



CLINICAL RESEARCH ARTICLE

Duration of breastmilk feeding of NICU graduates who live with individuals who smoke

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BACKGROUND: Breast milk has many benefits for infants, but initiating breastfeeding/pumping can be difficult for mothers of preterm infants, especially those who smoke (or live with individuals who smoke). The primary aim of this study was to identify risks for breastfeeding/pumping cessation with neonatal intensive care unit (NICU) infants' mothers who smoke or live with individuals who smoke, using a novel survival-analytic approach.

METHODS/DESIGN: Mothers ($N = 360$) were recruited for a secondhand smoke prevention intervention during infants' NICU hospitalizations and followed for ~6 months after infant discharge. Data were obtained from medical records and participant self-report/interviews.

RESULTS: The sample was predominantly ethnic/racial minorities; mean age was 26.8 (SD = 5.9) years. One-fifth never initiated breastfeeding/pumping ($n = 67$; 18.9%) and mean time-to-breastfeeding cessation was 48.1 days (SD = 57.2; median = 30.4 [interquartile range: 6.0–60.9]). Education, length of stay, employment, race/ethnicity, number of household members who smoke, and readiness-to-protect infants from tobacco smoke were significantly associated with breastfeeding cessation. Further, infants fed breast milk for ≥ 4 months had 42.7% more well-child visits ($p < 0.001$) and 50.0% fewer respiratory-related clinic visits ($p < 0.05$).

CONCLUSIONS: One-quarter of infants admitted to NICUs will be discharged to households where individuals who smoke live; we demonstrated that smoking-related factors were associated with mothers' breastfeeding practices. Infants who received breast milk longer had fewer respiratory-related visits.

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IMPACT:

- One-quarter of NICU infants will be discharged to households where smokers live.
- Initiating/sustaining breastfeeding can be difficult for mothers of preterm NICU infants, especially mothers who smoke or live with others who smoke.
- Education, employment, race/ethnicity, length of stay, household member smoking, and readiness-to-protect infants from tobacco smoke were significantly associated with time-to-breastfeeding cessation.
- Infants fed breast milk for ≥ 4 months had 42.7% more well-child visits and 50.0% fewer respiratory-related clinic visits, compared to infants fed breast milk < 4 months.
- Data support intervention refinements for mothers from smoking households and making NICU-based healthcare workers aware of risk factors for early breastfeeding cessation.

INTRODUCTION

Providing breast milk to infants has well-documented benefits (e.g., immune protection and regulation of metabolism), and may reduce maternal risks for postpartum stress, type-2 diabetes, and some cancers.^{1,2} Infants admitted to the neonatal intensive care unit (NICU) are often at risk for significant health consequences, increasing the importance of breastfeeding.^{3,4} For example, necrotizing enterocolitis (NEC) is significantly less prevalent in infants admitted to NICUs who were fed breast milk compared to

infants exclusively fed formula.^{5,6} Breast milk feeding is also associated with a lower risk for respiratory diseases^{7,8}—a critical consideration for vulnerable infants hospitalized in a NICU due to their increased risk for bronchopulmonary dysplasia, pneumonia, and asthma.⁹ Despite health risks from early breastfeeding cessation, fewer preterm infants and infants admitted to a NICU for other reasons receive any breast milk compared to term infants at the same postnatal ages.¹⁰ A majority of mothers of infants admitted to a NICU must breastfeed indirectly (i.e., pump breast

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milk and feed it to their infants via bottle, gastrostomy tube, or other methods) until infants are developmentally able to feed at the breast (i.e., coordinate sucking, swallowing, and breathing.^{11,12}) Therefore, our definition of early breastfeeding cessation includes cessation of breast pumping and subsequent cessation of all indirect breastfeeding.

The American Academy of Pediatrics recommends exclusive breastmilk feeding for the first 6 months of life and encourages continued breastmilk feeding through 1 year or longer.¹³ Similarly, the World Health Organization recommends exclusive breastmilk feeding until 6 months of age, after which safe and adequate complementary foods are introduced while continuing to breastfeed until up to age 2 years.¹⁴ Five-year US estimates (from 2011–2016) show increases for infants who received *any* breast milk;^{1,15} however, 16.2% never receive any breast milk and 42.7% have stopped receiving breast milk by 6 months of age, with even fewer receiving breast milk exclusively.¹⁵ For preterm infants (born <37 weeks) and other vulnerable infants, receiving breast milk for 6 months may hold the greatest health benefits.^{12,16} However, at least one study documented benefits of receiving breast milk for at least 4 months (i.e., infants not receiving breast milk had triple the risk for severe respiratory tract illness-related hospitalizations, compared to infants exclusively breastfed for 4 months or longer⁸).

Dozens of reasons exist for stopping breastfeeding early.^{11,13,16} Unique risk factors for failure-to-initiate or early cessation of breastfeeding are known for mothers of preterm infants^{11,12,16} (e.g., late preterm infants [LPI; born between 34 0/7 and 36 6/7 weeks gestation] fatigue more easily), and difficulties are exacerbated for infants born <34 weeks. Extended NICU hospitalizations can also impose socioeconomic difficulties (e.g., returning to work before infant discharge¹⁷) for sustaining adequate breastmilk reserves.

Maternal smoking and smoke exposure has also been found to play a considerable role in non-initiation or early discontinuation of breastfeeding.^{6,18,19} Smoking while breastfeeding should be discouraged due to associations with adverse infant health outcomes (e.g., sudden infant death syndrome²⁰) and low milk supply.^{21,22} Overall benefits of breast milk, however, are perceived by many health professionals to outweigh the risk of harm from infants' exposure to tobacco smoke constituents (e.g., carcinogens).^{23–25} Mothers who smoke or live with individuals who smoke comprise a quarter of mothers of NICU infants,²⁶ and this sizeable population of mothers may receive mixed messages or worry about breastfeeding while living in an environment saturated with secondhand and thirdhand smoke,²⁷ putting them at elevated risk for early breastfeeding cessation.²⁸ Interventions to increase breastfeeding with this population may need adaptation after a better understanding of risk factors for early cessation.

Our prior work demonstrated that mothers who smoke or live with individuals who smoke, and had an infant at high-respiratory risk in the NICU, tended to initiate breastfeeding at relatively low levels (52.9%), with mothers who smoke reporting the lowest levels (41.7%).²⁸ However, these analyses did not explore breastfeeding duration or factors associated with early cessation. Identifying modifiable risk factors and planning for difficulties that influence initiation or continued breastfeeding holds significant value.²⁹ The primary aim of this secondary-data analysis employed a novel statistical approach³⁰ to maximize identification of modifiable risk factors for breastfeeding cessation with mothers of infants in the NICU, who also smoked or lived with individuals who smoke. Secondary aims explored associations between duration of breastfeeding and infants' medical visits and reported mothers' reasons for breastfeeding cessation. We hypothesized that maternal smoking and lower socioeconomic status (income, education) would be associated with shorter breastfeeding

duration (e.g., refs. ^{29,31}) and that longer breastfeeding duration would be associated with fewer medical visits due to infant illnesses.

METHODS

This study was approved by our institutional and hospital institutional review boards (parent study clinicaltrials.gov registration: NCT01726062).^{32,33}

Participants and design

Data were collected during a parallel, two-group randomized controlled trial (RCT) that assessed a motivational intervention to reduce infant exposure to secondhand smoke post-NICU discharge.^{32,33} Mothers ($N=360$) were recruited from a large, urban children's hospital with 1400 admissions/year from September 2012 to June 2018. Eligible participants had infants admitted to the NICU, reported ≥ 1 individual who smokes living in the home, spoke English or Spanish, and lived ≤ 50 -mile hospital radius (due to home-based assessments). Participants with severe cognitive or psychiatric impairment were ineligible.

Measures

Structured participant interviews with research assistants (RAs) occurred at baseline (during hospitalization) and at three home-based follow-ups after infant discharge. Baseline participant and household characteristics (e.g., education, pregnancy/delivery history [e.g., number of other children, infant birthweight]), and smoking history were collected via self-report. Electronic health records were abstracted for NICU length of stay.

All predictor variables were measured at baseline and are listed in Table 1 and spanned several broad categories potentially related to breastfeeding duration. Variables included infant health variables, participant/household socio-demographics, participant depression/anxiety/stress subscales, neighborhood variables and subscales, processes-of-change subscales, pregnancy-related variables, treatment condition (of parent RCT), and smoking-/smoke exposure-related variables and subscales (including subscales assessing baseline readiness-to-protect infants from tobacco smoke). Table 2 summarizes scales/subscales completed by participants.

The primary outcome variable, length-of-time breastfeeding (days of infant life), was measured by RAs interviewing mothers on an exhaustive list of possible infant-feeding methods at each study visit (i.e., gastrostomy tube [breast milk or formula], intravenously, bottle [breast milk or formula], breastfeeding at the breast, solid food, or other). No mothers endorsed infants receiving donor breast milk. Mothers reported precise time ranges the infant received breast milk (in total) based on chronological (unadjusted) infant age and reported reasons for stopping (see Table 3).

Mothers were queried at each post-hospitalization assessment about the number of doctors' (outpatient), emergency room/urgent care, hospital, and ICU visits since discharge (or since the previous visit). Visit reasons (well-child, respiratory, or non-respiratory) were collected.

Procedure

Participants were approached in the NICU and randomized to a motivational interviewing plus financial incentives intervention (intervention condition) or conventional care. Assessments took ~45 min. Baseline (NICU) assessments occurred on average 1–2 weeks after delivery and NICU admission.³³ Three follow-up (post discharge), home-based assessments occurred ~2 weeks, 2 months, and 6 months post-NICU discharge. Participants gave informed consent and received gift card compensation for completing visits.

Table 1. Proportional hazards model results of baseline predictors of length of breastmilk provision to infants from a NICU.

Predictor	M (SD)	Univariate Cox proportional hazards regression (32 separate models)			Penalized Cox proportional hazards regression			Multiple Cox proportional hazards regression (reduced model)			
		Estimate (SE)	Hazard ratio (95% CI)	p Value	Penalized estimate	Penalized hazard ratio	Hazard ratio % change	Estimate (SE)	Hazard ratio (95% CI)	p Value	Hazard ratio % change
Birth weight (kg), M (SD)	2.2 (1)	0.12 (0.06)	1.13 (1.01, 1.26)	0.035	0.065	0.065	12.6%	0.007	1.007	0.007	0.7%
Maternal age (years), M (SD)	26.8 (5.9)	-0.02 (0.01)	0.98 (0.96, 1.00)	0.065	0.107	0.107	-1.8%	0.019	1.019	0.019	1.9%
Number of children ^a , M (SD)	2.5 (1.5)	0.10 (0.04)	1.10 (1.03, 1.18)	0.006	0.030	0.030	10.3%	-0.054	0.947	-0.054	-5.3%
Education (years), M (SD)	12.7 (2)	-0.12 (0.03)	0.88 (0.84, 0.93)	<0.001	<0.001	<0.001	-11.5%	-0.015	0.985	-0.015	-1.5%
Income ^b , M (SD)	1.9 (2)	-0.06 (0.03)	0.94 (0.89, 0.99)	0.025	0.059	0.059	-6.2%	0.014	1.014	0.014	1.4%
Prenatal visit initiation (week), M (SD)	10.2 (6.3)	0.02 (0.01)	1.02 (1.00, 1.04)	0.021	0.057	0.057	2.2%	0.017	1.017	0.017	1.7%
Age when started smoking (years), M (SD)	8 (9.2)	0.01 (0.01)	1.01 (1.00, 1.03)	0.017	0.051	0.051	1.5%	0.028	1.028	0.028	2.8%
Number of individuals who smoke in the home, M (SD)	1.5 (0.8)	0.25 (0.07)	1.28 (1.12, 1.48)	<0.001	0.006	0.006	28.4%	0.020	1.020	0.020	2.0%
Encourage/discourage smoking, M (SD)	-4.2 (4.2)	0.04 (0.01)	1.04 (1.01, 1.07)	0.003	0.021	0.021	4.2%	-0.003	0.997	-0.003	-0.3%
Confidence to avoid secondhand smoke, M (SD)	59.1 (12.9)	-0.01 (0.01)	0.99 (0.98, 1.00)	0.032	0.065	0.065	-0.9%	-0.019	0.981	-0.019	-1.9%
CES-D total score (depression), M (SD)	16.9 (11.1)	0.00 (0.01)	1.00 (0.99, 1.01)	0.923	0.923	0.923	0.0%	-0.004	0.996	-0.004	-0.4%
Environmental Tobacco Knowledge Scale, M (SD)	7.2 (1.8)	-0.09 (0.03)	0.92 (0.86, 0.98)	0.007	0.030	0.030	-8.3%	-0.004	0.996	-0.004	-0.4%
Generalized anxiety, M (SD)	6.6 (5.8)	-0.01 (0.01)	0.99 (0.97, 1.01)	0.402	0.513	0.513	-0.8%	-0.031	0.969	-0.031	-3.1%
Readiness-to-protect from tobacco (home), M (SD)	8.9 (2.2)	-0.06 (0.02)	0.95 (0.90, 0.99)	0.024	0.059	0.059	-5.4%	-0.010	0.990	-0.010	-1.0%
Readiness-to-protect from tobacco (car), M (SD)	8.7 (2.5)	-0.06 (0.02)	0.95 (0.91, 0.99)	0.011	0.039	0.039	-5.4%	0.009	1.009	0.009	0.9%
Readiness-to-protect (all tobacco sources), M (SD)	8.8 (2.3)	-0.08 (0.02)	0.92 (0.88, 0.97)	0.001	0.006	0.006	-7.9%	0.007	1.007	0.007	0.7%
MILES NICU Stress: sights and sounds, M (SD)	1.7 (0.8)	-0.16 (0.08)	0.85 (0.73, 0.99)	0.034	0.065	0.065	-14.9%	0.007	1.007	0.007	0.7%
MILES NICU Stress: infant appearance, M (SD)	2.6 (1.1)	-0.07 (0.05)	0.93 (0.84, 1.03)	0.150	0.228	0.228	-7.2%	0.007	1.007	0.007	0.7%
MILES NICU Stress: parental role alteration, M (SD)	3.5 (1.3)	-0.09 (0.04)	0.91 (0.83, 0.99)	0.035	0.065	0.065	-9.0%	0.007	1.007	0.007	0.7%
Neighborhood problems, M (SD)	15.6 (4.5)	0.02 (0.01)	1.02 (1.00, 1.05)	0.074	0.117	0.117	2.2%	0.007	1.007	0.007	0.7%
Neighborhood help, M (SD)	13.8 (5.8)	0.01 (0.01)	1.01 (0.99, 1.03)	0.453	0.530	0.530	0.7%	0.007	1.007	0.007	0.7%
Neighborhood social cohesion, M (SD)	16.9 (3.5)	-0.02 (0.02)	0.98 (0.95, 1.02)	0.314	0.415	0.415	-1.6%	0.007	1.007	0.007	0.7%
Neighborhood vigilance, M (SD)	17.2 (3.7)	0.00 (0.01)	1.00 (0.97, 1.02)	0.738	0.781	0.781	-0.5%	0.007	1.007	0.007	0.7%
Processes of Change: Experiential Scale, M (SD)	15.8 (4.9)	-0.01 (0.01)	0.99 (0.96, 1.01)	0.292	0.399	0.399	-1.3%	0.007	1.007	0.007	0.7%
Processes of Change: Behavioral Scale, M (SD)	19 (5)	-0.01 (0.01)	0.99 (0.97, 1.02)	0.570	0.649	0.649	-0.7%	0.007	1.007	0.007	0.7%
PSS total score (stress), M (SD)	6 (3)	-0.01 (0.02)	1.00 (0.96, 1.03)	0.803	0.823	0.823	-0.5%	0.007	1.007	0.007	0.7%

Table 1. continued

Predictor	M (SD)	Univariate Cox proportional hazards regression (32 separate models)			Penalized Cox proportional hazards regression			Multiple Cox proportional hazards regression (reduced model)					
		Estimate (SE)	Hazard ratio (95% CI)	p Value	FDR p value	Hazard ratio % change	Penalized estimate	Penalized hazard ratio	Hazard ratio % change	Estimate (SE)	Hazard ratio (95% CI)	p Value	Hazard ratio % change
Gestational age (weeks), M (SD)	33.8 (4.6)	0.03 (0.01)	1.03 (1.01, 1.05)	0.013	0.041	2.9%	0.014	1.014	1.4%	-0.03 (0.01)	0.97 (0.95, 0.99)	<0.001	-3.0%
Infant length of stay (weeks), M (SD)	43.1 (52.2)	-0.03 (0.01)	0.97 (0.95, 0.98)	<0.001	0.004	-3.2%	-0.052	0.950	-5.0%				
Social deprivation index, M (SD)	76.1 (25.6)	0.01 (0.01)	1.00 (1.00, 1.01)	0.037	0.065	0.5%	0.002	1.002	0.2%				
MI condition (REF = CC) ^c , n (%)	178 (50.1%)	0.04 (0.11)	1.04 (0.84, 1.29)	0.705	0.781	4.3%							
Working (REF = not working), n (%)	269 (75.8%)	-0.37 (0.13)	0.69 (0.53, 0.89)	0.005	0.030	-31.0%	-0.028	0.972	-2.8%	-0.28 (0.14)	0.76 (0.58, 0.99)	0.043	-24.1%
Has car access (REF = no car access), n (%)	239 (67.3%)	-0.32 (0.12)	0.73 (0.58, 0.91)	0.006	0.030	-27.4%	-0.021	0.980	-2.0%	-0.23 (0.12)	0.80 (0.63, 1.02)	0.071	-20.2%
Pregnancy was planned (REF = not planned), n (%)	265 (74.7%)	-0.15 (0.13)	0.86 (0.67, 1.11)	0.242	0.355	-13.8%							
Has partner (REF = no partner), n (%)	306 (86.2%)	-0.18 (0.16)	0.83 (0.61, 1.14)	0.260	0.368	-16.6%							
Home smoking ban active (REF = no home ban), n (%)	214 (60.3%)	-0.31 (0.11)	0.73 (0.59, 0.92)	0.007	0.030	-26.5%	-0.019	0.981	-1.9%				
Car smoking ban active (REF = no car ban), n (%)	203 (57.8%)	-0.09 (0.11)	0.91 (0.73, 1.14)	0.413	0.513	-8.8%							
Current smoker (REF = non-smoker), n (%)	68 (19.2%)	0.28 (0.14)	1.33 (1.01, 1.74)	0.043	0.074	32.5%	0.002	1.002	0.2%				
Married or living together (REF = not single), n (%)	222 (62.5%)	-0.25 (0.11)	0.78 (0.62, 0.98)	0.031	0.065	-21.8%	-0.011	0.989	-1.1%				
White (REF = Black ^d), n (%)	38 (10.7%)	-0.06 (0.18)	0.94 (0.66, 1.34)	0.743	0.781	-5.7%							
Other race (REF = Black ^d), n (%)	28 (7.9%)	-0.53 (0.21)	0.59 (0.39, 0.88)	0.011	0.039	-41.2%	-0.031	0.969	-3.1%	-0.48 (0.21)	0.62 (0.41, 0.94)	0.026	-37.8%
Hispanic (REF = Black ^d), n (%)	69 (19.4%)	-0.11 (0.14)	0.90 (0.68, 1.18)	0.435	0.524	-10.3%							

Note: The univariate Cox proportional hazards regressions' (32 separate models) and multiple Cox proportional hazards regression (Reduced Model) coefficients are unstandardized and the penalized Cox proportional hazards regression coefficients are standardized.

^aNumber of children in the home included the hospitalized NICU infant.

^bIncome was measured on an author-constructed scale (and analyzed as a continuous variable), 0 = "<\$15,000 per year"; 1 = "\$15,000-\$24,999 per year"; 2 = "\$25,000-\$34,999 per year"; 3 = "\$35,000-\$44,999 per year"; 4 = "\$45,000-\$54,999 per year"; 5 = ">\$55,000 per year".

^cThis refers to whether the participant was in the parent trials intervention condition (or control condition [CC]) (33).

^dBlack was the reference group for race/ethnic comparisons (n = 220; 62.0%).

Statistical analyses

Five infants were missing the breastfeeding outcome variable. In general, frequency-related variables were analyzed dichotomously (e.g., maternal smoking [yes/no]), unless >2 response options are reported (e.g., income). Variables reported as means were analyzed as continuous variables.

Cox proportional hazards regression

Univariate Cox proportional hazards regression modeled time-to-breastfeeding cessation as a function of 41 covariates (after dummy-coding categorical predictors; see Table 1) via the *coxph()* and *cox.zph()* functions in R³⁴ with the *survival* package³⁵. The false discovery rate (FDR; ref. ³⁶) accounted for multiplicity across models. The proportional hazards assumption was evaluated via statistical testing of weighted residuals and graphical analysis of Schoenfeld residual plots.

Penalized Cox proportional hazards regression

Elastic-net penalized Cox proportional hazards regression concurrently modeled time-to-breastfeeding cessation as a function of all 41 covariates in one model. This optimized pure outcome prediction and explicated relationships between covariates and the primary outcome. The elastic-net machine-learning algorithm applies a multi-purpose shrinkage penalty to each model coefficient (e.g., coefficient magnitude reduction to zero and removal from the statistical equation), providing de facto variable selection. Shrinkage also alleviates multicollinearity issues via reduced variance in parameter estimation. The elastic-net shrinkage penalty biases estimate toward zero, minimizing changes to coefficients during variable selection. Full elastic-net details are beyond this manuscript's scope (see ref. ³⁰ for additional details). Elastic net was performed in R using the package *penalized*.³⁷

Model reduction

The final optimized model, determined via elastic net may be further simplified to maximize parsimony (with an increase in estimation bias and potential loss of predictive power) in a process called model reduction. Specifically, a stepwise-selection machine-learning algorithm, *backwards elimination*, reduces the elastic-net-derived model by iteratively removing predictors from the statistical equation until the Akaike information criterion (AIC) is no longer reduced by removing additional predictors. A simplified model that retains ~95% of the elastic-net-model fit may be considered a successful reduction,³⁸ maximizing interpretability and optimizing the parameter-to-sample-size ratio. However, the introduced bias inflates regression coefficients and generates potentially misleading *p* values, and as such should be viewed as exploratory. This two-stage modeling procedure has demonstrated utility in building parsimonious models in several areas.^{30,39,40} Model reduction was performed in R using the package *MASS*.⁴¹

Medical utilization models

We modeled medical-visit utilization across four settings (out-patient settings, emergency departments, hospitals, and ICUs) as a function of breastfeeding status at 4 and 6 months chronological (infant) age. Both timeframes have been associated with health benefits for infants in previous studies, as described in the "Introduction." Each setting was modeled as a count outcome using generalized linear modeling via the negative binomial distribution (determined by the lowest AIC compared to competing distributions; e.g., Poisson, and zero-inflated negative binomial distributions).

RESULTS

Sample Description

The final sample consisted of *N* = 355 participants, 334 (94.1%) of whom did not initiate or stopped breastfeeding during the study.

Participants were predominantly Medicaid recipients (*n* = 310; 87.3%) and Black/African-American (*n* = 220; 62.0%), with a mean age and mean education of 26.8 (SD = 5.9) and 12.7 (SD = 2.0) years, respectively. Typical of level-4 NICUs, significant variation was demonstrated on infant gestational age (range: 23–43 weeks; median [interquartile range (IQR)]: 35.0 [31.0–37.0] weeks) and birthweight (range: 0.43–5.52 kg; median [IQR]: 2.24 [1.48–2.92] kg). See Table 1 for other characteristics.

Time-to-breastfeeding cessation

The mean time-to-breastfeeding cessation was 48.1 (SD = 57.2) days (median = 30.4 [IQR: 6.0–60.9] days). A sizable minority (*n* = 67; 18.9%) never initiated breastfeeding. A Kaplan–Meier survival plot for time-to-breastfeeding cessation is presented in Fig. 1. A small minority were still breastfeeding ≥4 months (*n* = 57; 16.1%) and ≥6 months after infant birth (*n* = 11, 3.1%). However, some 6-month breastfeeding data were censored, as a few women were still breastfeeding when they completed their final assessment, but their infants were not yet 6 months old (*n* = 17 [of 355]; 4.8%).

Univariate Cox proportional hazards regression

Table 1 provides the summary statistics for each univariate model. Mild but statistically significant violations of proportional hazards were noted in four predictors; graphical analysis judged these violations safe to disregard. After FDR correction, 13 predictors yielded a statistically significant relationship with time-to-breastfeeding cessation. For simplicity, we discuss variables as "protective" (if hazard ratios [HRs] are negative [–]) and "risk" factors (if HRs are positive) (see Table 1). We chose reference groups a priori for dichotomous variables. Per standard convention, HRs for continuous/ordinal variables and scales are interpreted in relation to ascending (low-to-high) values.

One of the strongest protective factors of time-to-breastfeeding cessation in the univariate models was education, where each additional year of education was associated with an 11.5% lower hazard. Other significant socio-demographic protective factors were working, having access to a car, and being from an "other" race/ethnicity (relative to Black/African-American participants). A longer length of stay in the NICU was also protective. Several tobacco/smoking-related variables were protective including greater knowledge about tobacco, higher levels of readiness-to-protect infants from all sources of tobacco smoke, and banning smoking in the home.

One of the strongest risk factors for early breastfeeding cessation was the total number of household members who smoked, where each additional household smoker was associated with a 28.4% higher hazard. Other risk factors associated with early breastfeeding cessation were: greater numbers of children in the home, greater gestational age, and greater reported encouragement of smoking by friends/family/others.

Penalized Cox proportional hazards regression

Time-to-breastfeeding cessation was then modeled using elastic-net penalized Cox proportional hazards regression. All 41 predictors were modeled simultaneously and 16 predictors' coefficients were reduced to zero, effectively removing them from the statistical equation. Retained predictors included the 13 (FDR) statistically significant predictors in the univariate models and 12 additional predictors (see Table 1). Penalized coefficients reinforced univariate findings in a multiple-predictor context and provided a baseline model for subsequent model reduction.

Model reduction

The 25 predictors retained in the previous step were fit to a non-penalized model to establish a baseline model for comparison during model reduction (with all predictors in their raw, unstandardized metric). This model was reduced to nine

Table 2. Summary of key scales and subscales modeled as predictors.

Construct/measure name	Description (citation[s])	Possible numeric range
Encourage/Discourage Smoking Scale	Social support for not smoking in the home/car was adapted from a scale measuring social support for not smoking. The influence of 12 different groups of people (i.e., partner, mother, father, siblings, other children, grandparents, aunt(s), uncle(s), friends, co-worker(s), healthcare provider (s), and others) on the participants' attitudes toward smoking was summed, with higher (positive) scores indicating a greater degree of attitudes that encouraged smoking ⁵¹	-12 to +12
Confidence to Avoid Secondhand Smoke Scale	A scale of confidence to avoid secondhand smoke was adapted from self-efficacy work. ⁵² Higher scores indicated greater confidence to avoid secondhand smoke ³²	14-70
Center for Epidemiologic Studies Depression Scale (CES-D)	The 20-item CES-D ⁵³ measured depressive symptoms over the past week, with higher scores indicative of higher depressive symptoms. Scoring 16 or higher is suggestive of symptoms of clinical depression ^{54,55}	0-60
Environmental Tobacco Knowledge Scale	A 10-item scale measuring participants' knowledge of health-related harms from environmental tobacco smoke exposure (ETSE) was adapted from work on attitudes toward and knowledge about ETSE. ⁵⁶ Greater scores indicate greater knowledge about ETSE ³²	0-10
Generalized anxiety disorder-7 (GAD-7)	Generalized anxiety was measured by the GAD-7. ⁵⁷ Higher scores indicated higher levels of anxiety	0-21
Readiness-to-protect infants from tobacco	The Contemplation Ladder ⁵⁸ was adapted to assess participants' readiness to protect their infant from tobacco smoke exposure. Three one-item questions separately assessed readiness in the car, home, and all locations. Greater scores indicate higher readiness ³³	0-10 (on each item)
MILES NICU Stress Scales	The MILES NICU Stress Scale has three subscales to measure stress that parents experience in the NICU (i.e., sights and sounds, parental role alteration, and infant appearance). The mean score is taken for all items in a subscale with higher scores indicating more NICU-related stress on each subscale ⁵⁹	1-5 (on each subscale)
Neighborhood Scales	Functional neighborhood characteristics were measured on four subscales (neighborhood problems, social cohesion, help, and vigilance). ⁶⁰⁻⁶³ Greater scores on each subscale indicate higher levels of neighborhood problems (possible range: 10-30), cohesion (possible score: 5-25), helping behavior (possible score: 5-25), and vigilance to threats (possible score: 6-30), respectively.	Varies by subscale (see description)
Processes of Change Scales	The 10-item Processes of Change Scale has two subscales (experiential [cognitive/affective] and behavioral change processes). Higher mean scores on each subscale indicate higher engagement in the processes of change, related to secondhand smoke ^{64,65}	5-25 (on each subscale)
Perceived Stress Scale (PSS)	The 4-item PSS ⁶⁶ measured the degree to which individuals appraise situations in their lives as stressful. Greater scores represent higher levels of perceived stress.	0-16
Social deprivation index	This is an index derived from 17 socio-economic variables obtained from census-track data with 9-digit zip codes. Higher scores denote higher levels of deprivation. The index has a mean of 100 and a standard deviation of 20 ⁶⁷	See description

predictors using the backward-elimination machine-learning algorithm (Table 1).⁴² A mild and statistically significant violation of proportional hazards was found for the length of stay; all other predictors and the overall model demonstrated proportional hazards.

The 9-predictor reduced model retained 87.4% of the fit provided by the baseline model, providing parsimony with a small loss of variance explained. Six predictors in the reduced model were statistically significant. Specifically, greater education (HR % change: -8.6%/year) and being employed (HR: -24.1%) were associated with longer time-to-breastfeeding cessation. Further, the small group of mothers who reported being from an Asian or "Other" race/ethnicity ($n = 28$) breastfed for longer than Black/African-American mothers (HR: -37.8%). A longer length of stay in the NICU (HR: -3.0%/week) and higher readiness-to-protect infants from all sources of tobacco smoke exposure (HR: -7.3% for each 1-point readiness-scale increase) were both protective. Conversely, greater numbers of individuals who smoke

living in the home were associated with earlier cessation of breastfeeding (HR: +18.2%/smoker).

Reasons for breastfeeding cessation

Mothers often reported several reasons for stopping breastfeeding (see Table 3). Running out of milk ($n = 129$; 52.7%) was the most common reason given. Potential reasons unique to households with individuals who smoked included worries about nicotine in breast milk ($n = 16$; 6.5%) and "other" (unspecified) reasons ($n = 46$; 18.8%). Three (of the 16) mothers with concerns about nicotine in their breast milk reported being non-smokers for the entire study.

Associations between breastfeeding and infants' medical utilization

Infant visits to four separate medical settings were modeled as a function of receiving breast milk at 4 months of chronological age. Further, we modeled all types of illness-related visits and respiratory-related visits separately for all four settings, and we

Table 3. Reasons for stopping breastfeeding or pumping.

Reason for stopping	n (%)
You ran out of milk	129 (52.7%)
Your baby didn't get enough nourishment from breast milk	58 (23.7%)
It took too much time	41 (16.7%)
It was painful or uncomfortable	41 (16.7%)
It was difficult because you were returning to work or school	39 (15.9%)
You breastfed as long as you planned to	37 (15.1%)
It "tied you down" too much	32 (13.1%)
You were worried about nicotine in breast milk	16 (6.5%)
Latching difficulty	15 (12.1%)
Your partner didn't want you to breastfeed	3 (1.2%)
Other	46 (18.8%)

Note: Reasons were not mutually exclusive. Noteworthy, latching difficulties were added to the list of response options approximately halfway through recruitment.

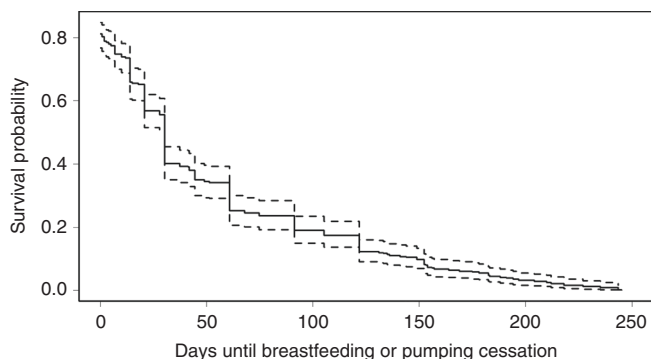


Fig. 1 Kaplan-Meier survival curve for the number of days to breastfeeding or pumping cessation. The cumulative probability of continuing to breastfeed or pump (i.e., survival; y-axis) is depicted for days of infant life (x-axis). The 95% confidence bands are depicted in dashed lines.

modeled well-child and sick visits separately for outpatient settings (see Table 4). Mothers of infants receiving breast milk at 4 months reported 34.5% more visits to outpatient settings ($p < 0.01$; across all visit types), driven by 42.7% more well-child visits ($p < 0.001$); breastfeeding status was not related to "sick" visits ($p = 0.72$). Further, infants receiving breast milk reportedly had fewer (-50.0% ; $p < 0.05$) visits to outpatient settings for respiratory-related illnesses. No significant differences were found across ED, hospital, or ICU settings for any type of visit or only respiratory-related visits. Similar results were found for infants being fed breast milk at 6 months.

DISCUSSION

Analyses in the present study utilized a novel approach to determine the strongest risk factors for early cessation of breastfeeding in a sample of mothers of infants admitted to a NICU, who also smoked and/or lived with individuals who smoked. A data-driven, machine-learning approach identified six significant predictors, two of which were unique to mothers who resided in households with individuals who smoke. Further, medical-setting utilization analyses demonstrated that mothers who breastfed for ≥ 4 months reportedly took their infants to more well-child visits and fewer respiratory-related visits.

Similar socio-demographic and other maternal characteristics (e.g., lower education, unemployment) have been found in previous studies^{6,18} to be predictive of non-initiation or early cessation of breastfeeding among mothers, regardless of whether infants were admitted to a NICU. For example, mothers who had ≤ 12 years education or were on Medicaid or WIC during delivery and pregnancy, initiated breastmilk feeding at proportions $< 80\%$, well below the national average.¹⁰ Although some of these characteristics are non-modifiable, NICU healthcare providers should be aware that these factors are associated with increased risk for early cessation of breastfeeding. Early preventative interventions offering extra support can be developed and implemented with these women at high risk of early breastfeeding cessation. Also, in our sample longer infant length of stay was a significant protective factor against breastfeeding cessation and may be viewed as an important proxy variable, often correlated with infant medical severity at delivery (e.g., preterm infants born at earlier gestational ages tend to have lengthier hospitalizations). We theorize that longer infant stays may give lactation specialists and nurses more time to convey pro-breastfeeding messages and intervene with and support mothers who might otherwise terminate breastfeeding early.

Interestingly, two smoking-related factors highlighted unique considerations for healthcare providers to evaluate when working with mothers who smoke or live with individuals who smoke. Specifically, a greater number of individuals who smoke living in an infant's household was associated with shorter lengths-of-time breastfeeding in this sample. It is possible that this is related to a more generally unhealthy environment and includes multiple behaviors (e.g., non-initiation of breastfeeding, no home smoking bans). Alternatively, with more smoking in the home environment, mothers may be increasingly concerned about the effects of cigarette toxicants on their infants via breastfeeding. Smoking considerations have been found to influence feeding decisions in other studies.⁴³

Our study also found that greater readiness-to-protect one's infant from all sources of environmental tobacco exposure was correlated with increased time spent breastfeeding. It is likely that mothers who are concerned about one health behavior, such as secondhand smoke, are also concerned about multiple other health behaviors, such as breastfeeding, which may represent a more general perspective with regard to individual and family health. Further, it is possible that interventions targeting one health behavior may positively influence others (e.g., refs. ^{44,45}). Notably, very few mothers reported concerns about nicotine present in their breast milk as a reason for stopping breastfeeding, but we did not explore the 46 "other" reasons for breastfeeding cessation, some of which may have been unique concerns for mothers who do not smoke but live with others who do. Furthermore, mothers who never initiated breastfeeding were not queried about their reasons for not initiating breastfeeding and may have chosen to avoid breastfeeding due to fears about nicotine contamination. Future work will improve on this limitation of our design.

We also replicated previous work (e.g., ref. ⁸) that demonstrated a negative correlation between length-of-time breastfeeding and medical visits for respiratory-related reasons. Specifically, mothers who reported breastfeeding for longer durations reported fewer respiratory-related visits to their infants' doctors' offices. These mothers also reported more overall doctors' visits (particularly well-child visits), suggesting that mothers who breastfeed for ≥ 4 months may be more attuned to healthy medical practices for their infants (e.g., getting vaccines, monitoring growth).

This novel approach to exploring breastfeeding with a unique and vulnerable population may help refine breastfeeding interventions for an often overlooked group of mothers, but limitations must be acknowledged. To maximize all available data, we combined mothers who smoked with mothers who abstain from

Table 4. Medical utilization predicted by breastfeeding at 4 months.

Outcome	M (SD)	Median (IQR)	Estimate (SE)	Hazard ratio (exp [estimate] with 95% CI)	p Value	Hazard ratio % change in visit utilization
Doctor visits (all visits)	6.77 (5.39)	5 (4–8)	0.297 (0.090)	1.345 (1.128–1.608)	0.001	+34.5%
Doctor visits (sick visits only)	1.20 (2.47)	1 (0–2)	−0.078 (0.219)	0.925 (0.605–1.428)	0.723	−7.45%
Doctor visits (well-child)	5.59 (4.74)	4 (3–7)	0.356 (0.093)	1.427 (1.190–1.715)	<0.001	+42.7%
Doctor visits (respiratory only)	0.45 (0.96)	0 (0–1)	−0.692 (0.349)	0.500 (0.246–0.976)	0.047	−50.0%
Emergency-department visits (all visits)	0.75 (1.16)	0 (0–1)	0.108 (0.222)	1.114 (0.720–1.722)	0.626	+11.4%
Emergency-department visits (respiratory only)	0.31 (0.77)	0 (0–0)	−0.346 (0.394)	0.708 (0.321–1.524)	0.380	−29.2%
Hospital visits (all visits)	0.29 (0.72)	0 (0–0)	0.398 (0.340)	1.489 (0.764–2.918)	0.242	+48.9%
Hospital visits (respiratory only)	0.14 (0.47)	0 (0–0)	−0.355 (0.536)	0.701 (0.229–1.943)	0.507	+29.9%
ICU visits (all visits)	0.65 (0.74)	1 (0–1)	−0.317 (0.442)	0.729 (0.276–1.608)	0.474	−27.1%
ICU visits (respiratory only)	0.38 (0.71)	0 (0–1)	−0.499 (0.659)	0.607 (0.135–1.956)	0.449	−39.3%

Note: "All visits" = well-child, sick (for any reason) in outpatient settings or illness-related visits in emergency department, hospital, or ICU settings. "Respiratory only" = visits for respiratory-related reasons only (e.g., asthma, wheezing).

smoking but live with others who smoke. Larger samples may yield important and distinct breastfeeding-cessation risk factors for these two populations. We also did not prospectively collect data on mothers from non-smoking households, which may have highlighted other key cultural and behavioral practices between smoking and non-smoking households.

Furthermore, as the intention of the parent trial was to study a behavioral intervention to reduce secondhand smoke exposure, several variables previously associated with breastfeeding were not measured. For example, we did not capture data on alcohol and drug use, due in part to the challenges of universal drug screening with pregnant women (or new mothers), especially in states with punitive or adverse outcomes (e.g., child custody investigations) for mothers who test positive at delivery.⁴⁶ Further, the setting of this study (Houston, TX, USA) is important to consider, as Texas lacks several statutes (e.g., breastfeeding friendly infant-feeding policies in hospitals⁴⁷) associated with increased breastmilk feeding at discharge, placing Texas among states with lower proportions of very low birthweight (<1500 g) infants discharged on breast milk.⁴⁸ Similarly, the lack of universal maternity leave policies and universal healthcare in the United States may increase the risk of early breastfeeding cessation for some mothers who must return to work soon after delivery, although in our sample employment appeared to have a protective benefit for breastfeeding. Our infant-feeding data were self-reported by mothers and did not contain the detail needed to analyze the proportion of feeds that contained breast milk or the proportion of breast milk contained within feeds that may have been supplemented with formula (a common practice to encourage infant weight gain during NICU hospitalizations). Our data have advantages over other analyses of breastfeeding with NICU and LPI populations, however, as PRAMS datasets do not have breastfeeding data beyond 10 weeks.¹⁶

CONCLUSION

Mothers who smoke or reside with individuals who smoke comprise a quarter or more of all families with an infant in the NICU^{26,33} and these mothers face greater risks for early breastfeeding cessation.²⁸ Given the potentially protective benefits of being fed breast milk, such as fewer respiratory-related infections, NICUs may wish to devote more resources to engaging and supporting young mothers of infants admitted to the NICU, who may be struggling to initiate or maintain breastfeeding. NICU-based

interventions with mothers who smoke or reside with household members who smoke would ideally address tobacco smoke exposure,^{26,33} breastfeeding,²⁸ and other health-promoting behaviors. These messages are synergistic and may facilitate multiple changes in the home, across all household members. For example, a positive effect of smoking cessation on breastfeeding duration has been demonstrated,^{49,50} making smoking cessation an important target by itself and a potential mediator of breastfeeding duration. Our data support future work to refine interventions for mothers who smoke or live with individuals who smoke.

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AUTHOR CONTRIBUTIONS

T.F.N. conceptualized the manuscript in consultation with A.L.S. and R.S. A.L.S. was the PI of the parent study and T.F.N. served as a co-investigator and project director. T.F.N. interpreted data-analytic results, wrote the initial draft of the manuscript, and finalized the submitted manuscript. A.L.S. contributed writing in several sections of the manuscript. R.S. and C.G. were co-investigators and provided statistical expertise and wrote relevant data-analytic and "Results" sections of the manuscript. A.K. was a co-investigator of the study and provided clinical oversight and content expertise. M.R.K. assisted in study management and provided conceptual contributions to the manuscript. All authors provided edits and revisions on several drafts of the manuscript.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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