1113–1114

65. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology.* 1990;1(1):43–46

66. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ.* 1998; 316(7139):1236–1238

67. Goodman SN. Toward evidence-based medical statistics. 1: the P value fallacy. *Ann Intern Med.* 1999;130(12):995–1004