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Effects of 3D ultrasonography and 3D printed images on maternal-fetal attachment and its correlation with overall smoking within pregnancy: a pilot study

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Abstract

Background Smoking in pregnancy continues to cause significant morbidity to mothers and babies and contributes to tremendous costs to society. Maternal-fetal attachment (MFA) may differentiate smokers who quit or pregnant smokers from non-smokers. Researchers have recommended utilizing interventions that improve MFA to help decrease smoking within pregnancy.

Methods We performed a randomized clinical trial of pregnant smokers ($n = 33$) using an MFA-informed, intention-to-treat protocol. We recruited pregnant smokers and provided timeline follow back (TLFB) interviews from 27 weeks of pregnancy until 6 weeks post-partum. Salivary cotinine was also collected at five different time points. 3D ultrasonography was performed, and patients were randomly assigned a 3D picture or a 3D model of their fetus.

Results Overall, the average percent reduction in cigarette use was 37.03% (SD = 31.18). The main effect of 3D type was not significant (3D Model vs. 3D Print Estimate = -0.09, 95% CI: −0.19 to 0.01, $p = 0.066$). A total of 4 patients (12%) quit smoking within one week of delivery. A 10% reduction in cigarette use was associated with a 30.57 g increase in birth weight (Estimate = 30.57, 95% CI: -14.15 to 75.29); a 10% reduction in cigarette use was associated with a 0.14 week increase in estimate gestational age at delivery (Estimate = 0.14, 95% CI: -0.01 to 0.28).

Conclusions Patients who smoke in pregnancy decrease the number of cigarettes smoked after receiving either a 3D picture or 3D model of their fetus.

Trial registration clinicaltrials.gov (NCT04541121).

Keywords 3D-printing, Maternal-fetal attachment, Smoking, Pregnancy

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Background

Smoking during pregnancy continues to be a leading preventable risk factor for pre-term delivery (PTD), low birth weight (LBW), neonatal intensive care unit (NICU) admission, and intrauterine fetal demises (IUFD) [1]. The current American College of Obstetricians and Gynecologists (ACOG) recommendations for smoking cessation emphasize the 5 A's ('Ask', 'Advise', 'Assess', 'Assist', and 'Arrange') [2]. Despite these well-established guidelines, healthcare providers have low rates of 'Assisting' and 'Arranging' and smoking cessation interventions are underutilized [3]. Ultrasonography in pregnancy is routine and established and has been shown to increase MFA in multiple studies [4, 5]. There is mounting evidence that 3D ultrasonography improves MFA scores more than 2D ultrasonography [5]. Additionally, 3D printed physical models will improve MFA scores statistically more than 3D ultrasonography alone [4]. Ironically, patients receiving 3D pictures and 3D models increase MFA scores equally [5]. MFA is also linked to smoking behavior with researchers recommending the next steps to included examining if MFA informed interventions could assist in smoking cessation efforts [6–8]. To our knowledge there are no studies that have examined MFA interventions and smoking in pregnancy. The aims of the current study were to compare the effectiveness of two easily implemented MFA-informed smoking interventions on smoking habits during pregnancy.

Materials and methods

All procedures described were approved by the Institutional Review Board of Creighton University. Participants were thirty English-speaking actively smoking pregnant adults with single gestations recruited from clinics in a medium-sized city in the Midwestern U.S. between 26 and 31 weeks of gestation (Fig. 1). Following informed consent procedures, we collected data described below from participants at the following timepoints: Time 1-enrollment (M=28.8 weeks, SD=1.4); Time 2-intervention (M=29.9 weeks, SD=1.4); Time 3-one week after intervention (M=30.9 weeks, SD=1.5); Time 4-two weeks post-partum; Time 5-six weeks post-partum.

3D images

After completing the MAAS questionnaires along with the demographics, patients were block randomized with equal allocation and block sizes of four, to a 3D model or 3D picture and then underwent a 15–20-minute ultrasonography examination at M=28.8 weeks (SD=1.4) using a General Electric (GE) Voluson™ E10 ultrasonography machine to capture a 3D image of the fetal face. After the patient left the clinic, the ultrasonographer either printed one of the 3D images on thermal paper or they exported a stereolighography (STL) file to a thumb drive to be modified. The STL file had artifacts removed and a 3D model was printed with a TAZ 6 Workhorse™ 3D printer using skin tone appropriate polylactic acid (PLA). Either the 3D picture or 3D model were presented to the corresponding patients one week after their ultrasonography (Time-2) (Fig. 2).

Smoking

Smoking was assessed from 27 weeks of pregnancy until 6 weeks post-partum using the TLFB method, the gold standard quantitative measure of patterns of substance use over time [9]. At each of the 5 timepoints participants reported how much they smoked on each day during the 2-week period immediately preceding the visit. Additionally, patients provided saliva samples also at each of the five timepoints . Saliva samples were stored at -80 degrees Celsius before shipment to Salimetrics (State College, PA). Samples were assayed using the Salimetrics Salivary Cotinine Assay Kit Cat. No. 1-2002, without modifications to the manufacturers' protocol. Samples were thawed to room temperature, vortexed, and then centrifuged for 15 min at approximately 3,000 RPM immediately before performing the assay. Samples were tested using a high sensitivity enzyme immunoassay (Cat. No. 1-2002). Sample volume was 20 μL of saliva per determination. The assay has a lower limit of sensitivity of 0.15 ng/mL, a standard curve ranges from 0.8 to 200 ng/mL.

Analytic Strategy

To assess change in cigarettes smoked during pregnancy, we estimated a piecewise mixed-effects Poisson regression model. The first segment estimated cigarette use from study enrollment until receiving a 3D ultrasound, this 7-day period was identical for both the 3D print and the 3D model group. The second segment estimated cigarette use from the day of 3D ultrasound until delivery, which varied across patients. Then, we evaluated the change in cigarettes smoked during pregnancy by time and 3D type. This final piecewise model included four fixed effects: time pre-3D ultrasound, time post-3D ultrasound, 3D types, and the time post-3D ultrasound-by-3D type interaction effect. The interaction effect evaluated whether 3D type moderated the effect of time. Residual pseudo-likelihood estimation was used. Time was modeled as a continuous variable (days). We accounted for the correlation of observations from the same patient by estimating random subject effects.

Secondary objectives

We evaluated the relationship between cigarette reduction and birth weight. Cigarette reduction was quantified as the percent reduction in cigarettes smoked between the 7-day period prior to receiving the 3D ultrasound and

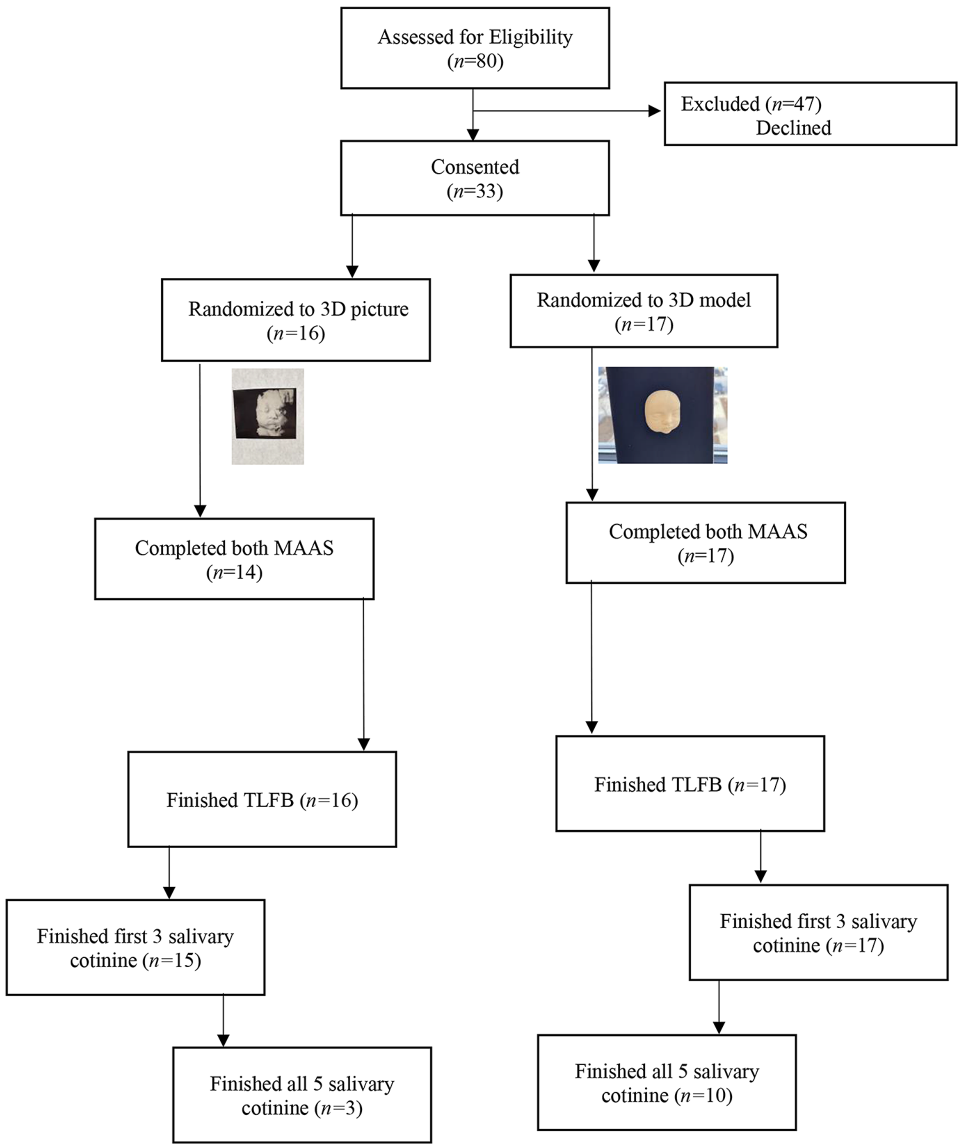

Fig. 1 CONSORT flow diagram

the 7-day period prior to delivery. Lastly, we estimated two linear regression models with birth weight and estimated gestational age at delivery as the outcomes and percent cigarette reduction as the predictors. All analyses used SAS v. 9.4 with two-tailed $p<0.05$ indicating statistical significance.

Results

Descriptive-demographics

A total of 33 patients were randomized: 3D picture ($N=16$) vs. 3D model ($N=17$). Demographic and obstetric patient data are presented in Table 1. Descriptive characteristics were similar between the 3D picture and the 3D model group.

Primary objective

In the 7-days prior to receiving the 3D ultrasound, the main effect of time was not significant (Estimate = -0.03, 95% CI: -0.09 to 0.02, $p=0.200$; Fig. 3). The main effect of 3D type was not significant (3D Model vs. 3D Picture Estimate = -0.09, 95% CI: −0.19 to 0.01, $p=0.066$; Fig. 3). The time-by-3D type interaction was significant indicating that 3D type moderated the effect of time (interaction $p<0.001$; Fig. 3). After receiving a 3D picture, the number of cigarettes smoked decreased by 0.4 cigarettes each 7-day period (Estimate = -0.04, 95% CI:=−0.05 to -0.03, $p<0.001$; Fig. 3). After receiving a 3D model, the number of cigarettes smoked decreased by 0.01 cigarettes each 7-day period (Estimate = -0.01, 95% CI:=−0.02 to 0.00, $p=0.243$; Fig. 3).

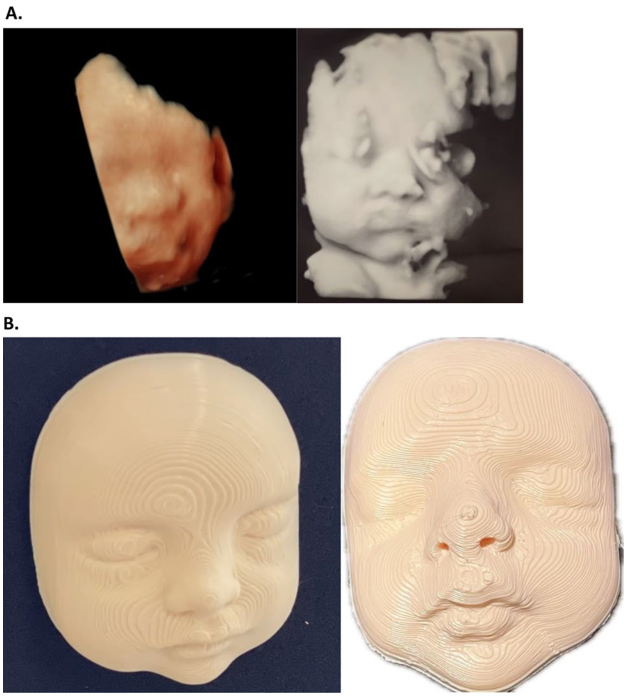

Fig. 2 Patients were randomized and received 3D pictures (**A**) or 3D models (**B**) one week after their 3D ultrasound was performed

The average percent reduction in cigarette use was 37.03% (SD=31.18). For the 3D picture and 3D model groups, the average reduction in cigarette use was 43.33% (SD: 32.12%) and 31.52% (SD=30.26%), respectively. There was no statistical difference in percent cigarette reduction between the 3D picture and the 3D model group (3D Model vs. 3D Picture Difference = -11.81%, 95% CI: -35.16–11.53%, p=0.309). Based on TLFB interviews for all the patients, 12% (N=4) quit smoking within a week of delivery.

Salivary cotinine levels had an average intra-assay coefficient of variation of 6.38%, and an average inter-assay coefficient of variation 6.63%. Currently, a cotinine cut point of 3ng/mL has been recommended for distinguishing smokers from non-smokers [10]. Of the patients with salivary cotinine data at Time-4 (2-weeks after delivery; N=19), 11% (N=2) had smoking cessation chemically confirmed.

Secondary objectives

Post-birth outcomes are presented in Table 2. Notably, 36.26% (N=12) of patients experienced preeclampsia. A 10% reduction in cigarette use was associated with a 30.57 gram increase in birth weight (Estimate=30.57, 95% CI: -14.15 to 75.29, p=0.173; Fig. 4a). A 10% reduction in cigarette use was associated with a 0.14 week increase in estimate gestational age at delivery (Estimate=0.14, 95% CI: -0.01 to 0.28, p=0.063; Fig. 4b).

Discussion

Previous research has focused on interventions to improve MFA scores in pregnancy, yet this is the first study to examine the effects of 3D fetal models or 3D pictures on smoking in pregnancy. Our findings showed no difference between 3D interventions; yet our within-subject design showed improvement in smoking reduction for both MFA interventions and is particularly impactful when considering the effects of smoking on birth outcomes in the general population.

A Cochrane review of interventions promoting smoking cessation in pregnancy found that there was limited evidence of reduced smoking in late pregnancy but that where reductions were biochemically validated there was no significant evidence of reduced smoking (RR 1.27, 95% CI 0.84 to 1.91) [11]. A review of behavioral interventions for smoking cessation in pregnancy found no significant difference in risk of preterm birth between those who smoked and who did not smoke (RR, 0.93 [95% CI 0.77–1.11]; 19 trials; n=9222). However, they found that those who smoked during pregnancy had a higher mean birth weight compared to controls (mean difference, 55.60 g [95% CI, 29.82–81.38]; 26 trials; n=11 338) and found those who smoked had a 17% risk reduction for LBW babies (RR, 0.83 [95% CI, 072-0.94]; 18 trials; n=9402) [12]. Because ultrasonography in pregnancy is routine and established (Moncrieff et al., 2021) our findings highlight an ability to augment the 'Assist' and 'Arrange' portions of the 5 A's that can be difficult for practitioners.

Multiple studies suggested the rate of LBW and PTD in smokers can be 2–3 times greater than in non-smokers, yet our findings suggest an improved LBW and PTD rate for pregnancy smokers after the interventions with only a 6% rate of LBW and PTD compared to the national 8.6% and 10.38% respectively [13, 14]. Consistant with other studies, we found that decreasing smoking may increase the risk of pre-eclampsia [15]. Notably, our findings support the need to evaluate these interventions on a larger scale.

Current recommendations contend that the use of ultrasound without a medical indication to view the fetus is inappropriate and contrary to responsible medical practice [16]. This recommendation has its roots in the "as low as reasonably achievable" (ALARA) principle. Interestingly, these organizations emphasize that ultrasound is a safe and risk-free method for prenatal diagnosis as "the literature does not include a single study reporting a risk to the fetus as a result of ultrasound" [17]. While the responsible use of fetal ultrasound is important the chilling effect these recommendations have on the use of ultrasonography is a slippery slope. In fact, a German ordinance has made any non-medical ultrasound exposure of a fetus a violation of the law that can be punished as a misdemeanor [18].

Table 1 Patient descriptives stratified by 3D product

	Overall	3D Product	
		Print	Model
Age, years	28 (23–31)	27 (22–31)	28 (24–32)
Baseline Body Mass Index, kg/m2	32 (27–37)	31 (25–37)	32 (27–35)
Baseline cotinine level, ng/mL	170 (104–257)	170 (93–259)	170 (142–257)
Baseline MAAS score	84 (80–87)	84 (82–87)	85 (77–87)
Race, N (%)			
White	22 (66.67)	11 (68.75)	11 (64.71)
Black	10 (30.30)	4 (25.00)	6 (35.29)
Hispanic	1 (3.03)	1 (6.25)	0 (0)
Married, N (%)	29 (87.88)	15 (93.75)	14 (82.35)
Medicaid insurance, N (%)	31 (93.94)	15 (93.75)	16 (94.12)
Income $, N (%)			
0–20	19 (65.52)	11 (73.33)	8 (57.14)
20–40	5 (17.24)	3 (20.00)	2 (14.29)
40–65	4 (13.79)	1 (6.67)	3 (21.43)
65–100	1 (3.45)	0 (0)	1 (7.14)
Education, N (%)			
Some high school	7 (21.21)	4 (25.00)	3 (17.65)
Highschool graduate	19 (57.58)	9 (56.25)	10 (58.82)
Some college/college graduate	7 (21.21)	3 (18.75)	4 (23.53)
Gravida, N (%)			
1 pregnancy	9 (27.27)	4 (25.00)	5 (29.41)
2 pregnancies	7 (21.21)	2 (12.50)	5 (29.41)
3 + pregnancies	17 (15.52)	10 (62.50)	7 (21.18)
Para, N (%)			
0 previous deliveries	14 (42.42)	6 (37.50)	8 (47.06)
1 previous delivery	5 (15.15)	1 (6.25)	4 (23.53)
2 + previous deliveries	14 (42.42)	9 (56.25)	5 (29.41)
History of secondhand smoke exposure, N (%)	22 (66.67)	10 (62.50)	12 (70.59)
History of e-cigarette use, N (%)	7 (21.21)	2 (12.50)	5 (29.41)

Continuous variables are presented as median (interquartile range). Categorical variables were presented as frequency (percent)

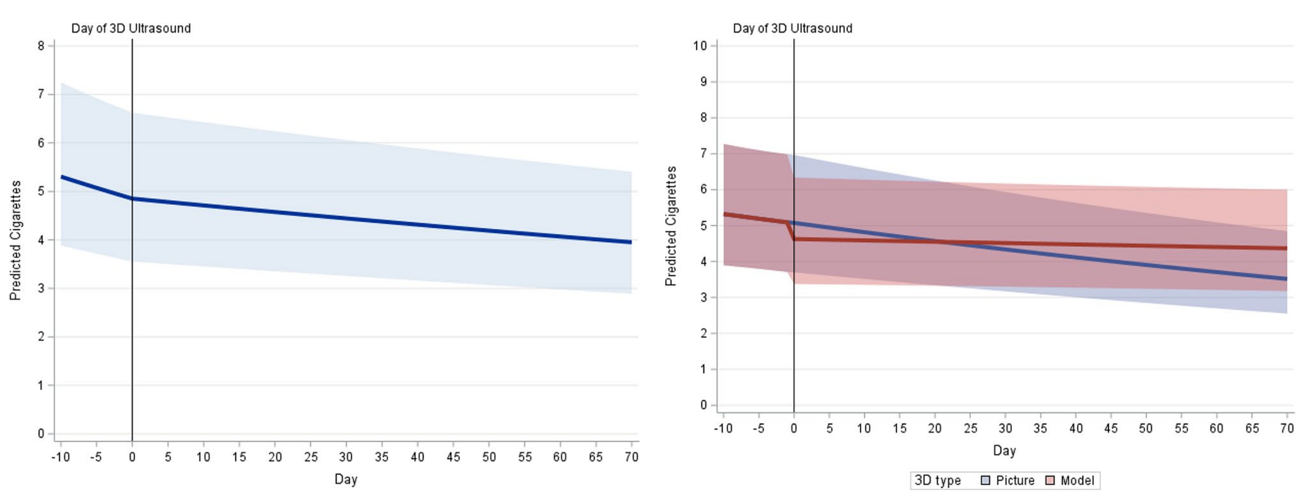

Fig. 3 Cigarette use throughout pregnancy stratified by 3D print and 3D model

Certain ultrasound techniques and advancements in the technological aspects of ultrasonography increase MFA scores, some more than others. Specifically, both 2D and 3D ultrasonography have been shown to increase MFA scores, yet 3D ultrasound images increase scores more than 2D ultrasound images on average [5]. This may be because the visual recognizability and perception of the fetus is higher with a 3D image compared to

Table 2 Birth outcomes stratified by 3D product

	Overall	3D Product		*p*
		Print	Model	
Estimated gestational age at delivery, weeks	39 (38–39)	39 (39–40)	39 (37–39)	0.090
Birth weight, g	3,130 (2,985-3,350)	3,135 (2,990-3,365)	3,100 (2,820-3,350)	0.614
Low birth weight, %	3 (9.09)	0 (0)	3 (17.65)	0.227
Neonatal intensive care unit admission, N (%)	2 (6.06)	0 (0)	2 (11.76)	0.485
Pre-eclampsia, N (%)	12 (36.36)	6 (37.50)	6 (37.50)	0.895

a. Continuous variables are presented as median (interquartile range)

b. LBW was defined as a birth weight less than 2,020 g for females and less than 2,730 g for males

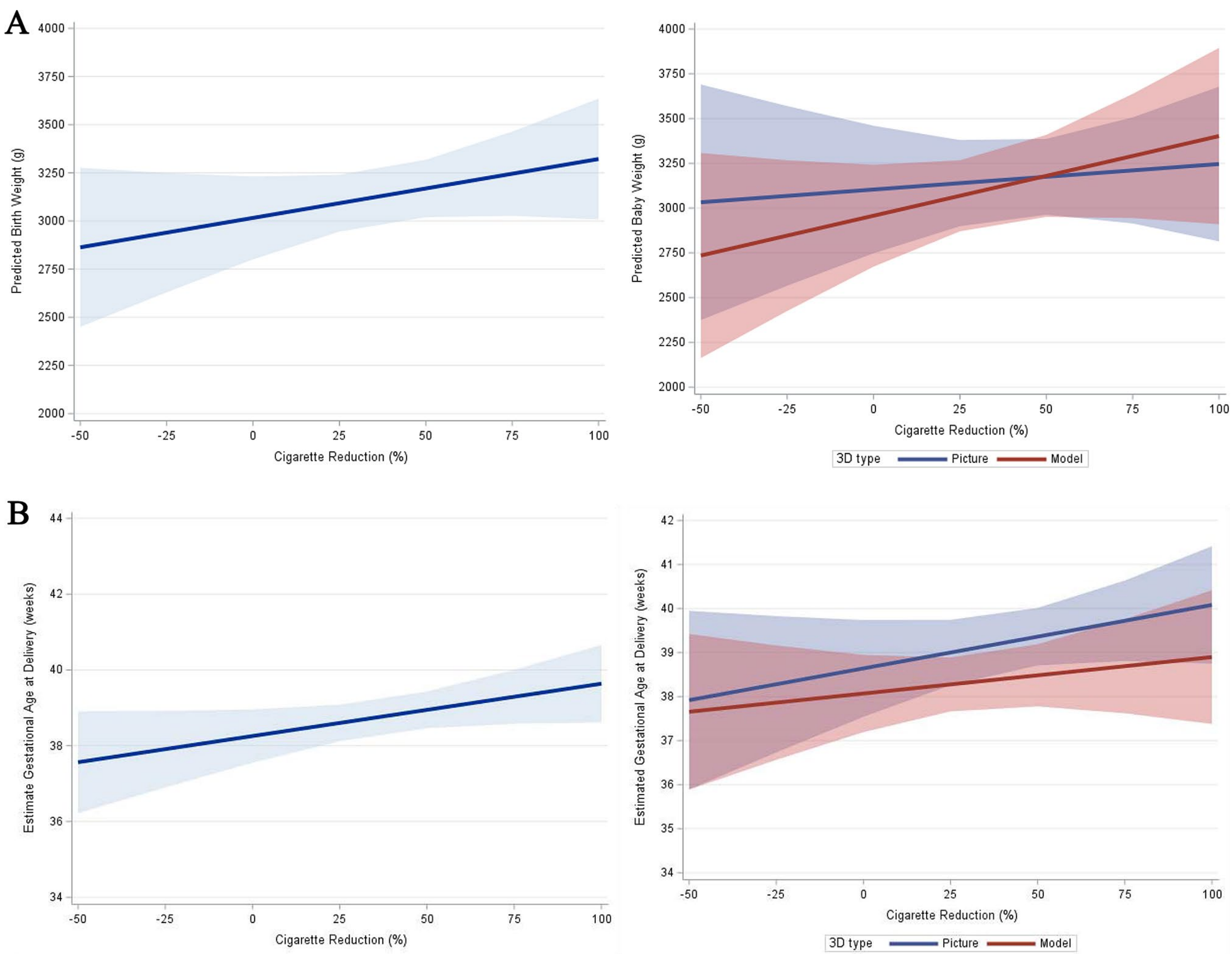

Fig. 4 (**a**) Association between cigarette reduction and birth weight stratified by 3D print and 3D model. (**b**) Association between cigarette reduction and estimated gestational age at delivery stratified by 3D print and 3D model

a 2D image and is consistant with neural correlates seen with facial processing [19, 20]. Unfortunately, the ultrasound experience and effects on MFA may be short lived. Westerneng et al., 2022 evaluated the effect of offering a routine ultrasound on MFA and found that an ultrasound may be associated with higher MFA score after a third trimester ultrasound only at lower baseline MFA scores [21]. Unfortunately, their ultrasound was done between Time 1 (mean 24.1 +/- 1.96) and Time 2 (32.1 +/- 0.72) but with no comparison of when the ultrasonography was performed. Our recent comparison of 3D ultrasonography to a 3D facial model supports the ability of the 3D images to increase MFA and reinforces the potential of the physical representation of the fetal face to increase MFA scores and continue to do so over time [4].

Our study had a few limitations. First, because this was a pilot study, the sample size limits any conclusion we can make about the interventions and smoking. The unforeseen pandemic along with lower-than-expected smoking rates will necessitate a multi-center trial going forward. Second, there was not a no intervention control group; however, ethical implications, and the fact that the standard of care encourages providers to intervene with the 5As argues against the appropriateness of not offering a portion of the patients an intervention that may be useful. The greatest weakness of not having a control group is that smoking might be expected to decline without intervention from 27 to 36 weeks or so following rising progesterone which is known to reduce cravings across sexes and substances. Lastly, we did not perform a cost benefit analysis comparing 3D models to 3D pictures. In light of restrictive healthcare spending, it would be important for future research to compare 3D printed models to 3D printed pictures for any cost savings.

There are no statistics on the percentage of patients who receive an image of their fetus at the time of their ultrasound. It is the assumption that the "keepsake" ultrasound has no medical indication which may inhibit the universal production and distribution of these images to patients. Our findings bring to light the possibility that advocacy for 3D ultrasonography and by extension 3D printed images may play a larger role than just "entertainment". Larger, multi-center trials are still needed.

Conclusions

This is the first study to evaluate MFA associated interventions in smoking cessation. The results are encouraging and build an impressive argument for utilizing ultrasonography and 3D printing to improve smoking rates in pregnant patients. Comparing outcomes (overall birth weight, birth weight percentile, low birth weight (LBW) percentile, neonatal intensive care unit (NICU) admissions, preterm delivery (PTD) rates and hypertensive diseases of pregnancy rates) to current baseline rates of pregnant smokers and non-smokers support a recommendation of utilizing 3D printed technologies to help decrease smoking in pregnancy.

Abbreviations

ACOG	American College of Obstetricians and Gynecologists
ALARA	As low as reasonably achievable
CI	Confidence interval
GE	General Electric
IUFD	Intrauterine fetal demise
LBW	Low birth weight
MFA	Maternal-fetal attachment
µL	Microliter
mL	Milliliter
ng	Nanogram
NICU	Neonatal intensive care unit
PLA	Polylactic acid
PTD	Preterm delivery
RPM	Revolutions per minute
SAS	Statistical analysis system
SD	Standard deviation
STL	Stereolithography
TLFB	Timeline follow back
U.S.	United States

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Author contributions

J.C. and A.B.B. contributed to the study conception or data acquisition, analysis, interpretation, drafting or critical revision, final approval and accountability of this article. All other authors (R.C., D.D., S.M., P.D., B.C., R.K.) contributed to analysis, interpretation, drafting or critical revision, final approval and accountability of this article. The author(s) read and approved the final manuscript.

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Data availability

Data utilized for this manuscript can be found at https://doi.org/10.5281/zenodo.10901063.

Declarations

Ethical approval

This research was approved by the Creighton's Institutional Review Board (protocol number 2001287), registered at clinicaltrials.gov (NCT04541121), carried out in accordance with The Code of Ethics of the World Medical Association for experiments involving humans, and all participants were provided informed consent.

Consent for publication

While no identifying information was utilized, consent for 3D images utilized in Figs. 1 and 2 was obtained.

Competing interests

JC, RC and BC are related to the owner of the company that produced the 3D models for the study at cost. All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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