A Randomized Trial of Parental Behavioral Counseling and Cotinine Feedback for Lowering Environmental Tobacco Smoke Exposure in Children With Asthma

Results of the LET'S Manage Asthma Trial

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Background: Secondhand tobacco smoke exposure impairs the control of pediatric asthma. Evidence of the efficacy of interventions to reduce children's exposure and improve disease outcomes has been inconclusive.

Methods: Caregivers of 519 children aged 3 to 12 years with asthma and reported smoke exposure attended two baseline assessment visits, which involved a parent interview, sampling of the children's urine (for cotinine assay), and spirometry (children ≥ 5 years). The caregivers and children ($n = 352$) with significant documented exposure (cotinine ≥ 10 ng/mL) attended a basic asthma education session, provided a third urine sample, and were randomized to the Lowering Environmental Tobacco Smoke: LET'S Manage Asthma (LET'S) intervention ($n = 178$) or usual care ($n = 174$). LET'S included three in-person, stage-of-change-based counseling sessions plus three follow-up phone calls. Cotinine feedback was given at each in-person session. Follow-up visits at 6 and 12 months postrandomization repeated the baseline data collection. Multivariate regression analyses estimated the intervention effect on the natural logarithm of the cotinine to creatinine ratio (lnCCR), use of health-care services, and other outcomes.

Results: In the sample overall, the children in the LET'S intervention had lower follow-up lnCCR values compared with the children in usual care, but the group difference was not significant (β coefficient = -0.307 , $P = .064$), and there was no group difference in the odds of having > 1 asthma-related medical visit (β coefficient = 0.035 , $P = .78$). However, children with high-risk asthma had statistically lower follow-up lnCCR values compared with children in usual care (β coefficient = -1.068 , $P = .006$).

Conclusions: The LET'S intervention was not associated with a statistically significant reduction in tobacco smoke exposure or use of health-care services in the sample as a whole. However, it appeared effective in reducing exposure in children at high risk for subsequent exacerbations.

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Abbreviations: CCR = cotinine to creatinine ratio; LET'S = Lowering Environmental Tobacco Smoke: LET'S Manage Asthma; lnCCR = natural logarithm of the cotinine to creatinine ratio; UC = usual care

Secondhand tobacco smoke is an important trigger of childhood asthma.^{1,2} Eliminating exposure, which can come from multiple sources, requires significant and often difficult behavioral change on the part of parents and caregivers.³ Parents frequently underestimate their child's level of tobacco smoke exposure.³ Cotinine is an objective indicator and biomarker of

tobacco exposure,^{1,4-7} and it can give parents a more accurate understanding of the extent of their child's exposure to this respiratory irritant.

Experimental research to date is not conclusive about the ability of behavioral counseling, coupled with cotinine feedback, to reduce the tobacco smoke exposure of children with asthma or to improve clinical

outcomes. One study that provided a letter to parents reporting their child's urinary cotinine level and a telephone call advising a home smoking ban or smoking cessation found no difference between the intervention and control groups in home or car smoking bans or in the child's cotinine to creatinine ratio (CCR).⁸ Another study of smoke-exposed children with asthma observed that, compared with the control group care, an intervention that combined behavior-based counseling with cotinine feedback was associated with a lower likelihood of having > one asthma-related acute medical visits in the follow-up year and with a trend toward lower urinary cotinine levels at the 12-month follow-up visit.⁹

The Lowering Environmental Tobacco Smoke: LET'S Manage Asthma (LET'S) randomized, controlled trial evaluated the efficacy of an enhanced, behaviorally based cotinine feedback and monitoring intervention, based on one author's (S. R. W.) previous research,⁹ to reduce tobacco smoke exposure, lower the use of health-care services, and improve other health outcomes for smoke-exposed children aged 3 to 12 years with asthma.

MATERIALS AND METHODS

Study methods were approved by the Institutional Review Board of the Kaiser Foundation Research Institute (No. CN-01HFARB-01-H). Additional methods and results information is available in e-Appendix 1.

Participants and Setting

Kaiser Permanente is a large, nonprofit, vertically integrated health maintenance organization with > 3.2 million members in northern California (http://physiciancareers.kp.org/nw/opportunities/Permanent_Medical_Group_Brochure.pdf). Children aged 3 to 12 years who were Kaiser Permanente Northern California members for ≥ 1 year and had medication use and/or a physician diagnosis suggesting persistent asthma were identified from computerized databases. Other eligibility criteria included parent-reported exposure of the child to secondhand tobacco smoke, confirmation of exposure by a urinary cotinine level ≥ 10 ng/mL

from ≥ one baseline visit test result, ≥ one asthma-related medical visit in the past year, intent to remain members for the next year, English-speaking ability, and no other significant comorbidities. Consent to participate was obtained prior to performing the baseline assessments and randomization.

Data Collection

Assessments (caregiver interview, urine collection, and spirometry) were performed at two prerandomization visits (visits 1 and 2), urine collection was performed a third time at the prerandomization basic asthma education visit, and baseline data collection was repeated at the 6- and 12-month follow-up visits. Study staff who performed follow-up assessments were blinded to group assignment. For children randomized to the intervention, urine samples also were collected at the three intervention visits. Feedback on test results was provided only to intervention-group parents.

Primary Caregiver Interview: The interviewer-administered questionnaire covered demographic information; the child's asthma history; the smoking status of the primary caregiver, household members, and home visitors; whether smoking occurred inside the home or in nonhome locations where the child spent significant amounts of time (eg, day care); parental efforts (if any) to make the home smoke free; and asthma's impact on the family's quality of life.

Urine Testing: As detailed previously,³ urinary cotinine levels were measured using the OraSure Cotinine Saliva Micro-Plate EIA assay (OraSure Technologies, Inc; Bethlehem, Pennsylvania), which is sensitive in the range of 5 to 100 ng/mL typically associated with secondhand exposure. Urinary creatinine levels were measured using the QuantiChrom Creatinine Assay Kit (BioAssay Systems; Hayward, California), which is sensitive in the range of 0.10 to 100 mg/dL. To correct for differences in urine concentration, the urinary CCR was calculated as $[100 \times \text{cotinine in ng/mL}] / [\text{creatinine in mg/dL}]$.¹⁰

Spirometry: For children ≥ 5 years, spirometry (KoKo Spirometer; Pulmonary Data Systems; Longmont, Colorado) was performed before and after bronchodilator use (two puffs of albuterol [0.18 mg] via AeroChamber VHC; Monaghan Medical; Plattsburgh, New York). A pediatric pulmonologist (H. J. F.), blind to patient identity and group assignment, reviewed all maneuvers. Maneuvers with > 1 s maximal effort but incomplete exhalation were rejected except for FEV₁.

Administrative and Clinical Records: All asthma-related data on health-care services use (any visit with a physician-coded diagnosis of asthma; code 493.xx from the *International Classification of Diseases, 9th edition*) and all asthma-medication-dispensing data from the 12 months prerandomization to 12 months postrandomization were extracted from Kaiser Permanente computerized records.

Basic Asthma Education Session

The basic asthma education session, a 45-min prerandomization visit, served to remove a lack of asthma education and medication adjustments as potential intervention confounders, provided structured asthma education (eg, pathophysiologic characteristics, triggers and avoidance measures, medication use, and, if appropriate, instruction on peak flowmeter use), and provided a review of the child's current treatment regimen and level of asthma control. If not consistent with then-current asthma treatment guidelines,¹¹ the treatment regimen was adjusted in consultation with the child's primary care physician. A written asthma action plan for each child was given to the parent.

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Randomization

A computerized adaptive randomization algorithm¹² ensured a better-than-chance balance between the experimental groups on five variables: child's age (< 5 years or ≥ 5 years), baseline median urinary cotinine levels (10–29 ng/mL or ≥ 30 ng/mL), primary caregiver smoking status (smoker or not a smoker), number of asthma-related health-care visits in the past year (≤ 1 visit or ≥ 2 visits), and high-risk asthma status.

High-Risk Asthma Criteria

Children were considered to have high-risk asthma per Kaiser Permanente criteria if one or more of the following occurred in the preceding 6 months: the child had an asthma-related hospitalization or ED visit, ≥ 6 units of short-acting β-agonist medication were dispensed, and/or asthma medication was prescribed by three or more physicians.¹³

Intervention Protocol

Additional details about the intervention protocol are included in e-Appendix 1. Briefly, parents of children randomized to the LET'S intervention and the child, if appropriate, attended three cotinine feedback and behavioral counseling visits in approximately 6 weeks after randomization for the purpose of identifying sources of secondhand smoke exposure, identifying and formalizing strategies to reduce the child's exposure based on the sources of the child's exposure (which may or may not have included the primary caregiver smoking in the home) and the caregiver's readiness to make the necessary changes, and creating a written smoke-exposure-reduction plan.

The interventionist made three follow-up telephone calls approximately 2, 4, and 6 weeks following visit 3. The interventionist provided additional cotinine feedback and strove to maintain and continue progress on the parents' smoke-exposure-reduction plan.

Primary Outcomes

Secondhand smoke exposure was assessed using the CCR. The baseline CCR was the pooled mean of the three prerandomization values, and the follow-up CCR was the pooled mean of the 6- and 12-month follow-up visit values. The respective sets of data points were pooled to increase precision and reduce variability. For children who were missing one of the follow-up visit values ($n = 25$, $n =$ five who were at high risk), the available CCR value was used as their mean follow-up value. The natural logarithms of the baseline and follow-up visit CCR values were used in the analysis to reduce skew. Prior to log-transformation, a constant of 0.25 was added to nonmissing cotinine values to avoid values of zero.

The second primary outcome, asthma-related use of health-care services, was specified as being > 1 asthma-related visit of any type. A visit was considered asthma-related if the physician designated asthma (code 493.xx from the *International Classification of Diseases, 9th edition*) as one of the visit diagnosis codes. Visit types included urgent care and ED visits and hospitalizations as well as routine office visits. Two additional use outcomes were also calculated separately for the 12 months before and after randomization: the total number of asthma-related visits and whether the child had ≥ 1 asthma-related hospitalizations or ED visits. Information about secondary outcomes is provided in e-Table 1.

Medication Dispensing Outcomes

An annual cumulative medication acquisition index^{14–16} was used to estimate prescription filling and refilling behavior as a proxy for adherence. The annual cumulative dose of all controller medica-

FIGURE 1. Case progress through the LET'S study. * = Includes patients whose primary care providers were not notified, did not respond, and did not assent, or whose parents could not be successfully contacted. † = Includes patients whose parents failed to keep two or more LET'S prerandomization appointments. ‡ = Reasons for ineligibility include failure to meet the urinary cotinine criterion of > 10 ng/mL from one or more of the three prerandomization urine analyses. LET'S = Lowering Environmental Tobacco Smoke: LET'S Manage Asthma trial.

tions dispensed for the child was measured as beclomethasone canister-equivalents, using weights developed by Schatz et al.¹⁷

Statistical Methods

Group differences at the follow-up visits were analyzed using multivariate generalized linear or logistic regression. Because we considered detecting an intervention-associated difference in CCR to be most meaningful when accompanied by a significant difference in the use of health-care services, statistical significance was set at $P < .01$ for tobacco smoke exposure and $P < .04$ for

Table 1—Baseline Characteristics of Participants, by Group

Characteristic ^a	Overall (N = 352)	LET'S Intervention (n = 178)	UC (n = 174)
Mean baseline cotinine level, ng/mL ^b	22.8 ± 12.8	23.0 ± 12.8	22.6 ± 12.8
Mean baseline CCR ^b	25.1 ± 18.0	26.2 ± 18.8	24.1 ± 17.1
Age, y	7.9 ± 2.9	8.0 ± 2.8	7.8 ± 3.0
< 5 y	55 (15.6)	26 (14.6)	29 (16.7)
≥ 5 y	297 (84.4)	152 (85.4)	145 (83.3)
Child's gender			
Male	214 (60.8)	112 (62.9)	102 (58.6)
Female	138 (39.2)	66 (37.1)	72 (41.4)
Identified as at high risk per Kaiser-Permanente criteria ^c			
Yes	67 (19.0)	35 (19.7)	32 (18.4)
No	285 (81.0)	143 (80.3)	142 (81.6)
Asthma health-care visits in prerandomization year, No.			
≤ 1	205 (58.2)	105 (59.0)	100 (57.5)
> 1	147 (41.8)	73 (41.0)	74 (42.5)
Primary caregiver smoker ^d			
Yes	145 (41.7)	73 (41.2)	72 (42.1)
No	203 (58.3)	104 (58.8)	99 (57.9)
Sites of exposure ^e			
Child's primary home	255 (72.4)	134 (75.3)	121 (69.5)
Grandparents' home	35 (9.9)	16 (9.0)	19 (10.9)
Other child-care setting ^f	71 (20.2)	32 (18.0)	39 (22.4)
Race/ethnicity			
White	87 (24.7)	42 (23.6)	45 (25.9)
Black	112 (31.8)	61 (34.3)	51 (29.3)
Asian/Pacific Islander	32 (9.1)	18 (10.1)	14 (8.1)
Hispanic	36 (10.2)	18 (10.1)	18 (10.3)
American Indian/Alaska Native	1 (0.3)	0 (0.0)	1 (0.6)
> one race/ethnicity reported	81 (23.0)	37 (20.8)	44 (25.3)
Unknown or not reported	3 (0.9)	2 (1.1)	1 (0.6)
Education of primary caregiver ^g			
Less than high school diploma	20 (5.9)	11 (6.4)	9 (5.3)
High school diploma/some college	273 (80.1)	140 (81.4)	133 (78.7)
4-y college degree or higher education	48 (14.1)	21 (12.2)	27 (16.0)
Household income/y ^h			
≤ \$40,000	135 (43.0)	71 (44.1)	64 (41.8)
> \$40,000	179 (57.0)	90 (55.9)	89 (58.2)
Study site			
Diablo	68 (19.3)	32 (18.0)	36 (20.7)
Hayward	23 (6.5)	11 (6.2)	12 (6.9)
Napa-Solano	170 (48.3)	88 (49.4)	82 (47.1)
Oakland	19 (5.4)	10 (5.6)	9 (5.2)
Richmond	37 (10.5)	19 (10.7)	18 (10.3)
Santa Clara	9 (2.6)	6 (3.4)	3 (1.7)
San Francisco	10 (2.8)	4 (2.2)	6 (3.5)
South San Francisco	16 (4.6)	8 (4.5)	8 (4.6)

Data are presented as mean ± SD or No. (%). CCR = cotinine to creatinine ratio; LET'S = Lowering Environmental Tobacco Smoke: LET'S Manage Asthma trial; UC = usual care.

^aThere were no significant differences between the intervention and control groups.

^bMean values were calculated from the results of the three prerandomization urine tests.

^cSee "Materials and Methods" section for Kaiser Permanente criteria for high-risk classification of pediatric asthma.

^dIncludes those who quit within the past 6 mo; No. = four missing.

^ePercentages add to > 100% because of multiple sites of exposure.

^fOther child-care settings include day-care centers, the day-care provider's home, relative or sitter care in the child's home, Head Start programs, and preschool, elementary school, or middle school.

^gNo. = 11 missing.

^hNo. = 38 missing.

asthma-related use of health-care services, thereby balancing the inherent difference in the intrinsic power of comparisons on dichotomous vs continuous variables and reducing the chance of a type II error for the use-of-health-care-services outcome. The $P < .05$ criterion was applied for all secondary outcomes.

A separate multivariate model was used to estimate each outcome. All reported baseline values are unadjusted, and all follow-up values and β -coefficients are fully adjusted for the five randomization variables and the baseline value of the outcome variable. Per the MacArthur criteria,¹⁸ we evaluated the

randomization-balancing variables as potential intervention effect modifiers. All analyses were performed using SAS, version 9.0 (SAS Institute; Cary, North Carolina).

RESULTS

Recruitment occurred from April 2003 to September 2005. Three hundred eighty-four families met all eligibility criteria for participation, and 352 were randomized (Fig 1). Three hundred thirty-four (94.9%) provided questionnaire data and/or a urine sample at the 6-month follow-up visit, and 336 (95.5%) at the 12-month follow-up visit. Baseline and follow-up data on the use of health-care services and pharmacy dispensing were available for all participants.

Baseline Characteristics

The intervention and control groups were comparable at baseline on all of the balancing variables (Table 1), including primary caregiver smoking status. Nearly all primary caregivers were high school graduates (94.1%), and 14.1% had a college degree. Overall, 72.4% of the children were exposed to tobacco smoke in their home, and 41.7% had a primary caregiver who smoked. The majority of children were boys (60.8%), the average age was 7.9 years, the sample was ethnically diverse, and 19.0% had "high-risk" asthma.

Primary Outcomes

Secondhand Smoke Exposure: The mean CCR decreased in both groups (Fig 2). The intervention was associated with a lower mean follow-up for the natural logarithm of the cotinine to creatinine ratio (lnCCR) compared with that seen in children who received usual care, but the intervention effect did not reach the preestablished $P \leq .01$ significance criterion (β coefficient = -0.307 ; 95% CI, -0.633 to

FIGURE 2. Distribution of the mean baseline and mean follow-up log CCR values, by group. The mean value is represented by the + sign, and the median value is represented by the horizontal line in the box. The box represents the interquartile range of values (25th-75th percentiles). The lowest and highest hash marks represent the minimum and maximum observations, respectively. The mean baseline lnCCR is based on the mean of the three pre-randomization urinalyses. The mean baseline lnCCR in the LET'S group = $2.53 (\pm 1.07)$, and in the usual care (UC) group = $2.68 (\pm 1.07)$. The mean follow-up lnCCR is based on the mean of the 6-month and 12-month follow-up urinalyses. The mean baseline lnCCR in the LET'S group = $1.11 (\pm 1.84)$, and in the UC group = $0.98 (\pm 1.83)$. □ = UC group; ■ = LET'S intervention group. CCR = cotinine to creatinine ratio; lnCCR = natural logarithm of the cotinine to creatinine ratio. See Figure 1 legend for expansion of the other abbreviation.

0.018 ; $P = .064$) (Table 2). Consistent with the pooled analysis, there was not an overall intervention effect on the lnCCR at either the 6-month or 12-month follow-up visits (data not shown).

Asthma Health-care Services Use: In the follow-up year, the number of asthma visits decreased slightly in both groups (Figs 3A, 3B). There was no evidence of an

Table 2—Effect of LET'S Intervention at Follow-up Visits, Relative to Usual Care, on Primary Outcomes and Medication Use

Outcomes at Follow-up Visit	No.	β Coefficient ^a for LET'S Intervention ^b	95% CI for β Coefficient	P Value
Primary outcomes				
lnCCR	337	-0.307	$(-0.633 \text{ to } 0.018)$	.064
Asthma-related HCU (> 1 ; ≤ 1)	348	0.035^c	$(-0.208 \text{ to } 0.277)$	.78
Asthma-related HCU counts	348	0.072	$(-0.272 \text{ to } 0.417)$	.68
Asthma-related ED visits/hospitalizations (≥ 1 ; < 1)	348	0.164^c	$(-0.282 \text{ to } 0.610)$	.47
Medication use				
Controller CMA	331	-0.039	$(-0.104 \text{ to } 0.026)$	.24
Beclomethasone canister equivalents	331	-0.239	$(-0.809 \text{ to } 0.331)$	.41

CMA = cumulative medication acquisition; HCU = health-care services use; lnCCR = natural logarithm of the cotinine to creatinine ratio. See Table 1 legend for expansion of other abbreviations.

^aExcept where noted, the β coefficient is a linear regression coefficient estimated from a fully adjusted generalized linear regression model. The full model is adjusted for group, balancing variables, site, and baseline value of specific outcome.

^bUrinary creatinine level is the referent.

^cThe β coefficient is log odds estimated from a fully adjusted logistic regression model. The full model is adjusted for group, balancing variables, site, and baseline value of specific outcome.

FIGURE 3. A, Distribution of asthma-related medical visits during the prereandomization year, by group. The LET'S group = 1.66 visits per year (± 1.86), the UC group = 1.72 visits per year (± 2.13). B, Distribution of asthma-related medical visits during the follow-up year, by group. The LET'S group = 1.26 visits per year (± 1.73), the UC group = 1.30 visits per year (± 1.94). $\square$ = UC group; $\blacksquare$ = LET'S intervention group. See Figure 1 and 2 legends for expansion of the abbreviations.

intervention effect on the odds of having > 1 asthma-related visit (β coefficient = 0.035; 95% CI, -0.208 to 0.277 ; $P = .78$) (Table 2). Results for the secondary outcomes are available in e-Table 1.

Parental Behavioral Change

At the follow-up visits, many parents in both groups reported engaging in behaviors aimed at reducing their child's tobacco smoke exposure (Table 3). After accounting for the baseline home smoking policy, there was a trend toward greater odds of a home smoking ban for the intervention group (OR = 1.81; 95% CI, 0.98-3.33; $P = .057$) (Table 4). The intervention was not differentially associated with other individually relevant and potentially beneficial parental behaviors.

Reduced Tobacco Smoke Exposure in Children at High Risk

High-risk status was the single balancing variable that appeared to modify the intervention effect on lnCCR (Fig 4). In the baseline year, children at high risk had a significantly higher rate of asthma-related medical visits, including ED visits and hospitalizations, and significantly more asthma controller and rescue medications were dispensed for them than for children who were not at high risk (data not shown). In the multivariable model, the group by high-risk status interaction term was significantly associated with follow-up lnCCR (β coefficient = -0.994 ; 95% CI, -1.810 to -0.178 ; $P = .017$). Among children at high risk (but not children at lower risk), the intervention was associated with a significantly lower follow-up lnCCR than for children who received usual care (β coefficient = -1.068 ; 95% CI, -1.816 to -0.319 ; $P = .006$).

The results were somewhat similar when the follow-up data points were kept separate, with the intervention associated with a lower lnCCR at the 6-month follow-up visit among children at high risk (β coefficient = -1.057 ; 95% CI, -1.973 to -0.142 ; $P = .02$) and a beneficial but nonsignificant effect on lnCCR at the 12-month follow-up visit (β coefficient = -0.884 ; 95% CI, -1.833 to 0.065 ; $P = .07$). However, the sizes of the intervention effect did not differ substantially between the 6-month and 12-month follow-up visits.

Health-care Services Use in Children at High Risk

Unlike tobacco smoke exposure, there was no observed effect among children at high risk who received the intervention in terms of reduced use of health-care services (β coefficient = -0.0150 ; 95% CI, -1.204 to 1.174 ; $P = .98$).

Behavioral Change in Parents of Children at High Risk

Because of the apparent role of high-risk status as an effect modifier, we reexamined the four parental

Table 3—Proportionate Distribution of Parental Behaviors Related to Their Child's Secondhand Smoke Exposure at Baseline and Follow-up Visits, by Group

Characteristic	Baseline			12-mo Follow-up Visit		
	LET'S Intervention	UC	P Value	LET'S Intervention	UC	P Value
Home smoking policy ^a						
No smoking allowed	117 (65.7)	116 (66.7)	.85	142 (84.0)	131 (77.1)	.11
Smoking allowed	61 (34.3)	58 (33.3)	...	27 (16.0)	39 (22.9)	...
Caregiver smoking status ^b						
Nonsmoker	104 (58.8)	99 (57.9)	.87	93 (62.8)	108 (70.6)	.15
Smoker	73 (41.2)	72 (42.1)	...	55 (37.2)	45 (29.4)	...
Exposed in day care ^{c,d}						
Yes	29 (16.4)	39 (22.5)	.15	19 (11.2)	15 (8.8)	.46
No	148 (83.6)	134 (77.5)	...	150 (88.8)	155 (91.2)	...
No. of exposure sources ^e						
None	1 (0.6)	3 (1.7)	.10	22 (14.9)	24 (15.5)	.79
One	122 (68.5)	98 (56.3)	...	80 (54.1)	90 (58.1)	...
Two	46 (25.8)	60 (34.5)	...	44 (29.7)	40 (25.8)	...
Three	9 (5.1)	13 (7.5)	...	2 (1.4)	1 (0.6)	...

Data are presented as No. (%) or P value. See Table 1 legend for expansion of abbreviations.

^aSample size: at baseline, LET'S, n = 178; UC, n = 174; at follow-up visit, LET'S, n = 169; UC, n = 170.

^bSample size: at baseline, LET'S, n = 177; UC, n = 171; at follow-up visit, LET'S, n = 148; UC, n = 153.

^cSample size: at baseline, LET'S, n = 177; UC, n = 173; at follow-up visit, LET'S, n = 169; UC, n = 170.

^dTobacco smoke exposure in day care includes all children; children not in day care were categorized as having no day-care exposure.

^eSample size: at baseline, LET'S, n = 178; UC, n = 174; at follow-up visit, LET'S, n = 148; UC, n = 155.

DISCUSSION

behaviors, stratified by high-risk status (Table 4). Similar to the overall sample, children at high risk in the intervention group had a trend toward greater odds (OR = 5.08; 95% CI, 0.87-29.7; *P* = .07) of living in a home with smoking prohibitions at the follow-up visits than did children at high risk in the usual care group. There was no intervention effect among children at high risk for the other smoke exposure reduction behaviors (Table 4).

Asthma Controller Medication Use

Both groups acquired sufficient controller medication for use as prescribed on approximately 30% of the days during the prerandomization year. During the 12-month follow-up period, controller medication acquisition remained essentially the same in both treatment groups (Table 2).

In the overall sample, the LET'S intervention did not have a statistically or clinically significant effect on any of the primary or secondary outcomes. This is a disappointing outcome, but one that is not unusual in the history of the development of what have subsequently become effective tobacco control interventions.

However, in children who were at high risk for subsequent exacerbations, the intervention was associated with substantially (~90%) and significantly lower secondhand smoke exposure compared with children who received usual care, suggesting that parents whose children were having more asthma-related problems were more motivated to reduce their children's exposure. Smoke exposure is likely to have been one of the factors contributing to their high-risk status. Such children stand to benefit substantially from exposure reduction, and indeed,

Table 4—LET'S Intervention Effect on the Relative Odds of Parental Behaviors Aimed at Reducing Secondhand Smoke Exposure, for the Sample Overall and by High-risk Status

Behavior	Overall Sample		High-Risk Status		No High-Risk Status	
	OR ^a (95% CI)	P Value	OR ^b (95% CI)	P Value	OR ^b (95% CI)	P Value
No smoking in the home	1.81 (0.98-3.33)	0.057	5.08 (0.87-29.7)	.07	1.54 (0.8-2.98)	.20
No sources of tobacco smoke exposure	0.99 (0.52-1.9)	0.98	1.36 (0.36-5.12)	.64	0.90 (0.43-1.9)	.78
Caregiver does not smoke	0.68 (0.35-1.34)	0.27	0.73 (0.16-3.35)	.69	0.67 (0.32-1.42)	.30
No tobacco smoke exposure at day care	0.66 (0.31-1.39)	0.27	0.18 (0.02-1.64)	.13	0.86 (0.37-1.98)	.72

See Table 1 legend for expansion of abbreviation.

^aORs estimated from logistic regression models controlling for group and parental behavior at baseline.

^bORs estimated from logistic regression models controlling for group, high-risk status, parental behavior at baseline, and the group by high-risk status interaction term.

FIGURE 4. Distribution of mean baseline and follow-up log CCR values, by group and high-risk status. The mean value is represented by the + sign, and the median value is represented by the horizontal line in the box. The box represents the interquartile range of values (25th-75th percentiles). The lowest and highest hash marks represent the minimum and maximum observations, respectively. The mean baseline lnCCR is based on the mean of the three prerandomization urinalyses. The mean follow-up lnCCR is based on the mean of the 6-month and 12-month follow-up urinalyses. Among children who are at high risk, the mean baseline lnCCR in the LET'S group = 2.72 (± 1.15), and in the UC group = 2.49 (± 0.99). The mean follow-up lnCCR in the LET'S group = 0.32 (± 1.82), and in the UC group = 1.07 (± 1.81). Among children who are not at high risk, the mean baseline lnCCR in the LET'S group = 2.67 (± 1.05), and in the UC group = 2.53 (± 1.09). The mean follow-up lnCCR in the LET'S group = 1.15 (± 1.80), and in the UC group = 1.12 (± 1.86). □ = UC group; ■ = LET'S intervention group. See Figures 1 and 2 legends for expansion of the abbreviations.

65% of the children at high risk in the intervention group had undetectable levels of urinary cotinine at the end of the study. The LET'S intervention could potentially be further strengthened by extending its duration and by the provision of pharmacotherapy for treatment of caregiver tobacco dependence.¹⁹ Forty-two percent of the children in both the full sample and the high-risk subgroup had primary caregivers (generally mothers) who were smokers, and approximately 73% lived in homes with some person (generally a parent) who smoked.

The significant *P* value associated with the interaction between children with high-risk status and those in the experimental group (*P* = .017) is suitably low so that the intervention effect is unlikely to be a false positive. Nevertheless, given the modest sample of participants who were at high risk (*n* = 67) and the inherently complex nature of subgroup analyses,²⁰ the observed benefit needs to be confirmed in larger samples of children at high risk, especially in populations with a higher baseline rate of use of health-care

services and poorer clinical status than the children in the LET'S sample. The present study was not planned to have adequate power to detect subgroup effects in these variables.

Prohibiting smoking in the home was the only behavior of the four examined that was associated with the intervention, suggesting a potential explanatory mechanism for the decrease in exposure. The benefit of establishing a smoke-free-home policy has been demonstrated previously.²¹⁻²³ Although not definitive, the present finding with regard to parental behavioral change should be confirmed in future research, including in larger studies of children at high risk.

The LET'S intervention was not associated with a higher rate of smoking cessation on the part of the child's primary caregiver. This is perhaps not surprising since reduction of the child's exposure, rather than caregiver smoking cessation specifically, was the primary intervention goal, and this goal is appropriate given the significant exposure observed in children screened for the LET'S study whose primary caregivers did not smoke. This exposure came from other household members, regular visitors to the home, grandparents, and day-care providers.³ In the present study, less than half of the primary caregivers were smokers, and exposure to a day-care provider who smoked was associated with cotinine levels comparable to those of children whose primary caregiver smoked, and when both smoked, the exposure was additive.

Further, smoking cessation remains a significant challenge for all interventions that target individuals who are not seeking assistance in quitting. However, since cessation would benefit both the child and the adult, offering pharmacotherapy and behavioral counseling for cessation to all of the child's smoking caregivers, in conjunction with the basic LET'S approach, could potentially increase its effectiveness.

This study expands on prior research findings by Wilson et al⁹ in which an earlier version of the LET'S cotinine feedback and behavioral counseling intervention resulted in a significant reduction in the use of health-care services and a (nonsignificant) trend toward lower urinary cotinine levels in the intervention group. The overall intervention effect estimates in the two studies are very similar, despite the substantial differences between the populations—demographically, socioeconomically, and in the sources of their medical care. However, the effect in children at high risk in the present study was much larger than the overall effect in the prior study. It is possible that a similar subgroup effect existed in the earlier study and was responsible for the observed overall trend. However, high-risk status was not determined in the earlier sample.

In observational studies, a lack of or very low levels of tobacco smoke exposure have been associated with lower rates of asthma-related use of health-care services,²⁴ and both exposure and use of health-care services for asthma tend to decrease with age during childhood. Unlike the previous study, we did not observe a differential reduction in the use of health-care services in either the sample overall or the high-risk subset. The present high-risk subset was smaller than the prior study's overall sample, and the LET'S trial was not powered to detect the hypothesized difference in the use of health-care services in subgroup analyses. The LET'S trial participants also had relatively low asthma-related use of health-care services in the prerandomization year. It is possible that a greater reduction in exposure and/or a greater focus on children with more frequent asthma-related use of health-care services would have been necessary in order to detect an effect on use in the present subset.

Use of High-Risk Asthma Lists

When this study was conducted, Kaiser Permanente Northern California routinely generated high-risk lists and circulated them to patients' primary care providers. Providers were encouraged to reach out to these patients to improve their asthma control, but no specific assessment of secondhand smoke exposure was performed and no tobacco-related messages were given except at the initiative of individual physicians. In the present study, the results of the urinary cotinine measurements were not provided to the child's primary care provider or placed in the child's medical record. Even though the study was not able to demonstrate clinical benefits associated with the intervention (ie, reduced health-care visits, improved symptoms, and increased lung function), the results suggest that the intervention can be effective in reducing smoke exposure for this subgroup of patients with asthma who are at high risk, given both identification of the children at high risk and objective assessment of their exposure, which constitutes a significant step forward toward an intervention that can improve clinical outcomes as well.

Strengths and Limitations

The strengths of this study include its randomized and tightly controlled experimental design and the use of objective outcome measures with multiple measurements before and after randomization. The stage-of-change-based intervention addressed the caregiver's readiness to make each of the changes that would be required to eliminate the individual child's exposure from specific sources. Finally, the sample size was reasonably large and broadly representative. The limitations of the study include the

relatively small number of children at high risk and the lack of statistical power for subgroup analyses of either main effects or potential mediators.

CONCLUSIONS

The study did not demonstrate an effect of the LET'S intervention on secondhand tobacco smoke exposure in the reference population of children with asthma. However, it did provide some evidence, short of conventional statistical proof, of an effect in children whose use of health-care services and overuse of rescue medication would classify them as having high-risk asthma.

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Dr Wilson: contributed to the conception and design of the trial, obtaining of funding, supervision of the study protocol and data acquisition, interpretation of data analyses, and drafting and critical revision of the manuscript.

Dr Farber: contributed to the conception and design of the trial, obtaining of funding, and supervision of clinical personnel, and is responsible for the quality control review of the spirometry measurements. Dr Farber also contributed to the interpretation of the data analyses and the drafting and critical revision of the manuscript.

Dr Knowles: contributed to the statistical analysis and interpretation of the data and the drafting and critical revision of the manuscript.

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Additional Information: The e-Appendix and e-Table can be found in the Online Supplement at <http://chestjournal.chestpubs.org/content/139/3/581/suppl/DC1>.

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