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Biomarker feedback intervention for smoking cessation among Alaska Native pregnant women: Randomized pilot study

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ABSTRACT

Objective: There is some evidence for biomarker feedback when combined with cessation counseling for reducing smoking in pregnancy. This randomized controlled pilot study evaluated feasibility and potential efficacy of a social-cognitive theory (SCT)-based biomarker feedback intervention among pregnant Alaska Native (AN) smokers.

Methods: Participants were randomly assigned to receive three study calls (10–20 min each): (1) biomarker feedback intervention ($n = 30$) including personalized cotinine results and feedback on their baby's likely exposure to carcinogen metabolite NNAL, or (2) contact control usual care condition based on the 5*As* ($n = 30$). Assessments were conducted at baseline, post-treatment, and delivery.

Results: High rates of treatment compliance, study retention, and treatment acceptability were observed in both groups. 7-day point prevalence smoking abstinence rates at delivery verified with urinary cotinine were the same in both study groups (20% intent-to-treat analysis, 26% per-protocol). SCT-based measures did not change differentially from baseline by study group.

Conclusion: This trial supports the feasibility and acceptability of providing biomarker feedback within the clinical care delivery system, but the intervention did not promote increased smoking cessation during pregnancy compared to usual care.

Practice Implications: Efforts are needed to promote the usual care and to develop alternative biomarker feedback messaging for pregnant AN women.

1. Introduction

Cigarette smoking during pregnancy is a major public health problem, with documented adverse effects on maternal, fetal, and infant health [1–3]. Among U.S. women who delivered a live birth in 2010, 11% reported smoking during the last three months of pregnancy with the highest prevalence of 26% among American Indian/Alaska Native (AI/AN) females [4]. Recent nationally representative estimates of smoking in pregnancy (at 3–5 months gestation) are 14–26%, but prevalence was not reported for AI/AN women [5,6]. Among Alaskans, smoking prevalence during pregnancy is 36% for AN women versus 13% for non-Native women [7].

Substantial progress has been made with evidence-based interventions for pregnant cigarette smokers [8,9]. The 2017 Cochrane review [8] included 77 trials involving 29,000 pregnant smokers and found that counseling interventions such as motivational interviewing were more effective than usual care.

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Six trials evaluated biomarker feedback interventions where the mother was provided with information about the fetal health status derived from ultrasound monitoring, maternal expired air carbon monoxide, or urine cotinine measurements. Providing biomarker feedback was effective only when combined with cessation counseling and compared to usual care (e.g., 15% vs. 4% in the Cope et al. [10] study).

Only one published study focused on AI/AN pregnant women [8,11,12], a pilot trial in rural Alaska using a culturally adapted 5*A*'s counseling intervention [13]. The intervention had low reach and was not effective in promoting tobacco cessation. Program feedback suggested women desired "objective" information on tobacco harms for babies.

The *Biomarker Feedback to Motivate Tobacco Cessation in Pregnant Alaska Native Women* (MAW) study includes three research phases that incorporate feedback on infant exposure to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) for prenatal smoking cessation. NNAL is a major metabolite of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), the main tobacco specific nitrosamine in tobacco and a potent carcinogen thought to contribute to lung and pancreatic cancer [14,15]. NNAL is found in the urine of tobacco-exposed individuals and is also carcinogenic [14,15]. Phase 1 demonstrated a strong correlation between maternal smoking and maternal urine cotinine concentration and neonatal exposure to NNAL [16]. Phase 2 qualitatively assessed application and acceptability of information derived from Phase 1 to develop the intervention [17]. AN women and partners/family members preferred general information about fetal exposure to carcinogens combined with individual cotinine testing to motivate smoking cessation [17].

The current pilot randomized, controlled trial (Phase 3) evaluated feasibility and efficacy of a social cognitive theory (SCT)-based biomarker feedback intervention for smoking cessation among pregnant AN women. The intervention's conceptual basis was SCT because of the role of perceived disease risk or harm potential in behavior change [18], along with self-efficacy or confidence to change, and the expectation that changes lead to reduced risk (ie, response efficacy) [18,19]. We hypothesized the intervention would be feasible and result in a higher biochemically verified smoking abstinence rate at delivery than the control condition. We also expected SCT-based variables would show differential change from baseline with the intervention compared to the control condition.

2. Methods

Building on a successful research partnership between Mayo Clinic and the Alaska Native Tribal Health Consortium (ANTHC) and Southcentral Foundation (SCF), the study received approval by the Alaska Area and Mayo Clinic Institutional Review Boards, as well as the ANTHC and SCF boards of directors. A community advisory board was formed for all MAW study phases [16]. The trial was registered with clinicaltrials.gov (NCT 02431611).

2.1. Participants

The targeted sample size was 60 participants based on recommendations for Stage I behavioral addictions treatment development [20–23]. While the study was not adequately powered to detect significant treatment differences on smoking abstinence, our goal was to obtain effect size estimates for planning a definitive trial. A doubling of the abstinence rate for the intervention vs. control condition at the end of pregnancy (ie, delivery assessment) was considered to be of clinical significance and warrant proceeding to a Stage II efficacy trial [24].

We conducted the study in Anchorage, enrolling AN women receiving prenatal care at the SCF Primary Care Center (PCC) between March 2015 and July 2016. Recruitment flyers were available in clinics and distributed to providers. After updating tobacco use status in the medical record, clinic medical assistants asked smokers about their interest in speaking with research staff about the study. Research staff approached interested women before or after their prenatal care appointment to provide information.

Research staff conducted screening in person or by telephone to determine eligibility: (1) AN woman eligible for care at SCF PCC, (2) aged $\geq$18 years, (3) willing to provide written informed consent, (4) currently pregnant ($\leq$28 weeks gestation with a singleton pregnancy), (5) resided in Anchorage, (6) planned to deliver at the Alaska Native Medical Center (ANMC), (7) current smoker (any cigarettes smoked during the past seven days), and (8) willing to enroll into the SCF clinical "Quit Tobacco Program" (QTP). Participants could use other forms of tobacco if cigarettes were the primary tobacco used. Exclusionary criteria were: (1) use of nicotine replacement therapy (NRT) or other medications or behavioral treatment for tobacco cessation within the past 30 days, and (2) another woman from the same household had enrolled. To account for varying levels of readiness to quit, setting a quit date was not required; this differed from current SCF QTP standard of care. Women ineligible or not interested were offered tobacco cessation information.

2.2. Procedures

We used a two-arm, parallel groups, randomized controlled design. Sixty participants were randomized with 1:1 allocation to the biomarker feedback intervention or contact control condition. Prior to the trial, the study statistician generated the random allocation sequence based on the stratification variable of readiness to quit (low, medium/high). Participants completed baseline assessments before being informed of their study assignment. To enhance sustainability and external validity, both study treatments were incorporated within the existing clinical care delivery system and conducted by SCF counselors. Research staff administered interview-based assessments in-person or by phone at baseline, one week post-treatment (week 5), and at the time of delivery before hospital discharge. Urine specimens were collected at baseline and delivery. At each assessment, participants received a $25 gift card for their time.

2.3. Treatments

2.3.1. Treatment components common to both study groups

Participants were enrolled into the SCF QTP, the program offered to AN people living in the Anchorage area. Counselors provide proactive one-on-one counseling phone calls, supportive follow-up calls, quit guide booklet and educational flyers on risks of smoking and benefits of quitting during pregnancy, and access to NRT. Based on evidence-based 5 *A*'s [9] counselors: (1) *ask* about tobacco use, (2) provide *advice* to quit emphasizing that no amount of smoking is safe during pregnancy, (3) *assess* readiness to set a quit date using motivational interviewing, (4) *assist* with quitting using behavioral and problem-solving strategies, and (5) *arrange* follow-up.

Prior to this study, QTP enrollees were required to set a quit date with the first counseling call set for the week of the quit date (ie, week 1), and then at weeks 2 and 3. Follow-up counseling calls are conducted at weeks 6, 12, 26, and for up to 1 year after enrollment. For this study, participants were not required to set a quit date, thus we modified the QTP contact schedule. Three study calls lasting approximately 10–20 min each occurred at weeks 2, 3, and 4 after QTP enrollment, allowing for cotinine results to be available for the first counseling session for those assigned to the biomarker

feedback condition. No incentives were offered for call completion. After receiving the three study calls, all participants were encouraged to remain in the QTP to continue receiving the standard of care follow-up calls.

2.3.2. Control condition

Participants were mailed a generic welcome letter and brochure on smoking risks while pregnant. During the three study calls, the QTP counselor delivered the standard of care (described above) without providing individual cotinine results or any additional treatment.

2.3.3. Biomarker feedback intervention

Participants were mailed a welcome letter informing them they would receive their cotinine test results during the first study call. They also received the brochure developed in Phase 2 [17] to help describe the cotinine results. The factual-based brochure graphically illustrated the correlation between maternal urine cotinine concentrations and neonatal urine NNAL levels (Phase 1 findings [16]) to provide feedback on their baby's likely exposure to NNAL. During the three study calls, as part of the 5*A*'s, the QTP counselor reviewed the biomarker data and emphasized tobacco exposure risks to mother and baby, using motivational interviewing [25].The participant was asked to discuss her interpretation of her personalized cotinine results relative to the generalized infant urine NNAL results including assessment of her thoughts, feelings, and reactions to the information and perceived impact on current cigarette use (counselor manual is provided as supplemental item S1). Based on SCT, counselors provided risk exposure information and reinforced behavior change by providing information on how smoking cessation will reduce harmful consequences. To enhance self-efficacy, counselors assisted participants to set short term goals (e.g., reducing exposure to second hand smoke) within the context of her broader values and goals (e.g., healthy baby, healthy family).

2.3.4. Counselors, training, and treatment fidelity

Three QTP counselors (certified tobacco treatment specialists) were trained to conduct the three study calls; two conducted the biomarker feedback and one conducted the control treatment. The intervention and control group calls were delivered by separate counselors to enhance fidelity and minimize potential for cross-treatment contamination.

All QTP counselors (whether or not they conducted study calls) received four hours of training on site in Alaska by the study team including: study background and overview, refresher training in motivational interviewing, and updates on tobacco use among pregnant AN women and recommended guidelines for NRT use during pregnancy. Four additional hours of training were conducted by telephone with the two intervention counselors consisting of information and assigned readings on biomarkers of tobacco exposure (cotinine, NNAL) and SCT, role-plays, and mock phone sessions.

A counselor manual for each condition guided delivery of study calls. Test calls were done to assess proficiency and certify study counselors. To assess treatment fidelity, 10% of the early, middle, and late treatment sessions were selected randomly and reviewed by study staff who listened in on these calls and documented intended treatment components delivered [26]. Counselor adherence was 94% for the intervention and 98% for the control condition.

2.4. Measures

2.4.1. Baseline characteristics

Baseline assessments documented age, marital status, education, spouse/partner smoking status, and use of other tobacco or nicotine products, as well as the Fagerström Test for Cigarette Dependence [27] and Contemplation Ladder (readiness to quit) [28] scores.

2.4.2. Feasibility

Recruitment data included number of potential participants screened and excluded. Study retention was based on proportion of participants completing the delivery assessment including providing a urine sample for cotinine analysis. Completion of study counseling calls and duration was recorded by QTP counselors, with treatment adherence defined as completing three study calls. At week 5, participants completed treatment acceptability items [13] (e.g., if they would recommend the program to other women, perceived program helpfulness for quitting smoking), with 4-point Likert-type response options. Biomarker feedback participants were additionally asked to rate the perceived helpfulness of each intervention component.

2.4.3. Smoking status

Seven-day point-prevalence, self-reported cigarette smoking status was obtained at week 5 and at delivery [9]. Urinary cotinine was used to verify self-reported smoking status at delivery [29], through analysis at the Alaska State Public Health Laboratory using liquid chromatography tandem mass spectrometry (LC/MS/MS) [30]. Participants self-reporting no cigarette smoking (not even a puff) in the last seven days verified with urinary cotinine concentration <50 ng/mL were classified as non-smokers [29,31]. Follow-up assessments documented concomitant NRT/smoking cessation medication use, smokeless tobacco (ST), and electronic cigarette use.

2.4.4. SCT-based measures

At baseline and week 5, we used validated measures to assess self-efficacy to quit smoking [32], internalized motivation to quit [33,34], perceived risk of self and baby for developing lung cancer [35], and response efficacy [35,36].

2.5. Statistical methods

To assess the adequacy of the randomization, baseline demographics were compared between study groups using the chi-square (exact) test for categorical and two-sample *t*-test for continuous variables. We used the chi-square test to compare the proportion of assessment completion, treatment adherence, setting a quit date, and treatment acceptability items between study groups. Two sample t-tests compared study groups on counseling call duration. The chi-square test examined the proportion of participants abstinent from smoking at week 5 and at delivery based on: (1) intent-to-treat (ITT) analysis of all randomized participants ($n = 30$ per study group), and (2) per-protocol analysis of only participants completing delivery assessments ($n = 23$ per group). Participants missing data on self-reported smoking status or not providing a urine sample were classified as smoking [29,31]. For SCT-based measures, the two-sample *t*-test compared study conditions on mean baseline score. Analysis of covariance (ANCOVA) assessed changes in these measures; the week 5 assessment was the dependent variable and treatment group and the baseline assessment were independent variables. All analyses used two-sided tests with $p \leq .05$ denoting statistical significance.

3. Results

3.1. Participants

Smoking status was assessed for 969 women scheduled for a prenatal care visit; 612 were non-smokers. Of the 357 smokers

approached, 90 expressed interest, and 60 were eligible and enrolled (see Fig. 1).

3.1.1. Baseline characteristics

Study groups were comparable at baseline except more control participants were married/partnered (41% vs. 17%, $p = .05$) (Table 1). None reported ST use; 3% in each study group reported use of electronic cigarettes.

3.1.2. Feasibility

Fig. 1 illustrates study flow. All three counseling calls were completed by 80% of participants in both study groups. For intervention participants, mean duration in minutes [standard deviation, range] for the three calls was: (1) 15.4 [4.0, 6–24]; (2) 11.4 [8.7, 5–46]; and (3) 9.5 [4.1, 5–18]. For control participants, call duration was: (1) 14.9 [5.9, 5–34]; (2) 14.2 [6.3, 4–35]; and (3) 11.6 [5.2, 4–23] (all $p > .05$).

For both conditions, the week 5 assessment was completed by 80% of participants and the delivery assessment was completed by 77%. Reasons for attrition were early miscarriage, withdrawal from the study, and losses to follow-up (refused or unable to contact). Treatment acceptability was high with 87% of intervention and 71% of controls indicating they would definitely recommend the program ($p = .29$), and 62% of intervention and 79% of controls reported the program was very helpful ($p = .20$). Biomarker feedback participants rated intervention components as highly acceptable (supplemental item S2).

3.1.3. Smoking status

The proportion setting a quit date was significantly ($p = .04$) higher for biomarker feedback than control participants (87% vs. 63%). However, there were no significant differences detected between study groups at week 5 for self-reported quit attempt or smoking abstinence based on per protocol or intent-to-treat analyses (Table 2). At delivery, biochemically confirmed smoking abstinence rates were the same in both study groups (20% based on ITT; 26% based on per-protocol analysis). NRT use was reported by 3% of participants in each study group at week 5 and at delivery; these participants self-reported smoking. None reported use of other smoking cessation medications, ST, or electronic cigarette use at either time point.

3.1.4. SCT-based measures

No theory-based variables changed differentially with the intervention; all ($p > .05$) (Table 3). In post-hoc analyses, we examined if perceived risk was a mechanism for lack of benefit of the intervention using logistic regression (adjusting for study group). Week 5 lung cancer risk perception scores for self or baby were not significantly associated with biochemically verified smoking abstinence at week 5 or at delivery. We also addressed whether women smoking fewer cigarettes per day post-intervention reported less risk perceptions using linear regression adjusting for study group. At week 5, greater number of cigarettes smoked per day was associated with increased risk perception scores for self ($p = .02$), but not for baby.

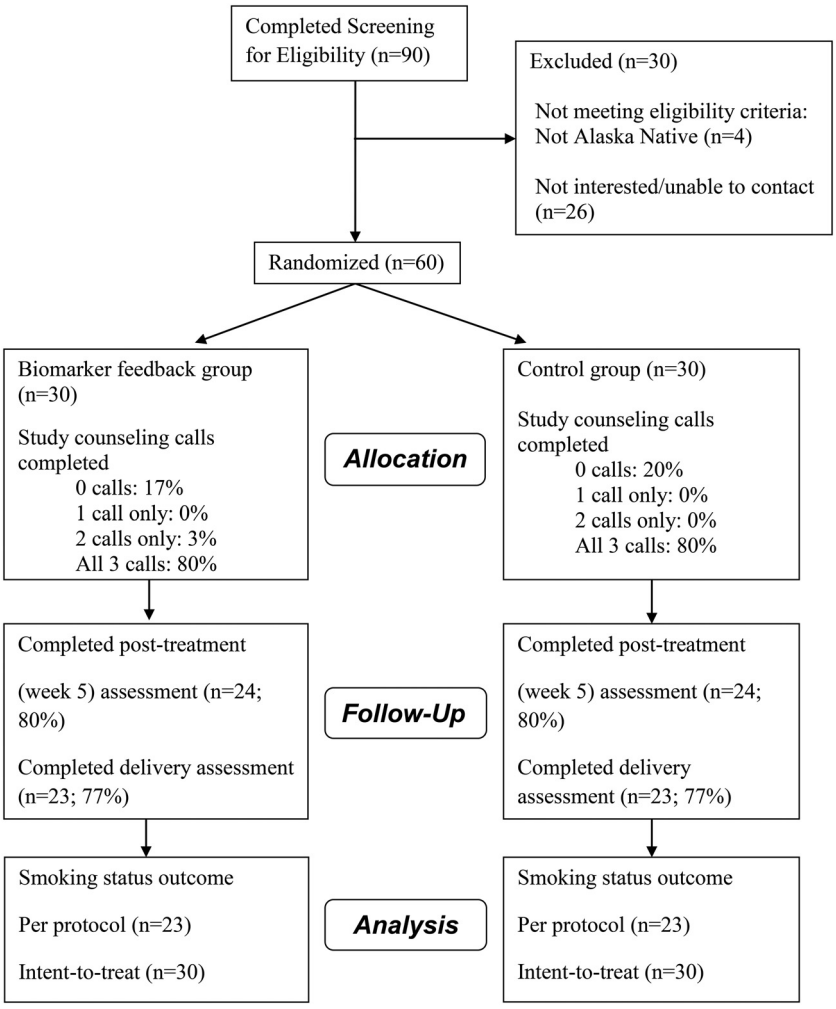

Fig. 1. Participant flow.

Table 1
Baseline Characteristics by Treatment Group: MAW Phase 3 Pilot Study ($n = 60$)[a,b].

	Biomarker Feedback Group	Control Group	p value[c]
Age	26.1 ± 5.0	27.8 ± 4.9	0.17
Range	18-36	20-38	
Married/partner	5 (17)	12 (41)	0.05
Education			0.46
Less than high school	9 (30)	8 (28)	
High school/GED	7 (23)	11 (38)	
Some college	14 (47)	10 (34)	
Number weeks gestation	14.3 ± 6.1	15.2 ± 7.1	0.57
Range	5-27	6-28	
Number of biological children			0.74
0	5 (17)	6 (21)	
1 or more	25 (83)	22 (79)	
Spouse/partner smokes[d]	4 (80)	10 (83)	0.87
Home smoking ban (includes artic entry)	28 (93)	24 (83)	0.56
Hours exposed to cigarette smoke each day	4.0 ± 3.6	4.5 ± 3.3	0.59
Range	1-14	0-12	
Lives with other smokers	21 (70)	25 (86)	0.13
Contemplation Ladder score	7.4 ± 1.5	6.9 ± 2.0	0.21
Low (0-3)	0 (0)	0 (0)	
Medium (4-6)	7 (23)	14 (48)	
High (7-10)	23 (77)	15 (52)	
Cigarettes per day	4.6 ± 2.9	4.9 ± 3.0	0.73
Range	1-13	1-12	
FTCD total score[e]	2.4 ± 2.0	2.6 ± 2.1	0.69
Range	0-6	0-8	
Urinary cotinine - creatinine corrected (ng/mg-creat)	593.3 ± 548.0	667.5 ± 757.9	0.67
Median	436.0	468.0	
Range	7-2310	2-2839	

[a] $n = 30$ for intervention group. $n = 29$ for control group; data are missing for 1 participant.
[b] Data are reported as n (%) or mean ± SD and range as appropriate.
[c] Two sample t-test or chi-square test as appropriate.
[d] For those reporting a spouse/partner; $n = 5$ intervention group, $n = 12$ control group.
[e] FTCD = Fagerström Test for Cigarette Dependence. Possible scores range from 0 to 10.

Table 2
Smoking Abstinence Outcomes at Post-Treatment and at Delivery: MAW Phase 3 Study.

	Post-treatment (Week 5)			Delivery		
Outcome[a]	Biomarker Feedback Group	Control Group	p-value[b]	Biomarker Feedback Group	Control Group	p-value[b]
Self-reported, 7-day point prevalence smoking abstinence, (n) %						
Per protocol (n = 23)	(4) 17	(6) 26	0.22	(6) 26	(7) 30	1.0
Intent-to-treat (n = 30)	(4) 13	(7) 23	0.51	(6) 20	(7) 23	1.0
Biochemically confirmed abstinence, (n) %						
Per protocol (n = 23)	–	–	–	(6) 26	(6) 26	1.0
Intent-to-treat (n = 30)	–	–	–	(6) 20	(6) 20	1.0
Quit attempt since enrolled in study, (n) %						
Per protocol (n = 23)	(14) 61	(19) 83	0.23	(15) 65	(19) 83	0.31
Intent-to-treat (n = 30)	(18) 60	(19) 63	1.0	(19) 63	(20) 67	1.0

[a] Intent-to-treat includes all women randomized to study conditions, $n = 30$ in both study groups. Per protocol analyses include women who completed the delivery assessment and provided a urine sample for cotinine analysis ($n = 23$ in both study groups). One participant was included in the per protocol analysis who did not provide a urine sample; this individual did not deliver at the ANMC and research staff were not able to obtain the sample, reported smoking abstinence, and used NRT at both follow-up time points.
[b] Chi-square or Fisher's exact test as appropriate.

4. Discussion and conclusion

4.1. Discussion

The biomarker feedback intervention demonstrated feasibility and acceptability among pregnant AN women, but it was no more effective than usual care with respect to smoking abstinence at week 5 or at delivery. Based on ITT analysis, both study groups achieved identical biochemically verified smoking abstinence rates of 20% (26% per-protocol) at delivery. The current study addressed important gaps in the field on tobacco treatment for AI/AN pregnant women [11,12]. Moreover, no prior work has presented information on fetal NNAL exposure for biomarker feedback among pregnant women [8].

Strengths of our intervention and study design are that biomarker feedback information was presented along with cessation counseling and compared to usual care. Smoking abstinence rates at delivery for both study groups compare favorably to cessation rates reported in the Cochrane review [8]. Psychosocial interventions were effective when compared to usual care, with biochemically verified smoking abstinence rates of 10%

Table 3
Baseline and Post-Treatment (Week 5) Theory-Based Measures by Study Group: MAW Phase 3 Pilot Study.

	Baseline			Week 5		
Measure	Biomarker Feedback Group	Control Group	p-value[a]	Biomarker Feedback Group	Control Group	p value[b]
TRSQ autonomous quitting motivation[c]	5.7 ± 1.4	5.7 ± 1.1	0.84	6.0 ± 1.3	6.3 ± 0.8	0.08
Range	2.2-7.0	2.8-7.0		2.5-7.0	4.0-7.0	
Self-efficacy to quit[d]	6.8 ± 2.3	6.3 ± 2.3	0.44	7.3 ± 2.1	7.1 ± 1.9	0.94
Range	3-10	2-10		3-10	5-10	
Cancer Risk Perceptions Scale[e]						
Self	3.4 ± 0.8	3.3 ± 0.7	0.54	3.4 ± 0.9	3.3 ± 0.9	0.99
Range	1.8-5.0	2.0-4.8		1.3-5.0	1.0-4.5	
Baby	2.8 ± 0.9	3.0 ± 0.9	0.54	2.7 ± 0.9	2.9 ± 0.9	0.68
Range	1.0-5.0	1.0-5.0		1.0-4.5	1.0-4.0	
Response efficacy[f]						
Self	3.6 ± 0.5	3.6 ± 0.9	0.91	3.6 ± 0.6	3.9 ± 1.2	0.31
Range	3.0-4.0	2.0-7.0		2.0-4.0	2.0-9.0	
Baby	3.4 ± 1.0	3.7 ± 0.5	0.12	3.8 ± 0.5	3.5 ± 0.9	0.13
Range	1.0-4.0	3.0-4.0		2.0-4.0	1.0-4.0	

Note. Data are reported as mean ± standard deviation (SD) and range.
[a] Two-sample *t*-test comparing study groups at the baseline assessment. Analyses were also adjusted for marital status which did not change the results (all $p > 0.05$).
[b] Analysis of Covariance (ANCOVA) assessing change in measures. For these analyses, the week 5 assessment was the dependent variable and study group and the baseline assessment were the independent variables. Analyses were also adjusted for marital status, which did not alter the results (all $p > 0.05$).
[c] TRSQ = Treatment Self-Regulation Questionnaire, 6-item autonomous quitting motivation subscale assessing reasons to quit or remain abstinent from smoking. Items are rated on a 1–7 point scale (1=not at all true, 4=somewhat true, 7=very true). The score reflects the mean of the six items with higher scores indicating greater internalized (versus external) sources of motivation to quit smoking.
[d] Single item "How confident are you in your ability to quit using tobacco?" rated on a scale from 1 (not at all confident) to 10 (completely confident).
[e] Perceived risk of developing lung cancer for self (4 items) and baby (4 items). Items are rated on a 5 point Likert scale. Scores for each of the self and baby subscales reflect the mean of 4 items with a possible score of 1–5; higher scores indicate greater lung cancer risk perceptions.
[f] Two items assessing benefits of quitting tobacco for self (1 item) and baby (1 item). Mean scores for each item can range from 1 to 4, with higher scores indicating greater perceived benefits.

vs. 8% respectively (14% vs. 11% in trials that used self-report or biochemical verification). One explanation for the high abstinence rate in our control condition is that it may be more intensive than most "usual care" comparisons that only provide information on the risks of smoking in pregnancy and brief advice to quit [8]. In contrast, our control condition, representative of the current clinical care delivery system, included 5*A*'s counseling with repeated contacts.

It is not possible to obtain urine NNAL concentrations in the fetus. We were only able to provide the mother with generalized feedback on the newborn's likely exposure to NNAL based on her urine cotinine results, which may have been less effective at helping her to understand the risks of smoking during pregnancy.

None of the theory-based measures changed differentially in the intervention, and no descriptive trends were observed. Moreover, risk perceptions post-intervention were not associated with smoking abstinence. Alternative theories may better inform development of new approaches to convey NNAL risk information. It is also possible the messaging lacked salience [38] or may have had unintended effects through processes such as cognitive dissonance not measured in this study [39,40].

Our findings suggest efforts to promote reach and use of standard of care counseling for pregnant AN smokers are warranted as this clinical program is currently underutilized by pregnant AN women. Placing the QTP in the SCF PCC increased program visibility, promoting referral. Incorporating clinic staff in the study recruitment process reinforced the need to assess tobacco status as a standard of care. Training QTP staff to conduct study treatments suggests future program modifications could be feasible and sustainable.

This study builds on long-standing community/research partnerships. Additional strengths include a biomarker feedback intervention developed with advice from pregnant AN women and community members, use of an experimental design, inclusion of a contact-control group, and well-specified treatments delivered with high fidelity. Having the intervention embedded within standard clinical care enhanced external validity and sustainability, and demonstrated high rates of study retention and treatment adherence in both groups, with biochemical verification of smoking abstinence.

Weaknesses of this study are the small sample size inherent in a Phase I treatment development [20–24] and the study was confined to one geographic region of Alaska, limiting generalizability [43]. All women were willing to enroll in a QTP and readiness to quit was high in this sample. It is possible differences were not detected between study groups because control women were already concerned about smoking effects on the fetus. To increase reach, future interventions may need to be tailored to the woman's stage of change (readiness to quit).

Our results point to new directions for research. Studies are needed to evaluate alternative conceptual frameworks, messaging appeals, and delivery channels at both individual (pregnant and/or postpartum women) and population (community) levels for communicating risk information on fetal NNAL exposure such as using storytelling [37] [41] which has been found to be culturally acceptable to AN people [42].

4.2. Conclusion

This pilot trial supports the feasibility and acceptability of providing biomarker feedback within the clinical care delivery system, but the intervention did not promote increased smoking cessation during pregnancy compared to usual care.

4.3. Practice implications

Clinically, our results demonstrate the importance of usual prenatal care that consistently assesses smoking status at every encounter, educates women on the effects of prenatal smoking, provides referral to smoking cessation programs embedded in the

prenatal clinic, and offers NRT to women expressing readiness to quit. In an era when health care costs increase dramatically with each additional test performed, our study demonstrates that simple improvements in usual care may prove to be less costly yet equally as effective as more sophisticated biometrics in reducing tobacco use in this population sector. Efforts are needed to promote reach and use of standard of care counseling for pregnant AN smokers, such as educating providers.

Informed consent and patient details

We confirm that all patient/personal identifiers have been removed so they are not identifiable and cannot be identified through the manuscript.

Declaration of interests

NLB is a consultant to several pharmaceutical companies that market medications to aid smoking cessation and has served as a paid expert witness in litigation against tobacco companies. The other authors have no conflicts to disclose.

Contributors

Authors CAP, KRK, CAF, VYH, CAH, AWW, PAD, CB, NJM, DH, NLB, and TKT contributed to the conception and design of the study. Authors CAF, CAH, TAB, MK, and DG contributed to the acquisition of data. Authors CAP, KRK, CAF PAD, KF, TAB, and TKT contributed to the analysis and/or interpretation of data. Authors CAP, KRK, CAF, CAH, PAD, and TKT contributed to drafting of the manuscript. All authors reviewed the draft manuscript providing critical intellectual contributions, and all authors approved the final submitted manuscript.

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Appendix A. Supplementary data

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References

[1] L. Bauld, C. Oncken, Smoking in pregnancy: an ongoing challenge, Nicotine Tob. Res. 19 (2017) 495–496, doi:http://dx.doi.org/10.1093/ntr/ntx034.
[2] S.C. Curtin, T.J. Matthews, Smoking prevalence and cessation before and during pregnancy: data from the birth certificate, 2014, Natl. Vital Stat. Rep. 65 (2016) 1–14.
[3] U.S. Department of Health and Human Services, The Health Consequences of Smoking: 50 years of progress. A Report of The Surgeon General, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta, GA, 2014.
[4] V.T. Tong, P.M. Dietz, B. Morrow, D.V. D'Angelo, S.L. Farr, K.M. Rockhill, L.J. England, Centers for Disease Control and Prevention (CDC), Trends in smoking before, during, and after pregnancy–Pregnancy Risk Assessment Monitoring System, United States, 40 sites, 2000-2010, MMWR Surveill. Summ. 62 (2013) 1–19.
[5] A.N. Kurti, R. Redner, A.A. Lopez, D.R. Keith, A.C. Villanti, C.A. Stanton, D.E. Gaalema, J.Y. Bunn, N.J. Doogan, A. Cepeda-Benito, M.E. Roberts, J. Phillips, S.T. Higgins, Tobacco and nicotine delivery product use in a national sample of pregnant women, Prev. Med. 104 (2017) 50–56, doi:http://dx.doi.org/10.1016/j.ypmed.2017.07.030.
[6] O. Alshaarawy, J.C. Anthony, Month-wise estimates of tobacco smoking during pregnancy for the United States, 2002-2009, Matern. Child Health J. 19 (2015) 1010–1015, doi:http://dx.doi.org/10.1007/s10995-014-1599-4.
[7] Alaska Native Epidemiology Center, Statewide Data: Prenatal Tobacco Use, (2016) . (Accessed 1 June 2017) http://anthctoday.org/epicenter/assets/data/statewide/prenatal_tobacco_use_statewide_3_31_2016.pdf.
[8] C. Chamberlain, A. O'Mara-Eves, J. Porter, T. Coleman, S.M. Perlen, J. Thomas, J. E. McKenzie, Psychosocial interventions for supporting women to stop smoking in pregnancy, Cochrane Database Syst. Rev. 2 (2017) CD001055, doi:http://dx.doi.org/10.1002/14651858.CD001055.pub5.
[9] M.C. Fiore, C.R. Jaen, T.B. Baker, W.C. Bailey, N.L. Benowitz, S.J. Curry, S.F. Dorfman, E.S. Froelicher, M.G. Goldstein, C.G. Healton, P.N. Henderson, R.B. Heyman, H.K. Koh, T.E. Kottke, H.A. Lando, R.E. Mecklenburg, R.J. Mermelstein, P.D. Mullen, C.T. Orleans, L. Robinson, M.L. Stitzer, A.C. Tommasello, L. Villejo, M.E. Wewers, Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline, Public Health Service, U.S. Department of Health and Human Services, Rockville, MD, 2008.
[10] G.F. Cope, P. Nayyar, R. Holder, Feedback from a point-of-care test for nicotine intake to reduce smoking during pregnancy, Ann. Clin. Biochem. 40 (2003) 674–679, doi:http://dx.doi.org/10.1258/000456303770367289.
[11] G.S. Gould, C. Patten, M. Glover, A. Kira, H. Jayasinghe, Smoking in pregnancy among indigenous women in high-income countries: a narrative review, Nicotine Tob. Res. 19 (2017) 506–517, doi:http://dx.doi.org/10.1093/ntr/ntw288.
[12] Y. Washio, H. Cassey, Systematic review of interventions for racial/ethnic-minority pregnant smokers, J. Smok. Cessat. 11 (2016) 12–27, doi:http://dx.doi.org/10.1017/jsc.2014.12.
[13] C.A. Patten, R.A. Windsor, C.C. Renner, C. Enoch, A. Hochreiter, C. Nevak, C.A. Smith, P.A. Decker, S. Bonnema, C.A. Hughes, T. Brockman, Feasibility of a tobacco cessation intervention for pregnant Alaska Native women, Nicotine Tob. Res. 12 (2010) 79–87, doi:http://dx.doi.org/10.1093/ntr/ntp180.
[14] N.L. Benowitz, C.C. Renner, A.P. Lanier, R.F. Tyndale, D.K. Hatsukami, B. Lindgren, I. Stepanov, C.H. Watson, C.S. Sosnoff, P. Jacob 3rd., Exposure to nicotine and carcinogens among Southwestern Alaskan Native cigarette smokers and smokeless tobacco users, Cancer Epidemiol. Biomarkers Prev. 21 (2012) 934–942, doi:http://dx.doi.org/10.1158/1055-9965.EPI-11-1178.
[15] S.S. Hecht, Biochemistry, biology, and carcinogenicity of tobacco-specific N-nitrosamines, Chem. Res. Toxicol. 11 (1998) 559–603, doi:http://dx.doi.org/10.1021/tx980005y.
[16] C.A. Flanagan, K.R. Koller, A.W. Wolfe, T.K. Thomas, N.L. Benowitz, C.C. Renner, C. Hughes, D.K. Hatsukami, C. Bronars, N.J. Murphy, G. Day, P.A. Decker, C.A. Patten, Fetal exposure to carcinogens with tobacco use in pregnancy: phase 1 MAW study findings, Nicotine Tob. Res. 18 (2016) 2162–2168, doi:http://dx.doi.org/10.1093/ntr/ntw134.
[17] K.R. Koller, C.A. Flanagan, G.E. Day, T.K. Thomas, C.A. Smith, A.W. Wolfe, C. Meade, C.A. Hughes, V.Y. Hiratsuka, N.J. Murphy, C.A. Patten, Developing a biomarker feedback intervention to motivate smoking cessation during pregnancy: phase II MAW study, Nicotine Tob. Res. 19 (2017) 930–936, doi:http://dx.doi.org/10.1093/ntr/ntw330.
[18] A. Bandura, Health promotion by social cognitive means, Health Educ. Behav. 31 (2004) 143–164, doi:http://dx.doi.org/10.1177/1090198104263660.
[19] E. Seydel, E. Taal, O. Wiegman, Risk-appraisal, outcome and self-efficacy expectancies: cognitive factors in preventive behaviour related to cancer, Psychol. Health 4 (1990) 99–109, doi:http://dx.doi.org/10.1080/08870449008408144.
[20] M. Campbell, R. Fitzpatrick, A. Haines, A.L. Kinmonth, P. Sandercock, D. Spiegelhalter, P. Tyrer, Framework for design and evaluation of complex interventions to improve health, BMJ. 321 (2000) 694–696, doi:http://dx.doi.org/10.1136/bmj.321.7262.694.
[21] S.M. Czajkowski, L.H. Powell, N. Adler, S. Naar-King, K.D. Reynolds, C.M. Hunter, B. Laraia, D.H. Olster, F.M. Perna, J.C. Peterson, E. Epel, J.E. Boyington, M.E. Charlson, From ideas to efficacy: the ORBIT model for developing behavioral treatments for chronic diseases, Health Psychol. 34 (2015) 971–982, doi:http://dx.doi.org/10.1037/hea0000161.
[22] G.A. Lancaster, S. Dodd, P.R. Williamson, Design and analysis of pilot studies: recommendations for good practice, J. Eval. Clin. Pract. 10 (2004) 307–312, doi:http://dx.doi.org/10.1111/j.2002.384.doc.x.
[23] B.J. Rounsaville, K.M. Carroll, L.S. Onken, A stage model of behavioral therapies research: getting started and moving on from stage I, Clin. Psychol. Sci. Pract. 8 (2001) 133–142, doi:http://dx.doi.org/10.1093/clipsy.8.2.133.

[24] H.C. Kraemer, D.J. Kupfer, Size of treatment effects and their importance to clinical research and practice, Biol. Psychiatry 59 (2006) 990–996, doi:http://dx.doi.org/10.1016/j.biopsych.2005.09.014.
[25] W.R. Miller, S. Rollnick, Motivational Inverviewing: Helping People Change, 3rd ed., Guilford Press, New York City, New York, 2012.
[26] A.J. Bellg, B. Borrelli, B. Resnick, J. Hecht, D.S. Minicucci, M. Ory, G. Ogedegbe, D. Orwig, D. Ernst, S. Czajkowski, Treatment Fidelity Workgroup of the N.I.H.B.C. C., Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium, Health Psychol. 23 (2004) 443–451, doi:http://dx.doi.org/10.1037/0278-6133.23.5.443.
[27] K. Fagerström, Determinants of tobacco use and renaming the FTND to the Fagerström Test for Cigarette Dependence, Nicotine Tob. Res. 14 (2012) 75–78, doi:http://dx.doi.org/10.1093/ntr/ntr137.
[28] L. Biener, D.B. Abrams, The Contemplation Ladder: validation of a measure of readiness to consider smoking cessation, Health Psychol. 10 (1991) 360–365, doi:http://dx.doi.org/10.1037/0278-6133.10.5.360.
[29] SRNT Subcommittee on Biochemical Verification, Biochemical verification of tobacco use and cessation, Nicotine Tob. Res. 4 (2002) 149–159, doi:http://dx.doi.org/10.1080/14622200210123581.
[30] P. Jacob 3rd., L. Yu, M. Duan, L. Ramos, O. Yturralde, N.L. Benowitz, Determination of the nicotine metabolites cotinine and trans-3'-hydroxycotinine in biologic fluids of smokers and non-smokers using liquid chromatography-tandem mass spectrometry: biomarkers for tobacco smoke exposure and for phenotyping cytochrome P450 2A6 activity, J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 879 (2011) 267–276, doi:http://dx.doi.org/10.1016/j.jchromb.2010.12.012.
[31] J.R. Hughes, J.P. Keely, R.S. Niaura, D.J. Ossip-Klein, R.L. Richmond, G.E. Swan, Measures of abstinence in clinical trials: issues and recommendations, Nicotine Tob. Res. 5 (2003) 13–25, doi:http://dx.doi.org/10.1080/1462220031000070552.
[32] N.A. Rigotti, E.R. Park, S. Regan, Y. Chang, K. Perry, B. Loudin, V. Quinn, Efficacy of telephone counseling for pregnant smokers: a randomized controlled trial, Obstet. Gynecol. 108 (2006) 83–92, doi:http://dx.doi.org/10.1097/01.AOG.0000218100.05601.f8.
[33] C.S. Levesque, G.C. Williams, D. Elliot, M.A. Pickering, B. Bodenhamer, P.J. Finley, Validating the theoretical structure of the Treatment Self-Regulation Questionnaire (TSRQ) across three different health behaviors, Health Educ. Res. 22 (2007) 691–702, doi:http://dx.doi.org/10.1093/her/cyl148.
[34] R.M. Ryan, J.P. Connell, Perceived locus of causality and internalization: examining reasons for acting in two domains, J. Pers. Soc. Psychol. 57 (1989) 749–761, doi:http://dx.doi.org/10.1037/0022-3514.57.5.749.
[35] P. Lyna, C. McBride, G. Samsa, K.I. Pollak, Exploring the association between perceived risks of smoking and benefits to quitting: who does not see the link? Addict. Behav. 27 (2002) 293–307, doi:http://dx.doi.org/10.1016/S0306-4603(01)00175-7.
[36] E.R. Park, J.S. Ostroff, W. Rakowski, I.F. Gareen, M.A. Diefenbach, S. Feibelmann, N.A. Rigotti, Risk perceptions among participants undergoing lung cancer screening: baseline results from the National Lung Screening Trial, Ann. Behav. Med. 37 (2009) 268–279, doi:http://dx.doi.org/10.1007/s12160-009-9112-9.
[37] T. McAfee, K.C. Davis, R.L. Alexander Jr., T.F. Pechacek, R. Bunnell, Effect of the first federally funded US antismoking national media campaign, Lancet. 382 (2013) 2003–2011, doi:http://dx.doi.org/10.1016/S0140-6736(13)61686-4.
[38] G.S. Gould, Y. Cadet-James, A.R. Clough, Getting over the shock: taking action on Indigenous maternal smoking, Aust. J. Prim. Health 22 (2016) 276–282, doi:http://dx.doi.org/10.1071/PY15066.
[39] L.T. Kessels, R.A. Ruiter, B.M. Jansma, Increased attention but more efficient disengagement: neuroscientific evidence for defensive processing of threatening health information, Health Psychol. 29 (2010) 346–354, doi:http://dx.doi.org/10.1037/a0019372.
[40] K. Witte, K.A. Cameron, J.K. McKeon, J.M. Berkowitz, Predicting risk behaviors: development and validation of a diagnostic scale, J. Health Commun. 1 (1996) 317–341, doi:http://dx.doi.org/10.1080/108107396127988.
[41] N.A. Rigotti, M. Wakefield, Real people, real stories: a new mass media campaign that could help smokers quit, Ann. Intern. Med. 157 (2012) 907–909, doi:http://dx.doi.org/10.7326/0003-4819-156-1-201201010-00541.
[42] M. Cueva, R. Kuhnley, L. Revels, N.E. Schoenberg, M. Dignan, Digital storytelling: a tool for health promotion and cancer awareness in rural Alaskan communities, Int. J. Circumpolar Health 74 (2015) 28781, doi:http://dx.doi.org/10.3402/ijch.v74.28781.
[43] C.A. Patten, C.C. Renner, P.A. Decker, E. O'Campo, K. Larsen, C. Enoch, K.P. Offord, R.D. Hurt, A. Lanier, J. Kaur, Tobacco use and cessation among pregnant Alaska Natives from Western Alaska enrolled in the WIC program, 2001-2002, Matern. Child Health J. 12 (Suppl 1) (2008) 30–36, doi:http://dx.doi.org/10.1007/s10995-008-0331-7.